Cancer Pathogenesis and Therapy 3 (2025) 163–172

Contents lists available at ScienceDirect

Cancer Pathogenesis and Therapy

journal homepage: www.journals.elsevier.com/cancer-pathogenesis-and-therapy

Research article

# Factors affecting the place of death in patients with liver cancer in China, 2013–2020: A population-based study

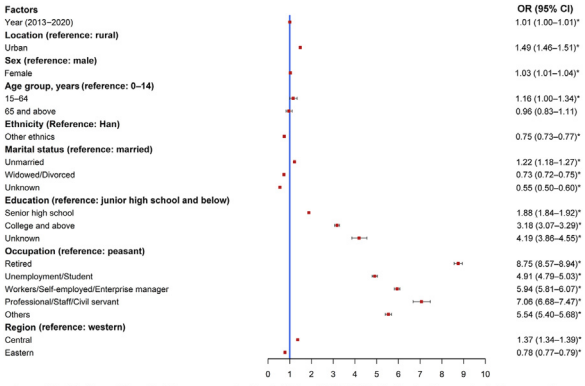
Xiaosheng Ding [a,1], Weiwei Shi [b,1], Jinlei Qi [c,1], Juan An [a], Weiran Xu [a], Hui Shi [a], Xixi Zheng [a], Xiaoyan Li [a,*]

[a] Department of Oncology, Beijing Tiantan Hospital, Capital Medical University, Beijing 100070, China
[b] Department of Oncology, PLA General Hospital, Beijing 100853, China
[c] National Center for Chronic and Noncommunicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing 100050, China

## HIGHLIGHTS

- Examines place of death (POD) impact factors of patients with liver cancer in China.
- Used data from the National Mortality Surveillance System from 2013 to 2020.
- Analysis demonstrated that 440,079 (72.29%) died at home and 158,291 (26.00%) died in hospitals.
- Hospital death is more likely for urban Han female patients aged from 0 to 14 years.
- Also more likely for married, educated, some professional, or retired patients.
- Home remained the preferred POD among patients with liver cancer.

## GRAPHICAL ABSTRACT




**Associated factors of hospital liver cancer deaths in China, 2013–2020: Estimated from a logistic regression. *$P < 0.05$. Western: Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Xizang, Shaanxi, Gansu, Qinghai, Ningxia, and Xinjiang; Central: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, and Hunan; Eastern: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Hainan. CI: Confidence interval; OR: Odds ratio.**

## ARTICLE INFO

Managing Editor: Peng Lyu

*Keywords:*
Liver neoplasms
Place of death
Socioeconomic status
China

## ABSTRACT

*Background:* Despite the country's substantial liver cancer burden, there is limited research on the factors influencing the place of death (POD) of patients with liver cancer in China. This study aimed to delineate POD distribution among patients with liver cancer, identify the factors associated with hospital deaths, and offer valuable insights for the government to develop healthcare policies.

*Methods:* Data from 2013 to 2020 were obtained from the National Mortality Surveillance System (NMSS) of China. This analysis focused on the distribution of POD among individuals who succumbed to liver cancer. Variations in characteristic distributions across different categories were evaluated using a chi-squared test. We also applied a multilevel logistic regression analysis to identify the factors associated with hospital liver cancer deaths. The proportional change in variance was computed to evaluate the contributions of different factors in the model.

* Corresponding author: Department of Oncology, Beijing Tiantan Hospital, Capital Medical University, No. 119 Nansihuan West Road Fengtai District, Beijing 100070, China.
*E-mail address:* lixiaoyan@bjtth.org (X. Li).

[1] Xiaosheng Ding, Weiwei Shi, and Jinlei Qi contributed equally to this work.

https://doi.org/10.1016/j.cpt.2024.04.001
Received 16 January 2024; Received in revised form 1 April 2024; Accepted 7 April 2024

*Results:* From 2013 to 2020, the NMSS reported a total of 608,789 liver cancer-related deaths, of which 440,079 (72.29%) died at home, and 158,291 (26.00%) died in the hospital. Home remained the preferred POD among patients with liver cancer. The results demonstrated that female patients, aged between 0 and 14 years, of Han ethnicity, living in urban areas, unmarried, highly educated, and either employed in a professional, staff, or civil servant capacity, or retired patients tended to end their lives in the hospital.
*Conclusions:* In China, home continues to be the predominant POD for patients with liver cancer, with demographic and socioeconomic factors significantly influencing whether a hospital is their POD. Enhancing healthcare policymakers' understanding of the factors influencing the place of death for patients with liver cancer may assist in creating a more equitable distribution of healthcare resources and providing a variety of choices for minorities with distinct preferences for end-of-life care.

## Introduction

Primary liver cancer encompasses three distinct pathological types: hepatocellular carcinoma, which constitutes 75–85% of cases; intrahepatic cholangiocarcinoma, accounting for 10–15%; and combined hepatocellular cholangiocarcinoma, which differs significantly in pathogenesis, biological behavior, histopathology, treatment methods, and prognosis.[1,2] According to Global Cancer Statistics 2020, liver cancer is the sixth most commonly diagnosed cancer and the third leading cause of cancer-related deaths.[3] The incidence of liver cancer has grown in the past decade, with 905,677 new cases and 830,180 deaths in 2020. These figures account for 4.7% of the 19.3 million new cases and 8.3% of the 10 million cancer-related deaths globally.[3] Moreover, the mortality rate was higher in male patients compared to women and increased in older patients. More than half of the new global cases and fatalities of liver cancer have been reported in China, primarily because of the high chronic infection rates of hepatitis B and C viruses. From 1995 to 1999, China experienced an increase in the mortality rate from liver cancer, which has been on a downward trend since 2004.[4] However, despite the consistent decrease in mortality rates, liver cancer continues to impose a substantial health burden.

The question of who is more likely to die in a hospital or at home falls within the scope of epidemiological research and has sociological research value. Globally, place of death (POD) is considered a significant indicator of the quality of care delivered in the final days or hours of life, serving both as a reliable metric for evaluating end-of-life (EOL) care and as an outcome measure for such care.[5,6] Despite the notable preference among many patients with end-stage disease or advanced cancer to die at home, the majority ultimately die in hospital settings. Furthermore, the provision of aggressive medical treatments has not been demonstrated to enhance the quality of life, nor has it alleviated the grief experienced by caregivers. Healthcare policymakers and researchers have increasingly emphasized this essential quality indicator for EOL care, leading several countries to implement policies that enhance the capacity for home-based palliative care and align it with patient preferences.[7,8]

Numerous studies have revealed that, especially in developed countries, the home might be the preferred place for patients in the terminal phase of their illness.[9–12] A systematic review indicated that POD is determined by the interplay of factors associated with illness, individual characteristics, and the environmental context.[13,14] China is the world's most populous developing nation, with a rich mosaic of cultures and ethnicities. It has also been associated with a substantial burden of liver cancer in recent decades. This scenario offers a unique opportunity to delve into the dynamics of POD and pinpoint the key factors shaping POD trends across patients with liver cancer, leveraging data from China.

However, to the best of our knowledge, there have been limited investigations into the factors associated with POD or hospital fatalities in patients with liver cancer. In this study, we aimed to map the distribution of POD among individuals with liver cancer and explore the factors contributing to deaths due to liver cancer in a hospital setting, thereby offering reasonable explanations. Strengthening the understanding of the factors influencing the place of death for liver cancer patients in China may help healthcare policymakers develop accessible and sustainable end-of-life care services for groups with different preferences for end-of-life care.

## Methods

### *Data sources*

Liver cancer death data were obtained from the National Mortality Surveillance System (NMSS) of the Chinese Center for Disease Control and Prevention (CDC). The NMSS encompasses all death registrations in China from 2013 to 2020, including information on the decedents' residential location and region, gender, age at death, ethnicity, marital status, education, and occupation.

### *Mortality data extraction*

The underlying cause of death in the NMSS was recorded using the International Classification of Diseases 10th Revision (ICD-10). We extracted all deaths between 2013 and 2020 with disease codes C22.0–C22.9, indicating deaths attributed to liver cancer.

### *Variables*

We classified POD into five categories: hospitals, homes, nursing homes, on the way to hospital, and others or unknown. For explanatory variables, we included residential location (for which we defined districts as urban areas and counties as rural areas), residential region (which we categorized into western, central, and eastern regions based on patients' provinces), demographics (gender, age at death, ethnicity, and marital status), and socioeconomic factors (including education and occupation). We analyzed age at death (years) as an ordinal three-category variable (0–14, 15–64, 65, and above) rather than a continuous variable to facilitate interpretation and comparison with other studies. For ethnicity, we divided patients into Han ethnicity and other ethnicities. Marital status was categorized as married, unmarried, widowed/divorced, or unmarried. Educational level was classified as junior high school or below, senior high school, college or above, or unknown. Occupations included farm workers, retired, unemployed/student, self-employed/enterprise manager, professional/staff/civil servant, or unknown.

### *Statistical analysis*

We used a chi-squared test to examine the differences in variables among different groups. Subsequently, we applied a multilevel logistic regression analysis to identify the factors associated with hospital liver cancer deaths. We classified POD at home, nursing homes, on the way to the hospital, and others/unknown as "out-of-hospital liver cancer deaths." Multiple models were constructed for the analysis. Model 1 was an ordinary null model that included fixed and random intercepts that were fitted to investigate spatial variations across multiple scales, among which random intercepts accounted for the clustering of participants (level 1) within the provinces (level 2). Random effects at the individual level were translated into the median odds ratio (MOR), which indicates

the median value of the odds between the area with the highest outcome probability and the area with the lowest one.[15–17] To explore the extent to which these personal and contextual variables affected the probability of liver cancer patients dying in the hospital, demographics (Model 2), socioeconomic factors (Model 3), and contextual phenomena (Model 4) were entered stepwise into the multivariate logistic model, and the proportional change in variance (PCV) was calculated for each model. PCV generally indicates how several factors contribute to a model and reflects the proportion of variance associated with newly added variables.[18–20] In this way, we identified the variables that indicate the choice of POD at the hospital.[21,22] In all hypothesis tests, a $P$ value $< 0.05$ was considered statistically significant. All relevant analyses were performed using the R version 4.2.1 (R Core Team, Vienna, Austria).

## Results

### *Characteristics of the place of death distribution among liver cancer patients*

The flow diagram of this study is illustrated in Figure 1. A total of 608,789 liver cancer-related deaths were reported by the NMSS in China from 2013 to 2020, including patients who died at home (440,079, 72.29%), in a hospital (158,291, 26.00%), in nursing homes (1798, 0.29%), on the way to hospital (4361, 0.72%), and others (4260, 0.70%) [Table 1]. Home remained the most common POD among patients with liver cancer, and differences in POD distribution according to key characteristics were also assessed. There was no significant change in the POD distribution from 2013 to 2020, with home ranking first, followed by hospitals [Figure 2A]. Compared to female patients, male patients with liver cancer were more likely to die in hospitals, with a proportion of 26.75% (compared to 23.88% for female patients); we also observed a higher frequency of younger patients choosing to die in hospitals, while older people died in homes irrespective of their gender [Figure 2B].

In addition, among the provinces of mainland of China, Beijing ranked first in medical institution deaths, followed by Shanghai, Heilongjiang, and Jilin [Figure 2C]. Similar to Figure 2A, there were no apparent differences in POD distribution in patients with liver cancer over time [Figure 3A]. However, patients from urban areas preferred to die in hospitals compared to those from rural areas (urban areas: 40.37%, rural areas: 18.41%). Remarkably, a higher proportion of liver cancer patients living in urban areas opted for hospital death, regardless of their age [Figure 3B]. In all 31 provinces, patients from urban areas were more likely to spend their EOL time in hospitals, particularly in Beijing and Xinjiang [Figure 3C]. Compared with other age groups, patients with liver cancer aged <20 years and those aged >100 years were more likely to die in the hospital, which was consistent over time [Supplementary Figure 1]. Another interesting finding was that Beijing and Shanghai were the two provinces with the highest number of liver cancer patients dying in hospitals, whereas Jiangsu and Zhejiang ranked high for at-home deaths of liver cancer patients [Supplementary Figure 2].

### *Factors contributing to hospital deaths*

We also conducted a multivariate logistic analysis to screen for factors associated with liver cancer-related deaths in hospitals. The MOR of all four multivariate models was <1, indicating that provincial variations did little to explain individual differences in choosing POD. Nevertheless, our results demonstrated that differences in demographics (age, gender, ethnicity, marital status) and individual socioeconomic factors (education, occupation) substantially contributed to explaining 20.79% of spatial variations among liver cancer-related deaths in hospitals below the province scale when comparing Model 1 with Model 4 [Table 2], and the probability of dying in the hospital changed little over time (odds ratio [OR]: 1.01, 95% confidence interval [CI]: 1.01–1.01).

In summary, patients who were female (OR: 1.04, 95% CI: 1.02–1.06), living in urban areas (OR: 1.42, 95% CI: 1.40–1.44), aged between 0 and 14, Han ethnicity, unmarried (OR: 1.24, 95% CI: 1.19–1.29), highly educated (OR: 3.44, 95% CI: 3.31–3.57), and either professionals, staff or civil servants (OR: 7.21, 95% CI: 6.81–7.63), or retired (OR: 9.07, 95% CI: 8.86–9.28) tended to die in hospitals. Conversely, the probability of liver cancer-related deaths in hospitals was lower in patients who were from ethnic minorities (OR: 0.64, 95% CI: 0.61–0.66) and those who were widowed or divorced (OR: 0.71, 95% CI: 0.70–0.73). These associations were further verified using a logistic regression [Figure 4], which yielded consistent results [Table 2].

## Discussion

In this population-based study, we utilized nationally representative mortality data to illustrate POD patterns among patients with liver cancer and explored the factors that could influence whether they died in a hospital. Our study revealed that home was the primary POD for patients with liver cancer between 2013 and 2020. Furthermore, being female, young, Han, unmarried, retired, urban, and highly educated made it more likely that the patients would die in hospitals.

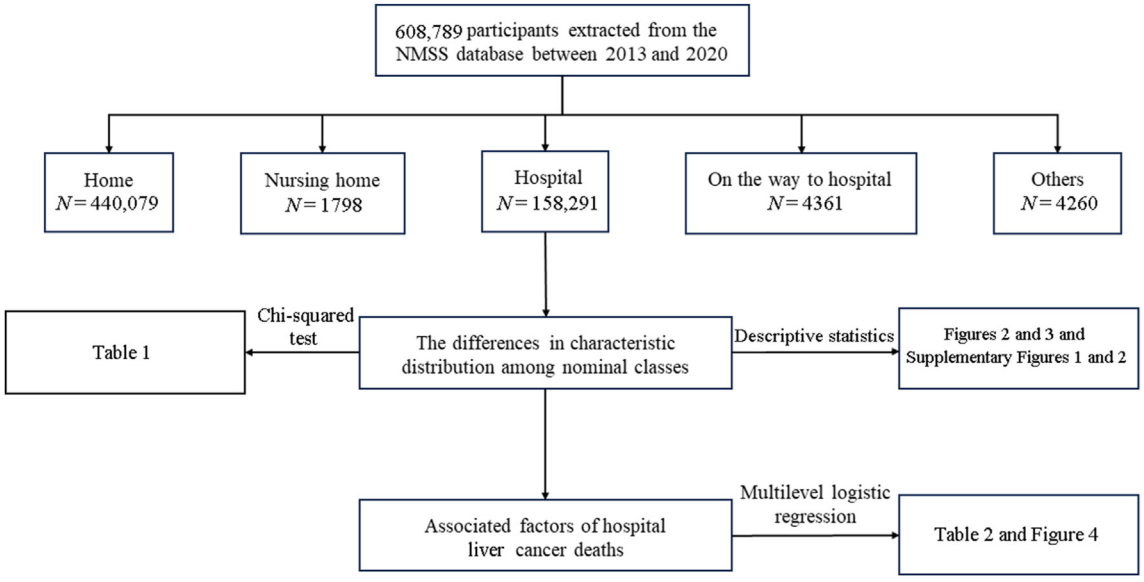



**Figure 1.** Study flow of the study. NMSS: National Mortality Surveillance System.

**Table 1**
Characteristics of POD distribution among liver cancer deaths from the NMSS in China, 2013–2020.

| Characteristics | Total, *N* | Medical and healthcare institutions, *n* | Out of medical and healthcare institutions | | | |
|---|---|---|---|---|---|---|
| | | | Home, *n* | Nursing homes, *n* | On the way to the hospital, *n* | Others/unknown, *n* |
| Total | 608,789 | 158,291 | 440,079 | 1798 | 4361 | 4260 |
| Location | | | | | | |
| Urban | 210,452 | 84,954 | 121,439 | 929 | 1462 | 1668 |
| Rural | 398,337 | 73,337 | 318,640 | 869 | 2899 | 2592 |
| Chi-squared statistic and *P* value | 35,269.0 | <0.001 | | | | |
| Region | | | | | | |
| Eastern | 261,551 | 63,950 | 193,609 | 911 | 1642 | 1439 |
| Central | 198,802 | 57,996 | 136,945 | 495 | 1866 | 1500 |
| Western | 148,436 | 36,345 | 109,525 | 392 | 853 | 1321 |
| Chi-squared statistic and *P* value | 2036.2 | <0.001 | | | | |
| Gender | | | | | | |
| Male | 449,622 | 120,277 | 321,631 | 1314 | 3240 | 3160 |
| Female | 159,167 | 38,014 | 118,448 | 484 | 1121 | 1100 |
| Chi-squared statistic and *P* value | 508.2 | <0.001 | | | | |
| Age group, years | | | | | | |
| 0–14 | 1073 | 325 | 715 | 2 | 19 | 12 |
| 15–64 | 295,916 | 81,594 | 209,110 | 514 | 2269 | 2429 |
| ≥65 | 311,800 | 76,372 | 230,254 | 1282 | 2073 | 1819 |
| Chi-squared statistic and *P* value | 1232.7 | <0.001 | | | | |
| Ethnicity | | | | | | |
| Han | 574,469 | 151,637 | 413,018 | 1673 | 4156 | 3985 |
| Other ethnicities | 34,320 | 6654 | 27,061 | 125 | 205 | 275 |
| Chi-squared statistic and *P* value | 846.7 | <0.001 | | | | |
| Marital status | | | | | | |
| Married | 503,378 | 135,156 | 360,672 | 769 | 3659 | 3122 |
| Unmarried | 18,750 | 5050 | 12,904 | 444 | 120 | 232 |
| Widowed/divorced | 83,134 | 17,262 | 64,289 | 555 | 552 | 476 |
| Unknown | 3527 | 823 | 2214 | 30 | 30 | 430 |
| Chi-squared statistic and *P* value | 11,734.0 | <0.001 | | | | |
| Education | | | | | | |
| Junior high school and below | 510,364 | 102,619 | 399,623 | 1524 | 3282 | 3316 |
| Senior high school | 74,319 | 37,825 | 34,824 | 195 | 802 | 673 |
| College and above | 20,991 | 15,963 | 4578 | 76 | 206 | 168 |
| Unknown | 3115 | 1884 | 1054 | 3 | 71 | 103 |
| Chi-squared statistic and *P* value | 64,096.0 | <0.001 | | | | |
| Occupation | | | | | | |
| Agricultural-related personnel | 424,111 | 54,322 | 363,737 | 856 | 2751 | 2445 |
| Retired | 57,553 | 35,995 | 20,487 | 355 | 404 | 312 |
| Unemployment/student | 32,501 | 15,132 | 16,677 | 177 | 276 | 239 |
| Worker/self-employed/enterprise manager | 56,414 | 32,373 | 22,817 | 160 | 583 | 481 |
| Professional/staff/civil servant | 7085 | 4933 | 1977 | 11 | 103 | 61 |
| Others/unknown | 31,125 | 15,536 | 14,384 | 239 | 244 | 722 |
| Chi-squared statistic and *P* value | 134,860.0 | <0.001 | | | | |

Western: Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Xizang, Shaanxi, Gansu, Qinghai, Ningxia, and Xinjiang; Central: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, and Hunan; Eastern: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Hainan. NMSS: Natrowheadional Mortality Surveillance System; POD: Place of death.

*Home was the most common place of death among liver cancer patients*

Between 2013 and 2020, 72.29% (440,079) of 608,789 liver cancer deaths occurred at home, whereas 26.00% (158,291) occurred in hospitals. The observation that most liver cancer deaths occurred at home is consistent with the findings of previous studies on other diseases. For example, in the United States, 40% of women who die of gynecologic malignancies die in their homes.[23] In 2021, a descriptive cross-sectional study was conducted in Iran, revealing that the majority of cancer patients selected their homes as the preferred location for end-of-life care and final disposition.[24] Similarly, a study of cancer-related deaths in the United States from 1999 to 2015 revealed a decline in hospital deaths from 36.6% to 24.6%, whereas the proportion of deaths at home increased from 38.4% to 42.6%.[25] Similar conclusions were drawn from a meta-analysis of 27 studies, indicating that over half of cancer patients expressed a preference for dying at home.[26]

However, some findings yielded results that differ from those of the present study. In Germany, the predominant location of death in patients with dementia is a retirement or nursing home, followed by hospitals and homes.[27] Moreover, a study conducted in England revealed that hospitals were the primary location of death in patients with liver diseases.[7] There are multifaceted reasons for this discrepancy. Previous studies proposed a three-stage evolutionary hypothesis that could be employed to interpret national variations in the distribution of POD over the past century.[28,29] In the first stage, home deaths constituted >90% of all fatalities in the early 20th century and were primarily attributed to limited healthcare resources and underdeveloped medical technologies. In the second stage, the percentage of hospital deaths gradually increased, comprising 70%–80% of all fatalities in most developed countries after the 1970s. This shift has been predominantly propelled by advancements in medical technology and enhanced access to healthcare services.

Advancing to the third stage, there has been a decline in-hospital deaths in the United States and Western countries. This shift can be attributed to an amplified focus on the quality of EOL care and a concurrent increase in deaths at home. According to this hypothesis, most developed countries are currently in Stage 2 or transitioning from Stage 2 to Stage 3, contingent upon the advancement of palliative care. We propose that China, as the world's largest developing country, is presently in its initial stage or is transitioning from Stage 1 to Stage 2 due to its substantial population base, uneven distribution of healthcare resources, and the nascent stage of palliative care implementation.

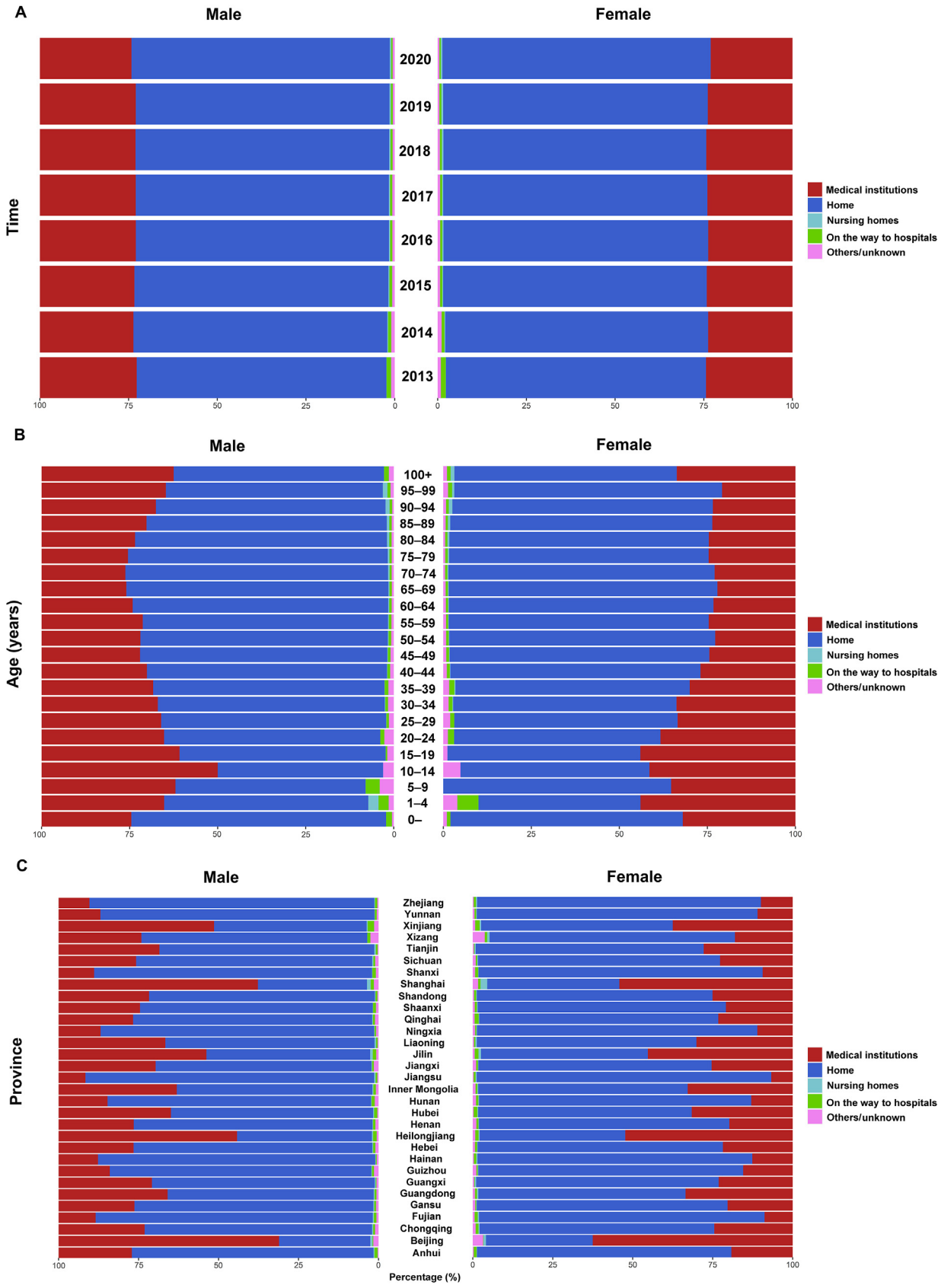



**Figure 2.** Percentage of POD distribution among liver cancer deaths from the NMSS in China by gender. (A) Percentage of POD distribution among liver cancer deaths in China 2013–2020. (B) Percentage of POD distribution among liver cancer deaths in China by age. (C) Percentage of POD distribution among liver cancer deaths in China by province. NMSS: National Mortality Surveillance System; POD: Place of death.

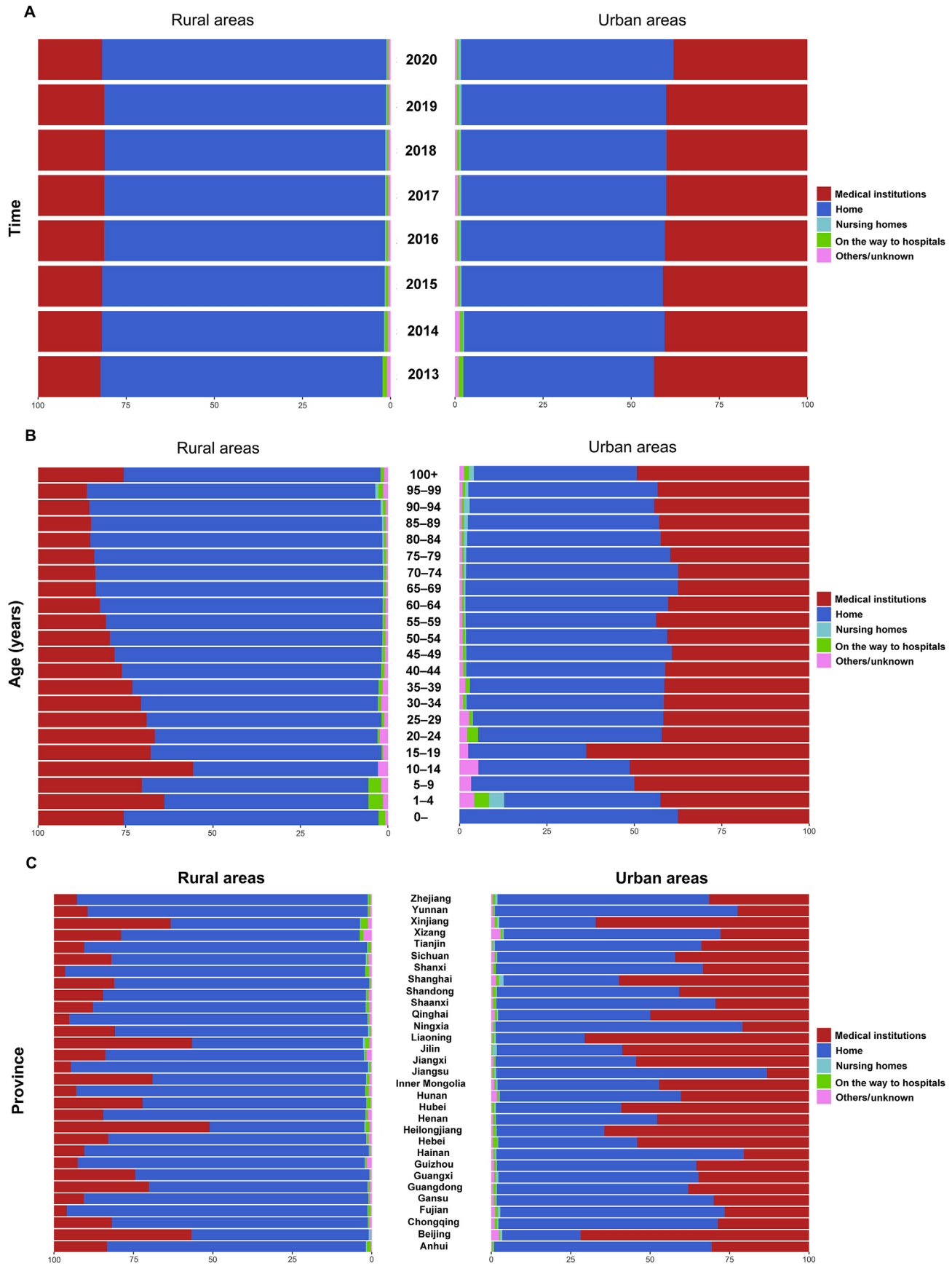



**Figure 3.** Percentage of POD distribution among liver cancer deaths from the NMSS in China by rurality status. (A) Percentage of POD distribution among liver cancer deaths in China 2013–2020. (B) Percentage of POD distribution among liver cancer deaths in China by age. (C) Percentage of POD distribution among liver cancer deaths in China by province. NMSS: National Mortality Surveillance System; POD: Place of death.

**Table 2**
Associated factors of hospital liver cancer deaths from the NMSS in China, 2013–2020: 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) |
|---|---|---|---|---|
| **Fixed effect** | | | | |
| Constant | 0.33 (0.29–0.39)[a] | 0.34 (0.29–0.41)[a] | 0.11 (0.09–0.14)[a] | 0.11 (0.09–0.14)[a] |
| Year (2013–2020) | – | 1.00 (1.00–1.00) | 1.01 (1.01–1.01)[a] | 1.01 (1.01–1.01)[a] |
| Location (reference: rural) | | | | |
| Urban | – | 3.15 (3.11–3.19)[a] | 1.42 (1.40–1.44)[a] | 1.42 (1.40–1.44)[a] |
| Gender (reference: male) | | | | |
| Female | – | 0.91 (0.89–0.92)[a] | 1.04 (1.02–1.06)[a] | 1.04 (1.02–1.06)[a] |
| Age groups, years (reference: 0–14) | | | | |
| 15–64 | – | 0.72 (0.65–0.80)[a] | 0.99 (0.88–1.11) | 0.99 (0.88–1.12) |
| ≥65 | – | 0.63 (0.56–0.70)[a] | 0.83 (0.74–0.93)[a] | 0.83 (0.73–0.93)[a] |
| Ethnicity (reference: Han) | | | | |
| Other ethnicities | – | 0.63 (0.61–0.65)[a] | 0.63 (0.61–0.66)[a] | 0.64 (0.61–0.66)[a] |
| Marital status (reference: married) | | | | |
| Unmarried | – | 1.07 (1.04–1.11)[a] | 1.24 (1.19–1.29)[a] | 1.24 (1.19–1.29)[a] |
| Widowed/divorced | – | 0.70 (0.69–0.72)[a] | 0.71 (0.70–0.73)[a] | 0.71 (0.70–0.73)[a] |
| Unknown | – | 0.63 (0.58–0.68)[a] | 0.50 (0.45–0.54)[a] | 0.50 (0.45–0.54)[a] |
| Education (reference: junior high school and below) | | | | |
| Senior high school | – | – | 1.92 (1.89–1.96)[a] | 1.92 (1.89–1.96)[a] |
| College and above | – | – | 3.44 (3.31–3.57)[a] | 3.44 (3.31–3.57)[a] |
| Unknown | – | – | 4.11 (3.79–4.45)[a] | 4.11 (3.78–4.46)[a] |
| Occupation (reference: agricultural-related personnel) | | | | |
| Retired | – | – | 9.07 (8.86–9.28)[a] | 9.07 (8.86–9.28)[a] |
| Unemployment/student | – | – | 4.72 (4.60–4.85)[a] | 4.72 (4.60–4.85)[a] |
| Worker/self-employed/enterprise manager | – | – | 6.31 (6.17–6.46)[a] | 6.31 (6.17–6.46)[a] |
| Professional/staff/civil servant | – | – | 7.21 (6.81–7.63)[a] | 7.21 (6.81–7.63)[a] |
| Others/unknown | – | – | 5.23 (5.09–5.38)[a] | 5.23 (5.09–5.38)[a] |
| Region (reference: Eastern) | | | | |
| Central | – | – | – | 1.44 (0.98–2.11)[a] |
| Western | – | – | – | 0.87 (0.64–1.19)[a] |
| **Random effects** | | | | |
| Variance among provinces (SE) | 0.58 (0.76) | 0.54 (0.73) | 0.50 (0.71) | 0.46 (0.68) |
| MOR | 0.73 | 0.70 | 0.67 | 0.65 |
| PCV (%) | | 7.86 | 14.06 | 20.79 |

[a] $P < 0.05$. Western: Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Xizang, Shaanxi, Gansu, Qinghai, Ningxia, and Xinjiang; Central: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, and Hunan; Eastern: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Hainan. CI: Confidence interval; MOR: Median odds ratio; NMSS: National Mortality Surveillance System; OR: Odd ratio; PCV: Proportional change in variance; SE: Standard error.

Moreover, traditional Chinese culture significantly influences EOL choices, where the concept of home extends beyond mere physical location to encompass emotional support. It is also convenient for family members to be present and perform certain ceremonies as part of EOL care. Finally, liver cancer typically has a poor prognosis. Doctors may have fewer treatment options for palliative care at home, especially for those in advanced stages. These findings shed light on the divergent POD for terminally ill patients in developed countries and China. We infer that these differences may be attributed to national variations in healthcare resources, advancements in medical technology, the development of palliative care, and cultural influences.

*Determining factors contributing to liver cancer deaths in hospitals*

Multilevel logistic regression analysis was conducted to identify factors influencing the preferred POD among patients with liver cancer who expressed a preference for hospitals. This analysis revealed relevant factors at both individual and provincial levels that may have contribute to in-hospital deaths.

We found that geographical location, region of residence, gender, age, marital status, and ethnicity were associated with liver cancer-related deaths in hospitals. Individuals residing in urban areas are more likely to die in hospitals than those residing in rural areas. A systematic review based on the location of deaths among cancer patients revealed that, compared to low-income individuals, those with higher incomes were more inclined to die in hospitals.[30] In China, residents of urban areas typically enjoy higher incomes than those of rural areas. Furthermore, urban residents who had access to urban employees' basic medical insurance were able to meet hospital expenses better than beneficiaries of the new rural cooperative medical scheme.[31]

Concerning gender, Model 4 suggested that female patients were more likely to experience hospital deaths than their male counterparts, and the OR for gender in the model was close to 1 (with reference to males). Certain studies have observed that gender-specific mortality rates for patients with liver cancer are approximately equal.[32,33] While female patients were noted to have higher odds of dying in hospitals for diseases such as cardiovascular disease, it is possible that gender may not be an influencing factor for patients with liver cancer when it comes to selecting POD.[34]

Regarding age, the findings revealed that pediatric patients were more prone to hospital deaths than individuals in other age groups. We also obtained findings comparable to those of another study suggesting that children with life-limiting conditions are more likely to die in hospitals.[35] Pediatric liver cancer typically requires a complex treatment regimen. Chinese parents are often willing to do everything in their power to ensure that their sick child receives comprehensive medical services and supervision in the hospital until the end of the child's life.[36] However, liver cancer is relatively rare in children and can lead to delayed diagnosis and treatment, thereby increasing the risk of hospital death for these patients. Conversely, older liver cancer patients may choose to return home, influenced by the traditional belief that "falling leaves return to their roots," coupled with their children's refusal to pursue further medical treatment.

In our study, we observed that patients belonging to the Han ethnic group were more likely to experience in-hospital death than those of other ethnicities, demonstrating that ethnic differences also play a significant role in POD.[37,38] Religious and cultural disparities may significantly contribute to the distinct patterns of POD between the Han and other ethnicities. Ethnic minorities with religious beliefs hold high regard for peaceful deaths at home in China.[39] Moreover, we observed that

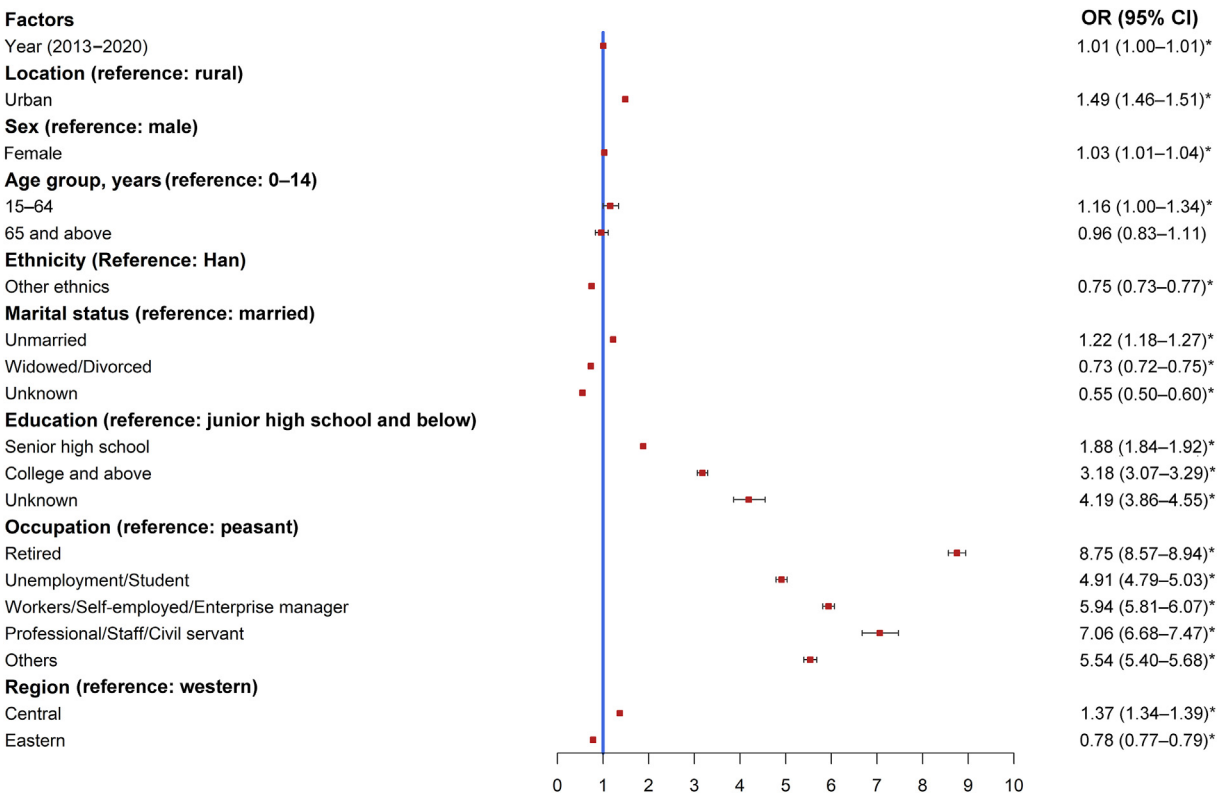



**Figure 4.** Associated factors of hospital liver cancer deaths in China, 2013–2020: Estimated from a logistic regression. *$P < 0.05$. Western: Inner Mongolia, Guangxi, Chongqing, Sichuan, Guizhou, Yunnan, Xizang, Shaanxi, Gansu, Qinghai, Ningxia, and Xinjiang; Central: Shanxi, Jilin, Heilongjiang, Anhui, Jiangxi, Henan, Hubei, and Hunan; Eastern: Beijing, Tianjin, Hebei, Liaoning, Shanghai, Jiangsu, Zhejiang, Fujian, Shandong, Guangdong, and Hainan. CI: Confidence interval; OR: Odds ratio.

being unmarried tended to be a crucial factor associated with hospital deaths compared to other marital statuses; this trend has also been noted in other findings related to cancer.[40] Married patients may receive ample social support from their spouses or family members, which allows them to opt for home-based treatment. The intimate psychological connection between patients and their caregivers may serve as a compelling rationale for selecting the home as the preferred location for EOL care. Conversely, unmarried patients who live alone may experience loneliness and may resort to therapy exclusively from medical institutions.

Another potential contributing factor is that end-stage liver cancer frequently presents with severe clinical symptoms such as hematemesis and jaundice. Although some families prefer home care, they often lack the readiness or capability to handle acute symptoms at home. Compared with other care settings, patients tend to feel safer when hospitalized. These findings underpin the creation of a comprehensive model designed to assess the risk factors influencing in-hospital mortality in patients with liver cancer.

An anthropological study conducted in Yunnan, China, revealed that individuals with higher socioeconomic status (SES) have an increased likelihood of hospital death.[14] Zhang and Lu highlighted that the quality of EOL care is influenced by accessibility, affordability, and the provision of professional support.[41] We also verified whether SES factors affected the probability of hospital deaths. We examined patients' education regarding their POD choices and observed a correlation. Patients with higher degrees were more likely to experience in-hospital deaths. This finding is not surprising as patients with higher education are likely to possess better financial status, maintain a more optimistic outlook, and actively embrace treatment and nursing care. Due to work-related and financial limitations, agricultural workers may be less likely to seek certain medical care, resulting in the lowest odds of hospital death compared with individuals in other occupations. However, our findings concerning the SES characteristics contradict those of some Western studies. Retrospective cohort studies conducted in Canada and Spain indicated that patients with a lower SES were more likely to die in medical institutions, whereas those with a higher SES were more likely to die at home. This scenario could be attributed to individuals with higher SES having the means to secure and utilize premium healthcare services domestically in developed nations, which is in stark contrast to the circumstances in China.

As the world's most populous developing country, China encounters formidable challenges in providing comprehensive home-based care services across its vast population despite the considerable advancements made in its healthcare system following the New Healthcare Reform in 2009. Undoubtedly, SES significantly affects patients' preferences regarding their POD. However, the variability in affordability and medical resource accessibility across different nations means that SES could shape decisions regarding death locations for patients in Eastern *vs.* Western settings differently.

Furthermore, we investigated the impact of geographical regions on the preferred POD. We classified the residences of patients with liver cancer according to their provinces (eastern, central, and western). Our findings revealed that patients from the eastern and central regions were more prone to hospital deaths than those from the western regions. This phenomenon can be attributed to the more substantial economic development in China's eastern and central regions, enhanced support from health insurance, increased access to medical services, the likelihood of more frequent health screenings, and heightened awareness of health risks. In some rural areas of the western part, the phenomena of "falling into poverty due to illness" and "returning to poverty due to illness" still exist. Especially against the backdrop of young labor force migration, which leads to left-behind and empty-nest situations, the phenomenon of some rural older adults choosing suicide, because they cannot afford

medical treatment and do not want to burden their families, is common. Additionally, there are significant differences in ethnic cultures, customs, and religious beliefs among the eastern, central, and western regions of China, which also influence the distribution of places of death.

Finally, there is a significant lack of education on perspectives toward life and death in our society, with death still considered a taboo in traditional Chinese culture. In the terminal stages of cancer, most patients may no longer be able to express their inner demands and may not have established a "living will" in time. Thanks to the development of advanced life support technologies, such as defibrillation, cardiopulmonary resuscitation, and tracheal intubation, vital signs can be maintained. However, whether this extension of life truly reflects the wishes of the dying has always been controversial. Family members often exercise their right to choose the place and manner of death on behalf of the terminally ill. Due to the consolation of their souls or avoidance of moral hazards, family members objectively increase the likelihood of patients dying in hospitals. Life begins, inevitably leading to its end. Thus, death is inherently natural. Strengthening education about life and death can assist family members in better understanding and accepting the significance of life and death and is essential for fostering the healthy development of society.

## Implications

The present characteristics of POD distribution among liver cancer deaths can be attributed to the complex interplay among multiple factors. With the profound influence of traditional culture and religious beliefs, the predominant POD among patients with liver cancer remains at home. We found that various demographic and socioeconomic factors significantly influenced POD choice. Therefore, we proposed recommendations to enhance the quality of EOL care for patients with liver cancer.

First, owing to the considerable percentage of patients dying at home, it is crucial to establish and develop home-based EOL care programs to better cater to the needs of patients with liver cancer. Second, we found that individuals with a lower SES were less likely to experience hospital deaths. This observation suggests an unbalanced allocation of medical resources and a lack of health awareness within specific subpopulations. Third, healthcare resources should be properly allocated based on the geography and demographics of the patients. These approaches aim to promote the quality of medical care for vulnerable patients by ensuring both accessibility and affordability of healthcare services.

To the best of our knowledge, this study represents the most extensive investigation into the trends in POD distribution among patients with liver cancer in China. Moreover, a multivariate analysis demonstrated the associated determinants of POD in patients with end-stage liver cancer and provided an interpretation of the contributions of each demographic and socioeconomic factor. However, our study has several limitations. We must recognize the potential biases in identifying factors that determine the preferred POD among patients with liver cancer. These biases stem partly from limitations in the data gathered by the NMSS, which failed to include crucial variables such as family income, employment status, and family background. Future studies should aim to incorporate these missing elements to provide a more comprehensive understanding. Another limitation is that NMSS is an online database that relies on death certificates. Subsequently, any inaccuracy in the coding of the death certificates may have distorted the results.

In conclusion, in China, the home remains the most likely location for EOL care among liver cancer patients, with demographic and socioeconomic factors playing a significant role in shaping their decisions toward hospital-based deaths. Enhancing healthcare providers' comprehension of palliative care for cancer patients and prioritizing the accessibility of services are crucial for improving the quality of EOL care. Such strategies guarantee a fair distribution of healthcare resources and offer a variety of choices for minorities with distinct preferences for EOL care.

## Authors contribution

Xiaosheng Ding: data curation, and writing - original draft preparation; Weiwei Shi: conceptualization, data curation, and writing - original draft preparation; Jinlei Qi: formal analysis and contribution to the interpretation and analysis of the results; Weiran Xu: data curation and formal analysis; Hui Shi: data curation and formal analysis; Juan An: data curation and formal analysis; Xixi Zheng: data curation and formal analysis; Xiaoyan Li: conceptualization, formal analysis, and writing - review & editing. All the authors critically revised and approved the final version of the manuscript.

## Ethics statement

This study was conducted in accordance with the principles of the *Declaration of Helsinki*. The Ethical Review Board of Beijing Tiantan Hospital, Beijing, China (Approval No. YW2022-015-10) approved the study protocol, and the requirement for informed consent was waived owing to the retrospective nature of the study. Identity information was excluded from this study.

## Declaration of Generative AI and AI-assisted technologies in the writing process

The authors declare that generative artificial intelligence (AI) and AI-assisted technologies were not used in the writing process or any other process during the preparation of this manuscript.

## Funding

This study was supported by grants from the National Natural Science Foundation of China (Nos. 81974361 and 82272768) and the Beijing Municipal Education Commission-Beijing Natural Science Foundation Union Program (No.KZ202010025046).

## Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgments

None.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cpt.2024.04.001.

## Data availability statement

The datasets generated and/or analyzed in the current study are available from the corresponding author upon reasonable request.

## References

1. Bragazzi MC, Venere R, Ribichini E, Covotta F, Cardinale V, Alvaro D. Intrahepatic cholangiocarcinoma: evolving strategies in management and treatment. *Dig Liver Dis*. 2024;56:383–393. https://doi.org/10.1016/j.dld.2023.08.052.
2. Xie DY, Zhu K, Ren ZG, Zhou J, Fan J, Gao Q. A review of 2022 Chinese clinical guidelines on the management of hepatocellular carcinoma: updates and insights. *Hepatobiliary Surg Nutr*. 2023;12:216–228. https://doi.org/10.21037/hbsn-22-469.
3. Sung H, Ferlay J, Siegel RL, et al. 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. https://doi.org/10.3322/caac.21660.
4. IHME. *GBD compare*. Seattle: Institute for Health Metrics and Evaluation; 2023. https://vizhub.healthdata.org/gbd-compare/. [Last accessed on 10/2023].

5. Jennings N, Chambaere K, Deliens L, Cohen J. Trends in place of death in a small developing country: a population-level study using death certificate data. *J Epidemiol Community Health*. 2020;74:580–585. https://doi.org/10.1136/jech-2019-213285.
6. van Doorne I, van Rijn M, Dofferhoff SM, Willems DL, Buurman BM. Patients' preferred place of death: patients are willing to consider their preferences, but someone has to ask them. *Age Ageing*. 2021;50:2004–2011. https://doi.org/10.1093/ageing/afab176.
7. Peng JK, Higginson IJ, Gao W. Place of death and factors associated with hospital death in patients who have died from liver disease in England: a national population-based study. *Lancet Gastroenterol Hepatol*. 2019;4:52–62. https://doi.org/10.1016/S2468-1253(18)30379-0.
8. Charalambous H, Pallis A, Hasan B, O'Brien M. Attitudes and referral patterns of lung cancer specialists in europe to specialized palliative care (SPC) and the practice of early palliative care (EPC). *BMC Palliat Care*. 2014;13:59. https://doi.org/10.1186/1472-684X-13-59.
9. Weng L, Hu Y, Sun Z, et al. Place of death and phenomenon of going home to die in Chinese adults: A prospective cohort study. *Lancet Reg Health West Pac*. 2022;18:100301. https://doi.org/10.1016/j.lanwpc.2021.100301.
10. Shepperd S, Gonçalves-Bradley DC, Straus SE, Wee B. Hospital at home: home-based end-of-life care. *Cochrane Database Syst Rev*. 2021;3:CD009231. https://doi.org/10.1002/14651858.CD009231.pub3.
11. Teno JM, Curtis JR. Family perspectives on aggressive cancer care near the end of life. *JAMA Oncol*. 2016;2:957–958. https://doi.org/10.1001/jamaoncol.2016.0441.
12. Bajwah S, Oluyase AO, Yi D, et al. The effectiveness and cost-effectiveness of hospital-based specialist palliative care for adults with advanced illness and their caregivers. *Cochrane Database Syst Rev*. 2020;9:CD012780. https://doi.org/10.1002/14651858.CD012780.pub2.
13. Gomes B, Higginson IJ. Factors influencing death at home in terminally ill patients with cancer: systematic review. *BMJ*. 2006;332:515–521. https://doi.org/10.1136/bmj.38740.614954.55.
14. Yuan Z, Gao L. Social gradient and culture alternative in medicalization of death. *Soc Sci Beijing*. 2018;1:86–93. https://doi.org/10.13262/j.bjsshkxy.bjshkx.180108.
15. Worku MG, Alamneh TS, Teshale AB, et al. Multilevel analysis of determinants of anemia among young women (15-24) in sub-Sahara Africa. *PLoS One*. 2022;17:e0268129. https://doi.org/10.1371/journal.pone.0268129.
16. Robba C, Graziano F, Rebora P, et al. Intracranial pressure monitoring in patients with acute brain injury in the intensive care unit (SYNAPSE-ICU): an international, prospective observational cohort study. *Lancet Neurol*. 2021;20:548–558. https://doi.org/10.1016/S1474-4422(21)00138-1.
17. Butwick AJ, Druzin ML, Shaw GM, Guo N. Evaluation of US state-level variation in hypertensive disorders of pregnancy. *JAMA Netw Open*. 2020;3:e2018741. https://doi.org/10.1001/jamanetworkopen.2020.18741.
18. Merlo J, Chaix B, Yang M, Lynch J, Råstam 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. https://doi.org/10.1136/jech.2004.023473.
19. Adam NS, Twabi HS, Manda SOM. A simulation study for evaluating the performance of clustering measures in multilevel logistic regression. *BMC Med Res Methodol*. 2021;21:245. https://doi.org/10.1186/s12874-021-01417-4.
20. Shayo FK, Nakamura K, Al-Sobaihi S, 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. https://doi.org/10.1016/j.ijid.2020.12.062.
21. Sharma R, Dwivedi LK, Jana S, et al. 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. https://doi.org/10.1016/j.ssmph.2022.101252.
22. Sangaramoorthy M, Shariff-Marco S, Conroy SM, et al, Joint associations of race, ethnicity, and socioeconomic status with mortality in the multiethnic cohort study. *JAMA Netw Open*. 2022;5:e226370. https://doi.org/10.1001/jamanetworkopen.2022.6370.
23. Puechl AM, Chino F, Havrilesky LJ, Davidson BA, Chino JP. Place of death by region and urbanization among gynecologic cancer patients: 2006–2016. *Gynecol Oncol*. 2019;155:98–104. https://doi.org/10.1016/j.ygyno.2019.07.013.
24. Fereidouni A, Salesi M, Rassouli M, et al. Preferred place of death and end-of-life care for adult cancer patients in Iran: a cross-sectional study. *Front Oncol*. 2022;12:911397. https://doi.org/10.3389/fonc.2022.911397.
25. Chino F, Kamal AH, Leblanc TW, Zafar SY, Suneja G, Chino JP. Place of death for patients with cancer in the United States, 1999 through 2015: racial, age, and geographic disparities. *Cancer*. 2018;124:4408–4419. https://doi.org/10.1002/cncr.31737.
26. Fereidouni A, Rassouli M, Salesi M, Ashrafizadeh H, Vahedian-Azimi A, Barasteh S. Preferred place of death in adult cancer patients: a systematic review and meta-analysis. *Front Psychol*. 2021;12:704590. https://doi.org/10.3389/fpsyg.2021.704590.
27. Dasch B, Bausewein C, Feddersen B. Place of death in patients with dementia and the association with comorbidities: a retrospective population-based observational study in Germany. *BMC Palliat Care*. 2018;17:80. https://doi.org/10.1186/s12904-018-0334-0.
28. Gu D, Liu G, Vlosky DA, Yi Z. Factors associated with place of death among the Chinese oldest old. *J Appl Gerontol*. 2007;26:34–57. https://doi.org/10.1177/0733464806296057.
29. Tang ST, McCorkle R. Determinants of place of death for terminal cancer patients. *Cancer Invest*. 2001;19:165–180. https://doi.org/10.1081/cnv-100000151.
30. Nilsson J, Blomberg C, Holgersson G, Carlsson T, Bergqvist M, 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. https://doi.org/10.1111/ajco.12678.
31. Li Z, Hung P, He R, et al. Disparities in end-of-life care, expenditures, and place of death by health insurance among cancer patients in China: a population-based, retrospective study. *BMC Publ Health*. 2020;20:1354. https://doi.org/10.1186/s12889-020-09463-1.
32. Sun Y, Wang Y, Li M, et al, Long-term trends of liver cancer mortality by gender in urban and rural areas in China: An age-period-cohort analysis. *BMJ Open*. 2018;8:e020490. https://doi.org/10.1136/bmjopen-2017-020490.
33. Álvarez CS, Espinosa-Tamez P, López-Ridaura R, et al. Liver cancer mortality in Mexico: trend analysis from 1998 to 2018. *Salud Publica Mex*. 2022;64:14–25. https://doi.org/10.21149/12518.
34. Wang W, Liu Y, Ye P, et al. 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. https://doi.org/10.1016/j.lanwpc.2022.100383.
35. Lin SC, Huang MC, Yasmara D, Wuu HL. Impact of palliative care on end-of-life care and place of death in children, adolescents, and young adults with life-limiting conditions: a systematic review. *Palliat Support Care*. 2021;19:488–500. https://doi.org/10.1017/S1478951520001455.
36. Pire A, Tambucci R, De Magnée C, et al. Living donor liver transplantation for hepatic malignancies in children. *Pediatr Transplant*. 2021;25:e14047. https://doi.org/10.1111/petr.14047.
37. Estrada LV, Agarwal M, Stone PW. Racial/ethnic disparities in nursing home end-of-life care: a systematic review. *J Am Med Dir Assoc*. 2021;22:279–290. https://doi.org/10.1016/j.jamda.2020.12.005.
38. Temkin-Greener H, Yan D, Wang S, Cai S. Racial disparity in end-of-life hospitalizations among nursing home residents with dementia. *J Am Geriatr Soc*. 2021;69:1877–1886. https://doi.org/10.1111/jgs.17117.
39. Ho JFV, Marzuki NS, Meseng NSM, et al. 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. https://doi.org/10.1177/10499091211048767.
40. Öhlén J, Cohen J, Håkanson C. Determinants in the place of death for people with different cancer types: a national population-based study. *Acta Oncol*. 2017;56:455–461. https://doi.org/10.1080/0284186X.2016.1250946.
41. Zhang Y, Lu J. Suffering or serene: an empirical study on determinants affecting the dying status of Chinese elderlies (In Chinese). *Popul Dev*. 2017;23:80–91