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ORIGINAL RESEARCH

Economic burden of advanced lung cancer patients treated by gefitinib alone and combined with chemotherapy in two regions of China

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ABSTRACT

Aim: To assess the economic burden of different chemotherapies for lung cancer patients and influencing factors in China.

Materials and methods: The economic burden of lung cancer, including direct, indirect and intangible costs was measured within three months after diagnosis and treatment. Direct cost included the cost of hospitalization, outpatient visits, out-of-pocket drug purchases, costs of transportation, accommodation and meal expenses while seeking treatments in hospitals. Cost information was attained from questionnaire and patients' medical record. Indirect cost was measured by the patients' and their caregivers' productive days lost due to outpatient visits and hospitalization for lung cancer treatment. Intangible cost was obtained through the willingness-to-pay method from a questionnaire completed by the patient.

Results: Among the total cost of CNY71,401.92, direct cost, indirect cost and intangible cost constituted 89.02%, 4.29%, and 6.69% respectively. Educational level, occupation, family income, lung cancer classification, and the city of residence significantly influenced the total cost.

Limitations: Limitations in our study included: First, our follow-up period of three months was relatively short compared to the whole survival period of lung cancer patients. Second, the sample size of the chemotherapy combined with targeted therapy group was not large enough, and the cost data obtained would need confirmation in future studies. Third, participants came from only two localities, which may somewhat limit the representativeness of the study results for the whole of China.

Conclusions: The economic burden of lung cancer treatment mainly came from the cost of the drugs. Patients taking chemotherapy had significantly higher cost compared to patients using targeted therapy. The cost was generally higher for those with higher educational level, those with higher family income, and those living in an economically more developed city. Patients with NSCLC had higher cost compared to patients with SCLC.

PLAIN LANGUAGE SUMMARY

In China, lung cancer is the leading cause of cancer-related deaths and imparts a heavy economic burden. Most lung cancer patients are treated with chemotherapeutic and/of targeted agents because they are usually diagnosed at an advanced stage (IIIB or IV). The use of targeted therapy has achieved high response rates, longer overall survival, and longer progression-free survival compared with conventional chemotherapies. Adverse reactions with targeted therapeutic agents are usually mild compared with conventional chemotherapy. However, targeted drugs for lung cancer are usually more expensive than conventional chemotherapeutic drugs. It should be noted that the adverse effects and toxicities caused by chemotherapeutic drugs are generally more serious compared to targeted drugs; therefore, a number of measures are needed to prevent or relieve these reactions clinically. This can increase the financial burden of lung cancer treatment. Does these two treatments have a different cost? Our results showed that educational level, occupation, family income, classification of lung cancer, and the city of residence significantly influenced the total cost. Patients taking chemotherapy had significantly higher cost compared to patients using targeted therapy. This result suggests that targeted therapy for lung cancer is a better choice than chemotherapy.

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Introduction

Lung cancer is the major cause of cancer-related deaths globally, accounting for nearly one-fifth of all cancer deaths, which equates to approximately 1.8 million deaths worldwide annually [1]. In China, lung cancer is also the leading cause of cancer-related deaths, with 590,000 deaths for both genders in 2013 and 610,200 in 2015 [2–4]. Financially, lung cancer imparts a heavy economic burden to patients, their families, and society at an estimated cost of US$188 billion globally, which far outweighs the economic burden of all other cancers [5–7]. It also accounts for the largest number of healthy life years lost globally at 15.5% [5]. In China, the average economic burden was estimated at US$43,336 for each lung cancer patient [6], and the annual total cost of inpatients with lung cancer increased from US$2.51 billion in 2017 to US$3.01 billion, US$4.04 billion, and US$5.34 billion in 2020, 2025, and 2030, accounting for 0.121%, 0.131%, and 0.146% of China's gross domestic productivity(GDP), respectively [8].

Cost-of-illness (COI) studies are commonly used to evaluate the economic burden of lung cancer. COI studies generally include direct cost, indirect cost, and intangible cost associated with managing the specific disease. In general, direct costs measure the opportunity cost of resources spent on treating a particular disease, while indirect costs measure the value of resources lost as a result of a disease. Meanwhile, intangible costs are associated with factors (e.g. pain, anxiety or fatigue) resulting from a disease or disease treatment.

A variety of clinical treatments, including surgery, chemotherapy, radiotherapy, targeted therapy, and immunotherapy can be used either alone or in combination to maximize lung cancer treatment outcomes, prolong survival, and minimize treatment toxicity. Most lung cancer patients are treated with chemotherapeutic agents because they are usually diagnosed at an advanced stage (IIIB or IV) [9]. In recently years, targeted therapy has been widely used in lung cancer patients, after recent advances in identifying the gene mutation status. The use of targeted therapy has achieved high response rates, longer overall survival, and longer progression-free survival compared with conventional chemotherapies [10]. Adverse reactions with targeted therapeutic agents are usually mild compared with conventional chemotherapy [11–14]. However, targeted drugs for lung cancer are usually more expensive than conventional chemotherapeutic drugs. For example, gefitinib costs Chinese Yuan (CNY)7500/month compared to gemcitabine which costs CNY4500/month. It should be noted that the adverse effects and toxicities caused by chemotherapeutic drugs are generally more serious compared to targeted drugs; therefore, a number of measures are needed to prevent or relieve these reactions clinically. This can increase the financial burden of lung cancer treatment.

Multiple overseas studies on the economic burden caused by lung cancer treatment have been published [15–17]. Recently, more researchers are focusing on the study of the economic burden of lung cancer in China [6,18,19]. However, most studies to date have been limited to the cost of surgery or chemotherapy for lung cancer patients, and few have examined the cost of targeted lung cancer therapies. In addition, these studies have been limited to calculating the direct and/or indirect cost of drug therapy for lung cancer patients and have not examined the intangible cost of clinical treatment for lung cancer patients. Actually, intangible cost can be a substantial component of total cancer treatment cost as shown by a Swedish study that also estimated intangible cost in the management of breast cancer [20]. As targeted therapies in lung cancer often cause fewer side effects than conventional chemotherapies, thus affecting the patients' quality of life. Any studies on the total economic burden of lung cancer should include indirect and intangible costs, particularly in countries like China with an increasing prevalence of lung cancer [21].

Therefore, the aim of this study was to assess the economic burden of different drug therapies for lung cancer patients in China, including direct cost, indirect cost and intangible cost. Besides, factors influencing the cost of lung cancer was identified. Our findings could provide a more comprehensive view of the cost of lung cancer treatment to assist in health care policy decisions and planning as well as resource allocation. The results would also provide some interesting data for comparison for clinicians and policy makers in other jurisdictions.

Methods

Study population

Lung cancer patients from three tertiary hospitals in China (Guangdong Academy of Medical Sciences & Guangdong General Hospital in Guangdong Province, the First Affiliated Hospital of Bengbu Medical College in Anhui Province, and the Affiliated Hospital of Jinan College in Guangdong Province) were recruited. The study was approved by the human ethics committee at the University of Newcastle and the three study sites (Reference No: H-2018-0435) and the three study sites. The study was conducted from April 2018 to March 2020.

Sample size

The sample size of this study was calculated according to nQuery Advisor – a clinical trial design platform commonly used for calculating sample size and statistical power (nQuery Advanced 8.7, Statsols). In the sample size calculation, the test significance level was set as 0.05. This was a 2-sided test and the mean for each group represented the utility: $\pi 1$ for control group, $\pi 2$ for patient group, and the hazard ratio was obtained from a previous publication [22]. Total numbers of events required (E) were 42 or 56 when the power was set as 80% or 90%, respectively. Sample size was calculated by E and incidence rate: E/incidence rate (e.g. mortality). The incidence rate of 1-year overall survival of gefitinib was estimated as 35.7% [23]. Therefore, the minimum sample size required was 157 (as calculated from: E/Incidence rate= 56/0.357).

Study design

After obtaining informed consent from each participant, their socio-demographic information (i.e. age, gender, education level, marital status, occupation, family income, number of family member, person responsible for the treatment cost, classification of lung cancer, stage of lung cancer, type of therapy, and city of residence) was collected. COI information was attained from the questionnaire completed by participants and from patients' medical record. This study calculated the cost of lung cancer for patients within three months after diagnosis and treatment. This time point was chosen based on lung cancer patients typically undergoing 4–6 cycles of chemotherapy, which takes roughly three months [9]. Participants were also asked to complete the willingness-to-pay (WTP) questionnaire.

Cost of illness information

In this study, the economic burden of lung cancer was calculated by including direct cost, indirect cost, and intangible cost. Direct cost included the cost of hospitalization, outpatient visits, out-of-pocket drug purchases, transportation to and from the hospital, and costs associated with accommodation and meal expenses while lung cancer patients were seeking treatments in hospitals. Among these items, the cost of hospitalization, outpatient visits, and out-of-pocket drug purchases were considered direct medical costs and the others were considered direct non-medical costs. The direct cost was calculated by the sum of the direct medical cost and direct non-medical cost.

Indirect cost was defined as the number of productive days lost by patients and their family caregivers as a result of outpatient visits and hospitalization for lung cancer treatment. They were calculated by multiplying the minimum income of local residents (CNY70/day in Guangzhou and CNY42/day in Bengbu) by the number of days of hospitalization. In China, the mandatory retirement age is 60 years for men and 50 years for women. Therefore, this study did not consider the productivity loss of patients and their families beyond this age.

Intangible cost was measured by WTP questionnaire. The contingent valuations (CV) method is widely used for eliciting the WTP for non-market goods [24]. There are four major methods for CV studies: open ended questions, bidding game, payment card, and dichotomous choice approach (single or double bounded) [24]. In this research, we used the double-bounded dichotomous choice approach. The respondents' answers were divided into four groups: "yes, yes," "yes, no," "no, yes" and "no, no" in this method. In comparison to other methods, this approach has been proven to have the most significant statistical efficiency [25]. A large number of health studies have been conducted using the double-bounded dichotomous choice method over the last few decades, and its validity and reliability have been demonstrated [24].

Statistical analyses

Means, standard deviations (SD), and frequencies were used to describe patients' characteristics. Kruskal-Wallis test and post hoc analysis were conducted to compare different groups with non-normal distribution. Analysis of variance (ANOVA) was used to analyse the relative impact of age, gender, marital status, education level, occupation, family income, number of family member, person responsible for the treatment cost, classification of lung cancer, stage of lung cancer, type of therapy, and the patients' city of residence. All analyses were two-tailed and a P-value of <0.05 was considered statistically significant. All analyses were performed using the software SPSS version 26.0 (IBM Corporation, Armonk, NY, USA).

Results

Patient characteristics

Characteristics of the 275 participants are presented in Table 1. Most came from Bengbu of Anhui Province (82.9%) and the rest came from Guangzhou of Guangdong Province. The majority of participants were male (70.5%) and were married (88.4%). The median age was 62.0 years (SD 10.17), which ranged from 24 to 90 years. The highest proportion of the participants had 2 or 3 family members (45.8%).

There were 158 patients with a low level of education (primary school or lower), accounting for the highest proportion (57.5%) and only 8 patients (2.4%) received college/university diploma/degree education. More than half of the patients ($n = 191$) were peasants, which accounted for the highest proportion of employment category (69.5%). Peasants are people who own a small allotment of land in the countryside and engage in agricultural production as their main source of income in China.

There were 123 participants (43.1%) with a household income of less than CNY2000/month, and only 3.3% exceeded CNY20000/month. The majority of the participants (86.6%) had Urban Residents' Basic Health Insurance or Rural Residents' Basic Health Insurance – the two major health insurances in China. There were 30 patients (10.9%) from low-income families or destitute families, which means that almost all of their medical costs can be covered by the Chinese government.

Among the participants, 202 (73.5%) were diagnosed with non-small cell lung cancer (NSCLC) and most had stage IV lung cancer (70.9%). In terms of the type of therapy, the majority of patients received chemotherapy (70.9%), while 20.4% received targeted therapy and 8.7% received a combination of chemotherapy and targeted therapy.

Economic burden of lung cancer

In this study, participants had an average of 3.43 (SD 1.09) hospitalizations and 32.87 hospital days (SD 15.29) within three months after diagnosis and receiving treatment in hospitals. Total economic burden (total cost) of lung cancer was

Table 1. Characteristics of participants ($n = 275$).

Characteristic	Number (%)
Age, years	
Mean (SD)	61.98 (10.17)
Min, max	24, 90
Gender	
Male	194 (70.5)
Marital status	
Married	243 (88.4)
Cohabitating	1 (0.4)
Widowed	20 (7.3)
Divorced	5 (1.8)
Single, never married	6 (2.2)
Education level	
Primary school or lower	158 (57.5)
Did not graduate from high school	69 (25.1)
Graduated from high school	40 (14.5)
College/university diploma/degree	8 (2.9)
Occupation	
Worker	47 (17.1)
Peasant	191 (69.5)
Business person	20 (7.3)
Professional person (e.g. doctor, teacher)	11 (4.0)
Full-time homemaker, student	6 (2.2)
Family income (CNY/month)	
<2000	123 (44.7)
2000–5000	73 (26.5)
5001–10000	40 (14.5)
10001–20000	30 (10.5)
>20000	9 (3.3)
Number of family member	
1	12 (4.4)
2–3	126 (45.8)
4–5	66 (24.0)
6–7	49 (17.8)
>7	22 (8.0)
Person responsible for the treatment cost	
Self-pay	7 (2.5)
Urban residents' basic health insurance	58 (21.1)
Rural residents' basic health insurance	180 (65.5)
Low income/destitute families	30 (10.9)
Classification of lung cancer	
NSCLC	202 (73.5)
SCLC	73 (26.5)
Stage of lung cancer	
Stage III	80 (29.1)
Stage IV	195 (70.9)
Type of therapy	
Chemotherapy	195 (70.9)
Targeted therapy	56 (20.4)
Chemotherapy + targeted therapy	24 (8.7)
City of residence	
Bengbu, Anhui Province	228 (82.9)
Guangzhou, Guangdong Province	47 (17.1)

Note: Data are presented as n (%), min, max or mean ± standard deviation (range); Exchange rates was US$1 = CNY6.6996 on 05/03/2019.

estimated by aggregating direct cost, indirect cost, and intangible cost.

Direct cost

The direct cost in this study within 3 months after diagnosis was CNY63562.76, which comprised 89.02% of the total cost. Further breakdown revealed that the cost of drugs was CNY28,395.57 per patient (representing 24.61% of the total treatment cost), the cost of laboratory tests was CNY9,244.09 (12.95% of the total cost), and the cost of imaging tests was about CNY3,888.59 (5.45% of the total cost) (Table 2).

The direct non-medical cost included the cost of transportation, which was calculated on fuel usage and toll fee. The average direct non-medical cost was CNY1,248.51, which comprised 1.74% of the total cost. Transportation cost (CNY983.27) represented the highest share (78.8%) of direct non-medical cost and accounted for 1.38% of the total cost. In summary, the direct cost was CNY63562.76, comprising the highest share of the total cost at 89.02%.

Table 2. Cost (CNY) of lung cancer patients within 3 months after diagnosis ($n = 275$).

Type of cost	Mean	SD	Min	Max	%
Direct cost	63562.76	36403.68	10529.40	281899.75	89.02
Direct medical cost	62314.26	36167.88	9101.40	281459.75	87.27
Drug cost	28395.57	19903.76	2054.63	174387.64	39.77
Laboratory test cost	9244.09	5122.78	736.50	30304.05	12.95
Imaging test cost	3888.59	3536.43	70.00	22064.93	5.45
Direct non-medical cost	1248.51	1257.18	0	10116.20	1.75
Transportation cost	983.27	1195.84	0	10000	1.38
Indirect cost	3062.42	2296.39	0	10080.00	4.29
Patient	1552.31	2151.52	0	6300.00	2.17
Family caregiver	1521.40	869.60	0	9660.00	2.13
Intangible cost	4776.73	6965.78	0	80000.00	6.69
Total cost	71401.92	38369.82	12453.40	301559.75	100

Note: Data are presented as n (%), min, max or mean ± standard deviation (range); Exchange rates was US$1 = CNY6.6996 on 05/03/2019.

Indirect cost

Table 2 shows that indirect cost was CNY3,062.42. This was calculated based on the lost productivity of patients and family caregivers, which accounted for the smallest proportion of the total cost at 4.29%. Of the indirect cost, the cost of lost productivity was about the same for patients with family caregiver (CNY1,552.31 vs. CNY1,521.40).

In our study, the productivity loss of family caregiver was mainly caused by accompanying patients to and from hospital and during hospitalization. During the three-month follow-up period, the average length of hospitalization was 32.87 days and the number of hospitalization was 3.46. The total number of days in hospital was significantly longer for patients in Bengbu than in Guangzhou, but there was no significant difference in the number of hospitalization between the two locations.

Intangible cost

Intangible cost was performed by WTP valuation in this study. It was calculated as CNY4,776.73 for each patient and represented 6.69% of the total cost (Table 2).

Total cost

From the aforementioned results, the total cost to lung cancer patients in this study within 3 months after diagnosis and clinical treatment was CNY71,401.92, with direct cost comprising the most share (Table 3).

Factors influencing the total cost of lung cancer patients

Table 4 shows the impact of various factors (e.g. gender, age, educational level, marital status, occupation, family income, number of family member, cost payer, stage of lung cancer, type of lung cancer, and city of residence) on the

Table 3. Cost (CNY) of lung cancer within 3 months after diagnosis for patients with different therapies in China [mean (SD)].

	Chemotherapy ($n = 195$)	Targeted therapy ($n = 56$)	Chemotherapy + targeted therapy ($n = 24$)	P value
Direct medical cost	61529.39 (34422.55)	58400.58 (39792.05)	77823.32 (38849.06)	0.075
Direct non-medical cost	1359.57 (1260.23)	808.84 (1113.50)	1372.04 (1369.84)	0.013
Direct cost (total)	62888.96 (34561.59)	59209.42 (40386.36)	79195.36 (38817.05)	0.070
Indirect cost	3169.44 (2287.59)	2282.00 (1985.61)	4013.92 (2594.19)	**0.004**
Intangible cost	4402.05 (5408.86)	5546.43 (10865.06)	6025.00 (6687.97)	0.336
Total cost	70460.45 (35407.32)	67037.85 (44893.50)	89234.27 (41942.64)	0.049

Note: Data are presented as n (%), or mean ± standard deviation (range); Bold values are significant at a p value < 0.05; Exchange rates was US$1 = CNY6.6996 on 05/03/2019.

Table 4. Factors influencing total cost (CNY) of lung cancer patients in China 3 months after treatment ($n = 275$).

Total cost	n	Mean	SD	P value
Gender				
Male	201	69066.61	32557.88	0.118
Female	74	76995.15	49398.82	
Age				
<40	7	100177.77	44162.57	0.095
40–50	33	79199.42	50823.93	
50–60	74	72730.50	39096.34	
60–70	99	70457.78	35125.00	
70–80	59	62570.78	31876.06	
>80	3	90550.50	44085.65	
Education level				
Primary school or lower	158	67414.72	34774.93	**0.008**
Did not graduate from high school	69	71364.21	39165.00	
Graduated from high school	40	79429.53	43726.01	
College/university diploma/degree	8	110336.53	49923.65	
Marital status				
Married	243	70895.06	38125.65	0.677
Cohabitating	1	52495.17	–	
Widowed	20	71467.59	43064.33	
Divorced	5	72686.58	29626.90	
Single, never married	6	93791.56	43470.96	
Occupation				
Worker	47	75333.10	32526.33	**<0.001**
Peasant	191	66667.71	34215.46	
Business person	20	94976.70	49944.75	
Professional person (e.g. doctor, teacher)	11	65948.84	21340.21	
Full-time homemaker, student	6	122728.28	98071.98	
Family income (CNY/month)				
<2000	123	68607.54	33801.70	**0.041**
2000–50000	73	65881.23	32841.34	
5001–10000	40	81881.72	41597.63	
10001–20000	30	85563.63	56254.13	
>20000	9	60899.30	39626.80	
Number of family member				
1	12	67686.81	22487.66	0.054
2–3	126	65658.69	29228.59	
4–5	66	82790.73	43019.90	
6–7	49	73809.69	52026.91	
>7	22	66792.25	35980.57	
Person responsible for the treatment cost				
Self-pay	7	69467.04	32169.24	0.195
Urban residents' basic health insurance	58	78071.55	36757.11	
Rural residents' basic health insurance	180	67921.18	37613.01	
Low income/destitute families	30	79843.22	45489.90	
Classification of lung cancer				
NSCLC	202	77161.15	39933.88	**<0.001**
SCLC	73	55465.44	28288.40	
Stage of lung cancer				
Stage III	80	77679.29	44132.07	0.082
Stage IV	195	68826.59	35543.30	
City of residence				
Bengbu, Anhui Province	228	65816.23	34116.97	**<0.001**
Guangzhou, Guangdong Province	47	98498.50	46050.96	

Note: Data are presented as n (%), or mean ± standard deviation (range); Bold values are significant at a p value < 0.05; Exchange rates was US$1 = CNY6.6996 on 05/03/2019.

total cost of lung cancer patients. It can be seen that educational level, occupation, family income, classification of lung cancer, and the city of residence significantly influenced the total cost. From these analyses, education level played a significant role in the costs of lung cancer patients, affecting all costs including direct cost ($p = 0.033$), indirect cost ($p = 0.003$), and intangible cost ($p = 0.037$). The difference in direct cost was mainly caused by the difference in the cost of drugs ($p = 0.026$), imaging tests ($p = 0.042$), and medical materials ($p = 0.009$).

The impact of different occupations on total cost was mainly due to the direct medical cost ($p = 0.001$). The cost of full-time homemaker and student were significantly higher than other occupations except for business person, thereby showing a significant variability in the cost of drugs ($p = 0.001$), imaging tests ($p = 0.011$), and medical materials ($p = 0.002$).

The impact of family income on the burden of lung cancer patients mainly influenced indirect cost. Family income was significantly affected by lost productivity from both patients ($p = 0.002$) and family caregivers ($p = 0.005$). Similarly, the difference in total cost due to different classifications of lung cancer was caused by the difference in direct medical costs ($p < 0.001$), which were mainly drug cost ($p < 0.001$) and laboratory test cost ($p < 0.001$).

The result also showed that the city of residence affected both direct cost ($p < 0.001$) and indirect cost ($p < 0.001$). Direct cost showed significant difference across many components such as cost of hospital accommodation ($p = 0.016$), medical materials ($p = 0.006$), laboratory tests ($p = 0.028$), and drugs for treatment ($p < 0.001$). Patients from Bengbu stayed more days in hospital ($p < 0.001$) compared to those from Guangzhou. Regarding indirect cost, there were significant differences in both the cost of lost productivity of patients ($p < 0.001$) and family caregiver ($p = 0.005$).

Discussion

COI studies are often used to understand the economic burden of a disease and to assist in decisions about health resource allocation. To our knowledge, our study is the first to compare all direct cost, indirect cost and intangible cost as well as influencing factors resulting from treating lung cancer in different districts in China. In addition, we compared the cost of chemotherapy, targeted therapy, and chemotherapy plus targeted therapy for NSCLC and SCLC. At the same time, we also analysed the various influencing factors that affected the cost of lung cancer treatment.

Lung cancer confers a heavy economic burden to patients, their families, and society [5–7] – which was further confirmed by the data in this study. China's per capita disposable income in 2018 was CNY28,228/year according to

data published by China's National Bureau of Statistics. In our study, the total cost of lung cancer patients within 3 months after diagnosis and clinical treatment was CNY71,401.92 – which is approximately three times of the per capita disposable income. We showed that direct medical cost accounted for 98.03% of the direct cost of lung cancer patients. This is similar to the results of other studies in the US (85%) and Turkey (84.2%) [26,27]. Medication cost was the main driver of direct cost (39.8%) and this is consistent with studies conducted in Turkey (29%) (28), Italy (35%) [28], the Netherlands (67.53%) [29], and Korea (53%) [30]. However, intangible cost was not included in the total cost in these studies.

Contrasting results have been reported in some other studies. For example, Cicin et al. showed that indirect cost accounted for the major portion of the total cost at 68.6% [27], whereas our study demonstrated direct cost to be the major component of the total cost (89.02%). Interestingly, our results were consistent with other studies conducted in China by Zhu et al. (98.16% direct cost) [6] and Wang et al. (85% direct cost) [31]. This is likely due to our participants being mainly peasants and our use of the local minimum income level when calculating indirect cost. However, the Canadian study by Seung et al. obtained result consistent with ours and showed that direct medical cost accounted for 66.3% of the total cost [17].

In our current study, total cost and indirect cost were significantly different among patients receiving chemotherapy, targeted therapy, and chemotherapy plus targeted therapy. Patients receiving chemotherapy plus targeted therapy incurred the highest cost and targeted therapy the lowest cost. A partial explanation may be that although drugs for targeted therapy are generally more expensive than chemotherapeutic drugs, some chemotherapeutic drugs are also quite expensive (e.g. pemetrexed). Furthermore, we found that a proportion of the direct cost of patients using chemotherapy was for the treatment of adverse reactions. Combined with higher administrative cost (chemotherapy is always administered in a hospital setting compared to oral targeted drugs that do not require hospitalization), the use of chemotherapy ultimately results in higher total cost than targeted therapy [29]. At the same time, the vast majority of patients treated with oral targeted drugs do not need to be hospitalized, thus providing further savings in indirect cost for patients and caregivers. As such, the main challenge with these targeted therapies is the high initiation drug acquisition cost. Outcome-based contract could be a practical solution with targeted therapies, such as Gefitinib, to realise their greater benefits for more patients seeking better and more affordable treatment for cancer [32,33].

As expected, we found the cost of lung cancer treatment was influenced by many factors. Our results showed for the first time in China that patients with higher educational levels were associated with higher total cost, which includes direct cost, indirect cost, intangible cost, cost of drug, imaging test cost, medical materials cost, and the loss of patients' productivity. The higher level of education of the patient may reflect a higher income and the ability to use better medical treatments. Furthermore, higher the level of education was also associated with higher demand for better quality of life and the willingness to pay for better treatments. Possibly for the same reason, higher family income is likely associated with significantly higher indirect cost, including both cost of home caregivers and loss of productivity.

Our results also showed occupation as an influential factor in the economic burden of lung cancer patients. The cost for full-time family homemaker and student was significantly higher than other occupations. It was speculated that these patients were generally younger and had a stronger desire to survive, therefore were willing to spend more for their treatment. However, the number of cases in this group of patients was relatively small and would need confirmation in future studies.

Another observation was that the total cost of NSCLC was significantly higher than SCLC. This is mainly due to the use of new therapeutic treatments for NSCLC such as targeted drugs and third-generation chemotherapeutic agents [34,35]. Consistent with the findings of an US study by Davis et al. [26], we also found different location of residence can affect the cost of lung cancer management. Our findings showed that both direct cost and indirect cost were significantly higher for lung cancer patients in Guangzhou city compared to those in Bengbu city. This may be related to the local income level and consumption level. Guangzhou city is known to be one of the most developed cities in China and its economic development level is much higher than Bengbu city.

Furthermore, a study by Zhu et al. showed that the cost of lung cancer was related to gender, age, and insurance status [18]. These factors were not found to have an effect in our study. The differing results are possibly due to the difference in the baseline characteristics of the participants, whereby the patients studied by Zhu et al. came from the city and the majority of the participants in our study were peasants from the countryside – thus they were under different insurance cover.

Several limitations should be noted in our study. First, our follow-up period was three months, which was relatively short compared to the whole survival period of lung cancer patients. This study calculated the cost of lung cancer patients within three months after diagnosis and treatment because lung cancer patients typically undergo 4–6 cycles of chemotherapy, which takes roughly three months. The median survival time of stage IV patients with NSCLC was only 7 months according to the seventh edition of the tumor staging manual of American joint committee on cancer. The 5-year survival rate of patients with stage III SCLC in China was about 8% and stage IV was less than 3%. For patients with NSCLC in China, the above data were 15% and 5%, respectively [9]. Therefore, the cost as measured in this study would cover most cost of chemotherapy. However, a Canadian study that measured all costs of managing lung cancer patients over a five-year period found that cancer clinic visits and physician services accounted for a significant proportion of total cost [17]. This suggests that our study lacks cost data on lost productivity of patients and caregivers

during the recovery period, which may underestimate indirect costs. Second, the sample size of the group treated by chemotherapy combined with targeted therapy group was not large enough. Hence, the cost data obtained in this group would need confirmation in future studies. Third, participants came from only two local cities, which may somewhat limit the representativeness of the study results for the whole of China. It is well known that China is a very large country and the level of economic development and healthcare standard and delivery vary greatly among different regions. Additionally, some other potential confounders such as labour market status [36] as it was reported that the health status of those who end up unemployed was lower than those in continuous employment.

Conclusions

Our results showed that the economic burden of lung cancer undergoing drug treatment mainly came from direct cost, with the cost of the drugs being the main component. Patients taking chemotherapy had significantly higher cost compared to patients using targeted therapy. Factors that impacted the cost of lung cancer treatment included patients' education level, occupation, family income, classification of lung cancer, and the location of their residence. An important contribution of our study is the measurement of intangible cost through WTP evaluation. This component is seldom reported in COI studies, and our findings would provide some reference value for comparison in future studies and other jurisdictions. Overall, the results of this study would provide valuable background data for comparison when newer treatment options for lung cancer become available in China.

Transparency

Declaration of financial/other relationships

No potential conflict of interest was reported by the authors.

Author contributions

SCL, SH, KY contributed to the conception or design of the study. KY, WW, CY and XZ contributed to the acquisition of clinical data. SCL and KY contributed to the analysis of data. KY wrote the first draft of the manuscript, SCL and SH revised it critically.

Data availability statement

All data generated or analyzed during this study are included in this published article.

Previous presentations

This article was developed from a dissertation that is available here: https://nova.newcastle.edu.au/vital/access/manager/Index.

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