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Advancements and improvements in general hospital psychiatry

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Advancements and improvements in general hospital psychiatry

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Editorial: Advancements and improvements in general hospital psychiatry

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Editorial on the Research Topic
Advancements and improvements in general hospital psychiatry

Since the deinstitutionalization of major psychiatric centers, general hospital psychiatry has been playing a more and more important role in providing psychiatric services to the public. But general hospital psychiatry does more than providing services to psychiatric patients in general hospital settings; it also provides consultation-liaison(C-L) services to physical patients with psychiatric comorbidity or psychiatric symptoms due to physical conditions. There is a high prevalence of psychiatric comorbidity in general hospital inpatients of various physical departments. Psychiatric comorbidity results in difficulty in clinical communication, longer hospitalization, worse clinical outcomes, and higher costs. However, psychiatric comorbidities are often neglected and untreated.

Many models of C-L services are designed to best fit tasks such as making diagnoses and prescribing pharmaceuticals, helping with physical patients' distressing emotions, helping with clinical communications between patients and their doctors, and so on.

In this Research Topic focusing on advancements in general hospital psychiatry, nine research papers from across the globe cover topics including psychiatric service delivery in various general hospital settings(inpatients, emergency, and outpatients), infection prevention strategy in psychiatric patients in general hospitals, pharmaceutical treatment of organic psychiatric disorders (neuropsychiatric systemic lupus erythematosus), and common psychiatric burdens in patients with physical conditions/symptoms(diabetes, postpartum, chest pain, etc.).

Work methods in different settings

Caspi et al. reported the feasibility of providing home care via online services to suitable psychiatric patients after emergency care with a multi-disciplinary team at Sheba Medical Center, Israel. With the advancement of technologies, patients' biological status can also be monitored online. This may inspire other clinicians, since medical resources are commonly limited and some patients would prefer home treatment.

In the study of Lundqvist et al., a comprehensive and continuous outpatient service was provided to 373 adult patients registered at 15 psychiatric outpatient clinics in three regions in central and southern Sweden. The outpatient service improved patients' quality of life via both symptom relief and recovery. Patient-staff relationship was found to have an independent effect on recovery. Simply put, a continuous outpatient service with humane warmth further relieves patients helps them recover.

Casey et al. reviewed medical conditions of 163 patients with primary psychiatric complaints presenting to Ochsner Louisiana State University Shreveport Psychiatric Crisis Unit, USA. In their findings, 50.3% of the patients received interventions prior to medical clearance. Elevated creatine kinase (in 31 patients) was the most common cause for intervention. Additional medical conditions that resulted in medical interventions included tachycardia, elevated serum ethanol level, dehydration, and acute kidney injury. Although the characteristics of patient populations may differ between regions and settings, this study reminds clinicians of the importance of paying attention to medical conditions in general hospital inpatients and emergency patients.

Han et al. reported a bundle management strategy in reducing hospital-acquired pneumonia in hospitalized patients with mental disorders at the mental health center of a tertiary general hospital in Wuhan, China. Infection prevention, isolation of infected patients, environment disinfection, and paying attention to antipsychotics and underlying diseases were applied in combination. The rate of HAP occurrence decreased from 0.95 to 0.52%.

In the study of Dai et al., a questionnaire evaluating hospitalized patients' expectations for treatment is reported as part of the consultation-liaison effort to help general hospital inpatients and their doctors better communicate treatment expectations in a tertiary general hospital in Beijing, China. Better doctor-patient communication and mutual understanding of medical diagnosis, treatment, and prognosis is integral to shared decision making, increases patient's compliance to treatment, and improves clinical outcome.

Studies of psychiatric disorders in physical conditions

One general rule is that the relationship between psychiatric disorders and physical conditions are bi-directional. But it is always difficult to tell how and to what extent one influences another. Specific diseases/conditions merit specific research.

Geng et al. reviewed the records of 160 inpatients with systemic lupus erythematosus (SLE) who required psychiatric consultation for further therapeutic intervention in a tertiary general hospital in Beijing, China. In these patients, 86.3% met the diagnostic criteria of at least one mental disorder, the most common being delirium. Patients with delirium have the highest mortality rate in patient groups. Antipsychotic usage was found to decrease death risk for patients with neuropsychiatric systemic lupus erythematosus (NPSLE). This stresses the importance of early recognition and treatment of psychiatric symptoms in SLE patients.

In the study of Sun et al., postpartum mental disorders were diagnosed in a sample of 284 parturients in a tertiary general hospital in Beijing, China. The risk of postpartum depression, anxiety disorders, and obsessive-compulsive disorder was 9.125 times, 7.310 times, and 6.259 times higher in postpartum women with high psychological stress levels related to delivery than in those with low psychological stress levels respectively. Future interventions focusing on psychological stress related to delivery could be very valuable in postpartum mental disorder prevention.

Both diabetes and depression are very common and cause a significant global health burden. A lot of research into their comorbidity have been done. In the study of Kim et al., the relationship between type 2 diabetes and depression was reconsidered using the National Health Insurance Sharing Service (NHISS) database of the National Health Insurance Service (NHIS) of South Korea. In contrast to the common impression that depression can increase the risk of type 2 diabetes, in this study it was found that depression and antidepressant medications were not contributory factors for type 2 diabetes after adjusting for other physical comorbidities.

The study of Zarean et al. Investigated depression and anxiety in healthy controls, patients with cardiac chest pain, and patients with non-cardiac chest pain in multiple medical centers across Shahrekord, Iran. Patients with non-cardiac chest pain had higher levels of depression and anxiety and lower quality of life than patients with cardiac chest pain and healthy controls.

In summary, this edition includes several new studies on setting specific work methods and disease/condition-specific psychiatric comorbidity in general hospital psychiatry. But these are only a some of the wide topics that need to be investigated in the field. We look forward to more nuanced studies into methodological and scientific aspects of general hospital psychiatry in the future.

Author contributions

JC: Writing – original draft. YZ: Writing – original draft. JW: Writing – review & editing.

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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Bundle management strategy in reducing hospital-acquired pneumonia in hospitalized patients with mental disorders

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Introduction: The incidence of hospital-acquired pneumonia (HAP) is high in the medical setting for mental disorders. To date, effective measurements for preventing HAP in hospitalized mental disorder patients are unavailable.

Methods: This study was conducted at the Large-Scale Mental Health Center of Renmin Hospital of Wuhan University (Wuhan, China) in two phases: baseline phase (January 2017–December 2019) and intervention phase (May 2020–April 2022). In the intervention phase, the HAP bundle management strategy was implemented in the Mental Health Center, and the data on HAP were collected continuously for analysis.

Results: A total of 18,795 and 9,618 patients were included in the baseline and intervention phases, respectively. The age, gender, ward admitted to, type of mental disorder, and Charlson comorbidity index did not differ significantly. After intervention, the rate of HAP occurrence decreased from 0.95 to 0.52% ($P < 0.001$). Specifically, the HAP rate decreased from 1.70 to 0.95% ($P = 0.007$) in the closed ward and from 0.63 to 0.35% ($P = 0.009$) in the open ward. The HAP rate in the subgroups was higher in patients with schizophrenia spectrum disorders (1.66 *vs*. 0.74%) and organic mental disorders (4.92 *vs*. 1.41%), and in those ≥65 years old (2.82 *vs*. 1.11%) but decreased significantly after intervention (all $P < 0.05$).

Conclusion: The implementation of the HAP bundle management strategy reduced the occurrence of HAP in hospitalized patients with mental disorders.

KEYWORDS

mental disorders, healthcare-associated pneumonia, infection control, inpatients, management strategy

Introduction

According to the statistics of the World Health Organization (WHO), >1 billion people are affected by mental disorders, deeming them a global public health issue that cannot be ignored and that has brought heavy healthcare and financial burden worldwide (1). China is leading with the burden of mental disorders (2); >1.6 million patients were hospitalized for mental disorders in China in 2015 (3).

Hospital-acquired pneumonia (HAP) is defined as pneumonia not incubating at the time of hospital admission and occurring ≥48 h after hospital admission (4, 5). Previous studies have shown that HAP incidence is high in Chinese patients with mental disorders (6, 7). For instance, a large-scale specialized hospital for mental disorders in Sichuan (China) reported

that the HAP incidence was 7.8% in middle-aged and elderly patients (≥50 years old) with schizophrenia (6). A large-scale specialized hospital for mental disorders in Taiwan reported that the HAP incidence was 14.7/1000 person-years in patients with severe mental disorders (>80% had schizophrenia or schizoaffective disorders) (7).

In recent years, the incidence of ventilator-associated pneumonia (VAP) in medical settings has been decreasing, while that of non–ventilator-associated HAP is increasing (8) with an incidence of about 1% (5, 9). Moreover, the total number of patients with HAP is 2-fold higher than the number of patients with VAP (9, 10). Most HAP (70.8%) occurs in the wards rather than the intensive care unit (ICU) (10). The disease could prolong the hospital stay, increase the overall medical cost, and mortality rate (11); however, it is the most underestimated hospitalization-related safety and economic issue. HAP is mainly induced by the aspiration or inhalation of pathogenic microorganisms in the form of aerosols or hydrogel microparticles (4, 5). Compared to regular patients, the occurrence of HAP in mental disorder patients has several unique characteristics, such as dietary and behavioral changes, different degrees of social function impairment, longer hospital stay, dysphagia (12), somatic comorbidity (13, 14), and dry mouth, drooling, and sedation induced by antipsychotics. Schizophrenia is a chronic and disabling mental illness. The previous findings suggest that HAP is particularly prevalent in patients with schizophrenia (6, 7). Moreover, organic mental disorders are more likely to be associated with older age and physical comorbidities such as dementia and cerebrovascular disease, and this may lead to an elevated risk of pneumonia and death. In addition to individualized factors, the transmission of pathogens capable of inducing pneumonia in the hospital also causes HAP. Previously, mental health settings/units have reported various outbreaks of *Streptococcus pneumonia* (15) and influenza (15, 16), indicating that hospitalized mental disorder patients may have a high risk of respiratory diseases.

Several studies have investigated the measures of preventing and managing VAP (9, 10, 17), and a perfect prevention and management system has been established. However, scientific evidence on the prevention and management of HAP is still limited. The major predictive factors for HAP could vary in patients without mechanical ventilation (18, 19). Previous studies have shown that interventional measures, such as improving hand hygiene, early activities, recognizing and managing dysphagia, and preventing viral infection (20), could reduce HAP occurrence in patients. The commonly applied infection prevention measures, such as hand hygiene, quarantine precautions, personal protective devices (gloves and masks), and disinfection of equipment and the environment, effectively reduce the risk of pathogen transmission in hospitals (21). However, the measures for effectively preventing the occurrence of HAP in mental disorder patients have not yet been investigated. Another survey showed that staff and patients in mental health settings have low overall compliance to infection prevention measures (22), which are manifested as follows: (1) mental disorder patients may exhibit cognitive impairment and thus are incapable of abiding by the infection prevention measures; (2) the understanding and implementation of common infection prevention and control measures could be insufficient for medical staff (23); (3) the hospitalization environment could be poor (24); (4) some essential equipment, such as ethanol sanitizer, could not be used due to safety concerns (25); (5) mental health settings encourage social interactions, group activities, and freedom of actions (26), which could increase the opportunity of cross-infection. Therefore, implementing infection prevention measures in mental health settings/units (27) is rather complex and could be influenced by factors, such as patients, medical staff, and organization (22). The bundle management strategy is the gathering of a series of evidence-based treatments and nursing, which plays a major role in effectively reducing VAP (28). In light of the current status and challenges in HAP prevention and management in mental disorder patients, as well as previous findings (20, 21), the present study developed a HAP bundle management strategy with respect to the levels of patients, medical staff, and organization and explored the effects on HAP in mental disorder patients.

Patients and methods

Study setting and subjects

This study was performed in the Mental Health Center of Renmin Hospital of Wuhan University (Wuhan, China) between January 2017 and April 2022. Patients hospitalized between January and April 2020 were not included due to the coronavirus disease-2019 (COVID-19) epidemic. This hospital is a large-scale general teaching institution with a large-scale mental health center with the highest number of beds for psychiatric patients in general hospitals in China (350 beds including 225 beds in open wards and 125 in closed wards across six wards). COVID-19 patients were not admitted to the Mental Health Center during the study period or included in the study.

The inclusion criteria were as follows: 1) hospitalized patients with the primary diagnosis of mental disorders according to the criteria described in the International Classification of Diseases-10 (ICD-10, codes F00-F99) and 2) Patients were hospitalized for >48 h.

The exclusion criteria were as follows: (1) incomplete data for analysis; (2) patients who died or were spontaneously discharged within 48 h after hospitalization; and (3) underwent mechanical ventilation.

The clinical research ethics committee of Renmin Hospital of Wuhan University approved this study (WDRY2022-K163), and informed consent was waived by the Ethics Committee of the hospital.

Study design and intervention

This 5-year study consisted of two phases: baseline phase (January 2017–December 2019) and intervention phase (May 2020–April 2022).

In the baseline phase, the target surveillance of HAP was not performed in the mental health center, and pneumonia symptoms were not monitored daily for all hospitalized patients. Only a few

patients and some medical staff wore masks, and management of patients with pneumonia or immunodeficiency was insufficient. Compliance with implementation of environmental cleaning and disinfection work was poor, such as environment disinfection was performed only 1 time/day, or unperformed in some wards sometimes, especially the disinfection of public areas. Hand hygiene was poor, and the monitoring of antipsychotics and side effects was limited. In May 2020, with the cooperation of the leaders of the hospital and multiple departments, including infection control, medicine, nursing, cleaning and disinfection management, and the mental health center, the risk was assessed according to the characteristics of mental disorder patients. Subsequently, a literature search was conducted according to evidence-based medicine-related guidelines and studies (18–28), and finally, the sophisticated management strategy was developed as follows:

1) Performing target surveillance of HAP: suspicious symptoms of pneumonia, such as cough, expectoration, and fever, were monitored daily for all the hospitalized patients to identify pneumonia patients in time. HAP occurrence was summarized and analyzed every month.
2) Improving the management of pneumonia patients: disinfection, hand hygiene, and wearing masks, were essential for contact isolation and respiratory isolation. For patients with pathogens detected, especially the infection or colonization of several drug-resistant microorganisms such as *Methicillin-resistant Staphylococcus aureus*, *Extended-spectrum-β-lactamases-producing Escherichia coli* or *Klebsiella pneumoniae, Carbapenem-resistant Escherichia coli* or *Klebsiella pneumoniae, Pseudomonas aeruginosa* or *Acinetobacter baumannii,* and respiratory viruses such as influenza, infection prevention measures were challenging; hence, isolation management was strengthened.
3) Enhancing disinfection, hand hygiene, and reasonable use of personal protective equipment: environment disinfection was performed two times/day, and additional attention was paid to the disinfection of public areas, such as activity rooms and recreation rooms for patients, toilets, elevators, and shared equipment and devices. The windows were opened regularly two times/day for ventilation. Compliance with hand hygiene was improved based on the WHO hand hygiene indications of "five moments for hand hygiene" (29). The antiseptic foam (water not required) was carried by doctors and nurses during ward rounds and also hung on the nursing cart (under supervision). Medical staff wore medical surgical masks during work; also, patients were required to wear masks. Extra bed was avoided. Regular education was conducted in all patients, such as hand hygiene, prevention, and control knowledge of HAP.
4) Protecting susceptible population: severe mental disorder patients with immunodeficiency, such as granulocytopenia or granulocytosis, and substantial malnutrition, "protective isolation," was prescribed and effectuated.
5) Enhancing the surveillance of antipsychotics uses and focusing on the underlying diseases: management and surveillance of antipsychotics, such as clozapine, were enhanced. For instance, antipsychotic concentrations were monitored, and therapeutic drug monitoring (TDM) was strengthened, especially when adjusting drug dosage or suspecting poisoning or insufficient dosage in patients. The drug side-effect scale was filled. Information, including sialorrhea, dysphagia, and bedrest time of patients, was collected in the ward rounds every day, and symptomatic treatments were performed promptly. The patients resting in bed or with low mobility were encouraged to conduct off-bed activities, and the doses of sedatives were adjusted in time. Then, underlying diseases, blood glucose, liver and renal functions, albumin, and body weight were monitored, and the corresponding treatments were strengthened.
6) Standard training for this sophisticated HAP bundle management strategy, which was designed for hospitalized patients with mental disorders, was conducted for patients, medical staff, and organization. Implementation of all measures was supervised, and feedback was acquired, which promoted the effective and accurate implementation of the measures. The overall compliance of patients, medical staff, and organization to infection prevention measures is important for effectively preventing the occurrence of HAP in mental disorder patients (21, 22).

Definition of HAP

Hospital-acquired pneumonia was diagnosed according to the criteria issued by the Centers for Disease Control and Prevention (USA) based on the comprehensive analysis of clinical manifestations, imaging findings of the chest, and laboratory examination results (30).

Definition of mental disorders

The diagnoses of the mental disorders were made by professional psychiatrists in accordance with the 10th revision of the International Classification of Mental Disorders (ICD-10, codes F00-F99). According to the incidence rate of HAP of different types of mental disorders (6, 7) and the sample size of different types of mental disorders in this study, we divide the types of mental disorders into four categories. Schizophrenia spectrum disorder referred to Schizophrenia, schizotypal and delusional disorders (ICD-10 categories F20–F29), Mood-affective disorder referred to ICD-10 categories F30–F39, Organic mental disorder referred to ICD-10 categories F00–F09, and other mental disorders referred to ICD-10 categories F10–F19, F40–F48, F50–F59, F60–F69, F70–F79, F80–F89, F90–F98, and F99.

Data collection

Clinical information, body temperature, blood routine results, and imaging findings of the lungs were collected through the real-time nosocomial infection surveillance system. Daily monitoring of suspicious symptoms was strengthened for all the hospitalized

patients, and target surveillance of HAP was performed. Charlson comorbidity index (CCI) was used to assess the severity of somatic comorbidities (31). Hospital stay refers to the length of hospital stay from the patient's admission to discharge. The length of time until HAP occurrence refers to the hospitalization time from the patient's admission to the onset of HAP. HAP rate refers to the number of HAP events per 100 admissions or the number of HAP events per 1,000 days. HAP was diagnosed by professionals in infection control and doctors in charge of the bed, ensuring data quality. According to The World Health Organization hand hygiene observation method (29), Compliance to hand hygiene (%) = actual times of executing hand hygiene in the observation time/anticipated times of executing hand hygiene×100%. Correctness of hand hygiene (%) = times of correctly executing hand hygiene in the observation time/actual times of executing hand hygiene×100%.

Statistical analysis

The data were analyzed using SPSS 22.0 (IBM Corp., Armonk, NY, USA) and Prism 8 (GraphPad Software, San Diego, CA, USA). Measurement data were tested for normality using the Kolmogorov–Smirnov method (sample size ≥50) or Shapiro–Wilk method (sample size <50). Normally distributed measurement data are presented as the mean ± standard deviation (SD) and compared between groups using the t-test for independent samples. Non-normally distributed measurement data are shown as median [interquartile range (IQR)] and compared between groups using the Mann–Whitney U-test. Count data are presented as frequency (percentage) and analyzed using the chi-squared test or Fisher's exact test. The incidence before and after the intervention was compared using the unadjusted incidence relative risk (RR) ratios, defined as the ratio of events for a defined period. A *P*-value of <0.05 was considered statistically significant.

Results

General characteristics of included patients

The age, gender, ward admitted to, type of mental disorder, and CCI did not differ significantly between the patients in the baseline and intervention phases (Table 1).

Occurrence rate of HAP in mental disorder patients in different wards

The rates of HAP occurrence in mental disorder patients in baseline and intervention phases are shown in Table 2 and Figure 1. HAP occurred in 178 patients in the baseline phase, of which 94 (52.81%) were in the closed ward. After intervention, the HAP rate reduced from 0.95 to 0.52% ($P < 0.001$). Specifically, the HAP rate reduced from 1.70 to 0.95% ($P = 0.007$) in the closed ward and reduced from 0.63 to 0.35% ($P = 0.009$) in the open ward. The hospital stay of patients was also significantly different between the baseline and intervention phases ($P < 0.001$).

Rate of HAP occurrence in patients with different types of mental disorders

In the baseline phase, HAP occurred in 62 (34.83%), 72 (40.45%), 29 (16.29%), and 15 (8.43%) patients with schizophrenia spectrum, mood affective, organic mental, and other mental disorders, respectively. After intervention, the HAP rate reduced from 1.66 to 0.74% ($P = 0.005$) in patients with schizophrenia spectrum disorders and from 4.92 to 1.41% ($P = 0.012$) in the organic mental disorders (Table 3 and Figure 2).

Rate of HAP occurrence in patients of different age groups

In the baseline phase, HAP occurred in 10 (5.62%), 85 (47.75%), 58 (32.58%), and 25 (14.04%) patients aged <18 years, 18–44 years, 45–64 years, and ≥65 years, respectively. After intervention, the HAP rate reduced from 0.42 to 0% ($P = 0.002$) in patients aged <18 years, from 0.73 to 0.44% ($P = 0.030$) in patients aged 18–44 years, and from 2.82 to 1.11% ($P = 0.045$) in patients aged ≥65 years (Table 4 and Figure 3).

Implementation of HAP bundle management strategy

After the implementation of the HAP bundle management strategy, the compliance of medical staff with hand hygiene increased from 76.32% (58/76) to 93.29% (139/149) ($P < 0.001$), and the correct rate of hand hygiene in medical staff increased from 71.05% (54/76) to 89.93% (134/149) ($P < 0.001$). The consumption of antiseptic foam (water not required) increased from 11,850.00 mL/ward/year (0.37 mL/day/bed) to 45,833.33 mL/ward/year (1.57 mL/day/bed). The consumption of chlorine-containing disinfectants increased from 400 g active chlorine/ward/month to 600 g active chlorine/ward/month. The consumption of medical surgical masks increased from 250 masks/ward/month to 2,575 masks/ward/month.

Discussion

To the best of our knowledge, this is the first study exploring the rate of HAP occurrence in mental disorder patients in a general hospital and the effectiveness of implementing the bundle management strategy in reducing HAP occurrence. The findings of this 5-year study showed that the implementation of the HAP bundle management strategy reduced the occurrence of HAP in mental disorder patients.

The findings of this study showed that in the baseline phase, the HAP rate was 0.95% (0.47/1,000 patient-days) in the hospitalized mental disorder patients, which was similar to the HAP rate in regular patients hospitalized in other general hospitals (approximately 1%) (5, 9); however, it was lower than the HAP rate in middle-aged or elderly patients with schizophrenia (6) or severe mental disorders (7) admitted in specialized hospitals for mental

TABLE 1 General characteristics of study subjects during the baseline and intervention phases.

Characteristic	Total (n = 28,413)			Closed ward (n = 8,254)			Open ward (n = 20,159)		
	Baseline (n = 18,795)	Intervention (n = 9,618)	P-value	Baseline (n = 5,519)	Intervention (n = 2,735)	P-value	Baseline (n = 13,276)	Intervention (n = 6,883)	P-value
Gender, n (%)			0.091			0.425			0.214
Male	7,980(42.46%)	3,983(41.41%)		2,937(53.22%)	1,430(52.28%)		5,043(37.98%)	2,553(37.09%)	
Female	10,815(57.54%)	5,635(58.59%)		2,582(46.78%)	1,305(47.72%)		8,233(62.02%)	4,330(62.91%)	
Age (years), n (%)			0.956			0.054			0.242
≥65	886 (4.71%)	452 (4.70%)		191 (3.46%)	118 (4.31%)		695 (5.24%)	334 (4.85%)	
<65	17,909(95.29%)	9,166(95.30%)		5,328(96.54%)	2,617(95.69%)		12,581(94.76%)	6,549(95.15%)	
Ward admitted to, n (%)			0.103						
Closed ward	5,519 (29.36%)	2,735(28.44%)							
Open ward	13,276(70.64%)	6,883(71.56%)							
Type of mental disorder, n (%)			0.697			0.686			0.785
Schizophrenia spectrum disorder[a]	3,735 (19.87%)	1,878(19.52%)		1,762(31.93%)	841 (30.75%)		1,973 (14.86%)	1,037(15.07%)	
Mood affective disorder[b]	10,828(57.61%)	5,565(57.86%)		2,817(51.04%)	1,411(51.59%)		8,011 (60.34%)	4,154(60.35%)	
Organic mental disorder[c]	590 (3.14%)	284 (2.95%)		211 (3.82%)	104 (3.80%)		379 (2.85%)	180 (2.62%)	
Others[d]	3,642 (19.38%)	1,891(19.66%)		729 (13.21%)	379 (13.86%)		2,913 (21.94%)	1,512(21.97%)	
Charlson comorbidity index, n (%)			0.925			0.164			0.243
0–1 points	16,557(88.09%)	8,477 (88.14%)		4,892(88.64%)	2,409(88.08%)		11,665(87.86%)	6,068(88.16%)	
2 points	1,130 (6.01%)	584 (6.07%)		283 (5.13%)	128 (4.68%)		847 (6.38%)	456 (6.62%)	
3 points and above	1,108 (5.90%)	557 (5.79%)		344 (6.23%)	198 (7.24%)		764 (5.75%)	359 (5.22%)	

[a]Schizophrenia spectrum disorder (ICD-10 categories F20–F29).
[b]Mood-affective disorder (ICD-10 categories F30–F39).
[c]Organic mental disorder (ICD-10 categories F00–F09).
[d]Others (ICD-10 categories F10–F19, F40–F48, F50–F59, F60–F69, F70–F79, F80–F89, F90–F98, F99).

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TABLE 2 HAP rate and hospital stay in inpatients with mental disorders in total, closed ward, or open ward during the baseline and intervention phases.

Characteristic	Total (n = 28,413)				Closed ward (n = 8,254)				Open ward (n = 20,159)			
	Baseline (n = 18,795)	Intervention (n = 9,618)	RR (95% CI)	P-value	Baseline (n = 5,519)	Intervention (n = 2,735)	RR (95% CI)	P-value	Baseline (n = 13,276)	Intervention (n = 6,883)	RR (95% CI)	P-value
No. of HAP patients	178	50			94	26			84	24		
No. of inpatients	18,795	9,618			5,519	2,735			13,276	6,883		
No. of patient-days	375,362	175,104			132,249	57,085			243,113	118,019		
HAP rate (%)	0.95%	0.52%	0.55 (0.40–0.75)	<0.001	1.70%	0.95%	0.55 (0.36–0.86)	0.007	0.63%	0.35%	0.55 (0.35–0.87)	0.009
HAP rate (per 1,000 days)	0.47‰	0.29‰	0.60 (0.44–0.82)	0.001	0.71‰	0.46‰	0.64 (0.42–0.99)	0.043	0.34‰	0.20‰	0.59 (0.37–0.93)	0.020
Hospital stay (days), median (IQR)	16.0 (11.0, 25.0)	16.0 (11.0, 22.0)		<0.001	20.0 (13.0, 30.0)	18.0 (13.0, 26.0)		<0.001	15.0 (10.0, 23.0)	15.0 (11.0, 21.0)		0.001
Length of time until HAP occurrence (days),[a] median (IQR)	9.5 (6.0, 19.0)	11.0 (7.0, 20.0)		0.299	11.0 (8.0, 18.5)	13.0 (7.0, 25.0)		0.564	8.0 (5.5, 14.5)	10.0 (7.0, 17.5)		0.317

[a]Length of time from admission to HAP occurrence.

HAP, hospital-acquired pneumonia; RR, relative risk; 95% CI, 95% confidence interval; IQR, interquartile range.

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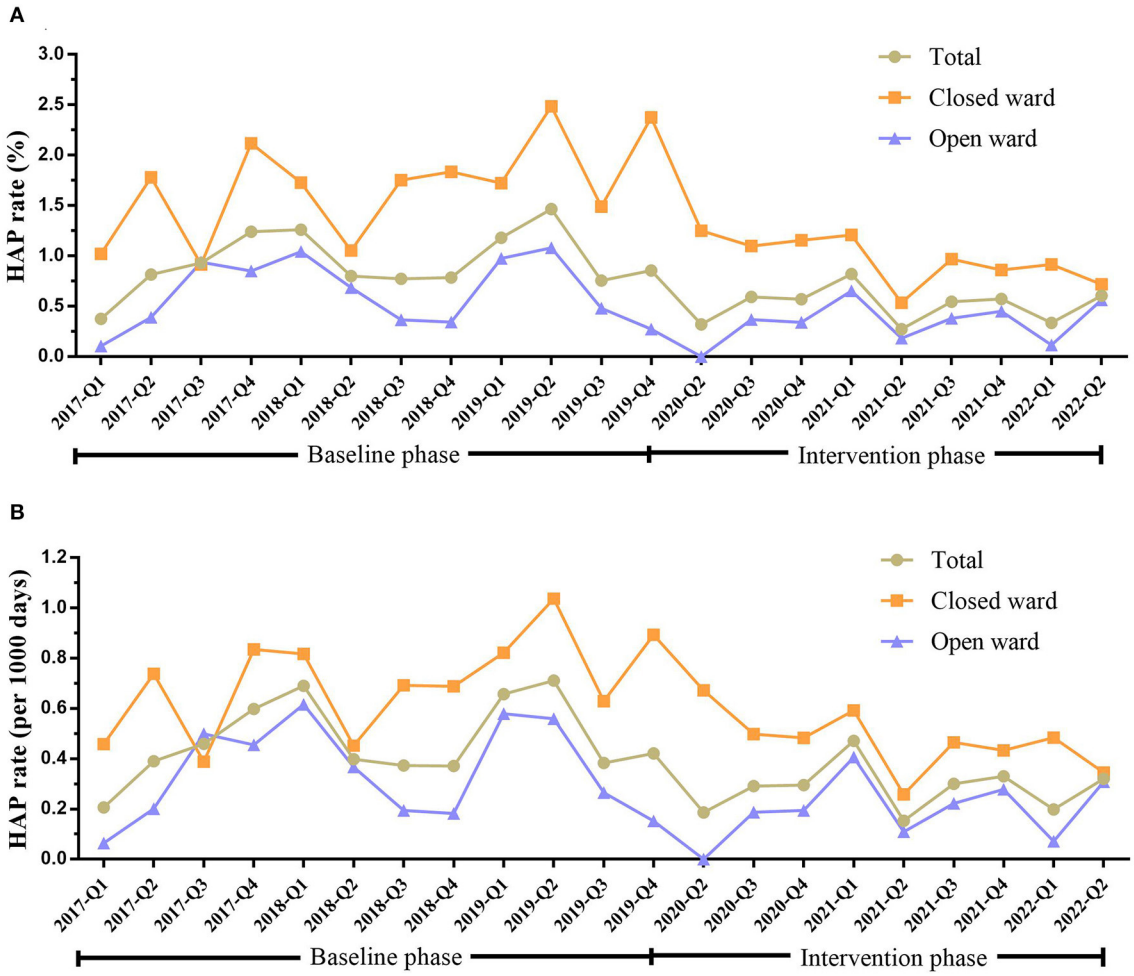

FIGURE 1
HAP rate in inpatients with mental disorders in total, closed ward, or open ward during the baseline and intervention phases. **(A)** HAP rate (%) in patients in total, closed ward, or open ward during the baseline and intervention phases. **(B)** The HAP rate (per 1,000 days) in patients in total, closed ward, or open ward during the baseline and intervention phases. HAP, hospital-acquired pneumonia; Q, quarter.

disorders. The HAP rate was higher in closed wards, in patients with schizophrenia spectrum disorders, in patients with organic mental disorders, and in patients aged ≥65 years than in regular patients in other general hospitals (5, 9). After the HAP bundle management strategy was implemented, the HAP rate in mental disorder patients reduced from 0.95 to 0.52%, and the hospital stay was reduced.

In this study, the high HAP rate in the closed ward could be associated with the characteristics of hospitalized patients. Patients hospitalized in the closed ward also exhibited severe mental disorders; the capability of self-perception and social functions was damaged to different degrees, and restraining the patients was difficult. Such patients had poor self-caring and self-controlling capabilities and poor personal hygiene. Therefore, closed wards require stringent environment disinfection, open window for ventilation, and hand hygiene. Patients with severe mental disorders might also have dysphagia. The treatment of severe mental disorders was complex, which increased the possibility of using drugs, such as clozapine, while long-term use of high-dose antipsychotics induces side effects and somatic diseases. The findings of this study showed that the HAP rate was high in patients with organic mental disorders or schizophrenia spectrum disorders. Schizophrenia is the most common chronic disabling mental disease (32). Previous studies have demonstrated a high incidence of pneumonia in schizophrenia patients (33). Patients with organic mental disorders could have an underlying "organic basis" that could lead to comorbid physical illnesses (34). For instance, several patients with advanced age, dementia, cerebrovascular disorders, and various comorbidities faced an increased risk of pneumonia and death.

According to features of mental disorders and the low compliance to infection-preventing measures in mental health settings/units (22), the present study developed and implemented the HAP bundle management strategy with respect to the levels of patients, medical staff, and organization and explored the effects on HAP in mental disorder patients. This HAP bundle management strategy focused on the characteristics of wards for mental disorders and features of diseases, ensuring the scientific relevance and feasibility of the management strategy. For instance, the strategy highlighted the importance of terminating the

TABLE 3 HAP rate and hospital stay in inpatients with different types of mental disorders during the baseline and intervention phases.

Characteristic	Schizophrenia spectrum disorder[a] (*n* = 5,613)				Mood affective disorder[b] (*n* = 16,393)				Organic mental disorder[c] (*n* = 874)				Others[d] (*n* = 5,533)			
	Baseline (*n* = 3,735)	Intervention (*n* = 1,878)	RR (95% CI)	*P*-value	Baseline (*n* = 10,828)	Intervention (*n* = 5,565)	RR (95% CI)	*P*-value	Baseline (*n* = 590)	Intervention (*n* = 284)	RR (95% CI)	*P*-value	Baseline (*n* = 3,642)	Intervention (*n* = 1,891)	RR (95% CI)	*P*-value
No. of HAP patients	62	14			72	24			29	4			15	8		
No. of inpatients	3,735	1,878			10,828	5,565			590	284			3,642	1,891		
No. of patient-days	89,799	42,834			213,412	97,814			9,764	4,498			62,387	29,958		
HAP rate (%)	1.66%	0.74%	0.44 (0.25–0.80)	0.005	0.66%	0.43%	0.65 (0.41–1.03)	0.063	4.92%	1.41%	0.28 (0.10–0.79)	0.012[e]	0.41%	0.42%	1.03 (0.44–2.43)	0.951
HAP rate (per 1000 days)	0.69‰	0.33‰	0.47(0.26–0.84)	0.010	0.34‰	0.24‰	0.73 (0.46–1.15)	0.175	2.97‰	0.89‰	0.30 (0.10–0.85)	0.016[e]	0.24‰	0.27‰	1.11 (0.47–2.62)	0.810
Hospital stay (days), median (IQR)	19.0 (12.0, 29.0)	19.0 (13.0, 28.0)		0.549	17.0 (11.0, 25.0)	15.0 (11.0, 22.0)		<0.001	14.0 (8.0, 20.0)	13.0 (10.0, 19.0)		0.464	15.0 (10.0, 21.0)	14.0 (10.0, 20.0)		0.117
Length of time until HAP occurrence (days),[f] median (IQR)	13.5 (7.0, 23.0)	11.5 (5.0, 24.0)		0.737	10.0 (5.5, 20.0)	11.5 (7.0, 21.0)		0.244	7.0 (5.0, 11.0)	7.0 (5.5, 16.0)		0.852	7.0 (5.5, 9.5)	11.0 (7.5, 13.5)		0.040

[a]Schizophrenia spectrum disorder (ICD-10 categories F20–F29).
[b]Mood-affective disorder (ICD-10 categories F30–F39).
[c]Organic mental disorder (ICD-10 categories F00–F09).
[d]Others (ICD-10 categories F10–F19, F40–F48, F50–F59, F60–F69, F70–F79, F80–F89, F90–F98, F99).
[e]Fisher's exact probability method.
[f]Length of time from admission to HAP occurrence.
HAP, hospital-acquired pneumonia; RR, relative risk; 95% CI, 95% confidence interval; IQR, interquartile range.

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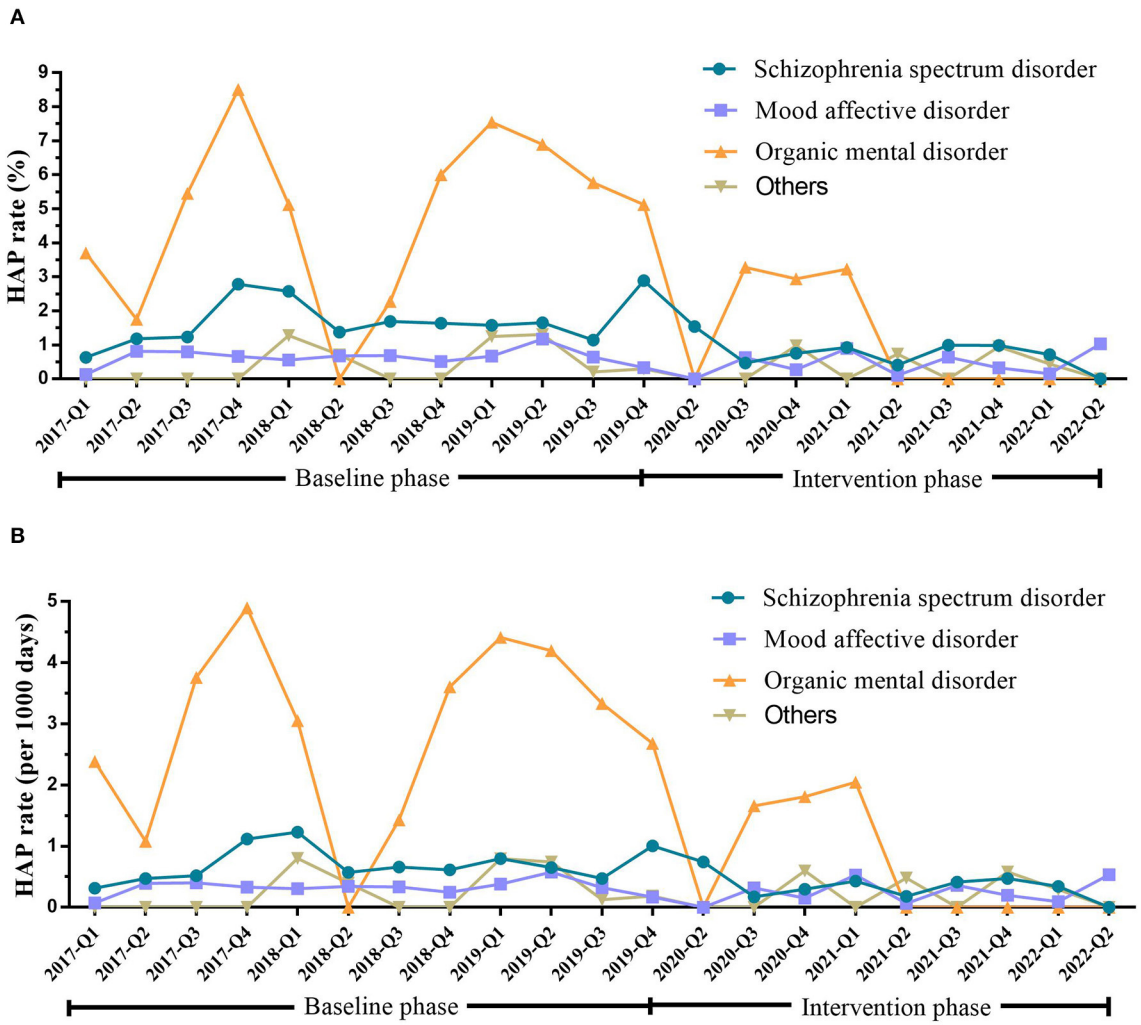

FIGURE 2
HAP rate in inpatients with different types of mental disorders during the baseline and intervention phases. **(A)** HAP rate (%) in patients with different types of mental disorders during the baseline and intervention phases. **(B)** HAP rate (per 1,000 days) in patients with different types of mental disorders during the baseline and intervention phases. Schizophrenia spectrum disorder (ICD-10 categories F20–F29; $n = 5{,}613$). Mood-affective disorder (ICD-10 categories F30–F39; $n = 16{,}393$). Organic mental disorders (ICD-10 categories F00–F09; $n = 874$). Others (ICD-10 categories F10–F19, F40–F48, F50–F59, F60–F69, F70–F79, F80–F89, F90–F98, F99; $n = 5{,}533$). HAP, hospital-acquired pneumonia; Q, quarter.

transmission in the hospital, such as enhancing the management of infected patients, cutting off the transmission route, and protecting the susceptible population as mental disorder patients might have cognitive impairment and are incapable of abiding by the measures of infection prevention. In order to consider patients' safety, the doctors and nurses carried antiseptic foam (water not required) during ward rounds and hung it on the nursing cart (under supervision). Regarding the poor environment in the psychiatric ward, training on air disinfection in the ward, material surface, public area, and public equipment, and management of disinfection frequency was enhanced. Regarding the encouragement of social interactions, and group activities for mental disorder patients (26), this study enhanced the disinfection in the activity rooms/recreation rooms for patients and prevented the gathering of pneumonia patients with other patients. Furthermore, this study enhanced the attention and management of antipsychotics and underlying diseases, monitored the antipsychotics concentrations, filled the "drug side-effect scale," and focused on sialorrhea, dysphagia, and duration of bedrest. The cooperation and overall compliance of patients, medical staff, and organization to infection prevention measures is important for effectively preventing the occurrence of HAP in mental disorder patients (21, 22). An intensive focus by hospital leaders and mental health center staff guarantees the successful implementation of the bundle management strategy. The target surveillance of HAP promotes the implementation of preventive measures and ensures the standardization of outcome estimation.

Limitations

First, the study quality could be improved further. This study was not a randomized controlled trial (RCT), and concurrent controls were not included; thus, the evidence-based

TABLE 4 HAP rate and hospital stay in inpatients of different age brackets during the baseline and intervention phases.

Characteristic	<18 years-old (*n* = 4,614)				18–44-years-old (*n* = 16,869)				45–64-years-old (*n* = 5,592)				≥65-years-old (*n* = 1,338)			
	Baseline (*n* = 2,370)	Intervention (*n* = 2,244)	RR (95% CI)	*P*-value	Baseline (*n* = 11,659)	Intervention (*n* = 5,210)	RR (95% CI)	*P*-value	Baseline (*n* = 3,880)	Intervention (*n* = 1,712)	RR (95% CI)	*P*-value	Baseline (*n* = 886)	Intervention (*n* = 452)	RR (95% CI)	*P*-value
No. of HAP patients	10	0			85	23			58	22			25	5		
No. of inpatients	2,370	2,244			11,659	5,210			3,880	1,712			886	452		
No. of patient-days	48,102	39,327			240,135	98,169			71,020	30,163			16,105	7,445		
HAP rate (%)	0.42%	0 %	0.10 (0.01–0.82)	0.002[a]	0.73%	0.44%	0.60 (0.38–0.96)	0.030	1.49%	1.28%	0.86 (0.52–1.41)	0.543	2.82%	1.11%	0.38 (0.15–1.01)	0.045
HAP rate (per 1,000 days)	0.21‰	0‰	0.12 (0.02–0.96)	0.003[a]	0.35‰	0.23‰	0.66 (0.42–1.05)	0.077	0.82‰	0.73‰	0.89 (0.55–1.46)	0.651	1.55‰	0.67‰	0.43 (0.16–1.13)	0.078
Hospital stay (days), median (IQR)	17.0 (11.0, 26.0)	15.0 (11.0, 21.0)		<0.001	17.0 (11.0, 26.0)	16.0 (12.0, 23.0)		<0.001	15.0 (10.0, 22.0)	15.0 (11.0, 21.0)		0.986	14.0 (10.0, 20.0)	14.0 (10.0, 21.0)		0.754
Length of time until HAP occurrence (days),[b] median (IQR)	16.7± 12.1	0.0		0.220	11.0 (6.0, 20.0)	11.0 (7.2, 20.0)		0.691	8.0 (5.2, 16.5)	9.0 (6.8, 14.5)		0.589	7.0 (5.0, 10.0)	22.0± 16.7		0.034

[a]Fisher's exact probability method.

[b]Length of time from admission to HAP occurrence.

HAP, hospital-acquired pneumonia; RR, relative risk; 95% CI, 95% confidence interval.

IQR, interquartile range.

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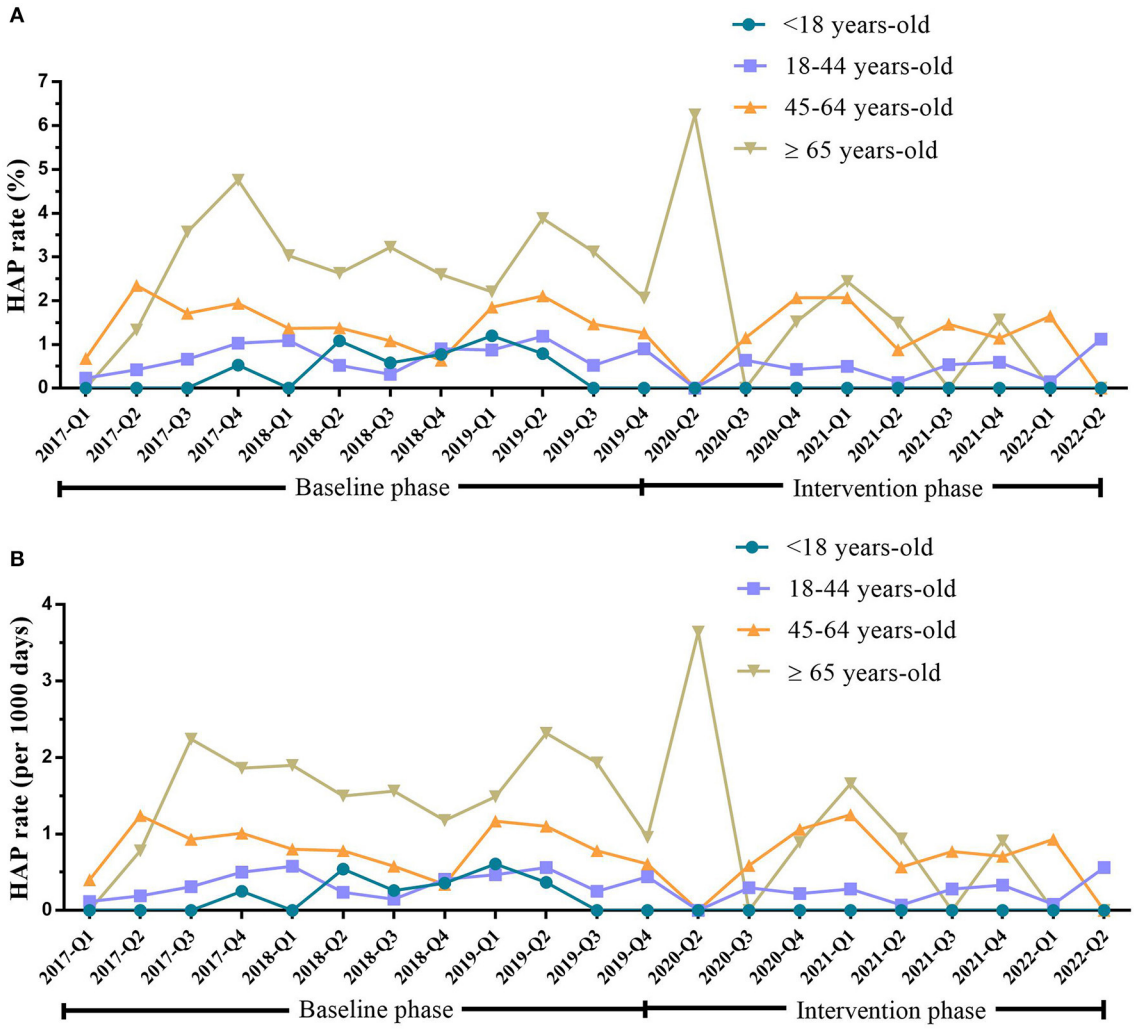

FIGURE 3
HAP rate in inpatients with mental disorders <18 years old, 18–44 years old, 45–64 years old, and ≥65 years old during the baseline and intervention phases. **(A)** HAP rate (%) in inpatients with mental disorders of <18 years old, 18–44 years old, 45–64 years old, and ≥65 years old during the baseline and intervention phases. **(B)** HAP rate (per 1,000 days) in inpatients with mental disorders of <18 years old, 18–44 years old, 45–64 years old, and ≥65 years old during the baseline and intervention phases. HAP, hospital-acquired pneumonia; Q, quarter.

evidence grade was low. Therefore, the present study could not provide definite conclusions on the effectiveness of specific interventional measures. Thus, we speculated that the HAP bundle management strategy reduces the occurrence of HAP in mental disorder patients. Second, this was a single-center study, and thus the results should be interpreted with caution. Third, the study was performed in the mental health center of a tertiary general hospital, and additional discussions are needed for the bundle management strategy of HAP related to other disorders or specialized hospitals. Finally, the sample size was large, and the severity of mental disorders was classified by manual scaling in the early phase of this study; thus, the severity of mental disorders of all patients could not be acquired on admission.

Conclusion

This study underscored the importance of HAP surveillance in hospitalized mental disorder patients, while implementing the HAP bundle management strategy reduced HAP occurrence in mental disorder patients hospitalized in closed or open wards.

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 authors.

Ethics statement

The Clinical Research Ethics Committee of Renmin Hospital of Wuhan University approved this study (WDRY2022-K163). Written informed consent was waived by the Ethics Committee of the hospital.

Author contributions

JH, YR, and GW conceived and designed the experiment and contributed to revise the manuscript. JH performed the research, collected the data, analyzed the results, wrote the manuscript, carried out literature search, and submitted the paper. JH and DL analyzed the data. All authors read and approved the final manuscript.

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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.

Publisher's note

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Refining medical clearance protocol for patients with primary psychiatric complaints in the emergency department

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Introduction: Medical clearance for patients with primary psychiatric complaints presenting to the emergency department has been debated for decades. Emergency physicians have argued that clearance labs are unnecessary, yet psychiatrists may still order or require them. A retrospective review was conducted to evaluate the continued need for labs of psychiatric patients and help identify high risk groups that may need additional intervention prior to medical clearance.

Methods: Charts of 163 patients from Ochsner LSU Shreveport Psychiatric Crisis Unit (PCU) were reviewed with data collected of history, physical examination, review of systems, vitals and routine lab work including complete blood count (CBC), comprehensive metabolic panel (CMP), urine drug screen (UDS), serum ethanol level (EtOH), urinalysis (UA), creatine kinase (CK), urine pregnancy test (UPT), and rapid COVID-19.

Results: Review identified 82 patients (50.3%) that received interventions prior to medical clearance. Most common intervention was intravenous (IV) fluids (n = 59; 45%) followed by admission to other service (n = 15; 8.4%), imaging (n = 10; 7.6%), antihypertensive medication (n = 3; 3.1%), cardiac workup (n = 3; 2.3%), antibiotics (n = 3; 2.3%), lorazepam for undocumented reasons (n = 2; 1.5%). Additional interventions completed once included immunizations, antiseizure medication, pain medication, and additional lab work. Causes for IV fluids were reviewed with elevated creatine kinase (CK) (n = 31; 50.8%) being most common. Additional causes included undocumented (n = 12; 19.7%), tachycardia (n = 6; 9.8%), elevated EtOH level (n = 3; 4.9%), dehydration (n = 2; 3.3%), acute kidney injury (AKI) (n = 2; 3.3%), leukocytosis following a seizure (n = 1; 1.6%), elevated CK and leukocytosis (n = 1; 1.6%), and AKI and elevated CK (n = 1; 1.6%). Most common cause for medical admission was elevated CK being cited in 8 out of 15 admissions (53.3%). Additional causes for admission included AKI (n = 2; 14.3%), seizures and leukocytosis (n = 1; 6.7%), rule out of acute coronary syndrome (ACS) (n = 1; 6.7%), alcohol withdrawal (n = 1; 6.7%), encephalopathy with drop in hemoglobin and white blood cell count (n = 1; 6.7%), and encephalopathy with elevated CK (n = 1; 6.7%).

Discussion: Our results support the recommended guidelines set by AAEP for laboratory testing in addition to history, vital signs and physical examination prior to medical clearance. Certain laboratory testing such as CK and CMP were

identified to have higher utility for medical intervention while other lab work such as UA and UDS had less of an impact. Further, we suggest that specifically a CK and CMP be obtained on patients presenting with any of the following: agitation, abnormal vital signs, intoxication, or a history of or current stimulant use as these were factors correlated with lab abnormalities that led to interventions.

KEYWORDS

ED labs, CK, medical clearance, psychiatry, ED clearance

Introduction

Inpatient psychiatric facilities often have limited capabilities to treat emergent or even urgent medical problems, and while some facilities have a hospitalist on staff to evaluate and treat medical needs, others do not. Additionally, some patients have medical causes for their psychiatric symptoms that require admission to other services besides psychiatry. Therefore, psychiatric facilities usually rely on the referral source to exclude serious medical causes, address medical issues that either require urgent or emergent treatment, and to ensure that patients are appropriate for admission. This process is typically called medical clearance.

Mandatory routine labs have been a part of the clearance process for decades (1–3). One assertion that has been used in the past as justification for routine screening labs is that psychiatric patients do not reliably or accurately report symptoms to guide testing. However, one study found that the initial medical complaints correlated directly with the need for medical clearance (4). Other studies have indicated that those with normal physical exams, stable vital signs, and no physical complaints do not require laboratory testing (4, 5).

The American Association for Emergency Psychiatry published guidelines in 2017 with eight recommendations for the process of medical clearance of adult psychiatric patients. They recommended universal screening involving, at a minimum, vital signs, history, physical examination, and assessment of mentation. They recommended that the decision for further evaluation be based on the emergency physician's assessment. They also identified further areas requiring investigation, one of which was the question of which criteria would define groups at high risk for medical disease (6).

At our institution, standard labs without clinical indication are required in the emergency department primarily because most receiving facilities do not accept patients without them. This retrospective chart review was conducted to evaluate the need for the routine labs on our panel. More specifically we evaluated their usefulness based on whether they directly led to interventions and whether they affected final disposition. Secondarily, this study was conducted to attempt to separate high-risk groups requiring further laboratory testing from low-risk groups who may not require labs.

Materials and methods

This retrospective chart review included psychiatric patients screened in our ED for admission to inpatient psychiatric facilities between 3/2/2021 and 9/1/2021. Patients were included if they presented to the ED with a primary complaint that was psychiatric in nature. Patients were excluded if they: did not have symptoms that required admission, were prisoners, were employees of the hospital, expired in the ED, were younger than 18, or did not have all routine labs obtained.

We reviewed 300 charts meeting inclusion criteria. Of those, 163 also met exclusion criteria. At our institution, a psychiatric crisis unit (PCU) exists where patients are admitted after medical clearance in the ED but prior to transfer to inpatient units. Admission to the PCU served as a proxy for admission to an inpatient unit since all patients admitted to the PCU required routine labs and because all transfers to inpatient units occurred after admission to the PCU. Charts were reviewed by accessing ED notes written by emergency department residents and psychiatry residents working in the PCU and by reviewing lab results.

Data collected from the notes included HPI, review of systems (ROS), physical examination, vital signs, and assessment and plan. ROS was recorded as negative if no systems were positive besides psychiatric. However, within the psychiatric ROS, we recorded agitation as positive due to the well-known requirement for intervention at times by ED staff in the form of chemical sedation. The physical exam was marked negative if no findings were documented and if the initial blood pressure, pulse rate, respiratory rate, and oxygen saturation were within normal limits. The blood pressure range considered normal in this study was 90–139 systolic and 60–79 diastolic. The pulse rate range considered normal was 60–100. The respiratory rate range considered normal was 12–20. The oxygen saturation cutoff for normal was 95%. The specific physical exam findings documented were recorded.

Labs included in the routine testing panel were complete blood count (CBC), complete metabolic panel (CMP), urinalysis (UA), urine pregnancy test (UPT), urine drug screen (UDS), serum EtOH, serum creatine kinase (CK), and rapid COVID-19. The specific levels or CK and EtOH were recorded. For the CBC, CMP, UA, UPT, and COVID-19, results were recorded simply as either normal or abnormal. For the UDS, the specific substance or substances that were detected were recorded. We recorded the final disposition in the ED and PCU notes as well as any interventions performed by the ED and PCU residents.

Results

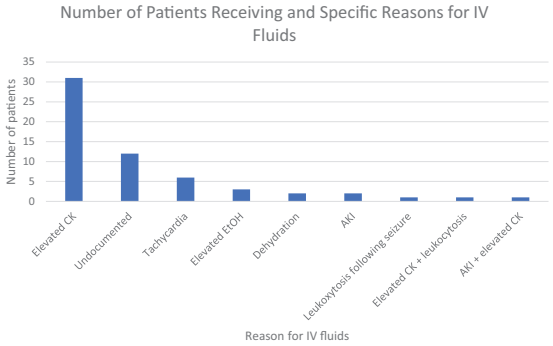
The demographic data of the patient population is presented below:

Demographics	
Age	Mean = 36
	Median = 33
	Range = 18–72
Sex	M = 67%
	F = 33%

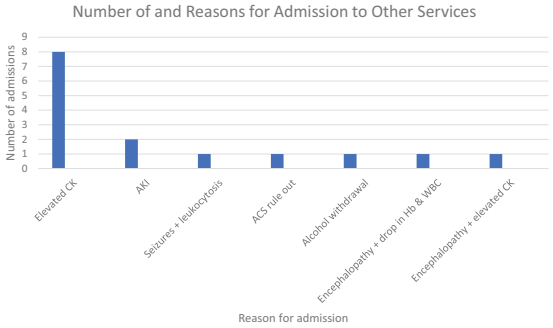
Of the 163 patients meeting inclusion and exclusion criteria, 82 patients (50.3%) received interventions, and a total of 105 interventions were performed by the ED. The interventions performed were as follows in descending order of frequency: intravenous (IV) fluids (n = 59; 45.0% of all interventions), admission to other services (n = 15; 11.5%), potassium replacement (n = 13; 9.9%), PRN medications for agitation (n = 11; 8.4%), imaging (n = 10; 7.6%), antihypertensive medication for high blood pressure (n = 4; 3.1%), cardiac workup (n = 3; 2.3%), antibiotics (n = 3; 2.3%), consults to other services (n = 3; 2.3%), and lorazepam for undocumented reasons (n = 2; 1.5%). Other interventions that were only performed once included acetaminophen administration for pain, folic acid and thiamine administration for alcohol use, laceration repair, tetanus immunization for a wound, repeat hemoglobin level, chlordiazepoxide administration for elevated alcohol level, thyroid panel for a history of thyroid nodule, and levetiracetam administration for seizure.

Interventions performed in the ED	
Intervention	Number of patients
IV fluids	59
Admission to other services	15
Potassium replacement	13
PRN medications for agitation	11
Imaging	10
Antihypertensives	4
Cardiac workup	3
Antibiotics	3
Consultation to other services	3
Lorazepam	2
Acetaminophen	1
Tetanus immunization	1
Repeat hemoglobin level	1
Chlordiazepoxide	1
Thyroid panel	1
Levetiracetam	1

IV fluids were given for the following documented reasons in descending order of frequency: elevated CK (n = 31; 50.8% of all IV fluids), undocumented (n = 12; 19.7%), tachycardia (n = 6; 9.8%), elevated EtOH level (n = 3; 4.9%), dehydration (n = 2; 3.3%), acute kidney injury (AKI) (n = 2; 3.3%), leukocytosis following a seizure (n = 1; 1.6%), elevated CK and leukocytosis (n = 1; 1.6%), and AKI and elevated CK (n = 1; 1.6%). Elevated CK alone was also the most cited sole factor for all interventions at 29.5%.



The commonest reason for admission to another service was elevated CK, which was cited for 8 of out the 15 admissions (53.3%). Patients were also admitted for AKI (n = 2; 14.3%), seizures and leukocytosis (n = 1; 6.7%), rule out of acute coronary syndrome (ACS) (n = 1; 6.7%), alcohol withdrawal (n = 1; 6.7%), encephalopathy with drop in hemoglobin and white blood cell count (n = 1; 6.7%), and encephalopathy with elevated CK (n = 1; 6.7%).



Imaging was obtained for 3 patients due to pain, for one due to cough, and for one due to an undocumented reason. A head CT was obtained for new onset psychosis for 4 patients and for a wound for one patient.

Antibiotics were given to one patient for cellulitis. They were given to 2 other patients for urinary tract infections, both of which were asymptomatic.

Consults to neurology, oral and maxillofacial surgery, and ophthalmology were placed for seizures, fracture, and photophobia, respectively.

One patient had an abnormal hemoglobin level repeated, which was normal.

Discussion

The preferred method of medical clearance in the ED has been debated (5, 7). In some EDs, a specific set of labs is ordered as a screening panel regardless of findings on history and

physical exam (2, 5, 7). These labs can be costly. For example, one study published in 2012 found that when the psychiatry service ordered laboratory or radiographic studies on 191 patients for whom emergency physicians did not order ancillary testing for medical clearance, the monetary impact based on Medicare reimbursement rates was $37,682 (2). Of those 191 patients, only one patient's disposition was altered. Another major reason why they continue to be required is that some psychiatric facilities have limited medical resources and therefore rely on EDs to obtain labs prior to admission. On the other hand, previous research and guidelines have indicated that routine labs on all psychiatric patients are not needed. Our results support the AAEP guideline recommending laboratory testing be guided by history, physical exam, and vital signs.

Our results highlight the need for fluids in a surprising number of patients. They were by far the commonest intervention. The primary documented reasons for fluids were elevated CK levels, elevated EtOH levels, CMP results, and vital signs, although for 19.7% of those receiving fluids there was no specific documented reason. Dehydration was cited as a reason, and in one case the patient was tachycardic and disoriented. The other patient was agitated. In two cases, leukocytosis was cited as one, but not the only, factor. In all cases except one, at least one of the following findings on history and physical was present: elevated blood pressure, tachycardia, incomplete ROS due to mental status, substance abuse reported by the patient, history of substance abuse, intoxication, agitation, violence, and exercising reported by a psychotic patient. The lone case for which none of these was found on history and physical examination also had no documented reason for IV fluids. The patient was a 23-year-old homeless male but had no history of drug use, did not report drug use, and had normal vital signs. IV fluids were given prior to labs drawn, and the patient's labs, once drawn, were unremarkable. Possibly, homelessness could be a component of the history that suggests a need for further lab evaluation or IV fluids.

CMP results led to both interventions and admissions. AKIs in our study were associated with agitation, tachycardia, elevated blood pressure, or a history of or current amphetamine use in all cases. For two patients, fluids were given in the ED solely for AKIs and partially for an AKI in another case. These patients were admitted to the PCU. Two others were admitted to internal medicine solely for AKIs. Of the 13 patients receiving potassium replacement, each had at least one of the following findings: tachycardia, elevated blood pressure, history of substance abuse, intoxication, or agitation. Therefore, a BMP or CMP should be considered in patients who have agitation, intoxication, abnormal vital signs, a history of amphetamine use, or current amphetamine use reported by the patient. In addition, since all of these patients for which interventions were performed had at least one of the above findings, the CMP appears better utilized as a lab directed by specific findings rather than as part of a general screening process for all psychiatric patients.

CK results alone led directly to both the most interventions performed in the ED (23.6%) and the most admissions (53.8%), and it was cited as part of the reason for interventions and admissions in still more cases. In all cases (100%) involving either CK or AKI, one of the following abnormalities was present on history and physical examination: agitation, tachycardia, elevated blood pressure, and either a history of amphetamine use or current amphetamine use reported by the patient. Therefore, our results suggest that patients with agitation, tachycardia, elevated blood pressure, a history of amphetamine use, or current amphetamine use reported by the patient should have a CK level and at least a basic metabolic panel (BMP), if not CMP, drawn. The results also suggest that the decision to obtain CK levels could be guided by the above findings rather than as part of a routine lab panel for all patients.

While in our study only amphetamines were associated with AKI and elevated CK levels, other stimulants have also been associated with elevated CK levels, rhabdomyolysis, and AKIs (8–11). Therefore, it seems reasonable to obtain CK levels and a BMP or CMP in these patients.

As for the utility of the CBC, in only one out of 163 cases was it cited as the only lab as a reason for intervention. In this case, the hemoglobin was low, but the CBC was repeated and the hemoglobin returned normal. The CBC was cited as one of the reasons for fluids in two cases. In one, fluids were given for leukocytosis and a seizure. In this case, laboratory testing including a CBC would have been indicated based on the seizure. In the other case, the other factor cited was elevated CK. In none of these cases was the disposition affected. It was cited as part of the reason for admission in one case of encephalopathy. However, encephalopathic findings on physical exam would typically necessitate collection of CBC, and this patient also had a history of HIV. Therefore, our results do not support the use of the CBC as part of routine labs for screening of all psychiatric patients.

The remaining patients admitted had clear indications for lab testing. The patient admitted for alcohol withdrawal was symptomatic. The patient admitted for ACS rule out had chest pain and shortness of breath.

The UPT was negative in all cases. However, this is required by most if not all facilities as they either do not accept pregnant patients or only accept patients whose pregnancies have not progressed beyond a certain stage. This is for safety. Therefore, a UPT will still be required as part of the screening process.

UA results led to treatment with oral antibiotics in some cases, but it did not change the disposition in any case. Therefore, its utility in general medical clearance, *per se*, based solely on our results is low since oral antibiotics can be started or continued on inpatient units. However, given the association of urinary tract infections and delirium in the elderly (>65 years), a urinalysis seems a reasonable component of the general screening process in the geriatric population (12).

The COVID-19 test was negative in all cases. However, it still seems a reasonable part of the screening process as of today because this will determine whether a patient requires admission to a dedicated COVID unit at an inpatient psychiatric facility. Most facilities do not have COVID units and therefore could not accommodate these patients.

The EtOH level alone was cited as the reason for fluids for 3 patients. This did not affect the disposition for any of these patients. One of these patients was tachycardic and hypertensive. The other two patients were hypertensive and agitated. Thus, all these patients had components of their physical exam and vital signs that could have been used to direct diagnostic testing, including an EtOH level.

UDS results were not cited as the reason for any intervention. This suggests that its role as part of the screening process is limited. Our results are consistent with a literature review that found the UDS was unlikely to affect management in the ED (13).

15 patients were admitted to other services. 10 were admitted to medicine services solely due to elevated CK, and each of them had agitation, abnormal vital signs, or amphetamine use reported by the patient. The remaining 5 patients admitted had clear indications for lab testing. The patient admitted for alcohol withdrawal was symptomatic. The patient admitted for ACS rule out had chest pain and shortness of breath. Two patients were admitted for encephalopathy, and the last was admitted for seizures. Therefore, these findings suggest labs be used as part of a diagnostic process guided by history and physical exam rather than as part of a general screening of all psychiatric patients.

Limitations

As our hospital is a residency training hospital, the level of training among residents varied. In addition, a psychiatry resident evaluated each patient after evaluation by an ED resident, and many EDs do not have a psychiatrist on site to evaluate patients prior to transfer for admission. Another limitation concerns the closeness of the relationship between our psychiatric emergency area and the main ED. Patients who are medically cleared are quickly and easily sent to the PCU, and patients initially cleared but inappropriately so can easily be transferred back to the main ED. This sometimes leads to a hastier clearance process in our ED, whereas at other EDs that do not have an emergency psychiatric service this may not be the case. In our experience with psychiatric hospitals in the state, some are unwilling to accept patients with certain lab values that our PCU is willing to accept. For example, some do not accept patients whose CK levels are above 500 U/L, whereas our PCU allows CK levels sometimes above 1,000 U/L depending on the psychiatry resident at the time. This indicates that the number of interventions in our ED for elevated CK levels may be lower at our hospital than at others. Finally, our study was limited to a single site and used a small sample size.

Conclusion

In their 2017 consensus recommendations, the AAEP outlined the need to define groups at high risk for medical disease (6). Our results further delineate certain groups and the specific laboratory tests that should be obtained. We suggest that a CK level, EtOH level, and a CMP or BMP be considered as part of the diagnostic process for patients presenting with agitation, abnormal vital signs, intoxication, or a history of or current stimulant use. Patients with at least one of these elements required interventions including IV fluids in the ED and admission to other services. The UDS had the least utility in the medical clearance process as it was not cited as the reason for any intervention or admission, and our results are consistent with previous research indicating low utility in the clearance process (6, 14). However, it does direct treatment planning for subsequent care, and the AAEP recommendations advised similarly (6). Inpatient units can obtain a UDS, but it is best utilized for this purpose as soon as possible on arrival to the ED due to rapid metabolism of certain illicit substances. Therefore, while not necessary for medical clearance, *per se*, it still has value in the ED. The CBC was also of low utility, consistent with previous research (15). UA results led to oral antibiotic treatment in some cases. However, since no patient was admitted to another service and since oral antibiotics can be started or continued on inpatient units, the UA appears to be of low utility in the general medical clearance process. It may be better utilized in a more directed manner, such as in elderly patients to screen for delirium (12). Although COVID-19 results and the UPT were negative in all cases, these tests are still required as most inpatient units are not equipped for patients testing positive for these.

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 Matthew Vetkoetter Louisiana State University Health Shreveport. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

CC wrote the primary manuscript, developed the study, and performed chart reviews. JG wrote the abstract. MS, NW, PM, and RR performed chart reviews. JP supervised the study. All authors contributed to the article and approved the submitted version.

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.

Publisher's note

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Technologically assisted intensive home treatment: feasibility study

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Introduction: In recent year, many attempts have been made to provide patients with alternatives to psychiatric hospitalization during acute distress. Although several hospitalization alternatives have been offered, most of them still require patients to be distanced from their families, friends, and the social environment.

Methods: In this report we describe the implementation of a novel approach to psychiatric care termed "Technologically assisted Intensive Home Treatment", where patients arriving to emergency settings are directed to home care with technological aids that enable close monitoring and ongoing contact with their therapists.

Results: We describe the rationale and treatment principles of the treatment, and provide an elaborative description of the implementation process during the first year of implementation.

Discussion: Additional attention is given to factors associated with early dropout from the program, in order to inform readers of predictors to optimal care. Limitations and directions for future research and practice are discussed.

Clinical Trial Registration: The study was registered in the database of clinical trials (registration number SHEBA-19-6555-MW-CTIL) and in the Ministry of Health (registration number MOH_2022-08-22_011992).

KEYWORDS

psychiatric hospitalization, admission, technology, technologically assisted intensive home treatment, psychiatric services

Introduction

Psychiatric inpatients settings are considered the most routine and traditional route to provide care to patients with acute mental outbreaks. Nonetheless, in recent years attention has been brought to the potential adverse effects of admission to psychiatric hospitals for individuals with severe mental disorders. These adverse effects are reported to include self-esteem impairment (1), social maladaptation (2) and symptomatic deterioration (3). Studies which explored reasons for patients' non-adherence with the psychiatric system have reported lack of self-control, adverse experiences with the treating staff (4, 5), feeling foreign from the therapeutic system (6) and social and self-stigma (7, 8) as some of the potential reasons for reduced compliance. These effects, as well as economical considerations pertaining to inpatient costs, have led scholars, clinicians and policy makers to explore alternatives to the traditional model of psychiatric hospitalization so as to mitigate these adverse consequences.

Alternative forms of psychiatric care during acute states have been established relatively early. In the late 1960s and early 1970s the Soteria model was suggested by Lauren Mosher in California (9), as means to address the needs of young people with severe mental disorders and specifically facilitate community integration and adjustment to the neighborhood's social norms. Crisis homes, which include community facilities staffed 24/7 by clinical staff and provide a short-term stay for individuals with mental disorders has also been described (10, 11). Nonetheless, some of the models were struggling to balance medical and social models of care, or were more fitted to specific populations (9, 10, 12). More importantly, most of them require patients to undergo their crisis away from their close and familiar environment.

The use of technology during the COVID-19 pandemic has provided further evidence for the potential of technological aids to act as therapeutic means for patients, even in their own homes. Intensive Home Treatment (IHT) typically involves treatment in patients' home and a facilitation of a decision-making process. During home treatment, a professional team visits the patient more than once a day (13). In a recent study comparing the effectiveness of home-based care to inpatient hospitalization, similar effectiveness in improving clinical symptoms was observed, along with a reduction in hospitalization days over the 2 years following the intensive home treatment (14). Studies aimed to explore the effectiveness of therapies provided online have demonstrated their non-inferiority to face-to-face treatments, thus supporting the notion that treatments given during hospitalization may be provided online (15). Studies that focused on treatment processes have indicated that the quality of the therapeutic alliance created in online therapy is similar to the quality of face-to-face therapy (16, 17). In medical settings, online medical counseling was found to be as effective as face-to-face treatment in terms of quality of communication and accessibility to treatment (18). Furthermore, Hickson et al. (18) suggested that online care may lead to increased access to care by reducing patients' travel costs. These findings suggest that technology might assist clinicians and patients to overcome the barriers and challenges of psychiatric hospitalization, by providing home care through the utilization of online services.

In 2019 clinicians in Sheba Medical Center in Israel initiated the implementation of "Technologically assisted Intensive Home Treatment". The project was initiated by the support of the Maccabi and healthcare services. The idea of remote hospitalization is that individuals with severe mental outbreaks will be treated at home using technological aids. The service was aimed to ameliorate stigma and significantly improve patients and families' experiences with the public mental health system. To reach this aim, a complex technological system managing multi-disciplinary therapeutic interventions was developed so as to allow access to treatment records by clinicians, as well as to monitor patients' physical status *via* sensors and self-report measures. Because the model does not depend on location, the remote service allowed the treating team to be continuously available to accompany the patient. The presence of a primary care giver, a family relative or close friend, who is with the patient most of the day, helped the treating staff to monitor potential risk. During the treatment, information was collected mainly through a smart watch, in order to assist in clinical assessments and decision making. The services followed the principles of continuity of care, therefore, the same professional staff accompanied the patients throughout the treatment at varying levels of intensity, depending on the patient's needs.

In this article we present the implementation process of the first technologically assisted intensive home treatment in Israel. Studies suggest that the effectiveness of novel treatments depends largely on the implementation process, with effective implementation associated with better therapeutic outcomes (19). Thus, this study is aimed to explore the benefits and drawbacks of technologically assisted intensive home treatment, and provide a full account of the challenges faced by the treating staff. Specifically, the following objectives were pursued: (a) providing a full description of the treatment model; (b) describing the nature of the patients participating in the implementation process; (c) discuss terms and conditions needed to reach therapeutic success in this model; and (d) provide directions for future research and suggestions to other groups which may be interested in implementing such services.

Methods

Basic principles of technologically assisted intensive home treatment

The basic model of the technologically assisted intensive home treatment is based on a sequence of interventions which overall can last for up to 2 years. This sequence starts with assessment of suitability, followed by remote hospitalization. During remote hospitalization patients receive therapeutic interventions, assessments and online monitoring, as well as in-person online meetings held in fixed intervals. The treatments are personal, conducted by a multi-professional team, and are customized to fit the needs of the patient and his primary caregiver; All treatments are managed by a case manager, and include psychiatric medical follow-up, psychological therapy and social assistance by a social worker, as well as continuous monitoring of behavioral and physical health. Continuous measurements of behavioral data such sleep patterns, level of physical activity, medication adherence, and vital signs including physiological measures (body temperature, blood pressure, and heart rate) was performed, and patients had mobile phone reminders to take medications and attend follow-up appointments. Therapists could also utilize the system for individual and group interventions through video conferencing. The service technology was based on a tablet with a dedicated application developed by Datos, a smartwatch measuring blood pressure and heart rate, a thermometer, a saturation monitor. The Datos application also enabled messaging communication and video calls with the healthcare team. The smartwatch also monitored sleep patterns and physical activity through step tracking. Blood pressure, temperature, and oxygen saturation data were transmitted to the Datos application on the tablet via Bluetooth.

Staff was compiled of a multi-disciplinary professional team that includes a psychiatrist, psychologist, social worker, nurse, occupational therapist and nutritionist. Patients participating in the program had 24/7 telephone availability of a psychiatric nurse. Data security measures are utilized to safeguard patient's confidentiality and privacy. During hospitalization, the degree of suitability of the patient to the service is constantly examined, so as to avoid potential risk. The medical doctor prescribes medications in the patient's medical record at Sheba Medical Center, which automatically transfers to a dedicated application accessible to the patient. Afterwards, family physician in the

community submits a request to the health insurance fund for dispensing the medications. In cases of low compliance with medications, a smart medication dispenser sends reminders for intake and alerts the healthcare team.

Treatment procedure

The acute stage of treatment includes high intensity care, and usually lasts 4–6 weeks. The first stage is initial assessment, where patients are referred to remote hospitalization after an examination in a psychiatric emergency room, a psychiatric clinic (community or hospital) or during a psychiatric hospitalization that does not exceed 2 days. After starting the program, the comprehensive care package is offered and is supported, if necessary, by community caretakers. Patients are equipped with a home kit with full communication platform to make video calls, send two-way messages, collect information through sensors, reminded to take medication and schedule follow-up appointments. The kit is based on a tablet computer. Significant clinical exacerbations, transfer to full hospitalization, incidents of self-harm and suicide and events of new physical illness are documented and reported to the risk management department at Sheba Medical Center.

TABLE 1 Demographic and clinical characteristics of the study sample.

Characteristics	Technologically assisted intensive home treatment (N = 57)
Age (M, SD)	37.52 (15.99)
Gender (% females)	40 (69)
Diagnoses	
Personality disorder (%)	15 (26.3)
Anxiety disorder (%)	9 (15.8)
Mood disorder (%)	25 (43.9)
Schizophrenia and psychosis (%)	8 (14)

Criteria for inclusion and exclusion

The service is designated for patients who need urgent psychiatric hospitalization, as clinically evaluated by a senior psychiatrist. Patients starting full hospitalization are eligible to transfer into the home care. Patients with one of the following diagnoses can join the services: psychotic disorder in its early stages (up to 5 years from the first psychotic episode), mood disorders, postpartum depression, or psychosis. The inclusion of a patient in the service is conditioned on the immediate availability of a primary caregiver such as a parent or spouse with good support capacity. Patients with one of the following definitions will not be included in the service: patients with immediate risk as a result of the mental illness to aggression or suicide, patients admitted for forced hospitalization, current drug or alcohol abuse, low levels of response to treatment, developmental intellectual disability or other disability which might cause difficulty in technological operation, significant physical illness requiring hospitalization, refusal to take part in treatment as part of the service.

Results

Table 1 presents the demographic characteristics of the patients admitted to the service during the first year of implementation. The total sample included 58 people, 69% were women. The average age was 37.52 (SD = 15.99). The most common diagnostic category was mood disorders with a frequency of 43.9% (n = 25), personality disorders with a frequency of 26.3% (n = 15), anxiety disorders with a frequency of 15.8% (n = 9) and schizophrenia and psychosis with a frequency of 14% (n = 8).

Table 2 presents the clinical outcomes of the technologically assisted intensive home treatment. The average number of days in technologically assisted intensive home treatment was 193.17 (SD = 208.6). Of all participants, 59% (n = 34) completed hospitalization and 41% (n = 24) dropped out prior to official discharge. Of those who dropout from hospitalization, 33% (n = 8) dropped out during the first month. The most common reason for leaving in the first month is lack of cooperation (n = 5, 62%, including transfer to another treatment),

TABLE 2 Outcomes of the first year of implementation.

Category	Sub-category	N (%)
Overall time in service (M, SD)		193.17 (208.6)
Status	Completes (%)	34 (58.6)
	Dropped (%)	24 (41.4)
Dropped time	In the first month (%)	8 (33.3)
	After the first month (%)	16 (66.6)
Reasons for leaving service in the first month (n = 8)	Aggravation or lack of improvement (%)	2 (25.0)
	Lack of cooperation (%)	5 (62.5)
	Release on a technical or other (%)	1 (12.5)
Reasons for leaving service after the first month (n = 16)	Aggravation or lack of improvement (%)	9(56.2)
	Lack of cooperation (%)	3 (18.7)
	Release on a technical or other (%)	4 (25.0)
Overall number of patients to full hospitalization (n = 15)	Involuntary (%)	12 (80)
	Consensual (%)	3 (20)

TABLE 3 Characteristics of patients who dropped out of the service ($n = 24$).

Characteristics		
Age	M, SD	35.71 (18.20)
Sex	% Female	17 (70.8%)
Diagnosis	Personality disorder	7 (29.2%)
	Mood/anxiety disorder	12 (50.0%)
	Schizophrenia	5 (20.8%)
Total days in service	M, SD	128.83 (113.31)
Team position	Unfitted to service	3 (12.5%)
	Needs full hospitalization	12 (50%)
	Should continue treatment	3 (12.5)
	Release due to various reasons	6 (25.0%)

aggravation or lack of improvement ($n = 2$, 25%), and dropout due to technical reason ($n = 1$, 12%). The most common reason for leaving after the first month is aggravation or lack of improvement ($n = 9$, 56%), dropout due to lack of cooperation (including transfer to other treatment $n = 3$, 19%) and dropout due to technical reason ($n = 4$, 25%). Of the total sample of dropouts, the majority (62%) moved to full hospitalization, with 80% of them transferring to involuntary hospitalization and 20% moving to consensual hospitalization. These numbers demonstrate the main complexity of technologically assisted intensive home treatment in balancing acute states.

Table 3 presents the demographic and clinical characteristics of patients who dropped out of the service ($n = 24$). The average age of the dropouts is 35.71 (SD = 18.20). Out of all the dropouts, 17 are women (70.8%). Average days in service is 128.83 (SD = 113.31). The most common diagnosis among the dropouts is Anxiety/Mood disorder with about 50% ($n = 12$), followed by Personality disorder with 29.9% ($n = 7$), and the disorder with the lowest frequency among the dropouts is Schizophrenia with 20.8% ($n = 5$). The most frequent staff position for the dropouts is that the patient needed full hospitalization (50%, $n = 12$), followed by release due to various reasons with 25% ($n = 6$), that the patient was unfitted to service with 12.5% ($n = 3$) or should continue treatment (12.5%, $n = 3$).

Discussion

This study was aimed to provide a full account of the first implementation of technologically assisted intensive home treatment in Israel, based on the first 58 patients who entered this program at Sheba Medical Center in Israel. To the best of our knowledge, this is the first program in Israel and worldwide to implement full psychiatric hospitalization while monitoring the psychological, medical, pharmacological, occupational and social treatment of patients using technological aids.

The results of the first year of recruitment to the program indicated that the vast majority of patients completed the treatment program. Nonetheless, 24 patients, which constitute 41% of the total sample, did not complete the treatment. Eight patients also failed to complete the first month of hospitalization. Several hypotheses can be made to explain these attrition rates. An analysis of the characteristics of the patients who dropped out of the program indicates that staff position was that these patients needed full hospitalization. Furthermore, most of the patients leaving the program did so due to aggravation in their clinical state, or due to lack of cooperation with the offered treatment program. The implementation process might have also differentially affected patients with different clinical characteristics. For example, it is possible that patients with severe anxiety and additional underlying pathology could not tolerate the experiential nature of the service and therefore were more likely to dropout. Thus, it is possible that for some patients, home environment is not sufficient for acute stabilization. Studies conducted in full psychiatric hospitalization settings demonstrate the importance of having clinical staff with the patient 24 h a day. (20) explained that the presence of the care staff 24 h a day makes it possible to anticipate future crisis events and prevent them. It is therefore possible that for some patients, the 24-h presence of professionals is paramount.

An analysis of the main characteristics of the dropouts from the technologically assisted intensive home treatment reveals that most of the dropouts were women with mood or anxiety disorder, followed by personality disorder. Schizophrenia had the lowest frequency of dropout, although the number of patients with schizophrenia recruited to the service was low to begin with. The high frequency of dropouts with mood and anxiety disorders may be associated with an underlying personality disorder (21), which may have been difficult to handle without a designated treatment approach. Furthermore, the majority of patients who dropped out entered full hospitalization. This may be associated with the novelty of the treatment approach, as compared to the familiarity of the inpatient care. Studies indicate that the credibility of the treatment approach, the fact that it well known, affects patients' trust and comfortless with the approach. Furthermore, Frovenholt et al. (22) found that the perceptions of credibility of the therapeutic procedure may affect both the therapeutic alliance and the treatment outcomes. It is therefore possible that once this alternative care will be disseminated, patients will be more comfortable with the treatment approach. Such an hypothesis remained to be examined in future initiatives.

The technology used in the implementation of the Technologically assisted Intensive Home Treatment included a tablet with a dedicated application developed by Datos, a smartwatch measuring blood pressure and heart rate, a thermometer, a saturation monitor. The technology was most helpful in videoconferencing and management of sleep disturbances. On the other hand, alerts of timing of medications and requests to report medication adherence was sometimes uncomfortable to some of the patients. Although no emergency alert was designated in the software, patients could call a nursing staff unit 24/7. Future developments of technologically-assisted services might use these conclusions to tailor other more adaptive functions, such as emergency button or more convenient management of patients' medications.

As this is the first implementation of remote hospitalization using technology, it is also possible that other factors related to the implementation and dissemination process affected the outcomes of the first year. Studies indicate that the effectiveness of a new treatment depends largely on the quality of its assimilation. More specifically, it has been found that effective assimilation is associated with better treatment outcomes among mental health patients (23). DuBois et al. (24) found that programs which were monitored during implementation obtained effect sizes three times larger than programs

that reported no monitoring. Moreover, Tobler (25) reported that 29% of the outcomes derived from 143 drug prevention studies were drawn from interventions that were improperly implemented, and comparisons suggested that well-implemented programs achieved effect sizes 0.34 greater than poorly implemented programs. These findings stress the importance of empirically evaluating treatment programs to improve patients' care.

The findings of the present study have several clinical and research implications. First and foremost, the results indicate that technologically assisted intensive home treatment is a feasible alternative. Furthermore, it was evident that some patients can receive treatment in their own house, and that a continuous psychiatric care can be delivered using technological aids. This ability to provide healthcare from afar is especially important in light of the adverse social effects of psychiatric hospitalization, such as social stigma (8), and potential feelings of alienation from the inpatient system (6). The fact that patients can stay in their own home and within their own community environment fosters the social concept of inclusion and tolerance, and may also impact social norms. As the length stay in the technologically assisted intensive home care is relatively long, this service may also be considered as a service that might replace hospitalization, but then continues as remote outpatient care. Empirically, the description of the process of implementation may encourage additional scientific explorations pertaining to the conditions needed to optimize this line of treatment.

Several limitations should also be noted. First, since this is the first technologically assisted intensive home treatment in Israel, the study and treatment staff were faced with many challenges which likely affected the overall implementation process. Future studies should explore the outcomes of this implementation after full dissemination of the treatment program. This study did not include in-depth interviews with patients, caregivers and their families to assess patients' and social partners' level of satisfaction with this novel service. Future studies should explore whether patients and their families may have suggestions to improve the quality of technologically assisted intensive home treatment. Finally, the outburst of the COVID-19 pandemic has dramatically affected the number of patients arriving to receive acute care, and therefore also affected the overall number of patients participating in the program. Additional studies are needed to further illuminate the strengths and limitations of this treatment program. Taken together, the efforts of implementation support the feasibility of technologically assisted intensive home treatment, and provide a new horizon to inform research and clinical practice.

Data availability statement

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

Ethics statement

The studies involving human participants were reviewed and the study was approved by the institutional review board of Sheba Medical Center in Israel (reference number: 6555-19-SMC) in January 2020. The patients/participants provided their written informed consent to participate in this study.

Author contributions

AC, DT, OiH, and OrH conceptualized the study design and methodology, did the literature search, wrote the original draft, contributed to validation, curation, analysis, interpretation of the data, reviewed, edited, and finalized the manuscript. AF and TA contributed to validation, curation, analysis, interpretation of the data, writing, reviewing, and editing. GB, EZ, OS, MS, AZ, and MW conceptualized the study design and methodology, contributed to project administration, investigation, data acquisition, curation, validation, writing, reviewing, and editing. All authors contributed to the article and approved the submitted version.

Conflict of interest

DT received research grants from the American Psychological Foundation and from Pfizer.

The remaining 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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Antipsychotics reduces mortality in patients with neuropsychiatric systemic lupus erythematosus: a retrospective study of psychiatric consultation cases

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Objective: This study aimed to identify the presence of psychiatric comorbidities as well as investigate the relationship between psychiatric interventions for mental symptoms and mortality in patients with systemic lupus erythematosus (SLE).

Method: We retrospectively evaluated the records of 160 inpatients with SLE who required psychiatric consultation for further therapeutic intervention from 2013 to 2020 in a tertiary general hospital. We collected clinical data, including diagnoses, medications, and mortality rate. We compared clinical characteristics among the diagnosis groups and correlations between variables.

Results: A total of 138 (86.3%) patients met the diagnostic criteria for at least one mental disorder, with the most common being delirium (54.4%). The average Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score significantly differed among the diagnosis groups ($p = 0.003$). The mortality rate among patients with delirium was significantly higher than that in the other patient groups ($x^2 = 12.967$, $p = 0.024$). SLEDAI-2K score was not significantly correlated with mortality ($r = 0.123$, $p = 0.087$). Antipsychotics use was associated with mortality (odds ratio 0.053, $p = 0.021$).

Conclusion: Antipsychotic use may decrease death risk for patients with NPSLE. Early psychiatric consultation is necessary for patients with SLE who have developed or have suspected psychiatric symptoms in order to establish a comprehensive intervention plan.

KEYWORDS

neuropsychiatric systemic lupus erythematosus, referral consultation, antipsychotics, consultation-liaison psychiatry, China

1. Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease that often causes multi-organ damage. Neuropsychiatric SLE (NPSLE), which is characterized by the involvement of the central or peripheral nervous system, leads to increased risk of mortality (1); further, it is associated with disabilities, reduced social participation, unemployment, and poor quality of life (2, 3). The estimated prevalence of NPSLE is 14–95% (4–6), with this wide range being attributed to the broad spectrum of presentable psychiatric symptoms. The American College of Rheumatology (ACR) defines 19 NPSLE syndromes, including delirium (acute confusional state), psychosis, mood disorder, and cognitive dysfunction (7).

Psychotropic medications have been considered for the symptomatic treatment of NPSLE (8). The present study aimed to describe the diagnostic spectrum and psychiatric interventions for the mental manifestations of SLE, as well as their correlation with mortality.

2. Methods

We evaluated the case records of inpatients with SLE who required psychiatric consultation for further therapeutic intervention between April 2013 and July 2020. There were 160 case records. All the patients were admitted to the Department of Rheumatology and Clinical Immunology at the Peking Union Medical College Hospital, which is a tertiary general hospital in Beijing. Medical records were retrospectively reviewed for clinical information, including general demographic characteristics, clinical characteristics, laboratory and magnetic resonance imaging (MRI) results, and medical and psychiatric medications.

Treating rheumatologists diagnosed each patient with SLE according to the ACR revised criteria for the classification of SLE (9) and performed an evaluation of disease activity using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) (10). The SLEDAI-2K is a validated 24-item scale encompassing clinical and laboratory variables (10). A SLEDAI-2K score < 5 suggests no or very low disease activity, while a score ≥ 15 suggests high disease activity (10).

Consultation-liaison psychiatrists administered standard mental status examinations during the first and follow-up consultation visits to determine the psychiatric diagnoses. Delirium, psychosis, mood disorder, and cognitive dysfunction were diagnosed based on the International Classification of Diseases 10th Revision (ICD-10) (11).

Statistical analyzes were performed using IBM SPSS Statistics 21.0.0.0 (IBM Corp., Armonk, NY, United States). Quantitative variables are described as mean ± standard deviation or median (interquartile range [IQR]) based on the normality of distribution. Categorical variables are described as frequencies (percentages). The Kruskal–Wallis test was used for among-group comparisons of continuous non-normally distributed variables. The Chi-square test or Fisher's exact test was used for among-group comparisons of categorical variables. The correlation between clinical variables was examined using Spearman's correlation test. Binary logistic regression analyzes were used to determine factors related to mortality. A two-tailed p value <0.05 was considered statistically significant.

3. Results

The median age of the 160 patients with SLE was 28 (IQR 23–39) years. Most patients (90.6%) were female. The median disease course was 1.5 years (IQR 0.3–6). Moreover, 75.6% of the patients showed multi-organ or -system involvement of SLE. The most commonly affected organ was the kidney (62.5%). The average SLEDAI-2K score was 20 (IQR 12–24). Ten patients (6.2%) died during hospitalization. The average length of hospital stay was 30 days (IQR: 22–43 days).

Table 1 presents the psychiatric diagnoses and clinical characteristics of all 160 patients. A total of 138 (86.3%) patients met the diagnostic criteria for at least one mental disorder, with the most common being delirium (54.4%). Out of the 132 patients who underwent head MRI, abnormal results were found in 85 individuals (64.4%). Among them, 14 had ischemic lesions, 44 had inflammatory lesions, 6 had both ischaemic and inflammatory lesions, and 21 showed other types of lesions. It was observed that there were no significant differences in the head MRI outcomes among patients with various psychiatric diagnoses (as shown in Table 1). Table 2 lists items in the SLEDAI-2K and their frequencies. The most prevalent descriptor was low complement (65.6%), followed by increased DNA binding (52.5%) and proteinuria (45.0%).

Patients with mania/hypomania showed the highest proportion of antipsychotic use (92.3%), followed by patients with psychosis (89.5%). Sedatives were used in one-third of the patients, with 53.8% (highest proportion) and 7.7% (lowest proportion) of these patients using them for mania/hypomania and depression, respectively. Four patients with negative symptoms were prescribed antipsychotics. One patient with catatonia received benzodiazepines. Moreover, 17 patients required consultation due to psychosocial stress and were subsequently recommended for psychotherapy.

As shown in Table 1, the mean SLEDAI-2K score differed significantly among the diagnosis groups (test value = 18.045, $p = 0.003$). However, if item "psychosis" and item "organic brain syndrome" were excluded, there was no significant among-group difference for the remaining diagnoses (test value = 8.392, $p = 0.136$). Patients with depressive disorder had lower SLEDAI-2K scores than patients with delirium ($p = 0.037$) and cognitive dysfunction ($p = 0.025$). Patients with delirium had a significantly higher mortality rate than the other patient groups ($\chi^2 = 12.967$, $p = 0.024$).

All 10 deceased patients were diagnosed with delirium during their hospitalization. Supplementary material S1 shows the multiple factors associated with mortality. The correlation between SLEDAI-2K score and mortality was not statistically significant ($r = 0.123$, $p = 0.087$). Logistic regression analysis indicated that the main mortality-related factors were antipsychotic use, cumulative cyclophosphamide dose, proteinuria, pericarditis, and thrombocytopenia (Figure 1).

4. Discussion

We assessed the diagnostic spectrum and psychiatric interventions of the mental manifestations in 160 adult patients with SLE. In our study, most of the patients met the diagnostic criteria for at least one mental disorder, with delirium showing the highest prevalence (54.4%). Antipsychotic use and cumulative cyclophosphamide dose were negatively correlated with mortality.

The reported prevalence rates of mental disorders among patients with SLE range from 14 to 95% (4–6). This wide range can

TABLE 1 Psychiatric diagnoses and clinical characteristics.

Diagnoses	Delirium (87)	Cognitive disorder (40)	Psychosis (19)	(Hypo) mania (13)	Depression (13)	None (22)	Total (160)
SLEDAI-2 K score	21 (17, 26)	21 (16, 27)	16 (9, 25)	16 (12, 19)	12 (6, 19)	16 (12, 22)	20 (12, 24)
SLEDAI-2 K score excluding NP symptoms	13 (9, 19)	13 (9, 19)	9 (3, 17)	9 (5, 12)	8 (4, 14)	14 (8, 20)	12 (8, 18)
Disease course (years)	0.5 (0.2, 4)	1.8 (0.3, 6.8)	3.5 (0.8, 9.0)	6 (2.3, 9.5)	3 (0.3, 12)	2 (0.2, 5.3)	1.5 (0.3, 6)
Multiple (≥3) organ/systems affected	73 (83.9%)	30 (75.0%)	11 (57.9%)	11 (84.6%)	9 (69.2%)	17 (77.3%)	121 (75.6%)
Hospital stay (days)	31 (24, 46)	35 (27, 49)	26 (18, 43)	27 (19, 33)	25 (15, 36)	29 (24, 41)	30 (22, 43)
Death	10 (11.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	10 (6.3%)
MRI abnormalities	45/72(62.5%)	25/38 (65.8%)	10/16 (62.5%)	6/10 (60.0%)	6/11 (54.5%)	14/17 (82.4%)	85/132 (64.4%)
Ischaemic	7 (15.5%)	5 (20.0%)	1 (10.0%)	1 (16.7%)	0 (0%)	4 (28.6%)	14 (16.4%)
Inflammatory	22 (48.9%)	8(32.0%)	7 (70.0%)	4 (66.6%)	4 (66.6%)	6 (42.9%)	44 (51.8%)
Ischemic + Inflammatory	3 (6.7%)	2 (8.0%)	1 (10.0%)	0 (0%)	1 (16.7%)	1 (7.1%)	6 (7.1%)
Others	13 (28.9%)	10 (40.0%)	1 (10.0%)	1 (16.7%)	1 (16.7%)	3 (21.4%)	21 (24.7%)
Antipsychotics use	66 (75.9%)	29 (72.5%)	17 (89.5%)	12 (92.3%)	5 (38.5%)	4 (18.2%)	103 (64.4%)
Sedatives use	38 (43.7%)	13 (32.5%)	7 (36.8%)	7(53.8%)	1 (7.7%)	1 (4.5%)	52 (32.5%)

SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; MRI, magnetic resonance imaging; NP, neuropsychiatric.

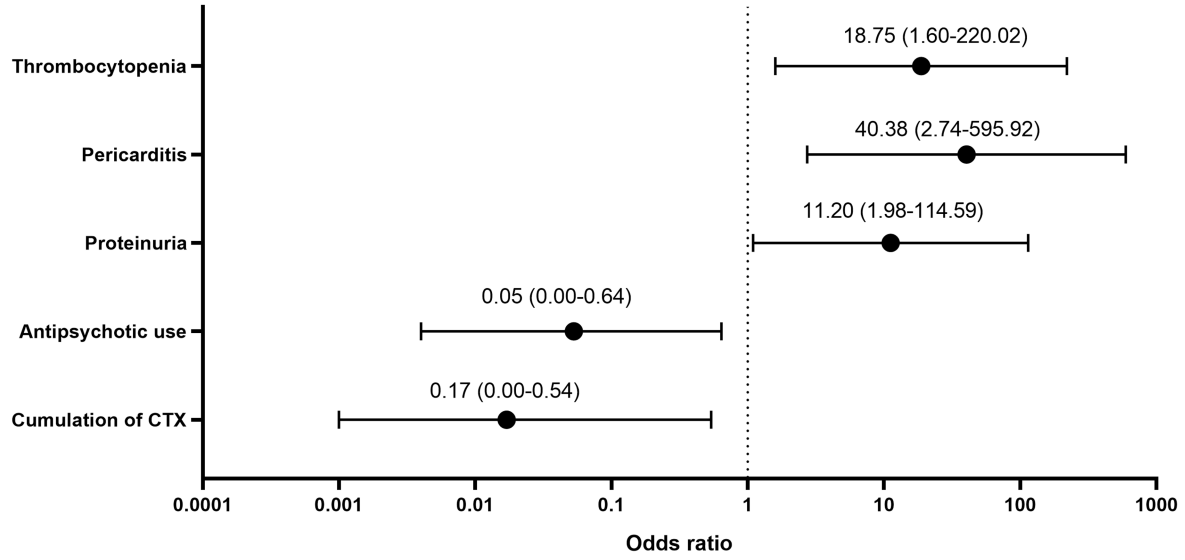
be attributed to differences in the population characteristics and diagnostic instruments. In our study, 86.3% of the patients had at least one mental disorder, which is higher than some previously reported values (12, 13). These differences could be attributed to the study population since most studies investigated general patients with SLE, while we focused on patients who required psychiatric consultation; therefore, mild or asymptomatic cases were probably not included.

Delirium and psychosis are considered relatively uncommon neuropsychiatric manifestations of SLE compared with other common ones such as mood disorder and cognitive dysfunction (5). In our study, delirium was diagnosed in more than half of the patients. Patients with SLE are predisposed to multiple risk factors for delirium given its multi-organ/−system involvement. Our patients had a mean SLEDAI-2K score of 20, which suggests severe disease activity; moreover, 75.6% of the patients had involvement of multiple organs or systems, which may explain the high prevalence of delirium in our study. In our study, the prevalence of cognitive dysfunction was 25%; further, the prevalence of psychosis was 11.9%, which is higher than previously reported values (12, 14, 15). This could also be attributed to participant bias. In clinical settings, it is sometimes difficult to attribute a mood episode solely to SLE (16). We found that disease activity was significantly lower in patients with depression than in patients with delirium and psychosis. We cautiously interpret this result as depression being less organic than the other two disorders. Our findings are consistent with the 2019 European League Against Rheumatism/ACR SLE diagnostic criteria (17), which only include delirium and psychosis as psychiatric manifestations. However, similar to other studies (18, 19), we observed psychiatric symptoms other than those in ACR case definitions for patients with SLE, such as catatonia, that required interventions such as sedative administration. Ultimately, psychiatric symptoms result from abnormal brain function (20–22). Autoimmune inflammation may cause encephalitis, which could be diagnosed based on evidence such as cerebrospinal fluid examinations, electroencephalography, and MRI results. NPSLE, with its vascular and immunological mechanisms that affect the brain, may cause all kinds

TABLE 2 SLEDAI-2K item frequencies of 160 patients.

Items	Frequencies (percentage)
Seizure	29 (18.1%)
Psychosis	50 (31.3%)
Organic brain syndrome (delirium)	71 (44.4%)
Visual disturbance	6 (3.8%)
Cranial nerve disorder	2 (1.3%)
Lupus headache	13 (8.1%)
CVAs	6 (3.8%)
Vasculitis	11 (6.9%)
Arthritis	28(17.5%)
Myositis	10 (6.3%)
Urinary casts	7 (4.4%)
Hematuria	39 (24.4%)
Proteinuria	72 (45.0%)
Pyuria	4 (2.5%)
Rash	28 (17.5%)
Alopecia	57 (35.6%)
Mucosal ulcers	28 (17.5%)
Pleurisy	32 (20.0%)
Pericarditis	22 (13.8%)
Low completement	105 (65.6%)
anti-DNA antibodies	84 (52.5%)
Fever	53 (33.1%)
Thrombocytopenia	69 (43.1%)
Leukopenia	64 (40.0%)

CVAs, cerebrovascular accidents.



FIGU RE 1
Odds ratio of mortality-related factors.

of psychiatric symptoms that may be seen in patients with primary mental disorders. Due to the limited clinical data available in our retrospective study, we were unable to determine the proportion of patients diagnosed with encephalitis. Future research can expand upon this point to comprehensively illustrate the correlation between brain function and psychiatric symptoms.

The differences between psychiatric diagnoses and SLEDAI-2K descriptors, specifically for delirium and psychosis, were remarkable. These differences may originate from different definitions of the same psychiatric term in the SLEDAI-2K and NPSLE (10, 17). For example, in the SLEDAI-2K, psychosis is defined including hallucinations, incoherence, marked loose associations, and bizarre or disorganized behaviors. In the NPSLE diagnostic definitions, psychosis refers only to hallucinations and delusions with delirium ruled out. Therefore, the frequency of the psychosis descriptor in the SLEDAI-2K should be higher than the diagnosis. The definition of organic brain syndrome in the SLEDAI-2K is the same as delirium in the NPSLE, although in our study, the frequency of delirium items was lower. We presume that this inconsistency was due to the clinical setting. The SLEDAI-2K is usually rated by rheumatologists as soon as a patient is hospitalized earlier than in the psychiatric consultation. It is highly possible that the general condition of some patients deteriorates during the first days of hospitalization; therefore, the number of cases fulfilling the diagnosis of delirium increases after consultation. It is also possible that some psychiatric manifestations are categorized as psychosis symptoms in the first evaluation and regrouped as manifestations of delirium after consultation. This phenomenon strengthens the importance of interdisciplinary collaboration for a more precise diagnoses and evaluations of patients with SLE.

Previous studies have shown that neuroanatomical abnormalities are more prevalent in patients diagnosed with NPSLE (23). MRI has been found to be a sensitive diagnostic tool in detecting ischemic lesions in SLE patients, while inflammatory NPSLE is associated with cognitive dysfunction (24). In a review of the diagnosis and management of NPSLE, the author concluded that vascular lesions are more commonly linked to cognitive dysfunction, while autoimmune inflammatory lesions lead to more diffuse symptoms, such as psychosis and acute confusional state (25). In our current study, we did not observe significant differences in MRI lesions among patients with different diagnoses, which precludes us from drawing firm conclusions about the relevance of specific lesions to any particular diagnosis.

The mortality rate in our study was 6.3%. Although the SLEDAI-2K score was not significantly correlated with mortality, we found that several descriptors in the SLEDAI-2K, including proteinuria, pericarditis, and thrombocytopenia, were related to death. High disease activity and multiple organ/system involvement are associated with mortality in patients with SLE. Ahn et al. (2) reported a three-fold increased mortality risk in patients with NPSLE. Additionally, a large multi-centre Chinese cohort study on hospitalized patients with SLE (26) reported that the mortality rate was 1.22%; further, age at diagnosis, NPSLE, hematological abnormalities, lupus nephritis, and infection were associated with mortality. A single-centre retrospective study of 194 patients with NPSLE reported a mortality rate of 8.2% (27). Patients with elevated serum creatinine levels, hypocomplementemia, and SLEDAI−2K scores ≥15 had shorter survival periods, which suggests that renal insufficiency and high disease activity are predictive of poor prognoses in patients with NPSLE. Pinto et al. (28) reported a 16.4% mortality rate in an Indian cohort of patients with NPSLE; furthermore, NPSLE relapse was associated with death.

Upon diagnosis of SLE, hydroxychloroquine, glucocorticoids, and immunosuppressive agents are considered as the fundamental treatment options (8). High-dose glucocorticoids and intravenous cyclophosphamide remain the main treatment regimens for patients with severe symptoms (29). Among all immunosuppressive interventions, the use of cyclophosphamide was correlated with disease outcome. Antipsychotics and sedatives are usually used for symptomatic treatment; furthermore, they are crucial for attaining improvement in severe cases, especially for agitated patients (8). Impaired consciousness impedes functional recovery, which in turn impedes clinical management (30). In our study, patients with SLE who presented with psychomotor agitation, including patients with

psychosis, delirium, and hypomania, were mostly prescribed psychotropic medications. Additionally, antipsychotic use was negatively correlated with mortality, especially in patients with delirium. Since benzodiazepines were not associated with fewer deaths, do antipsychotics help treat the "brain"? This may merit further study.

The main strength of our study was the precise psychiatric diagnosis and appropriate intervention for NPSLE symptoms under a multidisciplinary collaboration. However, this study has several limitations. First, given the retrospective design of the study, certain data were missing; moreover, we could not clarify the causal relationship between correlated factors. Second, there could have been patient selection bias; moreover, this was a single-centre study, which limits the generalizability of our findings. Further large-scale, multi-centre, longitudinal studies are warranted to confirm our findings.

5. Conclusion

Antipsychotic use may decrease death risks for patients with NPSLE. We recommend psychiatric consultation for each patient to establish a proper psychiatric diagnosis and comprehensive intervention plan.

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 Ethical Committee of Peking Union Medical College Hospital (I-23YJ349). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

WG, SZ, JC, BZ, YD, XH, and JW had access to the data and played a role in writing the manuscript. WG, JC, XH, and JW conceived and designed the study. Data were collected by WG, SZ, and YD. Statistical analyzes were performed by WG and BZ. WG, SZ, and JC wrote the first draft of the manuscript. All authors contributed to the article and approved the submitted version.

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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.

Publisher's note

Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2023.1189940/full#supplementary-material

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Depression, antidepressant use, and the risk of type 2 diabetes: a nationally representative cohort study

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Background: Previous studies have reported that depression can increase the risk of type 2 diabetes. However, they did not sufficiently consider antidepressants or comorbidity.

Methods: The National Health Insurance Sharing Service database was used. Among the sample population, 276,048 subjects who had been diagnosed with depression and prescribed antidepressants (DEP with antidepressants group) and 79,119 subjects who had been diagnosed with depression but not prescribed antidepressants (DEP without antidepressants group) were found to be eligible for this study. Healthy controls (HCs) were 1:1 matched with the DEP with antidepressants group for age and sex. We followed up with them for the occurrence of type 2 diabetes.

Results: In the group of DEP with antidepressants, although the risk of type 2 diabetes increased compared to HCs in a crude analysis, it decreased when comorbidity was adjusted for. In the group of DEP without antidepressants, the risk of type 2 diabetes decreased both in the crude model and the adjusted models. The risk varied by age group and classes or ingredients of antidepressants, with young adult patients showing an increased risk even in the fully adjusted model.

Conclusion: Overall, those with depression had a reduced risk of type 2 diabetes. However, the risk varied according to the age at onset, comorbidity, and type of antidepressants.

KEYWORDS

depression, antidepressants, type 2 diabetes, diabetes mellitus, risk factors

Introduction

Depression is a common mental disease with a lifetime prevalence of 7.7% in South Korea (1) and a global lifetime risk of ~1 in 6 individuals (2). It is associated with a significant morbidity (3). When a patient is diagnosed with depression, he or she is recommended to

undergo pharmacotherapy (mostly, antidepressants), psychotherapy, or combined treatment (4). Even after a depressive episode is remitted through a successful treatment, many patients relapse or go through a chronic course. Type 2 diabetes is also a prevalent disease. Globally, 537 million people were estimated to have diabetes in 2021, with type 2 diabetes accounting for more than 90% of diabetes (5). High morbidity and mortality associated with microvascular and macrovascular complications in type 2 diabetes can cause great distress to patients and caregivers with a large economic burden (6, 7).

Previous studies have suggested that depression might be a risk factor for type 2 diabetes. The pooled relative risk of incident type 2 diabetes in people with depression ranges from 1.18 to 1.60 (8–12). However, since antidepressant medications are commonly prescribed in patients with depression, they could mediate the relationship between depression and the subsequent occurrence of type 2 diabetes. A recent meta-analysis has reported that the use of antidepressants is generally associated with an increased risk of type 2 diabetes with a pooled hazard ratio of 1.24 (13). However, previous studies have limitations such as not limiting study participants to patients with depression (14–16), enrolling only a specific age group (17–20), relying on self-report for diagnosis of diabetes (19), not considering comorbid physical diseases (21–23), or not considering the type of antidepressants (18, 20–22, 24).

Considering the high prevalence and morbidity of depression and type 2 diabetes in addition to their high correlation, identifying risk factors for type 2 diabetes in patients with depression can be an important strategy for screening and early detection of type 2 diabetes. However, since psychiatric medications (particularly, antidepressants) and several physical conditions could affect the relationship between depression and type 2 diabetes, an analysis considering these factors is crucial.

Thus, the objective of this study was to examine the association between depression, antidepressant use, and the occurrence of type 2 diabetes considering its potential risk factors using a nationally representative population.

Methods

Study design and data source

This was a retrospective cohort study using data from the National Health Insurance Sharing Service (NHISS) database of the National Health Insurance Service (NHIS) of South Korea (25, 26). NHIS is a public organization responsible for operating a mandatory universal health insurance program. It covers nearly 97% of the total South Korean population. The remaining 3% is covered by the Medical Aid Program. The NHISS database includes data of medical services and claims such as inpatient, outpatient, emergency room visits, pharmacy data, and health screening programs.

NHISS data are anonymized. The Institutional Review Board of Samsung Medical Center exempted this study from review as it involved retrospective analyses of de-identified data (no. SMC 2019-09-030).

Case identification

Data of a sampling population of major psychiatric disorders extracted from the NHIS database were used. The sample population included those initially diagnosed with psychotic disorders, bipolar disorders, or depressive disorders between 2003 and 2017 who had no diagnostic codes for these diseases, hypertension, diabetes, or dyslipidemia in 2002. The sample population comprised 712,950 subjects with major psychiatric disorders after random sampling 20% of the total, stratified by sex, age, region, and income classes.

From this sample population, people with depression were extracted as the target population for this study. A total of 569,321 subjects were diagnosed with depression and prescribed antidepressants, and 136,384 subjects were diagnosed with depression but not prescribed antidepressants between 1 January 2003, and 31 December 2017. The diagnosis of depression (F32 and F33) was defined according to the International Statistical Classification of Disease and Related Health Problems 10th revision (ICD-10). Diagnostic codes were entered by physicians when they saw patients. The use of antidepressants was defined as having a history of prescribing oral antidepressants from the initial diagnosis of depression to the follow-up period. We excluded those with incomplete baseline information, those who were diagnosed with hypertension, any diabetes, or dyslipidemia within 1 year before the diagnosis of depression, those under the age of 18, and those who were diagnosed with bipolar disorder with a primary diagnostic code. Finally, 276,048 subjects who were diagnosed with depression (DEP) and prescribed antidepressants ("DEP with antidepressants" group) and 79,119 subjects who were diagnosed with depression but not prescribed antidepressants ("DEP without antidepressants" group) were eligible to be included in the analyses. Their medical records until 31 December 2018 were reviewed.

We also set a healthy control (HC) group. A total of 405,111 subjects not diagnosed with any major psychiatric disorder during the study period and who were not diagnosed with hypertension, diabetes, or dyslipidemia in 2002 were included in the HC group. Among them, 276,048 subjects who met the eligibility criteria were matched with subjects in the group of DEP and antidepressants by exact age and sex (Supplementary Figure S1).

Outcomes

The primary endpoint was newly diagnosed type 2 diabetes (ICD-10 codes of E11–E14 and prescription history of diabetes medications).

Covariates

Income levels at baseline were divided into quartiles according to payment of health insurance. To consider the effect of individuals' comorbidity, the Charlson comorbidity index (CCI) (27) was calculated by weighting pre-established diagnosis (dementia, pulmonary disease, connective tissue disorder, peptic ulcer, liver disease, paraplegia, renal disease, cancer, metastatic cancer, severe liver disease, and human immunodeficiency virus infection), excluding the diagnosis of metabolic and cardiovascular diseases

corresponding to exclusion criteria of subject identification. Disabilities included mental disability, intellectual disability, and physical disability that were caused by a brain lesion, visual disability, and hearing impairment, and speech impairment. As psychiatric factors comorbid personality disorders, psychiatric medication use (antipsychotics, benzodiazepines, stimulants, mood stabilizers, and zolpidem), psychotic symptoms (F32.3 and F33.3), recurrent depression (F33), symptoms severity (mild: F32.0 and F33.0; moderate: F32.1 and F33.1; severe: F32.2, F32.3, F33.2, and F33.3), and history of admission to psychiatry (claim for at least one hospitalization) were identified. CCI, disability, and psychiatric factors were identified based on all claims during the observation period.

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD), and categorical variables are presented as numbers and percentages. Analysis of variance (ANOVA) and chi-square tests were used to compare differences in factors between the groups. Cox proportional hazards regression analyses were conducted to identify the risk of type 2 diabetes by groups and censored by the occurrence of type 2 diabetes or death. The index date in depression patients with or without antidepressants was the date of the first occurrence of the diagnostic code for depressive disorder. In HCs, it was defined as the date of the first claim through a visit to a medical institution under any diagnostic code during the observation period. The proportional assumption was assessed using log–log survival plots. Hazard ratios (HRs) and corresponding 95% confidence intervals (CIs) are presented to show the magnitude of the risk of type 2 diabetes according to groups or variables. Analysis models were classified according to adjustment of variables, including crude (non-adjusted), Model 1 (adjusted for age and sex), Model 2 (adjusted for age, sex, and CCI), and Model 3 (adjusted for age, sex, CCI, income, disability, personality disorders, antipsychotic use, benzodiazepine use, stimulant use, mood stabilizer use, and zolpidem use). Sensitivity analyses including analyses within various groups, which were divided according to classes of antidepressants or detailed antidepressant ingredients, were performed. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, United States).

Results

Characteristics of study subjects

Table 1 shows the characteristics of the study subjects. The proportion of women in each group was distributed between 65% and 67%. The mean age at initial diagnosis of depression was 39.1 years (SD, 14.6 years) for the group of DEP without antidepressants, which was younger than that (39.9 years, SD, 13.9 years) of the group of DEP with antidepressants group and HCs ($p < 0.001$). Compared to HCs, the group of DEP with antidepressants and the group of DEP without antidepressants showed higher scores of CCI ($p < 0.001$). Compared to the group of DEPs without antidepressants, the group of DEP with antidepressants showed a higher proportion of all kinds of psychiatric medication use, psychotic symptoms, and admission to psychiatry. Regarding the symptom severity, the proportion of those with moderate or severe symptoms was higher in the group of DEP with antidepressants, while the proportion of those with mild symptoms was higher in the group of DEP without antidepressants.

Incidence of type 2 diabetes

In the group of DEP with antidepressants, during an average follow-up period of 8.5 years (SD, 4.7 years), 14,860 subjects were newly diagnosed with type 2 diabetes with an incidence rate of 6.5 per 1,000 person-years. Among those in the group of DEP without antidepressants, during an average follow-up period of 7.8 years (SD, 4.8 years), 2,898 subjects were newly diagnosed with type 2 diabetes with an incidence rate of 4.8 per 1,000 person-years. Among HCs, during an average follow-up period of 14.9 years (SD, 3.2 years), 24,577 subjects were newly diagnosed with type 2 diabetes with an incidence rate was 6.2 per 1,000 person-years. The incidence rate tended to increase with age (Supplementary Figure S2).

Risk of type 2 diabetes by groups

Table 2 presents HRs and 95% CIs for type 2 diabetes according to groups. In the crude model, compared to HCs, the group of DEP with antidepressants showed an increased risk of type 2 diabetes (HR, 1.16; 95% CI, 1.14–1.19), and the group of DEP without antidepressants showed a decreased risk (HR, 0.86; 95% CI, 0.83–0.90). However, in the fully adjusted model, compared to HCs, both the group of DEP with antidepressants (adjusted hazard ratio [aHR], 0.86; 95% CI, 0.83–0.88) and the group of DEP without antidepressants (aHR 0.78; 95% 0.74–0.81) showed a decreased risk of type 2 diabetes.

Table 3 presents HRs and 95% CIs according to age groups categorized as 18–39 years, 40–64 years, and ≥ 65 years. Among those aged 18–39 years, compared to HCs, the group of DEP with antidepressants (aHR, 1.24; 95% CI, 1.16–1.32) and the group of DEP without antidepressants (aHR, 1.17; 95% CI 1.08–1.27) showed increased risks for type 2 diabetes after full adjustment. Among those aged 40–64 years, compared to HCs, both the group of DEP with antidepressants (aHR, 0.81; 95% CI, 0.78–0.84) and the group of DEP without antidepressants (aHR, 0.74; 95% CI, 0.70–0.78) showed decreased risks of type 2 diabetes after full adjustment. Among those aged ≥65 years, compared to HCs, both the group of DEP with antidepressants (aHR, 0.69; 95% CI, 0.63–0.75) and the group of DEP without antidepressants (aHR, 0.70; 95% CI, 0.62–0.78) showed decreased risks of type 2 diabetes after full adjustment.

Risk of type 2 diabetes by antidepressant use

Table 4 shows HRs and 95% CIs according to combinations of antidepressant use and DEP without antidepressants on type 2 diabetes compared to HCs. In the fully adjusted model, compared to HCs, those who had used tricyclic antidepressants (TCAs) only (aHR, 1.25; 95% CI, 1.20–1.30) showed increased risks of type 2 diabetes. The remaining groups showed decreased risks of type 2 diabetes.

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TABLE 1 Baseline characteristics of the study subjects.

	DEP with antidepressants (*N*=276,048)	DEP without antidepressants (*N*=79,119)	Healthy controls (*N*=276,048)	Bonferroni corrected P		
				DEP with antidepressants vs. DEP without antidepressants	DEP with antidepressants vs. Healthy controls	DEP without antidepressants vs. Healthy controls
Sex				<0.001	1	<0.001
Male	91,997 (33.3)	27,735 (35.1)	91,997 (33.3)			
Female	184,051 (66.7)	51,384 (65.0)	184,051 (66.7)			
Age (years)	39.9 ± 13.9	39.1 ± 14.6	39.9 ± 13.9	<0.001	1	<0.001
Age group				<0.001	1	<0.001
18–39 years	144,487 (52.3)	44,279 (56.0)	144,487 (52.3)			
40–64 years	115,835 (42.0)	30,078 (38.0)	115,835 (42.0)			
≥65 years	15,726 (5.7)	4,762 (6.0)	15,726 (5.7)			
Income				0.007	<0.001	<0.001
Q1 (lowest)	70,480 (25.5)	19,828 (25.1)	68,050 (24.7)			
Q2	57,521 (20.8)	16,380 (20.7)	62,388 (22.6)			
Q3	66,842 (24.2)	19,208 (24.3)	72,144 (26.1)			
Q4 (highest)	81,205 (29.4)	23,703 (30.0)	73,466 (26.6)			
Charlson comorbidity index				<0.001	<0.001	<0.001
0	181,856 (65.9)	58,466 (73.9)	268,639 (97.3)			
1	57,281 (20.8)	14,936 (18.9)	6,379 (2.3)			
2	21,789 (7.9)	4,103 (5.2)	772 (0.3)			
≥3	15,122 (5.5)	1,614 (2.0)	258 (0.1)			
Disability	13,555 (4.9)	3,929 (5.0)	6,268 (2.3)	0.526	<0.001	<0.001
Personality disorders	9,229 (3.3)	1,447 (1.8)	342 (0.1)	<0.001	<0.001	<0.001
Antipsychotic use	27,154 (9.8)	6,356 (8.0)	63 (0.0)	<0.001	<0.001	<0.001
Benzodiazepine use	186,978 (67.7)	41,427 (52.4)	12,602 (4.6)	<0.001	<0.001	<0.001
Stimulant use	4,718 (1.7)	1,123 (1.4)	701 (0.3)	<0.001	<0.001	<0.001
Mood stabilizer use	12,011 (4.4)	2,340 (3.0)	321 (0.1)	<0.001	<0.001	<0.001
Zolpidem use	42,768 (15.5)	6,515 (8.2)	98 (0.0)	<0.001	<0.001	<0.001
Psychotic symptoms	3,448 (1.3)	947 (1.2)	0 (0.00)	0.251	<0.001	<0.001
Recurrent depression	18,324 (6.6)	5,131 (6.5)	0 (0.00)	0.129	<0.001	<0.001
Symptom severity				<0.001	<0.001	<0.001
Mild	64,648 (23.4)	21,445 (27.1)	0 (0.0)			
Moderate	59,984 (21.7)	12,941 (16.4)	0 (0.0)			
Severe	19,906 (7.2)	4,391 (5.6)	0 (0.0)			
Other	131,510 (47.6)	40,342 (51.0)	0 (0.0)			
Admission to psychiatry	57,94 (2.1)	1,165 (1.5)	110 (0.0)	<0.001	<0.001	<0.001

DEP, depression. Data are expressed as the mean ± standard deviation, or *n* (%).

Supplementary Tables S1–S6 show results of sensitivity analyses including analyses within various groups divided according to classes of antidepressants or detailed antidepressant components. Compared to HCs, the risk of type 2 diabetes was generally reduced in patients with depression regardless of the use of antidepressants or the type of drugs. However, the use of TCAs was associated with an increased risk of type 2 diabetes compared to the DEP without antidepressants group.

Subgroup analysis

We performed a subgroup analysis for depression patients with diagnostic codes having symptom severity information. A total of 144,538 (52.4%) participants in the group of DEP with antidepressants and 38,608 (49.0%) participants in the group of DEP without antidepressants had diagnostic codes with symptom severity information. In the regression model additionally adjusted

TABLE 2 Hazard ratios and 95% confidence interval on type 2 diabetes according to groups.

	Subjects (*N*)	Events (*N*)	Follow-up duration (person-year)	Incidence rate (per 1000 person-years)	Hazard ratio (95% Confidence interval)			
					Crude	Model 1[a]	Model 2[b]	Model 3[c]
Healthy controls	276,048	24,577	3,954,318	6.2	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
DEP with antidepressants	276,048	14,860	2,283,663	6.5	1.16 (1.14–1.19)***	1.06 (1.04–1.08)***	0.95 (0.93–0.98)***	0.86 (0.83–0.88)***
DEP without antidepressants	79,119	2,898	603,168	4.8	0.86 (0.83–0.90)***	0.88 (0.85–0.92)***	0.85 (0.82–0.88)***	0.78 (0.74–0.81)***

DEP, depression. *p <0.05, **p <0.01, ***p <0.001.
[a]Adjusted for age (years) and sex.
[b]Adjusted for age (years), sex, and Charlson comorbidity index.
[c]Adjusted for age (years), sex, Charlson comorbidity index, income, disability, personality disorders, antipsychotic use, benzodiazepine use, stimulant use, mood stabilizer use, and zolpidem use.

TABLE 3 Hazard ratios and 95% confidence interval on type 2 diabetes according to the age group.

Age group	Group	Subjects (*N*)	Events (*N*)	Follow-up duration (person-year)	Incidence rate (per 1000 person-years)	Hazard ratio (95% Confidence interval)			
						Crude	Model 1[a]	Model 2[b]	Model 3[c]
18–39 years	Healthy controls	144,487	5,302	2,170,803	2.4	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	DEP with antidepressants	144,487	3,197	1,135,441	2.8	1.59 (1.52–1.67)***	1.54 (1.47–1.61)***	1.40 (1.34–1.48)***	1.24 (1.16–1.32)***
	DEP without antidepressants	44,279	837	349,550	2.4	1.34 (1.24–1.44)***	1.33 (1.23–1.43)***	1.28 (1.19–1.38)***	1.17 (1.08–1.27)***
40–64 years	Healthy controls	115,835	16,286	1,622,580	10.0	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	DEP with antidepressants	115,835	9,587	1,012,624	9.5	1.02 (1.00–1.05)	1.02 (0.99–1.04)	0.89 (0.86–0.92)***	0.81 (0.78–0.84)***
	DEP without antidepressants	30,078	1,674	227,041	7.4	0.80 (0.77–0.85)***	0.83 (0.79–0.88)***	0.80 (0.76–0.84)***	0.74 (0.70–0.78)***
≥65 years	Healthy controls	15,726	2,989	160,935	18.6	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
	DEP with antidepressants	15,726	2,076	135,598	15.3	0.80 (0.76–0.85)***	0.80 (0.76–0.85)***	0.71 (0.67–0.77)***	0.69 (0.63–0.75)***
	DEP without antidepressants	4,762	387	26,577	14.6	0.75 (0.67–0.83)***	0.75 (0.67–0.84)***	0.73 (0.65–0.81)***	0.70 (0.62–0.78)***

DEP, depression. *p <0.05, **p <0.01, ***p <0.001.
[a]Adjusted for age (years) and sex.
[b]Adjusted for age (years), sex, and Charlson comorbidity index.
[c]Adjusted for age (years), sex, Charlson comorbidity index, income, disability, personality disorders, antipsychotic use, benzodiazepine use, stimulant use, mood stabilizer use, and zolpidem use.

TABLE 4 Hazard ratios and 95% confidence intervals of antidepressant combinations and DEP without antidepressants group on type 2 diabetes compared to healthy controls.

	Subjects (*n*)	Events (*n*)	Follow-up duration (person-year)	Incidence rate (per 1000 person-years)	Hazard ratio (95% confidence interval)			
					Crude	Model 1[a]	Model 2[b]	Model 3[c]
Healthy controls	276,048	24,577	3,954,318	6.2	1 (Ref.)	1 (Ref.)	1 (Ref.)	1 (Ref.)
DEP without antidepressants	79,119	2,898	603,168	4.8	0.86 (0.83–0.90)***	0.88 (0.85–0.92)***	0.85 (0.82–0.88)***	0.78 (0.74–0.81)***
SSRI only	70,108	2,117	455,491	4.6	0.85 (0.81–0.89)***	1.07 (1.02–1.12)**	1.02 (0.97–1.07)	0.86 (0.81–0.90)***
TCA only	48,754	5,098	439,207	11.6	2.04 (1.98–2.11)***	1.61 (1.56–1.66)***	1.41 (1.37–1.46)***	1.25 (1.20–1.30)***
SSRI+TCA	41,358	2,275	413,002	5.5	0.97 (0.93–1.01)	0.89 (0.85–0.93)***	0.77 (0.74–0.81)***	0.66 (0.63–0.70)***
Other combinations	115,828	5,370	975,963	5.5	0.97 (0.95–1.00)	0.85 (0.82–0.87)***	0.73 (0.71–0.75)***	0.60 (0.58–0.63)***

DEP, depression; SSRI, selective serotonin reuptake inhibitors; TCA, tricyclic antidepressant. *p <0.05, **p <0.01, ***p <0.001.
[a]Adjusted for age (years) and sex.
[b]Adjusted for age (years), sex, and Charlson comorbidity index.
[c]Adjusted for age (years), sex, Charlson comorbidity index, income, disability, personality disorders, antipsychotic use, benzodiazepine use, stimulant use, mood stabilizer use, and zolpidem use.

for symptom severity, risks of type 2 diabetes for the group of DEP with antidepressants (aHR, 0.81; 95% CI: 0.77–0.85) and the group of DEP without antidepressants (aHR, 0.74; 95% CI: 0.69–0.79) compared to HCs were similar to the main outcomes (Supplementary Table S7).

Discussion

In this study, we examined associations of depression and antidepressant use with the occurrence of newly diagnosed type 2 diabetes. As a result, after adjustments, the overall risk of type 2

diabetes was lowered in patients with depression compared to that in HCs regardless of the use of antidepressants. However, the risk considerably varied according to the age of patients, comorbid physical diseases, and type of antidepressants used.

This study found that the risk of type 2 diabetes was lower in patients with depression than in HCs, which is inconsistent with previous studies. The difference seemed to be largely attributable to comorbid metabolic disorders. In this study, people with a previous history of hypertension or dyslipidemia besides diabetes were excluded from subject identification. Hypertension and dyslipidemia together with abdominal obesity are components that constitute the metabolic syndrome, sharing underlying mechanisms such as insulin resistance and genetic predisposition. It is widely accepted that they can increase the risk of diabetes (28, 29). Considering their high prevalence and the fact that depression often accompanies people with these diseases (30), hypertension and dyslipidemia can act as strong confounders in the relationship between depression and type 2 diabetes. Therefore, we tried to identify the association between depression and type 2 diabetes in relatively metabolically healthy subjects by excluding those who had a diagnostic history of these diseases before the index date. This methodology seemed to have caused different results compared to previous studies.

Moreover, among depression patients with antidepressants, Cox regression analyses showed increased risks of type 2 diabetes in the crude model and the model adjusted for age and sex. However, the risk was decreased when physical comorbidity was additionally adjusted. This suggests that comorbid illness can increase the risk of type 2 diabetes, rather than antidepressants themselves being a direct risk factor for type 2 diabetes in patients with depression taking antidepressants. Although depression and antidepressants do not substantially increase the risk of type 2 diabetes, the high comorbidity of depression in other physical illnesses (which are risk factors for type 2 diabetes) might have made it appear as if depression and antidepressants were risk factors. Moreover, in the fully adjusted model, when other factors such as psychiatric comorbidity (i.e., personality disorder) and other psychiatric medication use were additionally included, the risk of type 2 diabetes was further decreased both in the group of DEP with antidepressants and the group of DEP without antidepressants. This suggests that other psychiatric conditions and medications could also affect the risk of type 2 diabetes.

As an explanation for the decreased risk of type 2 diabetes among depression patients, changes in appetite or weight, which are symptoms of depression, could affect the results of this study. While the manifestation of symptom clusters is heterogeneous among patients with depression, they often experience decreased appetite and weight loss, which could be protective against type 2 diabetes. However, the risk of type 2 diabetes varies depending on the age at the onset of depression. In young adults, the risk increased even after adjusting for CCI and other potential risk factors for type 2 diabetes, which was contrary to the result for those aged ≥40 years. To explain this, two aspects can be considered. First, young adults with depression correspond to having early-onset depression. Earlier onset age is known to be associated with a higher genetic burden (31). A previous study has reported that young people at increased familial risk of depression are likely to have diminished insulin sensitivity even without depressive symptoms, suggesting vulnerability to diabetes (32). In addition, young adults are more likely to have depression with atypical features, which shows the reverse of neurovegetative symptoms such as increased appetite and weight gain while those with other types commonly have a poor appetite and weight loss as their depressive symptoms (33). These metabolically opposite manifestations of depressive symptoms between young adult patients and older patients might have led to opposite outcomes.

In all age groups, the increased risk due to taking antidepressants was not significantly different from the risk in the group not taking antidepressants. In fully adjusted models, the difference ranged only 1%–8%. However, among those with depression, compared to those without antidepressants, the risk varied depending on the class of antidepressants. In particular, the risk of type 2 diabetes was reduced in those who had used only SSRIs, but the risk was increased in those who had used only TCAs. The weight gain liability of each antidepressant or clinical aspects considered when they were prescribed might have affected these results. However, since this study did not include the dose or duration of the drug used, further research is needed to examine the causal inference.

Caution is needed when interpreting the results of the present study showing that depression is a preventive factor for type 2 diabetes, especially in those after middle age. Although a decreased risk was observed when potential confounders that could affect the relationship between depression and type 2 diabetes were corrected, in the crude model, especially in people who had used antidepressants, an increased risk was observed compared to that for HCs. Moreover, the subsequent risk for type 2 diabetes could be higher if we also considered those who previously had metabolic diseases such as hypertension or dyslipidemia. Therefore, while we found that having depression itself does not lead to a high risk for type 2 diabetes, it should be noted that the occurrence of subsequent diabetes can often be observed in clinical settings considering the high comorbidity of depression in other physical illnesses which are associated with type 2 diabetes. Rather, if a patient with depression has many metabolic risk factors such as obesity, hypertension, and hyperlipidemia, more clinical attention should be paid to the detection of diabetes since depressive symptoms such as decreased motivation or energy level can prevent them from participating in health-promoting behaviors such as health checkups or seeking adequate physical care even if they have symptoms or signs of diabetes.

This study provides novel findings that depression and antidepressants are generally associated with a decreased risk of type 2 diabetes after adjusting for other physical comorbidities rather than being a risk factor as described in the results of previous studies. On the other hand, the increase in risk was noteworthy in young adult patients with depression. Compared to the group not taking antidepressants, there was a difference in the risk according to classes of antidepressants. These results suggest that an individualized approach that considers age at onset, physical comorbidity, and other metabolic risk factors is needed for screening and detecting type 2 diabetes rather than viewing those with depression as a population at high risk.

This study has some limitations. First, the diagnosis of depression was identified only through diagnostic codes without any structured evaluation because we used claims data. However, in South Korea, a patient can see a specialist without a referral from a primary care physician. Therefore, it is assumed that most of the initial diagnosis of depression was made by psychiatrists. Second, since the depression group included only cases diagnosed by visiting a medical institute, there might be people who met the criteria for the depressive disorder but did not visit a hospital who might have been included in HCs. Third, because the data source included claims data from 2002 with a clean period set as 1 year, those who had previously been diagnosed

with depression but did not visit a medical institution in 2002 (the clean period) and then visited again for depression that could be considered as new-onset depression were included in the analyses. Moreover, the possibility of such bias would increase as the age of subjects increased. This should be considered particularly when interpreting results according to age group. Fourth, we extracted and matched HCs based only on DEP with the antidepressant group. There was no separate matched control group based on the group of DEP without antidepressants. Due to the lack of matching in the DEP without antidepressants group, age and sex were included as adjusting variables in the analysis models. Moreover, matching was done based on data in 2002. Thus, time-related bias might have occurred due to differences in index year and follow-up period between patients with depression and HCs. Fifth, while we tried to include factors that could affect the relationship between depression, antidepressants, and type 2 diabetes in our analyses, some factors such as family history, lifestyle factors, overweight/obesity, and polycystic ovarian syndrome were not included in the analyses. Moreover, regarding the use of antidepressants, we focused on whether antidepressants were used and the classes or ingredients of antidepressants. However, other clinical factors related to antidepressant use (e.g., the timing of the antidepressant exposure, the use of multiple antidepressants, changes in dose, or drug discontinuation) could also affect the relationship between depression and the occurrence of type 2 diabetes. They should be the focus of future research. In addition, while the severity of depressive symptoms could affect the use of antidepressants, it was included only in the subgroup analyses, but not in the main analyses since only about half of the subjects in depression groups had severity information in their diagnostic codes. Finally, we excluded those who had hypertension or dyslipidemia at baseline and 1 year before the index date considering their potentially strong confounding effects because these diseases are strong risk factors for type 2 diabetes and the prevalence of depression is high in people with these diseases. Although excluding those with these conditions was to examine more direct effects of depression and antidepressants on type 2 diabetes in a relatively metabolically healthy population, caution is needed when interpreting our results and applying them to real-world clinical settings.

In conclusion, in this nationally representative cohort study, we found that depression and antidepressant medications *per se* were not contributory factors for type 2 diabetes. Clinical attention is needed for patients with depression for the detection of type 2 diabetes, especially in those with early age at onset, those with physical comorbidity, and those with metabolic risk factors.

Data availability statement

Publicly available datasets were analyzed in this study. This data can be found here: https://nhiss.nhis.or.kr/.

Ethics statement

The studies involving humans were approved by Institutional Review Board of Samsung Medical Center. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because As it involved retrospective analyses of de-identified data.

Author contributions

HK: Conceptualization, Methodology, Writing – original draft, Writing – review & editing. Y-BL: Methodology, Writing – review & editing. JL: Formal analysis, Methodology, Visualization, Writing – review & editing. DK: Writing – review & editing. GK: Writing – review & editing. S-MJ: Writing – review & editing. JK: Writing – review & editing. KH: Conceptualization, Methodology, Project administration, Writing – review & editing. HJ: Conceptualization, Methodology, Project administration, Writing – review & editing.

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Conflict of interest

JL and DK were employed by Hanmi Pharm. Co., Ltd.

The remaining 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 author(s) declared that they were an editorial board member of Frontiers, at the time of submission. This had no impact on the peer review process and the final decision.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2023.1275984/full#supplementary-material

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High psychological stress levels related to delivery can increase the occurrence of postpartum mental disorders

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Objective: The study sought to explore the relationship between high psychological stress levels related to delivery and postpartum mental disorders.

Methods: A total of 284 parturients were included in the study from July 2021 to January 2022. The stress level at 1 month postpartum was assessed by the Impact of Event Scale-Revised (IES-R). Parturients with an IES-R score ≤ 9 were included in the low psychological stress level group, and those with an IES-R score > 9 were included in the high psychological stress level group. The Edinburgh Postnatal Depression Scale (EPDS), Union Physio-Psycho-Social Assessment Questionnaire (UPPSAQ-70), Symptom Checklist-90 (SCL-90) and Mini-International Neuropsychiatric Interview (M.I.N.I.) were conducted at 42 ± 7 days postpartum to assess the mental health of parturients. The parturients' mental health after birth was assessed by the EPDS, UPPSAQ-70, and SCL-90. Semi-structured diagnostic interviews were conducted at 42 ± 7 days postpartum by using the M.I.N.I.

Results: The incidence rate of postpartum mental disorders was 20.42% (58/284), the incidence rates of postpartum depression, anxiety disorders, obsessive-compulsive disorder and posttraumatic stress disorder were 17.96% (51/284), 11.97% (34/284), 4.58% (13/284) and 1.41% (4/284), respectively, and the comorbidity rate was 58.62% (34/58). A history of mental disorders and pregnancy complications were risk factors for postpartum depression ($p = 0.028$, $p = 0.040$, respectively); a history of mental disorders, a lack of physical exercise, partner violence and pregnancy complications were risk factors for postpartum anxiety disorders ($p = 0.003$, $p = 0.007$, $p = 0.031$, $p = 0.048$, respectively); and the delivery of female infants was a risk factor for postpartum obsessive-compulsive disorder ($p = 0.022$). The risk of postpartum depression, anxiety disorders and obsessive-compulsive disorder was 9.125 times (95% CI = 3.900 ~ 21.349, $p < 0.01$), 7.310 times (95% CI = 2.588 ~ 20.649, $p < 0.01$) and 6.259 times (95% CI = 1.347 ~ 29.093, $p < 0.01$) higher in postpartum women with high psychological stress levels related to delivery than in those with low psychological stress levels, respectively.

Conclusion: The incidence of postpartum mental disorders is high and has a positive correlation with the level of psychological stress. This may lead to a new perspective of the effect of psychological stress on postpartum mental

disorders and attract more attention to other mental disorders in addition to postpartum depression.

KEYWORDS

postpartum, psychological stress, mental disorders, pregnancy, parturient

1 Introduction

Childbirth is one of the most influential factors inducing mental illness. All types of mental disorders may occur after childbirth (1). In addition to depression and anxiety disorders, postpartum mental disorders (PMD) also include acute stress disorder and posttraumatic stress disorder (PTSD), eating disorders, obsessive-compulsive disorder (OCD) and psychotic disorders. PMD will harm the physical and mental health of mothers and can even lead to suicide. For the offspring of mothers with these disorders, the risk of developmental delays, emotional regulation difficulties, poor cognitive development and social behavior problems in infancy (2, 3) and mental disorders in adolescence is increased (4). In addition, depression and anxiety symptoms are increased in fathers when mothers suffer from mental disorders (5), which has a devastating impact on family relations. Therefore, the ability to predict a person's risk for developing PMD has clinically actionable implications. We can intervene early to reduce risk factors or conduct close psychological follow-up assessments on high-risk parturients.

A recent report from Simone explored a clinical risk index for common PMD. The independently associated variables include several sociodemographic and obstetric characteristics, such as mental health diagnosis history and medications during pregnancy, conception type and complications, lactation intention and so on (6). Ayer's research suggests that childbirth can lead to PTSD, and the psychological stress reaction related to childbirth overlaps with various PMD, which lays the foundation for paying attention to maternal mental health from the perspective of stress reactions (7). Based on these thoughts, we try to explore the risk for PMD from the perspective of stress.

In this way, we explored the level of parturition-related physiological-psychosocial stress and its correlation with postpartum mental disorders through a diagnostic interview tool. We hope our study can provide a reference for the early detection and prevention of postpartum mental disorders.

2 Materials and methods

2.1 Research subject

The subjects of the study were pregnant women who filing and prenatal examination in obstetrics department of Peking Union Medical College Hospital from July 2021 to January 2022. The inclusion criteria were as follows: (1) 18–45-year-old females; (2) women who could read and write; and (3) women who signed the informed consent form. The exclusion criteria were as follows: (1) language, writing or reading disabilities; (2) abortion or stillbirth; and (3) questionnaires in which the number of completed items was less than 2/3 of the total items or the content was illogical.

2.2 Outcome measures

2.2.1 Impact of event scale-revised (IES-R)

The IES-R, which is divided into 3 factors and has 22 items, is a self-evaluation scale for evaluating subjective responses to trauma. According to the severity of symptoms, a score of 0 to 4 points is given: 0 points for no impact, 1 point for a mild impact, 2 points for a moderate impact, 3 points for a severe impact, and 4 points for an extremely severe impact. The total score ranges from 0 to 88 points. A higher score predicts more serious symptoms. The internal consistency of IES-R is 1 in foreign studies and 0.89–0.96 in domestic studies. The split half reliability is 0.93 and.

3-week retest reliability is 0.51–0.94 (8). The IES-R has no strict cutoff value; in the study of nonobstetric trauma, it is generally considered that a score less than or equal to 9 indicates a low stress level (9).

2.2.2 Edinburgh postnatal depression scale (EPDS)

The EPDS is a self-evaluation scale used for screening, auxiliary diagnosis and the evaluation of depression in perinatal women. There are 10 items in total. Each item is scored on a 4-point scale from 0 (never) to 3 (usually) according to the frequency of symptoms, and the total score ranges from 0 to 30 points. A higher score predicts a greater risk of depression. The internal consistency coefficient of the scale is 0.87, and the split half reliability is 0.88. Compared with the diagnostic criteria for depression used in the study, the sensitivity was 86% and the specificity was 78% (10). In China, a score of 9/10 points indicates the possibility of postpartum depression (the sensitivity is 0.82, and the specificity is 0.86) (10, 11); therefore, puerpera with an EPDS score $\geq$ 9 points were considered to have positive screening results in this study.

2.2.3 Symptom checklist 90 (SCL-90)

The SCL-90, also known as the Self-Reporting Inventory, has 90 items, including items for wide range of psychiatric content such as feelings, emotions, thinking, consciousness, interpersonal relationships, diet and sleep. The SCL-90 is widely used in symptom measurement. Each item adopts a 5-point scoring system from 1–5 according to the severity of symptoms (1 for no, 2 for very light, 3 for medium, 4 for heavy, and 5 for serious). A total of 9 factors are included: somatization (12 items), obsessive-compulsive symptoms (10 items), interpersonal sensitivity (9 items), depression (13 items), anxiety (10 items), hostility (6 items), phobia (7 items), paranoia (6 items), and psychosis (10 items). The total SCL-90 score reflects the severity of disease. A higher score indicates more serious disease; factor scores reflect the characteristics of symptom groups. If the total score exceeds 160 points, the number of positive items exceeds 43, or any factor score exceeds 2 points, the screening is considered positive.

According Derogatis's report, the validity coefficients of each symptom in SCL-90 are 0.77–0.99, $p < 0.01$. Domestic and foreign comprehensive hospitals often use this scale to understand the mental symptoms of patients with physical diseases and believe that the results are satisfactory (12).

2.2.4 Union physio-psycho-social assessment questionnaire (UPPSAQ-70)

The UPPSAQ-70 is a health screening self-assessment scale with three dimensions (physiological, psychological, social) that was independently developed and designed by the Department of Psychological Medicine of Beijing Union Medical College Hospital. The Chronbach's α coefficient of each factor in UPPSAQ-70 is between 0.823 and 0.904. The Chronbach's α coefficient of the full scale is 0.847, and there is a significant correlation between the two retests ($p < 0.05$) (13, 14). There are 70 items in the questionnaire, including 8 factors: emotions (9 items), sleep (8 items), anxiety and physical discomfort (18 items), pain (3 items), sexual function (5 items), happiness and satisfaction (9 items), hypochondriasis (12 items), and social interactions (6 items). Each item is scored according to the frequency or severity of symptoms on a 4-point scale from 0 to 3, with a total score ranging from 0 to 210 points. The higher the score is, the higher the symptom severity. If the total score of the equivalent table is ≥65 points or the average score of a single factor is ≥1 point, the screening result is considered positive.

2.2.5 Mini-international neuropsychiatric interview (M.I.N.I.)

The M.I.N.I. is a short structured diagnostic tool for mental disorders. All items in the questionnaire are answered with yes/no, starting with screening questions and ending with diagnostic blocks, to check whether a patient meets the diagnostic criteria. This study used the Chinese version of M.I.N.I. 5.0, and the selected modules were as follows: A: major depressive episode (MDE); B: dysthymic disorder; C: suicidal tendency; D: (hypo) manic episode; E: panic disorder (PD); F: agoraphobia; G: social anxiety disorder; H: OCD; I: PTSD; J: alcohol abuse and dependence; K: nonalcohol psychoactive substance use disorder; L: psychotic disorder; M: anorexia nervosa; N: bulimia nervosa; and O: generalized anxiety disorder (GAD) (15). Studies in the United States, France, and Japan have found that the reliability Kappa values of M.I.N.I. are all greater than 0.75, with 70% of modules above 0.90 (12).

2.3 Study process

This study adopted a cross-sectional study design and a convenience sampling method to collect general information on mothers after childbirth in Peking Union Medical College Hospital. The information included the following age, nationality, occupation, medical insurance status, marital status, residence, education level, life status, family *per capita* income, height, weight, whether the pregnancy was planned, whether partner violence occurs, physical exercise (cardiorespiratory and/or resistance training, >30 min/day), drinking history (a pattern of pathological alcohol use or impairment in social or occupational functioning due to alcohol, and either tolerance or withdrawal), history of psychosocial diseases, partner history of mental and psychological diseases, whether the child was the first-born, mode of delivery, whether full-term delivery occurred, whether pregnancy complications (gestational diabetes and pregnancy-induced hypertension syndrome, hyperemesis gravidarum and placental abnormalities) occurred, and whether diabetes was diagnosed during pregnancy. The IES-R, EPDS, UPPSAQ-70 and SCL-90 were used to comprehensively evaluate and screen the conditions of the puerpera 42 ± 7 days after delivery. The time range of IES-R is 1 month postpartum, and the other scales evaluate the status of the past 1 week.

Parturients with an IES-R score ≤ 9 were included in the low psychological stress level group, and those with an IES-R score > 9 were included in the high psychological stress level group. Puerpera considered to have positive screening results were assessed and diagnosed with mental disorders by the M.I.N.I. 5.0. On the other hand, 30 % of the women with negative screening results were randomly selected for assessment with the M.I.N.I. The evaluation of this study was jointly completed by psychiatrists and graduate students qualified by the standardized training certificate in the department of psychiatry and mental health.

The research protocol, research process and informed consent form of this study were reviewed by the Ethics Review Committee of Peking Union Medical College Hospital with approval number ZS-2865. All subjects signed informed consent forms.

2.4 Statistical methods

This study used EpiData 3.1 to enter data into the database and IBM SPSS 25.0 to analyze the data. A 95% confidence interval was used in the test, and a two-sided t test was conducted. Differences were statistically significant at $p < 0.05$.

Descriptive statistics: the mean and standard deviation ($\bar{X} \pm s$) were used to describe measurement data verified to conform to a normal distribution (comply with the principle of three standard deviations principles), and the frequency (n) and constituent ratio (%) were used to describe enumeration data.

Intergroup comparison: an independent sample t test was used for comparisons between measurement data groups that met the normal distribution, and the chi-square test or Fisher's exact test was used for comparisons between counting data groups.

Correlation analysis: pearson correlation analysis was used for intergroup comparisons of measurement data.

Regression analysis: first, single-factor analysis was performed; then, statistically significant variables were incorporated into the multivariate binary logistic regression model to analyze the influencing factors. The unconditional logistic regression model was selected to correct for confounding factors, and the odds ratio (OR) and 95% confidence interval were calculated.

3 Results

3.1 Sociodemographic characteristics and obstetric data

A total of 337 parturients signed the informed consent form, of which 22 were not included in the study because the number of items completed in the scale was less than 2/3 of the total number of items.

Eight parturients could not be contacted during the study, and 23 parturients refused to undergo the Concise International Neuropsychiatric Interview. Therefore, a total of 284 parturients were included in the study, and the response rate was 84.27%. The average age was 33.20 ± 3.62 years old, and most of the parturients were married (99.30%, 282/284), in-service (96.13%, 273/284), living with others (98.59%, 280/284), had a high education level (95.77%, 272/284) and had good economic status (85.56% had a family average monthly income of 8,000 yuan or above).

Combined with previous studies (12), the revised version of the impact scale with 284 maternal events used in this study was determined according to the distribution within the group. The median IES-R score was 9, which was defined as the cutoff value. Parturients with an IES-R score ≤ 9 were included in the low psychological stress level group, and those with an IES-R score > 9 were included in the high psychological stress level group. Comparing the sociodemographic characteristics of the high and low psychological stress level groups, there was no significant difference in age, nationality, occupation, marital status, living conditions, monthly income, drinking history, body mass index (BMI), or physical exercise level between the two groups ($p > 0.05$). The education level of the high psychological stress level group was higher than that of the low psychological stress level group. There was no significant difference in the composition between the two groups (Table 1).

Among the 284 parturients included in this study, most delivered their first-born child (77.46%, 220/284), had a planned pregnancy (86.97%, 247/284), had a full-term delivery (89.08%, 253/284), and had a vaginal delivery (61.62%, 175/284), and the male-to-female ratio of newborns was balanced. The obstetric characteristics of the high and low stress level groups were compared. There was no significant difference between the two groups in terms of the mode of conception, whether the child was the first-born, whether the pregnancy was planned, newborn sex, whether the delivery occurred full-term, whether pregnancy complications and maternal complications occurred, and whether gestational diabetes mellitus (GDM) was diagnosed during pregnancy ($p > 0.05$) (Table 2).

TABLE 1 Sociodemographic characteristics.

Variable	Population ($n = 284$)	Low stress level group ($n = 145$)	High stress level group ($n = 139$)	t/χ^2	P
Age (years)	33.20 ± 3.62	33.43 ± 3.81	32.96 ± 3.42	1.078	0.282
Nationality *n* (%)				1.271	0.260
Han	257 (90.49)	134 (92.41)	123 (88.49)		
Others	27 (9.51)	11 (7.59)	16 (11.51)		
Occupation *n* (%)				0.056	0.813
In service	273 (96.13)	139 (95.86)	134 (96.40)		
Unemployment	11 (3.87)	6 (4.14)	5 (3.60)		
Marital status *n* (%)				0.001	0.976
Married	282 (99.30)	144 (99.31)	138 (99.28)		
Other	2 (0.70)	1 (0.69)	1 (0.72)		
Education level *n* (%)				8.269	0.005
Above bachelor	272 (95.77)	134 (92.41)	138 (99.28)		
Under bachelor	12 (4.23)	11 (7.59)	1 (0.72)		
Living conditions *n* (%)				0.931	0.623
Not living alone	280 (98.59)	142 (97.93)	138 (99.28)		
Living alone	4 (1.41)	3 (2.07)	1 (0.72)		
Per monthly income *n* (%)				0.099	0.866
Above ¥8,000	243 (85.56)	125 (86.21)	118 (84.89)		
Under ¥8,000	41 (14.44)	20 (13.79)	21 (15.11)		
Drinking history				0.939	0.372
Yes	193 (67.9)	102 (70.34)	91 (65.47)		
No	91 (32.04)	43 (29.66)	48 (34.53)		
BMI (kg/m ^{2})	23.08 ± 2.77	23.21 ± 2.53	22.95 ± 3.01	0.494	0.622
Physical exercise *n* (%)				0.045	0.893
Yes	210 (73.94)	108 (74.48)	102 (73.38)		
No	74 (26.06)	37 (25.52)	37 (26.62)		

BMI, body mass index.

TABLE 2 Obstetric data.

Factor	Population (n = 284)	Low stress level group (n = 145)	High stress level group (n = 139)	χ^2	P
Mode of production n (%)				0.329	0.566
Delivery	175 (61.62)	87 (60.00)	88 (63.31)		
Cesarean section	109 (38.38)	58 (40.00)	51 (36.69)		
Primary n (%)				0.436	0.571
Yes	220 (77.46)	110 (75.86)	110 (79.14)		
No	64 (22.54)	35 (24.14)	29 (20.86)		
Planned pregnancy n (%)				0.001	1.000
Yes	247 (86.97)	126 (86.90)	121 (87.05)		
No	37 (13.03)	19 (13.10)	18 (12.95)		
Newborn sex n (%)				0.051	0.822
Male	147 (51.76)	76 (52.41)	71 (51.08)		
Female	137 (48.24)	69 (47.59)	68 (48.92)		
Term production n (%)				0.099	0.753
Yes	253 (89.08)	130 (89.66)	123 (88.49)		
No	31 (10.92)	15 (10.34)	16 (11.51)		
Pregnancy complications n (%)				0.101	0.753
Yes	48 (16.90)	21 (14.48)	27 (19.42)		
No	236 (83.10)	124 (85.52)	112 (80.58)		
Gestational diabetes mellitus n (%)				1.234	0.273
Yes	62 (21.83)	28 (19.31)	34 (24.46)		
No	222 (78.17)	117 (80.69)	105 (75.54)		

3.2 Prevalence and clinical characteristics of postpartum mental disorders

The incidence of postpartum mental disorders was 20.42% (58/284). Among the 284 parturients, 51 (17.96%) had a depressive episode, 2 of whom had suicidal tendencies, accounting for 3.92% of the sample. Five parturients had major depressive episodes with melancholic features, and 14 reported a history of depressive disorder before delivery; 4 (1.41%) were in a (mild) manic state; 3 had panic disorder (1.06%); 5 had phobias regarding places (1.76%); and 2 had social phobia (0.70%). There were 28 patients (9.86%) with generalized anxiety disorder (GAD). There are a total of 34 individuals diagnosed with anxiety disorders, with an incidence rate of 11.97%. Three patients reported a history of anxiety disorder before delivery, 13 reported OCD (4.58%), and 4 reported PTSD (1.41%). The comorbidity rate of mental disorders was 58.62% (34/58) (Table 3).

TABLE 3 Prevalence of postpartum mental disorders.

Mental disorders	Number of people (n)	Incidence (%)
Depressive episode	51	17.96
Suicidal tendencies	2	0.70
(mild) manic state	4	1.41
Anxiety disorder	34	11.97
Panic disorder	3	1.06
Place phobia	5	1.76
Social phobia	2	0.70
Generalized anxiety disorder	28	9.86
Obsessive compulsive disorder	13	4.58
Post-traumatic stress disorder	4	1.41
Mental disorders	58	20.42

3.3 Risk factors for postpartum mental disorders

The risk factors for postpartum mental disorders included age, nationality, occupation, medical insurance status, marital status, residence, education level, living condition, family *per capita* monthly income, BMI, whether the pregnancy was planned, whether partner violence occurred, physical exercise level, drinking history, history of mental illness, history of partner mental illness, whether the child was the first-born, mode of delivery, whether full-term delivery occurred, and whether pregnancy and maternal complications occurred. The univariate analysis of whether GDM diagnosed during pregnancy was a risk factor for postpartum mental disorders showed that compared with the healthy group, in the postpartum depression group, the

distribution of physical exercise levels, history of mental and psychological diseases, premature birth, pregnancy complications and maternal complications were significantly different. There were significant differences in the distribution of partner violence (including physical violence, psychological violence, and sexual violence), physical exercise levels, history of mental and psychological disease, premature birth, pregnancy complications and maternal complications between the puerpera with postpartum anxiety disorders and the healthy group. There were significant differences in neonatal sex and pregnancy and maternal complications between the puerpera with postpartum OCD and the healthy group (Table 4).

The factors with significant differences in univariate analysis were included in multivariate binary logistic regression analysis. A history of mental illness, pregnancy complications and maternal complications were risk factors for postpartum depression. A history of mental illness, partner violence, pregnancy complications and maternal complications were risk factors for postpartum anxiety disorders, and physical exercise was a protective factor against postpartum anxiety disorders. Neonatal sex was associated with postpartum OCD (the incidence of postpartum OCD was higher in women who delivered female neonates). The risk of postpartum depression and anxiety disorders in puerperal women with a history of mental and psychological disease was 3.542 times and 6.734 times than that in puerperal women without a history of mental and psychological disease, respectively (Table 5).

3.4 Relationship between high psychological stress levels related to childbirth and postpartum mental disorders

The incidence of postpartum mental disorders (including depression, generalized anxiety disorder, OCD, and PTSD) in the high psychological stress level group and the low psychological stress level group significantly differed ($p < 0.05$), and the incidence of mental disorders in the high psychological stress level group was higher (Table 6).

According to the results of the M.I.N.I., the psychological stress levels of postpartum women with mental disorders and healthy women were compared, and there were significant differences between the two groups. Postpartum women with depression, social phobia, OCD, PTSD and anxiety disorders had significantly higher levels of psychological stress related to childbirth than healthy women ($p < 0.05$) (Table 7).

The risk of depressive disorder, anxiety disorder and OCD were 9.125 times, 7.310 times and 6.259 times higher in the high psychological stress level group than in the low psychological stress level group, respectively ($p < 0.05$). A high psychological stress level related to childbirth had the greatest impact on the occurrence of postpartum depression, as shown in Table 8.

TABLE 4 Univariate analysis of risk factors for postpartum mental disorders.

Factor	Depression disorder Anxiety disorder Obsessive-compulsive disorder					
	χ^2/t	*P*	χ^2/t	*P*	χ^2/t	*P*
Age	0.607	0.545	1.050	0.294	1.224	0.222
Nation	0.949	0.247	0.021	0.591	0.052	0.644
Occupation	0.000	0.618	0.419	0.388	0.549	0.592
Medical insurance	0.066	0.633	0.036	0.595	0.344	0.718
Marital status	0.441	0.673	0.274	0.775	0.097	0.910
Residence	1.342	0.301	0.834	0.462	0.294	0.753
Educational level	2.742	0.088	1.704	0.210	0.601	0.563
Living conditions	0.888	0.451	0.552	0.599	0.195	0.828
Household *per capita* monthly income	0.359	0.549	0.233	0.798	0.502	0.700
BMI	1.263	0.209	0.804	0.423	0.496	0.621
Planned pregnancy	0.570	0.450	0.096	0.757	1.214	0.232
Partner violence	4.272	0.073	8.411	0.024	0.294	0.753
physical exercise	4.046	0.044	8.843	0.003	1.088	0.297
History of mental illness	4.780	0.045	10.484	0.008	0.405	0.437
History of partner mental illness	0.220	0.820	0.136	0.880	0.048	0.954
Primipara	0.851	0.356	2.567	0.129	1.719	0.310
Mode of production	0.595	0.441	0.538	0.463	0.334	0.772
Newborn sex	1.851	0.174	1.733	0.188	7.220	0.009
Term production	4.830	0.028	6.320	0.012	0.146	0.574
Pregnancy complications	5.536	0.019	7.879	0.005	3.888	0.049

BMI, body mass index.

TABLE 5 Multivariate binary logistic regression analysis of influencing factors of postpartum depression, anxiety disorder and OCD.

	Factor	β	Se	Wald χ^2 value	P	Or
Postpartum depression	History of mental illness	1.265	0.574	4.848	0.028	3.542
	Pregnancy complications	0.778	0.378	4.237	0.040	2.176
Postpartum anxiety	History of mental illness	1.907	0.636	9.002	0.003	6.734
	physical exercise	1.115	0.413	7.292	0.007	0.328
	Partner violence	2.058	0.956	4.637	0.031	7.831
	Pregnancy complications	0.893	0.452	3.905	0.048	2.442
Postpartum OCD	Fetal sex	1.786	0.781	5.223	0.022	0.168

OCD, obsessive-compulsive disorder.

TABLE 6 Comparison of the incidence of mental disorders between the high psychological stress level group and the low psychological stress level group.

Mental disorders	Low stress level group (n = 145)	High stress level group (n = 139)	χ^2	P
Depressive disorder n (%)	7 (4.83)	44 (31.65)	34.667	< 0.001
Anxiety disorder n (%)	5 (3.45)	29 (20.86)	20.424	< 0.001
Generalized anxiety disorder	4 (2.76)	24 (17.27)	*	< 0.001
Panic disorder	1 (0.69)	2 (1.44)	*	0.616
Place phobia	1 (0.69)	4 (2.88)	*	0.206
Social phobia	0	2 (1.44)	*	0.239
OCD n (%)	2 (1.38)	11 (7.91)	*	0.010
PTSD n (%)	0	4 (2.88)	*	0.040
Mental disorder n (%)	10 (6.90)	48 (34.53)	33.351	< 0.001

*Was using Fisher exact test.
OCD, obsessive-compulsive disorder.

TABLE 7 Comparison of psychological stress levels between postpartum mental disorder group and normal group.

Mental disorders	Psychological stress level ($\bar{x} \pm s$)		T	P
	Diseased group	Normal group		
Depressive disorder	25.02 ± 9.94	9.94 ± 9.47	9.800	< 0.001
(mild) mania	28.00 ± 4.24	12.54 ± 11.47	1.903	0.058
Panic disorder	14.67 ± 7.51	12.63 ± 11.55	0.305	0.761
Agoraphobia	15.60 ± 7.733	12.59 ± 11.56	0.578	0.564
Social phobia	33.00 ± 15.56	12.50 ± 11.38	2.535	0.012
OCD	24.15 ± 12.27	12.10 ± 11.20	3.777	< 0.001
Post-traumatic stress disorder	43.75 ± 0.50	12.20 ± 10.97	5.746	< 0.001
Generalized anxiety disorder	25.79 ± 12.87	11.21 ± 10.41	6.864	< 0.001
Mental disorders	24.02 ± 12.34	9.73 ± 9.27	9.736	0.003

OCD, obsessive-compulsive disorder.

4 Discussion

Under acute stress, the sympathetic adrenal medullary system (SAM) and hypothalamic–pituitary axis (HPA) are highly activated, releasing catecholamines (mainly epinephrine) and glucocorticoids to accelerate glucose oxidation and glycolysis, promoting protein and fat breakdown, and ensuring normal organ function (16). However, when the stress level is too high, the HPA is hyperexcitable, and cortisol levels increase significantly. Studies have found that an increase in cortisol levels is related to the development of depression (17). Pregnancy and childbirth are stressful life events for women of childbearing age. Mental disorders are prone to occur due to substantial changes in physiology and the continuous stimulation caused by mental stress (18). Our study found that a variety of mental disorders occurred in the postpartum period, and comorbidities were very common. There was a significant positive correlation between the level of psychological stress related to delivery and postpartum mental disorders. This result may lead to a new perspective of the effect of psychological stress on postpartum mental disorders and attract more attention to other mental disorders in addition to postpartum depression.

4.1 Incidence of postpartum mental disorders

Postpartum depression was the most common mental disorder in the perinatal period. The incidence of depressive episodes in this study was 17.96%, which was comparable to Hahn Holbrook's review of 291 studies worldwide (19). Maternal suicide is a serious adverse consequence of postpartum depression. In this study, 3.92% of postpartum women with depression had suicidal tendencies. Brockington et al. (20) found that 4.5% of 535 postpartum patients with depression were at risk of suicide. It is necessary to screen and evaluate the suicidal tendency of patients with postpartum depression. It is also important to note that 1.41% of postpartum women showed a (mild) manic state. Previous studies indicate that the first episode of postpartum depression may indicate potential bipolar disorder (21). At present, medical staff mostly focus on postpartum depression, and we should prevent missed diagnoses of bipolar disorder.

Postpartum anxiety is very common but is also misunderstood as a normal phenomenon for new mothers. In this study, the incidence of anxiety disorder in the postpartum period was 11.97%. A previous study of patients in nonpsychiatric outpatient departments of 9

TABLE 8 Correlation between high psychological stress level in childbirth and postpartum mental disorder.

Variable	Model 1			Model 2		
	OR	95%CI	*P*	OR	95%CI	*P*
Postpartum mental disorder						
Low stress level	1.000			1.000		
High stress level	7.121	3.427 ~ 14.796	< 0.001	7.108	3.337 ~ 15.138	< 0.001
Postpartum depression						
Low stress level	1.000					
High stress level	9.131	3.945 ~ 21.135	< 0.001	9.125	3.900 ~ 21.346	< 0.001
Postpartum anxiety disorder						
Low stress level	1.000			1.000		
High stress level	7.382	2.767 ~ 19.696	< 0.001	7.310	2.588 ~ 20.649	< 0.001
Postpartum obsessive-compulsive disorder						
Low stress level	1.000			1.000		
High stress level	6.145	1.337 ~ 28.246	0.020	6.259	1.347 ~ 29.093	0.019

Model 1, unadjusted confounders; Model 2, adjusted for risk factors.
CI, confidence interval.

general hospitals in three cities found that the detection rate of anxiety disorder was 7.6% (22), and the incidence of anxiety disorders in the postpartum period was relatively high. Panic disorder, place phobia, social phobia, and generalized anxiety disorder occur in the postpartum period and may coexist. It is very important to educate postpartum women and their families to understand anxiety disorders and seek help as soon as possible.

Similarly, compared with the general population, women are more likely to suffer from OCD after childbirth (23). In previous studies, the incidence of postpartum first-episode OCD was approximately 2.3–11% (24, 25). The incidence in this study was 4.58%. Both obsessive-compulsive thoughts and behaviors occurred and were related to newborns. In our interviews, some respondents had obsessive-compulsive symptoms, but the severity did not constitute OCD. This part of the population also deserves attention and early intervention to prevent the development of OCD.

Traumatic experiences during pregnancy and traumatic childbirth can cause PTSD. In this study, the incidence of postpartum PTSD was 1.41%. Foreign countries previously reported that the prevalence of postpartum PTSD in high-income countries was approximately 1–2%, while the prevalence in low-income countries was higher, at approximately 5–8% (26–28).

In this study, the incidence of mental disorders 42 ± 7 days after birth was 20.42%, and more than half of the patients had comorbidities. Previous studies have shown that postpartum depression is often comorbid with anxiety disorder (29), and PTSD is highly comorbid with depression (30). This study supports the above conclusions. The conditions of patients with comorbidities are complex and serious, which makes their diagnosis and treatment challenging, and these patients should be given more attention.

4.2 Influencing factors of postpartum mental disorders

In this study, there was a correlation between a history of previous mental illness and the occurrence of postpartum depression and anxiety disorders, which was consistent with the results of previous studies. A prospective study in Germany found that having a history of depression before pregnancy increases the risk of postpartum depressive symptoms (31). A literature review by Robertson suggested that anxiety or depression during pregnancy or a history of depression were the strongest predictors of postpartum depression (32). Women with a history of depressive disorder were 2.6 times more likely to have postpartum anxiety symptoms than women without a history of depression (33). Women with a history of mental illness face complex problems of disease recurrence and prognosis during pregnancy and the postpartum period, and their risk of mental disorders increases after childbirth. Medical staff should pay more attention to mothers with a history of mental and psychological diseases, remind them of possible changes in their condition, and pay close attention to changes in their symptoms.

Pregnancy complications and maternal complications are risk factors for postpartum depression. The results of a population-based mother-infant cohort in Crete, Greece, showed that women with pregnancy-induced hypertension and preeclampsia had more postpartum depressive symptoms (34), which was consistent with the findings of Blom et al. (35). Women with pregnancy complications and other complications are more prone to premature birth. Worrying about the health of herself and her newborn can make a mother more stressed and prone to emotional problems.

According to our results, regular exercise during pregnancy is a protective factor against postpartum anxiety disorder. Koltyn et al. (36) studied postpartum women and found that after 60 min of low-intensity aerobic exercise, maternal anxiety scores were significantly reduced, and emotions were significantly improved; Cram Ag and others also reached the same conclusion using the State–Trait Anxiety Inventory (STAI) to evaluate the emotional state of pregnant women after exercise. A large randomized controlled trial involving 189 pregnant women in Iran found that (37) lifestyle interventions, including physical exercise during pregnancy, can significantly reduce the postpartum anxiety score. In addition, there is sufficient evidence to prove that moderate and regular physical exercise can also prevent the occurrence of depressive disorder to a

certain extent (38, 39). Moderate physical exercise during pregnancy is very beneficial.

In this study, domestic violence was a risk factor for postpartum anxiety disorders. Domestic violence committed by partners against women during pregnancy mainly includes physical violence, psychological violence (including verbal or emotional abuse), and sexual violence, of which psychological violence is the most common (40). A cross-sectional study of 373 pregnant women enrolled in the Nigerian primary health center conducted by Mapayi et al. (41) showed that women who experienced domestic violence were 10 times more likely to report anxiety than those the control group. A systematic review and meta-analysis of 67 papers showed that (42) domestic violence was significantly associated with high levels of postpartum anxiety, which was consistent with the findings of this study. Domestic violence is a global public health problem. In addition to the increase in postpartum anxiety, studies have also found that domestic violence increases the risk of adverse outcomes such as miscarriage, premature birth, fetal distress, and low birth weight (43). Perinatal nursing and health care professionals should pay attention to the identification of domestic violence, especially psychological violence, and provide timely support and assistance to pregnant and postpartum women. It may be of great significance to reduce postpartum anxiety.

At present, there are few studies on the risk factors for postpartum OCD. Studies that link neonatal sex with postpartum mental disorders mainly focus on postpartum depression, and no unified conclusion has been reached. Studies in Western countries have not found a significant association between neonatal sex and postpartum depression (39), but studies in low-income countries such as India and Nigeria have found a significant correlation between the birth of female infants and postpartum depression (44, 45). Xie et al.'s (46) research results in China showed that after adjusting for potential confounders, the risk of postpartum depression in women who gave birth to female infants was twice that of women who gave birth to male infants. The researchers speculated that this was related to the social and cultural background. Family members may have more negative reactions to the birth of female infants, so mothers may receive less family support. In this study, giving birth to girls may be associated with maternal postpartum OCD. In addition, an increasing number of studies have found that fetal sex can specifically affect the maternal immune and endocrine systems. For example, male fetal sex is related to the increase in maternal proinflammatory cytokines, and fetal sex can lead to changes in maternal reproductive hormone levels (47, 48). This provides the basis for the link between neonatal sex and postpartum mental disorders. Our study found that neonatal sex may be associated with the occurrence of postpartum OCD, which provides a new idea for the follow-up study of postpartum OCD.

4.3 Correlation between high psychological stress levels related to childbirth and postpartum mental disorders

Our study showed that the risk of postpartum depression in the high stress level group was 9.125 times higher than that in the low stress level group. This is consistent with the view of Soderquist et al. (49) that there is a correlation between postpartum acute stress and postpartum depression. Childbirth-related psychological stress and depression disorders have overlapping symptoms, such as a continuous inability to experience positive emotions, sleep disorders, and difficulty concentrating (50). From the perspective of high-risk groups, people with low self-evaluation, pessimism, sensitivity, avoidant coping styles, and a lack of social support are prone to higher stress when exposed to external stimuli, and these personality characteristics are also risk factors for depression. In terms of pathogenesis, previous studies have shown that stressful life events can change the epigenetic modification of genes, and women with postpartum depression have different methylation patterns of the hp1bp3 and ttc9b genes (51, 52). Stress stimuli can produce many free radicals. When the body's antioxidant reduction capacity is exceeded, the body enters a state of oxidative stress. Similarly, patients with depression have oxidative stress damage in their brain and peripheral blood (53). Stress causes the HPA axis to be hyper functional, and the level of cortisol steroids increases continuously, which can lead to changes in the structure and function of brain tissue, thus causing depression. Psychological stress causes immune cell behavior disorders, which may increase cytokines in the brain to pathological levels, interfere with signal transmission, neurotransmitter synthesis, reuptake and release, and affect the emotional and cognitive functions of the nervous system (54).

In this study, the risk of postpartum anxiety in the high stress level group was also higher. Stress can lead to increased levels of norepinephrine (NE), which can stimulate thalamic α receptors, leading to increased alertness and inducing strong feelings of anxiety, fear, and anxiety-like behavior (16). Under high psychological stress, the activity of the limbic system, including the amygdala, anterior cingulate gyrus and prefrontal cortex, increases. Studies have found that the increase in volume and activity of these parts of the brain are positively correlated with the severity of symptoms of generalized anxiety disorder (55). Previous studies have also found that people with high anxiety traits are more susceptible to traumatic events, experience more symptoms and have higher stress levels after trauma, and these people are also at high risk for postpartum generalized anxiety disorder (3).

After adjusting for possible confounding factors, the risk of OCD in puerpera with high stress levels was 6.259 times higher than that in those with low stress levels. Research on psychological and behavioral responses to stress has found that people often have repeated ineffective and involuntary thoughts or actions when faced with strong stimuli or major setbacks (24). From the perspective of behavioral theory, patients may take certain actions to alleviate the anxiety caused by some situations. After patients believe that these compulsive or ritual behaviors can alleviate anxiety, they gradually increase compulsive behaviors through conditioned reflexes and even generalize these behaviors (25). For example, in clinical practice, a new mother may worry about her inability to take care of her child or that her child will have health problems, and she may repeatedly wash baby bottles and other baby supplies to alleviate this worry. In the long run, the behavior of repeatedly washing baby supplies is continuously strengthened and even generalized to washing other items and forcing her family to wash items. Encountering strong psychological stress or difficulties and setbacks that cannot be resolved will activate maladaptive thinking and behavior patterns.

In conclusion, in this study, a psychiatric diagnostic interview tool, the M.I.N.I., was used to evaluate the mental status of parturients.

It was found that a variety of mental disorders occurred, including depressive disorders (mild) manic episode, generalized anxiety disorder, OCD, panic attacks, etc. The comorbidity rate was more than 50%, which seriously threatened the health of mothers and newborns. At present, the focus of postpartum health care is mainly on postpartum depression, while other types of postpartum mental disorders are rarely mentioned. For the mental and physical health of mothers and infants, it is very important to popularize science and education on a variety of mental disorders. More attention and support should be given to groups at high risk of postpartum mental disorders, such as individuals with a history of mental illness, pregnancy complications, partner violence, and no physical exercise, and early intervention should be carried out to prevent the occurrence and development of postpartum mental disorders. The results of this study showed that a high level of psychological stress may have a certain correlation with the occurrence of postpartum depression, anxiety disorders and OCD. It is necessary to evaluate the level of psychological stress related to childbirth and carry out early interventions. In our further work, we plan to incorporate IES-R evaluation into postpartum routine follow-up on 42 ± 7 days after delivery. Puerpera with IES-R score > 9 should be referred to our department of psychological medicine for systematic evaluation and necessary diagnosis and treatment. We hope our study will contribute to more comprehensive maternal mental and psychological health care.

4.4 Limitation

Regretfully, because of ethical limitations, the research could not be designed as a cohort study. What's more, the stress levels were assessed within 1 month after delivery and some possible confounders, such as medications used after the delivery and history of psychological disorders were not be collected. In our further study, the stress levels during pregnancy, regular follow-up after childbirth and key details infected result should be brought into a more accurate evaluation.

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 humans were approved by the Ethics Review Committee of Peking Union Medical College Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

Author contributions

RS: Writing – original draft, Visualization. MZ: Data curation, Formal analysis, Investigation, Writing – original draft. LM: Resources, Writing – review & editing. YD: Writing – review & editing. JW: Funding acquisition, Resources, Supervision, Writing – review & editing.

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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.

Publisher's note

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Development and psychometric validation of the hospitalized patients' expectations for treatment scale-clinician version

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Objective: Patient safety management systems in general hospitals require a comprehensive tool for assessing the expectations of inpatients across different wards. This study aimed to develop and psychometrically validate a new scale, the hospitalized patients' expectations for treatment scale-clinician version (HOPE-C), to meet this requirement.

Methods: We interviewed 35 experts and 10 inpatients while developing the HOPE-C scale. The scale was initially designed with three dimensions: clinicians' expectations regarding doctor-patient communication, clinicians' expectations regarding treatment outcome, and clinicians' expectations regarding disease management. We recruited 200 inpatients from a general hospital in China. At the same time, 51 clinicians were assigned to the enrolled patients who completed the HOPE-C to examine the reliability, validity, and psychometric characteristics of the questionnaire. We applied item analysis, assessed construct validity, evaluated internal consistency, and conducted a test-retest reliability analysis over 7 days.

Results: Both exploratory and confirmatory analyses supported a 2-dimensional structure, comprising doctor-patient communication expectations and treatment outcome expectations, with favorable model fit parameters (root mean square residual [RMR] = 0.042, root mean square error of approximation [RMSEA] = 0.049, comparative fit index [CFI] = 0.989, Tucker-Lewis index [TLI] = 0.984). Item analysis demonstrated appropriate item design (r = 0.744–0.961). The scale exhibited strong internal consistency, with Cronbach's α values of 0.884, 0.816, and 0.840 for the overall scale, the doctor-patient communication expectation subscale, and the treatment outcome expectation subscale, respectively. The 7-day test-retest reliability was 0.996 ($p < 0.001$).

Conclusion: Our findings suggest that the HOPE-C is a reliable and valid assessment tool for measuring the expectations of inpatients in general hospitals. It effectively identifies patients' expectations concerning doctor-patient communication and treatment outcomes.

KEYWORDS

clinician, general hospital, treatment expectation, doctor-patient relationship, patient safety

1 Introduction

In healthcare, understanding physicians' expectations for treatment is paramount for optimizing patient care. Since physicians play a pivotal role in patient treatment, their expectations can considerably impact healthcare delivery, patient outcomes, and the overall quality of healthcare services. With a growing emphasis on patient-centered care and shared decision-making, understanding physicians' expectations for treatment has become a central concern (1). First, physicians are responsible for diagnosing and treating medical conditions and establishing and maintaining the patient-physician relationship, serving as the foundation of patient-centered care (2). Second, as trusted healthcare providers, physicians bring their own expectations, beliefs, and preferences into their clinical practice, influencing the clinical decisions they make for their patients (3). Furthermore, trust and communication between physicians and patients are pivotal in achieving optimal health outcomes, patient satisfaction, and adherence to treatment plans (4).

The importance of understanding physicians' expectations lies in its potential to improve healthcare outcomes. A deeper comprehension of what physicians expect can help healthcare institutions and policymakers design strategies and interventions to align these expectations with patient-centered care goals. It can also enhance medical education and training by tailoring curricula to address areas where expectations differ from patient needs and preferences.

Physicians' expectations are a notable factor influencing clinical practice, which might affect patient outcomes. Previous studies demonstrated a gap in patient-physician communication regarding expectations of patient treatment outcomes (5). In cancer survivorship care, patients and physicians have discordant expectations (6, 7). Moreover, an enhanced agreement between patients' preferences and physicians' expectations can improve communication and patients' satisfaction with treatment (8–10). Shared decision-making (SDM) with the incorporation of patient-reported outcomes can promote patient adherence and satisfaction (11). The concordance of treatment expectations is the key factor in SDM, potentially helping manage patient expectations for treatment and ultimately positively impacting their health-related quality of life (12). Patients often experience stress and anxiety related to their medical conditions and treatment. Positive expectations of physicians can help alleviate some of this stress and anxiety, leading to a better overall patient experience and potentially improved clinical outcomes (13). Clinical studies demonstrated that physicians' expectations can influence a patient's physiological response to treatment (14). Positive expectations might lead to the release of endorphins and other neurochemicals, contributing to an enhanced healing response and reduced pain perception (15). Moreover, the treatment expectations of physicians also reflect the treatment intention, which is associated with attitude, past behavior, perceived behavioral control, and subjective norms, thus influencing therapeutic modalities in clinical settings (16).

The current measures for assessing treatment expectations among clinicians in general hospitals remain insufficient. Many survey questionnaires have been developed for specific treatments or diseases, such as brain metastases in cancer (17), high tibial osteotomy for osteoarthritis (18), and idiopathic pulmonary fibrosis (19). Furthermore, the absence of a quantitative scale makes it challenging to quantitatively evaluate the impact of physicians' treatment expectations on overall patient management and hinders comparisons across different hospital departments. Consequently, there is a compelling need to establish a quantitative tool for evaluating physicians' treatment expectations that can be applied across various clinical departments. Therefore, we created the hospitalized patients' expectations for treatment scale-clinician version (HOPE-C) to enhance our understanding of physicians' treatment expectations and improve patient safety management systems.

Our study sought to validate a structured assessment tool to measure clinicians' expectations for treatment. The primary objective was to provide a dependable and practical assessment instrument for forthcoming clinical applications, addressing the increasing demand for personalized healthcare and reinforcing a robust patient safety framework. In a prior phase of our research, we effectively validated the hospitalized patients' expectations for treatment scale-patient version (HOPE-P), affirming its validity and reliability in assessing treatment expectations among hospitalized patients (20). In the present study, we leveraged a similar scale structure to that of HOPE-P to create an assessment tool focused on clinicians' expectations rooted in their perspective on clinical treatment. Our aim is to establish a comprehensive assessment system for the expectations of patients and clinicians for treatment in future clinical practice.

2 Materials and methods

2.1 Formulation of the scale

In this study, we developed the HOPE-C, building upon the prior scale developed for patients (HOPE-P). Thirty-five experts representing various medical fields, including psychiatry, surgery,

internal medicine, nursing, and medical management, collaborated in the development of this tool according to the inclusion criteria: (1) employment in general hospitals or psychiatric specialty hospitals within China; (2) specialization in fields such as clinical medicine, healthcare management, medical informatics, or nursing; (3) active engagement in doctor-patient relationship dynamics and patient safety management within their respective work and research areas. Additionally, we conducted interviews with 10 randomly selected inpatients at the Peking Union Medical College Hospital, covering a range of medical specialties, such as general surgery, orthopedics, vascular surgery, plastic surgery, gastroenterology, infectious medicine, and neurology. To refine the scale, we employed the Delphi method, gathering insights from both medical experts and patients. The question was, "What do patients expect from hospitalization and doctors? What do patients concern most?" After three rounds of extensive discussions, participants' responses converged on three domains: how a patient is treated on a person-to-person level by the doctor (doctor-patient communication), whether the clinical condition will improve during hospitalization (treatment outcomes), and condition as a long-term problem (perceptions of long-term disease management). We designed the HOPE-C in alliance with HOPE-P to make it convenient for clinical usage; hence, clinicians could easily identify misunderstandings between doctors and patients.

2.2 Participants

A total of 200 patients, spanning five different departments, were enrolled from the Peking Union Medical College Hospital in China between March 2023 and September 2023. Fifty-one clinicians were randomly assigned to manage the enrolled patients. To be eligible, participants must be aged $\geq$ 10 years, hospitalized for $>$ 24 h, anticipate discharge within a week, and demonstrate the ability to understand and cooperate with the study requirements. Exclusion criteria encompassed acute suicidal tendencies, limited writing proficiency, language barriers, organic brain disorders, cognitive impairment, dementia, and psychosis. All participants provided informed consent, indicating their understanding of the study's procedures by signing the consent form. For participants aged $<$ 18 years, supplementary informed consent was secured from their parents or legal guardians.

2.3 Administration

The HOPE-C scale was administered to clinicians within 24 h of their patients' admission to the ward. This process was facilitated through a smartphone applet developed and supported by the Department of Psychological Medicine at Peking Union Medical College Hospital, which served as the platform for completing the HOPE-C scale. Specially trained investigators provided information about the research to patients and their assigned clinicians. They also supplied a QR code for the applet. Patients who consented to participate scanned the QR code using their mobile phones, accessed the main interface, and signed an informed consent form. For patients aged $<$ 18 years, their parents or guardians authorized and signed additional informed consent forms.

Following the applet's instructions and with the investigator's assistance, the assigned clinicians provided essential information and completed the HOPE-C scale. The sociodemographic questionnaire collected data on age, gender, residence, marital status, family income, education level, employment status, and other pertinent details. Subsequently, 20 clinicians participated in a retest conducted 7 days after the initial completion of the HOPE-C scale to evaluate the test-retest reliability and the stability of the measurement tool over time.

2.4 Sample size evaluation

The sample size calculation was guided by "rules of thumb" or "blue chips." These guidelines suggest that a minimal sample size, typically exceeding 200, is necessary to ensure sufficient statistical power for data analysis. Furthermore, these rules of thumb propose that the ratio of the number of individuals (N) to the number of measured variables (p) should ideally fall within the range of 5–10, with a minimum requirement of $N > 100$. A widely accepted standard is to have 10 cases per indicator variable. Considering these factors, the total sample size was determined to be 200, and the Kaiser-Meyer-Olkin (KMO) was used to assess the adequacy of the sampling.

2.5 Statistical analysis

Data analysis was performed using IBM SPSS version 28.0 and AMOS version 26.0. The significance level was set at a two-tailed p-value < 0.05 for the entire analysis.

2.5.1 Descriptive statistics

Continuous variables were presented as median (25 and 75th percentiles), and categorical variables were represented as the count along with the corresponding percentage (n [%]). Kolmogorov–Smirnov test was applied to evaluate the normality of the data. Additionally, differences among groups in HOPE-C scores were assessed by the Mann–Whitney U test for 2-group comparison and the Kruskal–Wallis H test with Bonferroni adjustment for multiple-group comparison.

2.5.2 Item analysis

The HOPE-C total score was divided into two groups based on high and low scores, with the upper 27% and lower 27% of scores forming the respective groups. A t-test was conducted to compare these groups, leading to the calculation of critical ratio (CR) values. We calculated the corrected associations between items and the total score to assess the strength of correlations between each item and the overall scale score. If the item-total correlation coefficient exceeded 0.4, it was considered a satisfactory result (21).

2.5.3 Structural validity

We conducted an exploratory factor analysis (EFA) using IBM SPSS version 28.0 on a randomly selected half of the collected dataset to explore the previously unexamined structure of the HOPE-C scale. Before proceeding, we performed checks on the data suitability and sampling adequacy, which included the KMO

measure and Bartlett's test of sphericity. KMO > 0.70 and $p < 0.001$ for Bartlett's test indicated adequate data suitability and sampling adequacy, signifying a substantial correlation between the items suitable for structure detection. We applied varimax rotation and extracted factors with eigenvalues > 1. A total factor loading > 60% was considered satisfactory (22). A confirmatory factor analysis (CFA) was performed using AMOS version 26.0 on the other half of the sample. The following criteria determined global model fit appropriateness: a root mean square residual (RMR) value < 0.05, a root mean square error of approximation (RMSEA) value ≤ 0.10, along with comparative fit index (CFI), normed fit index, non-normed fit index, incremental fit index, Tucker-Lewis index (TLI), and goodness of fit index values > 0.9 (23).

We calculated Cronbach's α coefficients and McDonald's ω coefficients for both the complete scale and individual subscales to assess the internal consistency of the recently developed tool. Additionally, we provided 95% confidence intervals (95% CI). Internal consistency was considered high when Cronbach's α coefficient or McDonald's ω coefficient exceeded 0.7, while a value > 0.9 suggests redundancy (24). For evaluating the 7-day test-retest reliability, we determined the Pearson correlation coefficient or Spearman correlation coefficient based on the results of the Kolmogorov–Smirnov test between the initial test and the retest.

3 Results

3.1 Descriptive statistics

The study involved 200 patients, with an average age of 43.50 ± 14.34 years, and 122 (61.0%) of them were male (Table 1). Among the clinicians assigned to the enrolled patients, 51 completed the HOPE-C. The mean total score on the HOPE-C scale was 37.66 ± 4.31, out of a maximum possible score of 45. Subscale scores were as follows: 13.79 ± 1.78 for the doctor-patient communication expectations subscale (referred to as subscale A, covering items 1–3 with a maximal score of 15), 21.83 ± 2.92 for the clinicians' treatment outcome–related expectations subscale (referred to as subscale B, encompassing items 4–8, with a maximal score of 25), and 2.06 ± 1.03 for the disease management expectancy subscale (subscale C, with a maximal score of 5). No statistically significant differences were detected in HOPE-C total scores and subscale scores based on patients' gender, employment status, place of residence, monthly family income, or educational level.

However, notable variations were observed in the total HOPE-C scores among patients of different age groups ($H = 20.335$, $p < 0.001$) and among patients in various hospital departments ($H = 44.786$, $p < 0.001$). Patients aged 21–40 years achieved the highest total HOPE-C scores (41.00 [37.00, 42.00]). Notably, clinicians in the urology department obtained lower scores compared to those in orthopedics (36.00 [34.00, 39.00] vs. 40.00 [39.00, 41.00], $p < 0.001$) and general surgery (36.00 [34.00, 39.00] vs. 41.00 [39.00, 42.00], $p < 0.001$). Concerning subscale-A scores, no significant differences were found among patients of different ages; however, clinicians in urology attained significantly lower scores compared to those in endocrinology (13.00 [12.00, 15.00] vs. 15.00 [15.00, 15.00], $p < 0.001$). Regarding subscale B, there were significant differences among patients of different ages ($H = 21.483$, $p < 0.001$), with those aged 21–40 years achieving the highest scores (24.00 [21.00, 25.00]). Clinicians in urology exhibited significantly lower scores compared to those in general surgery (20.00 [20.00, 22.00] vs. 24.50 [23.00, 25.00], $p < 0.001$). Furthermore, significant differences were observed among hospital departments in subscale C ($H = 33.647$, $p < 0.001$). Clinicians in the cardiology department expressed a greater expectation for long-term disease management compared to those in orthopedics, urology, and general surgery (1.00 [1.00, 1.00] vs. 2.00 [1.00, 3.00], $p < 0.001$; 1.00 [1.00, 1.00] vs. 2.00 [2.00, 2.00], $p < 0.001$; 1.00 [1.00, 1.00] vs. 2.00 [1.00, 3.00], $p < 0.001$). Considering medical conditions, 101 (50.5%) patients were diagnosed with cancer in different wards; however, there were no statistically significant differences in the HOPE-C score between distinct medical conditions.

3.2 Item analysis

The CR values for items 1–8 fell within the range of 8.528 to 13.598, and the distinctions between low- and high-scoring groups were all statistically significant. The scores for items 1–8 and the total score demonstrated significant correlations, with coefficients ranging from 0.744 to 0.927, all exceeding 0.40. Notably, item 9 had the lowest CR value (1.316) and displayed an insignificant correlation with the total score, indicating that this item fails to discern response variations among different investigators. This item lacked meaningful relevance in the survey and should be removed. The item analysis results are presented in Table 2.

3.3 Structural validity analysis

Based on the item analysis results and the scale's design concept, an EFA was conducted on a randomly selected half of the sample ($n = 100$) to ascertain the number of factors. According to the results of item analysis, EFA based on eight items conducted with the KMO statistics yielded a value of 0.875, with Bartlett's test of sphericity showing $\chi^2 = 617.936$ ($p < 0.001$), indicating the suitability of the data for factor extraction. Subsequently, principal component analysis with varimax rotation was performed, identifying a single factor with eigenvalues exceeding 1. The single factor explained 65.551% of the total variance. Detailed item factor loadings are provided in Table 3.

Concerning the design concept and principle of this scale, we conducted EFA based on nine items to explore whether HOPE-C can be divided into three factors. The KMO statistics yielded a value of 0.866, with Bartlett's test of sphericity demonstrating $\chi^2 = 627.329$ ($p < 0.001$). Three factors collectively explained 80.485% of the total variance. Upon thoroughly examining factor loadings, items 1–5 and 7–8 were grouped within one dimension, while items 6 and 9 were attributed to factors 2 and 3, respectively. As outlined in Supplementary Table 1, all items displayed factor loadings exceeding 0.6. However, the results of the EFA analysis using the 9-item scale did not align with the intended structure we designed for this scale.

Subsequently, a CFA using weighted least squares estimation was conducted on another randomly selected sample ($n = 100$)

TABLE 1 Demographic characteristics of the overall sample.

Variables	Number (%)	Overall Scale Mean ± SD	Subscale A Mean ± SD	Subscale B Mean ± SD	Subscale C Mean ± SD
Age	$N = 200$	$P < 0.001$*	$P = 0.063$	$P < 0.001$*	$P = 0.822$
10-20	2 (1.0%)	38.00 (35.00, -)	13.00 (11.00, -)	23.00 (21.00, -)	2.00 (1.00, -)
21-40	39 (19.5%)	41.00 (37.00, 42.00)	15.00 (14.00, 15.00)	24.00 (21.00, 25.00)	2.00 (1.00, 3.00)
41-60	79 (39.5%)	38.00 (36.00, 41.00)	15.00 (13.00, 15.00)	22.00 (20.00, 24.00)	2.00 (1.00, 2.00)
61-80	79 (39.5%)	37.00 (34.00, 40.00)	14.00 (12.00, 15.00)	20.00 (20.00, 23.00)	2.00 (2.00, 2.00)
>80	1 (0.5%)	35.00	12.00	21.00	2.00
Gender	$N = 200$	$P = 0.062$	$P = 0.479$	$P = 0.085$	$P = 0.444$
Male	122 (61.0%)	38.00 (34.00, 41.00)	15.00 (12.00, 15.00)	22.00 (20.00, 24.00)	2.00 (1.00, 2.00)
Female	78 (39.0%)	39.00 (36.00, 41.00)	15.00 (13.00, 15.00)	22.50 (20.00, 25.00)	2.00 (1.00, 3.00)
Residence	$N = 200$	$P = 0.201$	$P = 0.639$	$P = 0.205$	$P = 0.959$
Urban	175 (87.5%)	38.00 (35.00, 41.00)	15.00 (12.00, 15.00)	22.00 (20.00, 24.00)	2.00 (1.00, 2.00)
Rural	25 (12.5%)	39.00 (37.00, 41.00)	15.00 (14.00, 15.00)	22.00 (20.00, 25.00)	2.00 (1.00, 3.00)
Marital status	$N = 200$	$P = 0.077$	$P = 0.081$	$P = 0.128$	$P = 0.293$
Single	17 (8.5%)	40.00 (36.50, 41.50)	15.00 (12.50, 15.00)	23.00 (20.50, 25.00)	2.00 (1.00, 4.00)
Married	167 (83.5%)	38.00 (35.00, 41.00)	15.00 (12.00, 15.00)	22.00 (20.00, 24.00)	2.00 (1.00, 2.00)
Divorced	5 (2.5%)	39.00 (36.50, 40.50)	15.00 (13.50, 15.00)	22.00 (21.00, 24.50)	1.00 (1.00, 2.50)
Widowed	5 (2.5%)	35.00 (33.50, 36.00)	12.00 (12.00, 12.50)	20.00 (19.50, 21.00)	2.00 (2.00, 3.00)
Other	6 (3.0%)	39.00 (37.25, 41.50)	15.00 (12.50, 15.00)	23.00 (20.75, 25.00)	3.00 (1.00, 3.00)
Employment status	$N = 200$	$P = 0.060$	$P = 0.666$	$P = 0.106$	$P = 0.744$
Student	6 (3.0%)	40.50 (36.50, 43.25)	15.00 (11.00, 15.00)	25.00 (21.00, 25.00)	3.00 (1.00, 4.00)
Employed	74 (37.0%)	39.00 (36.00, 41.00)	15.00 (13.00, 15.00)	23.00 (20.00, 25.00)	2.00 (1.00, 2.25)
Unemployed	24 (12.0%)	38.00 (35.00, 41.00)	15.00 (12.00, 15.00)	22.00 (20.00, 24.75)	2.00 (1.00, 2.75)
Retired	84 (42.0%)	37.00 (34.00, 40.00)	14.00 (12.00, 15.00)	21.00 (20.00, 24.00)	2.00 (1.00, 2.00)
Other	12 (6.0%)	38.50 (37.00, 40.50)	15.00 (13.25, 15.00)	22.50 (21.25, 24.00)	2.00 (1.00, 2.75)
Educational level	$N = 200$	$P = 0.698$	$P = 0.815$	$P = 0.566$	$P = 0.968$
Elementary	12 (6.0%)	39.00 (37.25, 40.00)	14.50 (14.00, 15.00)	22.00 (20.25, 24.00)	2.00 (1.00,2.75)
Junior	21 (20.5%)	38.00 (34.50, 41.00)	14.00 (12.00, 15.00)	21.00 (20.00, 24.00)	2.00 (1.00, 3.00)
High school	41 (20.5%)	38.00 (34.50, 41.00)	15.00 (13.00, 15.00)	22.00 (20.00, 24.00)	2.00 (1.00, 2.00)
College or higher	106 (53.0%)	38.50 (35.00, 41.00)	15.00 (12.00, 15.00)	22.00 (20.00, 25.00)	2.00 (1.00, 2.00)
Monthly family income	$N = 200$	$P = 0.780$	$P = 0.986$	$P = 0.828$	$P = 0.519$
<4,000 RMB	41 (20.5%)	38.00 (35.00, 41.00)	15.00 (12.00, 15.00)	22.00 (20.00, 24.00)	2.00 (1.00, 3.00)
4,000-8,000 RMB	71 (35.5%)	38.00 (35.00, 41.00)	15.00 (12.00, 15.00)	21.00 (20.00, 25.00)	2.00 (1.00, 2.00)
>8,000 RMB	88 (44.0%)	39.00 (35.00, 41.00)	15.00 (12.00, 15.00)	22.00 (20.00, 24.00)	2.00 (1.00, 2.00)
Wards	$N = 200$	$P < 0.001$*	$P < 0.001$*	$P < 0.001$*	$P < 0.001$*
Orthopedics	31 (15.5%)	40.00 (39.00, 41.00)	15.00 (14.50, 15.00)	24.00 (22.00, 25.00)	2.00 (1.00, 3.00)
Urology	102 (51.0%)	36.00 (34.00, 39.00)	13.00 (12.00, 15.00)	20.00 (20.00, 22.00)	2.00 (2.00, 2.00)
General Surgery	26 (13.0%)	41.00 (39.00, 42.00)	15.00 (14.00, 15.00)	24.50 (23.00, 25.00)	2.00 (1.00, 3.00)
Cardiology	15 (7.5%)	40.00 (37.50, 41.00)	15.00 (14.50, 15.00)	24.00 (23.00, 25.00)	1.00 (1.00, 1.00)
Endocrinology	26 (13.0%)	38.50 (37.00, 40.00)	15.00 (15.00, 15.00)	22.00 (21.00, 23.00)	1.00 (1.00, 2.00)
Medical Condition					
Orthopedics	$N = 31$	$P = 0.290$	$P = 0.515$	$P = 0.677$	$P = 0.879$
Cervical Spondylosis	8 (25.8%)	40.00 (31.75, 41.00)	15.00 (15.00, 15.00)	23.00 (14.75, 25.00)	2.00 (1.00, 2.00)

(Continued)

TABLE 1 (Continued)

Variables	Number (%)	Overall Scale Mean ± SD	Subscale A Mean ± SD	Subscale B Mean ± SD	Subscale C Mean ± SD
Scoliosis	5 (16.1%)	41.00 (40.50, 43.00)	15.00 (14.50, 15.00)	25.00 (23.00, 25.00)	3.00 (1.00, 2.00)
Atlantoaxial Dislocation	4 (12.9%)	40.00 (36.25, 20.75)	15.00 (13.50, 15.00)	23.00 (20.75, 24.50)	2.00 (1.25, 2.00)
Lumbar Spinal Stenosis	11 (35.5%)	40.00 (39.00, 41.00)	15.00 (14.00, 15.00)	24.00 (22.00, 24.00)	2.00 (1.00,3.00)
Others	2 (9.7%)	41.00 (38.00, -)	15.00 (15.00, 15.00)	24.00 (20.00, -)	3.00 (1.00, -)
Urology	$N = 102$	$P = 0.103$	$P = 0.291$	$P = 0.081$	$P = 0.459$
Renal Tumor	24 (23.5%)	38.00 (35.00, 40.00)	14.50 (12.00, 15.00)	21.00 (20.00, 23.00)	2.00 (2.00,3.00)
Bladder Tumor	18 (17.6%)	34.50 (34.00, 38.25)	12.50 (12.00, 15.00)	20.00 (20.00, 20.50)	2.00 (2.00,2.25)
Prostatic Cancer	13 (12.7%)	34.00 (33.50, 36.50)	12.00 (12.00, 14.50)	20.00 (19.00, 20.50)	2.00 (1.50, 2.00)
Adrenal Tumors	27 (26.5%)	37.00 (34.00, 41.00)	13.00 (12.00, 15.00)	20.00 (20.00, 25.00)	2.00 (2.00, 3.00)
Urinary Caculus	10 (9.8%)	34.50 (34.00, 36.50)	12.00 (12.00, 13.25)	20.00 (20.00, 22.00)	2.00 (1.75, 2.50)
Others	10 (9.8%)	35.50 (33.00, 41.00)	13.00 (11.75, 15.00)	20.00 (19.75, 24.25)	2.00 (1.75, 4.00)
General Surgery	$N = 26$	$P = 0.593$	$P = 0.252$	$P = 0.132$	$P = 0.486$
Pancreatic Neoplasm	6 (23.1%)	40.00 (37.75, 43.00)	15.00 (14.00, 15.00)	22.50 (21.00, 24.25)	3.00 (1.75, 4.00)
Thyroid Nodule	4 (15.4%)	40.50 (36.25, 41.75)	14.00 (11.75, 14.75)	24.50 (21.75, 25.00)	2.00 (1.00, 3.75)
Thyroid Cancer	13 (50.0%)	41.00 (39.50, 41.50)	15.00 (14.00, 15.00)	25.00 (23.50, 25.00)	2.00 (1.00, 2.00)
Others	3 (11.5%)	42.00 (41.00, -)	15.00 (15.00, 15.00)	25.00 (25.00, 25.00)	2.00 (1.00, -)
Cardiology	$N = 15$	$P = 0.863$	$P = 0.384$	$P = 0.776$	$P = 0.253$
Coronary Atherosclerotic Heart Disease	7 (46.7%)	38.00 (37.00, 41.00)	15.00 (13.00, 15.00)	25.00 (23.00, 25.00)	1.00 (1.00, 1.00)
Atrial Fibrillation	4 (26.7%)	39.50 (39.00, 40.75)	15.00 (15.00, 15.00)	23.00 (23.00, 24.50)	1.00 (1.00, 1.75)
Others	4 (26.7%)	40.50 (16.75, 41.00)	15.00 (6.00, 15.00)	24.50 (9.75, 25.00)	1.00 (1.00, 1.00)
Endocrinology	$N = 26$	$P- = 0.909$	$P = 0.599$	$P = 0.815$	$P = 0.468$
Diabetes Mellitus	7 (26.9%)	38.00 (37.00, 40.00)	15.00 (15.00, 15.00)	21.00 (21.00, 24.00)	1.00 (1.00, 1.00)
Insulinoma	4 (15.4%)	38.50 (37.25, 39.75)	15.00 (15.00, 15.00)	21.50 (20.25, 22.75)	2.00 (1.25, 2.75)
Cushing Syndrome	3 (11.5%)	38.00 (38.00, -)	15.00 (15.00, 15.00)	22.00 (22.00, -)	1.00 (1.00, -)
Others	12 (46.2%)	39.00 (36.00, 40.50)	15.00 (14.25, 15.00)	22.50 (20.50, 23.00)	1.00 (1.00, 2.00)

Mann-Whitney U test was used for two group comparison and Kruskal-Wallis H test with Bonferroni adjustment for multiple group comparison.*$p < 0.01$.

to assess the 2-factor model based on eight items, encompassing satisfaction with treatment experience– and outcome–related expectations. The outcomes revealed that the majority of items in the CFA model exhibited factor loadings surpassing 0.6 (Figure 1), and all model fit indices indicated a favorable fit (χ^2/df = 1.237, RMSEA = 0.049, SRMR = 0.042, CFI = 0.989, TLI = 0.984).

3.4 Reliability analysis

An analysis of reliability using the 8-item 2-factor model demonstrated that the scale exhibited reliable performance. The McDonald's ω coefficient for the complete HOPE-C scale was calculated at 0.883 (95% CI = [0.857, 0.906]). The McDonald's ω coefficients for HOPE-C subscale A and subscale B were 0.820 (95% CI = [0.767, 0.856]) and 0.839 (95% CI = [0.802, 0.872]), respectively.

For the HOPE-C maximal scale, the Cronbach's α coefficient was 0.884 (95% CI = [0.857, 0.906]). The Cronbach's α coefficients for HOPE-C subscale A and subscale B were 0.816 (95% CI = [0.767, 0.856]) and 0.840 (95% CI = [0.802, 0.872]), respectively.

Furthermore, the test-retest reliability of the complete HOPE-C scale over a 7-day interval was 0.996 ($p < 0.001$). These analyses collectively indicated that the scale exhibits strong and reliable measurement properties.

4 Discussion

In this research, we enrolled 200 inpatients and 51 clinicians from a Chinese general hospital to investigate the reliability, validity, and psychometric characteristics of the HOPE-C scale. This scale was adapted from the HOPE-P and designed to assess clinicians' multifaceted expectations for patients in a general hospital setting. Initially including three dimensions and nine items, the scale measures expectations related to the doctor-patient relationship, treatment outcomes, and disease management in Chinese healthcare.

TABLE 2 Item analysis.

	Item	Critical ration	Corrected item-total correlation
Subscale A: doctor-patient communication expectation	Q1. I listen to patient's opinions on treatment	10.205**	0.830**
	Q2. During this hospitalization, I fully explains the state of illness and negotiates medical decision with patient	11.121**	0.879**
	Q3. During this hospitalization, I care my patient	10.499**	0.880**
Subscale B: treatment expectation	Q4. Through this hospitalization, the patient's disease can be definitely diagnosed	11.417**	0.927**
	Q5. Through this hospitalization, the patient's symptoms can be improved	10.294**	0.889**
	Q6. Through this hospitalization, the patient's disease can be cured	8.528**	0.744**
	Q7. Through this hospitalization, the patient can restore work/family functions	13.598**	0.961**
	Q8. Through this hospitalization, the patient can take care of themselves	10.498**	0.893**
Subscale C: disease management expectancy by doctor	Q9. After this hospitalization, the patient need to mental long-term treatment	1.316	0.155

**p <0.01.

TABLE 3 Results of exploratory factor analysis.

	Item	EFA (8 items)	EFA (9 items)		
		Loadings on factor	Loadings on factor 1	Loadings on factor 2	Loadings on factor 3
Subscale A: doctor-patient relationship expectation	Q1	0.681	0.742	−0.194	−0.210
	Q2	0.879	0.881	0.101	/
	Q3	0.871	0.850	0.164	−0.133
Subscale B: treatment expectation	Q4	0.851	0.842	0.178	0.140
	Q5	0.858	0.784	0.375	−0.118
	Q6	0.41		0.942	/
	Q7	0.912	0.885	0.228	/
	Q8	0.889	0.880	0.159	/
Subscale C: disease management expectancy by doctor	Q9	/	/	/	0.984

EFA, exploratory factor analysis.

Our findings indicated that the HOPE-C scale exhibits robust internal consistency, reliability, and validity. The results were consistent with a 2-factor model encompassing expectations tied to the treatment experience and satisfaction with treatment outcomes. This study confirmed the scale's overall strong reliability and demonstrated satisfactory reliability and validity for the first two subscales. Thus, the HOPE-C scale allows a practical and accessible assessment of clinicians' treatment expectations in Chinese healthcare culture.

The initial subscale of the HOPE-C evaluated expectations regarding doctor-patient communication and comprised three distinct items. Prior studies underscored variations in perceptions of doctor-patient communication between patients and clinicians (25). Consequently, Subscale A was tailored to measure doctor-patient communication expectations from the patient's perspective. Effective doctor-patient communication is pivotal in nurturing patient trust in their healthcare providers, bolstering overall satisfaction, and indirectly influencing health outcomes, including symptom management and adherence to medical regimens. Thus, ensuring effective and efficient communication is a foundational component of strategies to deliver high-quality healthcare (26).

Within the HOPE-C scale, the three items that pertain to doctor-patient communication specifically address clinicians' expectations regarding attentiveness to patient treatment opinions, transparent communication about the patient's medical condition, active patient involvement in medical decision-making, and the demonstration of a compassionate demeanor. These items closely align with the core tenets of previous research on doctor-patient communication, which reflect the principles of patient autonomy, SDM, and a humanitarian approach—critical aspects of personalized medicine (27, 28). Our study results revealed distinctions in doctor-patient communication expectations among different hospital wards. Significantly, clinicians in the urology department expressed lower expectations regarding doctor-patient

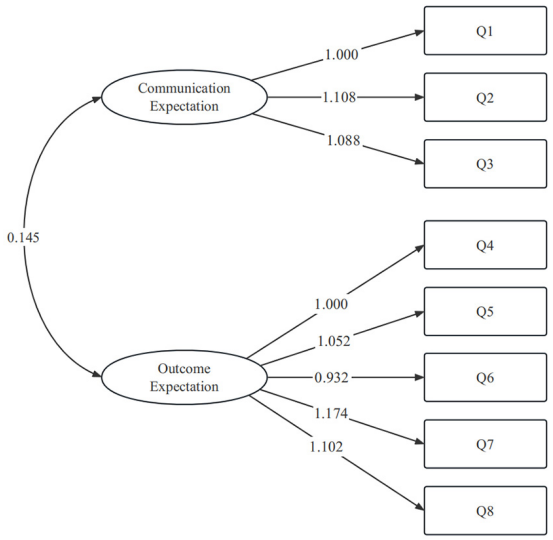

FIGURE 1
Factor structure of hospitalized patients' expectations for treatment scale-clinician version (HOPE-C), based on an eight-item two-factor model.

communication when compared to their counterparts in the orthopedics and endocrinology departments. This discrepancy suggests that perspectives on doctor-patient communication among clinicians still vary based on the clinical setting.

Extensive research on clinicians' therapeutic expectations yielded compelling insights into the impact of physicians' expectations regarding treatment outcomes on disease management results (29). In this study, outcome expectation pertains to a physician's personal assessment of the potential benefits associated with a specific treatment plan that they intend to prescribe to a patient, considering the patient's prognosis. Evaluating clinicians' treatment outcome expectations is critical, as it serves as a guiding factor in clinical practice and aids in predicting treatment outcomes. Items 4–8 within the HOPE-C scale are specifically designed to assess physicians' expectations concerning treatment outcomes. These items encompass various facets, including expectations for a clear diagnosis, disease improvement, recovery, and the restoration of functional capabilities. Additionally, patient age significantly influences physicians' expectations regarding treatment outcomes. Furthermore, the nature of a patient's specific medical condition can result in varying expectations regarding treatment outcomes and attitudes toward long-term disease management. Various treatment modalities and management approaches offered by clinicians, which are tailored to the unique characteristics of each medical condition, lead to diverse treatment experiences and outcomes. Consequently, this diversity affects the expectations of different clinicians in terms of treatment outcomes, aligning with the observations made in routine clinical practice. There is no apparent interaction between physicians' treatment outcome–related expectations and doctor-patient communication. This suggests that doctor-patient communication does not influence the formulation of treatment expectations by physicians before they make clinical decisions. This finding underscores that, in contrast to patient expectations, physicians' treatment outcome expectations are not substantially influenced by the quality of doctor-patient communication.

In line with our earlier investigation on the HOPE-P scale, this current study also does not support the inclusion of the disease management expectancy subscale within the HOPE-C. Several factors might contribute to this, including issues related to the item's design or its standalone nature. According to our findings, we compared various CFA models and opted for an 8-item, 2-factor model for further analysis. Nevertheless, it remains crucial to focus on the concept of disease management expectancy for a holistic assessment of hospitalized patients' treatment expectations, aiming to enhance personalized medical care. The CFA results revealed no correlation between individual items in the doctor-patient communication subscale and treatment-related outcome expectations, suggesting that clinicians' expectations regarding treatment outcomes are independent of SDM. This finding implies that the SDM process might not be fully integrated into the routine clinical practice of inpatient care within a general hospital setting in China. In future research, exploration of the disparities in treatment expectations between patients and clinicians is required. Furthermore, examining whether and how differences in treatment expectations between patients and doctors impact clinical practice outcomes is essential.

Nonetheless, there were several limitations in this study. The inclusion of inpatients was restricted to a relatively small selection of departments, primarily encompassing three surgical and two internal medicine departments. Future research should consider enlarging the sample size and containing a wider array of departments to improve generalizability. Furthermore, while the current set of items in the HOPE-C scale aims to encompass critical dimensions, there is a need for further investigation to identify potential dimensions that warrant attention, thereby enhancing the scale's comprehensiveness.

5 Conclusion

The HOPE-C scale demonstrates robust internal consistency, reliability, and validity, consistently aligning with the 2-factor satisfaction model. These two factors encompass doctor-patient communication and treatment outcome–related expectations, strengthening the scale's reliability and relevance for assessing clinicians' multifaceted treatment expectations.

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 humans were approved by the Ethics Committee of Peking Union Medical College Hospital. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

BD: Conceptualization, Data curation, Formal analysis, Writing – original draft. CX: Project administration, Writing – original draft. YW: Data curation, Writing – review & editing. TL: Resources, Writing – review & editing. YD: Resources, Writing – review & editing. YJ: Resources, Writing – review & editing. LS: Resources, Supervision, Writing – review & editing. XH: Resources, Writing – review & editing. WG: Resources, Writing – review & editing. JH: Project administration, Writing – review & editing. JC: Conceptualization, Supervision, Writing – review & editing. JW: Conceptualization, Funding acquisition, Supervision, Writing – review & editing.

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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.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fpsyt.2023.1325013/full#supplementary-material

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Influence of mental health service provision on the perceived quality of life among psychiatric outpatients: associations and mediating factors

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Objective: To investigate the relationship between perceived mental health service provision and quality of life (QoL) as perceived by patients in psychiatric outpatient care.

Methods: A total of 373 adult patients registered at 15 psychiatric outpatient clinics in three regions in central and southern Sweden were included in the study. Survey data were collected using a questionnaire on mental health service provision, symptom severity, recovery, clinical diagnosis, sociodemographics (serving as independent variables) and QoL (serving as the dependent variable). Three aspects of mental health service provision were used: patients' perceived quality of care, perceived staff-patient interaction, and patient reported psychiatric treatments. Structural equation modelling was used to model the relationship among the variables.

Results: Variables in mental health service provision showed few direct associations with patients' perceived QoL. Instead, the associations of mental health service provision on QoL were mainly mediated through symptom severity and recovery. These relationships were retained after adjusting for sociodemographic variables and clinical diagnoses. The final model achieved excellent goodness of fit ($\chi^2 = 49.502$, $p = 0.230$, RMSEA = 0.020, CFI = 0.997 and a SRMR = 0.024).

Conclusion: This study shows that mental health service provision is associated with patients' perceived QoL; however, this association is mostly indirect and mediated by reduced symptom severity and increased recovery. This finding can help inform the design of future interventions to enhance service provision to improve patients' QoL.

KEYWORDS

mediator model, mental health, outpatient psychiatric care, service provision, structural equation modelling, quality of life

1 Introduction

Psychiatric outpatient care is designed to offer comprehensive, continuous treatment and support for individuals to cope with mental health conditions to enabling them to sustain their everyday lives within their community (1). A primary goal of the provided care is to improve patients' quality of life (QoL) (2–6), which encompasses their perceptions of life circumstances within their cultural context, considering their aspirations, expectations, and concerns (7). However, beyond psychiatric clinical symptoms (3, 8–11), various sociodemographic, social, occupational, and financial factors may contribute to patients' QoL. For instance, studies have indicated that older age (12, 13), female gender (12, 14), relationship problems (11, 12), lower education levels (10, 13, 15), and unemployment (11, 13, 16–18) are associated with lower QoL in patients with mental illness.

However, the multitude of variables linked to QoL makes the research in this area fragmented and challenging to comprehend (19). While attempts have been made to propose models demonstrating the relationships between various variables and QoL (20–22), explicit models that effectively guide the understanding of how mental health service provision impacts QoL are still lacking. The relationship between mental health service provision and patients' perceived QoL is intricate and may not be adequately explained solely through simple correlations. Employing more complex modelling techniques, such as mediation analysis (23, 24), can help elucidate the complex relationships, where an intermediate (mediating) variable or factor may clarify the connection between the quality of mental health services and patients' perceived QoL.

Upon reviewing existing literature, it becomes evident that while numerous factors influence QoL, only a selected few have been thoroughly investigated as potential mediators impacting QoL. For instance, studies have delved into variables such as recovery (21, 25) and symptom severity (22, 25–27) but have yet to explore many others in depth. Within the scope of recovery, notable components encompass empowerment, agency, and hope (21, 25, 28). This emphasis on recovery has spurred a growing body of research over the past three decades, prompting mental health systems globally to advocate for recovery-oriented services. These services encourage active involvement and choice for individuals seeking treatment and support (29).

While the concept of recovery from mental illness traditionally involved symptom absence and restoration to a pre-illness state, the contemporary viewpoint extends beyond this notion. Modern perspectives emphasize personal growth and development, surpassing the adverse effects of mental illness to establish a fulfilling and meaningful life (30). Therefore, recovery encompasses more than mere symptom remission or a return to prior functioning levels. Interestingly, a meta-analysis of 20 articles highlights that individuals with schizophrenia can experience personal recovery despite persisting symptoms of psychosis (31). Consequently, recovery and symptom severity may function as partially independent markers of mental health status.

Building upon the findings of prior research, a conceptual model (Figure 1) has been proposed. According to this model, variables within mental health services can directly influence QoL or operate via mental health status variables that directly impact QoL. Additionally, sociodemographic variables directly influence QoL alongside patients' clinical diagnoses.

1.1 Aim

The aim is to examine the relationship between perceived mental health service provision and QoL among patients in psychiatric outpatient care.

2 Methods

2.1 Participants and procedure

The sample used in this study originated from 15 of totally 17 psychiatric outpatient clinics in three regions in central and southern Sweden (Region Kronoberg, Region Värmland, and Region Örebro län) including approximately 795,000 inhabitants. The clinics serve both the urban and the rural population. They are staffed by multi-professional teams. Patients with different mental illnesses can be admitted to the clinic by self-referral or by referral from other caregivers. A questionnaire containing five standardised instruments (described below) and questions concerning sociodemographic characteristics, diagnoses, and psychiatric treatments was distributed to the 15 outpatient clinics. Inclusion criteria for participants encompassed being 18 years of age or older, being able to understand and read Swedish, and cognitively able to answer the questionnaire. Patients eligible for participation were informed orally and in writing by a designated member of staff, who also ensured that the patients were able to answer the questionnaire in a valid way. Those who gave oral consent were asked to complete the questionnaire anonymously prior to leaving the clinic. A total of 706 questionnaires were returned; however, 333 questionnaires were discarded due to 15% or more missing items in any of the instruments included in the questionnaire. The final sample thus comprised 373 patient questionnaires. The patients were between 18 and 87 years old with a mean age of approximately 35 years. The majority of patients were women, had upper secondary education but only one in five patients was working. Characteristics of the study participants are shown in Table 1.

2.2 Measurements

2.2.1 Quality of life

The Swedish version (32) of the *Manchester Short Assessment of Quality of Life* (MANSA (33)) was used to assess the perceived QoL. The MANSA contains 12 items on global life satisfaction, job, financial situation, friendships, leisure activities, accommodation, personal safety, people that the person lives with, family and health. Items are scored on a 7-point scale from 1 (could not be worse) to 7 (could not be better). A higher score indicates perceived better QoL. The Swedish version has a satisfactory internal consistency with a Cronbach's alpha of 0.81 (32).

2.2.2 Mental health service provision

The *Quality in Psychiatric Care – Outpatient* (QPC-OP (34)) instrument was used to assess patients' perception of the quality of care. The QPC-OP consists of 30 items covering 8 dimensions: encounter (6 items), participation-empowerment (3 items), participation-information (5 items), discharge (3 items), support (4 items), environment (3 items), next of kin (2 items), and accessibility

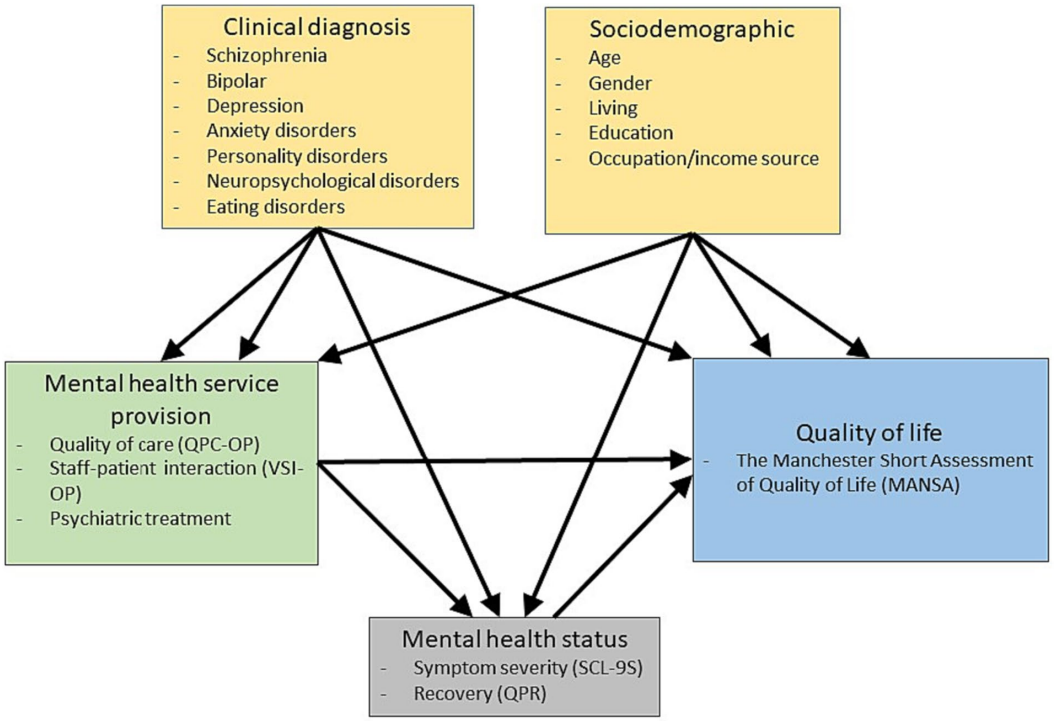

FIGURE 1
Conceptual model of mental healthcare service provision impact on patients' perception on quality of life.

(4 items). Each item begins with the wording "I experience that…" and is scored on a 4-point Likert-type scale from 1 (totally disagree) to 4 (totally agree) with a 'not applicable option.' A higher score represents perceived better quality of care. The QP-OP has an excellent internal consistency with a Cronbach's alpha of 0.95 (34).

The *Verbal and Social Interaction questionnaire for Psychiatric Outpatient Care* (VSI-OP (35)) was used to assess the patients' perceptions of the patient-staff relationship. The VSI-OP contains 17 items covering 3 dimensions: relationship (inviting the patient to establish a relationship, 6 items), interest (showing interest in the patients' feelings, experiences, and behaviour, 6 items) and helping (helping the patients to establish structure and routines in their everyday life, 5 items). The items are scored on 4-point Likert-type scales from 1 (not at all) to 4 (very high degree). A higher score reflects a perceived better patient-staff relationship. The internal consistency for VSI-OP is satisfactory, with a Cronbach's alpha of 0.81.

Psychiatric treatment. Patients were asked to report which psychiatric treatments they received from the outpatient clinic, e.g., pharmacological, electroconvulsive therapy, counselling, psychotherapy, and other psychiatric treatment. Patients could report having more than one treatment.

2.2.3 Mental health status

The *Symptom Checklist 9 short index* (SCL-9S (36)) was used to measure general psychological distress of patients. The SCL-9S is a unidimensional measure that comprises the nine items most indicative of each of the nine subscales of the Symptom Checklist-90-R (37). Each item is scored on a five-point Likert-type scale from 1 (not at all) to 5 (very much). The internal consistency for SCL-9S is satisfactory, with a Cronbach's alpha of 0.75 (36).

Questionnaire about the Process of Recovery (QPR). The Swedish 16-item one-factor version (28) of the original 22-item two-factor version (38) was used. Each item is scored using a five-point Likert-type scale from 1 (disagree strongly) to 5 (agree strongly). The Cronbach's alpha internal consistency of the QPR was excellent, with a Cronbach's alpha of 0.92 (28).

2.2.4 Sociodemographic characteristics

The following sociodemographic variables were used: age, gender, living with partner, education level, and occupation/income source.

2.2.5 Self-reported clinical diagnoses

The patients reported their diagnoses in free text on the questionnaire. The diagnoses were then categorised into eight categories: anxiety, bipolar, dependency disorder, depression, eating disorders, neuropsychological disorders, personality disorders, and schizophrenia. Patients could report having more than one diagnosis.

2.3 Data analysis

IBM SPSS 27 and AMOS 25.0 were used to analyse the data. The 333 questionnaires with 15% or more missing items were discarded prior to analysis. Imputation of missing values was performed for the remaining 373 questionnaires using the SPSS expectation-maximisation procedure. We used structural equation modelling to test the proposed model because of greater flexibility in model specification and estimation options, such as simultaneously testing the full model (24, 39). To examine direct and indirect associations we used bootstrapping because it does not make assumptions about

TABLE 1 Participant characteristics ($N = 373$).

Category	Variable	Frequency	%
Sociodemographic			
	Age (years)	35.1	12.87
	Gender		
	Woman	268	72%
	Man	105	28%
	Living		
	Alone	201	54%
	With partner	172	46%
	Education		
	Did not complete school	10	3%
	Compulsory school	59	16%
	Upper secondary school	234	63%
	Higher education	70	24%
	Occupation/income source		
	Work	86	23%
	Unemployed	25	7%
	Sick pay	118	32%
	Sickness compensation[b]	45	12%
	Activity compensation for reduced work capacity[c]	34	9%
	Retirement pension[d]	7	2%
	Student	33	9%
	Other	25	7%
Clinical diagnosis[a]			
	Anxiety disorders	110	30%
	Bipolar	39	11%
	Dependency disorder	2	1%
	Depression	83	22%
	Eating disorders	20	5%
	Neuropsychological disorders	90	24%
	Personality disorders	43	12%
	Schizophrenia	28	8%
	No diagnosis reported	90	24%
Mental health provision			
Treatment[a]			
	Pharmacological	306	82%
	ECT	25	7%
	Counselling	256	69%
	Psychotherapy	176	47%
	Other	78	21%
Previous visits			
	First time	11	3%
	1 time	13	4%
	2–5 times	57	15%
	6–10 times	71	19%
	>10 times	221	59%
		Mean	SD
Quality of care (1–4)			
	Encounter	3.58	0.61
	Participation: empowerment	3.12	0.78
	Participation: information	3.05	0.78
	Support	3.27	0.82
	Discharge	2.84	0.84
	Environment	3.38	0.66
	Next of kin	3.23	0.94
	Accessibility	2.82	0.83
Patient-staff interaction (1–4)			
	Establish relationship	3.50	0.62
	Showing interest	2.95	0.77
	Establish structure	2.24	0.94
Mental health outcomes			
Symptom severity (1–5)		2.48	0.76
Recovery (1–5)		3.33	0.71
Quality of life (1–7)		4.17	0.94

[a]Patients can have more than one diagnosis or psychiatric treatment. Thus, the per cent will not sum up to 100%.
[b]If the individual is between the ages of 19 and 64 and will never be able to work, now or in the future, due to sickness or a disability.
[c]If the individual is between 19 and 29 and cannot work for at least 1 year due to sickness or a disability.
[d]Individuals can apply for a retirement pension from the month they become 62 at the earliest.

the distribution of the variables, which circumvents deviations from multivariate normality (39).

Based on the conceptual model (Figure 1), we specified a testable model and analysed it stepwise. First, we tested the model for the association of variables in mental health care service provision with mental health status variables and QoL. We used an iterative process by deleting non-significant variables and modifying the model according to the modification indices until no more improvements could be made. Once the relationships were established, sociodemographic variables and clinical diagnoses were entered into the model to evaluate whether they still hold when adjusted for these variables.

Model adequacy was assessed with different fit indexes, including the chi-square test, the comparative fit index (CFI), the standardised root mean square residual (SRMR), and the root mean square error of approximation (RMSEA). A non-significant chi-square reflects agreement between the model and the data. CFI values ≥0.90 and ≥0.95 and SRMR and RMSEA values ≤0.08 and ≤0.05 were considered adequate and excellent levels of goodness of fit, respectively (23).

Differences between the goodness-of-fit indexes of the models were analysed to determine which model better fitted the data. Differences no greater than 0.01 between the CFI values (0.030 for the SRMR and 0.015 between the RMSEA values) were considered irrelevant when comparing the models (40). In such cases we chose the model that accomplished the desired level of explanation with as few parameters or predictor variables as possible.

3 Results

Twenty significant relationships were found after the iterative testing procedure (Table 2), and we reached a final mediation model (Table 3) that received excellent goodness of fit for all evaluated goodness-of-fit indices. The non-significant chi-square shows that the model did not deviate significantly from observed data. The R^2 indicates that the model explained 55% of the variance in quality of life, which was deemed adequate. Adjustment of the model with sociodemographic and diagnosis variables had a small and non-significant effect on the model fit ($\Delta\chi^2 = 17.04$ with a $\Delta df = 21$ giving a $p = 0.71$, a ΔRMSEA = 0.011, and a ΔCFI = 0.001), demonstrating that the associations between the variables in mental health service provision and QoL were not affected by the observed socioeconomic or diagnosis variables.

The final model indicated that the relationship between the variables in mental health service provision and the patient's perceived QoL is relatively complex. As shown in Figure 2, QoL was directly associated with six variables, whereas only one, participation information, was a service provision variable. Most service provision variables were mediated by the mental health status variables (symptom severity and recovery) mediating QoL. Among the quality-of-care variables, all but one were mediated by the discharge variable. Moreover, the patient-staff relationship, measured by the VSI, had an indirect association with QoL and a significant direct association with recovery. One treatment variable, psychotherapy, had a significant association with QoL, i.e., a mediated association via symptom severity and recovery, resulting in a total negative association with QoL.

Although sociodemographic and diagnosis variables had no significant effects on the model fit, some relationships with QoL were significant. Living with partner had a significant and direct positive association with QoL. For clinical diagnosis, bipolar disorder, schizophrenia, and anxiety had a significant positive association with QoL. Notably, the relationship between patients' anxiety and QoL was somewhat complex. Patients with anxiety were more likely than those with other diagnoses to receive psychotherapy. Those receiving psychotherapy (whether or not with anxiety) perceived slightly more severe symptoms and less QoL than those receiving other psychiatric treatments, resulting in a negative association between anxiety and QoL. In contrast, patients diagnosed with schizophrenia and bipolar disorders reported better QoL than patients with other diagnoses.

4 Discussion

This study examined the relationship between perceived mental health service provision and QoL among patients in psychiatric outpatient care. The final model achieved excellent goodness of fit, showing that variables in mental health service provision mainly had an indirect effect on patients' perceived QoL and that this effect was mediated by symptom severity and recovery.

This result is consistent with research indicating that service provision variables have a minor direct association with perceived QoL, suggesting that other factors beyond mental health care service are more impactful (5, 31, 40). Moreover, the results correspond to studies using complex mediator models. For instance, Fleury and colleagues (21) found that sociodemographic variables (gender and living) and clinical diagnosis variables (mood disorders and substance use disorders) were directly related to patients' perceived QoL but that only two of the service provision variables (service continuity and adequacy of help) were directly associated with QoL. Similarly, the present study shows that recovery serves as an important mediator but that symptom severity, which was not assessed by Fleury and colleagues (21), also acts as a mediator and has a similar magnitude of association with QoL, suggesting that both recovery and symptom severity have a vital role for patients' perceived QoL. However, in this study the association of symptom severity with QoL is primarily mediated by recovery, which correspond with findings by Saavedra and colleagues (24), suggesting that the symptom severity and QoL association may depend on the presence of recovery, which aligns with previous research (e.g., (30)). The present results thus suggest that symptom relief is unnecessary for recovery, but in relation to QoL, the absence of symptom relief will reduce recovery, resulting in a negative association with QoL. Hence, the model indicates that recovery would have less impact on patients' perceived QoL if there was no symptom relief.

Surprisingly, the discharge dimension was a mediator between most of the other service provision variables and recovery. It is not apparent why discharge has this role. However, visits to outpatient clinics are often intermittent and a regular discharge procedure does not always occur. Thus, the QPC-OP discharge dimension items are mainly about closure and the future. These aspects can be related to findings by Fleury and colleagues (21), who showed that recovery, which included elements found in patients' experience at discharge, was a mediating factor between service continuity and QoL. Discharge may thus be a significant event and a crucial component of the treatment process. As such, discharge is a creative process that can be customised to meet each patient's unique needs and comprehensively address them across multiple health systems in a continuous and coordinated manner (41). As mentioned above, the discharge process in outpatient care is less formal, and in this study, it was measured by questions including aspects of closure and the future. These questions encompass parts of the personal agency, an essential factor in understanding the 'service provision-recovery-quality of life' relationship (22).

From a clinical perspective, this finding raises questions about whether interventions in outpatient psychiatric care need to focus

TABLE 2 Standardised regression weights.

Predictor		Estimate	
Mental health service provision variables			
QPC Access	→	QPC Discharge	0.223***
QPC Next of kin	→	QPC Discharge	0.181***
QPC Support	→	QPC Discharge	0.122*
QPC Participation empowerment	→	QPC Discharge	0.154**
QPC Participation information	→	QPC Discharge	0.259***
QPC Participation information	→	Quality of life (MANSA)	0.062*
QPC Discharge	→	Symptom severity (SCL-9S)	−0.117*
QPC Discharge	→	Recovery (QPR)	0.204***
QPC Environment	→	Symptom severity (SCL-9S)	−0.143**
VSI Relationship	→	Recovery (QPR)	0.099*
Treatment: Psychotherapy	→	Symptom severity (SCL-9S)	0.169***
Mental health status variables			
Symptom severity (SCL-9S)	→	Recovery (QPR)	−0.529***
Symptom severity (SCL-9S)	→	Quality of life (MANSA)	−0.280***
Recovery (QPR)	→	Quality of life (MANSA)	0.499***
Sociodemographic and diagnosis variables			
Living	→	Quality of life (MANSA)	0.129***
Bipolar disorder	→	Quality of life (MANSA)	0.122***
Schizophrenia	→	Symptom severity (SCL-9S)	−0.101*
Schizophrenia	→	Quality of life (MANSA)	0.087*
Anxiety	→	Symptom severity (SCL-9S)	0.176***
Anxiety	→	Treatment: Psychotherapy	0.201***

Parameter estimate coefficients are standardised. QPC, The quality in psychiatric care – outpatient questionnaire; VSI, the verbal and social interaction questionnaire; SCL-9S, symptom checklist 9 short index; QPR, questionnaire about the process of recovery. *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$.

TABLE 3 Final mediation model of direct, indirect, and total effects on quality of life.

	Direct	Indirect	Total
Mental health service provision variables			
QPC Access		0.037***	0.037***
QPC Next of kin		0.030***	0.030***
QPC Support		0.020*	0.020*
QPC Environment		0.078**	0.078**
QPC Participation empowerment		0.025**	0.025**
QPC Discharge		0.165***	0.165***
QPC Participation information	0.062*	0.043*	0.105**
VSI Relationship		0.049*	0.049*
Treatment: Psychotherapy		−0.092***	−0.092***
Mental health status variables			
Symptom severity (SCL-9S)	−0.280***	−0.264***	−0.544***
Recovery (QPR)	0.499***		0.499***
Sociodemographic and diagnosis variables			
Living	0.129***		0.129***
Anxiety		−0.114***	−0.114***
Bipolar disorder	0.122***		0.122***
Schizophrenia	0.087**	0.073**	0.160**
Model fit			
Chi-square; degree of freedom; value of P	$\chi^2 = 49.502$; $df = 45$; $p = 0.230$		
RMSEA (90% CI)	0.020 (0.001; 0.042)		
CFI	0.997		
SRMR	0.024		
Model R^2	0.545		

Parameter estimate coefficients are standardised. RMSEA, root mean square error of approximation; CFI, comparative fit index; SRMR, standardised root mean squared residual; QPC, The quality in psychiatric care – outpatient questionnaire; VSI, the verbal and social interaction questionnaire; SCL-9S, symptom checklist 9 short index; QPR, questionnaire about the process of recovery. *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$.

more on agency rather than providing more support and that it is important to include questions about closure and the future from the start of the care process. Prospects encouraging hope can be positive for perceived QoL (42). The quality-of-service provision may also increase patients' capacity, allowing them to influence their future (43), potentially affecting their QoL. Our model aligns with the assumption that the experience of controlling and being able to master situations is an important recovery factor for developing a higher level of QoL. In this regard, our findings correspond with a holistic perspective on mental health service providers aiming to support recovery by focusing on both symptom reduction and increased well-being related to hope, self-esteem, social connectedness, and a sense of control of one's life (35–47). However, the current outcome on the role of the discharge dimension should be taken with caution until it has been replicated in independent studies. Further research is needed to clarify the link between the quality of the service provided and the patients' view of their future.

In addition to the discharge issues, the present results show that the patient-staff relationship, as measured by the VSI, may have an independent effect on recovery. Among the three elements of the patient-staff relationship measured by the VSI-OP, only *Inviting the patient to establish a relationship* had an association with QoL. This association was mediated entirely by recovery. In other words, the greater the patient-staff relationship, the greater

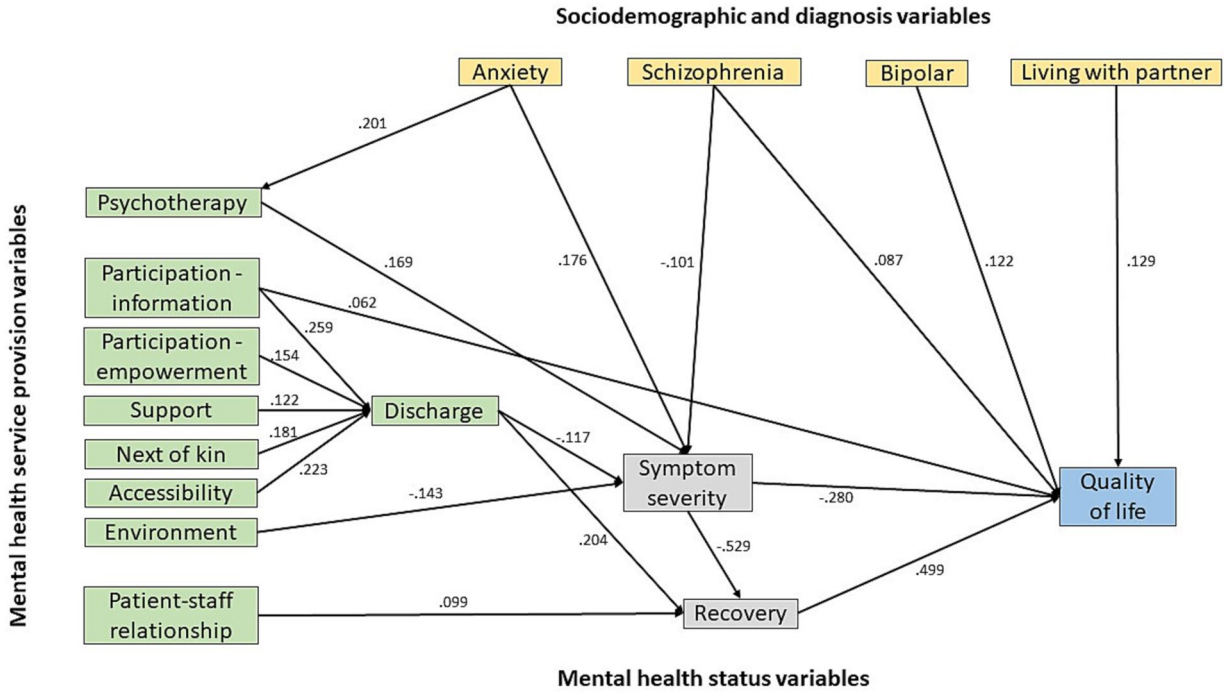

FIGURE 2
Final mediation model of the impact of mental health service provision on psychiatric outpatients' perception of quality of life. Coefficients are standardised.

the recovery and thus better QoL. A good patient-staff relationship has been noted as an important factor that can make a difference in recovery during an episode of mental illness, including involuntary admission (48). Using the VSI-OP, Rask and colleagues (35) showed that patients reported that *Inviting the patient to establish a relationship*, as well as, *Showing interest in patients' feelings, experiences, and behaviour* were rated as the most frequent actions performed by staff. In another study, using VSI for supported housing, the residents rated *inviting the patient to establish a relationship* as the most frequently performed and the most important facet of the patient-staff interaction (49). These findings confirm Green et al. (50), who reported that patients value a staff perceived as competent, caring, trustworthy, and trusting and that these factors were important for patient recovery. This position is in line with our findings that a positive patient-staff relationship, including staff showing interest in the patients' thoughts and experiences, is vital for patient recovery.

Concerning clinical diagnoses, schizophrenia and bipolar disorders were directly associated with QoL. The associations were positive, indicating that patients with schizophrenia and bipolar disorder perceived QoL better than patients with other mental diagnoses. In addition, schizophrenia was associated with less symptom severity, leading to a positive indirect association with QoL. This observation aligns with previous findings showing that patients with schizophrenia report higher self-reported QoL than patients with other mental disorders (51). However, our finding differed from the finding of Priebe et al. (51) that schizophrenia is associated with more severe reported symptoms.

Anxiety was not directly associated with QoL. Instead, the association between anxiety and QoL was mediated by psychotherapy and reported symptom severity, indicating that the relationship between anxiety and QoL is complex. Specifically, patients with anxiety reported receiving more psychotherapy compared to patients with other mental diagnoses and receiving psychotherapy was associated with reporting greater symptom severity, suggesting that patients with anxiety in ongoing psychotherapy also struggle with severe symptoms. This circumstance may thus explain why psychotherapy was associated with greater reported symptom severity.

Concerning the sociodemographic variables only one, living with a partner, was positively associated with QoL. Although associations between sociodemographic variables and QoL seem to depend on the study population, similar results have been demonstrated in studies on patients with schizophrenia (52).

4.1 Methodological considerations

The measurement of QoL in mental health services depends on the assessment instrument used. We chose the MANSA because it is an established and widely used instrument for QoL assessment in mental health practice and has good psychometric properties in Swedish patients who receive psychiatric outpatient services. Because QoL instruments may differ in definition and item content, results based on other tools may deviate from those we observed. Yet, our results are largely consistent with comparable results in studies using other QoL measures (e.g., (20, 21, 26)). In addition, the rigorous method of structural equation modelling made it possible to investigate the complex network of mediating variables and to model associations and hypothesised causal mechanisms between service provision and QoL.

This study has some limitations. First, the model hinges on the study variables. We have chosen variables based on previous research,

which does not rule out the possibility that other variables may have equal or better predictive values than those we chose. Second, as in any research involving recall, there exists the potential for the results to be influenced by recall bias. Nevertheless, in our study, patients complete the questionnaire immediately upon leaving the clinic. The short duration between their visit/consultation and answering the questionnaire significantly reduces the likelihood of substantial recall bias affecting the outcomes. Third, although the study included patients from several clinics in three regions in Sweden, the results may not be directly generalisable to other countries, especially those with different healthcare systems. Fourth, because the present data are cross-sectional, we cannot determine the temporal and causal relationships of the variables. This model must therefore be assessed in terms of the model matching the observed data, given that the model reflects an existing temporal/causal relationship. Thus, the results do not reflect actual causal relationships. Therefore, longitudinal or experimental studies should be performed to investigate the causality of the effects of mental health service provision on patients' QoL. In such an effort, the present study can thus be used to scrutinise potential causal relationships more closely.

5 Conclusion

The present study shows that patients' perception of mental health service provision is positively associated with their perceived QoL; however, this association is mostly indirect and mediated by reduced symptom severity and increased recovery. This finding can help design future interventions to enhance service provision and thus promote patients' QoL. Further studies are needed to capture a causal path to QoL.

Data availability statement

The datasets presented in this article are not readily available because of ethical restrictions. Requests to access the datasets should be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Swedish Ethical Review Authority. The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because the participants gave verbal informed consent to participate.

Author contributions

L-OL: Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. PR: Conceptualization, Writing – review & editing. MR: Conceptualization, Writing – review & editing. DB: Conceptualization, Writing – review & editing. TS: Conceptualization, Writing – review & editing. KG: Conceptualization, Writing – review & editing. IR: Conceptualization, Writing – review & editing. AS: Conceptualization, Funding acquisition, Writing – review & editing.

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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.

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Comparing depression, anxiety, and quality of life in individuals with cardiac and non-cardiac chest pain

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Background: Psychological factors are often overlooked as potential contributors to cardiovascular disease. This study aimed to investigate the relationship between depression, anxiety, and quality of life with chest pain origin.

Method: This cross-sectional study was performed from 2019 to 2020 and included participants from multiple medical centers across Shahrekord, Iran. Participants were recruited through advertisements in medical centers. Participants were divided into three groups: healthy control ($n = 67$), chest pain with cardiac origin (CCP) ($n = 70$), and chest pain with non-cardiac origin (NCCP) ($n = 73$). Data were collected using the Beck's Anxiety scale, Beck's Depression scale, and Short-Form Health Survey questionnaires. The chi-square, exact test, *t*-test, Kruskal–Wallis, and logistic regression models were used for statistical analysis. All analysis was performed using SPSS 26.

Results: The mean scores of depression and anxiety in the NCCP group (depression = 17.03 ± 11.93, anxiety = 17.18 ± 11.37) were significantly higher than those in the CCP (depression = 9.73 ± 5.76, anxiety = 8.77 ± 5.96) and healthy (depression = 7.00 ± 7.61, anxiety = 6.18 ± 7.63) groups ($p < 0.05$). The mean score of quality of life in the NCCP group (54.87 ± 12.66) was significantly lower than that in the CCP (76.31 ± 12.49) and healthy (80.94 ± 15.78) groups ($p < 0.05$). Patients with NCCP had higher odds of having depression (adjusted OR = 4.39, 95% CI: 1.25, 15.35) and lower odds for having mental quality of life scores than the CCP and health groups, respectively (adjusted OR = 0.90, 95% CI: 0.87, 0.94).

Conclusion: Our findings suggest that collaboration between psychiatrists and other specialists may be necessary to improve patients' health conditions and quality of life.

KEYWORDS

anxiety, cardiac, chest pain, depression, non-cardiac, quality

Introduction

Chest pain is one of the most common reasons for attendance at emergency medicine and cardiovascular clinics. The source of chest pain can be cardiac (coronary or non-coronary) and non-cardiac (1). Chest pain in a patient with known coronary artery disease indicates a new or unresolved medical or psychological problem (2). In people with non-cardiac chest pain (NCCP), no cardiac cause for chest pain is found (3). Pulmonary disorders, gastrointestinal disorders, osteoarthritis of the neck, and psychological factors are the most common causes of NCCP (4).

The prevalence of NCCP is up to 70%. NCCP may be diagnosed at all levels of the medical care system, including general practitioners, emergency departments, and chest pain and heart care units (5). Epidemiological studies in different countries such as Germany, Europe, the United States, China, and Australia show that the NCCP prevalence in patients with chest pain is reported to be between 20 and 40% (6). In the United States, cardiac chest pain (CCP) accounts for 38% of emergency department visits, and in only 13% of patients, acute coronary syndrome is identified as the cause of chest pain (7).

There are some evidence that mental health problems are common in patients with chest pain. Anxiety disorders (such as panic disorder and phobia), sleep problems, depressive disorders, poor quality of life (QOL), somatization, and alexithymia are common in patients with chest pain (8, 9). Psychological problems such as depression and anxiety not only have been associated with NCCP but also they are independent risk factors for coronary artery disease (CAD) (3, 10, 11). Furthermore, depression and anxiety can deteriorate the risk factors of CHD, consisting of smoking, high blood pressure, and hyperlipidemia (12, 13). Although 15 to 20% of patients with myocardial infarction were depressed for at least 6 months before the stroke, depression has not been considered in many of these patients (13).

In today's stressful life, one of the most common manifestations of anxiety and depression can be NCCP. Moreover, psychological problems can worsen the quality of life and sense of wellbeing among patients with either cardiac or non-cardiac chest pain. Numerous studies have examined anxiety, depression, and quality of life in diverse populations (14–17), but there is a lack of research specifically focusing on individuals with chest pain.

Due to the importance of this issue, in this study, we aimed to compare depression, anxiety, and quality of life in patients with chest pain (cardiac and non-cardiac) and healthy individuals referred to cardiac clinics. Studying the effects of chest pain on anxiety, depression, and quality of life in people will provide valuable insight into how chest pain affects individuals across different populations. This information can then be used to develop better treatments for those suffering from chest pain and its associated mental health issues.

Method

Design study and participant

This multi-center study examined the relationship between anxiety, depression, and quality of life in people with chest pain. This cross-sectional study was performed from 2019 to 2020 and included participants from multiple medical centers across Shahrekord, Iran. Participants were recruited through advertisements in medical centers. All participants had written consent to enter the study. The questionnaires were completed through face-to-face interviews.

The inclusion criteria for the study were adults aged over 45 years old. We considered adults aged 45 years for simple sample collection because ischemic heart diseases are more common in older people. The inclusion criteria for the NCCP and CCP groups were adults aged over 45 years old who have been diagnosed with chest pain and are currently receiving treatment for their condition. The exclusion criteria included musculoskeletal disorders, gastrointestinal disorders, gastroesophageal reflux disease, pulmonary disorders, heart valve disorders, neck osteoarthritis, and smoking (4, 6). At this stage, we used the restriction method, which is one of the ways to control confounders in the study design stage. We aimed to emphasize psychological factors as a probable causality for NCCP.

Subjects were in three groups: healthy, CCP, and NCCP. Individuals with chest pain (with and without cardiac origin) were selected with the approval of cardiologists and internists. Healthy individuals were recruited among patients referred for other reasons (without chest pain symptoms) based on the inclusion and exclusion criteria.

Sample size

Considering the Cohen medium effect size of 0.25 (18), three groups ($n_1 = n_2 = n_3$), 95% confidence level, and 90% power, the total sample size of the study was calculated as 207. G-Power software version 3.1.9.4 was used for this purpose. Finally, 210 individuals were included in the present study. The sampling method was convenient.

Instruments and variables

Data collection involved a survey administered to participants. The survey assessed anxiety, depression, and quality of life using validated scales. Beck's Depression Inventory (BDI) (19), Beck's Anxiety Inventory (BAI) (20), and the Short-Form Health Survey (SF-36) (21) were applied for data collection. Additionally, demographic information such as age, sex, and job were collected.

The BDI contains 21 items, a self-report rating inventory that measures characteristic attitudes and symptoms of depression. The BDI-II contains 21 items on a 4-point scale from 0 (symptom absent) to 3 (severe symptoms). Scoring is achieved by adding the highest ratings for all 21 items. The minimum score is 0, and the maximum score is 63. Higher scores indicate greater symptom severity. In this questionnaire, scores from 0 through 9 indicate no or minimal depression; scores from 10 through 18 indicate mild-to-moderate depression; scores from 19 through 29 indicate moderate-to-severe depression, and scores from 30 through 63 indicate severe depression (19).

The BAI consists of 21 items with a Likert scale ranging from 0 to 3 and raw scores ranging from 0 to 63. The BAI scores are classified as minimal anxiety (0 to 7), mild anxiety (8 to 15), moderate anxiety (16 to 25), and severe anxiety (30 to 63). Each item allows the patient four choices of no symptom to severe symptom. In each item, the patient is asked to report how she/he felt during the past week (20).

The SF-36 Health Survey is a general quality of life instrument that contains 36 questions. It considers the signs of perceived change in health-related quality of life over the past year. Each dimension was the score with a value range of 0–100. A higher score shows a better

quality of life. This questionnaire measures two general aspects: physical and mental. The validity and reliability of all questionnaires have already been confirmed in Iran (21–23).

Analysis

In descriptive analysis, mean, standard deviation (SD), frequency (n), and percentage (%) were used to summarize participant characteristics. The normality of age, depression, anxiety, and physical and mental quality of life was assessed using the Kolmogorov–Smirnov test. Non-parametric tests were used because of the non-normality of the data. In the analytical analysis, chi-square, exact test, t-test, Kruskal–Wallis with Tukey's HSD *post-hoc*, univariable logistic regression, and multivariable logistic regression were applied to examine the relationship between the source of pain and the psychological variables such as depression, anxiety, and quality of life.

We combined the CCP and healthy groups in logistic models as reference groups. Enter and backward approaches were applied in univariable and multivariable logistic regression models, respectively. We used Lemeshow's (2000) (24) strategy for assessing potential confounders and interaction forms. In the univariable models, variables with value of ps less or equal to 0.2 were entered into the multivariable model. We examined the interaction between pairs of included risk factors in the multivariable logistic regression model. A variance inflation factor (VIF) was used for checking multicollinearity, which measures the correlation and its strength between the predictor variables in a regression model. The VIF value was less than 10, which means there is no multicollinearity in the independent variables.

In logistic models, job, depression, and anxiety variables were considered binary due to the small sample size in some of their subgroups. The job variable was considered unemployed/housewife and employed, while the employed sub-variable was created from the sum of an employee, freelance job, farmer, worker, and other subscales. The depression and anxiety variables were considered no/mild, minimal/mild, and severe/moderate. All statistical analysis was conducted using SPSS software version 26. A p-value of <0.05 was considered statistically significant.

Ethics

Written informed consent was obtained from all the study participants. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1398.032).

Results

A total of 210 people participated in this study (67 persons were in the healthy group, 70 in the CCP group, and 73 in the NCCP group). In total, 61.9% of participants were women and unemployed/housewives (36.2%). The mean (SD) age of participants was 51.19 (± 6.14) years. Out of the total number of subjects, 4.8% had severe depression and 9% had anxiety. The mean ± SD score of quality of life in the physical and mental areas was 79.54 ± 12.94 and 70.33 ± 17.80, respectively (Table 1). According to chi-square analysis, there is a significant relationship between the pain origin and depression, anxiety, and physical and mental quality of life ($p < 0.05$). The status of demographic and psychological variables has been shown in Table 1.

Two-by-two groups of pain origin comparison based on the scores of depression, anxiety, and quality of physical and mental life can be seen in Table 2. The median score of depression and anxiety in the NCCP was higher than in the other groups ($p < 0.05$). These scores were higher in CCP compared with the health group ($p < 0.05$). The median score of physical and mental quality of life in the NCCP was much lower than the other two groups (health and CCP) ($p < 0.05$). This score was the highest in the healthy group.

The odds of moderate-to-severe depression and anxiety and quality of life status in the NCCP than CCP/health group are presented in Table 3. After controlling for other potential risk factors, we estimated that the NCCP group had more than four times higher odds of depression than the CCP/health group (adjusted OR = 4.39, 95% CI: 1.25, 15.35). The NCCP group had lower odds for better mental quality of life scores than the CCP group (adjusted OR = 0.90, 95% CI: 0.87, 0.94). We did not find any evidence that indicated the odds of severe or moderate anxiety had been increased in NCCP significantly. Furthermore, the NCCP group did not worsen the physical quality of life. None of the interaction forms entered into the multivariable model were significant. Moreover, there was no multicollinearity in the independent variables.

Discussion

In the present study, patients with NCCP had a higher chance of having moderate-to-severe depression and a lower quality of life than CCP or healthy people. The median score of depression and anxiety in people with NCCP was higher than in patients with CCP. These scores were higher in CCP compared to the control group.

In line with our study, a study in İzmir, Turkey, between 2015 and 2018 on patients aged 13–18 with unexplained chest pain showed that there was a significant association between unexplained chest pain with depression and impaired emotions (25). In Southeast Sweden, patients with NCCP and a history of cardiovascular disease (CD), compared to patients without CD had a poorer health-related quality of life (3). These results are similar to the present study, in which people with NCCP are associated with lower quality of life scores. Our findings are similar to those of Alkhatatbeh et al., who observed that anxiety and depression scores were higher in subjects with NCCP than healthy controls (26).

In contrast with the present study, a study in Hong Kong and Wuhan from 2004 to 2005 reported that the quality of life and psychological impact in patients with NCCP were not different from CCP (27). In another study conducted in Niš, Serbia, although the patients with NCCP had no associated psychiatric disorder, coronary patients were more depressed and hostile (28). These results may be due to differences in the study population and the questionnaires used.

People with NCCP may worry about the origin of symptoms. They may attribute their chest pain not only to the heart but also to other diagnoses, which can further lessen their quality of life (3). Anxiety and depression were supposed to be possible causes of NCCP (26). The coexistence of psychological disorders with NCCP (a pathophysiological mechanism) is very important (29). Some psychopharmacological treatments have been suggested to manage NCCP (30). Patients suffering from NCCP may have obsessional thoughts about the disease. They tend

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TABLE 1 Status of demographic variables in healthy, CCP[a], and NCCP[b] groups ($n = 210$).

Variables	Total *N* (%)	Healthy ($n = 67$) *N* (%)	Chest pain ($n = 140$)		*p*-value
			CCP ($n = 70$)	NCCP ($n = 73$)	
Age [year (mean ± SD)] Median (IQR)	51.19 ± 6.14 49 (4)	50.52 ± 5.68 49 (4)	50.97 ± 6.20 49 (3.5)	52.00 ± 6.47 49 (4.5)	0.317[c]
Sex					
Female	130 (61.9)	44 (65.7)	44 (62.9)	42 (57.5)	0.600[d]
Male	80 (38.1)	23 (34.3)	26 (37.1)	31 (42.5)	
Job					
Worker	7 (3.3)	0 (0)	5 (7.1)	2 (2.7)	0.202[e]
Farmer	6 (2.9)	1 (1.5)	4 (5.7)	1 (1.4)	
Freelance job	36 (17.2)	10 (14.9)	11 (15.7)	15 (20.5)	
Employee	61 (29.0)	23 (34.3)	16 (22.9)	22 (30.1)	
Unemployed/housewife	76 (36.2)	25 (37.3)	29 (41.4)	22 (30.1)	
Others	24 (11.4)	8 (11.9)	5 (7.1)	11 (15.1)	
Depression					
No	149 (71.0)	63 (91.0)	57 (81.5)	31 (42.5)	<0.001[e]
Mild	30 (14.2)	3 (4.5)	11 (15.7)	16 (21.9)	
Moderate	21 (10.0)	3 (4.5)	1 (1.4)	17 (23.3)	
Severe	10 (4.8)	0 (0.0)	1 (1.4)	9 (12.3)	
Anxiety					
Minimal	101 (48.1)	50 (74.6)	32 (45.7)	101 (48.1)	<0.001[d]
Mild	56 (26.7)	11 (16.4)	29 (41.4)	56 (26.7)	
Moderate	34 (16.2)	3 (4.5)	8 (11.4)	34 (16.2)	
Severe	19 (9.0)	3 (4.5)	1 (1.4)	19 (9.0)	
Quality of life					
Physical	79.54 ± 12.94	87.06 ± 10.30	80.10 ± 13.32	72.08 ± 10.45	<0.001[c]
Mental health	70.33 ± 17.80	80.94 ± 15.78	76.31 ± 12.49	54.87 ± 12.66	

[a]CCP, cardiac chest pain.
[b]NCCP, non-cardiac chest pain.
[c]Kruskal–Wallis test *p*-value.
[d]Chi-square *p*-value.
[e]Exact test *p*-value.

TABLE 2 A two-by-two comparison of healthy, CCP[a], and NCCP[b] groups according to psychological variables ($n = 210$).

Variables	Total Mean ± SD Median (IQR: Q3-Q1)	Healthy ($n = 67$) Mean ± SD Median (IQR: Q3-Q1)	Chest pain ($n = 140$)		*p*-value[c] (CCP & NCCP)	*p*-value[c] (CCP & Healthy)	*p*-value[c] (NCCP & Healthy)
			CCP ($n = 70$) Mean ± SD Median (IQR)	NCCP ($n = 73$) Mean ± SD Median (IQR)			
Depression	11.40 ± 9.39 9.00 (15.00–5.00)	7.00 ± 7.61 6.00 (10.00–3.00)	9.73 ± 5.76 9.00 (12.25–6.00)	17.03 ± 11.93 16.00 (23.00–9.00)	<0.001	0.023	<0.001
Anxiety	10.87 ± 9.85 8.00 (16.00–3.75)	6.18 ± 7.63 4 (8.00–2.00)	8.77 ± 5.96 8.00 (12.00–4.00)	17.18 ± 11.37 18.00 (24.00–7.00)	<0.001	0.009	<0.001
Quality of life (Physical)	79.54 ± 12.94 83.12 (89.37–72.50)	87.06 ± 10.30 90.00 (93.75–85.62)	80.10 ± 13.32 84.06 (87.65–77.81)	72.08 ± 10.45 73.12 (77.50–69.68)	<0.001	<0.001	<0.001
Quality of life (Mental)	70.33 ± 17.80 73.97 (85.40–55.05)	80.94 ± 15.78 87.87 (91.00–74.41)	76.31 ± 12.49 80.93 (84.75–71.34)	54.87 ± 12.66 54.66 (60.81–46.54)	0.022	<0.001	<0.001

[a]CCP, cardiac chest pain.
[b]NCCP, non-cardiac chest pain.
[c]Kruskal Wallis test (post-hoc: LSD).

TABLE 3 Univariable and multivariable logistic regression for assessing the association between pain source (NCCP[b] and CCP[a] or healthy) with demographic variables, depression, anxiety, and quality of life ($n = 210$).

Variables	Univariable		Multivariable	
	OR (95% CI)	*p*-value	AOR (95% CI)	*p*-value
Age (year)	1.03 (0.98, 1.08)	0.163*	1.04 (0.97, 1.10)	0.213
Sex				
Female	0.75 (0.42, 1.34)	0.342	–	–
Male	1	1	–	–
Job				
Unemployed/housewife	0.66 (0.36, 1.21)	0.184*	0.56 (0.24, 1.32)	0.190
Employed	1	1	1	1
Depression				
Severe/moderate	14.06 (5.30, 40.23)	<0.001*	4.39 (1.25, 15.35)	0.020**
No/mild	1	1	1	1
Anxiety				
Severe/moderate	8.83 (4.35, 17.88)	<0.001*	1.83 (0.71, 4.66)	0.205
Minimal/mild	1	1	1	1
Quality of life				
Physical	0.92 (0.89, 0.95)	<0.001*	1.02 (0.98, 1.07)	0.272
Mental health	0.90 (0.87, 0.92)	<0.001*	0.90 (0.87, 0.94)	<0.001**

[a]CCP, cardiac chest pain.
[b]NCCP, non-cardiac chest pain.
*Variables with a *p*-value of ≤ 0.2 and entered into the multivariable model.
** Statistical significance: *p*-value < 0.05.

to have disastrous interpretations of their bodily sensations. Therefore, psychological treatments can help them (31).

Some limitations of the current study are the convenient sampling method and the focus on people over 45 years old. We had to use the conventional method to select healthy and chest pain groups. One of the other limitations was self-report which is subject to recall bias and potential inaccuracies in participants' responses. The study was conducted in Shahrekord, Iran, which may restrict the generalizability of the findings to other populations or geographic locations.

The NCCP group had higher depression and anxiety and lower quality of life scores compared to the CCP and healthy groups. NCCP people had a higher chance for higher depression and lower mental quality of life. CCP participants had higher depression and anxiety scores and lower quality of life compared to healthy individuals. Therefore, it seems the cooperation of psychiatrists with other specialists is necessary to enhance patients' health conditions and quality of life.

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 humans were approved by the study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Shahrekord University of Medical Sciences (IR.SKUMS.REC.1398.032). The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin.

Author contributions

EZ: Conceptualization, Writing – original draft, Validation. ZS: Data curation, Investigation, Writing – review & editing. SK: Formal analysis, Methodology, Software, Writing – original draft. ST: Formal analysis, Methodology, Software, Writing – original draft, Conceptualization, Funding acquisition, Writing – review & editing.

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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.

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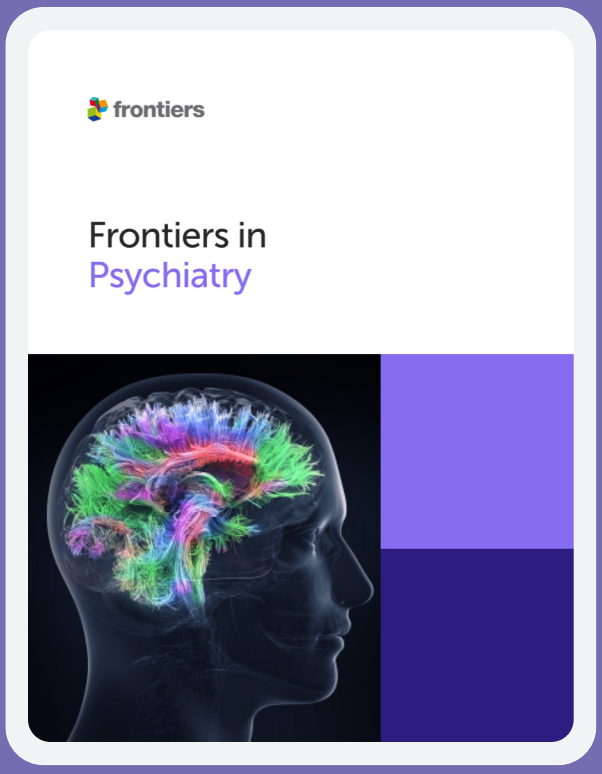

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