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Stomach disease as a terminal node in comorbidity networks among middle-aged and older adults: An integrated analysis of network topology and risk factors

Linya Lyu, Wei Fu*, Fang Dai, Jinji Huang, and Guobin Cheng

Department of Gastroenterology, The 925th Hospital of PLA Joint Logistics Support Force, Guiyang, Guizhou, China

Abstract

Background: Stomach disease is highly prevalent among middle-aged and older adults and often coexists with other chronic conditions, yet its comorbidity patterns remain unclear. This cross-sectional study aimed to construct a comorbidity network for stomach disease and identify its key associated factors using data from the China Health and Retirement Longitudinal Study (CHARLS, 2008–2020). **Methods:** A total of 19,541 participants were included. Data on 18 demographic variables and 14 chronic diseases were collected. Disease network analysis, extended Bayesian information criterion graphical least absolute shrinkage and selection operator (LASSO), the LASSO regression, and logistic regression were employed to examine network topology and factors associated with stomach disease. **Results:** A total of 19,541 unique participants were included. Among them, 26.17% (5,114/19,541) had stomach disease. Disease network analysis and regression analysis revealed significant, stable relationships among the included diseases. Nine diseases, including arthritis, dyslipidemia, and heart disease, were identified as independent factors associated with stomach disease. Among demographic characteristics, nine indicators, such as age, male sex, and current alcohol consumption, were independently associated with stomach disease ($p < 0.05$). **Conclusion:** Our study reveals that stomach disease in middle-aged and older adults primarily functions as a "terminal" phenomenon. It is statistically associated with core diseases within the network. Stomach disease is independently associated with multiple chronic conditions, such as arthritis, heart disease, and liver diseases, as well as factors like rural residence. These associations should be interpreted as statistical correlations rather than causal relationships, given the cross-sectional design. **Relevance for patients:** Stomach disease in older adults often reflects broader chronic disease burdens, warranting holistic rather than symptom-only management.

Keywords: Stomach disease; Middle-aged and older adults; CHARLS; Disease network analysis

***Corresponding author:**
Wei Fu
(fmmufw@foxmail.com)

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1. Introduction

The prevalence of stomach disease among middle-aged and older adults remains persistently high. This poses a significant public health burden.[1,2] This population often

suffers from multiple chronic conditions simultaneously. This reflects a widespread phenomenon of multimorbidity.[3] Traditional research methods on comorbidities primarily rely on constructing logit models or comparing the composition of disease types.[4,5] However, such approaches fall short of revealing the complex interactive networks among multiple diseases. In recent years, comorbidity network analysis has emerged as a novel, systematic perspective. It enables the visualization of the overall association patterns among diseases. It also helps identify central hub diseases within the network.[6] Nevertheless, studies specifically applying this approach to explore the comorbidity patterns of stomach disease in middle-aged and older adults remain scarce. The precise topological position of stomach disease within complex comorbidity networks and its interrelationships with other chronic conditions remain unclear. Therefore, based on the nationally representative longitudinal China Health and Retirement Longitudinal Study (CHARLS) database, this study aims to systematically construct a comorbidity network of chronic diseases among middle-aged and older adults. We focus on analyzing the characteristics and position of stomach disease within this network. We further identify its independent associated factors. This study is expected to provide new insights into the pathogenesis of stomach disease. It also offers a scientific basis for developing targeted, comprehensive prevention and management strategies.

2. Methods

2.1. Study population and design

This study utilized data from the CHARLS. CHARLS is a nationally representative longitudinal survey targeting individuals aged 45 and above in China.[7] The CHARLS project was approved by the Biomedical Ethics Committee of Peking University (Ethics Approval No.: IRB00001052-11015). All participants provided written informed consent.

Data from six waves of the CHARLS survey (2008, 2011, 2013, 2015, 2018, and 2020) were included. To maximize the sample size, a cross-sectional analytical approach was adopted. Leveraging the unique participant IDs in the CHARLS database, each ID was included only once. This ensured no duplication. A total of 25,874 unique individuals were included in the analysis (Figure 1). For participants diagnosed with stomach disease, only concurrent information from the same survey wave was used. For those who were never diagnosed with stomach disease in the available records, data from their most recent survey wave were included.

Participants with missing data on gastroduodenal disease status (n = 537) were first excluded. Subsequently, based on the completeness of the 32 variables considered in this study (including age, waist circumference, etc.), an additional 5,796 participants were excluded for missing data. The final analytical sample comprised 19,541 participants.

2.2. Definition of gastrointestinal disease

Identification of stomach disease was based on responses to the health status and functioning questionnaires in the 2008–2020 CHARLS. Participants were asked whether a doctor had ever diagnosed them with a gastrointestinal disease. According to the CHARLS instrument, digestive diseases are referred to as chronic conditions requiring medical management. These included gastritis, gastric/duodenal ulcers, inflammatory bowel disease, liver cirrhosis, and functional gastrointestinal disorders—excluding tumors or cancers. Those answering "Yes" were classified as having stomach disease. The surveys were administered by trained interviewers using standardized questionnaires aligned with international aging research protocols. This self-reported, doctor-diagnosed approach is a well-established method for assessing chronic disease prevalence in older populations. It has been widely adopted in large-scale epidemiological studies. However, this definition aggregates several clinically distinct conditions (e.g., gastritis, peptic ulcers, functional dyspepsia) into a single binary outcome. Such heterogeneity may introduce misclassification and limit the clinical interpretability of the findings.[8] A binary stomach disease variable (yes/no) was used for all subsequent analyses.

2.3. Ascertainment of other diseases

In accordance with the CHARLS user manual and with reference to literature[8], all diseases were ascertained based on participants' responses to the question "Have you been diagnosed by a doctor with the following diseases?" with assistance from the interviewers. The diseases assessed included 13 conditions: arthritis, asthma, cancer, diabetes, dyslipidemia, heart disease, hypertension, kidney disease, liver disease, lung disease, memory-related disorder, mental illness, and stroke. Considering that disability can significantly impact overall health status, it was also included in the comorbidity network analysis.

2.4. Demographic characteristics

A total of 18 demographic characteristics potentially associated with stomach disease were included in the analysis, based on data extracted from the CHARLS questionnaire. These variables were: age, body mass index (BMI), current alcohol drinking, current smoking,

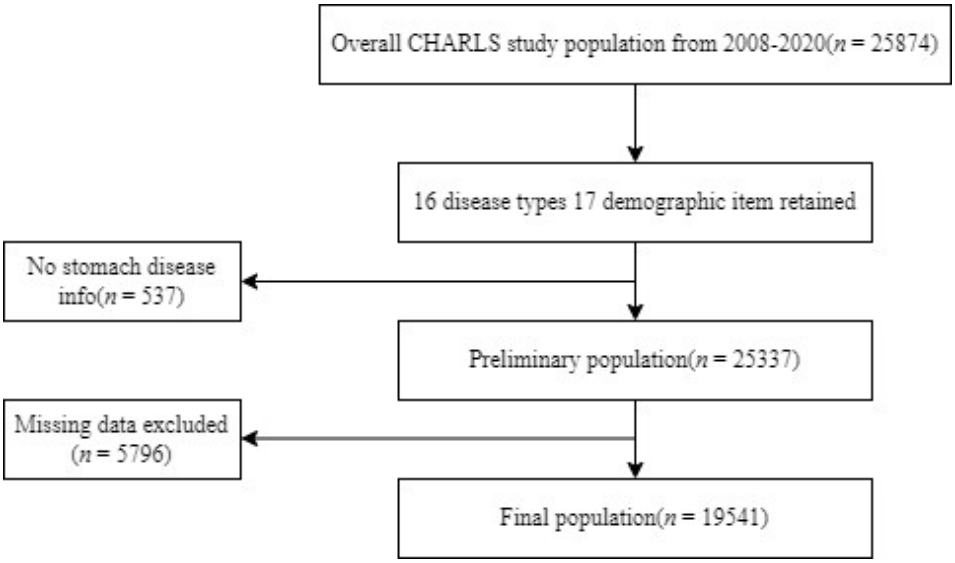

Figure 1. Sample selection flowchart
Abbreviation: CHARLS: China Health and Retirement Longitudinal Study.

education level, exercise habits, gender, Han ethnicity, enrollment in endowment insurance, history of hip fracture, marital status, enrollment in medical insurance, past alcohol drinking, place of residence (urban/rural), history of past falls, retirement status, access to running water, and waist circumference. Given the conceptual overlap between "past alcohol consumption and smoking status" and "current alcohol consumption and smoking status," these potentially overlapping variables were separately retained during the least absolute shrinkage and selection operator (LASSO) selection process to avoid presumptive exclusion.

2.5. Statistical analysis

All statistical analyses were performed using R software (version 4.5.2, R Foundation for Statistical Computing, Austria) within the RStudio environment. For data with less than 5% missingness per variable (overall 4.2%), complete-case analysis was used for primary analyses. Sensitivity analyses included multiple imputation (five datasets via mice), the missing-indicator method, and worst-case scenario analysis, all supporting the robustness of primary findings.

A comorbidity network was constructed from regularized partial correlations using the Extended Bayesian Information Criterion Graphical LASSO method to model conditional dependencies among chronic diseases after controlling for all other conditions. The initial correlation matrix was computed using qgraph::cor_auto() for mixed data types, followed by regularization ($\gamma = 0.5$) to enhance network sparsity and interpretability. Centrality measures—strength, betweenness, and closeness—were calculated from the weighted network using the igraph package to identify hub diseases. Network stability was assessed via nonparametric bootstrap analysis (n = 2,500) using the bootnet package. Co-occurrence strength between diseases was quantified using the Jaccard index and visualized in a multimorbidity network.

Network topology metrics were computed as follows: clustering coefficient (weighted transitivity), average path length (inverse of edge weights), network density, and small-world index compared to 100 random networks. The specific calculation formula is included in the Appendix.[9]

Modeling strategy: To identify factors associated with stomach disease, we employed a two-step approach: (i) variable selection via LASSO regression with 10-fold cross-validation (glmnet package, λ.1se criterion); (ii) multivariable logistic regression with selected variables to estimate adjusted odds ratios. This two-stage strategy addresses two key issues. First, given the multiple chronic disease variables and potential collinearity, LASSO's L1 regularization provides stable, efficient variable selection from high-dimensional data, overcoming limitations of traditional stepwise methods. Second, since inference based directly on LASSO coefficients can be biased, we fit a standard logistic model with the selected variables to obtain robust odds ratio estimates and valid confidence intervals, separating variable selection from formal inference. This methodology is supported by studies advocating LASSO-based screening for high-dimensional data.[10] The final

model included all variables selected by LASSO at the optimal λ (i.e., λ.1se) without further stepwise elimination, ensuring transparency in predictor inclusion.

All visualizations were created using the ggplot2 package. A two-sided p-value < 0.05 was considered statistically significant.

3. Results

3.1. Sample characteristics

Table 1 presents the sociodemographic characteristics of the 19,541 study participants. Among them, 61.6% (12,044/19,541) were diagnosed with two or more coexisting chronic conditions. The study population was predominantly female (53.24%, 10,405/19,541), Han Chinese (81.7%, 15,968/19,541) individuals residing in rural areas (60.7%, 11,852/19,541). The vast majority were covered by endowment insurance (89.2%, 17,440/19,541) and various forms of medical insurance (94.0%, 18,378/19,541). The majority reported healthy lifestyle behaviors: 66.2% (12,934/19,541) were non-smokers at the time of the survey, and 90.9% (17,770/19,541) reported engaging in regular exercise.

3.2. Results of comorbidity network analysis in middle-aged and older adults

The comorbidity network analysis of all diseases among the study participants revealed that chronic conditions in middle-aged and older adults form a tightly connected and efficient small-world network (clustering coefficient: 0.593, average path length: 0.07, network density: 0.495, small-world index: 25.384). Mental illness, hypertension, and liver disease were identified as central hubs within the network. They exhibited extensive connections and dominated disease associations. In contrast, although stomach disease widely coexisted with multiple other conditions, it primarily functioned as a "terminal" node rather than a hub in the network. This pattern suggests that its occurrence is significantly associated with core diseases. The identified network structure and the determination of core hubs have been validated through stability testing, confirming their reliability.

To evaluate the stability of the comorbidity network, we employed a nonparametric bootstrap approach (n = 2,500 bootstrap samples). As shown in Figure 2, the average edge weights calculated from the bootstrap samples (bootstrap mean) were observed to be closely aligned with the edge weights estimated from the original sample (sample). This indicates that the network structure constructed in this study is highly stable, and the disease associations observed within the network are robust and reliable.

The stability assessment of centrality metrics (Figure 3) demonstrated that strength centrality and closeness centrality exhibited excellent stability. The average correlation coefficients with the original sample remained above 0.95 and 0.75, respectively, even when up to 50% of cases were excluded. In contrast, betweenness centrality showed relatively poor stability, indicating its higher sensitivity to sample fluctuations. Therefore, we have high confidence in the identification of core diseases (such as heart disease and liver disease) based on strength and closeness centrality. The specific values of betweenness centrality, however, should be interpreted only as indicative of trends.

Heart disease, hypertension, and liver disease served as central hubs in the comorbidity network among middle-aged and older adults. They demonstrated high values in strength, betweenness, and closeness centrality (Figure 4, Table A1). In contrast, although stomach disease showed relatively high strength centrality—indicating direct comorbidity relationships with multiple other diseases—its extremely low betweenness centrality suggests that it does not serve as a critical bridge between disease communities. This pattern indicates that stomach disease is more likely to function as a "terminal" node in the comorbidity network, being statistically associated with core diseases rather than serving as a hub that drives the network structure.

Figure 5 depicts the disease co-occurrence network constructed based on CHARLS data. As shown, the chronic diseases form a tightly interconnected network structure. Node color represents the disease category. Node size corresponds to disease prevalence. Edge thickness indicates the strength of comorbidity associations. The network can be broadly divided into two main communities: "cardiometabolic and cerebrovascular" and "neuropsychiatric." Within this structure, mental illness and hypertension occupy central positions. They exhibit extensive connections with multiple disease categories, highlighting their pivotal hub roles in the comorbidity network. Of particular note, stomach disease shows direct and strong statistical associations with both mental illness and liver disease. This provides important visual clues for exploring the mechanisms of comorbidity.

3.3. Least absolute shrinkage and selection operator analysis of factors influencing stomach disease

To identify the independent factors influencing stomach disease, we first incorporated demographic characteristics and comorbidities. Each variable was appropriately coded: (i) Stomach disease, arthritis, asthma, cancer, currently drinking, currently smoking, diabetes, disability, dyslipidemia, Han ethnicity, having endowment insurance,

Table 1. Sample characteristics (*n* = 19,541)

Characteristics	Value
Age, mean (SD)	60.5 (10.02)
Waist circumference, mean (SD)	85.6 (11.27)
Body mass index, mean (SD)	26.19 (3.74)
Male, *n* (%)	9,136 (46.8)
Han ethnicity, *n* (%)	15,968 (81.7)
Retired, *n* (%)	3,599 (18.4)
Rural residence, *n* (%)	11,852 (60.7)
Married, *n* (%)	17,023 (87.1)
Past smoking, *n* (%)	8,677 (44.4)
Past alcohol consumption, *n* (%)	10,055 (51.5)
Currently smoking, *n* (%)	6,607 (33.8)
Currently drinking, *n* (%)	11,080 (56.7)
With endowment insurance, *n* (%)	17,440 (89.2)
Access to running water, *n* (%)	17,318 (88.6)
Past falls, *n* (%)	5,976 (30.6)
Educational attainment, *n* (%)	
Below primary school	8,249 (42.2)
Primary school	5,369 (27.5)
Middle school	3,783 (19.4)
High school and above	2,140 (11.0)
Exercise habits, *n* (%)	
No exercise	1,771 (9.1)
Light exercise	5,455 (27.9)
Moderate exercise	6,074 (31.1)
Heavy exercise	6,241 (31.9)
Number of comorbidities, *n* (%)	
0	3,179 (16.3)
1	4,318 (22.1)
2	4,223 (21.6)
3	3,159 (16.2)
≥4	4,662 (23.9)
Medical insurance, *n* (%)	
No insurance	1,163 (6.0)
Urban employee medical insurance	2,423 (12.4)
Urban and rural residents' medical insurance	157 (0.8)
Urban resident medical insurance	768 (3.9)
New rural cooperative medical insurance	14,847 (76.0)
Public medical care	158 (0.8)
Other medical insurance types	25 (0.1)

Abbreviation: SD: Standard deviation.

heart disease, hip fractures, hypertension, kidney disease, liver disease, lung disease, memory disorder, mental illness, past alcohol consumption, prior falls, retirement status, stroke history, and access to running water (1 = yes, 0 = no); (ii) Age, BMI, waist circumference (actual value); (iii) Gender (1 = male, 0 = female); (iv) Marriage (1 = married, 0 = others); (v) Place of residence (1 = village, 0 = city); (vi) Education (0 = below primary school, 1 = primary school, 2 = middle school, 3 = high school and above); (vii) Exercise habits (0= no exercise, 1 = light exercise, 2 = moderate exercise, 3 = heavy exercise); (viii) Medical insurance (0 = no medical insurance, 1 = urban employee basic medical insurance, 2 = urban and rural residents' basic medical insurance, 3 = urban resident basic medical insurance, 4 = new rural cooperative medical scheme, 5 = public medical care, 6 = other medical insurances). LASSO regression with cross-validation was employed for variable selection. As shown in Figures 6–7, when the model was optimized ($\lambda = 0.0005$), 24 key predictors with non-zero coefficients were identified from the 32 candidate variables. These retained variables were subsequently included in the multivariable regression model to further evaluate their independent association strength with stomach disease.

At the optimal tuning parameter ($\lambda = 5 \times 10^{-04}$), 24 key predictors with non-zero coefficients were selected from the 32 candidate variables under the minimum criteria. Alternatively, 17 variables were retained using the one-standard-error rule. Demographic characteristics include: age, BMI, currently smoking, currently drinking, education, exercise habits, gender, Han ethnicity, having endowment insurance, marriage, medical insurance, have drunk alcohol, past falls, place of residence, retirement, there is running water, waist circumference; comorbidity include: arthritis, asthma, cancer, diabetes, disability, dyslipidemia, heart disease, hypertension, hip fractures, kidney disease, lung disease, liver disease, mental illness, memory disorder, stroke.

3.4. Analysis of characteristics associated with stomach disease

Using stomach disease as the dependent variable and the LASSO-selected variables as independent variables, a logistic regression analysis was performed on all independent variables (i.e., those with non-zero coefficients at the optimal λ). No additional stepwise elimination was applied after LASSO selection. Nine demographic characteristics (age, male, currently drinking, have drunk alcohol, have endowment insurance, live in the countryside, past falls, waist circumference, exercise habit) and nine comorbidities characteristics (arthritis, dyslipidemia, heart disease, hypertension, kidney disease, lung disease, liver diseases, mental illness, stroke) were found to be

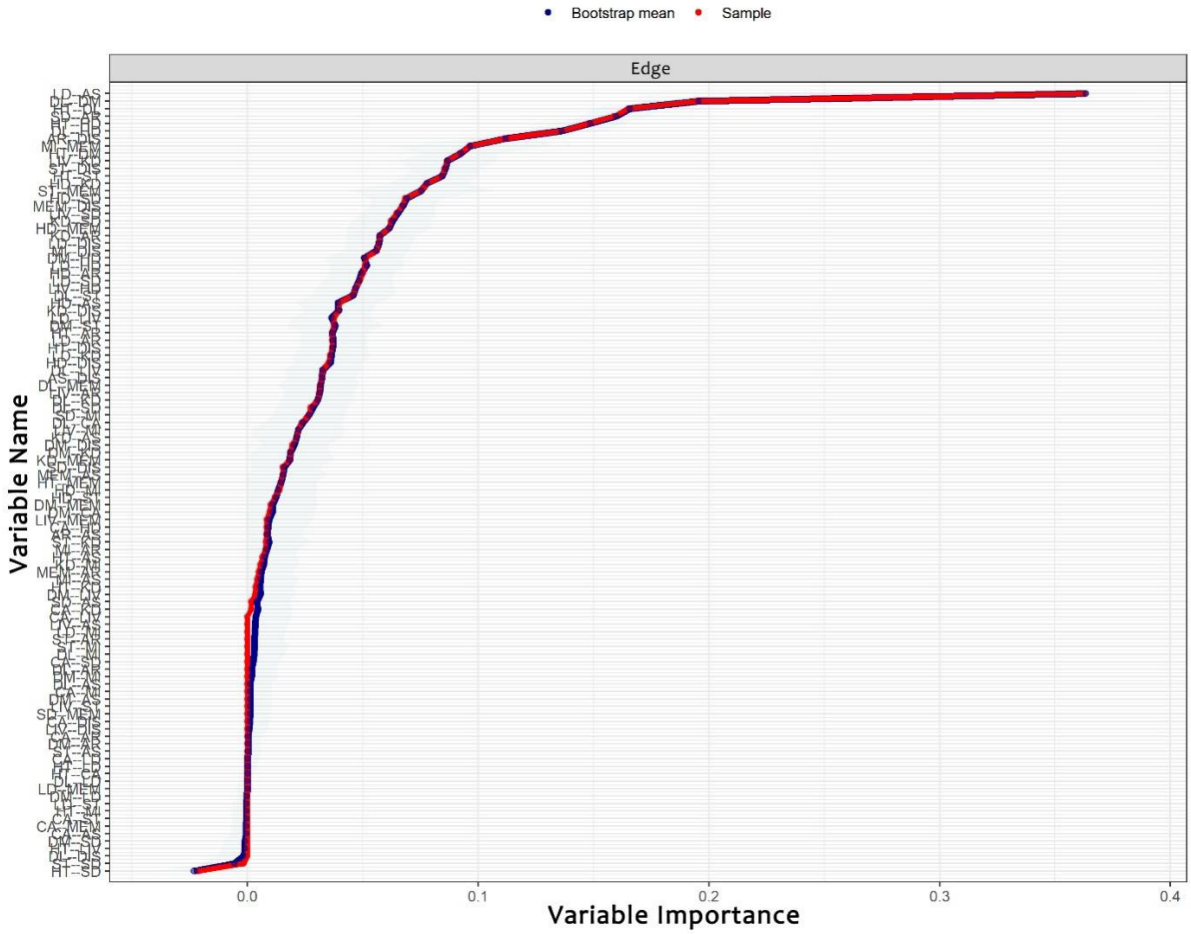

Figure 2. Edge stability analysis for the comorbidity network

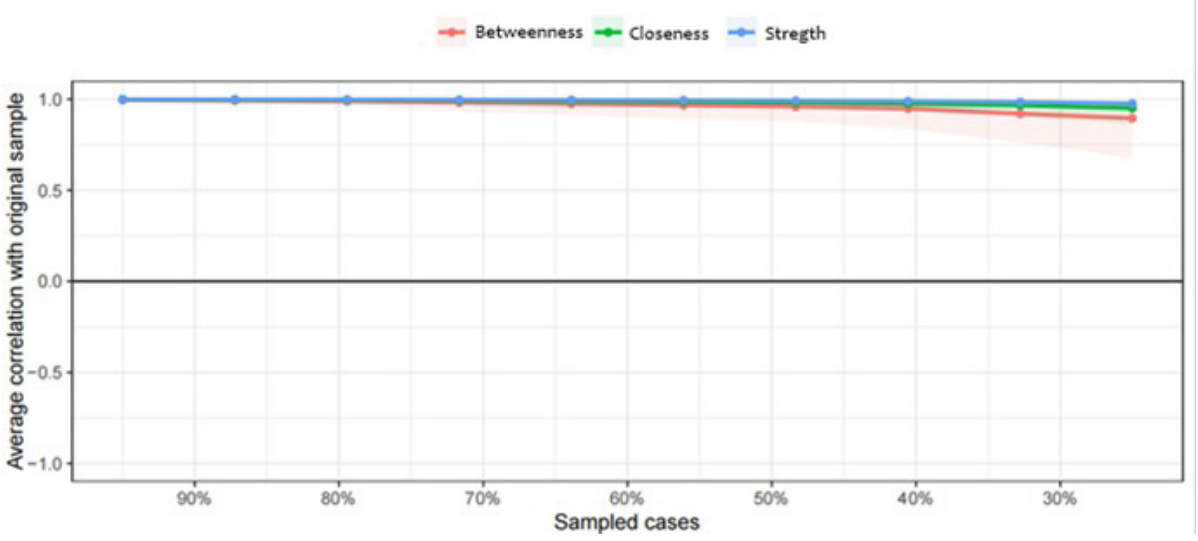

Figure 3. Centrality stability analysis for the comorbidity network

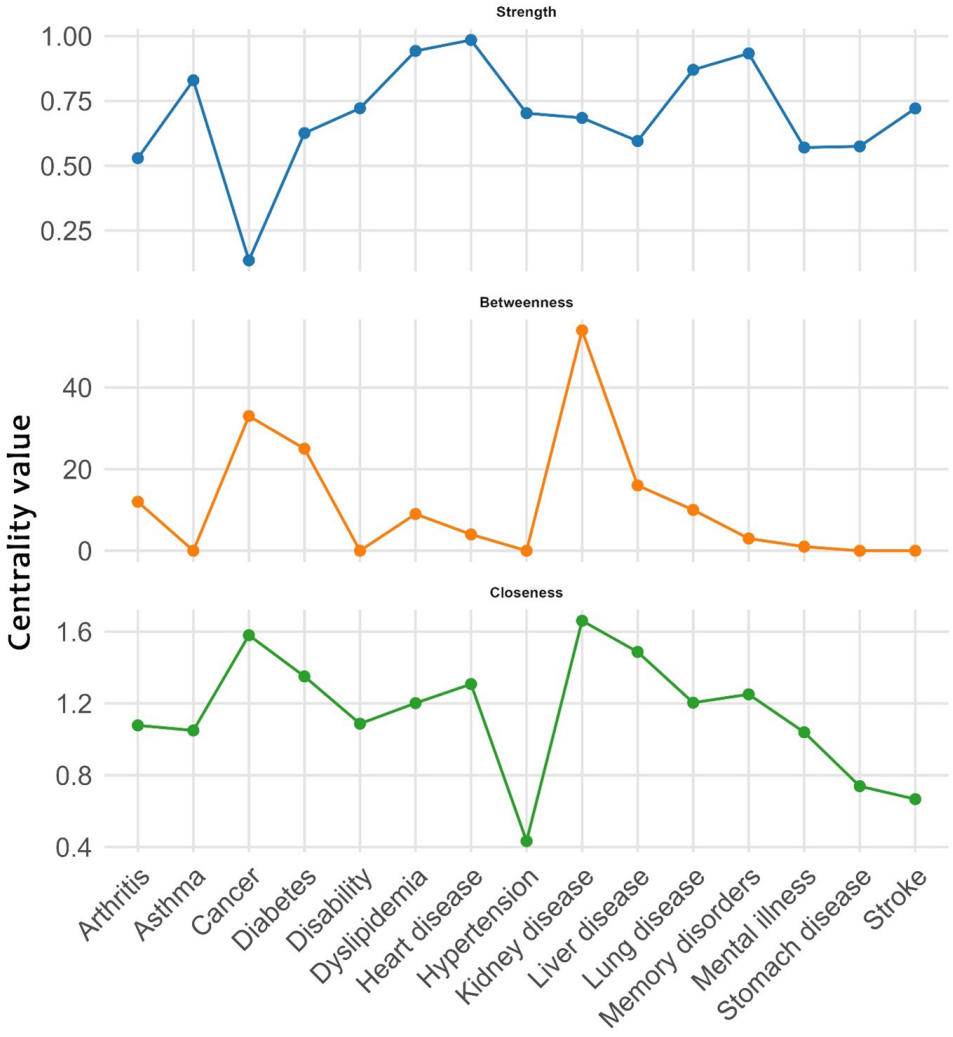

Figure 4. Centrality effects in the comorbidity network analysis

independently associated with stomach disease ($p < 0.05$) as shown in Table 2. Subsequently, we used $Log_{10}(P)$ to reflect the strength of the correlation of the variables in the table and ranked them. This analysis identifies key determinants of stomach disease through logistic regression. Comorbid conditions demonstrate the strongest associations. Arthritis (odds ratio [OR] = 2.078) and liver diseases (OR = 1.929) represent the most significant risk factors. Cardiovascular and metabolic conditions, including heart and kidney disease, also show substantial effects. As shown in Figure 8, demographic factors exhibit more modest associations. Alcohol consumption and past falls are risk factors, while male gender and exercise demonstrate protective effects. The prevalence of multiple comorbid conditions supports the notion that gastric diseases should be regarded as an important node in the network of geriatric comorbidities. They represent the convergence point of multiple pathological pathways in the aging population.

4. Discussion

The digestive system is the physiological structure most frequently exposed to exogenous factors such as food and drugs. Repeated stimulation by these factors can lead to chronic inflammatory responses in the digestive system. The stomach is particularly affected. This is a significant cause of chronic stomach disease.[8–10] Previous studies have also analyzed comorbidities of stomach disease with conditions such as diabetes[11] and hypertension[12] and confirmed their

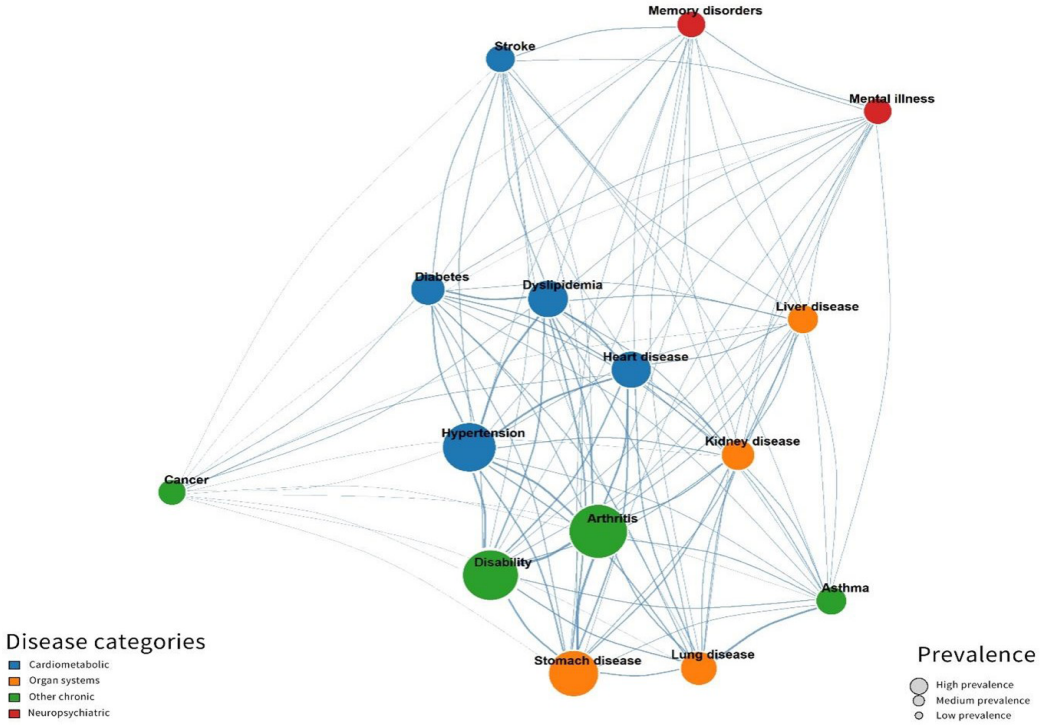

Figure 5. Disease co-occurrence network diagram

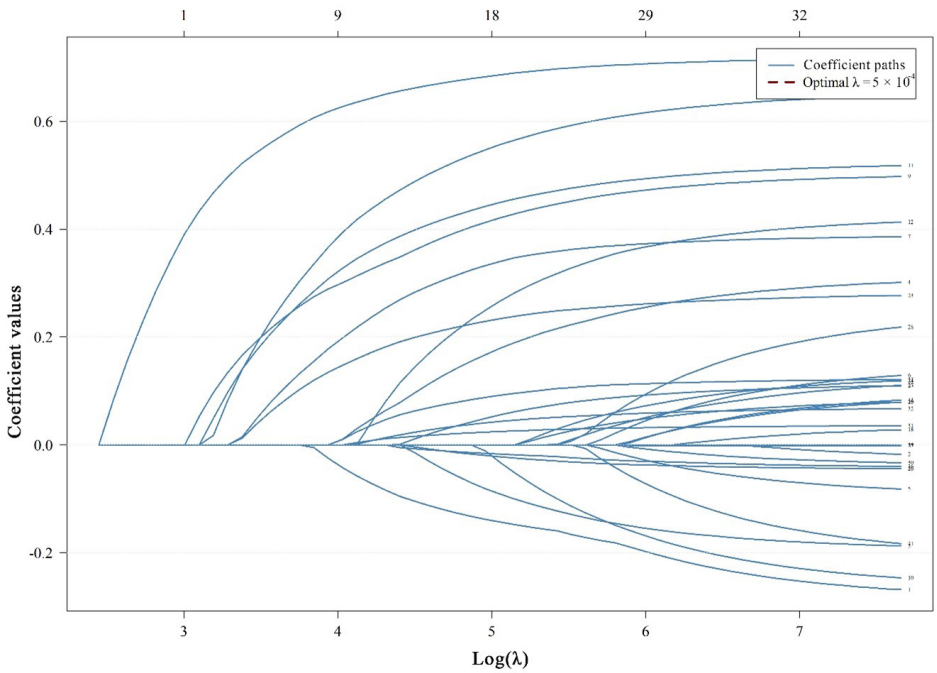

Figure 6. Coefficient path plot of least absolute shrinkage and selection operator regression for factors influencing stomach disease. As the regularization parameter λ (penalty intensity) increases, the number of variables retained in the model gradually decreases.

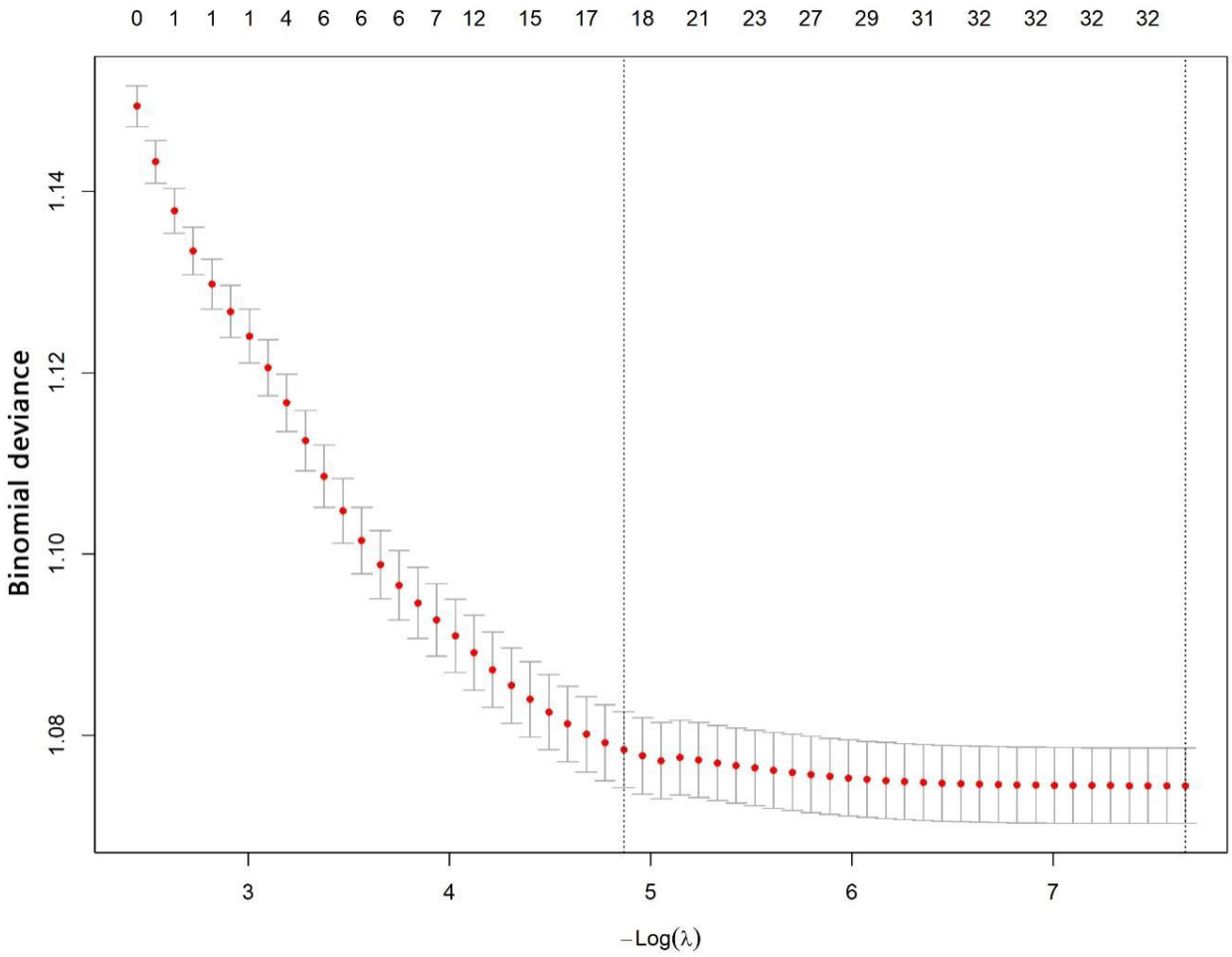

Figure 7. Cross-validation curve of least absolute shrinkage and selection operator regression for factors influencing stomach disease

correlations. Furthermore, *Helicobacter pylori* infection is a major factor influencing stomach disease. It has been demonstrated to be significantly associated with conditions such as atherosclerosis[13], dyslipidemia[14], and metabolic syndrome.[15] Our study extracted relevant data from the CHARLS database (2008–2020). By integrating network topology analysis with multivariable regression models, we systematically revealed the independent factors associated with stomach disease in middle-aged and older adults and their unique position within the comorbidity network. The results not only confirmed several known risk factors but, more importantly, revealed that stomach disease functions as a "terminal node" in the comorbidity network from a systems perspective. This indicates that their occurrence and development are driven by multiple core chronic diseases.

4.1. Association between demographic characteristics and stomach disease

This study identified several demographic characteristics significantly associated with stomach disease. Increased age showed an inverse association. This inverse association should be interpreted as an exploratory finding. It may be influenced by the relatively high proportion of "young-old" individuals in the study cohort, who might have better-preserved gastric function, or by survival bias. Given the cross-sectional design, this finding warrants cautious interpretation and requires confirmation in future longitudinal studies. Male sex was associated with lower odds, consistent with a previous study.[16] This is potentially attributable to differences in female hormone levels and neurological function.[17,18] Both current and past alcohol consumption were associated with increased odds of stomach disease. The direct irritation and damage of

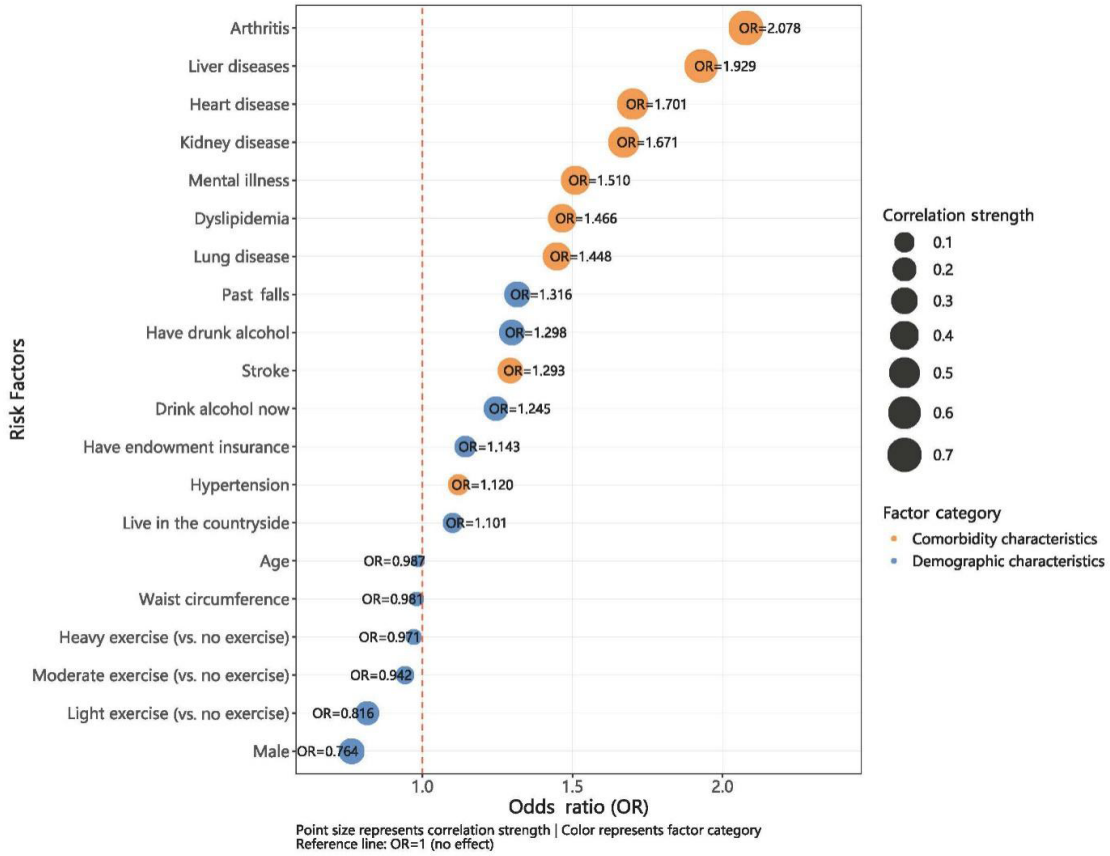

Figure 8. Ranking of correlation among independent related variables of stomach disease
Abbreviation: OR: Odds ratio.

alcohol to the gastric mucosa is the primary mechanism.[19,20] This study identified having endowment insurance and rural residence as factors associated with increased odds. This may reflect the combined influence of socioeconomic status, access to medical care, and dietary patterns (e.g., high salt, preserved foods). A history of past falls was associated with increased odds of stomach disease. While we found no direct evidence to explain this finding, it might stem from systemic factors underlying fall events. These include degeneration of neuromuscular control or a high burden of comorbidities, rather than indicating a direct causal relationship. The finding that increased waist circumference is associated with lower odds of stomach disease appears somewhat counterintuitive. This exploratory finding may reflect better nutritional status or be influenced by residual confounding from unmeasured factors, such as body fat distribution or muscle mass. Given the complex relationship between adiposity and metabolic health, this result should be interpreted with caution and warrants confirmation in future studies using more detailed body composition measurements. Finally, regular exercise, particularly mild exercise, showed an inverse association. This underscores the positive role of a healthy lifestyle in preventing stomach disease. Moderate exercise can effectively improve gut microbiota composition.[21] It can reduce endotoxemia[22] and prevent the onset of comorbidities[23], thereby helping to prevent stomach disease.

4.2. Comorbidity characteristics: Stomach disease as a convergence point for multiple chronic conditions

The core finding of this study is that stomach disease exhibits strong independent associations with a range of systemic chronic conditions. This provides key evidence for their role as a node within the comorbidity network. Among these, arthritis and liver disease showed the strongest associations with stomach disease. Potential underlying mechanisms suggest that various chronic conditions may be linked to stomach disease through shared or interconnected pathophysiological pathways: (i) Inflammation and medication-related injury: The systemic inflammatory state associated with conditions like

Table 2. Logistic regression analysis results of characteristics affecting stomach disease

Variable	β	SE	Wald	*p*	OR	95%CI
Demographic characteristics						
Age	−0.013	0.002	36.275	<0.001	0.987	0.983–0.991
Male	−0.270	0.051	28.368	<0.001	0.764	0.692–0.843
Currently drinking	0.219	0.057	14.819	<0.001	1.245	1.113–1.391
Have drunk alcohol	0.261	0.059	19.853	<0.001	1.298	1.157–1.456
Have endowment insurance	0.134	0.060	4.982	0.026	1.143	1.016–1.286
Live in the countryside	0.096	0.042	5.358	0.021	1.101	1.015–1.194
Past falls	0.275	0.037	54.450	<0.001	1.316	1.224–1.416
Waist circumference	−0.019	0.002	145.546	<0.001	0.981	0.978–0.984
Exercise habit			8.998	0.029		
No exercise					1.000	
Light exercise	−0.203	0.069	8.715	0.003	0.816	0.713–0.934
Moderate exercise	−0.059	0.047	1.581	0.209	0.942	0.859–1.034
Heavy exercise	−0.029	0.044	0.441	0.507	0.971	0.890–1.059
Comorbidity characteristics						
Arthritis	0.731	0.036	422.768	<0.001	2.078	1.938–2.228
Dyslipidemia	0.382	0.050	59.126	<0.001	1.466	1.330–1.616
Heart disease	0.531	0.048	121.593	<0.001	1.701	1.548–1.869
Hypertension	0.113	0.041	7.637	0.006	1.120	1.033–1.213
Kidney disease	0.514	0.061	70.184	<0.001	1.671	1.482–1.885
Lung disease	0.371	0.056	44.151	<0.001	1.448	1.299–1.616
Liver diseases	0.657	0.073	80.304	<0.001	1.929	1.671–2.227
Mental illness	0.412	0.122	11.385	0.001	1.510	1.188–1.918
Stroke	0.257	0.104	6.068	0.014	1.293	1.054–1.587

Abbreviations: CI: Confidence interval; OR: Odds ratio; SE: Standard error.

arthritis, along with the long-term use of medications such as non-steroidal anti-inflammatory drugs, may collectively affect the gastric mucosa.[24,25] (ii) Circulatory and metabolic dysregulation: Liver diseases (e.g., portal hypertension)[26–28], heart diseases (e.g., systemic congestion)[29,30], and chronic kidney disease (e.g., uremic toxins)[31] may contribute to stomach disease. They influence gastric blood flow, the local microenvironment, or cause direct mucosal injury. (iii) Neuro–immune axis dysfunction: Mental disorders[32] and stroke[33,34] may influence gastrointestinal function via the brain–gut axis. Chronic lung diseases[35] could be related to alterations in the microbiota mediated by the gut–lung axis. In summary, within the observed comorbidity network among the middle-aged and older adults, stomach diseases are extensively interconnected with chronic conditions across multiple systems. This pattern of association suggests that stomach disease may not represent an isolated endpoint. Rather, they function as a "convergent node" closely linked to systemic multi-organ conditions, embedded within a complex network of comorbid chronic diseases. They likely reflect the co-occurrence of metabolic, circulatory, immune, and neuropsychiatric dysregulations within individuals. Consistent with the cross-sectional design, these findings should be interpreted as statistical associations rather than mechanistic or causal pathways. The proposed mechanisms are speculative and intended to inform the generation of hypotheses for future longitudinal or mechanistic studies.

This study reveals that stomach disease exhibits a "convergence point" characteristic within comorbidity networks. This offers a new perspective for optimizing health management in the middle-aged and older adults. In terms of screening strategies, it is recommended to shift from universal screening to targeted assessment of gastrointestinal symptoms. This should focus on older adults already diagnosed with core chronic conditions

such as arthritis, heart disease, liver disease, or mental health disorders. Regarding care models, efforts should be made to transition from "specialty-specific single-disease management" to "patient-centered integrated multimorbidity management." This involves incorporating gastric health into comprehensive geriatric assessments. It also requires enhancing collaboration between gastroenterology and other relevant specialties to jointly develop treatment plans. This can improve overall prognosis and quality of life.

5. Conclusion

Based on the comprehensive analysis, this study indicates that among middle-aged and older adults, stomach disease exhibits topological characteristics of a "terminal node" within the chronic comorbidity network. Their presence indicates strong, independent associations with multiple core chronic conditions. Notably, these include arthritis, liver diseases, and heart disease. Associations are also seen with demographic factors, such as alcohol consumption and rural residence. These findings suggest that stomach issues in older adults may often reflect the clinical manifestation of accumulated systemic chronic disease burdens. Consequently, in clinical practice, it is advisable to emphasize screening for systemic comorbidities and integrated, patient-centered management for individuals with stomach disease. This is particularly important for those already diagnosed with the aforementioned core chronic conditions, rather than focusing exclusively on gastrointestinal symptoms.

Several limitations of this study should be acknowledged. First, the cross-sectional design limits the ability to infer causal or temporal directions in the observed associations. All reported associations should therefore be understood as statistical correlations rather than causal effects**.** Second, although multiple potential confounders were adjusted for, residual confounding from unmeasured variables cannot be ruled out. Third, all disease information was based on self-reported physician diagnoses. This may be affected by misclassification and recall bias. The broad and symptom-based definition of "stomach disease," which aggregates clinically heterogeneous conditions, such as gastritis, peptic ulcers, and functional dyspepsia, into a single binary outcome, may lead to over-reporting of minor conditions or under-detection of asymptomatic pathologies. This heterogeneity limits the clinical interpretability of the findings and may introduce bias into the estimated associations and network structure. Similarly, self-reporting of mental health conditions may be influenced by stigma or cognitive awareness, potentially compromising accuracy. Fourth, by treating stomach disease as a composite category, this analysis could not distinguish risk factors for specific subtypes. Finally, the study sample was drawn from a Chinese population. The findings may be influenced by local cultural, dietary, and healthcare system characteristics. Thus, generalization to other populations requires further validation.

Future studies would benefit from longitudinal designs. They should incorporate objective clinical or biomarker data, conduct subtype-specific analyses, and validate findings across diverse populations. This will help improve understanding of the role of stomach disease within comorbidity networks and inform more targeted prevention and management strategies.

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Conflict of interests

The authors declare no competing interests.

Author contributions

Conceptualization: Linya Lyu
Data curation: Linya Lyu, Fang Dai, Jinji Huang, Guobin Cheng
Formal analysis: Wei Fu, Fang Dai, Jinji Huang, Guobin Cheng
Funding acquisition: Wei Fu
Investigation: Wei Fu
Methodology: Wei Fu
Project administration: Wei Fu
Resources: Fang Dai, Jinji Huang, Guobin Cheng
Supervision: Wei Fu
Validation: Fang Dai, Jinji Huang, Guobin Cheng
Writing–original draft: Linya Lyu
Writing–review & editing: Fang Dai, Jinji Huang, Guobin Cheng

Ethics approval and consent to participate

The Medical Ethics Committee of the 925th Hospital granted ethical approval for the study under the reference number YNKT202503. Given that the researchers lacked access to identifying information, the data used in this study were anonymized and publicly available on the CHARLS website (https://charls.pku.edu.cn/). As a result, the 925th Hospital Review Board categorized this study as "non-human subjects" research.

Consent for publication

Not applicable.

Availability of data

This study utilized publicly available datasets, which can be accessed at the following link: https://charls.pku.edu.cn/

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Appendix

The supplementary calculation formula

Clustering coefficient: We employ the clustering coefficient of the weighted network, and the specific formula is as follows **(Equation A1):**

$$C = \frac{1}{n}\sum_{i=1}^{n} \frac{2\sum_{j<k} w_{ij} w_{ik} w_{jk}}{d_i(d_i - 1)} \quad \text{(A1)}$$

Among them, w_{ij} represents the edge weight between nodes i and j, and d_i is the degree of node i (i.e., the number of connected edges, after binarization). This formula is one of the common definitions of the weighted clustering coefficient.

Average path length: In a weighted network, the path length is defined as the sum of the reciprocals of the edge weights along the path (since the edge weights represent the connection strength, and the larger the weight, the shorter the distance). The specific formula is shown in **Equation A2:**

$$L = \frac{1}{n(n-1)}\sum_{i \neq j} d_{ij} \quad \text{(A2)}$$

Among these, d_{ij} is the shortest path length between nodes i and j (the sum of the reciprocals of the edge weights). Since the edge weights in our network are partial correlation coefficients (ranging from −1 to 1), we take their absolute values or transform them into positive weights (e.g., w'ij = $|w_{ij}|$ or w'ij = 1−$|w_{ij}|$) to calculate distances. In our calculations, we use the absolute values as the connection strength, and the distance is defined as $d_{ij} = 1/|w_{ij}|$. However, note that if an edge weight is 0, the distance is infinite. Therefore, we only perform calculations for existing edges (non-zero weights).

Network density: This study employs the standard formula for calculating network density in network science. Specifically, for an undirected network, the formula is as follows (**Equation A3**):

$$D = \frac{2L}{[N(N-1)]} \quad \text{(A3)}$$

Here, L represents the actual number of edges, and N represents the number of nodes. This definition serves as the fundamental metric for analyzing complex networks.

Small-world index: The small-world index (σ) is defined as the ratio of the clustering coefficient to the clustering coefficient of a random network divided by the ratio of the average path length to the average path length of a random network, as shown in **Equation A4:**

$$\sigma = \frac{C / C_{random}}{L / L_{random}} \quad \text{(A4)}$$

Among these, C_{random} and L_{random} are the clustering coefficient and the average path length of a random network, respectively. Typically, a σ value greater than 1 (σ > 1) indicates that the network exhibits small-world characteristics.[36]

Table A1. Network node graph calculation indicators

Node	Strength	Betweenness	Closeness	Strength_z	Betweenness_z	Closeness_z
Hypertension	0.703	0.000	0.433	0.037	−0.717	−2.107
Dyslipidemia	0.943	9.000	1.202	1.162	−0.137	0.177
Diabetes	0.626	25.000	1.351	−0.323	0.893	0.618
Cancer	0.135	33.000	1.580	−2.621	1.408	1.300
Lung disease	0.870	10.000	1.204	0.821	−0.073	0.184
Liver disease	0.595	16.000	1.487	−0.466	0.313	1.023
Heart disease	0.985	4.000	1.308	1.359	−0.459	0.491
Stroke	0.721	0.000	0.667	0.124	−0.717	−1.412
Kidney disease	0.685	54.000	1.661	−0.048	2.760	1.539
Stomach disease	0.575	0.000	0.739	−0.562	−0.717	−1.198
Mental illness	0.570	1.000	1.039	−0.583	−0.652	−0.306
Memory disorders	0.934	3.000	1.251	1.117	−0.524	0.322
Arthritis	0.529	12.000	1.078	−0.775	0.056	−0.192
Asthma	0.830	0.000	1.050	0.632	−0.717	−0.276
Disability	0.722	0.000	1.087	0.126	−0.717	−0.164