Trajectories of Comorbidity between Chronic Physical Illnesses and Mental Health Disorders: a Retrospective Study of an urban population in South China

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Abstract

Background: As yet the mechanisms that might drive such comorbidity between chronic physical illnesses and mental health disorders have not been fully clarified. Consequently, no effective prevention strategies been developed and put in place to reduce risk of complex co-morbidity trajectories.

Objective: A clearer understanding of underlying aetio-pathogenic complexity that exists between chronic physical illness and mental health offers an opportunity for improving clinical care of both long-term health conditions and social wellbeing.

Methods: In this retrospective study of mental health disorders in people living in the southern region of Guangdong, China, we have conducted an comprehensive analysis on the risk of comorbidity and constructed time-dependent trajectories between chronic physical illnesses and mental health disorders.

Results: In this study, electronic health records containing F codes (ICD) from cases over a period of 7 years were included. This contained 268,588 hospital admissions and discharges for 46,649 patients. 26,572 trajectories containing four diagnoses and approximate time duration intervals were identified. In addition, We analyzed the trajectory progression patterns in patient groups of different age groups and gender. These trajectories involved mainly one or more of the three categories of cerebrovascular diseases, organic mental disorders, neurotic stress related and somatoform diseases.

Conclusions: This study identified both the differences and commonalities in the disease trajectory and progression patterns of patient groups stratified by age and gender. This provided valuable insight and a preliminary basis for developing early prevention and control strategies of chronic physical illnesses and mental health disorders.

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Original Paper

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Keywords: Chronic physical illness; Mental health disorders; Comorbidity analysis; Disease trajectory

Introduction

According to the 2022 World Health Organisation (WHO) report, approximately one billion people worldwide are currently suffering from mental health problems [1]. Our social environment has changed dramatically in the aftermath of the COVID-19 pandemic and the global burden of disease for mental disorders has increased. Cases of major depressive disorder and anxiety disorder have risen by 28% and 26% respectively [1-4]. Mental health has been a neglected area of public health for decades and the WHO are calling for a change in the global mental health landscape [5]. Mental health disorders have not only a significant impact on the mental health of a patient, but patients also often suffer from serious chronic physical illnesses. These may include diabetes, chronic kidney disease, and cardiovascular disease along with other conditions.

In China, the lifetime weighted-prevalence of six types of mental disorders, excluding dementia in old age, is 16.6%. Thus, one in seven people develop at least one mental disorder during their lifetime [6]. According to the China Mental Health Survey, the lifetime prevalence of adult depressive disorders in China is currently 6.8%, of which 3.4% have depression. In China there are currently 95 million people suffering from depression, and approximately 280,000 people commit suicide each year of which forty per cent suffer from depression [7]. Following China's rapid economic and social development, the incidence of psychological and behavioral problems and the prevalence of mental disorders amongst children and adolescents have been gradually increasing. According to one survey about Chinese children and adolescents, the prevalence of mental disorders in the Chinese school population, between the ages of 6 and 16 years, was 17.5%. While, the proportion of adolescents who had received appropriate diagnosis and treatment was less than 20% [4, 8].

The widespread use of electronic health records (EHRs) and clinical registries has accelerated the collection of large-scale longitudinal patient health information. This has laid important foundations for performing large-scale data analyses that can reveal insight and temporal patterns of disease association that was previously impossible [9, 10]. Temporal interval sequencing of disease events has, as yet not been widely performed in large EPR data sets or in other clinical registries. Examination of the temporal dimensions and relationships of comorbidity development can reveal both subtle and complex patterns of comorbidity along with their characteristic interrelationships. This can as facilitate a deeper study of the trajectories of mental health disorders and their risk relationships with physical illness [11-13]. We have applied such approaches to large longitudinal data sets relating to the southern region of Guangdong, China. This focused on patients with mental health disorders over a 7-year period (2016 to 2022). As most complications associated with mental health disorders develop within a few years, these records both guide early prevention providing decisions and guidance and also examine the trajectory of comorbidity that leads to mental health disorders.

Early identification of patients at risk for developing mental health disorders can help prevent or delay the progression of mental health disorders, through allowing patients to make lifestyle changes or receive earlier treatment/intervention. Many risk identification models for early-stage patients with mental health disorders are widely used in clinical settings. However, most are based on studies of mental health disorders based on are analyses of one or limited comorbidity patterns. Thus, they do not consider comorbidity in terms of time-dependency or examine the trajectory of the disease within large-scale datasets. Furthermore, they primarily examine a particular type of mental health disorder over trajectories that lack a comprehensive approach [14-19]. For example, Jeong et al. developed a diagnostic progression network based on Health Insurance claims data with the aim of identifying global diagnostic patterns in Korea

[14]. However, the network only provided information on associations between diagnostic pairs and not on disease sequence trajectories. By incorporating temporal factors into co-morbidity studies and through the analysis of timelines of patients' disease episodes (i.e., disease history vectors) it is possible to predict such disease progression through time, potentially facilitating early prevention and treatment of other co-morbidities. Jensen et al pioneered the analysis of a large-scale dataset for a comprehensive set of disease trajectories [15]. Using data from an electronic health registry covering the entire Danish population, they proposed a discovery-driven approach for the analysis of temporal progression patterns of various disorders. This encompassed both some organic disorders and psychiatric / behavioural disorders as a result of psychoactive substance use. Their analysis of trajectory clusters also revealed the diseases at the core of the trajectory progression [15]. Jeong et al. also constructed clinical trajectories for Type 2 diabetes and underlying time-dependence based on Korean population health insurance claims data. This provided insight into key temporal associations between Type 2 diabetes and other diseases and identified differences in progression patterns across age and gender groups [16]. Few similar studies have been conducted and most of the trajectories identified are based on either cross-sectional studies or on healthcare records from developed countries. Predictive risk models for diseases such as for some cancers based on one specific population are often less useful or inappropriate for other populations. Thus, risk models looking at relationships between physical and mental health in one population may not be applicable to a Chinese population. This could be due to a variety of reasons including external and social environments, level and approach of healthcare, ethnicity, and socio-economics.

To address this, we have conducted a retrospective study of all patients who were admitted to hospital for mental health disorders in a city based in the southern region of Guangdong, China. The aim was to construct time-related trajectories of mental health disorders based on the analysis of their comorbidity with chronic physical illnesses, taking into account time-dependence and direction of association. We have also analysed the patterns of trajectory progression in patient groups of different ages and gender. These trajectories will help to explain the temporal correlation between mental health disorders and chronic physical illnesses.

Methods

Data source

Longitudinal electronic health record database of patients with a diagnosis of mental health disorders and living in the southern region of Guangdong, China were available for study. These data were restricted to the study period of January 1st 2016 to December 31st 2022. These data were derived from patient discharge reports collected from a number of hospitals in the area. Longitudinal clinical data were available for each hospital patient and each discharge report contained the patient's identity, age, date of consultation and discharge, primary diagnosis code and up to 15 secondary diagnosis codes. All disease diagnoses were classified using ICD-10 (International Classification of Diseases, 10th Revision) codes. A total of 102,409 individuals diagnosed with mental health disorders and admitted to inpatient care between 2016-2022, were included in this study. After excluding missing data (such as chronic medical history, time, and patient information), a total of 268,588 admission and discharge records containing 46,649 patients were combined with duplicate admission and discharge records. To exclude repeat admissions for the same diagnosis, we used only the first admission record for each diagnosis for each patient.

Disease selection

Diagnostic codes in clinical records used ICD-10, but as there are over 20,000 unique and active diagnostic codes in this coding format, it was impractical to analyse every ICD diagnostic code. To address this challenge, we processed the codes in the form of four-digit ICD-10 codes, which filtered and classified the codes into two categories: chronic physical illnesses and mental health disorders. Based on the existing literature, we performed prevalence statistics for the 60 chronic illnesses proposed elsewhere [20]. We selected chronic physical illnesses with a need for hospital admission prevalence of greater than or equal to 1% [10] (ICD-10 codes for illnesses that do not begin with an F) for inclusion in the examination. The prevalence of mental health disorders observed in the hospitals was also used as a basis for determining which conditions should be included and examined [11]. The age-sex information of patients with mental health disorders and the prevalence of mental health disorders are shown in Table 1. In total, forty-one chronic physical illnesses and eight mental health disorders were included in the study. These are summarised in Supplement.

Table 1 Age, gender and clinical breakdown of patients with mental health disorders

Sex	Total Number：46649	Average Age：62.1
Female	22313	

Male		24336 (52.17%)		
Age	Number (%.)	Average Age (yrs)	Female	Male
0-18	2835 (6.08%)	8.6	868	1967
18-45	12732 (27.29%)	35.0	4836	7896
45-60	9632 (20.64%)	54.3	5270	4362
60-80	13764 (29.51%)	70.9	7483	6281
80-	7686 (16.48%)	87.3	3856	3830

Diagnosis of major mental health disorders	**Disease Name**	**Number/ Prevalence** 45859 (98.31%)
F00-F09	Organic Mental Disorders	12273 (26.31%)
F10-F19	Mental and Behavioral Disorders Due to Psychoactive Substance Use	1094 (2.35%)
F20, F22, F24, F25, F28	Schizophrenia and Delusional Diseases	14634 (31.37%)
F30-F34, F38, F39	Depression and Mood Diseases	3601 (7.72%)
F40-F45, F48	Neurotic Stress Related and Somatoform Diseases	15877 (34.04%)
F50	Eating Disorders	82 (0.18%)
F51.0-F51.3	Sleep Disorders_F	612 (1.31%)
F60	Specific Personality Disorders	29 (0.06%)
F70-F79	Mental Retardation	3431 (7.35%)
F84	Pervasive Developmental Disorders	622 (1.33%)
F90-F98	Behavioral and Emotional Disorders with Onset Usually Occurring in Childhood and Adolescence	229 (0.49%)

Analysis of comorbidity networks

In the network analysis, we represented the ‘in-and-out’ records as a two-part graph whose nodes can be divided into two non-interacting subsets (patients and diseases). Modelling the patient and comorbidity relationship was used to describe the relationship between patients and diseases [17-19]. This was denoted by G = (u, v), where G denotes the generated undirected bi-partite graph, u denotes the set of patient nodes, v denotes the set of disease nodes, and when there exists an edge between a patient node and a disease node, it means that the patient has been diagnosed with this disease. A comorbidity network for representing the relationship between diseases was determined by applying a one-sided projection to the bi-partite graph G. Through this process, only the relationships between diseases are displayed. If two diseases are connected by at least one common patient node in the original bi-partite graph, there will be an edge between these two disease nodes in the comorbidity network indicating that there may be interactions and connections between them. At the same time, we then delete the network and only retain comorbidity combinations with more than 10 common patients to address any bias due to small sample size.

We evaluated the combinations of comorbidities associated with mental health disorders in the comorbidity network by considering the strength of their associations and their temporal ordering [10]. Using schizophrenia and diabetes as an example, we conducted a case-control study of patients with schizophrenia to determine the association between schizophrenia and diabetes. This was assessed by generating a 2 × 2 table (as shown in Figure 1A) and determining a relative risk / ratio ratios to measure the strength of the association [16]. Relative Risk (RR), Odds Ratio (OR) and their associated p-values were calculated by using the Fisher exact test with Bonferroni correction. RR and OR were used to quantify the correlation between two variables, with larger values of OR or RR indicating a larger effect of the exposure and greater strength of the association between exposure and outcome.

Disease pairs with corrected p-value < 0.001, RR > 1.2 and OR > 1 were considered significant [16, 21, 22], while disease pairs possessing significant temporal order and strength of association were stored for subsequent trajectory exploration.

Trajectory of comorbidity

Trajectories were derived from multiple combinations of comorbidities in chronological order. Again, we describe the comorbidity combination of schizophrenia → diabetes as an example of how we assessed their trajectories. To assess common temporal comorbidity trajectories shaped as D1 → D2 → D3 → D4, we refer to previously published methods [15, 16, 23] that combine disease pairs with significant directions into longer comorbidity trajectories of at least 3 consecutive diseases. The significance of the D1 → D2 trajectory was determined by comparing the D1 and non-D1 groups, and then we newly defined the groups with and without D2 after diagnosis of D1 as the case and control groups, respectively, and used these groups to test the significance of the D1 → D2 → D3 trajectory. In addition, we included the ORs of disease pairs in the examination at the same time, and used the same p-values, relative risks, and ratios throughout the analyses and applied the Fisher exact test with Bonferroni correction. To extract the trajectory of D1 → D2 → D3 → D4, we selected a group of patients who were diagnosed in the order of D2 and D3 after the diagnosis of D1 as a case group, and another group of patients who were diagnosed with D2 but not D3 after the diagnosis of D1 as a control group (as shown in Figure 1A). Finally, we counted the mean intervals (in days) and the number of patients in each chain for each of the four long trajectories.

To describe the overall comorbidity trajectories of patients with mental health disorders we split the four long trajectories into directed edges with weights; the nodes represent diagnostic categories (represented by rectangular boxes with different colours, and the size of the rectangular boxes indicates the prevalence rate of the disease in the group), the directed edges represent the direction of the chain between the two diseases. Edge colour indicates diagnostic intervals, with red and blue indicating shorter intervals (<211 days) and longer intervals (>211 days), respectively. The thickness of the edges is related to the number of patients between the two diseases, with the more patients included, the thicker the edges. Only trajectories with mean risk estimates ranking in the top thirty were considered to reduce the complexity of the graph. As an example, the trajectory of organic mental disorder → schizophrenia and delusional diseases → diabetes → heart failure is shown in Fig. 1B. The average interval and number of transfers for each segment are labelled.

Age and gender are potential factors affecting patients' health [10, 24, 25]. Given the current high prevalence of mental health disorders in our school-age population (6-16 years) [6, 7], we extended the age range of patients in our examination. To study age- and gender-related differences in the trajectories of comorbidity, we divided the data into 10 groups of patients by gender and by age (0-18, 18-45, 45-60, 60-80, and 80-).

Results

Analysis of Comorbidity Networks and Combinations

In Figure 2, we show an undirected comorbidity network which contains 49 nodes and 1124 edges. The width of the edges represents the number of co-morbidities of the two diseases, from which we can find a direct correlation with mental health disorders. We analysed the temporal order and strength of the associations, which revealed disease pairs with significant directional associations between physical and mental health disorders. Disease pairs with significant associations with mental health disorders are summarised in Table 2.

Some chronic physical illnesses had a higher frequency of un-directional significance after mental health disorders episodes were diagnosed, e.g. mental health and behavioral disorders due to psychoactive substance use → hypertension (RR=1.35 OR=1.41, N=171). A number of chronic physical illnesses had a high significance before mental health disorders were diagnosed; these included dyslipidemia → organic mental health disorders (RR=1.40, OR=1.49, N=2088), other metabolic diseases → schizophrenia and delusional diseases (RR=2.08, OR =2.18, N=928) and ear nose and throat diseases → organic mental disorders (RR=1.40, OR=1.49, N=803) amongst others. A number of other disorders were also identified that may precede or follow mental health conditions and these will require further investigation.

Table 2 Comorbidity combinations with significant directionality in the comorbidity network (all with p-value < 0.001, RR > 1.2, OR > 1 and number of comorbidities >= 100)

Disease Pair	RR	OR	N
Mental And Behavioral Disorders Due to Psychoactive Substance Use → Hypertension	1.35	1.42	171
Other Metabolic Diseases → Schizophrenia and Delusional Diseases	2.09	2.18	928
Other Respiratory Diseases → Mental and Behavioral Disorders Due to Psychoactive Substance Use	2.02	2.04	116
Other Cardiovascular Diseases → SLEEP DISORDERS_F	1.99	1.99	111
Heart Failure → SLEEP DISORDERS_F	1.76	1.77	109
Thyroid Diseases → Schizophrenia and Delusional Diseases	1.72	1.78	124
Dyslipidemia → Mental and Behavioral Disorders Due to Psychoactive Substance Use	1.48	1.48	136
Dyslipidemia → Organic Mental Disorders	1.40	1.49	2088
Ear Nose and Throat Diseases → Organic Mental Disorders	1.40	1.49	803
Other Metabolic Diseases → Mental Retardation	1.37	1.38	244

Development patterns of trajectories

To determine statistically significant temporal correlations between pairs of diagnoses, we also conducted a retrospective cohort study. From the complete dataset of patients with mental health disorders, we identified 1124 disease pairs. After excluding disease pairs unrelated to mental health disorders, a total of 305 distinct disease pairs containing mental health disorders were identified. Of these 305 disease pairs associated with mental health disorders, we performed a significant direction test to identify the specific order of onset of diseases (i.e. D1 and D2). Overall we identified 123 of these pairs with the D2 vs. D1 onset intervals within a 5-year time frame, as being significantly orientated and associated (RR>1.2, OR>1, Bonferroni-corrected p-value < 0.001, and number of transfers >10),. Using the same criteria, we identified 2,294 significant trajectories containing 3 diagnoses (D1 → D2 → D3) and finally 26,572 trajectories containing 4 diagnoses (D1 → D2 → D3 → D4).

To test the reliability of the trajectories observed, we counted the prevalence of each disease and the number of transfers between diseases, as well as calculating the RR and OR between diseases. In the trajectories we obtained, the relative risks between transferred diseases all exceeded 1.2, and the mean of the relative risks for the trajectories containing the four diagnoses exceeded 1.8. The trajectories other metabolic diseases → organic mental disorders → cataract and other lens diseases → other eye diseases had the highest mean relative risks. Hypertension → neurotic stress related and somatoform diseases were more common (number of transfers = 5,253).

The 30 trajectories with the highest average relative risk, are shown in Figure 3. In these trajectories, 'co-evolution' is the consecutive development of mental health disorders, which consists of one diagnosis before the diagnosis of another mental health disorders and two progressions after. The first diagnosis belongs to a chronic physical illness and is dominated by thyroid diseases, cardiac valve diseases and atrial fibrillation. The second one belongs to the mental health disorders and has the highest frequencies of organic mental disorders and neurotic stress related and somatoform diseases. The mean interval from diagnosis 1 to diagnosis 2 was relatively long (376.1 days). The mean intervals from diagnosis 2 to diagnosis 3 and from diagnosis 3 to diagnosis 4 were progressively shorter (276.9 and 62.2 days respectively). Hypertension, cataract and other lens diseases, and ischemic heart disease were the most common disease categories for the third diagnosis, acting as a bridge to the fourth diagnosis. The fourth diagnosis was highest for cerebrovascular disease and other eye diseases. In addition, we found that the trajectories observed mainly around cerebrovascular diseases, organic mental disorders, neurotic stress-related and somatoform diseases (referred to as central diseases), reflected the high risk of these three categories amongst the group of patients with mental health disorders.

Trajectory Development Model by Gender and Age Grouping

The complete dataset was further divided into 10 groups and analysed by sex and age to explore differences in trajectory progression patterns and extract significant trajectories in each group. Due to there being a lower prevalence of chronic physical illnesses and mental health disorders at younger ages, comorbidity trajectories were not extracted in the group of patients aged 0-18 years that included four diagnoses. The top 30 trajectories with the highest average relative risk for each group are shown in Figure 4.

Significant differences in the pattern of trajectory development between age-groups-genders were observed. The trajectory networks of the 45-60 years range female and 60-80 years range male patient groups were relatively dense, with a greater variety of disease diagnoses, the presence of more trajectory development patterns, and a higher number of transfers between diseases than in the other age-sex groups. Comparison of gender through the trajectory network identified variations, as shown in Table 3. Eight trajectory networks were all centred on one or more of cerebrovascular disease, organic mental disorders and neurotic stress related and somatoform disease. This suggested that at least one of these three groups of chronic physical illnesses is at high risk across the age-sex patient population range.

Table 3 Central diseases in patient groups stratified by age and sex

Patient group	Central disease (>10 occurrences in each trajectory)
Male patient group aged 18-45 years	Esophagus Stomach and Duodenum Diseases
	Neurotic Stress Related and Somatoform Diseases
	Other Metabolic Diseases
	Dyslipidemia
Female patient group aged 18-45 years	Esophagus Stomach and Duodenum Diseases
	Neurotic Stress Related and Somatoform Diseases
Male patient group aged 45-60 years	Neurotic Stress Related and Somatoform Diseases
	Cerebrovascular Disease
	Organic Mental Disorders
	Hypertension
	Ischemic Heart Disease
	Heart Failure
Female patient group aged 45-60 years	Neurotic Stress Related and Somatoform Diseases
	Cerebrovascular Disease
	Ischemic Heart Disease
	Dorsopathies
Male patient group aged 60-80 years	Cerebrovascular Disease
	Organic Mental Disorders
	Neurotic Stress Related and Somatoform Diseases
	Hypertension
Female patient group aged 60-80 years	Cerebrovascular Disease
	Neurotic Stress Related and Somatoform Diseases
	Hypertension
	Organic Mental Disorders
Male patient group	Organic Mental Disorders

aged 80- years	Cerebrovascular Disease
	Hypertension
Female patient group aged 80- years	Cerebrovascular Disease
	Neurotic Stress Related and Somatoform Diseases
	Hypertension
	Organic Mental Disorders

Discussion

In this study, we analysed time dependence and risk between mental health disorders and chronic physical illnesses by retrospectively examining the case histories of patients with mental health disorders. We constructed trajectories and visualised their progression patterns. Furthermore, we reconstructed trajectories by assembling patient groups according to age group and sex, and comparatively analysed what effect these had on trajectory progression. More trajectory progression patterns were present in the 45-60 years old female and 60-80 years old male patient groups, which confirms subjective clinical opinion. To the best of our knowledge, this is the first analysis of comorbidity trajectory reported between chronic physical and mental health conditions based on real-world longitudinal electronic health record data rather than self-reported survey data. Furthermore, we have analysed trajectory variability across different age-gender patient groups.

Consistent with previous studies, our study, focusing on network analysis, found that mental health disorders are associated with chronic physical illnesses and have complex interactions [11, 26-28]. We found that the trajectory of mental health disorders tends to encompass many somatic chronic conditions with a high intensity of comorbidity with mental illness, and that these comorbidities are consistent with previously published findings [11, 26, 29]. This finding validates the existence of a comorbidity relationship between somatic chronic diseases and mental health disorders, on which we further validate the temporal dependence of this comorbidity relationship by constructing comorbidity trajectories. In addition, our trajectories include a number of co-morbidities not previously recognised as common to mental health disorders. For example, some of the trajectories include spinal and musculoskeletal disorders, which, although some studies have suggested a relationship between back pain and mental health disorders, they are not considered as common comorbidities of mental health disorders and the specific mechanisms of comorbidity need to be further investigated in the clinical setting [30, 31]. At the same time, we found central diseases in the trajectories (cerebrovascular diseases, organic (including symptomatic) mental disorders and neurological-related somatic diseases) around which the trajectory network evolves, reflecting the high prevalence of these three diseases among patients with mental health disorders. In addition, there is also a trend in the literature that refers to the study of co-morbidity between body, mind and brain disorders.

Comorbidity between chronic physical illnesses and mental health disorders affects people of all ages, even hospitalised children and adolescents (age <= 18 years). Consistent with most of the previous studies related to comorbidity [10, 24, 32], we found variability in the trajectories of groups of patients of different age-gender, with different age-gender leading to significant variability in trajectories in terms of the central disease and comorbidity. For example, the trajectory network of the 18-45 years old group of patients was centred around esophagus stomach and duodenum diseases and neurotic stress related and somatoform diseases, whereas the trajectory network of the 60+ year old group of patients was centred around organic mental disorders, cerebrovascular disease, and hypertension, which may suggest that mental health disorders are caused by negative events and emotional stress in the younger age group of patients, while in the older age group of patients the mental health disorders are caused by organic lesions in the brain.

In addition, previous studies have shown a high prevalence of schizophrenia and delusional diseases, depression and mood diseases, and diabetes and asthma in children and adolescents due to genetic predisposition, lifestyle, diet and sleep, lack of space for activities, and academic stress [33-36]. Our findings suggest that the co-prevention of specific mental health disorders and chronic physical illnesses should be emphasised in specific age groups, especially in children and adolescents, as mental health problems in children and adolescents that are not attended to and intervened in a timely manner not only affect their physical and mental development, their learning and their social functioning, but also extend into adulthood and have life-long effects.

The main strengths of this study can be summarised as follows. Firstly, it is the first regional study to assess the trajectory of comorbidity between chronic physical illnesses and mental health disorders based on the medical record homepage, identifying chronic physical illnesses that are closely related to the onset of mental health disorders, and analysing the temporal sequencing of their development and the risk of developing them, as well as their differences in age and gender.

Secondly, the trajectories we propose can indicate the relative order of development between chronic physical illnesses and mental health disorders, which can provide the necessary decision support for the early prevention of mental health disorders and their related diseases. Furthermore, the method can be extended to other healthcare datasets to analyse the development of comorbidity trajectories.

There are a number of limitations to this study which should be considered. One limitation lies in our inability to access individual-level influences such as socioeconomic status, lifestyle, clinical data and treatments, which play a key role in understanding differences between trajectories of comorbidity. Secondly, because recording diseases in clinical data may lead to incomplete diagnosis, this study used medical data from a real-world situation. As clinical management data, the medical record homepage may be affected by a variety of biasing factors, such as the impact of the health insurance payment system reform and the performance evaluation of public hospitals, which may lead to bias in the completion of diagnostic information by doctors. Furthermore, there may be differences in the records between different doctors and at different points in time, which may lead to missing or inaccurate information. Thirdly, we only included diseases with a prevalence of hospitalisation greater than or equal to 1% within this group in our examination. Additionally, the patients studied were mainly part of a regional group in China, which is a single source of data, and the specific development of the trajectory of comorbidity and the analysis of the risk need further clinical verification. Fourthly, the intervals of the trajectories we proposed were obtained from the medical record homepage, which has some limitations and cannot be used to determine the exact time of comorbidity transfer simply based on the records. In addition, we used data spanning the period from 2020 to October 2022, when the COVID-19 occurred, and hospitalisations for co-morbidities were inevitably affected by the outbreak.

In the future, we plan to conduct a multi-centre study on chronic physical illnesses and mental health disorders across different geographic regions, and on the basis of a large-scale dataset, we are committed to integrating data from multiple sources, including lifestyle and socio-economic status, to build a more comprehensive and accurate assessment model to further elaborate the development of comorbidity trajectories and risk between chronic physical illnesses and mental health disorders. In addition, we plan to refine the trajectory development model among child and adolescent patient groups.

Conclusion

This regional study in China focuses on the comorbidity between chronic physical illnesses and mental health disorders and their sequencing. We established a trajectory of comorbidity between chronic physical illnesses and mental health disorders, and clarified the trajectory progression pattern of mental health disorders. At the same time, we grouped patient populations of different ages and genders and analysed the differences in the trajectory development patterns of each group. The findings suggest that differential measures based on patient age and gender are needed in clinical prevention and care management to achieve early prevention and treatment of the disease and to further reduce the burden associated with the disease.

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Author contributions:

L.L. organized and cleaned disease diagnosis datasets, as well as conceptualized and designed work, and drafted manuscripts. T.L. performed the literature investigation, experiments and data analysis, paper writing. W.O. contributed to analysis of experimental results and papers writing. Y.P. contributed to research methods, result analysis, and paper writing. C.C. designed research, improved methods and manuscript. Y.L. reviewed the draft of the paper, drafted and improved the manuscript.

All authors have revised and approved the final manuscript.

Competing interests:

The authors declare no competing interests.

Data availability:

Due to ethical limitations and potential risks of exposing patient privacy, the dataset during the current study period has not been fully disclosed. The author can be contacted for any needs, and all relevant data can be provided upon request and after appropriate ethical review. The processed anonymized data is provided with the article.

Code availability:

All data analyses and visualizations were conducted in Python v. 3.8. The key algorithm has been described in the literature.

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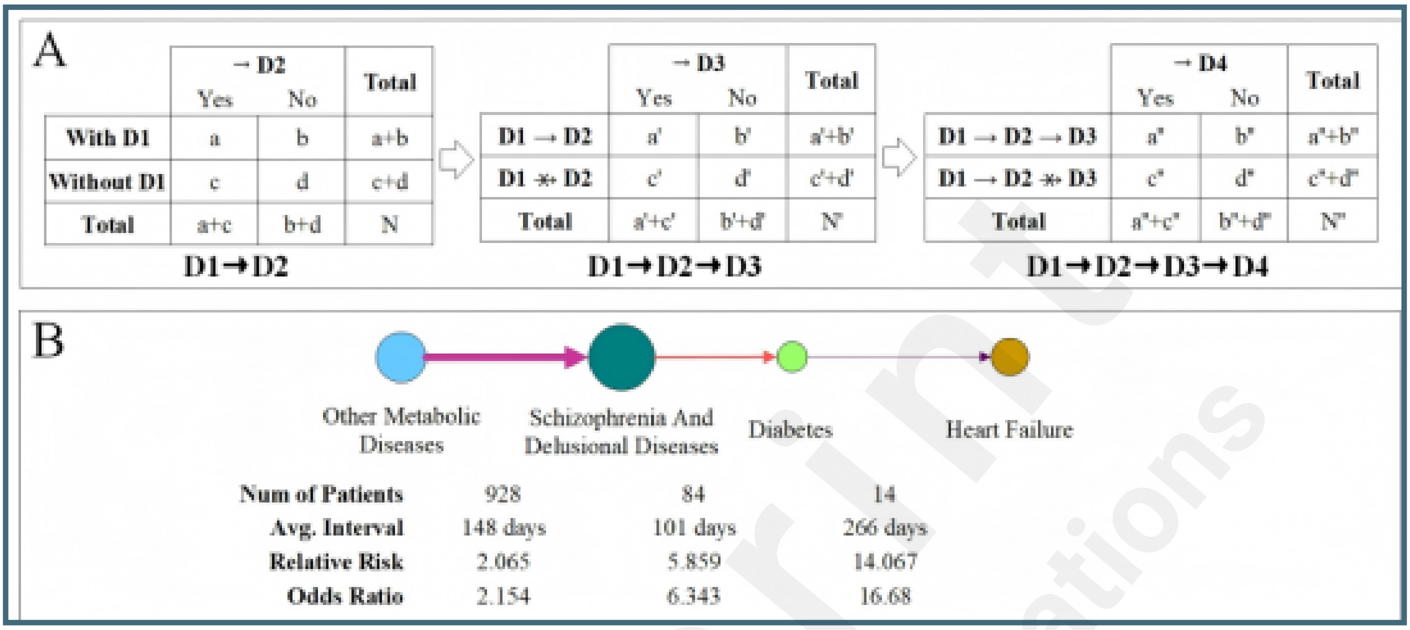
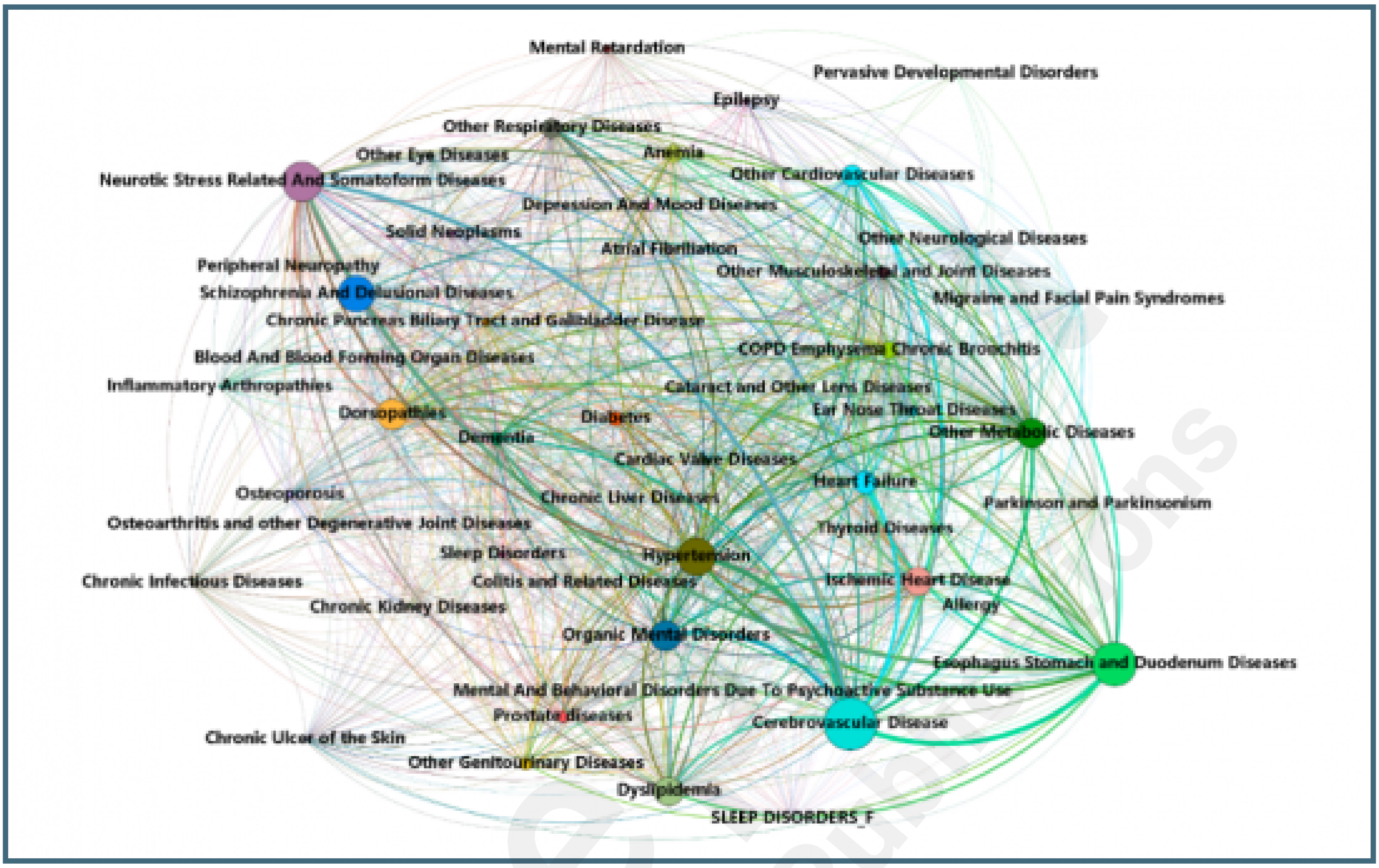
Supplementary Files

Figures

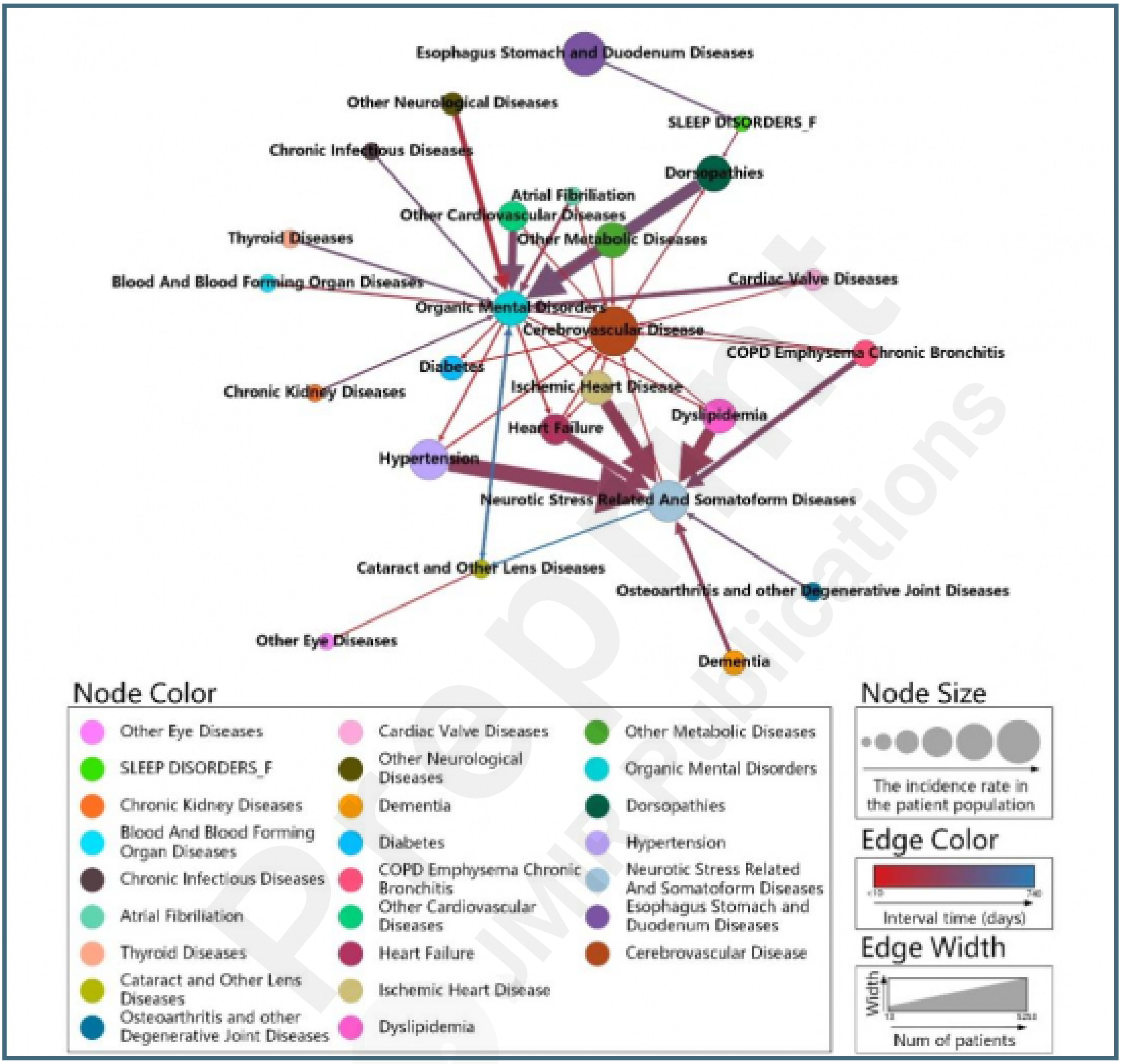
Flowchart for constructing comorbidity trajectories. (A) Identification of trajectories containing four types of diseases based on the definition of different case and control groups. (B) Using an example of a trajectory containing schizophrenia and diabetes mellitus, the number of patients, mean interval, RR, and OR were calculated for each segment.



Undirected network for comorbidity (Nodes represent diseases, represented in different colors. The size of the node represents the prevalence of the disease. The weight of edges and diseases is proportional, indicating the number of patients between them.).



Visualisation of the top 30 trajectories with the highest average risk across the patient population.



Visualisation of the top 30 trajectories with the highest average risk in each patient group after grouping by age-sex (A) Age 18-45yrs male (B) Age 18-45yrs female (C) Age 45-60 yrs male (D) Age 45-60 yrs female (E) Age 60-80 yrs male (F) Age 60-80 yrs female (G) Age >80yrs male (H) Age >80yrs female.