## Original Article Trends and determinants of place of death among Chinese lymphoma patients: a population-based study from 2013-2021

Xiao-Sheng Ding<sup>1\*</sup>, Jin-Lei Qi<sup>2\*</sup>, Wei-Ping Liu<sup>1\*</sup>, Peng Yin<sup>2</sup>, Li-Jun Wang<sup>2</sup>, Yu-Qin Song<sup>1</sup>, Mai-Geng Zhou<sup>2</sup>, Jun Ma<sup>3</sup>, Jun Zhu<sup>1</sup>

<sup>1</sup>Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Lymphoma, Peking University Cancer Hospital & Institute, Beijing 100142, China; <sup>2</sup>National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing 100050, China; <sup>3</sup>Department of Hematology & Oncology, Harbin Institute of Hematology & Oncology, Harbin 150010, Heilongjiang, China. <sup>\*</sup>Equal contributors.

Received May 23, 2023; Accepted June 26, 2023; Epub September 15, 2023; Published September 30, 2023

**Abstract:** Limited research exists on factors influencing the place of death (POD) or hospital deaths among lymphoma patients in China, despite the country's significant burden of lymphoid neoplasms. This study aimed to describe the distribution of POD among lymphoma patients and identify the factors associated with hospital lymphoma deaths to provide evidence for developing targeted healthcare policies. Data in this study were obtained from the National Mortality Surveillance System (NMSS). The distribution of POD among individuals who died from lymphoma was analyzed, and factors influencing the choice of dying in the hospital were examined. Chi-square test was employed to analyze the differences in characteristic distributions. Multilevel logistic regression analysis was identify the relationship between hospital deaths due to lymphoma and individual factors, as well as socioeconomic contextual variables. During 2013-2021, there were 66772 lymphoma deaths reported by the NMSS, including 44327 patients (66.39%) who died at home and 21211 (31.77%) died in the hospital. Female patients, those had a higher level of educational attainment, retired individuals, those died of non-Hodgkin lymphoma, residents of urban areas, patients between the ages of 0 and 14, and unmarried individuals had a higher probability of dying in hospitals. Improving health care providers' understanding of palliative care for cancer patients and prioritizing accessible services are essential to enhance the quality of end-of-life care. These approaches ensure the equitable allocation of healthcare resources and provide diverse options for minorities with specific preferences regarding end-of-life care.

Keywords: Lymphoma, place of death, China, trends, spatial variations, associated factors

#### Introduction

Lymphoma comprises a diverse range of tumors affecting the blood and lymph nodes, originating from lymphocyte abnormalities. Based on the corresponding pathological characteristics, there are two main subtypes of lymphoma, non-Hodgkin lymphoma (NHL) and Hodgkin lymphoma (HL), which account for 90% and 10% of lymphoma cases, respective-ly. According to GLOBOCAN statistics in 2020, the estimated numbers of HL and NHL cases were 83087 and 544352 worldwide, respectively, accounting for 3.2% of the 19.2 million new cancer cases in 2020 (0.4% due to HL and

2.8% due to NHL) [1]. There were 23376 and 259793 decedents due to HL and NHL, respectively, accounting for 2.8% of the 9.9 million cancer deaths worldwide in 2020 (0.2% due to HL and 2.6% due to NHL) [1].

Place of death (POD) has generally proven to be a sensitive and reliable indicator of care provision during the end of life (EOL) and an outcome measure of health care services worldwide [2, 3]. Healthcare policy-makers and scientists have increasingly focused on this crucial quality indicator of EOL care, and patients with endstage diseases deserve the opportunity to select their preferred POD. Some studies have corroborated that patients with end-stage diseases or advanced cancer prefer palliative care and to die at home [4-6]. China is currently the most populous developing country in the world, with highly multifarious cultures and ethnicities [7]. This presents a great opportunity to gain insights into the mechanisms of POD and identify the determining factors that influence POD patterns in patients with different diseases using Chinese data. Furthermore, this study provides pertinent guidance for the precise allocation of medical care and health services for patients with end-stage diseases.

China has been facing a dramatic disease burden of lymphoid neoplasms in recent decades, with an annual increase of 4.5% in the mortality of lymphoma and myeloma [8, 9]. Some studies have reported diverse POD distributions and corresponding related factors among patients with cancer, dementia, cardiovascular diseases and pediatric diseases [10-13]. To our knowledge, there have been few studies on the associated factors of POD or hospital deaths among patients with lymphoma. Grasping the characteristics of POD among lymphoma patients is beneficial in optimizing the utilization of healthcare resources and improving the quality of EOL care for lymphoma patients. In this study, we aimed to describe the POD distribution among lymphoma patients and probe the related factors of hospital lymphoma deaths, so as to provide plausible explanations.

## Methods

## Data sources

Data on lymphoma deaths were obtained from the National Mortality Surveillance System (NMSS), which is housed in the Chinese Center for Disease Control and Prevention (China CDC). The disease surveillance point system was primarily established in 1978 with 2 pilot surveillance points in Beijing [14]. After the subsequent development of surveillance mechanisms, surveillance points increased to 145 points covering 10 million people in 1990 and further expanded to 161 points covering 73 million people in 2004 [15]. The disease surveillance point system merged with the vital registration system in 2013, intending to provide provincially representative mortality surveillance information. The surveillance system encompassing 605 points of observation across 31 provinces monitored a population of over 300 million individuals, accounting for 24% of the total population [15]. The NMSS also gradually achieved internet-based reporting, which greatly improved the effect of mortality surveillance, making routine collections more convenient, efficient and thorough. The ethics committee of the Chinese Center for Disease Control and Prevention approved this study. The research was conducted without the accessibility of individual participant information.

## Mortality data extraction

The underlying cause of death (COD) in the NMSS is recorded by using the International Classification of Diseases 10<sup>th</sup> Revision (ICD-10). We extracted all deaths between 2013 and 2021 where lymphoma (NHL or HL) was identified as the underlying COD.

#### Variables

We grouped the POD of lymphoma patients into five categories: hospitals, home, nursing homes, on the way to hospitals and others/ unknown. For explanatory variables, we included location (for which we defined districts as urban areas and counties as rural areas), demographics (sex, age, ethnicity, marital status), socioeconomic status (SES, including the level of educational attainment and occupation), and disease-related factors (underlying COD, highest-level diagnostic institutions, highest-level diagnosis basis) [16, 17]. We analyzed age (years) as an ordinal 3-category variable (0-14, 15-64, 65 and above) rather than as a continuous variable to facilitate interpretation and comparison with other studies.

## Statistical analysis

We first depicted the POD distribution among lymphoma patients based crucial features from 2013 to 2021. Chi-square test was employed to examine the differences in characteristic distributions among nominal classes. Subsequently, we conducted multilevel logistic regression to identify the relationships of hospital lymphoma deaths with individual factors and socioeconomic contextual variables. Hence, we classified deaths at home, nursing homes, on the way to hospitals and others/unknown as "out-of-hospital lymphoma deaths". Multiple



Figure 1. Study flow.

models were constructed separately. First, Model 1 was the ordinary null model that included fixed and random intercepts and was fitted to investigate spatial variations across multiple scales, among which random intercepts accounted for the clustering of participants (level 1) within provinces (level 2). Random effects at the individual level were thus translated into the median odds ratio (MOR), which indicated the median value of the odds between the area with the highest outcome probability and the area with the lowest [18]. To explore the extent to which these personal and contextual variables affected the probability of patients with lymphoma dying in the hospital, demographics (Model 2), SES (Model 3), underlying COD (Model 4), and region (Model 5) were input into the multivariable logistic model, respectively, and the proportional change in variance (PCV) was calculated for each submodel. PCV generally indicates how several factors contribute to a model, but it reflected the proportion of variance associated with newly added variables in this study [19-22]. In this way, we could verify whether the potential impact of contextual variables on hospital lymphoma deaths was dependent on each individual-level variable [23-25]. Furthermore, an analogous analysis among NHL and HL deaths was specifically performed to identify corresponding factors that might be influential in the deaths of the two staple categories of lymphoma patients. In all hypothesis tests, a *P* value cutoff of 0.05 was considered statistically significant. All relevant analyses were performed in R 4.2.1 (R Core Team, Vienna, Austria) and the ArcGIS program.

## Role of the funding source

The funders of this study played no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors had full access to all the data in this study and held the final responsibility for the decision to submit for publication.

#### Results

# Characteristics of the POD distribution among lymphoma patients

The flow diagram used in this study is presented in Figure 1. During 2013-2021, there were 66772 lymphoma deaths reported by the NMSS, including 44327 patients who died at home (66.39%), 21211 in the hospital (31.77%), 301 in a nursing home (0.45%), 497 on the way to a hospital (0.74%) and 436 others (0.65%) (Table 1). Home was still the primary preferred POD among lymphoma patients, and disparities in the POD distribution by important characteristics were also present. Hospitals became a more common POD after 2013, although home was the leading POD for both male and female lymphoma patients (Figure 2). In contrast to rural areas, patients from urban areas were more likely to die in the hospital (Figure 3). Similar results were discovered in the POD distribution of lymphoma among provinces. In addition, we found that all age groups had a higher proportion of hospital deaths in urban areas. In contrast, younger patients were more likely to die in hospitals in rural areas. Furthermore, at a national level, there was no distinct change with time among each age

Characteristics	Total	Medical and healthcare institutions	Out of r	medical an	d healthcare i	nstitutions
			Home	Nursing	On the way	Others/
			потте	homes	to hospitals	Unknow
lotal	66772	21211	44327	301	497	436
Location						
Urban	28128	13850	13678	206	200	194
Rural	38644	7361	30649	95	297	242
P value	<0.001					
Region						
Eastern	33672	10599	22468	185	218	202
Central	19378	6176	12814	79	168	141
Western	13722	4436	9045	37	111	93
P value	<0.001					
Sex						
Male	41280	12928	27584	194	318	256
Female	25492	8283	16743	107	179	180
P value	0.008					
Age group, years old						
0-14	762	373	357	2	14	16
15-64	26117	8445	17156	74	223	219
65 and above	39893	12393	26814	225	260	201
P value	< 0.001	22000	2002.		200	
Ethnicity	-0.001					
Han	63745	20558	42019	283	462	423
Other ethnics	3027	653	2308	18	35	13
P value	<0.001	000	2000	10	00	10
Marital status	40.001					
Married	52728	17107	34753	150	393	325
Unmarried	3340	1415	1784	50	41	50
Widowed/Divorced	10425	2585	7630	99	60	50 51
,	279	104	160	99 2	3	10
Unknown		104	100	2	5	10
P value	<0.001					
Education	55400	40407	40000	007	200	225
Junior high school and below	55108	13197	40983	227	366	335
Senior high school	7179	4500	2495	45	73	66
College and above	4485	3514	849	29	58	35
<i>P</i> value	<0.001					
Occupation		100.1		07		100
Agricultural-related personnel	39490	4694	34288	87	222	199
Retired	10518	6903	3396	78	81	60
Unemployment/Student	4024	2009	1891	32	49	43
Worker/Self-employed/Enterprise manager	6671	3966	2533	36	84	52
Professional/Staff/Civil servant	675	514	143	1	14	3
Others/Unknown	5394	3125	2076	67	47	79
P value	<0.001					
Underlying cause of death						
HL	4087	1201	2810	19	32	25
NHL	62685	20010	41517	282	465	411
P value	0.02					

 Table 1. Characteristics of place of death (POD) distribution among lymphoma deaths from the National Mortality Surveillance System (NMSS) in China, 2013-2021

Region: Western: Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Tibet, Shaanxi, Gansu, Qinghai, Ningxia, Xinjiang; Central: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, Hunan; Eastern: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, Hainan. We used the chi-square test to examine the differences in characteristic distributions among nominal classes.



**Figure 2.** Percentage of place of death (POD) distribution among lymphoma deaths from the National Mortality Surveillance System (NMSS) in China, by sex. A: Percentage of POD distribution among lymphoma deaths in China, 2013-2021; B: Percentage of POD distribution among lymphoma deaths in China, by age; C: Percentage of POD distribution among lymphoma deaths in China, by province.



**Figure 3.** Percentage of POD distribution among lymphoma deaths from NMSS in China, by residence areas. A: Percentage of POD distribution among lymphoma deaths in China, 2013-2021; B: Percentage of POD distribution among lymphoma deaths in China, by age; C: Percentage of POD distribution among lymphoma deaths in China, by province.

group. Compared with elderly patients, lymphoma patients younger than 45 years old were more likely to spend their last days in the hospital before dying (Figure S1). Another interesting finding was that Beijing and Shanghai were the top two provinces with the highest proportions of hospital deaths, but Jiangsu and Zhejiang were the top two provinces with the highest proportions of at-home deaths, which were observed in both HL and NHL patients (Figures S2, S3 and S4). We analyzed the spatial patterns of hospital lymphoma deaths based on the average data of hospital lymphoma deaths in China from 2013 to 2021 (Figure S5).

# Associated factors of hospital lymphoma deaths

Furthermore, we constructed multilevel models to explore the relationships of hospital lymphoma deaths with individual factors and socioeconomic contextual variables. From 2013 to 2021, multilevel modeling results demonstrated that differences in demographics (age, sex, ethnicity, marital status) and individual SES (education, occupation) substantially contributed to explaining 23.27% of spatial variations among hospital lymphoma deaths below the province scale when comparing Model 1 with Model 3 (Table 2), Moreover, the MOR of Model 3 (1.79, greater than 1) also indicated significant regional variations and helped explain individual differences in POD. In Model 5, 23.29% of the variation (MOR of 1.75) was explained by both individual factors and contextual factors. Specifically, female patients (OR: 1.22, 95% CI: 1.17-1.27), those with a higher level of educational attainment (OR: 3.37, 95% CI: 3.09-3.67), retired individuals (OR: 9.62, 95% CI: 9.02-10.25), those died of NHL (OR: 1.12, 95% CI: 1.02-1.22), residents in urban areas (OR: 1.55, 95% CI: 1.48-1.63), patients between the ages of 0 and 14 (OR: 1.25, 95%) CI: 1.04-1.50), or unmarried individuals (OR: 1.24, 95% CI: 1.12-1.37) had a higher probability of dying in hospitals than their counterparts. In contrast, the probability of hospital lymphoma deaths was lower among patients who were ethnic minorities (OR: 0.58, 95% CI: 0.52-0.65) or were widowed or divorced (OR: 0.64, 95% CI: 0.60-0.68). Additionally, we further verified the associations between factors and NHL deaths (Figure 4). Sex and educational attainment were not prominent among potential contributing factors for NHL deaths. Among lymphoma patients, residents and children (aged between 0 and 14) in western China were more likely to die from NHL.

## Discussion

Using nationally representative mortality data for lymphoma, we depicted the distribution of POD among lymphoma decedents and explored the related factors that could potentially influence the decision to die in the hospital among lymphoma patients. The results of this study showed that from 2013 to 2021, home was the most frequent POD among lymphoma patients. Moreover, female patients, the youngest patient group, those of Han ethnicity, unmarried individuals, retired individuals, residents of urban areas, those with a higher SES, or those who died from NHL had a higher likelihood of dying in hospitals compared to their counterparts.

## Home was the leading POD among lymphoma patients

Among all the 66772 lymphoma decedents during 2013-2021, 66.39% (44327 patients) died at home, followed by those who died in hospitals (21211 deaths, 31.77%). In accordance with the distribution of POD in the third national retrospective survey on CODs from 2004 to 2005 in China (the rate of at-home deaths among Chinese residents was 72%), home was also the leading POD among lymphoma patients in China [26]. However, there are few studies on POD among lymphoma patients. Therefore, we compared our results with the POD of other leading diseases. Similarly, Gu et al. reported that in their prospective questionnaire study, 53.64% of terminally ill patients with cancer chose home as the preferred POD. which was the most common POD among patients [27]. Wang et al. also found that home was the leading POD among cardiovascular disease patients in China, the proportion of which was higher than 70% [28]. In Malaysia, a study conducted by Ho JFV et al. revealed that 52.1% of advanced cancer patients expressed a preference for dying at home, despite the high prevalence of symptoms [29]. Gomes et al. conducted a global survey on the preferences of terminally ill cancer patients regarding the POD and found that over two-thirds of the patients preferred to die at home [30]. In a

**Table 2.** Associated factors of hospital lymphoma deaths from National Mortality Surveillance System (NMSS) in China, 2013-2021: estimated from multilevel logistics regression

Factors	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)	Model 5 OR (95% CI)
Fixed effect					
Constant	0.48 (0.38-0.61)*	0.23 (0.18-0.29)*	0.11 (0.09-0.14)*	0.10 (0.08-0.12)*	0.08 (0.06-0.11)*
Year (2013-2021)	-	1.01 (1.01-1.02)*	0.99 (0.98-1.00)*	0.99 (0.98-1.00)*	0.99 (0.98-1.00)*
Location (Reference: Rural)					
Urban	-	4.06 (3.90-4.22)*	1.55 (1.48-1.63)*	1.55 (1.47-1.62)*	1.55 (1.48-1.63)*
Sex (Reference: Male)					
Female	-	1.08 (1.04-1.12)*	1.22 (1.17-1.27)*	1.22 (1.17-1.27)*	1.22 (1.17-1.27)*
Age groups, years old (Reference: 65 and above)					
0-14	-	1.94 (1.63-2.32)*	1.25 (1.04-1.50)*	1.25 (1.04-1.50)*	1.25 (1.04-1.50)*
15-64	-	1.08 (1.04-1.12)*	1.16 (1.10-1.21)*	1.16 (1.10-1.21)*	1.15 (1.10-1.21)*
Ethnicity (Reference: Han)					
Other ethnics	-	0.58 (0.53-0.64)*	0.59 (0.52-0.66)*	0.58 (0.52-0.65)*	0.58 (0.52-0.65)*
Marital Status (Reference: Married)					
Unmarried	-	1.54 (1.41-1.68)*	1.24 (1.12-1.37)*	1.24 (1.12-1.37)*	1.24 (1.12-1.37)*
Widowed/Divorced	-	0.61 (0.58-0.65)*	0.64 (0.60-0.67)*	0.64 (0.60-0.68)*	0.64 (0.60-0.68)*
Unknown	-	1.07 (0.82-1.40)	1.00 (0.75-1.34)	1.00 (0.75-1.34)	1.00 (0.75-1.34)
Education (Reference: Junior high school and below)					
Senior high school	-	-	2.09 (1.96-2.22)*	2.09 (1.96-2.22)*	2.09 (1.96-2.22)*
College and above	-	-	3.37 (3.09-3.67)*	3.37 (3.09-3.67)*	3.37 (3.09-3.67)*
Occupation (Reference: Agricultural-related personnel)					
Retired	-	-	9.60 (9.01-10.23)*	9.62 (9.02-10.24)*	9.62 (9.02-10.25)*
Unemployment/Student	-	-	5.06 (4.68-5.48)*	5.07 (4.68-5.48)*	5.07 (4.68-5.48)*
Worker/Self-employed/Enterprise manager	-	-	6.91 (6.44-7.41)*	6.92 (6.45-7.42)*	6.92 (6.46-7.42)*
Professional/Staff/Civil servant	-	-	9.30 (7.61-11.36)*	9.31 (7.62-11.37)*	9.31 (7.62-11.37)*
Others/Unknown	-	-	6.34 (5.86-6.86)*	6.35 (5.87-6.87)*	6.35 (5.87-6.87)*
Underlying cause of death (Reference: HL)					
NHL	-	-	-	1.12 (1.02-1.22)*	1.12 (1.02-1.22)*
Region (Reference: Eastern)					
Central	-	-	-	-	1.55 (0.90-2.66)
Western	-	-	-	-	1.29 (0.79-2.10)
Random effects					
Variance among provinces (SE)	0.47 (0.68)	0.43 (0.65)	0.37 (0.61)	0.37 (0.61)	0.34 (0.59)
MOR	1.92	1.87	1.79	1.79	1.75
PCV (%)		7.46	23.27	23.28	23.29

Abbreviations: OR, odd ratio; Cl, confidence interval; SE, standard error; MOR, median odds ratio; PCV, Proportional change in variance; "\*" means *P<0.05*. Region: Western: Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Tibet, Shaanxi, Gansu, Qinghai, Ningxia, Xinjiang; Central: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, Hunan; Eastern: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, Hainan.

Factors			OR (95%CI)
Year (2013-2021)		H	1.06 (1.04–1.07)*
Location (Reference: Rural)			
Urban			1.40 (1.30–1.51)*
Sex (Reference: Male)			
Female	F	<b>-</b>	1.01 (0.95–1.08)
Age groups, years old (Reference: 0-14)			
15-64	<b>—</b>		0.55 (0.37-0.78)*
65 and above			0.55 (0.37-0.78)*
Ethnicity (Reference: Han)			
Other ethnics		<b>⊢</b>	1.28 (1.09–1.52)*
Marital Status (Reference: Married)			
Unmarried	<b>—</b>		0.75 (0.65-0.88)*
Widowed/Divorced	H	•	0.97 (0.89–1.07)
Unknown	·		0.95 (0.60-1.62)
Education (Reference: Junior high school and below)			
Senior high school	,		1.07 (0.96–1.20)
College and above	⊢		1.03 (0.90–1.20)
Occupation (Reference: Peasant)			
Retired	<b>⊢</b>		0.81 (0.73–0.90)*
Unemployment/Student	⊢ <b></b>	-	0.86 (0.75–1.00)*
Worker/Self-employed/Enterprise manager	<b>⊢</b>		0.81 (0.72–0.91)*
Professional/Staff/Civil servant	► <b>=</b>		0.91 (0.66–1.30)
Others	<b>•</b>	+	0.94 (0.83–1.08)
Region (Reference: Western)			
Central	<b>⊢</b> ∎−		0.87 (0.79–0.95)*
Eastern		4	0.90 (0.82–0.98)*
	0.5	1 1.5	2

**Figure 4.** Associated factors of non-Hodgkin lymphoma (NHL) deaths in China, 2013-2021: estimated from multilevel logistics regression. Abbreviations: OR, odd ratio; CI, confidence interval; "\*" means *P*<0.05. Region: Western: Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Tibet, Shaanxi, Gansu, Qinghai, Ningxia, Xinjiang; Central: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, Hunan; Eastern: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, Hainan.

cross-sectional study, Cohen et al. collected data about the POD of people with cancer from 14 countries across 4 continents, and they reported that there was a large variation in the POD among countries, with the rate of cancer patients dying at home ranging from 12% (South Korea) to 57% (Mexico) [31]. Several factors could contribute to this phenomenon. First, previous studies have proposed a threestage evolutionary hypothesis to explain the variations in the distribution of POD over the past century [7, 32]. In the first stage, home deaths accounted for over 90% of all deaths in the early 20th century due to limited healthcare resources and underdeveloped medical technologies. In the second stage, the proportion of hospital deaths steadily increased, reaching 70% to 80% of all deaths in most developed countries after the 1970s, primarily driven by advancements in medical technologies and improved access to healthcare services. In the third stage, there has been a leveling off or decline in hospital deaths and a rise in home deaths in the United States and other Western countries, attributed to an increased emphasis on the quality of end-of-life care. According to the hypothesis, most developed countries are currently in stage 2 or transitioning from stage 2 to stage 3, depending on the level of palliative care. As the world's largest developing country, China is believed to at its first stage or in a transition from stage 1 to stage 2, owing to its substantial population base, imbalanced distribution of healthcare resources, and early stage of palliative care implementation. Besides, There is a Chinese proverb that says, "The falling leaves return to the roots". The Chinese culture makes a great impact on the end-of-life choices. Home brings a sense of belonging to suffering end-stage patients, so patients with lymphoma are more willing to die at home. In some cases, lymphoma patients do not respond to treatment, and further efforts are in vain. Chinese doctors might suggest this type of patient go home with palliative care [33].

# Factors affecting death in hospitals among lymphoma patients

To facilitate the rational allocation of healthcare services for lymphoma patients at the EOL, we identified relevant factors that might be influential in hospital deaths at both the individual and provincial levels. Overall, individual factors accounted for nearly half of the explained variations in hospital lymphoma deaths, while contextual socioeconomic factors contributed little to it.

We found that the following demographic variables were correlated with hospital lymphoma deaths: sex, age, marital status and ethnic group. Females were more likely to die in hospitals because their life expectancy was usually longer than that of males. Consequently, elderly men often continue to live with their spouses and stay at home even when they are in poor health conditions. In contrast, elderly women are more likely to be widowed or live alone in old age and choose institutional help as they became more debilitated [34]. Regarding age, the results exhibited that pediatric patients were more inclined to die in hospitals than patients in other age groups. Similar results were also found in England, where children diagnosed with a life-limiting conditions were more likely to die in hospitals [35]. Due to the inherent risk of death associated with lymphoma in children, despite the utilization of powerful therapies, it is not surprising that children turn to medical institutions for assistance and care. There was, in addition, one equally momentous point. These children were likely to receive bone marrow transplantation, which is associated with a high mortality [36]. In contrast, elderly patients with lymphoma might return home due to traditional concept of "The falling leaves return to the roots". Similar to other findings, we found that being unmarried tended to be a crucial risk factor for hospital lymphoma deaths compared with being married, and this has also been observed in other cancer-related findings [31, 37]. Married patients may obtain sufficient support from their spouses or other family members, enabling them to accept treatment at home. However, unmarried patients, who may live alone and experience feelings of loneliness. often rely on medical institutions as the primary support. Ethnic differences have proven to be influential in POD [38]. In our study, the ethnic minority group was also reported to have a lower probability of dying in hospitals, which might result from their sociocultural environment.

We also investigated whether SES-related variables influenced the probability of deaths occurring in hospitals. In our models, educational attainment and occupation had significant effects on lymphoma-related deaths in hospitals. The higher the level of education, the more likely patients were to die in hospitals. Conventionally, patients with higher education levels were likely to have better financial resources, be more optimistic, and actively accept treatment and nursing care. Compared with other occupations, agricultural workers may be limited by their work and payment capacity. Therefore, they might refuse to receive hospital medical care and consequently exhibit a decreased probability of passing away in a hospital setting. However, our results regarding SES characteristics are opposite to some Western findings. A retrospective cohort study conducted in Canada showed that patients with lower socioeconomic levels had higher odds of dying in medical institutions [39]. Similarly, a study in Spain reported that higher SES might result in a higher likelihood of dying at home [40]. A systematic review based on the POD among cancer patients found that, compared to low-income individuals, high-income individuals were more inclined to die at home [41]. This situation may result from individuals with a higher SES being able to afford and access high-quality healthcare services at home in developed countries, which is different from the reality of China. China is the most populous developing country in the world, so it presents challenges to provide sufficient homebased care services on a large scale.

## Implications

The current characteristics of POD distribution among lymphoma deaths can be attributed to a complex interplay of multiple factors. With a profound influence from the core values of Confucianism, especially the principles of loyalty, filial piety, and benevolence. It is expected that home deaths will continue to maintain their current patterns in the foreseeable future. Furthermore, individual-level factors are likely

to remain the primary contributors to the variations observed in POD choices. We offer recommendations for improving the quality of EOL care for lymphoma patients. First, recognizing that a significant proportion of patients pass away at home, it is essential to establish and enhance home-based EOL care programs. These programs should cater specifically to the needs of lymphoma patients during their final stages, aiming to bridge the gap between hospital and home care in the coming years. Second, we also found that some individuals with lower SES were less likely to die in the hospital. This disparity could indicate an inequitable allocation of medical and healthcare resources among various subpopulations. Third, substantial provincial variations in the distribution of POD hinted that the needs for region-specific and demographic-oriented strategies. Healthcare resource allocation should be tailored to address the specific needs of vulnerable subpopulations, aiming to improve the quality of medical care by providing accessible and affordable healthcare services.

## Limitations

To our knowledge, this is the first and largest study conducted to investigate the trends of POD distribution among lymphoma patients in China, and our study contributes to filling a gap in this field. Moreover, we performed multilevel analysis to demonstrate the associated determinants of POD for end-stage lymphoma patients and interpretated the contributions of each demographic, socioeconomic and contextual feature. However, there were several limitations to our study. We failed to cover sufficient potential factors that might be influential in hospital lymphoma deaths, such as personal preference, family care, and family income, Therefore, it is necessary to address these deficiencies in future studies by collecting more comprehensive and relevant information and employing a more refined classification of POD among lymphoma patients.

## Conclusion

In China, home remained the leading POD in lymphoma patients, and demographics and individual SES contributed a great deal to hospital deaths among lymphoma patients compared with contextual socioeconomic factors. These findings may support the promotion of home-based EOL care procedures in China and offer guidance for region-specific and demographic-oriented allocation of medical resources.

#### Acknowledgements

This research was funded by the National Natural Science Foundation of China (Nos. 82070205, 81870154, 81972807, 81670187, 81970179, and 81700197); Beijing Natural Science Foundation (Nos. 7202025 and 7202-026), Capital's Funds for Health Improvement and Research (Nos. 2020-2Z-2157, 2022-1-2152, 2022-4-2156) and Beijing Municipal Science & Technology Commission (Z18110-0001918019). Cultivation plan in Haidian District (HP2022-19-503004). Beijing Hospital Authority Cultivation plan (PX2022046).

#### Disclosure of conflict of interest

None.

Address correspondence to: Jun Zhu, Key Laboratory of Carcinogenesis and Translational Research (Ministry of Education), Department of Lymphoma, Peking University Cancer Hospital & Institute, No. 52 Fucheng Road, Haidian District, Beijing 100142, China. Tel: +86-10-88196109; E-mail: zhujun2017@outlook.com; Jun Ma, Department of Hematology & Oncology, Harbin Institute of Hematology & Oncology, No. 151 Diduan Street, Daoli District, Harbin 150010, Heilongjiang, China. Tel: +86-0451-84694406; E-mail: majun0322@126. com; Mai-Geng Zhou, National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, No. 27 Nanwei Road, Xicheng District, Beijing 100050, China. Tel: +86-10-63040442; E-mail: zhoumaigeng@ncncd.chinacdc.cn

## References

- [1] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2021; 71: 209-249.
- [2] Koroukian SM, Douglas SL, Vu L, Fein HL, Gairola R, Warner DF, Schiltz NK, Cullen J, Owusu C, Sajatovic M and Rose J. Incidence of aggressive end-of-life care among older adults with metastatic cancer living in nursing homes and community settings. JAMA Netw Open 2023; 6: e230394.

- [3] Driessen A, Borgstrom E and Cohn S. Placing death and dying: making place at the end of life. Soc Sci Med 2021; 291: 113974.
- [4] Shepperd S, Goncalves-Bradley DC, Straus SE and Wee B. Hospital at home: home-based end-of-life care. Cochrane Database Syst Rev 2021; 3: CD009231.
- [5] Wright AA, Keating NL, Ayanian JZ, Chrischilles EA, Kahn KL, Ritchie CS, Weeks JC, Earle CC and Landrum MB. Family perspectives on aggressive cancer care near the end of life. JAMA 2016; 315: 284-292.
- [6] Bajwah S, Oluyase AO, Yi D, Gao W, Evans CJ, Grande G, Todd C, Costantini M, Murtagh FE and Higginson IJ. The effectiveness and costeffectiveness of hospital-based specialist palliative care for adults with advanced illness and their caregivers. Cochrane Database Syst Rev 2020; 9: CD012780.
- [7] Gu D, Liu G, Vlosky DA and Yi Z. Factors associated with place of death among the Chinese oldest old. J Appl Gerontol 2016; 26: 34-57.
- [8] GBD 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the global burden of disease study 2016. Lancet 2017; 390: 1151-1210.
- [9] Liu W, Liu J, Song Y, Wang X, Zhou M, Wang L, Ma J and Zhu J; Union for China Leukemia Investigators of the Chinese Society of Clinical Oncology, Union for China Lymphoma Investigators of the Chinese Society of Clinical Oncology. Mortality of lymphoma and myeloma in China, 2004-2017: an observational study. J Hematol Oncol 2019; 12: 22.
- [10] Mayan I, Yaffe K, James J and Hunt LJ. The association between race and place of death among persons with dementia. J Pain Symptom Manage 2022; 64: e109-e114.
- [11] Cross SH, Kaufman BG, Mentz RJ, Kamal AH, Taylor DH Jr and Warraich HJ. Trends in place of death for individuals with cardiovascular disease in the United States. J Am Coll Cardiol 2019; 74: 1943-1946.
- [12] Renton K, Mayer AT, Alison L and Yeomanson D. Factors associated with place of death for children in South Yorkshire: a retrospective cohort study. BMJ Support Palliat Care 2020; 10: e10.
- [13] Vidal M, Rodriguez-Nunez A, Hui D, Allo J, Williams JL, Park M, Liu D and Bruera E. Placeof-death preferences among patients with cancer and family caregivers in inpatient and outpatient palliative care. BMJ Support Palliat Care 2022; 12: e501-e504.
- [14] Yang G, Hu J, Rao KQ, Ma J, Rao C and Lopez AD. Mortality registration and surveillance in China: history, current situation and challenges. Popul Health Metr 2005; 3: 3.

- [15] Liu S, Wu X, Lopez AD, Wang L, Cai Y, Page A, Yin P, Liu Y, Li Y, Liu J, You J and Zhou M. An integrated national mortality surveillance system for death registration and mortality surveillance, China. Bull World Health Organ 2016; 94: 46-57.
- [16] Li Z, Jiang S, Xu C, Lu F, He R, Pan Z, Zhang P and Zhang L. Determinants of place of death for end-stage cancer patients: evidence from China. Int J Qual Health Care 2020; 32: 41-47.
- [17] Sunuwar DR, Singh DR, Pradhan PMS, Shrestha V, Rai P, Shah SK and Adhikari B. Factors associated with anemia among children in South and Southeast Asia: a multilevel analysis. BMC Public Health 2023; 23: 343.
- [18] Worku MG, Alamneh TS, Teshale AB, Yeshaw Y, Alem AZ, Ayalew HG, Liyew AM, Tessema ZT and Tesema GA. Multilevel analysis of determinants of anemia among young women (15-24) in sub-Sahara Africa. PLoS One 2022; 17: e0268129.
- [19] Merlo J, Chaix B, Yang M, Lynch J and Rastam L. A brief conceptual tutorial of multilevel analysis in social epidemiology: linking the statistical concept of clustering to the idea of contextual phenomenon. J Epidemiol Community Health 2005; 59: 443-449.
- [20] Adam NS, Twabi HS and Manda SOM. A simulation study for evaluating the performance of clustering measures in multilevel logistic regression. BMC Med Res Methodol 2021; 21: 245.
- [21] Austin PC and Merlo J. Intermediate and advanced topics in multilevel logistic regression analysis. Stat Med 2017; 36: 3257-3277.
- [22] Shayo FK, Nakamura K, Al-Sobaihi S and Seino K. Is the source of domestic water associated with the risk of malaria infection? Spatial variability and a mixed-effects multilevel analysis. Int J Infect Dis 2021; 104: 224-231.
- [23] Boylan JM and Robert SA. Neighborhood SES is particularly important to the cardiovascular health of low SES individuals. Soc Sci Med 2017; 188: 60-68.
- [24] Sangaramoorthy M, Shariff-Marco S, Conroy SM, Yang J, Inamdar PP, Wu AH, Haiman CA, Wilkens LR, Gomez SL, Le Marchand L and Cheng I. Joint associations of race, ethnicity, and socioeconomic status with mortality in the multiethnic cohort study. JAMA Netw Open 2022; 5: e226370.
- [25] Sharma R, Dwivedi LK, Jana S, Banerjee K, Mishra R, Mahapatra B, Sahu D and Singh SK. Survey implementation process and interviewer effects on skipping sequence of maternal and child health indicators from national family health survey: an application of cross-classified multilevel model. SSM Popul Health 2022; 19: 101252.

- [26] Chen Z. Report of the third national retrospective survey on causes of death. China Union Med University Press 2008; 2: 11.
- [27] Gu X, Cheng W, Cheng M, Liu M and Zhang Z. The preference of place of death and its predictors among terminally ill patients with cancer and their caregivers in China. Am J Hosp Palliat Care 2015; 32: 835-840.
- [28] Wang W, Liu Y, Ye P, Liu J, Yin P, Qi J, You J, Lin L, Wang F, Wang L, Huo Y and Zhou M. Trends and associated factors in place of death among individuals with cardiovascular disease in China, 2008-2020: a population-based study. Lancet Reg Health West Pac 2022; 21: 100383.
- [29] Ho JFV, Marzuki NS, Meseng NSM, Kaneisan V, Lum YK, Pui EWW and Yaakup H. Symptom prevalence and place of death preference in advanced cancer patients: factors associated with the achievement of home death. Am J Hosp Palliat Care 2022; 39: 762-771.
- [30] Gomes B, Higginson IJ, Calanzani N, Cohen J, Deliens L, Daveson BA, Bechinger-English D, Bausewein C, Ferreira PL, Toscani F, Meñaca A, Gysels M, Ceulemans L, Simon ST, Pasman HRW, Albers G, Hall S, Murtagh FEM, Haugen DF, Downing J, Koffman J, Pettenati F, Finetti S, Antunes B and Harding R; PRISMA. Preferences for place of death if faced with advanced cancer: a population survey in England, Flanders, Germany, Italy, the Netherlands, Portugal and Spain. Ann Oncol 2012; 23: 2006-2015.
- [31] Cohen J, Pivodic L, Miccinesi G, Onwuteaka-Philipsen BD, Naylor WA, Wilson DM, Loucka M, Csikos A, Pardon K, Van den Block L, Ruiz-Ramos M, Cardenas-Turanzas M, Rhee Y, Aubry R, Hunt K, Teno J, Houttekier D and Deliens L. International study of the place of death of people with cancer: a population-level comparison of 14 countries across 4 continents using death certificate data. Br J Cancer 2015; 113: 1397-1404.
- [32] Tang ST and McCorkle R. Determinants of place of death for terminal cancer patients. Cancer Invest 2001; 19: 165-180.

- [33] Action L. Lymphoma and the end of life. https://lymphoma-action.org.uk/about-lymphoma/lymphoma-and-end-life. Accessed.
- [34] Dasch B, Blum K, Gude P and Bausewein C. Place of death: trends over the course of a decade: a population-based study of death certificates from the years 2001 and 2011. Dtsch Arztebl Int 2015; 112: 496-504.
- [35] Gibson-Smith D, Jarvis SW and Fraser LK. Place of death of children and young adults with a life-limiting condition in England: a retrospective cohort study. Arch Dis Child 2020; 106: 780-785.
- [36] Shah A, Diggens N, Stiller C, Murphy D, Passmore J and Murphy MF. Place of death and hospital care for children who died of cancer in England, 1999-2006. Eur J Cancer 2011; 47: 2175-2181.
- [37] Ohlen J, Cohen J and Hakanson C. Determinants in the place of death for people with different cancer types: a national population-based study. Acta Oncol 2017; 56: 455-461.
- [38] Estrada LV, Agarwal M and Stone PW. Racial/ ethnic disparities in nursing home end-of-life care: a systematic review. J Am Med Dir Assoc 2021; 22: 279-290, e1.
- [39] Wales J, Kalia S, Moineddin R and Husain A. The impact of socioeconomic status on place of death among patients receiving home palliative care in Toronto, Canada: a retrospective cohort study. J Palliat Care 2020; 35: 167-173.
- [40] Lopez-Valcarcel BG, Pinilla J and Barber P. Dying at home for terminal cancer patients: differences by level of education and municipality of residence in Spain. Gac Sanit 2019; 33: 568-574.
- [41] Nilsson J, Blomberg C, Holgersson G, Carlsson T, Bergqvist M and Bergström S. End-of-life care: where do cancer patients want to die? A systematic review. Asia Pac J Clin Oncol 2017; 13: 356-364.



Figure S1. Temporal trends of place of death (POD) distribution among lymphoma deaths in China, by age (years old), 2013-2021.



Figure S2. Temporal trends of POD distribution among total lymphoma deaths in China, by province, 2013-2021.



Figure S3. Temporal trends of POD distribution among HL deaths in China, by province, 2013-2021.



Figure S4. Temporal trends of POD distribution among NHL deaths in China, by province, 2013-2021.



Figure S5. Spatial patterns of hospital lymphoma deaths in China on average, 2013-2021.