

Epidemiology of pulmonary embolism in China, 2021: a nationwide hospital-based study



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Summary

Background Pulmonary embolism (PE) as a preventable and potentially fatal noncommunicable disease was believed to have a lower incidence in Asian populations compared to Western populations. However, the incidence and mortality rates of PE in China and the impact of venous thromboembolism (VTE) prevention system constructions on PE still lack nationwide evidence.

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Methods For this nationwide hospital-based observational study, we used data from the National Hospital Quality Monitoring System (HQMS) and public database in China. We estimated the incidence and in-hospital mortality rates of PE by age group, sex, and regions of geographical and socioeconomic level. VTE prevention and management system constructions were quantified by geographical density. We then calculated the incidence and mortality rates in different conditions of VTE prevention and management system construction.

Findings During the 12 months period between January and December 2021, a total number of 200,112 PE patients and 14,123 deaths were recorded from 5101 hospitals in the HQMS database. The incidence of PE was 14.19 (200,112, 95% CI 14.13–14.26) per 100,000 population and the mortality rate was 1.00 (95% CI 0.99–1.02) per 100,000 population. The incidence of PE was higher in male patients (14.43 per 100,000 population) than in female patients (13.95 per 100,000 population). Disparities of incidence and mortality rates were shown within age groups and geographical regions. The incidence and mortality rates of PE showed decreasing trend with increasing geographical density of VTE-related facilities and VTE prevention system developments.

Interpretation China had a substantially large number of PE patients. The incidence and mortality rates of PE showed disparities in terms of sex, age, and geography. The incidence and mortality rates of PE decrease across regions with increasing levels of socioeconomic development, potentially influenced by the existing VTE prevention and management systems. Optimizing the health policies and healthcare investment in VTE prevention may help reduce the disease burden of PE.

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Keywords: Pulmonary embolism; Incidence; Mortality; VTE prevention; Disease burden

Introduction

Acute pulmonary embolism (PE) is one of the important causes of unexpected death in hospitalized patients, which occurs in 39–115 individuals per 100,000 population in western countries.¹ Several studies have reported that the incidence of PE have increased considerably in the past years, including the data from eastern Asian. The incidence of PE in hospitalized patients increased fivefold from 2007 to 2016 in China, similar to the trends found in Japan and Korea.² These changes might be due to increased awareness, improvement of diagnostic imaging tests, medical conditions, and surgical risk contributing to the development of venous thromboembolism (VTE).

In the past two decades, a significant decrease of in-hospital mortality has been reported in European and America countries. The similar trends were also found in studies from East Asia. These results might be due to the improvement of early detection and proper management. Potential health resource utilities could also affect the mortality and fatality of acute PE.

As a preventable disease and major clinical challenge, the disease burden of PE, and proper healthcare management should be considered. In European and North American regions, when adjusted based on the European standard population, PE-related mortality rates ranged between 2.6 and 6.5 per 100,000

population.^{3,4} The mortality rate data reported by 123 countries in the WHO Mortality Database show a significant variance from 0 to 24 per 100,000 population, adjusted according to the WHO's standard population.⁵

According to the most recent report from the U.S., the mortality of high risk PE remains a challenging issue.⁶ Race, sex, and socioeconomic disparities persist in PE-related mortality Nationwide. Mortality rates are higher for Black compared with White individuals, similarly for higher in rural areas than in micropolitan and large metropolitan areas. Heterogeneity of age, sex, and geography structures can lead to variances for PE incidence and death. However, few studies reported the relationship between geography, medical environment, and the incidence and mortality of PE in eastern Asian countries. In addition, the demographic structure may differ in different population, and the correlation between the above factors and prognosis needs to be further elucidated.

The comprehensive evidence explaining the disease burden of PE and the potential prognostic factors are limited in Asia. It is still unknown whether healthcare resource allocation influences the clinical outcome of acute PE. Data from the patients' records have been widely used to describe disease burden. HQMS is a national database established by the National Health Commission of China from 2011 with the goal of

Research in context

Evidence before this study

We searched PubMed, Embase, and Web of Science using the search terms “incidence”, “prevalence”, “mortality”, “pulmonary embolism”, “venous thromboembolism”, “epidemiology”, and “systematic review”. We retrieved studies related to the epidemiology and review of PE published from January 1, 1980 to December 31, 2022. Previous studies have shown that PE is one of the most important causes of accidental death in hospitalized patients and imposes a substantial economic burden due to disability and chronic disease. According to the 2021 American Heart Association report, 389,000 PE cases occur annually in the United States, with an incidence of 60–120 per 100,000 person-years.

PE incidence is rising in Asian populations, making it a major health issue. Factors such as age, sex, race, and geography affected PE incidence and outcomes. Regional disparities in healthcare standards might also contribute to differences in PE mortality. The disease burden and regional distribution of PE in China remained unclear. China had implemented national-level VTE prevention system constructions and has achieved notable improvements, with prophylaxis rates markedly increasing. Epidemiological studies of PE based on a large sample of hospitalized patients in China were urgently needed to fill the evidence gaps and better guide the prevention and management of PE in China.

Added value of this study

Based on the HQMS data, we reported the incidence and mortality rates and their disparities within the age and geography of PE patients in China in 2021 using the ICD-10 codes. This study found that the incidence of PE in China in 2021 was 14.2 per 100,000, the mortality rate was 1.0 per 100,000. Our study found that PE incidence has increased

compared with previous epidemiological data, while the mortality rate remains lower than in European and American populations after population structure adjustment. The proportion of male PE patients in China was 52.0%, and the proportion of PE patients over 60 years old was 75.3%. The study also noted substantial age-related increases in PE incidence and mortality, with the highest rates in northern, northwestern, and southwestern regions, and the lowest in southern regions. To our knowledge, this is the first PE disease burden study based on the most significant sample of inpatients in China, filling key evidence gaps in PE research in China and even Asia.

Implications of all the available evidence

Our research highlights the increasing incidence and high mortality rates of PE in China, challenging the previous notion that PE incidence is significantly lower in Asian populations compared to Western regions. The findings underscore the urgent need for enhanced public awareness and appropriate thromboprophylaxis to address the rising PE burden. It cannot be neglected that the incidence and mortality rates of PE are increasing with age due to the progression of aging societies. The study also reveals significant disparities in PE incidence and mortality across different regions, sex, and age groups in China. Regions with well-developed VTE-related facilities and VTE prevention systems tend to have lower PE incidence and mortality rates, highlighting the need for optimizing VTE prevention policies while also enhancing healthcare investments and improving the overall quality of care. Therefore, it is crucial to conduct comprehensive, long-term epidemiological studies to better understand and manage PE.

improving the quality of medical care, which provides a background for disease distribution and healthcare resources. In this study, we used the national database of patient records, aiming to elucidate the incidence and mortality rates of PE and the potential impact of healthcare resources to fill the gap in the epidemiology of PE in the Chinese population and provide evidence to support the targeted reduction of PE disease burden.

Methods

Overview of the study design and data source

For this national cross-sectional study, the data were extracted from HQMS database from January 1 to December 31, 2021. All public hospitals from 31 provinces in mainland China are required to submit daily individual-level data on the front page of inpatient discharge records to the HQMS database, including information on socio-demographic, diagnoses, and hospitalization-related

characteristics, had accounted for 79% of the actual number of discharged patients across the nation in the year 2021 (Detailed coverage was provided in [Appendix Table S1](#)). As one of the most comprehensive national sources of information on hospital-based care in China, HQMS had been used regularly in previous health services research ([Appendix Table S2](#)).^{7–10} We also obtained the data of population size, distribution of VTE prevention related healthcare resources, and socioeconomic indicators from the public databases ([Appendix Methods S1](#)). All data collected were anonymous without any personally identifiable information. The study was approved by the Institutional Review Board of China-Japan Friendship Hospital (2024-KY-033).

Identification of PE patients and in-hospital outcome

PE patients were determined by combination of PE with/without deep vein thrombosis (DVT) diagnoses

(PE \pm DVT). The diagnoses of PE and DVT were identified and selected using discharge diagnoses by *International Classification of Diseases, Tenth Revision* (ICD-10) coding system in either principle or other discharge diagnoses. ICD-10 of I26.0 or I26.9 were labeled as PE codes, detailed PE-related codes were listed in [Appendix Table S3](#). We categorized PE \pm DVT patients into two subcategories: patients with both PE and DVT were classified as PE + DVT patients, while patients presenting with isolated PE were categorized as PE alone patients. Given the possibility of multiple hospitalizations for an individual, multi-hospitalizations for the same patient were considered as one patient in counting. The analysis was performed with the information from the patients' initial accessible hospitalization records in HQMS database. PE patients with a discharge status recorded as deceased were identified as death cases.

Data extraction and variable definition

We extracted data from the entire HQMS database on patients with PE-related diagnoses and discharged from hospital in 2021. The variables utilized in the analysis included hospital characteristics (grade and region) and patient demographic characteristics (age, sex, and discharge diagnosis). Age was stratified in five-year intervals. Multimorbidities were defined as the presence of the disease in either principle or other discharge diagnoses through the ICD-10 codes. We have geographically classified the 31 provinces and autonomous regions of China into seven regions, namely North, Northeast, Northwest, East, Central, South, and Southwest ([Appendix Table S4](#)).

Evaluation of VTE-related facilities and prevention systems

We evaluated the VTE-related facilities and prevention systems using two sets of indicators. The VTE-related healthcare resources included the number of institutions for the diagnosis and treatment of PE, the number of hospital beds, the annual number of hospitalizations, and the number of professional healthcare providers. The VTE prevention system developments comprised the number of QC staff and hospitals implementing VTE prevention, the number of hospitals participating in the National VTE Prevention Program, and the number of hospitals certified as VTE centres of excellence ([Appendix Table S5](#)). Certification as a VTE centres of excellence indicates that an institution possesses comprehensive resources and capabilities in areas such as management structure, medical technology, healthcare informatization, nursing management, and patient management, effectively supporting the prevention and management of VTE. Beijing and Shanghai, as the pinnacle of medical care in China, were excluded to minimize bias introduced by the substantial patients referred from nationwide locations.

Then, we assigned the remaining 29 provinces by Human Development Index (HDI) to seven groups ([Appendix Table S6](#)). Geographical density is defined as the number of each indicator per 1000 km² of geographical area ([Appendix Table S7](#)).

Statistical analysis

The PE incidence and mortality rates were defined as the number of patients and deaths with PE diagnosis divided by the total population from the seventh national population census data, respectively. Each rate was characterized and described through the stratification of the patients into four dimensions: sex, age groups demarcated by 5-year increments, provinces, and subcategories of PE. Meanwhile, we standardized the incidence and mortality rates of PE in different age groups using the 2010 census population in China, the 2000–25 world standard population published by WHO¹¹ and the 2013 European standard population¹² to allow comparison with previous studies in China² and international PE-related epidemiological researches^{3–5} ([Appendix Table S8](#)).

Characteristics of PE patients were summarized as numbers (%) for categorical data, and means and Standard Deviations for normally distributed continuous variables. All results of rates were summarized as count and proportion with 95% confidence intervals estimated by delta method. We depicted the proportion of incidence and mortality in age groups, sex, and geographical regions with heat maps. Linear regression models were used to analyze the association between the incidence, mortality, and regions of different HDI percentiles. All analyses were performed using R software, version 4.2.1 ([Appendix Table S9](#)).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

A total of 200,112 PE patients were identified and 14,123 PE patients died between January 1 and December 31, 2021. Among these patients, 120,997 were diagnosed with isolated PE and 79,115 were diagnosed with PE + DVT. More male inpatients were found than female inpatients (104,089 [52.0%] versus 96,023 [48.0%]). The mean age of patients with PE \pm DVT was 67.5 (SD 13.8) years, with female patients having a higher average age than male patients (68.2 [SD 13.5] versus 66.9 [SD 14.2]). Patients older than 60 years were the vast majority (150,705 [75.3%]). More than half patients were admitted in medical departments (120,431 [60.2%]). However, the proportion of PE + DVT patients (18,801 [23.8%]) admitted in surgical departments were twice than that among PE alone patients (12,680 [10.5%]) ([Table 1](#)).

Hypertension, ischemic heart diseases, and heart failure were ranked as the top three multimorbidities in PE patients. The lung (15,604 [7.8%]), colorectal (2936 [1.5%]), and stomach (2523 [1.3%]) were the top three cancer types with the highest proportion among PE patients with cancer (37,263 [18.6%]). Patients with PE alone showed more multimorbidities than patients with PE + DVT, especially in cardiovascular and respiratory diseases (Table 1).

The PE ± DVT incidence was 14.19 [95% CI 14.13–14.26] per 100,000 population in China. Among them, the incidence of isolated PE and PE + DVT were 8.58 [95% CI 8.53–8.63] per 100,000 population and 5.61 [95% CI 8.17–8.26] per 100,000 population, respectively. The incidence of PE was higher in male patients (14.43 per 100,000 population) than in female patients (13.95 per 100,000 population). Mortality rates were estimated to 1.00 [95% CI 0.99–1.02] per 100,000 population. In the population over 85 years, the mortality rate in male patients reaches double that of female patients (Fig. 1).

In terms of age-standardized rates, the incidence adjusted for the European population was the highest (19.30 [95% CI 19.23–19.37]), while that adjusted using the WHO world standard population was the lowest (13.95 [95% CI 13.89–14.01]). The incidence adjusted for the 2010 Chinese population was lower than that for the 2020 population data (15.84 [95% CI 15.78–15.91] versus 21.05 [95% CI 20.97–21.12]). Mortality rates changed in a way similar to incidence, with the highest being in the European standard population at 2.22 (95% CI 2.20–2.25), and the lowest in the WHO standard population (0.99 [95% CI 0.97–1.00]). The rates adjusted from 2010 were lower than those from 2020. The incidence and mortality rates adjusted for the European population exceeded those adjusted for the WHO population by more than twofold (Table 2).

The incidence and mortality rates were significantly increased with the growth of population age. The incidence of PE was slightly higher in males (14.43 per 100,000) compared to females (13.95 per 100,000). In terms of mortality rates, as the age increased, the mortality rate in male patients were increasingly higher than the rates in female patients. In the population aged 85 and above, male patients had a mortality rate more than twice that of female patients (21.00 per 100,000 versus 10.24 per 100,000). In males, the incidence rates ranged from 0.07 per 100,000 in the 0–4 age group to 135.65 per 100,000 in those aged 85 and above. In females the corresponding rates were 0.06 per 100,000 and 86.01 per 100,000 (Fig. 1). At geographical level, the highest incidence was shown in North, Northwest, and Southwest regions. The highest mortality rates were shown in Northwest, Southwest, and North regions. The South region was found with the lowest incidence and mortality rates (Fig. 2). The incidence in the Very low HDI group is higher compared to the Very high HDI group and mortality rates follow a similar trend.

	Total PE (n = 200,112)	PE alone (n = 120,997)	PE + DVT (n = 79,115)
Sex, n (%)			
Male	104,089 (52.0%)	63,907 (52.8%)	40,182 (50.8%)
Female	96,023 (48.0%)	57,090 (47.2%)	38,933 (49.2%)
Age, years (SD)	67.5 (13.8)	67.9 (14.1)	66.9 (13.5)
0–19 years, n (%)	716 (0.4%)	505 (0.4%)	211 (0.3%)
20–39 years, n (%)	8223 (4.1%)	5065 (4.2%)	3158 (4.0%)
40–59 years, n (%)	40,468 (20.2%)	23,254 (19.2%)	17,214 (21.8%)
60–69 years, n (%)	51,282 (25.6%)	30,102 (24.9%)	21,180 (26.8%)
70–79 years, n (%)	61,609 (30.8%)	37,481 (31.0%)	24,128 (30.5%)
≥80 years, n (%)	37,814 (18.9%)	24,590 (20.3%)	13,224 (16.7%)
Departments, n (%)			
Medical departments	120,431 (60.2%)	77,774 (64.3%)	42,657 (53.9%)
Respiratory	54,301 (27.1%)	33,426 (27.6%)	20,875 (26.4%)
Cardiology	30,583 (15.3%)	20,047 (16.6%)	10,536 (13.3%)
Neurology	6889 (3.4%)	4302 (3.6%)	2587 (3.3%)
Surgical departments	31,481 (15.7%)	12,680 (10.5%)	18,801 (23.8%)
General surgery	11,430 (5.7%)	3830 (3.2%)	7600 (9.6%)
Orthopedics	4362 (2.2%)	2395 (2.0%)	1967 (2.5%)
Cardiovascular surgery	3032 (1.5%)	927 (0.8%)	2105 (2.7%)
Thoracic surgery	2852 (1.4%)	1312 (1.1%)	1540 (2.0%)
Critical care units	11,393 (5.7%)	7767 (6.4%)	3626 (4.6%)
Obstetrics and gynecology	3060 (1.5%)	1814 (1.5%)	1246 (1.6%)
Others	33,747 (16.9%)	20,962 (17.3%)	12,788 (16.2%)
Multimorbidity, n (%)			
Hypertension	87,517 (43.7%)	53,316 (44.1%)	34,201 (43.2%)
Ischemic heart diseases	61,039 (30.5%)	40,001 (33.1%)	21,039 (26.6%)
Heart failure	61,770 (30.9%)	41,093 (34.0%)	20,616 (26.1%)
Respiratory failure	48,054 (24.0%)	30,728 (25.4%)	17,292 (21.9%)
Pneumonia	34,527 (17.3%)	20,294 (16.8%)	14,223 (18.0%)
Diabetes mellitus	34,142 (17.1%)	20,824 (17.2%)	13,287 (16.8%)
COPD	29,266 (14.6%)	20,312 (16.8%)	8934 (11.3%)
Ischemic stroke	28,712 (14.4%)	17,212 (14.2%)	11,477 (14.5%)
Cancer (total)	37,263 (18.6%)	23,099 (19.1%)	14,164 (17.9%)
Lung	15,604 (7.8%)	10,027 (8.3%)	5557 (7.0%)
Colon rectum carcinoma	2936 (1.5%)	1739 (1.4%)	1196 (1.5%)
Stomach	2523 (1.3%)	1551 (1.3%)	970 (1.2%)

Abbreviations: PE, pulmonary embolism; DVT, deep vein thrombosis; SD, Standard Deviation; COPD, Chronic Obstructive Pulmonary Disease.

Table 1: Demographic and clinical characteristics of PE patients from 5101 hospitals in China between Jan. and Dec. 2021.

However, there were no statistically significant linear relationship between HDI level and PE incidence ($p = 0.25$) or mortality rates ($p = 0.29$) (Fig. 1).

We observed noticeable downward trend with increasing geographical density of the majority indicators of VTE-related healthcare resources and VTE prevention system developments in the incidence ($p = 0.021$ for PE diagnosis and treatment institutions, $p = 0.021$ for hospital beds, $p = 0.023$ for hospitalizations, $p = 0.042$ for professional healthcare providers, $p = 0.076$ for thromboprophylaxis management, $p = 0.12$ for VTE program participations, $p = 0.012$ for VTE centres of excellence, and $p = 0.034$ for QC stuffs) and

Rates (per 100000 population)		Years of old																	
		0-4	5-9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70-74	75-79	80-84	>=85
Incidence																			
Entire population	14.19	0.06	0.12	0.17	0.57	1.20	1.70	2.21	3.05	4.25	6.26	9.74	17.32	26.21	43.30	67.10	90.70	105.60	105.65
Sex																			
Male	14.43	0.07	0.12	0.17	0.69	1.34	1.81	2.54	3.50	4.66	6.63	10.68	19.14	28.06	45.19	69.86	94.45	116.38	135.65
Female	13.95	0.06	0.11	0.16	0.43	1.04	1.57	1.86	2.57	3.81	5.89	8.79	15.49	24.35	41.48	64.48	87.34	96.81	86.01
Geographic area																			
North	20.04	0.05	0.25	0.31	0.72	1.50	1.95	2.50	3.86	4.98	7.10	11.24	21.56	35.72	62.14	99.84	140.76	154.67	160.06
Northwest	19.55	0.08	0.04	0.26	0.71	1.44	2.35	2.77	4.20	6.51	9.11	14.39	24.52	40.18	68.61	109.28	153.46	175.51	176.50
Southwest	17.02	0.03	0.03	0.14	0.74	1.76	2.22	2.84	3.81	6.14	8.00	12.69	22.70	29.14	46.17	69.90	99.64	129.76	142.41
East	13.03	0.07	0.19	0.15	0.41	1.03	1.32	1.77	2.50	3.17	4.90	7.89	14.54	23.16	38.50	61.57	81.55	92.62	92.10
Northeast	12.82	0.07	0.05	0.05	0.56	0.82	1.50	1.70	2.23	2.73	4.28	6.81	11.09	18.88	33.93	48.55	73.64	84.90	85.17
Central	11.31	0.05	0.09	0.11	0.52	0.94	1.65	2.18	2.76	3.84	5.91	8.54	15.66	21.93	33.37	51.00	61.88	73.08	72.11
South	9.63	0.09	0.06	0.19	0.58	0.96	1.48	2.33	2.90	4.27	6.42	10.21	16.61	23.55	39.31	56.41	65.98	78.86	82.66
HDI group*																			
Very high	11.95	0.09	0.05	0.18	0.53	1.09	1.37	2.04	2.53	3.40	5.10	7.87	15.05	23.89	40.60	63.04	83.31	96.74	97.82
High	17.23	0.13	0.43	0.24	0.47	0.96	1.54	1.99	2.84	3.90	6.23	9.71	17.33	26.47	47.56	76.23	110.29	117.25	106.74
Upper-middle	12.34	0.05	0.08	0.19	0.61	0.87	1.61	1.96	2.46	3.71	5.34	8.81	15.23	22.99	36.84	54.74	71.61	88.77	93.66
Middle	11.15	0.03	0.12	0.12	0.44	0.98	1.45	1.69	2.46	3.25	5.10	7.67	13.43	19.59	32.87	50.31	64.12	74.16	72.34
Lower-middle	16.01	0.03	0.05	0.11	0.52	1.17	1.78	2.21	3.52	4.90	7.48	11.62	20.62	32.68	51.26	81.87	117.18	130.25	120.69
Low	10.33	0.02	0.02	0.11	0.40	1.12	1.36	1.78	2.40	3.33	5.11	8.11	13.52	18.18	28.37	43.62	58.76	73.32	74.65
Very low	19.18	0.06	0.02	0.13	0.90	2.01	2.96	3.54	4.66	7.32	10.41	15.89	28.62	39.08	69.21	102.86	135.57	164.76	181.25
Mortality																			
Entire population	1.00	0.01	0.01	0.02	0.03	0.05	0.07	0.11	0.15	0.25	0.40	0.58	1.09	1.51	2.57	3.98	6.41	9.59	14.50
Sex																			
Male	1.18	0.01	0.01	0.02	0.04	0.05	0.07	0.12	0.18	0.30	0.44	0.69	1.37	1.83	3.35	5.16	8.11	11.88	21.00
Female	0.82	0.01	0.00	0.02	0.01	0.06	0.07	0.10	0.11	0.20	0.36	0.46	0.81	1.18	1.82	2.86	4.88	7.71	10.24
Geographic area																			
Northwest	1.53	0.00	0.01	0.05	0.08	0.12	0.13	0.22	0.26	0.56	0.65	0.87	1.90	2.40	4.85	6.77	11.50	18.06	28.51
Southwest	1.50	0.00	0.00	0.01	0.03	0.09	0.10	0.15	0.32	0.43	0.59	0.92	1.87	2.38	3.48	4.95	8.79	13.00	24.30
North	1.21	0.00	0.01	0.03	0.05	0.04	0.08	0.10	0.13	0.28	0.38	0.59	1.01	1.65	2.71	5.05	8.61	13.20	21.70
Northeast	1.19	0.03	0.00	0.00	0.02	0.09	0.08	0.08	0.12	0.20	0.28	0.61	0.86	1.53	2.59	4.04	6.90	10.76	14.05
Central	0.78	0.00	0.00	0.00	0.02	0.03	0.09	0.14	0.14	0.19	0.40	0.45	0.94	1.15	2.08	3.08	4.39	7.20	9.56
East	0.74	0.00	0.01	0.02	0.01	0.04	0.04	0.08	0.09	0.14	0.26	0.37	0.78	1.10	1.89	3.00	4.33	6.43	9.71
South	0.74	0.04	0.01	0.03	0.01	0.04	0.05	0.11	0.13	0.24	0.46	0.62	1.01	1.44	2.66	4.05	5.95	7.81	11.84
HDI group#																			
Very high	0.52	0.03	0.00	0.01	0.02	0.02	0.03	0.07	0.06	0.18	0.26	0.30	0.54	0.81	1.57	2.13	3.35	5.52	7.96
High	1.40	0.01	0.02	0.01	0.02	0.01	0.10	0.10	0.14	0.28	0.40	0.70	1.30	1.73	3.35	5.45	8.82	11.88	17.02
Upper-middle	1.05	0.00	0.00	0.02	0.04	0.08	0.08	0.13	0.15	0.28	0.32	0.67	1.14	1.56	2.62	4.07	6.26	8.99	16.60
Middle	0.71	0.00	0.00	0.00	0.04	0.06	0.05	0.09	0.10	0.16	0.25	0.44	0.74	1.15	1.73	3.00	4.33	6.81	6.62
Lower-middle	1.11	0.00	0.01	0.01	0.04	0.08	0.12	0.17	0.17	0.30	0.61	0.64	1.21	1.77	2.97	4.49	7.85	13.37	16.74
Low	1.02	0.01	0.01	0.02	0.01	0.09	0.10	0.13	0.21	0.23	0.46	0.63	1.24	1.70	2.42	3.66	5.70	8.03	13.64
Very low	1.21	0.00	0.00	0.02	0.03	0.07	0.07	0.15	0.37	0.45	0.59	0.81	1.89	1.95	3.75	4.94	8.96	12.69	23.55

Fig. 1: Incidence and mortality heatmap of the age groups by sex, geographic area, and HDI in China. *Suggests that there is no statistically significant linear relationship between HDI level and PE incidence ($p = 0.25$). *Suggests that there is no statistically significant linear relationship between HDI level and PE mortality ($p = 0.29$). Abbreviation: HDI, Human Development Index.

mortality rates of PE ($p = 0.058$ for PE diagnosis and treatment institutions, $p = 0.071$ for hospital beds, $p = 0.070$ for hospitalizations, $p = 0.075$ for professional healthcare providers, $p = 0.11$ for thromboprophylaxis management, $p = 0.19$ for VTE program participations, $p = 0.0050$ for VTE centres of excellence, and $p = 0.039$ for QC stuffs) (Fig. 3).

Discussion

To the best of our knowledge, this is the first study utilizing national data to elucidate the disparities in incidence and mortality rates and the impact on VTE facilities and prevention systems in China. Our findings indicated that the number of PE patients in 2021, has escalated to approximately 200,000, yielding an

	Total PE	PE alone	PE + DVT
Incidence (per 100,000 population, 95% CI)			
Incidence rates by 2020 standard population in China	14.19 (14.13, 14.26)	8.58 (8.53, 8.63)	5.61 (5.57, 5.65)
Age-standardized incidence rates by 2010 standard population in China	10.70 (10.64, 10.75)	6.45 (6.41, 6.49)	4.25 (4.21, 4.28)
Age-standardized incidence rates by WHO standard population	9.42 (9.37, 9.47)	5.70 (5.66, 5.74)	3.72 (3.69, 3.75)
Age-standardized incidence rates in European population	19.30 (19.23, 19.37)	11.82 (11.76, 11.87)	7.48 (7.44, 7.53)
Mortality (per 100,000 population, 95% CI)			
Mortality rates by 2020 standard population in China	1.00 (0.99, 1.02)	0.77 (0.76, 0.79)	0.23 (0.22, 0.24)
Age-standardized mortality rates by 2010 standard population in China	0.73 (0.72, 0.74)	0.57 (0.55, 0.58)	0.17 (0.16, 0.17)
Age-standardized mortality rates by WHO standard population	0.65 (0.64, 0.67)	0.51 (0.49, 0.52)	0.15 (0.14, 0.15)
Age-standardized mortality rates in European population	1.47 (1.45, 1.49)	1.13 (1.11, 1.15)	0.34 (0.33, 0.35)

Abbreviations: PE, pulmonary embolism; DVT, deep vein thrombosis; WHO, World Health Organization; CI, confidence interval.

Table 2: Incidence and mortality rates of PE standardized by differ standard population in China.

incidence rate of 14.19 per 100,000 population. Additionally, the mortality rate of PE patients was 1.00 per 100,000 population. This study provided comprehensive and large-scale data within the East Asian region, enhancing our understanding of the global epidemiological trends and disparities in disease burden associated with PE globally.

Our latest estimates indicate a significant increase in the PE incidence compared to prior data from China. Previous epidemiological studies have estimated that the incidence of PE surged fivefold over a decade from 1.1 per 100,000 individuals in 2007 to 6.3 per 100,000 individuals in 2016.² Similarly, in Hong Kong China, the incidence elevated from 3.9 per 100,000 in 2004 to 11.7 per 100,000 in 2022.^{13,14} The incidence results from our study mark a further twofold increase compared with the data from five years ago, indicating an ongoing escalation of PE incidence in China. The steady growth in the incidence of PE can be attributed to several factors. Awareness of diagnosis among physicians improved and diagnostic techniques were widespread. On the other hand, the patient scale admitted in Chinese hospitals has seen consistent expansion in recent years. The higher rate of PE + DVT in surgical settings may be attributed to systematic DVT screening strategies that improve detection compared to medical settings. Meanwhile, aging, obesity, and cancer had led to an increase in risk associated with PE. Obesity has been considered a significant risk factor for VTE in previous studies.^{15,16} BMI levels in China have risen from 22.7 kg/m² in 2004 to 24.4 kg/m² in 2018, and obesity prevalence has increased from 3.1% to 8.1% during the same period.¹⁷ COVID-19 is also an important independent risk factor for PE. During the study period, COVID-19 may have influenced the incidence of PE, with the risk ratio for PE being 33.05 during the first 30 days following COVID-19 infection.¹⁸ In patients with cancer, the risk of VTE is increasing steadily and reaching ninefold higher than that in the general population. In our study, patients with cancer constituted 18% of PE

patients, a significantly higher proportion than in the general population.¹⁸

We estimate that the most recent number of PE patients in China is approaching the latest figures statistics reported in the U.S. for 2022, where the number of PE hospitalizations reached 389,000 in 2018.¹⁹ Our study suggests that the current incidence and mortality of PE in China was higher than previous epidemiological data from Asia.¹³ However, the incidence among the PE population in Asia continues to rise conspicuously. In South Korea, the incidence rose from 3.7 per 100,000 in 2004 to 16.6 per 100,000 in 2013.²⁰ Furthermore, we found that the incidence of DVT patients in China reached 106.8 per 100,000 population, substantially exceeding the levels reported in previous Asian studies, where the incidence of DVT ranged between 15.9 and 30.0 per 100,000 population and was close to the incidence rates observed in Western regions (78–152 per 100,000 population).¹³

The WHO Mortality Database serves as a crucial source of data related to PE mortalities. Unfortunately, this database does not contain data from China, leading to an absence of recent data for PE-related deaths from China. Our study addressed the existing gap regarding the PE-related mortality data in China. The mortality rate data reported by 123 countries in the WHO Mortality Database show a significant variance from 0 to 24 per 100,000 population. However, the majority of countries globally report mortality rates within the range of 1–4 per 100,000 population adjusted according to the WHO's standard population.⁵ In European and North American regions, when adjusted based on the European standard population, the PE-related mortality rates ranged between 2.6 and 6.5 per 100,000 population.^{3,4} Our study employed both the WHO and European standard populations for adjustments to compared with studies globally. However, we utilized the all-cause in-hospital mortality rate among PE patients in our research, a measurement criterion that is typically broader compared to the WHO Mortality Database

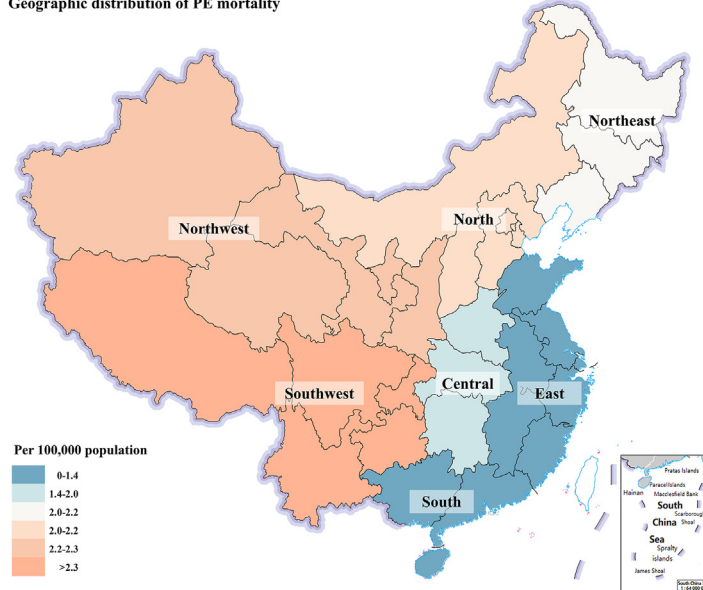
a Geographic distribution of PE incidence**b** Geographic distribution of PE mortality

Fig. 2: Geographic distribution of PE incidence and mortality in China. **a:** The incidence rates of PE were higher in the northern regions compared to the southern regions, with the northwest and southwest regions showing higher incidence than the eastern areas. **b:** The mortality rates of PE were greater in the northern than in the southern regions. Notably, the southwest, northwest, and northeast regions exhibited higher mortality rates than others. Abbreviation: PE, pulmonary embolism.

where PE is considered as the primary cause of death. Heterogeneity in population age structures can lead to variances in the adjusted results. Compared to the WHO standard population, the European standard

population has a higher proportion of older age groups. By adjusting for these different age structures, we can better understand the burden of PE disease in China, where the population is rapidly aging.

In terms of sex disparities, both incidence and mortality rates were observed higher in male than female patients in China. This finding is consistent with previous research, which suggested that males had a higher risk of first and recurrent venous thrombosis compared to females. Male patients had more multi-morbidities compared to females, such as respiratory diseases including chronic obstructive pulmonary disease (COPD), respiratory failure, and pneumonia. However, the mortality rates increase higher among males with age, which are different from the findings in Europe and North America regions.^{3,4} The decline in estrogen levels post-menopause is known to affect blood coagulation, potentially increasing the risk of thromboembolic events. A significant increase in PE incidence in women after the age of 45, which corresponds to the postmenopausal period, suggests that hormonal changes associated with menopause may contribute to an increased risk of PE.

The differences in geographic distributions of PE incidence and mortality are multifactorial. Several factors could contribute to these regional variations, such as disparities in socioeconomic development, differences in healthcare infrastructure and technology, variations in lifestyle and climate, among others. Studies have shown that socioeconomic status and access to healthcare can significantly influence the outcomes of PE incidence and mortality. Higher socioeconomic regions tend to have better healthcare infrastructure and preventive measures, leading to lower PE rates and improved outcomes.^{5,21} Additionally, climatic conditions such as colder temperatures and air pollution have been associated with increased risk of thromboembolic events.^{22,23}

In age disparities, the PE-related incidence, mortality rates were both observed to be increasing with age. However, younger women are present with specific risk factors for VTE, such as pregnancy and the use of oral contraceptive drugs.²⁴ In the face of declining fertility rates and increasing life expectancy, the progressive aging of China's society has escalated into a significant concern. China has the world's largest older population. In 2021, 14.2% of China's population was 65 years and older.²⁵ PE emerges as a significant coexisting condition within elder population. Like the challenges encountered by European countries, the overall medical, societal, and economic burden related to the increasing number of PE diagnoses and deaths are forecasted to persistently escalate. The UN General Assembly declared 2021–2030 the decade of healthy aging. It is necessary to implement thromboprophylaxis and optimize clinical pathways of diagnosis and treatment to improve the quality of care for older patients.

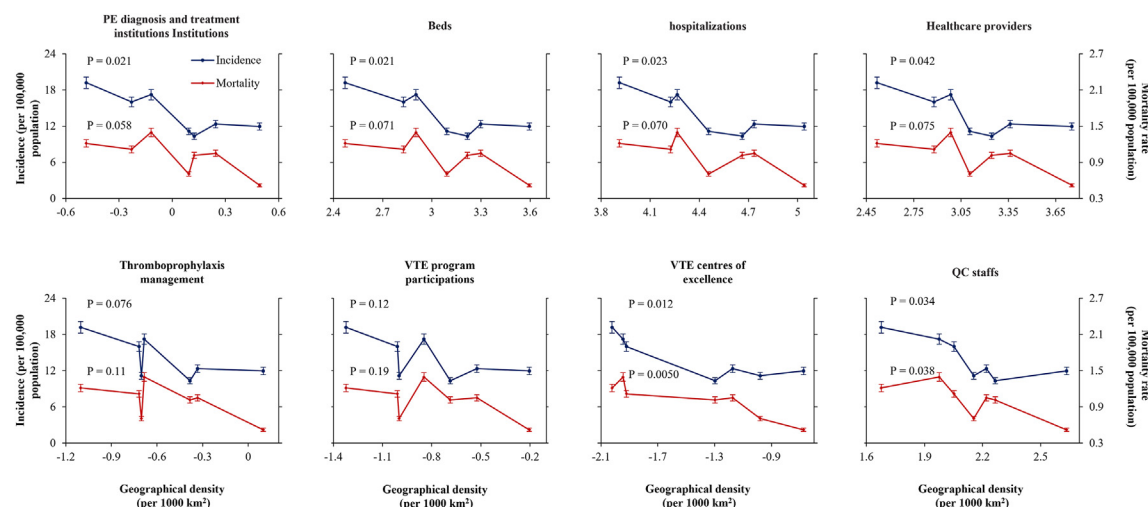


Fig. 3: PE-related incidence and mortality rates in PE patients in relation to the geographical densities of VTE-related facilities and prevention systems in China, 2021. Geographical densities per 1000 square kilometres were log-transformed. Detailed geographical densities of each indicator were listed in [Appendix Table S7](#). Error bars show 95% CIs of each rate. The definitions of each indicator of VTE-related facilities and prevention systems were as follows: PE diagnosis and treatment institutions Institutions was defined as the total number of secondary and tertiary public hospitals across Mainland China. Hospital bed counts represented the total number of actual and functional beds available at the end of the year. The hospitalizations were defined as the total number of patients discharged throughout the year of 2021. Professional healthcare providers included licensed physicians, assistant physicians, registered nurses, pharmacists, technicians, and interns, who provide medical care to patients. Thromboprophylaxis management denoted the number of hospitals implementing VTE prevention system according to the NCIS survey. VTE program participation implied the total number of hospitals engaged in the National VTE prevention program in China. VTE Centres of Excellence indicated that the institution possesses comprehensive resources and capabilities to effectively support the prevention and management of VTE. QC staffs were defined as the total numbers of specialized personnel engaged in medical quality management control. Abbreviations: PE, pulmonary embolism; VTE, venous thromboembolism; CI, confidence interval; NCIS, National Clinical Improvement System; QC, quality control.

Although the occurrence and death of PE are multifactorial, thromboprophylaxis serves a critical role in reducing the disease burden of PE.²⁶ Past studies have shown that the rate of VTE prophylaxis in China has been relatively low for a long time, with only 14.3% of hospitalized patients receiving VTE prophylaxis in 2016.²⁷ China's health administration had launched a national VTE prevention management program from 2018. Our latest survey in 2021 shows that the VTE prevention rate in China has now elevated to 37.9%. However, the global VTE prophylaxis rates had already reached 40%–60% back in 2008, as indicated by the Endorse study.²⁸ The most recent Meta-analysis reports the current global rate of VTE prophylaxis at 54.5%, with Europe and North America having the highest rates of 66.8% and 68.6%, respectively.²⁹ Thus, China's VTE prophylaxis rate is still significantly lower than the global levels. Further strategies need to be taken to improve the thromboprophylaxis among hospital patients to alleviate the disease burden of PE.

As a critical preventable noncommunicable disease, PE incidence and mortality rates were found to be lower in regions with better VTE prevention system construction. Regions with better VTE-related healthcare resources often lean towards to a marked decline in PE occurrences.

However, it contradicts the conclusion derived from 123 countries, which suggested a higher mortality rate in high-income countries.⁵ The indicators of VTE prevention and management play a crucial role in the construction of VTE prevention systems, which in turn significantly influence the incidence and outcomes of PE. Our findings demonstrate that the overall incidence and mortality rates of PE tend to decrease with the increasing geographical density of VTE facilities and prevention systems. This suggests that strengthening VTE prevention systems should be a priority to improve national prevention strategies and reduce the disease burden associated with PE. Furthermore, it is essential to recognize that the availability of healthcare resources significantly influence PE outcomes. High-income countries, despite their advanced healthcare systems, may face higher mortality rates due to factors such as healthcare access disparities, resource allocation, and quality of care. Therefore, while enhancing VTE prevention systems is crucial, equal attention must be given to improving overall healthcare management and quality of care.

Our study has several limitations. First, the estimated rates were based on a single year's data, which may lead to potential misestimation of the incidence rate, as some patients may diagnose and manage PE as

outpatient, some patients may have been diagnosed with PE prior to 2021 but were hospitalized for other reasons during the study period. Second, although the front page of the medical record has legal validity, the identification of PE patients relies on diagnostic codes entered by clinicians, lacking detailed diagnostic confirmation, and treatment information. Additionally, ICD codes at hospital discharge do not differentiate between ambulatory PE and hospital-acquired PE, which is crucial for improving VTE prevention during hospitalization. Third, out-of-hospital events may not be adequately captured, potentially leading to an underestimation of the incidence and mortality rates associated with PE. It is crucial to integrate comprehensive databases that thoroughly outline the causes of death to estimate a more accurate PE mortality rate. Fourth, the HQMS database covers approximately 79% of the total population, which may lead to an underestimation of the true rates of PE. Fifth, the potential impact of the COVID-19 pandemic should be further emphasized in future analyses, particularly to determine whether the change of incidence rates are related to circumstantial factors, underlying causes, or a combination of both, to assess their relative importance. While our research has highlighted and addressed several epidemiological aspects of PE in China, there remains a pressing need for systematic, long-term studies on epidemic trends.

Conclusion

China had a large number of PE population with a high mortality rate. The incidence and mortality of PE showed disparities in terms of sex, age, geography, and condition of VTE prevention system constructions. The incidence and mortality rates of PE showed decreasing trend with increasing geographical density of VTE facilities and prevention systems. It is necessary to conduct more comprehensive, long-term epidemiological and prospective research on thromboprophylaxis, diagnosis and treatment in PE. This study provides the national data for understanding the epidemiology of PE in China and even in the East Asia region from a global perspective.

Contributors

ZZhai and CW contributed to the conception and design of the study. KZ prepared the first draft and made the figures and tables. KZ, YT, LX, SW, and QG did the statistical analysis and data interpretation. YK, XM, DW, GF, and ZChen were involved in data preparation and verification. GF, YK, JL, and SW directed the statistical methods. ZZhang, CS, WW, and YZ sorted out the rules of coding conversion. JW, YY, ZL, YJ, JS, QY, GS, YG, NZ, ZCheng, LZ, ZheC, PY, WX, QH, SZ, XZ, LG, BL, and SC participated in data interpretation and provided professional guidance on the manuscript. All authors provided input into interpretation of the results and content of the paper. CJ, ZZhai, and CW had full access to all data in the study and verified the data and are responsible for the integrity and accuracy of the data and the decision to submit the manuscript. All authors revised the report and approved the final version before submission.

Data sharing statement

Data of the population structures and geographical area are listed by regions in the [Appendix](#). Data sources of VTE prevention system

constructions and HDI are listed by regions in the [Appendix](#). The coverage of the database of the HQMS hospital admission record by province are listed in the [Appendix](#). According to the Personal Information Protection Law of China, individual participant data in our study will not be made available publicly. The data from National VTE Prevention Program, including deidentified hospital participants, will be made available upon publication to members of the scientific and medical community for non-commercial use only, upon email request to vte20181013@126.com.

Editor note

The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

Declaration of interests

The authors have no conflict of interest or financial relationships to disclose. No form of payment was given to anyone to produce the manuscript.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.janwpc.2024.101258>.

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