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End-of-life cost and its determinants for patients with malignant neoplasms in urban China: A population-based retrospective study

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Abstract

Objective This study aimed to define end-of-life (EOL)healthcare utilisation and its cost and determinants for patients with malignant neoplasms (PMNs) and to proactively provide reference for related strategies in mainland China.

Design A population-based retrospective study.

Setting and Participants Data of 894 patients with PMNs were collected in the urban Yichang, China from 1 July 2015 to 30 June 2017.

Outcome measures Emergency department (ED) visits, hospitalisation, intensive care unit (ICU) admission and total costs were used as the main outcomes.

Results 66.78% of 894 patients were male, and the average age was 60.4 years. Among these patients, 37.58% died at home with an average of 4.86 outpatient services, 2.23 inpatient services and 1.44 ED visits. Additionally, 8.2% of these patients who died at home once visited of ICU. During the EOL periods, the costs in last 6 months, last 3 months, last 1 month and last 1 week were $18235, $13043, $6349 and $2085, respectively. The cost increased dramatically as death approached. The estimation results of generalised linear regression model showed that aggressive care substantially affects expenditure. Patients with Urban Employee Basic Medical

Insurance spent more than those with Urban Resident-based Basic Medical Insurance and New Rural Cooperative Medical Scheme. Place of death and survival time are also the risk factors for the increased EOL cost.

Conclusion The findings suggested that the health expenditure for PMNs is associated with aggressive care, insurance type and survival time. Timing palliative care is urgently needed to deal with the irrational healthcare utilisation and reduce the cost.

Trial registration This study was approved by the ethics committee of Tongji Medical College, Huazhong University of Science and Technology (IORG no. 2018S291). All the data used in this study were de-identified.

Keywords

cancer patients, end-of-life, utilisation, expenditure, retrospective study, urban China

Strengths and limitations

This population-based study was the first to systematically estimate the EOL health expenditure for patients with cancer in mainland China. Estimating the palliative care demand and guiding its system-building are important.

This study introduced EOL healthcare and cost in China and quantified the relationship between them.

This study will guide health policy regarding the delivery of high-quality, cost-effective cancer care system.

Given the anonymity of the data, we cannot obtain the health records from primary care facilities. Thus, the EOL healthcare cost might have been underestimated.

The unique socioeconomic status of the selected cohort population may reduce the generalisability of our findings. Further studies on the provincial or national level are essential to provide systematic evidence for policy makers.

Introduction

Cancer is the leading cause of mortality and accounts for 14.1 million new cancer cases and 8.2 million deaths worldwide, thereby resulting in 32.6 million individuals living with cancer in 2012 [1]. Cancer greatly affects low- and middle-income countries and is expected to account for 70% of the newly reported cancer by 2030 [2]. Given the considerable share of the total health expenditure on cancer (approximately 6% in European countries [3], 9.2% in Taiwan) [4 5]) and the staging 5/80 cancer disequilibrium between developed and developing countries[2], evaluating end-of-life (EOL) cost and identifying its key determinants have been a worldwide concern [6].

Several systematic reviews pointed out that EOL in-home care can improve patient satisfaction, thereby reducing hospital care utilisation and death [7 8]. These reviews also indicated that aggressive procedures do not improve the quality of life [9 10]. However, the health expenditure and utilisation show large geographic variations among patients in the USA with high medical care intensity at the EOL, thereby producing poor outcomes and confusing the patients' preference [11-13]. EOL hospitalisation relatively lacks value worldwide with unsustainable expenditure [14 15], and palliative care is relatively underutilised though is proven to save cost [16]. These phenomena thereby aggravate the inequality among patients with different economic levels or health insurance types and decrease the overall efficacy [17-19].

According to the Fifth Chinese National Health Services Survey in 2013, the incidences of malignant neoplasms in China reached 0.35% and 0.23% in the urban and rural areas, respectively, which are higher than those in 2008 [20]. The most common cancer types in China are lung cancer and stomach, liver and oesophageal cancer, accounting for 22% and 27%, respectively, of global new cancer cases and deaths [21]. Although the age-standardised 5-year relative survival has increased from 30.9% (2003–2005) to 40.5% (2012–2015), the geographical differences in cancer survival still remain [22]. The Program of Cancer Prevention and Control in China (2004–2010) reported that the decreased mortality rates and substantial geographic variation in the survival rate have become a burden to the health system, especially the high out-of-pocket (OOP) expenditure [21 23]. The Economist Intelligence Unit

pointed that China ranked 71st among 80 countries in a survey on the quality of death [24]. A cross-sectional study in China found that OOP expenditures account for 57.5% of the annual household income [25]; this percentage is higher than the household income (23.7%) in the USA [26]. Given the limitation of medical insurance coverage and reimbursement rate, patients with malignant neoplasms (PMNs) and their families face extremely high health expenditure [27 28]. Hospital type, education, insurance type and household income can also predict the expenditure of cancer care [25]. Research on the EOL healthcare cost in mainland China received considerable interest in terms of policy; studies pointed out that some treatments for PMNs in the tertiary hospital are unnecessary, especially during the patients' last days [21 29 30]. However, cross-sectional studies mainly focus on the total healthcare cost limited to single-institutional level, thus underestimating the actual expenditure [31]. Population-based study examining the EOL healthcare expenditure and its determinants has not been explored, especially in terms of the real-world data of the regional health system in urban China. According to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), the WHO version for 2016 [32], the present study selected patients diagnosed with C00-C97 in urban Yichang, China.

Methods

Data collection

Residents who died from malignant neoplasms from 1 July 2015 and 30 June 2017 in urban Yichang, China were continuously enrolled in this study. The demographic information of cancer decedents was collected from the National Population Death Registration and Management System established in 2013. Data on the place of death, cancer type and date of death were obtained from the National Decedent Registration Database. All healthcare utilisation and cost data were provided by the Yichang Health Management Centre affiliated to the Yichang Centre for Diseases Control and Prevention integrating hospital information system, health insurance database and population information database with the identification card number. This study was approved by the ethics committee of Tongji Medical College, Huazhong University of

Science and Technology (IORG no: 2018S291).

Variables

Patients were divided into three groups, such as those younger than 65 years, 65–80 years old and those 80 years or older when diagnosed [21]. Gender and survival time were also divided into four types [33], namely, education, marriage status, cancer type and medical insurance type. The place of death was routinely coded as a binary independent variable. The recommended benchmark measures for terminal cancer care were used to identify the aggressive and palliative procedures [34-38]. The primary outcome was healthcare utilisation, including hospitalisation services, outpatient services, emergency department (ED) visits and intensive care unit (ICU) admission. The secondary outcome was total expenditure. To compare the results, we converted the cost data to the international purchasing power parities by using rate for Chinese Yuan to US dollars (¥2.03=$1) in health from the International Comparison Program 2011[39].

Patient and public involvement

This study aimed to define end-of-life (EOL)healthcare utilisation and its cost and determinants for decedents with PMNs based on a population-based retrospective study. All the data were provided by the Yichang Health Management Centre affiliated to the Yichang Centre for Diseases Control and Prevention and de-identified before statistical analysis. Therefore, decedents were not involved in the recruitment or implementation of this study. The results will not be disseminated to the decedents.

Statistical analysis

Descriptive analysis was used to describe the detailed information about the enrolled population. Generalised linear model was used to evaluate the mechanism of the effect of independent variables on the EOL cost because the EOL data were severely positive skewed [40 41]. For the regression model, the EOL cost was the outcome variables, and the independent variables are as follows: (1) age (<65, 65–80 and 80 years and above), (2) gender (male/female), (3) education level, (4) marital status, (6) first cancer type, (7) medical insurance type, (9) number of ED visit, (10) number of ICU admission and (11) survival time. All the above-mentioned data were calculated

with Stata 14.0. Differences at $P<0.05$ were considered statistically significant.

Results

Table 1. Basic characteristics of the enrolled patients

Demographic characteristics	patients (N=894)	%
Age (year), Median (range)	69 (25,102)	
<65	315	35.23
65-80	440	49.22
>80	139	15.55
Gender		
Male	597	66.78
Female	297	33.22
Marital status		
Unmarried	9	1.01
Married	742	83.00
Widow	126	14.09
Divorced	17	1.90
Insurance type		
Urban Employee Basic Medical Insurance (UEBMI)	518	57.94
Urban Resident-based Basic Medical Insurance (URBMI)	181	20.25
New Rural Cooperative Medical Scheme (NRCMS)	195	21.81
Education		
Junior school or below	675	75.5
Senior school	141	15.77
college or above	78	8.72
Place of death (POD)		
Health institution	558	62.42
Home	336	37.58
Survival time from cancer diagnosis		
< 3 months	261	29.19
3-6 months	233	26.06
7-12 months	216	24.16
> 12 months	184	20.58

Characteristics of the patients and ICD-10 code

As shown in Table 1, 894 patients were identified. The median age of enrolled patients was 69 (range, 25–102) years, 35.23% of which were younger than 65 years, and 15.55% were older than 80 years. Over half (66.78%) of these of the patients were male, and 83% of these male patients were married. A total of 57.94% of the patients were enrolled in the Urban Resident-based Basic Medical Insurance (URBMI). Over 75% of the patients finished junior school or below, and 44.74%

survived for at least 6 months. A total of 62.42% of the patients died at hospitals. As shown in Table 2, The most common cancer types were lung cancer (34.68%), liver cancer (13.98%) and colorectal cancer (9.51%).

Healthcare utilisation and cost

As shown Table 3, the average number of outpatients and hospitalisation services were 4.86 and 2.23 times per capita, respectively. The ED visits and ICU were 1.44 and 0.06 times per capita, respectively. A total of 5.9% (53/894) of the patients were admitted once into the ICU, and 49.7% (444/894) visited ED only once. The average expenditures per capita during the last 1 week, 1 month, 3 months and 6 months were $2085, $6349, $13043and $18235, respectively. The costs in the last 1 week, 1 month and 3 were 11.4%, 34.8% and 71.5% of the last 6 months.

Table 2.The ICD-10 codes of first cancer type when diagnosed

First cancer type	codes	patients (N=894)	%
Lung	C34.x	310	34.68
Stomach	C16.x	60	6.71
Colorectum	C18.x, C19.x, C20.x	85	9.51
Liver	C22.x	125	13.98
Pancreas	C25.xl	39	4.36
Biliary tract	C23.x, C24.x	19	2.13
Blood	C81.x-C86.x, C91.x-C95.x	0	0
Prostate	C61.x	15	1.68
Breast	C50.x	28	3.13
Others	C00.x-C15.x, C17.x, C21.x,C26.x,C30.x-C33.x, C37.x-C41.x,C43.x-C49.x,C51.x-C58.x, C60.x,C62.x,C80.x,C88.x,C90.x,C96.x,C97.x	213	23.83

Table 3. Healthcare services utilization and cost*

Variable	mean	Std. error	median	range
Outpatient services	4.86	7.67	2	59
hospitalization services	2.23	2.16	2	39
Emergency department visit	1.44	2.91	1	13
Intensive care unit admission	0.06	0.25	0	2
Cost during the last 1 week	2085	6829	1195	66437
Cost during the last 1 month	6349	18469	6640	195182
Cost during the last 3 months	13043	37434	13901	431158
Cost during the last 6 months	18234	34583	19276	723144

* the International Purchasing Power Parities using rate for Chinese Yuan to US dollars (¥2.03=$1) in health from International Comparison Program (ICP) 2011.

Determinants of EOL healthcare cost

As shown in Table 4, all the results revealed proportionate increase/decrease in the health expenditures among different groups. In the four generalised linear models, the patients with different genders, marital statuses and education levels showed statistically insignificant differences in the four kinds of cost. High EOL healthcare expenditure was associated with the age of first diagnosis, insurance type, place of death, survival of time after diagnosis and aggressive care services. In terms of the cost in last 6 months, old patients (>80) spent 27.2% (*P*=0.010), which is less than of young patients (<65, 65–80) at 25.5% (*P*=0.011). The difference (OR=0.638, *P*=0.039) between old patients (>80) and relatively younger patients (65–80) increased the cost during in the last 1 week. Patients with the Urban Employee Basic Medical Insurance (UEBMI) spent higher than those with Urban Resident-based Basic Medical Insurance (URBMI) and the New Rural Cooperative Medical Scheme (NRCMS) groups did in the last 6 months (OR=1.691, *P*<0.001; OR=1.471, P=0.006), 3 months (OR=1.960, *P*<0.001; OR=1.474, *P*=0.011) and 1 month (OR1.840, *P*=0.001; OR=1.474, *P*=0.011). Patients with NRCMS spent 33.2% (*P*=0.019) and 66% (P=0.033) higher than the URBMI group did in the last 6 months and 1 week, respectively. The difference between the UEBMI and NRCMS groups was statistically insignificant (*P*=0.151). Patients who died in the hospitals spent 1.364- (*P*=0.002), 1,878- (*P*<0.001), 3.227- (*P*<0.001) and 5.362-fold higher (*P*<0.001) than those died at home during the four EOL periods. The healthcare expenditures during the last 6 months of the patients who survived for 3–6, 7–12 and >12 months were 30.4% (*P*=0.010), 43.8% (*P*=0.001) 39.2% (*P*=0.018) higher than those of the reference group, respectively (<3 months). For the healthcare expenditure during the last 3 months, the expenditures of the patients who survived for 7–12 and >12 months were lower than those of the reference group (<3 months). Differences between the four groups were also observed on the healthcare expenditure during last 1 month and 1 week. For the survival time, the mean costs estimated during the last 1 week of the groups who survived for 3–6 (OR=1.776, *P*=0.017) and 7–12 months (OR=1.557, *P*=0.342) were higher than those of the group with longest survival time (>12

months).

Discussion

In this study, patients with end-stage cancer have high rates of hospitalisation and an average admission of 2.23 times in the last 6 months of life. A total of 5.9% of the patients with cancer had used ICU services during the EOL period. A comparative study in 7 developed countries showed that 40.3% of patients were admitted in the ICU in USA and approximately 18% in the 6 other countries [59]. The mean cost is $18234 per capita which is lower than those of developed countries, such as Canada (US $21840), Norway (US $19783), the US (US $18500) [42], South Korea, Japan and Taiwan (annual cost of $68,773 in 2010) [43]. The cost increased dramatically as death approached. Considering the irrational utilisation and the EOL expenditures trajectory, the risk factors of the high EOL cost must be investigated.

High EOL healthcare expenditure was associated with young age due to high hospital care intensity. This result is consistent with those of previous studies [44-46]. Different studies indicated that gender [46 47] and marital status [48] were not facilitative determinants of the increased EOL healthcare cost. Striking disparities were also observed among the different medical insurances; this finding is consistent with the study of Zeng H et al. [49]. Patients enrolled in NRCMS spent more than those enrolled in URBMI during the last weeks. This phenomenon may be related to the traditional Chinese concept on death and suggests irrational utilisation and low-value service provision [50]. However, this finding is inconsistent with the patient's preference to receive relatively passive care in Taiwan [20]. Cost also depends on the place of death, and it increased rapidly as death approached. The percentage (62.42%) of patients who died in hospitals in China was higher than those in the USA (29.5%) and Canada (52%) [42]. However, 74% of non-hospice beneficiaries died in hospitals or skilled nursing facilities as compared with the 14% who died receiving hospice care in the USA [51]. When the effect of survival time on cost was examined, patients that survived for <3 months spent more than the other groups did. This result is different from the findings of Obermeyer Z, et al. [52], thereby suggesting that the patients with poor cancer prognosis in the present study

may have high rates of aggressive care at the EOL period. However, the ED visit in China is not a risk factor for the increase in cost, which may be due to the current operation process wherein patients are usually hospitalised once admitted during ED visits [53].

The above-mentioned results indicated that numerous health resources in China are irrationally used similar to in other countries [54]. The overuse of aggressive care during the EOL period can be harmful from the patient's perspective [18], and the patients receiving hospice care experience an improved quality of death [12]. Hence, the healthcare need of patients should be satisfied. The timely initiation of hospice or home care may reduce the low-value cancer healthcare services in China because EOL hospice or home care can reduce the hospital care and cost [55], and individuals in EOL period in home or hospice programs have twice as high possibility to have a home death than those with usual care [52].

Conclusion

According to real-world data, this study provides comprehensive evidence on the healthcare utilisation and expenditure for PMNs during the EOL period in China. This study revealed the potential irrational utilisation of the medical resources and the urgency to improve hospice care system in China. Overall, this study may aid in formulating specific measures to optimise cancer care delivery system, especially at the germination stage of hospice care system. Future studies should focus on the evaluation of the current system on the provincial or national level.

Abbreviation

EOL, End-of-life;

OOP, Out-of-pocket;

PMNs, patients with malignant neoplasms;

ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th Revision;

UEBMI, Urban Employee Basic Medical Insurance;

URBMI, Urban Resident-based Basic Medical Insurance;

NRCMS, New Rural Cooperative Medical Scheme;

CI, Confidence interval

AIC, Akaike Information Criterion

OR, Odds ratio

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Zhong Li, Zijin Pan, Pei Zhang, Liang Zhang and Boyang Li designed this study; Zhong Li, Zijin Pan, Chengzhong Xu, Fangfang Lu collected and analyzed the data; Zhong Li drafted the manuscript; Ruibo He, Shan Jiang, Boyang Li and Liang Zhang modified the manuscript. All authors read and approved the final manuscript.

Authors' information

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Data sharing statement

All the research data is available upon reasonable request.

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Table 4. Results of the generalized linear models

Variables	Group	OR (a)	*P*	*95% CI*	OR (b)	*P*	*95% CI*	OR (c)	*P*	*95% CI*	OR (d)	*P*	*95% CI*
Gender(e)	Female	0.941	0.461	0.774-1.106	0.929	0.494	0.751-1.148	0.869	0.243	0.687-1.100	0.915	0.555	0.680-1.230
Age(f)	65-80	0.967	0.701	0.811-1.152	1.017	0.887	0.805-1.284	1.118	0.387	0.868-1.439	1.280	0.142	0.921-1.778
	>80	0.728	**0.010**	0.572-0.926	0.789	0.148	0.573-1.087	0.883	0.491	0.621-1.257	0.816	0.393	0.511-1.302
Insurance	NRCMS	1.332	**0.019**	1.048-1.693	1.333	0.081	0.966-1.839	1.248	0.225	0.872-1.786	1.662	**0.033**	1.041-2.654
Type(g)	UEBMI	1.691	**<0.001**	1.316-2.172	1.960	**<0.001**	1.401-2.742	1.840	**0.001**	1.269-2.668	2.211	**0.001**	1.360-3.596
Marriage	Married	1.343	0.43	0.645-2.795	1.275	0.627	0.478-3.401	1.197	0.742	0.411-3.487	1.341	0.676	0.339-5.313
Status(h)	Widow	1.182	0.667	0.551-2.539	1.029	0.956	0.371-2.852	1.318	0.625	0.435-3.997	1.293	0.725	0.308-5.417
	Divorced	1.225	0.658	0.498-3.017	0.961	0.949	0.290-3.190	1.350	0.652	0.366-4.975	1.591	0.592	0.291-8.687
Education(i)	Senior	1.092	0.414	0.885-1.347	1.050	0.734	0.792-1.392	1.039	0.802	0.768-1.407	0.914	0.667	0.607-1.376
	= > College	0.903	0.467	0.687-1.188	1.037	0.846	0.717-1.501	1.275	0.230	0.858-1.894	1.272	0.353	0.765-2.114
POD(j)	Hospital	1.364	**0.002**	1.121-1.660	1.878	**<0.001**	1.438-2.453	3.227	**<0.001**	2.412-4.317	5.362	**<0.001**	3.664-7.847
Survival time(k)	3-6 months	1.304	**0.01**	1.065-1.595	0.802	0.118	0.609-1.057	0.590	**<0.001**	0.438-0.793	0.587	**0.008**	0.397-0.870
	7-12 months	1.438	**0.001**	1.150-1.795	0.625	**0.003**	0.458-0.851	0.584	**0.002**	0.419-0.815	0.515	**0.003**	0.331-0.801
	> 12 months	1.392	**0.018**	1.058-1.831	0.541	**0.002**	0.369-0.794	0.448	**<0.001**	0.300-0.670	0.331	**<0.001**	0.194-0.562
Outpatients		1.006	0.281	0.995-1.017	1.001	0.938	0.984-1.018	0.992	0.420	0.974-1.011	1.003	0.791	0.979-1.029
EMR		0.998	0.752	0.969-1.023	0.983	0.356	0.947-1.020	0.982	0.399	0.942-1.024	0.974	0.317	0.924-1.026
hospitalization		1.421	**<0.001**	1.347-1.500	1.398	**<0.001**	1.294-1.512	1.373	**<0.001**	1.262-1.495	1.373	**<0.001**	1.235-1.526
ICU		2.544	**<0.001**	1.865-3.470	3.169	**<0.001**	2.081-4.827	3.305	**<0.001**	2.128-5.133	3.411	**<0.001**	1.910-6.089
AIC	22.88				21.84			20.25			17.69		

(a) identified during the last 6 months; (b)identified during the last 3 months; (c)identified during the last 1 months; (d)identified during the last 1 week.

Reference Catogeries: (e)Male; (f)<65; (g) URBMI; (h)Unmarried; (i)Junior or below; (j)Home; (k)< 3 months

AIC, Akaike Information Criterion;OR, odds ratio, CI, Confidential Interval.

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End-of-life cost and its determinants for cancer patients in urban China: A population-based retrospective study

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Abstract

Objective This study aimed to define the end-of-life (EOL) healthcare utilisation and its cost and determinants for cancer patients and to proactively inform related strategies in mainland China.

Design A population-based retrospective study.

Setting and Participants Data from 894 cancer patients were collected in urban Yichang, China from 1 July 2015 to 30 June 2017.

Outcome measures Emergency department (ED) visits, outpatient and inpatient hospitalisation services, intensive care unit (ICU) admission and total costs were used as the main outcomes.

Results In this study, 66.78% of the 894 patients were male, and the average age was 60.4 years. Among these patients, 37.58% died at home, and patients had an average of 4.86 outpatient services, 2.23 inpatient hospitalisation services and 1.44 ED visits. Additionally, 5.9% of these patients visited the ICU at least once. During the EOL periods, the costs in the last 6 months, last 3 months, last 1 month and last 1 week were $18234, $13043, $6349 and $2085, respectively. The cost increased dramatically as death approached. The estimation results of generalised linear regression models

showed that aggressive care substantially affected expenditure. Patients with Urban Employee Basic Medical Insurance spent more than those with Urban Resident-based Basic Medical Insurance or the New Rural Cooperative Medical Scheme. The place of death and survival time are also risk factors for increased EOL cost.

Conclusion The findings suggested that the EOL cost for cancer patients is associated with aggressive care, insurance type and survival time. Timing palliative care is urgently needed to address irrational healthcare utilisation and to reduce costs.

Trial registration This study was approved by the Ethics Committee of the Tongji Medical College, Huazhong University of Science and Technology (IORG No: IORG0003571). All the data used in this study were de-identified.

Keywords

Cancer patients, end-of-life, utilisation, expenditure, retrospective study, urban China.

Strengths and limitations

This population-based study was the first to systematically estimate the EOL health expenditure for cancer patients in mainland China. It is important to estimate the palliative care demand and guide its system building.

This study introduced EOL healthcare utilisation and cost in China and quantified the relationship between them.

This study will guide health policy regarding the delivery of high-quality, cost-effective cancer care systems.

Given the anonymity of the data, we cannot obtain the health records from primary care facilities and healthcare utilisation outside Yichang. Thus, the EOL healthcare cost might have been underestimated.

The unique socioeconomic status of the selected population may reduce the generalisability of our findings. Further studies on the provincial or national levels are essential to provide systematic evidence.

Introduction

Cancer is the leading cause of mortality and accounts for 14.1 million new cancer cases and 8.2 million deaths worldwide, thereby resulting in 32.6 million individuals living with cancer in 2012 [1]. Cancer greatly affects low- and middle-income countries and is expected to account for 70% of the newly reported cancer cases worldwide by 2030 [2]. Given the considerable share of the total health expenditure on cancer (approximately 6% in European countries [3], 9.2% in Taiwan [4 5]) and the great gap in the cancer healthcare delivery system between developed and developing countries [2], evaluating the end-of-life (EOL) cost and identifying its key determinants have been a worldwide concern [6].

Several systematic reviews have noted that in-home EOL care can improve patient satisfaction, thereby reducing inpatient hospitalisation utilisation and hospital death [7 8]. These reviews also indicated that aggressive procedures do not improve the quality of life [9 10]. However, health expenditure and utilisation show large geographic variations among patients in the USA with high medical care intensity during the EOL period, thereby producing poor outcomes and confusing the patients' preference [11-13]. EOL hospitalisation relatively lacks value worldwide with its unsustainable expenditure [14 15], whereas palliative care is relatively underutilised, though it is proven to save costs [16]. These phenomena thereby aggravate inequality among patients with different socioeconomic statuses and decrease overall efficacy [17-19].

According to the Fifth Chinese National Health Services Survey in 2013, the incidences of malignant neoplasms in China reached 0.35% and 0.23% in the urban and rural areas, respectively, which are higher than those in 2008 [20]. The most common cancer types in China are lung and stomach cancers, accounting for 22% of new global cancer cases and deaths, and liver and oesophageal cancers, accounting for 27% of new global cancer cases and deaths [21]. Although the age-standardised 5-year relative survival rate has increased from 30.9% (2003–2005) to 40.5% (2012–2015), geographical differences in cancer survival still remain [22]. The Program of Cancer Prevention and Control in China (2004–2010) reported that the decreased mortality rates and the substantial geographic variation in the survival rates have become a burden to the health system,

especially with the high out-of-pocket (OOP) expenditure [21 23]. The Economist Intelligence Unit noted that China ranked 71st among 80 countries in a survey on the quality of death [24]. A cross-sectional study in China found that OOP expenditures for cancer patients accounted for 57.5% of the annual household income [25]. This percentage is higher than the household income (23.7%) in the USA [26]. Given the limitations of medical insurance coverage and reimbursement rate, cancer patients and their families face extremely high health expenditures [27 28]. Hospital type, education, insurance type and household income can also predict the expenditure of cancer care [25]. Research on the EOL healthcare cost in mainland China has received considerable interest in terms of policy. Studies have noted that some treatments for cancer patients in tertiary hospitals are unnecessary, especially during the patients' last days [21 29 30]. However, cross-sectional studies mainly focus on the total healthcare cost limited to the single-institutional level, thus underestimating the actual expenditure [31]. A population-based study examining EOL healthcare expenditure and its determinants hasnot been explored, especially in terms of the real-world data of the regional health system in China. Therefore, in this study, we aimed 1) to define the EOL healthcare utilisation and its cost among cancer patients, 2) to investigate the determinants of EOL healthcare cost, and 3) to inform related policy making and implementation in China.

Methods

Data collection

According to the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), and the WHO version for 2016 [32], the present study selected patients diagnosed with C00-C97 in urban Yichang, China. Residents who died from cancer from 1 July 2015 and 30 June 2017 in were continuously enrolled in this study. The demographic information of cancer patients, data on the place of death, cancer type was collected from the National Population Death Registration and Management System established in 2013. All healthcare utilisation and cost data were provided by the Yichang Health Management Centre affiliated with the Yichang Centre for Disease Control and Prevention integrating hospital information system, health insurance database and population information database with the identification card

number. This study was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (IORG No: IORG0003571).

Variables

Patients were divided into three groups: those younger than 65 years, those 65–80 years old and those 80 years or older when diagnosed [21]. Survival was divided into four types [33], namely, education, marital status, cancer type and medical insurance type. The place of death was routinely coded as a binary independent variable. The recommended benchmark measures for terminal cancer care were used to identify the aggressive and palliative procedures [34-38]. The primary outcome was healthcare utilisation, including outpatient and inpatient hospitalisation services, emergency department (ED) visits and intensive care unit (ICU) admission. The secondary outcome was total expenditure. To compare the results, we converted the cost data to the international purchasing power parities by using the rate for Chinese Yuan to US dollars (¥2.03=$1) in health from the International Comparison Program 2011[39].

Patient and public involvement

All the data were provided by the Yichang Health Management Centre affiliated with the Yichang Centre for Disease Control and Prevention and de-identified before statistical analysis. Therefore, identifiable cancer patients were not involved in the recruitment or implementation of this study.

Statistical analysis

Descriptive analysis was used to describe the detailed information about the enrolled population. Generalised linear models were used to evaluate the mechanism of the effect of independent variables on the EOL cost because the EOL data were severely positively skewed [40 41]. Four regression models were conducted for patients with different lengths of survival, the EOL costs were the outcome variables, and the independent variables were as follows: (1) age (<65, 65–80, and 80 years and above), (2) gender (male/female), (3) education level, (4) marital status, (6) first cancer type, (7) medical insurance type, (8) number of outpatient services, (9) number of ED visits, (8) number of inpatient hospitalisation services, (11) number of ICU admissions and (12) survival. All the above mentioned data were calculated with Stata 14.0. Differences

at $P<0.05$ were considered statistically significant.

Results

Characteristics of the patients and ICD-10 code

As shown in Table 1, 894 patients were included in this study. The median age of enrolled patients was 69 (range, 25–102) years, 35.23% of which were younger than 65 years, and 15.55% were older than 80 years. Over half (66.78%) of these patients were male, and 83% of the 894 patients were married. A total of 57.94%, 20.25%, and 21.81% of the patients were enrolled in the Urban Employee Basic Medical Insurance (UEBMI), Urban Resident-based Basic Medical Insurance (URBMI) and the New Rural Cooperative Medical Scheme (NRCMS), respectively. Over 75% of the patients finished junior school or below, and 44.74% survived for at least 6 months. A total of 62.42% of the patients died in hospitals. As shown in Table 2, the most common cancer types were lung cancer (34.68%), liver cancer (13.98%) and colorectal cancer (9.51%).

Healthcare utilisation and cost

As shown in Table 3, the average number of outpatient and inpatient hospitalisation services were 4.86 and 2.23 times per capita, respectively. The ED visits and ICU visits were 1.44 and 0.06 times per capita, respectively. A total of 5.9% (53/894) of the patients were admitted once into the ICU, and 49.7% (444/894) visited the ED only once. The average expenditures per capita during the last 1 week, 1 month, 3 months and 6 months were $2085, $6349, $13043 and $18235, respectively. The population-level costs in the last 1 week, 1 month and 3 months were, on average, 11.4%, 34.8% and 71.5%, respectively, of the last 6 months.

Determinants of EOL healthcare cost

As shown in Table 4, all the results revealed proportionate changes in health expenditures among the different groups. In the four generalised linear models, the gender, marital status and education levels of the patients showed statistically insignificant differences in the costs in the four different EOL periods. High EOL healthcare expenditure was associated with the age of first diagnosis, insurance type, place of death, survival after diagnosis and aggressive care services.

For age, we can see that patients aged between 65-80 years spent 66.8% and 34.7%

more than the oldest groups (OR=1.322, P=0.033, 95% CI=1.022-1.710) and younger patients (OR=1.347, P=0.036, 95% CI=1.02-1.779) on the cost during the last 6 months and 3 months, respectively. Patients with UEBMI spent more than those with URBMI, and the NRCMS in the last 6 months (OR=1.79, P<0.001, 95% CI=1.313-2.44; OR=1.480, P=0.002, 95% CI=1.160-1.887), 3 months (OR=2.172, P<0.001, 95% CI=1.464-3.222; OR=1.668, P=0.002, 95% CI=1.206-2.305) and 1 month (OR=2.132, *P*<0.00195% CI=1.46-3.113; OR= 1.581, P=0.004, 95% CI=1.161-2.152). Patients with the NRCMS spent between 98.2% (OR=1.982, P=0.005, 95% CI=1.228-3.2) and 153.2% (OR=2.532, P<0.001, 95% CI=1.548-4.139) higher than the URBMI group during the last week. Patients who died in the hospitals spent 1.488- (*P*=0.002, 95% CI: 1.187-1.864), 2.323- (*P*<0.001, 95% CI: 1.712-3.151), 3.481- (*P*<0.001, 95% CI: 2.585-4.688) and 3.246-fold higher (*P*<0.001, 95% CI: 2.427-4.341) than those who died at home during the four EOL periods.

For the survival time, the difference between the patients who survived for 7-12 months and those who survived for longer than 12 months was not statistically significant (OR=1.026, P=0.787, 95% CI=0.854-1.231). The cost during the last 3 months for patients who survived longer than 12 months was 31.7% (OR=0.682, P=0.032, 95% CI=0.482-0.968) less than that of the reference group (<3-6 months). Differences between the four groups were also observed on the cost during the last 1 week. The mean costs estimated during the last 1 week of the groups who survived for 3–6 months (OR=0.624, P=0.023, 95% CI=0.416-0.937), 7–12 months (OR=0.54, P=0.007, 95% CI=0.346-0.845) and longer than 12 months (OR=0.346, P<0.001, 95% CI=0.199-0.599) were less than patients who survived less than 3 months. Moreover, patients with 7-12 months (OR=0.554, P=0.017, 95% CI=0.341-0.900) and longer survival spent less than patients surviving between 3-6 months (OR=1.602, P=0.023, 95% CI=1.067-2.405). Patients with more than 12 months of survival also spent (OR=0.640, P=0.048, 95% CI=0.411-0.997) less than those who survived 7-12 months. For the inpatient hospitalisation and ICU services, once the inpatient hospitalisation and ICU services increased by one time, the cost with the four periods increased 30.5% (P<0.001, 95% CI=1.25-1.362) and 83.5% (P<0.001, 95% CI=1.292-2.606), 35.3% (P<0.001, 95%

CI=1.187-1.864) and 113.7% (P<0.001, 95% CI=1.253-1.461), 35.7% (P<0.001, 95% CI=1.248-1.477) and 202.5% (P<0.001, 95% CI=1.994-5.152), 35.3% (P<0.001, 95% CI=1.245-1.471) and 222.9% (P<0.001, 95% CI=2.07-5.038), respectively.

Discussion

Many studies have noted that aggressive treatment during the EOL of a patient can lead to higher costs [17-18]. In this study, patients with end-stage cancer had high rates of hospitalisation and an average admission of 2.23 times in the last 6 months of life. A total of 5.9% of the cancer patients had used ICU services during the EOL period. A comparative study in 7 developed countries showed that 40.3% of patients were admitted to the ICU in the USA and approximately 18% of patients were admitted to the ICU in the 6 other countries [42]. The mean cost in China is $18234 per capita, which is lower than those of developed countries, such as Canada (US $21840), Norway (US $19783), the US (US $18500) [42], South Korea, Japan and Taiwan (annual cost of $68,773 in 2010) [43]. The cost increased dramatically as death approached, similar to the results that SEER-Medicare costs revealed [44]. We also found that cost increased rapidly in the last one month, indicating excessive treatment and unnecessary medical expenses. Considering the current status of EOL healthcare utilisation and the expenditures trajectory, the risk factors of the high EOL cost must be investigated.

In this study, several determinants were identified that were associated with the higher EOL cost. First, high EOL healthcare expenditure was associated with young age due to high hospital care intensity. This result is consistent with those of previous studies [44-46]. Many studies indicated that gender [46 47] and marital status [48] were not facilitative determinants of the increased EOL healthcare cost. Second, striking disparities were also observed among the different medical insurances, which is consistent with the study of Zeng H et al. [49]. Patients enrolled in NRCMS spent more than those enrolled in URBMI during the last week. This phenomenon may be related to the traditional Chinese concept of death and suggests irrational utilisation and low-value service provision [50]. However, this finding is inconsistent with the conclusion that patients prefer to receive relatively passive care in Taiwan [43]. Third, cost also depends on the place of death, and it increased rapidly as death approached. The

percentage (62.42%) of patients who died in hospitals in China was higher than patients in the USA (29.5%) and Canada (52%) [42]. However, in the USA, 74% of non-hospice beneficiaries died in hospitals or skilled nursing facilities compared with the 14% who died receiving hospice care [51]. Fourth, the effect of survival on EOL cost differed among patients with different survival periods, suggesting that the patients with poor cancer prognosis in the present study may have high rates of aggressive care at the EOL period. Moreover, inpatient hospitalisation and ICU services were risk factors for high EOL cost. An ED visit in China is not a risk factor for the increase in cost, which may be due to the current operation process wherein patients are usually hospitalised once admitted during ED visits [52]. One study by Obermeyer Z et al. [53] revealed that Medicare fee-for-service beneficiaries with poor-prognosis cancer, which were enrolled in the hospice care programme, used less hospitalisation, intensive care unit admissions, and invasive procedures with a lower total cost than the non-hospice group. Hence, there is great potential for the development of hospice care programmes in China.

The abovementioned results indicated that numerous health resources in China might be irrationally used, similar to other countries [54]. Studies have noted that patients receiving hospice care or early palliative care intervention could experience better palliation of pain and symptom management [55] and improved the likelihood of the place of death they preferred [12, 52]. The overuse of aggressive care during the EOL period can be harmful from the perspective of the patient, including care-related financial strain [14] and the inability to palliate the bereavement of the families [18, 56]. Given the potential benefits of hospice care and early palliative care intervention, the healthcare need of patients should be satisfied. The timely initiation of hospice or home care may reduce the low-value cancer healthcare services in China.

Conclusion

According to real-world data, this study provides comprehensive evidence on healthcare utilisation and expenditure for cancer patients during the EOL period in China. This study revealed the potential irrational utilisation of medical resources and the urgency to improve hospice care systems in China. Overall, this study may aid in

formulating specific measures to optimise the current cancer care delivery system, especially at the developing stages of the hospice care system. Future studies should focus on the evaluation of the current system on the provincial or national levels.

Abbreviation

EOL, End-of-life;

OOP, Out-of-pocket;

ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th Revision;

UEBMI, Urban Employee Basic Medical Insurance;

URBMI, Urban Resident-based Basic Medical Insurance;

NRCMS, New Rural Cooperative Medical Scheme;

CI, Confidence interval;

AIC, Akaike Information Criterion.

OR, Odds ratio

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Zhong Li, Zijin Pan, Pei Zhang, Liang Zhang and Boyang Li designed this study; Zhong Li, Zijin Pan, Chengzhong Xu, Fangfang Lu collected and analyzed the data; Zhong Li drafted the manuscript; Ruibo He, Shan Jiang, Boyang Li and Liang Zhang modified the manuscript. All authors read and approved the final manuscript.

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Data sharing statement

All the research data is available upon reasonable request.

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Table 1. Basic characteristics of the enrolled patients

Demographic characteristics	patients (N=894)	%
Age (year), Median (range)	69 (25,102)	
<65	315	35.23
65-80	440	49.22
>80	139	15.55
Gender		
Male	597	66.78
Female	297	33.22
Marital status		
Unmarried	9	1.01
Married	742	83.00
Widow	126	14.09
Divorced	17	1.90
Insurance type		
Urban Employee Basic Medical Insurance (UEBMI)	518	57.94
Urban Resident-based Basic Medical Insurance (URBMI)	181	20.25
New Rural Cooperative Medical Scheme (NRCMS)	195	21.81
Education		
⩽ Junior school	675	75.5
Senior school	141	15.77
⩾ College	78	8.72
Place of death (POD)		
Health institution	558	62.42
Home	336	37.58
Survival time from cancer diagnosis #		
< 3 months	260	29.25
3-6 months	231	26.0
7-12 months	219	24.6
> 12 months	179	20.14

Survival time of five patients was not obtained.

Table 2. The ICD-10 codes of first cancer type when diagnosed

First cancer type	codes	patients (N=894)	%
Lung	C34.x	310	34.68
Stomach	C16.x	60	6.71
Colorectum	C18.x, C19.x, C20.x	85	9.51
Liver	C22.x	125	13.98
Pancreas	C25.xl	39	4.36
Biliary tract	C23.x, C24.x	19	2.13
Blood	C81.x-C86.x, C91.x-C95.x	0	0
Prostate	C61.x	15	1.68
Breast	C50.x	28	3.13
Others	C00.x-C15.x, C17.x, C21.x,C26.x,C30.x-C33.x, C37.x-C41.x,C43.x-C49.x,C51.x-C58.x, C60.x,C62.x,C80.x,C88.x,C90.x,C96.x,C97.x	213	23.83

Table 3. Healthcare services utilization and cost of the enrolled patients*

Variable	mean	Std. error	median	range
Outpatient services	4.86	7.67	2	59
Inpatient hospitalization services	2.23	2.16	2	39
Emergency department visit	1.44	2.91	1	13
Intensive care unit admission	0.06	0.25	0	2
Cost during the last 1 week	2085	6829	1195	66437
Cost during the last 1 month	6349	18469	6640	195182
Cost during the last 3 months	13043	37434	13901	431158
Cost during the last 6 months	18234	34583	19276	723144

* The International Purchasing Power Parities using rate for Chinese Yuan to US dollars (¥2.03=$1) in health from International Comparison Program (ICP) 2011.

Table 4. Results of the four generalized linear models

Variables	Group	Model 1			Model 2			Model 3			Model 4		
		OR	***P***	***95% CI***	**OR**	***P***	***95% CI***	**OR**	***P***	***95% CI***	**OR**	***P***	***95% CI***
Gender(e)	Female	0.906	0.305	(0.751,1.094)	1.016	0.903	(0.789,1.308)	0.824	0.127	(0.643,1.056)	0.946	0.722	(0.694,1.288)
Age(f)	65-80 (2)	1.098	0.369	(0.895,1.347)	**1.347**	**0.036**	(1.02,1.779)	1.017	0.901	(0.779,1.329)	1.241	0.212	(0.885,1.74)
	>80 (3)	0.831	0.224	(0.616,1.12)	1.043	0.834	(0.702,1.551)	0.767	0.156	(0.531,1.107)	0.932	0.778	(0.568,1.527)
Insurance	NRCMS (2)	1.21	**0.230**	(0.886,1.652)	1.302	0.215	(0.858,1.977)	1.349	0.117	(0.928,1.961)	1.982	**0.005**	(1.228,3.2)
Type(g)	UEBMI (3)	1.79	**<0.001**	(1.313,2.44)	2.172	**<0.001**	(1.464,3.222)	2.132	**<0.001**	(1.46,3.113)	2.532	**<0.001**	(1.548,4.139)
Marriage	Married (1)	2.457	0.069	(0.933,6.468)	1.205	0.757	(0.371,3.919)	1.07	0.906	(0.349,3.276)	1.239	0.764	(0.305,5.031)
status(h)	Widow (2)	2.163	0.132	(0.792,5.905)	0.893	0.855	(0.264,3.017)	1.27	0.687	(0.397,4.064)	1.004	0.996	(0.231,4.355)
	Divorced (3)	2.504	0.112	(0.808,7.763)	1.074	0.922	(0.257,4.489)	1.248	0.746	(0.327,4.772)	1.572	0.607	(0.28,8.824)
Education(i)	Senior (2)	1.143	0.242	(0.913,1.431)	1.004	0.978	(0.73,1.382)	1.043	0.791	(0.767,1.418)	0.921	0.702	(0.605,1.403)
	≥College (3)	0.996	0.981	(0.737,1.346)	1.227	0.358	(0.794,1.897)	1.255	0.277	(0.833,1.891)	1.244	0.406	(0.743,2.086)
POD(j)	Hospital	1.488	**0.001**	(1.187,1.864)	2.323	**<0.001**	(1.712,3.151)	3.481	**<0.001**	(2.585,4.688)	5.371	**<0.001**	(3.653,7.897)
Survival(k)	3-6 months (2)							0.648	**0.008**	(0.47,0.893)	0.624	**0.023**	(0.416,0.937)
	7-12 months (3)				0.827	0.186	(0.623,1.096)	0.661	**0.02**	(0.466,0.937)	0.54	**0.007**	(0.346,0.845)
	> 12 months (4)	1.026	**0.787**	(0.854,1.231)	0.683	**0.032**	(0.482,0.968)	0.507	**0.002**	(0.333,0.771)	0.346	**<0.001**	(0.199,0.599)
OS		1.007	0.13	(0.998,1.016)	0.998	0.842	(0.981,1.015)	0.993	0.441	(0.974,1.011)	1.005	0.679	(0.98,1.031)
EMR		0.997	0.824	(0.975,1.02)	0.98	0.267	(0.945,1.016)	0.98	0.343	(0.941,1.022)	0.971	0.273	(0.922,1.023)
'H'IS		1.305	**<0.001**	(1.25,1.362)	1.353	**0.001**	(1.253,1.461)	1.357	**<0.001**	(1.248,1.477)	1.369	**<0.001**	(1.229,1.526)
ICU		1.835	**0.001**	(1.292,2.606)	2..378	**<0.001**	(1.438,3.932)	3.205	**<0.001**	(1.994,5.152)	3.456	**<0.001**	(3.456,6.299)
No		398			629			**807**			868		

Model 1: cost during the last 6 months; Model 2:cost during the last 3 months; Model 3: cost during the last 1 months; Model 4: cost during the last 1 week. # Reference: (e)Male; (f)<65; (g) URBMI; (h)Unmarried; (i) Junior or below; (j)Home; (k)< 3 months In Model 1 and 2, we took the patients survived 7-12 months and

3-6 months as reference, respectively. Results of additional models: Model 1: Agegroup: 2 vs.3 (OR=1.322, P=0.033, 95% CI=1.022-1.710); Insurnace type: 3 vs.2 (OR=1.480, P=0.002, 95% CI=1.160-1.887); Model 2: Insurnace type: 3 vs.2 (OR=1.668, P=0.002, 95% CI=1.206-2.305); Model 3: Insurnace type: 3 vs.2 (OR= 1.581 , P=0.004, 95% CI=1.161-2.152); Model 4: Survival: 4 vs.2 (OR=0.554, P=0.017, 95% CI=0.341-0.900); 5 vs.2 (OR=1.602, P=0.023, 95% CI=1.067-2.405);4 vs.3 (OR=0.640, P=0.048, 95% CI=0.411-0.997); OS, outpatient services; IHS, inpatient hospitalization services; No, number of observation; AIC, Akaike Information Criterion; OR, odds ratio, CI, Confidential Interval.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not required
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*4-5*
Bias	9	Describe any efforts to address potential sources of bias	4-5
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4-5
		(*b*) Describe any methods used to examine subgroups and interactions	4-5
		(*c*) Explain how missing data were addressed	4-5
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	4-5

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6-7
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	6-7
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	6-7
		Cross-sectional study—Report numbers of outcome events or summary measures	6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7
		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8-9, 1
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9, 1
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9, 1

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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End-of-life cost and its determinants for cancer patients in urban China: A population-based retrospective study

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End-of-life cost and its determinants for cancer patients in urban China: A population-based retrospective study

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Abstract

Objective This study aimed to define the end-of-life (EOL) healthcare utilisation and its cost and determinants for cancer patients and to proactively inform related strategies in mainland China.

Design A population-based retrospective study.

Setting and Participants Data from 894 cancer patients were collected in urban Yichang, China from 1 July 2015 to 30 June 2017.

Outcome measures Emergency department (ED) visits, outpatient and inpatient hospitalisation services, intensive care unit (ICU) admission and total costs were used as the main outcomes.

Results In this study, 66.8% of the 894 patients were male, and the average age was 60.4 years. Among these patients, 37.6% died at home, and patients had an average of 4.86 outpatient services, 2.23 inpatient hospitalisation services and 1.44 ED visits. Additionally, 5.9% of these patients visited the ICU at least once. During the EOL periods, the costs in the last 6 months, last 3 months, last 1 month and last 1 week were $18234, $13043, $6349 and $2085, respectively. The cost increased dramatically as death approached. The estimation results of generalised linear regression models

showed that aggressive care substantially affected expenditure. Patients with Urban Employee Basic Medical Insurance spent more than those with Urban Resident-based Basic Medical Insurance or the New Rural Cooperative Medical Scheme. The place of death and survival time are also risk factors for increased EOL cost.

Conclusion The findings suggested that the EOL cost for cancer patients is associated with aggressive care, insurance type and survival time. Timing palliative care is urgently needed to address ineffective and irrational healthcare utilisation and to reduce costs.

Trial registration This study was approved by the Ethics Committee of the Tongji Medical College, Huazhong University of Science and Technology (IORG No: IORG0003571). All the data used in this study were de-identified.

Keywords

Cancer patients, end-of-life, utilisation, expenditure, retrospective study, urban China.

Strengths and limitations

This population-based study was the first to systematically estimate the EOL health expenditure for cancer patients in mainland China. It is important to estimate the palliative care demand and guide its system building.

This study introduced EOL healthcare utilisation and cost in China and quantified the relationship between them.

This study will guide health policy regarding the delivery of high-quality, cost-effective cancer care systems.

Given the anonymity of the data, we cannot obtain the health records from primary care facilities and healthcare utilisation outside Yichang. Thus, the EOL healthcare cost might have been underestimated.

The unique socioeconomic status of the selected population may reduce the generalisability of our findings. Further studies on the provincial or national levels are essential to provide systematic evidence.

Introduction

Cancer is the leading cause of mortality and accounts for 14.1 million new cancer cases and 8.2 million deaths worldwide, 32.6 million individuals living with cancer in 2012 [1]. Cancer greatly affects low- and middle-income countries and is expected to account for 70% of the newly reported cancer cases worldwide by 2030 [2]. Given the considerable share of the total health expenditure on cancer (approximately 6.0 % in European countries [3], 9.2 % in Taiwan [4 5]) and the great gap in the cancer healthcare delivery system between developed and developing countries [2], evaluating the end-of-life (EOL) cost and identifying its key determinants have been a worldwide concern [6].

Several systematic reviews have noted that in-home EOL care can improve patient satisfaction, as well as reducing inpatient hospitalisation utilisation and hospital death [7 8]. These reviews also indicated that aggressive procedures do not improve the quality of life [9 10]. However, health expenditure and utilisation show large geographic variations among patients in the USA with high medical care intensity during the EOL period, thereby producing poor outcomes and confusing the patients' preference [11-13]. EOL hospitalisation relatively lacks value worldwide with its unsustainable expenditure [14 15], whereas palliative care is relatively underutilised, though it is proven to save costs [16]. These phenomena thereby aggravated inequality among patients with different socioeconomic statuses and decrease overall efficacy [17-19].

According to the Fifth Chinese National Health Services Survey in 2013, the incidences of malignant neoplasms in China reached 0.35% and 0.23% in the urban and rural areas, respectively, higher than those in 2008 [20]. The most common cancer types in China are lung and stomach cancers, accounting for 22% of new global cancer cases and deaths, and liver and oesophageal cancers, accounting for 27% of new global cancer cases and deaths [21]. Although the age-standardised 5-year relative survival rate has increased from 30.9% (2003–2005) to 40.5% (2012–2015), geographical differences in cancer survival still remain [22]. The Program of Cancer Prevention and Control in China (2004–2010) reported that the decreased mortality rates and the substantial

geographic variation in the survival rates have become a burden to the health system, especially with the high out-of-pocket (OOP) expenditure [21 23]. The Economist Intelligence Unit noted that China ranked 71st among 80 countries in a survey on the quality of death [24]. A cross-sectional study in China found that OOP expenditures for cancer patients accounted for 57.5% of the annual household income [25]. This percentage is higher than that (23.7%) in the USA [26]. Given the limitations of medical insurance coverage and reimbursement rate, cancer patients and their families face extremely high health expenditures [27 28]. Hospital type, education, insurance type and household income can also predict the expenditure of cancer care [25]. Research on the EOL healthcare cost in mainland China has received considerable interest in terms of policy. Studies have noted that some treatments for cancer patients in tertiary hospitals are unnecessary, especially during the patients' last days [21 29 30]. However, cross-sectional studies mainly focus on the total healthcare cost limited to the single-institutional level, thus underestimating the actual expenditure [31]. A population-based study examining EOL healthcare expenditure and its determinants is not explored, especially in terms of the real-world data of the regional health system in China. Therefore, in this study, we aimed 1) to define the EOL healthcare utilisation and its cost among cancer patients, 2) to investigate the determinants of EOL healthcare cost, and 3) to inform related policy making and implementation in China.

Methods

Data collection

Based on the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), and the WHO version for 2016 [32], the present study selected patients diagnosed with C00-C97 in urban Yichang, China. Residents who died from cancer from 1 July 2015 and 30 June 2017 were continuously enrolled in this study. The demographic information of cancer patients, data on the place of death, cancer type was collected from the National Population Death Registration and Management System established in 2013. All healthcare utilisation and cost data were provided by the Yichang Health Management Centre affiliated with the Yichang Centre for Disease Control and Prevention integrating hospital information system, health

insurance database and population information database with the identification card number. This study was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology (IORG No: IORG0003571).

Variables

Patients were divided into three groups: those younger than 65 years, those 65–80 years old and those 80 years or older when diagnosed [21]. Survival was divided into four types [33], namely, education, marital status, cancer type and medical insurance type. The place of death was routinely coded as a binary variable. The recommended benchmark measures for terminal cancer care were used to identify the aggressive and palliative procedures [34-38]. The main outcome was healthcare utilisation, including outpatient and inpatient hospitalisation services, emergency department (ED) visits and intensive care unit (ICU) admission, and the EOL expenditures. To compare the results, we converted the cost data to the international purchasing power parities by using the rate for Chinese Yuan to US dollars (¥2.03=$1) in health from the International Comparison Program 2011[39].

Patient and public involvement

All the data were provided by the Yichang Health Management Centre affiliated with the Yichang Centre for Disease Control and Prevention and de-identified before statistical analysis. Therefore, identifiable cancer patients were not involved in the recruitment or implementation of this study.

Statistical analysis

Descriptive analysis was used to describe the detailed information about the enrolled population. Generalised linear models were used to evaluate the mechanism of the effect of independent variables on the EOL cost because the EOL data were severely positively skewed [40 41]. Four regression models were conducted for patients with different lengths of survival, the EOL costs were the outcome variables, and the independent variables were as follows: (1) age (<65, 65–80, and ⩾ 80 years), (2) gender (male/female), (3) education level, (4) marital status, (6) first cancer type, (7) medical insurance type, (8) number of outpatient services, (9) number of ED visits, (8) number of inpatient hospitalisation services, (11) number of ICU admissions and (12)

survival. All the above mentioned data were calculated with Stata 14.0. Differences at $P < 0.05$ were considered statistically significant.

Results

Characteristics of the patients and ICD-10 code

As shown in Table 1, 894 patients were included in this study. The median age of enrolled patients was 69 (range, 25–102) years, 35.2% of which were younger than 65 years, and 15.6% were older than 80 years. Two-thirds (66.8%) of these patients were male, and 83% of the 894 patients were married. A total of 57.9%, 20.3%, and 21.8% of the patients were enrolled in the Urban Employee Basic Medical Insurance (UEBMI), Urban Resident-based Basic Medical Insurance (URBMI) and the New Rural Cooperative Medical Scheme (NRCMS), respectively. 75.5 % of the patients finished junior school or below, and 44.7% survived for at least 6 months. A total of 62.4% of the patients died in hospitals. As shown in Table 2, the most common cancer types were lung cancer (34.7%), liver cancer (14.0 %) and colorectal cancer (9.5%).

Healthcare utilisation and cost

As shown in Table 3, the average number of outpatient and inpatient hospitalisation services were 4.86 and 2.23 times per capita, respectively. The ED visits and ICU visits were 1.44 and 0.06 times per capita, respectively. A total of 5.9% (53/894) of the patients were admitted once into the ICU, and 49.7% (444/894) visited the ED only once. The average expenditures per capita during the last 1 week, 1 month, 3 months and 6 months were $2085, $6349, $13043 and $18235, respectively. The population-level costs in the last 1 week, 1 month and 3 months were, on average, 11.4%, 34.8% and 71.5%, respectively, of the last 6 months.

Determinants of EOL healthcare cost

As shown in Table 4, all the results revealed proportionate changes in health expenditures among the different groups. In the four generalised linear models, the gender, marital status and education levels of the patients showed statistically insignificant differences in the costs during the four different EOL periods. High EOL healthcare expenditure was associated with the age of first diagnosis, insurance type, place of death, survival after diagnosis and aggressive care services.

For age, we can see that patients aged between 65-80 years spent 66.8% and 34.7% more than the oldest groups (OR=1.322, P=0.033, 95% CI=1.022-1.710) and younger patients (OR=1.347, P=0.036, 95% CI=1.02-1.779) on the cost during the last 6 months and 3 months, respectively. Patients with UEBMI spent more than those with URBMI, and the NRCMS in the last 6 months (OR=1.79, P<0.001, 95% CI=1.313-2.44; OR=1.480, P=0.002, 95% CI=1.160-1.887), 3 months (OR=2.172, P<0.001, 95% CI=1.464-3.222; OR=1.668, P=0.002, 95% CI=1.206-2.305) and 1 month (OR=2.132, P<0.001, 95% CI=1.46-3.113; OR= 1.581, P=0.004, 95% CI=1.161-2.152). Patients with the NRCMS spent between 98.2% (OR=1.982, P=0.005, 95% CI=1.228-3.2) and 153.2% (OR=2.532, P<0.001, 95% CI=1.548-4.139) higher than the URBMI group during the last week. Patients who died in the hospitals spent 1.488- (*P*=0.002, 95% CI: 1.187-1.864), 2.323- (*P*<0.001, 95% CI=1.712-3.151), 3.481- (*P*<0.001, 95% CI= 2.585-4.688) and 3.246-fold higher (*P*<0.001, 95% CI=2.427-4.341) than those who died at home during the four EOL periods.

For the survival time, the difference between the patients who survived for 7-12 months and those who survived for longer than 12 months was not statistically significant (OR=1.026, P=0.787, 95% CI=0.854-1.231). The cost during the last 3 months for patients who survived longer than 12 months was 31.7% (OR=0.682, P=0.032, 95% CI=0.482-0.968) less than that of the reference group (<3-6 months). Differences between the four groups were also observed on the cost during the last 1 week. The mean costs estimated during the last 1 week of the groups who survived for 3–6 months (OR=0.624, P=0.023, 95% CI=0.416-0.937), 7–12 months (OR=0.54, P=0.007, 95% CI=0.346-0.845) and longer than 12 months (OR=0.346, P<0.001, 95% CI=0.199-0.599) were less than patients who survived less than 3 months. Moreover, patients with 7-12 months (OR=0.554, P=0.017, 95% CI=0.341-0.900) and longer survival spent less than patients surviving between 3-6 months (OR=1.602, P=0.023, 95% CI=1.067-2.405). Patients with more than 12 months of survival also spent (OR=0.640, P=0.048, 95% CI=0.411-0.997) less than those who survived 7-12 months. For the inpatient hospitalisation and ICU services, once the inpatient hospitalisation and ICU services increased by one time, the cost with the four periods increased 30.5% (P<0.001, 95%

CI=1.25-1.362) and 83.5% (P<0.001, 95% CI=1.292-2.606), 35.3% (P<0.001, 95% CI=1.187-1.864) and 113.7% (P<0.001, 95% CI=1.253-1.461), 35.7% (P<0.001, 95% CI=1.248-1.477) and 202.5% (P<0.001, 95% CI=1.994-5.152), 35.3% (P<0.001, 95% CI=1.245-1.471) and 222.9% (P<0.001, 95% CI=2.07-5.038), respectively.

Discussion

Many studies have noted that aggressive treatment during the EOL of a patient can lead to higher costs [17-18]. In this study, patients with end-stage cancer had high rates of hospitalisation and an average admission of 2.23 times in the last 6 months of life. A total of 5.9% of the cancer patients had used ICU services during the EOL period. A comparative study in 7 developed countries showed that 40.3% of patients were admitted to the ICU in the USA and approximately 18% of patients were admitted to the ICU in the 6 other countries [42]. The mean cost is $18234 per capita, which is lower than those of developed countries, such as Canada (US $21840), Norway (US $19783), the US (US $18500) [42], South Korea, Japan and Taiwan (annual cost of $68,773 in 2010) [43]. The cost increased dramatically as death approached, similar to the results that SEER-Medicare costs revealed [44]. We also found that cost increased rapidly in the last one month, indicating excessive treatment and ineffective medical expenses. Considering the current status of EOL healthcare utilisation and the expenditures trajectory, the risk factors of the high EOL cost must be investigated.

In this study, several determinants were identified that were associated with the higher EOL cost. First, high EOL healthcare expenditure was associated with young age due to high hospital care intensity. This result is consistent with those of previous studies [44-46]. Many studies indicated that gender [46 47] and marital status [48] were not facilitative determinants of the increased EOL healthcare cost. Second, striking disparities were also observed among the different medical insurances, which is consistent with the study of Zeng H et al [49]. Patients enrolled in NRCMS spent more than those enrolled in URBMI during the last week. This phenomenon may be related to the traditional Chinese concept of death and suggests ineffective and irrational utilisation and low-value service provision [50]. However, this finding is inconsistent with the conclusion that patients prefer to receive relatively passive care in Taiwan [43].

Third, cost also depends on place of death, and cost increased rapidly as death approached. The percentage (62.42%) of patients who died in hospitals in China was higher than patients in the USA (29.5%) and Canada (52%) [42]. However, in the USA, 74% of non-hospice beneficiaries died in hospitals or skilled nursing facilities compared with the 14% who died receiving hospice care [51]. Fourth, the effect of survival on EOL cost differed among patients with different survival periods, suggesting that the patients with poor cancer prognosis in the present study may have high rates of aggressive care at the EOL period. Moreover, inpatient hospitalisation and ICU services were risk factors for high EOL cost. An ED visit in China is not a risk factor for the increase in cost, which may be due to the current operation process wherein patients are usually hospitalised once admitted during ED visits [52]. One study by Obermeyer Z et al. [53] revealed that Medicare fee-for-service beneficiaries with poor-prognosis cancer, which were enrolled in the hospice care programme, used less hospitalisation, intensive care unit admissions, and invasive procedures with a lower total cost than the non-hospice group. Hence, there is great potential for the development of hospice care programmes in China.

The abovementioned results indicated that numerous health resources in China might be ineffectively used, similar to other countries [54]. Patients receiving hospice care or early palliative care intervention could experience better management of pain and symptom[55] and an improved likelihood of dying at home if that was preferred [12, 52]. Given the potential benefits of hospice care and early palliative care intervention, the timely initiation of hospice or home care may reduce low value cancer healthcare services in China. The overuse of aggressive care during the EOL period can be harmful from the perspective of the patients, including additional care-related financial strain [14], no reduction in the bereavement of their families [18, 56]. Given the potential benefits of hospice care and early palliative care intervention, the healthcare need of patients should be satisfied. The timely initiation of hospice or home care may reduce the low-value cancer healthcare services in China.

Conclusion

According to real-world data, this study provides comprehensive evidence on

healthcare utilisation and expenditure for cancer patients during the EOL period in China. This study revealed the potential ineffective and irrational utilisation of medical resources and the urgency to improve hospice care systems in China. Overall, this study may aid in formulating specific measures to optimise the current cancer care delivery system, especially at the developing stages of the hospice care system. Future studies should focus on the evaluation of the current system on the provincial or national levels.

Abbreviation

EOL, End-of-life;

OOP, Out-of-pocket;

ICD-10, International Statistical Classification of Diseases and Related Health Problems 10th Revision;

UEBMI, Urban Employee Basic Medical Insurance;

URBMI, Urban Resident-based Basic Medical Insurance;

NRCMS, New Rural Cooperative Medical Scheme;

CI, Confidence interval;

AIC, Akaike Information Criterion.

OR, Odds ratio

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Zhong Li, Zijing Pan, Pei Zhang, Liang Zhang and Boyang Li designed this study; Zhong Li, Zijing Pan, Chengzhong Xu, Fangfang Lu collected and analyzed the data; Zhong Li drafted the manuscript; Ruibo He, Shan Jiang, Boyang Li and Liang Zhang modified the manuscript. All authors read and approved the final manuscript.

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Data sharing statement

All the research data is available upon reasonable request.

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Table 1. Basic characteristics of the enrolled patients

Demographic characteristics	patients (N=894)	%
Age (year), Median (range)	69 (25,102)	
<65	315	35.2
65-80	440	49.2
>80	139	15.6
Gender		
Male	597	66.8
Female	297	33.2
Marital status		
Unmarried	9	1.0
Married	742	83.0
Widow	126	14.2
Divorced	17	1.9
Insurance type		
Urban Employee Basic Medical Insurance (UEBMI)	518	57.9
Urban Resident-based Basic Medical Insurance (URBMI)	181	20.3
New Rural Cooperative Medical Scheme (NRCMS)	195	21.8
Education		
≤ Junior school	675	75.5
Senior school	141	15.8
≥ College	78	8.7
Place of death (POD)		
Health institution	558	62.4
Home	336	37.6
Survival time from cancer diagnosis #		
< 3 months	260	29.3
3-6 months	231	26.0
7-12 months	219	24.6
> 12 months	179	20.1

Survival time of five patients was not obtained.

Table 2. The ICD-10 codes of first cancer type when diagnosed

First cancer type	codes	patients (N=894)	%
Lung	C34.x	310	34.7
Stomach	C16.x	60	6.7

Colorectum	C18.x, C19.x, C20.x	85	9.5
Liver	C22.x	125	14.0
Pancreas	C25.xl	39	4.4
Biliary tract	C23.x, C24.x	19	2.1
Blood	C81.x-C86.x, C91.x-C95.x	0	0
Prostate	C61.x	15	1.7
Breast	C50.x	28	3.1
Others	C00.x-C15.x, C17.x, C21.x,C26.x,C30.x-C33.x, C37.x-C41.x,C43.x-C49.x,C51.x-C58.x, C60.x,C62.x,C80.x,C88.x,C90.x,C96.x,C97.x	213	23.8

Table 3. Healthcare services utilization and cost of the enrolled patients*

Variable	mean	Std. error	median	range
Outpatient services	4.86	7.67	2	59
Inpatient hospitalization services	2.23	2.16	2	39
Emergency department visit	1.44	2.91	1	13
Intensive care unit admission	0.06	0.25	0	2
Cost during the last 1 week	2085	6829	1195	66437
Cost during the last 1 month	6349	18469	6640	195182
Cost during the last 3 months	13043	37434	13901	431158
Cost during the last 6 months	18234	34583	19276	723144

* The International Purchasing Power Parities using rate for Chinese Yuan to US dollars (¥2.03=$1) in health from International Comparison Program (ICP) 2011.

Table 4. Results of the four generalized linear models

Variables	Group	Model 1			Model 2			Model 3			Model 4		
		OR	***P***	***95% CI***	**OR**	***P***	***95% CI***	**OR**	***P***	***95% CI***	**OR**	***P***	***95% CI***
Gender(e)	Female	0.906	0.305	(0.751,1.094)	1.016	0.903	(0.789,1.308)	0.824	0.127	(0.643,1.056)	0.946	0.722	(0.694,1.288)
Age(f)	65-80 (2)	1.098	0.369	(0.895,1.347)	**1.347**	**0.036**	(1.02,1.779)	1.017	0.901	(0.779,1.329)	1.241	0.212	(0.885,1.74)
	>80 (3)	0.831	0.224	(0.616,1.12)	1.043	0.834	(0.702,1.551)	0.767	0.156	(0.531,1.107)	0.932	0.778	(0.568,1.527)
Insurance	NRCMS (2)	1.21	**0.230**	(0.886,1.652)	1.302	0.215	(0.858,1.977)	1.349	0.117	(0.928,1.961)	1.982	**0.005**	(1.228,3.2)
Type(g)	UEBMI (3)	1.79	**<0.001**	(1.313,2.44)	2.172	**<0.001**	(1.464,3.222)	2.132	**<0.001**	(1.46,3.113)	2.532	**<0.001**	(1.548,4.139)
Marriage status(h)	Married (1)	2.457	0.069	(0.933,6.468)	1.205	0.757	(0.371,3.919)	1.07	0.906	(0.349,3.276)	1.239	0.764	(0.305,5.031)
	Widow (2)	2.163	0.132	(0.792,5.905)	0.893	0.855	(0.264,3.017)	1.27	0.687	(0.397,4.064)	1.004	0.996	(0.231,4.355)
	Divorced (3)	2.504	0.112	(0.808,7.763)	1.074	0.922	(0.257,4.489)	1.248	0.746	(0.327,4.772)	1.572	0.607	(0.28,8.824)
Education(i)	Senior (2)	1.143	0.242	(0.913,1.431)	1.004	0.978	(0.73,1.382)	1.043	0.791	(0.767,1.418)	0.921	0.702	(0.605,1.403)
	≥College (3)	0.996	0.981	(0.737,1.346)	1.227	0.358	(0.794,1.897)	1.255	0.277	(0.833,1.891)	1.244	0.406	(0.743,2.086)
POD(j)	Hospital	1.488	**0.001**	(1.187,1.864)	2.323	**<0.001**	(1.712,3.151)	3.481	**<0.001**	(2.585,4.688)	5.371	**<0.001**	(3.653,7.897)
Survival(k)	3-6 months (2)							0.648	**0.008**	(0.47,0.893)	0.624	**0.023**	(0.416,0.937)
	7-12 months (3)				0.827	0.186	(0.623,1.096)	0.661	**0.02**	(0.466,0.937)	0.54	**0.007**	(0.346,0.845)
	> 12 months (4)	1.026	**0.787**	(0.854,1.231)	0.683	**0.032**	(0.482,0.968)	0.507	**0.002**	(0.333,0.771)	0.346	**<0.001**	(0.199,0.599)
OS		1.007	0.13	(0.998,1.016)	0.998	0.842	(0.981,1.015)	0.993	0.441	(0.974,1.011)	1.005	0.679	(0.98,1.031)
EMR		0.997	0.824	(0.975,1.02)	0.98	0.267	(0.945,1.016)	0.98	0.343	(0.941,1.022)	0.971	0.273	(0.922,1.023)
'H'IS		1.305	**<0.001**	(1.25,1.362)	1.353	**0.001**	(1.253,1.461)	1.357	**<0.001**	(1.248,1.477)	1.369	**<0.001**	(1.229,1.526)
ICU		1.835	**0.001**	(1.292,2.606)	2..378	**<0.001**	(1.438,3.932)	3.205	**<0.001**	(1.994,5.152)	3.456	**<0.001**	(3.456,6.299)
No		398			629			**807**			868		

Model 1: cost during the last 6 months; Model 2:cost during the last 3 months; Model 3: cost during the last 1 months; Model 4: cost during the last 1 week. # Reference: (e)Male; (f)<65; (g) URBMI; (h)Unmarried; (i) Junior or below; (j)Home; (k)< 3 months In Model 1 and 2, we took the patients survived 7-12 months and 3-6 months as reference, respectively. Results of additional models: Model 1: Agegroup: 2 vs.3 (OR=1.322, P=0.033, 95% CI=1.022-1.710); Insurnace type: 3 vs.2 (OR=1.480, P=0.002, 95% CI=1.160-1.887); Model 2: Insurnace type: 3 vs.2 (OR=1.668, P=0.002, 95% CI=1.206-2.305); Model 3: Insurnace type: 3 vs.2 (OR= 1.581 , P=0.004, 95% CI=1.161-2.152); Model 4: Survival: 4 vs.2 (OR=0.554, P=0.017, 95% CI=0.341-0.900); 5 vs.2 (OR=1.602, P=0.023, 95% CI=1.067-2.405);4 vs.3 (OR=0.640,

P=0.048, 95% CI=0.411-0.997); OS, outpatient services; IHS, inpatient hospitalization services; No, number of observation; AIC, Akaike Information Criterion; OR, odds ratio, CI, Confidential Interval.

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*
Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	1-2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any pre-specified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4-5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not required
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*4-5*
Bias	9	Describe any efforts to address potential sources of bias	4-5
Study size	10	Explain how the study size was arrived at	4-5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4-5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	4-5
		(*b*) Describe any methods used to examine subgroups and interactions	4-5
		(*c*) Explain how missing data were addressed	4-5
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	4-5

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6
		(b) Indicate number of participants with missing data for each variable of interest	6-7
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	6
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	6-7
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	6-7
		Cross-sectional study—Report numbers of outcome events or summary measures	6-7
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	6-7
		(*b*) Report category boundaries when continuous variables were categorized	6-7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6-7
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6-7
Discussion			
Key results	18	Summarise key results with reference to study objectives	8-9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	8-9, 1
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-9, 1
Generalisability	21	Discuss the generalisability (external validity) of the study results	8-9, 1

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.