Original Research

Multimorbidity Patterns Reveal Heterogeneity Among Hospitalized Patients With Chronic Obstructive Pulmonary Disease: A Multicenter Retrospective Cross-Sectional Study in China

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Running Head: **Multimorbidity Patterns in Hospitalized COPD**

Keywords: chronic obstructive pulmonary disease; multimorbidity patterns; latent class analysis

Abbreviations:

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Abstract

Background Chronic obstructive pulmonary disease (COPD) is heterogeneous, but multimorbidity patterns are poorly characterized in China. We identified patterns among hospitalized patients with COPD and examined associations with healthcare burden and adverse in-hospital outcomes.

Methods This multicenter retrospective cross-sectional study analyzed electronic medical records from 17,828 patients hospitalized with COPD at six tertiary hospitals in China between 2019 and 2024. We retained each patient's first eligible hospitalization. Latent class analysis (LCA) was applied to 25 comorbidities with prevalence >3% to identify multimorbidity patterns. Multivariable logistic and linear regression models assessed associations between these patterns and healthcare burden and in-hospital outcomes, with adjustment for age, sex, marital status, ethnicity, insurance type, and occupation.

Results Among the 17,828 patients, 87.6% had at least one comorbidity. LCA identified five multimorbidity patterns: low comorbidity (53.7%), asthma (8.5%), metabolic disease (18.1%), cardiovascular disease (13.5%), and pulmonary hypertension (6.1%). The pulmonary hypertension class had the longest mean hospital stay (10.3 ± 7.47 days) and the highest median cost (¥17,204). Compared with the low comorbidity class, it also had the highest adjusted odds of mortality-related discharge (OR 2.04, 95% CI 1.39-2.91) and respiratory failure (OR 3.75, 95% CI 3.30-4.28; both P<0.001). The cardiovascular disease class also had higher healthcare use and more adverse outcomes.

Conclusion Five clinically distinct multimorbidity patterns were identified among hospitalized Chinese patients with COPD. Pulmonary hypertension and cardiovascular disease patterns were associated with greater healthcare burden and adverse in-hospital outcomes. These patterns may identify patients requiring closer multidisciplinary management.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a major global health challenge. In China, COPD imposes a substantial epidemiological and economic burden, with a national prevalence of approximately 8.6% among adults aged 20 years and older, affecting about 100 million individuals and ranking as a leading cause of hospitalization and mortality.[1 2] COPD exhibits inherent heterogeneity, with diverse clinical phenotypes such as chronic bronchitis-dominant, emphysema-dominant, and refined classifications like the non-exacerbator, eosinophilic exacerbator, and non-eosinophilic exacerbator[3 4]. These phenotypes guide personalized treatments, including targeted bronchodilators and exacerbation prevention, but they primarily focus on respiratory features while underemphasizing multimorbidity.

Multimorbidity, the coexistence of two or more chronic conditions, affects up to 86% of COPD patients, driven by shared risk factors and shared pathways like systemic inflammation and vascular dysfunction.[5-7] Common comorbidities in COPD patients include cardiovascular diseases, metabolic disorders, neuropsychiatric disorders, musculoskeletal disorders and respiratory conditions, which collectively amplify disease progression and therapeutic complexity.[6] Multimorbidity in COPD has profound clinical implications. Prior studies have shown that multimorbidity such as ischemic heart disease, hypertension, diabetes, and depression substantially elevate the risks of acute exacerbations and mortality in patients with COPD.[8 9] Accordingly, elucidating these comorbidity patterns is pivotal for enhancing disease management, facilitating targeted prevention, and tailoring therapeutic interventions.

Despite these insights, the majority of extant research on COPD multimorbidity has been constrained to isolated comorbidities or select common conditions, relying on prevalence-based summaries or conventional regression analyses that fail to capture the synergistic dynamics within comorbidity clusters[10]. Such approaches overlook synergistic interactions within clusters, which may drive heterogeneous therapeutic responses and escalate costs. Emerging methodologies, such as latent class analysis (LCA), offer a person-centered framework for uncovering unobserved subgroups based on comorbidity co-occurrence patterns, thereby

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illuminating novel phenotypes.[11-13] Yet, applications of LCA to COPD multimorbidity remain limited, particularly in China, where prior investigations have been hampered by reliance on self-reported diagnoses and limited by single-center designs or modest sample sizes, introducing potential selection biases[12 14]. These gaps block full views of multimorbidity phenotypes in Chinese COPD groups, calling for more studies to inform comorbidity-oriented interventions amid the nation's mounting COPD burden.

Therefore, in this study, we aimed to identify unique patterns of multiple comorbidities among hospitalized patients with COPD using the LCA method, based on electronic medical records from tertiary hospitals across six centers in China. We further assessed the association between these patterns and healthcare burden as well as short-term adverse events. By revealing the heterogeneity of comorbidities, this research lays the foundation for establishing COPD phenotypes centered on comorbidities, thereby providing evidence for precision medicine and resource allocation.

Methods

Study design and population

This retrospective cross-sectional study included patients admitted to six tertiary hospitals in China between January 2019 and December 2024 (Figure S1). Patients hospitalized for COPD were identified from the principal diagnosis recorded at discharge. Diagnoses were made by treating specialists using the complete hospitalization record; spirometry results and documentation of prior specialist confirmation were not available in the multicenter database. We retained the first eligible hospitalization for each patient during the study period and removed duplicate entries using patient identifiers and hospitalization information.

Multimorbidity selection and outcomes

Multimorbidity was defined as the coexistence of two or more chronic conditions in the same patient. Conditions were identified from primary and secondary diagnoses recorded at discharge and mapped to ICD-10 categories. The complete ICD-10 category list, prevalence estimates, and

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the indicators entered into the LCA are provided in Table S1. Healthcare burden outcomes included total hospitalization cost, length of stay, and number of hospitalizations recorded over five years. In-hospital outcomes included emergency admission, mechanical ventilation, tracheal intubation, respiratory failure, ICU admission, and in-hospital death. The severe-outcome composite included mortality-related discharge, intubation, ICU admission, or mechanical ventilation. Ventilatory support included invasive and noninvasive ventilation and was identified from a recorded ventilation duration greater than zero or matching procedure descriptions; intubation was identified from procedure descriptions. Table S2 gives the full outcome algorithms.

Statistical analysis

Descriptive statistics were used to summarize patient characteristics. Categorical variables are presented as n (%), and continuous variables as mean ± standard deviation (SD) or median (interquartile range [IQR]), as specified in each table. Fisher's exact test or the chi-square test was used to compare disease prevalence and multimorbidity patterns by sex and region.

Latent class analysis (LCA) was used to identify multimorbidity patterns. The number of classes was selected by considering the Akaike information criterion (AIC), Bayesian information criterion (BIC), likelihood-ratio statistic (G2), average maximum posterior probability, class size, parsimony, and clinical interpretability. Each patient was assigned to the class with the highest posterior probability. Associations between class membership and outcomes were estimated using multivariable logistic and linear regression models. Models used Class 1 as the reference and adjusted for age, sex, marital status, ethnicity, insurance type, and occupation.

To assess robustness, we repeated the outcome models after excluding patients aged over 80 years. In response to concern about possible COPD misclassification at younger ages, we also repeated the current analysis among patients aged 40 years or older. Both analyses retained the five-class assignments from the main analysis and used the same covariate adjustment set. All analyses were conducted in R version 4.4.3 (R Foundation for Statistical Computing, Vienna,

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Austria).

Results

Patient characteristics and burden of comorbidities

A total of 17,828 patients hospitalized with COPD were included; 80.61% were male and 70% were older than 65 years. Mechanical ventilation was recorded in 1,409 patients (7.9%), ICU admission in 1,233 (6.92%), and in-hospital death in 149 (0.84%) (Table S3). Patients had a mean of 2.41 comorbidities, and 87.6% had at least one comorbidity (Figure S2). The most common conditions were hypertension (26.5%), ischemic heart disease (21.9%), benign prostatic hyperplasia (14.3%), diabetes (14.1%), asthma (12.2%), heart failure (10.4%), bronchiectasis (10.3%), stroke (10.2%), pulmonary hypertension (9.7%), and hyperlipidemia (9.5%) (Figure S3). The number of comorbidities was positively associated with length of stay, admission count, and total hospitalization cost (Figure 1).

Latent class analysis of multimorbidity patterns

LCA included the 25 comorbidities with prevalence greater than 3%. AIC and G2 decreased as the number of classes increased, whereas BIC reached its minimum at seven classes. The average maximum posterior probability was 0.696 for five classes, compared with 0.642 and 0.638 for six and seven classes, respectively (Figure S4 and Table S4). We retained the five-class solution after considering model fit, classification certainty, class size, parsimony, and clinical interpretability. The five patterns were named low comorbidity (Class 1), asthma (Class 2), metabolic disease (Class 3), cardiovascular disease (Class 4), and pulmonary hypertension (Class 5) (Figure 2). Most patients were in the low comorbidity class (9,580; 53.7%), followed by the metabolic disease class (3,234; 18.1%), cardiovascular disease class (2,415; 13.5%), asthma class (1,508; 8.5%), and pulmonary hypertension class (1,091; 6.1%)(Table S5).

Characteristics of multimorbidity patterns

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Maximum-likelihood estimation generated posterior probabilities, and each patient was assigned to the class with the highest probability. Table 1 and Table S5 show the principal characteristics. Class 1 (low comorbidity) had the fewest comorbidities and the largest proportion of men. Class 2 (asthma) had high prevalences of asthma and rhinitis; these patients were the youngest and had the lowest admission count and hospitalization cost. Class 3 (metabolic disease) was characterized by hypertension and diabetes, with length of stay and costs similar to Class 1. Class 4 (cardiovascular disease) had high prevalences of hypertension, diabetes, ischemic heart disease, atrial fibrillation, and heart failure; it contained the oldest patients and had high healthcare use. Class 5 (pulmonary hypertension), the smallest class, had high prevalences of pulmonary hypertension, bronchiectasis, venous thromboembolism, and heart failure, together with the longest mean stay and highest median cost.

Association between multimorbidity patterns and medical costs and adverse hospital outcomes.

Adverse in-hospital outcomes differed across the five classes. Classes 4 and 5 had higher frequencies of in-hospital death, emergency admission, mechanical ventilation, intubation, respiratory failure, ICU admission, and the severe-outcome composite (Table 1). The adjusted regression analysis used the mortality-related discharge endpoint and Class 1 as the reference. Class 5 had higher odds of mortality-related discharge (OR 2.04, 95% CI 1.39-2.91), emergency admission (OR 1.33, 95% CI 1.14-1.55), mechanical ventilation (OR 3.31, 95% CI 2.79-3.91), and intubation (OR 3.58, 95% CI 2.51-5.04). It also had higher odds of respiratory failure (OR 3.75, 95% CI 3.30-4.28), ICU admission (OR 2.02, 95% CI 1.65-2.47), and the severe-outcome composite (OR 2.64, 95% CI 2.27-3.06). All models adjusted for age, sex, marital status, ethnicity, insurance type, and occupation (Figure 3 and Table S3; all $P<0.001$).

Results after excluding patients older than 80 years were similar (Figure S5 and Table S7). In the age ≥40 sensitivity analysis, 81 patients were excluded and 17,747 were retained. Class proportions changed by no more than 0.2 percentage points, and Class 5 remained associated

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with higher odds of mortality-related discharge (OR 2.04, 95% CI 1.39-2.91), respiratory failure (OR 3.75, 95% CI 3.29-4.28), and ICU admission (OR 2.03, 95% CI 1.66-2.48) (Figure S6 and Table S8).

Discussion

Using electronic medical records from six centers across China, this study identified five multimorbidity patterns among patients hospitalized with COPD: low comorbidity, asthma, metabolic disease, cardiovascular disease, and pulmonary hypertension. The classes differed in demographic characteristics, healthcare use, and in-hospital outcomes. The pulmonary hypertension class had the highest adjusted odds of mortality-related discharge and respiratory failure.

The burden of multimorbidity in COPD is substantial, as previous studies have demonstrated that most patients with COPD have at least one additional disease.[6] In our study, 87.6% of hospitalized COPD patients had at least one comorbidity, with an average of 2.41 comorbidities per patient. The most prevalent comorbidities were hypertension and ischemic heart disease, among other cardiovascular diseases, which aligns with findings from a prior COPD comorbidity study conducted in western China.[15] To provide a more comprehensive and accurate assessment of the impact of comorbidities on COPD, this study utilized LCA based on discharge diagnoses rather than prior knowledge, enabling us to explore under-assessed comorbidities. The observed heterogeneity across the five multimorbidity patterns reflects the complexity and multifaceted nature of COPD.

Patients in the pulmonary hypertension class had the highest hospitalization costs and the most adverse outcomes, including more than twofold odds of mortality-related discharge and more than threefold odds of respiratory failure. Pulmonary hypertension is a common complication of COPD and may arise through right ventricular dysfunction, systemic inflammation, and hypoxemia.[16] A meta-analysis of 38 studies across different levels of COPD severity reported a pulmonary hypertension prevalence of 39.2%.[17] Pulmonary hypertension in

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COPD has also been associated with worse functional status, reduced exercise tolerance, more exacerbations and hospitalizations, higher mortality, and greater healthcare use.[18] COPD can coexist with other causes of pulmonary hypertension, including pulmonary embolism, bronchiectasis, and left heart disease. Venous thromboembolism is relatively common in COPD and is associated with poor prognosis.[19] A previous small cluster analysis also identified a venous thromboembolism group with worse prognosis and higher hospitalization costs.[14]

On the other hand, the cardiovascular disease class exhibited increased hospitalization costs and a higher frequency of intensive care unit admissions and mechanical ventilation, likely due to the compounded effects of heart failure, ischemic heart disease, and other vascular disorders. The presence of these conditions may lead to greater treatment complexity, longer hospital stays, and higher medical costs owing to the need for intensive monitoring and therapy. These findings align with previous literature, which has consistently highlighted the negative impact of cardiovascular comorbidities on COPD prognosis.[20] The prevalence of cardiac diseases in COPD patients is high, particularly coronary artery disease, heart failure (especially heart failure with preserved ejection fraction), and atrial fibrillation, which may be attributable to shared risk factors (such as advanced age, smoking, sedentary lifestyle, and obesity) and pathophysiological mechanisms.[21] In contrast, patients in the metabolic disease class had a relatively favorable prognosis, as this class lacked concurrent cerebrovascular or cardiovascular comorbidities and primarily featured metabolic disorders such as hypertension, diabetes, and hyperlipidemia. A Korean study based on the Korea National Health and Nutrition Examination Survey reported that nearly one-third of patients with early-stage COPD had metabolic syndrome, which was associated with more frequent exacerbations, higher hospitalization rates, and increased medical costs.[22] The relatively better prognosis and lower medical expenditures in our metabolic disease class may be because patients with concurrent cardiac diseases were classified into another class. Consistent with this, prior research has identified metabolic syndrome in a substantial proportion of younger COPD patients and those with less severe disease.[23] Additionally, the metabolic and cardiovascular classes suggest a continuum in which metabolic issues often precede or

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accompany cardiac complications in COPD, driven by numerous complex factors including obesity-linked inflammation, oxidative stress, and physical inactivity.[24]

The asthma class had the lowest hospitalization burden and the most favorable short-term in-hospital outcomes, and its patients were the youngest. Among patients assigned to this class, 87.3% had an asthma diagnosis; rhinitis was also common. This pattern may represent asthma-COPD overlap. The class had more comorbidities than the low comorbidity class but better short-term outcomes, possibly because some patients had a reversible airway component responsive to anti-inflammatory treatment. Bai et al. reported lower mortality in patients with asthma-COPD overlap than in those with COPD alone, despite more frequent exacerbations.[25] These findings suggest that the configuration of comorbidities may provide information beyond the comorbidity count.

Clinically, the most widely recognized comorbidity clusters in COPD include cardiovascular diseases, metabolic disorders, neuropsychiatric disorders, musculoskeletal disorders, and respiratory conditions.[6,26] However, in this latent class analysis of hospitalized patients from respiratory departments in six tertiary hospitals in China, the five identified multimorbidity patterns did not include neuropsychiatric or musculoskeletal disorders. These two clusters primarily encompass anxiety, depression, osteoporosis, and musculoskeletal abnormalities. The low prevalence of these comorbidities in our study may be attributable to underdiagnosis and inadequate management by pulmonologists, highlighting the urgent need to enhance research and clinical capabilities in COPD comorbidity assessment, particularly for neuropsychiatric and musculoskeletal disorders. Potential measures include routine screening with anxiety and depression scales, as well as evaluations of skeletal muscle mass and nutritional status. Nonetheless, these multimorbidity patterns hold clinical significance and inform precision medicine in COPD. For instance, identifying high-risk clusters (Classes 4 and 5) could prompt targeted therapies such as pulmonary vasodilators for pulmonary hypertension or integrated cardiac-pulmonary rehabilitation, potentially reducing intensive care unit utilization and costs.[27] Recognizing the lower burden in the asthma class favors phenotype-tailored biologics for

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asthma-COPD overlap, while metabolic clusters call for lifestyle and pharmacologic interventions to prevent cardiovascular progression. This approach aids resource allocation in strained systems like China's, emphasizing multidisciplinary care for syndemic cases to improve outcomes.

This study has several limitations. First, the restriction to hospitalized patients favors more severe disease and limits generalizability to ambulatory or mild COPD. Second, the multicenter database did not contain spirometry, smoking history, forced expiratory volume in 1 second, treatment adherence, or reliable information on whether each secondary diagnosis was present before admission. COPD and comorbidities were therefore based on discharge diagnoses, and diagnostic misclassification remains possible, especially at younger ages. The age ≥40 analysis reduced this concern and produced similar estimates, but it cannot replace spirometric confirmation. Finally, the cross-sectional design does not support causal or prospective interpretations of the associations between latent classes and outcomes. Prospective studies with spirometry and standardized longitudinal follow-up are needed to validate these patterns.

Conclusions

This study identified five multimorbidity patterns among patients hospitalized with COPD. The pulmonary hypertension and cardiovascular disease patterns were associated with greater healthcare burden and more adverse in-hospital outcomes. Prospective studies should validate these patterns in patients with spirometry-confirmed COPD and longitudinal follow-up.

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Declarations

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethics Review Committees of the China-Japan Friendship Hospital and all other participating centers(2024-KY-364). The requirement for informed consent was waived by the ethics committee due to the retrospective and anonymized nature of this research.

Consent for publication

Not applicable as no individual personal health information is included in this article.

Availability of data and material

The data that support the findings of this study are available from the corresponding author, [Ke Huang], upon reasonable request.

Competing Interest

No potential conflict of interest was reported by the author(s).

Author contributions

Jisong Yan and Minghui Shi performed the analysis and drafted the manuscript. Qiong Zhou, Wei Chen, Quncheng Zhang, Ming Zhang, Xin Chen, Minghui Shi, Xingyao Tang, Wei Li, Tingting Huang, Yanan Cui, Yaodie Peng, Rui Su, and Zhifa Han contributed to the data collection. Ke Huang, and Ting Yang designed the study concept and revised it critically for important intellectual content. All authors reviewed and approved the final version of the manuscript.

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Tables

Table 1. Demographic characteristics and clinical characteristics of the five latent classes.

	Class 1 (N=9580)	Class 2 (N=1508)	Class 3 (N=3234)	Class 4 (N=2415)	Class 5 (N=1091)	P_overall
Age, years	70.0 (63.0-76.0)	65.0 (57.0-70.0)	71.0 (65.0-77.0)	**75.0 (69.0-81.0)**	73.0 (65.0-79.0)	<0.001
Age group, years						<0.001
18-35	28 (0.29%)	15 (0.99%)	2 (0.06%)	1 (0.04%)	3 (0.27%)	
36-45	74 (0.77%)	44 (2.92%)	9 (0.28%)	0 (0.00%)	10 (0.92%)	
46-55	592 (6.18%)	239 (15.8%)	157 (4.85%)	34 (1.41%)	62 (5.68%)	
56-65	2358 (24.6%)	493 (32.7%)	721 (22.3%)	291 (12.0%)	209 (19.2%)	
66-75	3885 (40.6%)	518 (34.4%)	1305 (40.4%)	927 (38.4%)	394 (36.1%)	
75+	2643 (27.6%)	199 (13.2%)	1040 (32.2%)	1162 (48.1%)	413 (37.9%)	
Gender						<0.001
Female	1591 (16.6%)	414 (27.5%)	655 (20.3%)	557 (23.1%)	239 (21.9%)	
Male	7989 (83.4%)	1094 (72.5%)	2579 (79.7%)	1858 (76.9%)	852 (78.1%)	
Insurance						<0.001
UEBMI	4205 (43.9%)	633 (42.0%)	1494 (46.2%)	1274 (52.8%)	446 (40.9%)	
URBMI	1715 (17.9%)	240 (15.9%)	526 (16.3%)	383 (15.9%)	260 (23.8%)	
NRCMS	1440 (15.0%)	267 (17.7%)	273 (8.44%)	222 (9.19%)	178 (16.3%)	
Others	1890 (19.7%)	335 (22.2%)	850 (26.3%)	467 (19.3%)	185 (17.0%)	
None	330 (3.44%)	33 (2.19%)	91 (2.81%)	69 (2.86%)	22 (2.02%)	
Length of stay, day	8.66 ±5.78	7.55 ±3.57	8.35 ±4.13	9.58 ±6.05	**10.3 ±7.47**	<0.001
Admission count, times	2.73 ±3.79	2.49 ±4.51	3.42 ±4.75	**4.09 ±6.58**	2.70 ±3.41	<0.001
Total hospitalization cost, Yuan	11892 (8106-18037)	10686 (7741-15409)	12630 (9180-18037)	14341 (9870-20646)	**17204 (11556-27393)**	<0.001
Emergency						<0.001
No	7908 (82.5%)	1346 (89.3%)	2752 (85.1%)	1924 (79.7%)	843 (77.3%)	
Yes	1672 (17.5%)	162 (10.7%)	482 (14.9%)	491 (20.3%)	**248 (22.7%)**	
Death						0.008
No	9500 (99.2%)	1505 (99.8%)	3209 (99.2%)	2390 (99.0%)	1075 (98.5%)	
Yes	80 (0.84%)	3 (0.20%)	25 (0.77%)	25 (1.04%)	**16 (1.47%)**	
ICU admission						<0.001
No	8956 (93.5%)	1453 (96.4%)	3076 (95.1%)	2152 (89.1%)	958 (87.8%)	
Yes	624 (6.51%)	55 (3.65%)	158 (4.89%)	263 (10.9%)	**133 (12.2%)**	
Ventilator use						<0.001
No	8889 (92.8%)	1467 (97.3%)	3040 (94.0%)	2154 (89.2%)	869 (79.7%)	
Yes	691 (7.21%)	41 (2.72%)	194 (6.00%)	261 (10.8%)	**222 (20.3%)**	

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Endotracheal intubation						<0.001
No	9462 (98.8%)	1503 (99.7%)	3211 (99.3%)	2367 (98.0%)	1044 (95.7%)	
Yes	118 (1.23%)	5 (0.33%)	23 (0.71%)	48 (1.99%)	**47 (4.31%)**	
Respiratory failure						<0.001
No	6828 (71.3%)	1304 (86.5%)	2520 (77.9%)	1566 (64.8%)	430 (39.4%)	
Yes	2752 (28.7%)	204 (13.5%)	714 (22.1%)	849 (35.2%)	**661 (60.6%)**	
Severe outcome						<0.001
No	8440 (88.1%)	1423 (94.4%)	2915 (90.1%)	2001 (82.9%)	805 (73.8%)	
Yes	1140 (11.9%)	85 (5.64%)	319 (9.86%)	414 (17.1%)	**286 (26.2%)**	
Number of comorbidities	1.42±1.16	2.46±1.30	3.72±1.44	**4.14 ±1.55**	3.27±1.41	<0.001

Note: Age and total hospitalization cost are presented as median (IQR). Length of stay, admission count, and number of comorbidities are presented as mean ± SD. Categorical variables are presented as n (%). UEBMI, Urban Employee Basic Medical Insurance; URBMI, Urban Resident Basic Medical Insurance; NRCMS, New Rural Cooperative Medical Scheme.

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Figure legends

Figure 1. Association between the number of comorbidities and healthcare burden among patients hospitalized with COPD. COPD, chronic obstructive pulmonary disease.

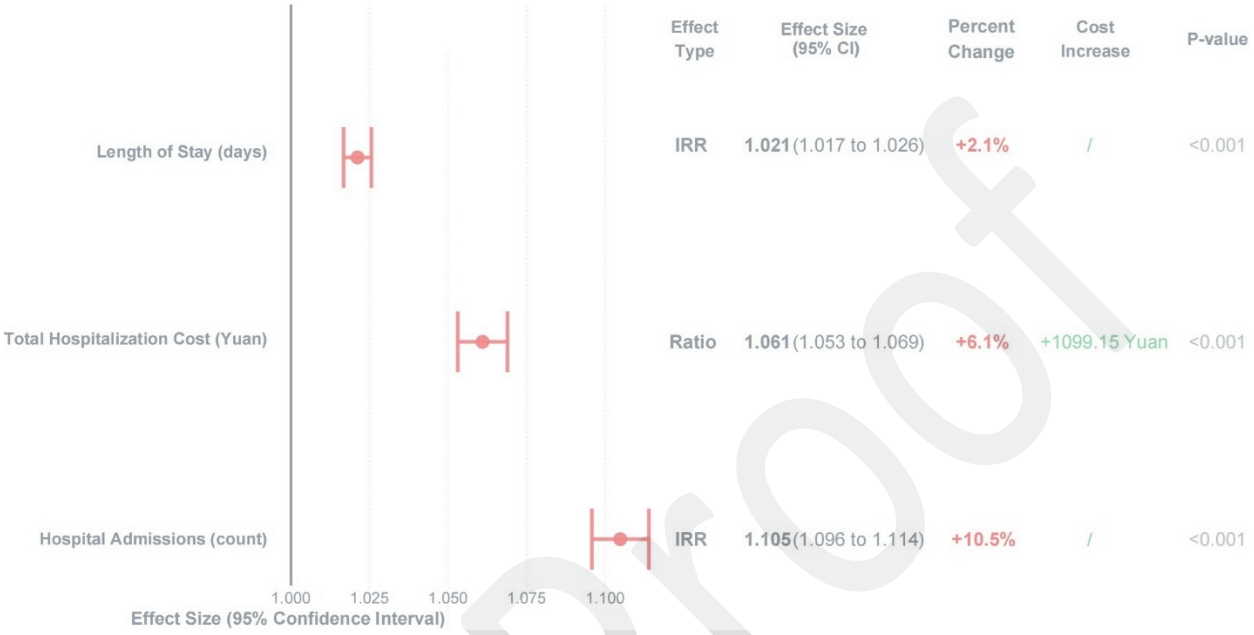

Figure 2. Conditional probabilities and the five most prevalent comorbidities in each latent class. The heat map shows model-estimated item-response probabilities. The bar charts show observed within-class prevalences after assignment to the class with the highest posterior probability, as reported in Table S5. These quantities are distinct and may differ. COPD, chronic obstructive pulmonary disease.

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Figure 3. Adjusted associations between multimorbidity patterns and adverse in-hospital outcomes. Class 1 is the reference.

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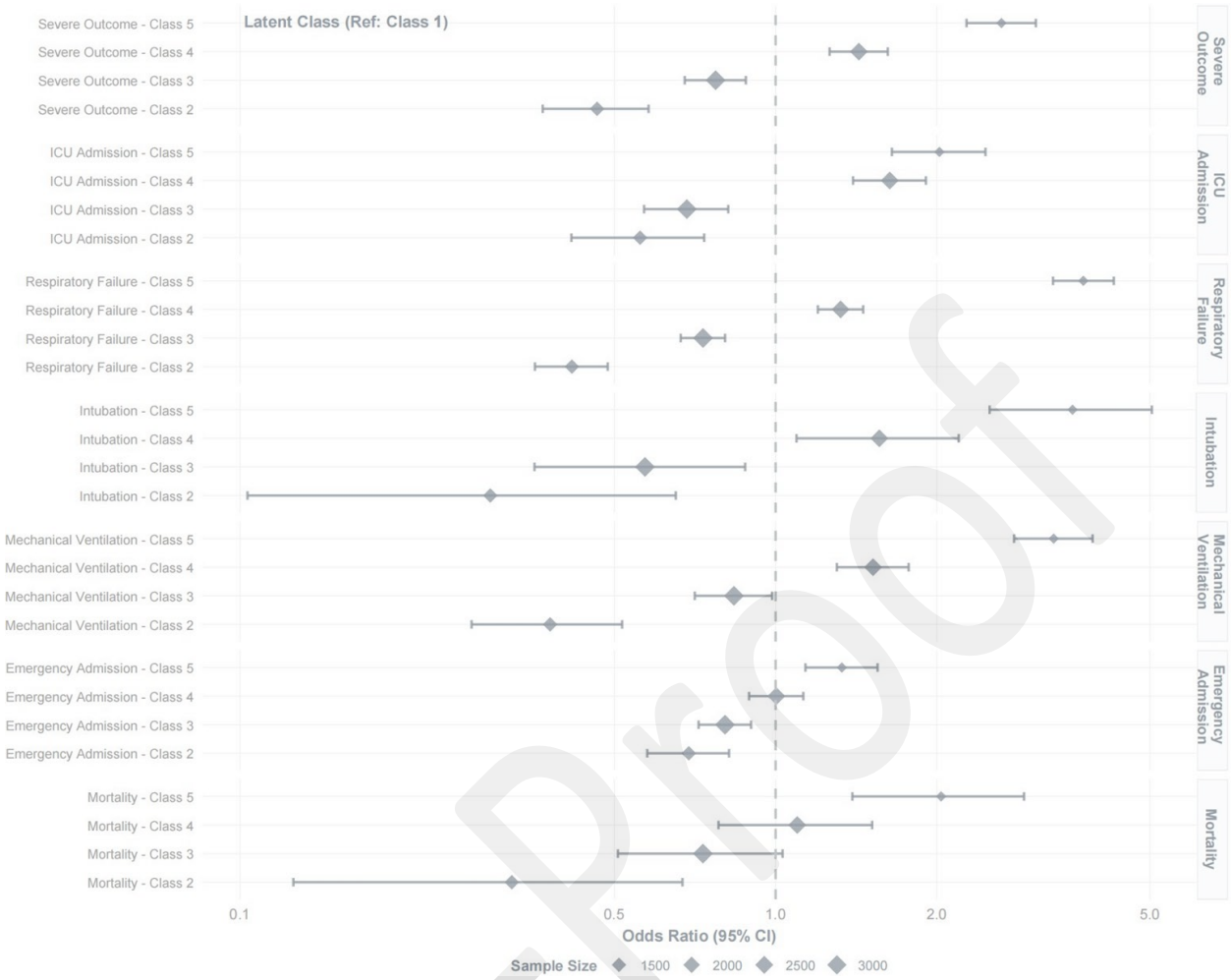

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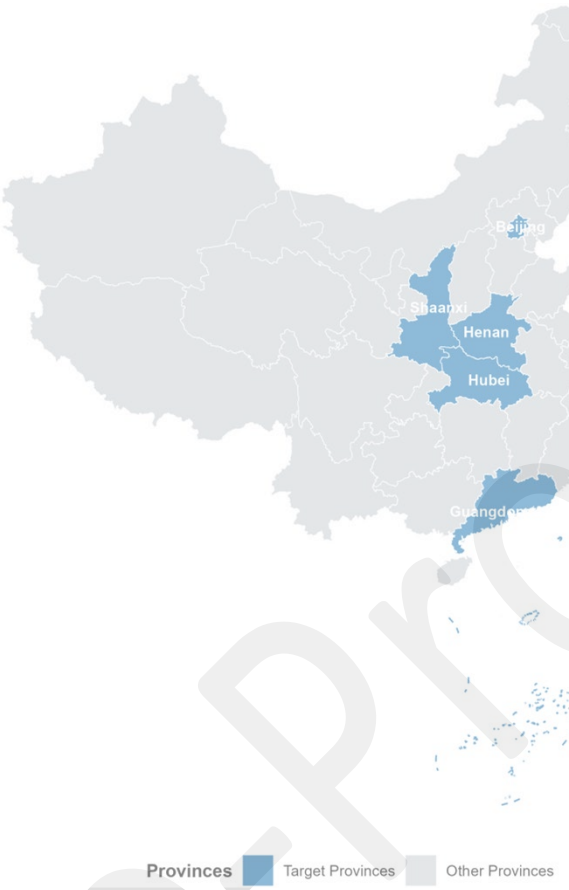

Figure S1. Geographical distribution of the six participating centers.

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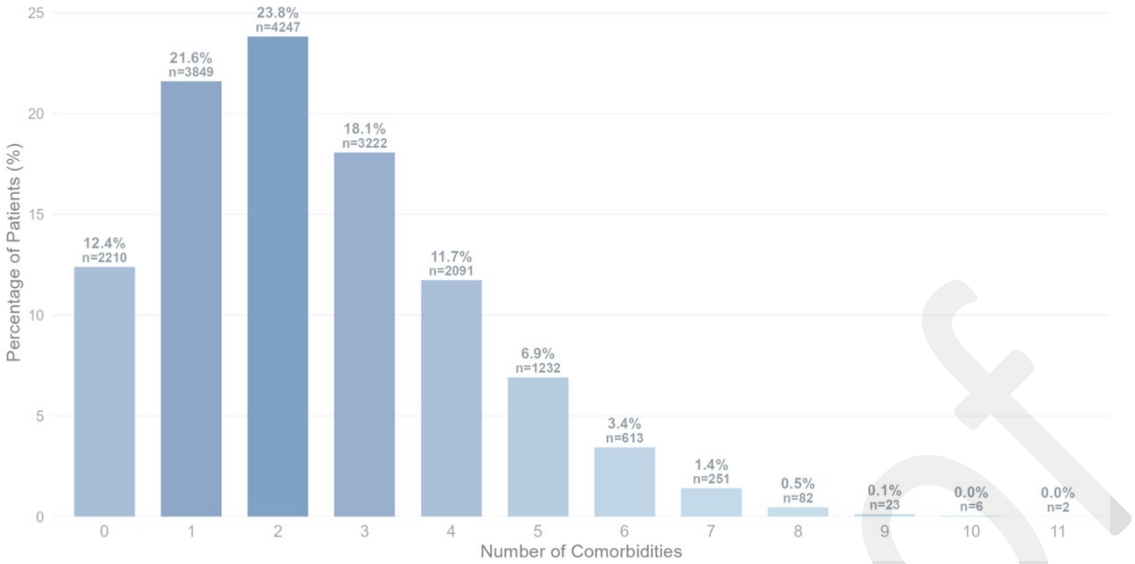

Figure S2. Distribution of the number of comorbidities among patients hospitalized with COPD.

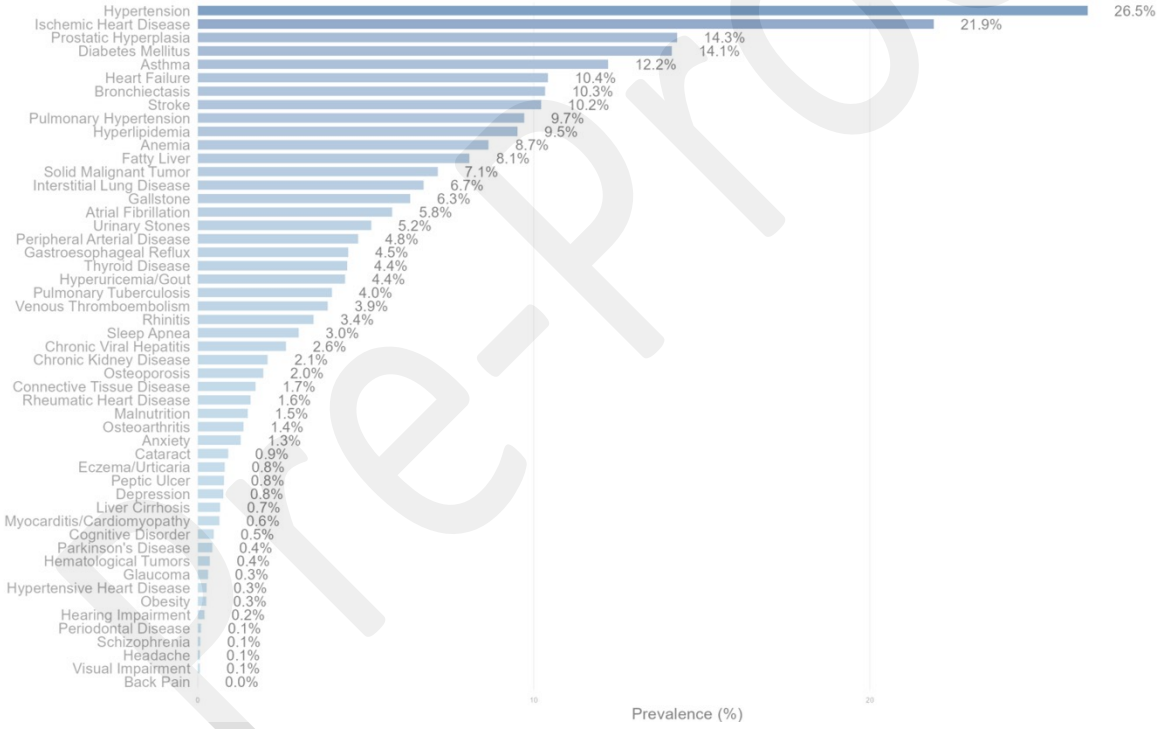

Figure S3. Prevalence of the 51 observed comorbidities included in the study.

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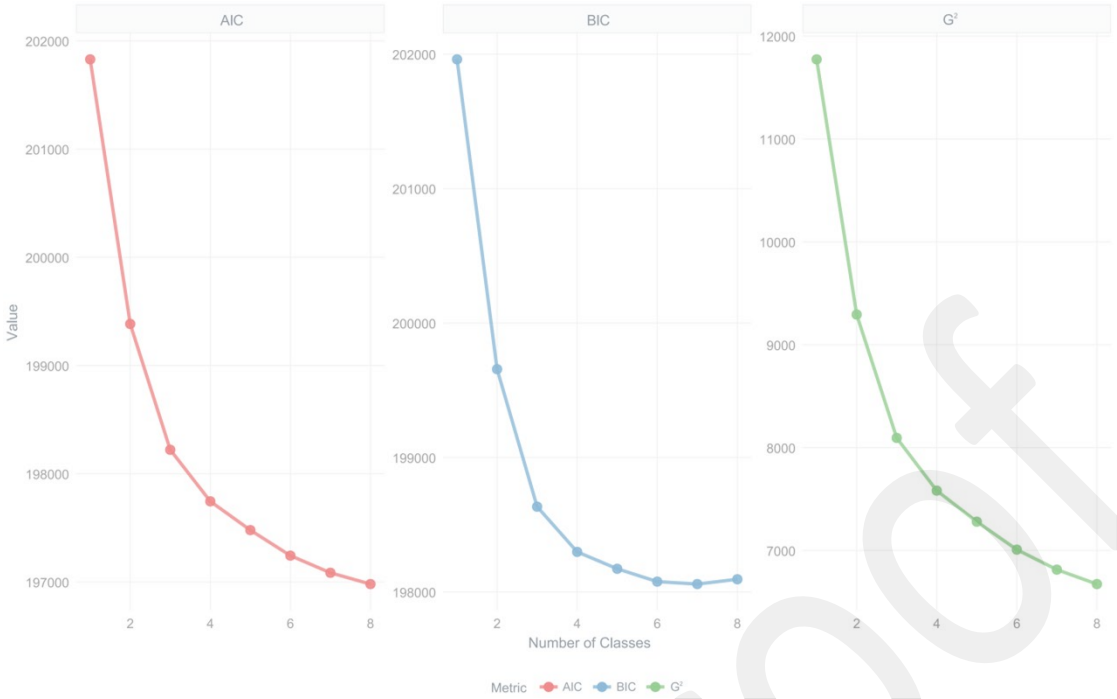

Figure S4. Latent class model-selection metrics. AIC and G2 decreased as the number of classes increased, whereas BIC reached its minimum at seven classes. The average maximum posterior probability was 0.696 for the five-class model and was lower for the six- and seven-class models (0.642 and 0.638). The five-class solution was retained after considering model fit, classification certainty, class size, parsimony, and clinical interpretability.

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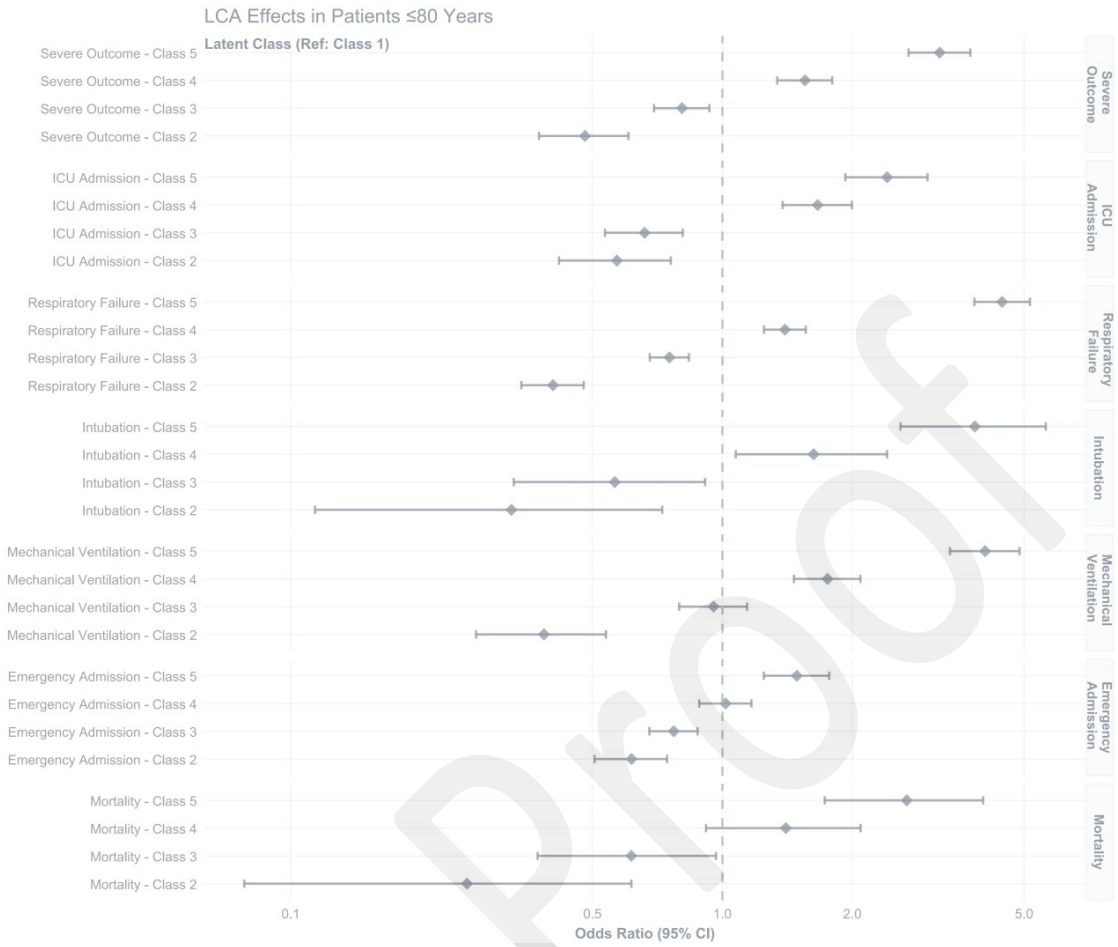

Figure S5. Associations between multimorbidity patterns and adverse in-hospital outcomes among patients aged ≤80 years. Odds ratios were estimated with Class 1 as the reference and adjusted for age, sex, insurance category, ethnicity, marital status, and occupation. CI, confidence interval.

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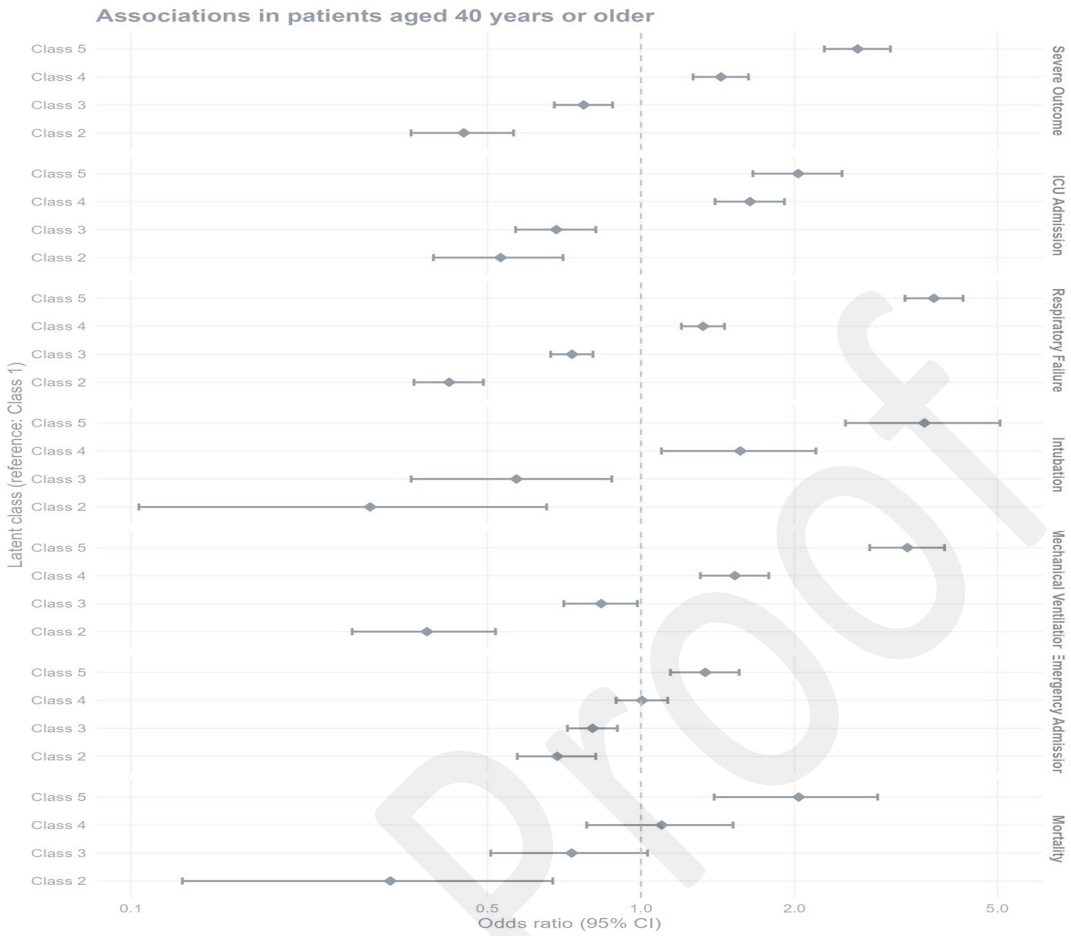

Figure S6. Associations between multimorbidity patterns and adverse in-hospital outcomes among patients aged ≥40 years. Odds ratios were estimated with Class 1 as the reference and adjusted for age, sex, insurance category, ethnicity, marital status, and occupation. CI, confidence interval.

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Table S1. ICD-10 categories, prevalence, and conditions entered into latent class analysis.

Condition	ICD-10 category	n (%)	Entered into LCA
Hypertension	I10-I15	4,720 (26.48%)	Yes
Ischemic heart disease	I20-I25	3,905 (21.90%)	Yes
Benign prostatic hyperplasia	N40	2,542 (14.26%)	Yes
Diabetes mellitus	E10-E14	2,514 (14.10%)	Yes
Asthma	J45-J46	2,177 (12.21%)	Yes
Heart failure	I50	1,857 (10.42%)	Yes
Bronchiectasis	J47	1,842 (10.33%)	Yes
Stroke	I60-I69	1,821 (10.21%)	Yes
Pulmonary hypertension	I27.0, I27.2	1,731 (9.71%)	Yes
Hyperlipidemia	E78	1,697 (9.52%)	Yes
Anemia	D50-D64	1,543 (8.65%)	Yes
Fatty liver disease	K76.0	1,441 (8.08%)	Yes
Solid malignant tumor	C00-C80	1,274 (7.15%)	Yes
Interstitial lung disease	J84	1,198 (6.72%)	Yes
Gallstone disease	K80	1,127 (6.32%)	Yes
Atrial fibrillation	I48	1,031 (5.78%)	Yes
Urinary stones	N20-N23	921 (5.17%)	Yes
Peripheral arterial disease	I70.2, I73.9	851 (4.77%)	Yes
Gastroesophageal reflux disease	K21	798 (4.48%)	Yes
Thyroid disease	E00-E07	793 (4.45%)	Yes
Hyperuricemia or gout	E79, M10	781 (4.38%)	Yes
Pulmonary tuberculosis	A15-A19	713 (4.00%)	Yes
Venous thromboembolism	I26, I80-I82	690 (3.87%)	Yes
Rhinitis	J30-J31	615 (3.45%)	Yes
Obstructive sleep apnea	G47.3	536 (3.01%)	Yes
Chronic viral hepatitis	B18	469 (2.63%)	No
Chronic kidney disease	N18	371 (2.08%)	No
Osteoporosis	M80-M82	348 (1.95%)	No
Connective tissue disease	M30-M36	306 (1.72%)	No

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Rheumatic heart disease	I05-I09	281 (1.58%)	No
Malnutrition	E40-E46	266 (1.49%)	No
Osteoarthritis	M15-M19	242 (1.36%)	No
Anxiety disorder	F40-F41	228 (1.28%)	No
Cataract	H25-H26	163 (0.91%)	No
Eczema or urticaria	L20-L30, L50	143 (0.80%)	No
Peptic ulcer	K25-K28	140 (0.79%)	No
Depressive disorder	F32-F33	135 (0.76%)	No
Liver cirrhosis	K74	119 (0.67%)	No
Myocarditis or cardiomyopathy	I40-I43	115 (0.65%)	No
Cognitive disorder or dementia	F00-F03, G30, R41.8	86 (0.48%)	No
Parkinson disease	G20-G21	77 (0.43%)	No
Hematologic malignancy	C81-C96	64 (0.36%)	No
Glaucoma	H40-H42	55 (0.31%)	No
Hypertensive heart disease	I11-I13	48 (0.27%)	No
Obesity	E66	46 (0.26%)	No
Hearing impairment	H90-H91	37 (0.21%)	No
Periodontal disease	K05	17 (0.10%)	No
Schizophrenia-spectrum disorder	F20-F29	14 (0.08%)	No
Visual impairment	H54	11 (0.06%)	No
Headache or migraine	R51, G43-G44	11 (0.06%)	No
Back pain	M54	3 (0.02%)	No

Note: The ICD-10 categories are provided for reference. The implemented extraction algorithm searched condition-specific diagnostic terms in the primary and secondary diagnoses recorded at discharge; a separate ICD-code field was not used as an independent filter. A condition was coded present when any term matched. The 25 observed conditions with prevalence >3% were entered into the LCA. ICD-10 categories were checked against the World Health Organization ICD-10 Version 2019 browser (https://icd.who.int/browse10/2019/en). LCA, latent class analysis.

Table S2. Ascertainment of healthcare burden and adverse in-hospital outcomes.

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Outcome	Definition
Length of stay	Recorded hospital length of stay
Total hospitalization cost	Total charge recorded for the hospitalization, in yuan
Admission count	Total number of hospitalizations recorded by participating hospitals during 2019-2024
Emergency admission	Admission route recorded as emergency
Mechanical ventilation	Ventilation duration >0 or a procedure description matching invasive or noninvasive ventilation
Tracheal intubation	Procedure description matching tracheal or endotracheal intubation
Respiratory failure	Matching respiratory-failure diagnosis in the discharge record
ICU admission	Recorded ICU admission
In-hospital death	Discharge disposition recorded as death; used for descriptive reporting
Mortality	In-hospital death or nonmedical discharge
Severe outcome	Mortality-related discharge, tracheal intubation, ICU admission, or mechanical ventilation

Note: ICU, intensive care unit.

Table S3. Baseline characteristics and number of multimorbidities in COPD hospitalized patients.

Variable	Category	N(%)	Number of multimorbidities (Mean ± SD)	P-value
Total	All patients	17828(100.00%)	2.41 ± 1.73	/
Gender	Female	3456(19.39%)	2.65 ± 1.76	<0.001
	Male	14372(80.61%)	2.35 ± 1.71	
Age group	18-35	49(0.27%)	1.45 ± 1.29	<0.001
	36-45	137(0.77%)	1.80 ± 1.46	
	46-55	1084(6.08%)	1.88 ± 1.45	
	56-65	4072(22.84%)	2.17 ± 1.66	
	66-75	7029(39.43%)	2.36 ± 1.68	
	75+	5457(30.61%)	2.77 ± 1.81	
Ethnicity	Minority	424(2.38%)	2.58 ± 1.74	0.036
	Han chinese	17404(97.62%)	2.40 ± 1.73	

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Marriage	Unmarried	145(0.81%)	2.30 ± 1.59	<0.001
	Married	16153(90.60%)	2.41 ± 1.72	
	Widowed	830(4.66%)	2.58 ± 1.85	
	Divorced	87(0.49%)	2.48 ± 1.59	
	Others	613(3.44%)	1.98 ± 1.64	
Insurance	UEBMI	8052(45.16%)	2.50 ± 1.76	<0.001
	URBMI	3124(17.52%)	2.38 ± 1.68	
	NRCMS	2380(13.35%)	1.98 ± 1.52	
	Others	3727(20.91%)	2.53 ± 1.79	
	None	545(3.06%)	2.17 ± 1.63	
Occupation	Civil servant	120(0.67%)	2.19 ± 1.87	<0.001
	Technical staff	112(0.63%)	2.48 ± 1.76	
	Clerk	285(1.60%)	1.98 ± 1.54	
	Enterprise manager	28(0.16%)	2.25 ± 1.67	
	Worker	213(1.19%)	2.07 ± 1.69	
	Farmer	3299(18.50%)	2.09 ± 1.56	
	Student	8(0.04%)	1.12 ± 1.25	
	Freelancer	135(0.76%)	1.86 ± 1.50	
	Self employed	82(0.46%)	2.07 ± 1.51	
	Unemployed	426(2.39%)	2.58 ± 1.83	
	Retired	5417(30.38%)	2.54 ± 1.75	
	Others	7703(43.21%)	2.48 ± 1.76	
Admission	Outpatient	14546(81.59%)	2.41 ± 1.74	0.14
	Emergency	3055(17.14%)	2.41 ± 1.68	
	Other institutions	227(1.27%)	2.23 ± 1.78	
Discharge	Medical discharge	16540(92.78%)	2.40 ± 1.72	0.166
	Medical transfer	194(1.09%)	2.68 ± 1.75	
	Medical transfer to primary care	617(3.46%)	2.43 ± 1.73	
	Non medical discharge	140(0.79%)	2.45 ± 1.54	
	Death	149(0.84%)	2.51 ± 1.67	
	Others	188(1.05%)	2.55 ± 1.96	
ICU	No	16595(93.08%)	2.40 ± 1.73	<0.001

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admission				
	Yes	1233(6.92%)	2.53 ± 1.63	<0.001
Respiratory failure	No	12648(70.94%)	2.38 ± 1.74	<0.001
	Yes	5180(29.06%)	2.48 ± 1.69	<0.001
Ventilator use	No	16419(92.1%)	2.39 ± 1.73	<0.001
	Yes	1409(7.9%)	2.60 ± 1.65	<0.001
Intubation	No	17587(98.65%)	2.41 ± 1.73	0.058
	Yes	241(1.35%)	2.54 ± 1.57	0.058

Note: Data are n (%) unless otherwise indicated; number of comorbidities is mean ± SD. UEBMI, Urban Employee Basic Medical Insurance; URBMI, Urban Resident Basic Medical Insurance; NRCMS, New Rural Cooperative Medical Scheme.

Table S4. Latent class model-selection and classification-quality metrics.

Classes	AIC	BIC	G2	Average maximum posterior probability	Maximum posterior probability ≥0.70
1	250,091.1	250,285.8	26,445.0	1.000	100.0%
2	247,321.2	247,718.4	23,623.1	0.827	76.4%
3	245,727.1	246,326.8	21,977.0	0.746	59.5%
4	245,136.3	245,938.5	21,334.2	0.729	58.5%
5	244,701.8	245,706.5	20,847.7	0.696	49.4%
6	244,424.9	245,632.1	20,518.7	0.642	31.2%
7	244,209.4	245,619.1	20,251.3	0.638	41.8%
8	244,037.1	245,649.3	20,027.0	0.644	42.3%

Note: Lower AIC, BIC, and G2 indicate better relative fit. BIC was lowest for seven classes. The five-class solution was retained after joint consideration of fit, classification certainty, class size, parsimony, and clinical interpretability. AIC, Akaike information criterion; BIC, Bayesian information criterion; G2, likelihood-ratio statistic.

Table S5. The prevalence of multimorbidities among the five latent classes.

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	Class 1(N=9580)	**Class 2(N=1508)**	**Class 3(N=3234)**	**Class 4(N=2415)**	**Class 5(N=1091)**	**P_overall**
Asthma						<0.001
No	9259 (96.6%)	191 (12.7%)	2951 (91.2%)	2209 (91.5%)	1041 (95.4%)	
Yes	321 (3.35%)	**1317 (87.3%)**	283 (8.75%)	206 (8.53%)	50 (4.58%)	
Bronchiectasis						<0.001
No	8555 (89.3%)	1385 (91.8%)	2906 (89.9%)	2253 (93.3%)	887 (81.3%)	
Yes	1025 (10.7%)	123 (8.16%)	328 (10.1%)	162 (6.71%)	**204 (18.7%)**	
Pulmonary hypertension						<0.001
No	8781 (91.7%)	1488 (98.7%)	3112 (96.2%)	2205 (91.3%)	511 (46.8%)	
Yes	799 (8.34%)	20 (1.33%)	122 (3.77%)	210 (8.70%)	**580 (53.2%)**	
ILD						<0.001
No	8860 (92.5%)	1495 (99.1%)	3000 (92.8%)	2293 (94.9%)	982 (90.0%)	
Yes	720 (7.52%)	13 (0.86%)	234 (7.24%)	122 (5.05%)	109 (9.99%)	
PTB						<0.001
No	9073 (94.7%)	1502 (99.6%)	3152 (97.5%)	2353 (97.4%)	1035 (94.9%)	
Yes	507 (5.29%)	6 (0.40%)	82 (2.54%)	62 (2.57%)	56 (5.13%)	
Rhinitis						<0.001
No	9549 (99.7%)	1087 (72.1%)	3121 (96.5%)	2370 (98.1%)	1086 (99.5%)	
Yes	31 (0.32%)	**421 (27.9%)**	113 (3.49%)	45 (1.86%)	5 (0.46%)	
IHD						<0.001

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No	8483 (88.5%)	1432 (95.0%)	2690 (83.2%)	338 (14.0%)	980 (89.8%)	
Yes	1097 (11.5%)	76 (5.04%)	544 (16.8%)	2077 (86.0%)	111 (10.2%)	
Atrial Fibrillation						<0.001
No	9383 (97.9%)	1497 (99.3%)	3192 (98.7%)	1906 (78.9%)	819 (75.1%)	
Yes	197 (2.06%)	11 (0.73%)	42 (1.30%)	**509 (21.1%)**	**272 (24.9%)**	
HTN						<0.001
No	8622 (90.0%)	1335 (88.5%)	1382 (42.7%)	783 (32.4%)	986 (90.4%)	
Yes	958 (10.0%)	173 (11.5%)	**1852 (57.3%)**	**1632 (67.6%)**	105 (9.62%)	
Heart failure						<0.001
No	9580 (100%)	1503 (99.7%)	3234 (100%)	1328 (55.0%)	326 (29.9%)	
Yes	0 (0.00%)	5 (0.33%)	0 (0.00%)	**1087 (45.0%)**	**765 (70.1%)**	
Peripheral arterial disease						<0.001
No	9469 (98.8%)	1475 (97.8%)	2819 (87.2%)	2210 (91.5%)	1004 (92.0%)	
Yes	111 (1.16%)	33 (2.19%)	415 (12.8%)	205 (8.49%)	87 (7.97%)	
Venous thromboembolism						<0.001
No	9309 (97.2%)	1504 (99.7%)	3156 (97.6%)	2271 (94.0%)	898 (82.3%)	
Yes	271 (2.83%)	4 (0.27%)	78 (2.41%)	144 (5.96%)	**193 (17.7%)**	
Gastroesophageal reflux						<0.001
No	9414	1396	2856	2338	1026	

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	(98.3%)	(92.6%)	(88.3%)	(96.8%)	(94.0%)	
Yes	166 (1.73%)	112 (7.43%)	378 (11.7%)	77 (3.19%)	65 (5.96%)	
Fatty liver						<0.001
No	9378 (97.9%)	1264 (83.8%)	2348 (72.6%)	2323 (96.2%)	1074 (98.4%)	
Yes	202 (2.11%)	244 (16.2%)	**886 (27.4%)**	92 (3.81%)	17 (1.56%)	
Gallstone						<0.001
No	9099 (95.0%)	1440 (95.5%)	2858 (88.4%)	2247 (93.0%)	1057 (96.9%)	
Yes	481 (5.02%)	68 (4.51%)	376 (11.6%)	168 (6.96%)	34 (3.12%)	
Diabetes mellitus						<0.001
No	9062 (94.6%)	1444 (95.8%)	2132 (65.9%)	1625 (67.3%)	1051 (96.3%)	
Yes	518 (5.41%)	64 (4.24%)	**1102 (34.1%)**	**790 (32.7%)**	40 (3.67%)	
Hyperlipidemia						<0.001
No	9337 (97.5%)	1299 (86.1%)	2209 (68.3%)	2206 (91.3%)	1080 (99.0%)	
Yes	243 (2.54%)	209 (13.9%)	**1025 (31.7%)**	209 (8.65%)	11 (1.01%)	
Thyroid disease						<0.001
No	9375 (97.9%)	1426 (94.6%)	2912 (90.0%)	2299 (95.2%)	1023 (93.8%)	
Yes	205 (2.14%)	82 (5.44%)	322 (9.96%)	116 (4.80%)	68 (6.23%)	
Hyperuricemia gout						<0.001
No	9443 (98.6%)	1457 (96.6%)	2800 (86.6%)	2324 (96.2%)	1023 (93.8%)	
Yes	137 (1.43%)	51 (3.38%)	**434 (13.4%)**	91 (3.77%)	68 (6.23%)	
Stroke						<0.001

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No	9103 (95.0%)	1469 (97.4%)	2477 (76.6%)	1958 (81.1%)	1000 (91.7%)	
Yes	477 (4.98%)	39 (2.59%)	757 (23.4%)	457 (18.9%)	91 (8.34%)	
Urinary stones						<0.001
No	9159 (95.6%)	1425 (94.5%)	2895 (89.5%)	2373 (98.3%)	1055 (96.7%)	
Yes	421 (4.39%)	83 (5.50%)	339 (10.5%)	42 (1.74%)	36 (3.30%)	
Prostatic hyperplasia						<0.001
No	8637 (90.2%)	1348 (89.4%)	2318 (71.7%)	2053 (85.0%)	930 (85.2%)	
Yes	943 (9.84%)	160 (10.6%)	916 (28.3%)	362 (15.0%)	161 (14.8%)	
Solid malignant tumor						<0.001
No	8657 (90.4%)	1501 (99.5%)	3069 (94.9%)	2253 (93.3%)	1074 (98.4%)	
Yes	923 (9.63%)	7 (0.46%)	165 (5.10%)	162 (6.71%)	17 (1.56%)	
Obstructive sleep apnea						<0.001
No	9475 (98.9%)	1422 (94.3%)	3054 (94.4%)	2299 (95.2%)	1042 (95.5%)	
Yes	105 (1.10%)	86 (5.70%)	180 (5.57%)	116 (4.80%)	49 (4.49%)	
Anemia						<0.001
No	8628 (90.1%)	1497 (99.3%)	3006 (92.9%)	2192 (90.8%)	962 (88.2%)	
Yes	952 (9.94%)	11 (0.73%)	228 (7.05%)	223 (9.23%)	129 (11.8%)	

Table S6. Association between multimorbidity patterns and adverse hospital outcomes.

Outcome	Classes	OR (95% CI)	P value
Mortality-related discharge	Class 2	0.32 (0.13-0.67)	0.007
	Class 3	0.73 (0.51-1.03)	0.083

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Outcome	Classes	OR (95% CI)	P value
	Class 4	1.10 (0.78-1.51)	0.580
	Class 5	2.04 (1.39-2.91)	<0.001
Emergency Admission	Class 2	0.69 (0.58-0.82)	<0.001
	Class 3	0.80 (0.72-0.90)	<0.001
	Class 4	1.00 (0.89-1.13)	0.956
	Class 5	1.33 (1.14-1.55)	<0.001
Mechanical Ventilation	Class 2	0.38 (0.27-0.52)	<0.001
	Class 3	0.84 (0.71-0.98)	0.034
	Class 4	1.52 (1.30-1.77)	<0.001
	Class 5	3.31 (2.79-3.91)	<0.001
Intubation	Class 2	0.29 (0.10-0.65)	0.008
	Class 3	0.57 (0.35-0.88)	0.015
	Class 4	1.56 (1.09-2.20)	0.012
	Class 5	3.58 (2.51-5.04)	<0.001
Respiratory Failure	Class 2	0.42 (0.36-0.49)	<0.001
	Class 3	0.73 (0.67-0.80)	<0.001
	Class 4	1.32 (1.20-1.46)	<0.001
	Class 5	3.75 (3.30-4.28)	<0.001
ICU Admission	Class 2	0.56 (0.42-0.74)	<0.001
	Class 3	0.68 (0.57-0.82)	<0.001
	Class 4	1.63 (1.40-1.91)	<0.001
	Class 5	2.02 (1.65-2.47)	<0.001
Severe Outcome	Class 2	0.46 (0.37-0.58)	<0.001
	Class 3	0.77 (0.68-0.88)	<0.001
	Class 4	1.43 (1.26-1.62)	<0.001
	Class 5	2.64 (2.27-3.06)	<0.001

Note: Reference: Class 1. ORs (95% CIs) were estimated by multivariable logistic regression in 17,828 patients, with adjustment for age, sex, insurance category, ethnicity, marital status, and occupation. ORs and confidence limits are reported to two decimal places.

Table S7. Association between multimorbidity patterns and adverse hospital outcomes in patients

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aged ≤80 years.

Outcome	Classes	OR (95% CI)	P value
Mortality-related discharge	Class 2	0.26 (0.08-0.62)	0.008
	Class 3	0.62 (0.37-0.97)	0.044
	Class 4	1.40 (0.92-2.09)	0.106
	Class 5	2.67 (1.73-4.02)	<0.001
Emergency Admission	Class 2	0.62 (0.51-0.74)	<0.001
	Class 3	0.77 (0.68-0.88)	<0.001
	Class 4	1.02 (0.88-1.17)	0.81
	Class 5	1.49 (1.25-1.77)	<0.001
Mechanical Ventilation	Class 2	0.39 (0.27-0.54)	<0.001
	Class 3	0.95 (0.79-1.14)	0.612
	Class 4	1.75 (1.46-2.09)	<0.001
	Class 5	4.06 (3.37-4.88)	<0.001
Intubation	Class 2	0.32 (0.11-0.73)	0.015
	Class 3	0.56 (0.33-0.91)	0.027
	Class 4	1.63 (1.07-2.41)	0.018
	Class 5	3.85 (2.59-5.61)	<0.001
Respiratory Failure	Class 2	0.41 (0.34-0.48)	<0.001
	Class 3	0.75 (0.68-0.84)	<0.001
	Class 4	1.40 (1.25-1.56)	<0.001
	Class 5	4.44 (3.84-5.16)	<0.001
ICU Admission	Class 2	0.57 (0.42-0.76)	<0.001
	Class 3	0.66 (0.53-0.81)	<0.001
	Class 4	1.66 (1.38-2.00)	<0.001
	Class 5	2.41 (1.93-2.99)	<0.001
Severe Outcome	Class 2	0.48 (0.38-0.61)	<0.001
	Class 3	0.81 (0.69-0.93)	0.004
	Class 4	1.55 (1.34-1.80)	<0.001
	Class 5	3.19 (2.70-3.75)	<0.001

Note: Reference: Class 1. ORs (95% CIs) were estimated by multivariable logistic regression among patients aged ≤80 years (n=14,949), with adjustment for age, sex, insurance category, ethnicity, marital status, and occupation. ORs and confidence limits are reported to two decimal places.

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Table S8. Associations between multimorbidity patterns and adverse outcomes among patients aged ≥40 years.

Outcome	Class	OR (95% CI)	P value
Mortality-related discharge	Class 2	0.32 (0.13-0.67)	0.007
Mortality-related discharge	Class 3	0.73 (0.51-1.03)	0.082
Mortality-related discharge	Class 4	1.10 (0.78-1.52)	0.578
Mortality-related discharge	Class 5	2.04 (1.39-2.91)	<0.001
Emergency Admission	Class 2	0.69 (0.57-0.82)	<0.001
Emergency Admission	Class 3	0.80 (0.72-0.90)	<0.001
Emergency Admission	Class 4	1.00 (0.89-1.13)	0.936
Emergency Admission	Class 5	1.34 (1.14-1.56)	<0.001
Mechanical Ventilation	Class 2	0.38 (0.27-0.52)	<0.001
Mechanical Ventilation	Class 3	0.84 (0.71-0.98)	0.034
Mechanical Ventilation	Class 4	1.53 (1.31-1.78)	<0.001
Mechanical Ventilation	Class 5	3.33 (2.81-3.94)	<0.001
Intubation	Class 2	0.29 (0.10-0.65)	0.008
Intubation	Class 3	0.57 (0.35-0.88)	0.014
Intubation	Class 4	1.57 (1.10-2.20)	0.011
Intubation	Class 5	3.60 (2.52-5.06)	<0.001
Respiratory Failure	Class 2	0.42 (0.36-0.49)	<0.001
Respiratory Failure	Class 3	0.73 (0.67-0.81)	<0.001
Respiratory Failure	Class 4	1.32 (1.20-1.46)	<0.001
Respiratory Failure	Class 5	3.75 (3.29-4.28)	<0.001
ICU Admission	Class 2	0.53 (0.39-0.70)	<0.001
ICU Admission	Class 3	0.68 (0.57-0.82)	<0.001
ICU Admission	Class 4	1.64 (1.40-1.91)	<0.001
ICU Admission	Class 5	2.03 (1.66-2.48)	<0.001
Severe Outcome	Class 2	0.45 (0.35-0.56)	<0.001
Severe Outcome	Class 3	0.77 (0.68-0.88)	<0.001
Severe Outcome	Class 4	1.43 (1.27-1.63)	<0.001
Severe Outcome	Class 5	2.66 (2.29-3.08)	<0.001

Note: Reference: Class 1. The analysis included 17,747 patients aged ≥40 years and retained the five-class

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assignments from the main analysis. Multivariable logistic regression adjusted for age, sex, insurance category, ethnicity, marital status, and occupation. CI, confidence interval; OR, odds ratio.

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