

WILLINGNESS TO PAY FOR LUNG CANCER TREATMENT: PATIENT VERSUS GENERAL PUBLIC VALUES

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Objectives: Lung cancer has been the most common cancer since 1985, accounting for 12–13 percent of cancer cases worldwide. Newer targeted therapies with potential increased survival benefits may not be affordable to patients. Many countries use arbitrary thresholds to determine whether a medical intervention is cost-effective. As such, many effective, albeit expensive, therapies are not being reimbursed. To understand the value placed on effective therapies, this study evaluates the patient and public willingness to pay (WTP) for a quality-adjusted life-year (QALY) for lung cancer treatments using Thailand as an example.

Methods: A total of 300 subjects responded to hypothetical lung cancer health states, described by three levels of severity and two levels of side effects, and provided their valuation of the level of quality of life and their WTP to improve from one state to another.

Results: The patients with the lowest income and general public were willing to pay more than twice the threshold for acceptability in Thailand (US Dollar 5,123/QALY [Thai Baht 160,000/QALY]). This increased significantly by wealth category. Patients' WTP was associated with quality of life, financial difficulties, health insurance, diarrhea, and wealth.

Conclusions: The current study highlights the value patients and general public place on effective lung cancer therapies.

Keywords: Lung cancer, Willingness-to-pay, Health economics, Cancer treatment, Pharmacoeconomics

Cancer continues to be one of the leading causes of health burden worldwide, with an estimated 12.66 million people being diagnosed and 7.56 million dying from cancer in 2008 (1). In 2008 alone, cancer was responsible for an estimated loss of 169.3 million healthy years (2). According to the World Health Organization, lung cancer has consistently been the most common cancer worldwide since 1985, accounting for 12–13 percent of all cancers.

Given the high cost of treatment for cancers and other diseases, health economics has become an increasingly important tool for governments and healthcare insurers to evaluate the value of treatment. Although health economics are being used for determining efficient allocation of limited funding, there has been particular emphasis on high cost treatments, such as oncology. Many countries evaluate the “value” of medical interventions using arbitrary thresholds to help in determining what would be considered a cost-effective therapy. As such,

many effective, albeit expensive, new therapies are not being reimbursed by insurers or governments.

The costs of these treatments are an important issue from the patient's perspective, because their ability to pay may ultimately determine their treatment course. The more expensive newer targeted therapies that may increase survival may not be affordable by the majority of patients. Universal Healthcare insurance is funded by the general public, so their perspectives on the inherent value of treatments and their willingness to fund such treatments is also of essential for policy makers to consider.

In health economic evaluations, the cost of interventions must be compared with health benefits to determine whether the value of these benefits exceed the costs incurred. The benefits of health interventions are frequently measured by means of quality-adjusted life-years, which account for the patient's quality of life (QOL) through their remaining life-years. Another approach is contingent valuation, or willingness to pay (WTP) method. Within the healthcare setting, the underlying premise is that a person's willingness to trade money for a defined improvement in health status is their assessment of the value of that intervention inclusive of treatments and procedures.

WTP for cancer treatment has not been greatly studied, specifically in the Asia region. Lang conducted a study to elicit

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willingness to copay for lung cancer medication in a Taiwanese population (3), but focused on lung cancer patients' perspective alone without including the public's view which many times are the payer of cancer treatment. We conducted a study to evaluate the WTP for lung cancer treatments using Thailand as an example to better understand patient and public's perceptions and values. Thailand is a middle income country with public health insurance and a health technology assessment agency; therefore, it is representative of many growing economies experiencing the same issues with healthcare funding. WTP threshold for Thailand in 2014 was announced at US Dollar (USD) 5,123 (Thai Baht [THB] 160,000) for 1 QALY (4) which came from 1.2 times of GNI (gross national income) per capita (September 1, 2012, exchange rate: USD 1: THB 31.23). This number was also benchmarked with the WTP results from societal value for Thailand threshold study which reported value at USD 4,995 (THB 156,000) (5). This quantification of the inherent value of treatments for patients is expected to add onto the understanding of lung cancer treatment in middle income countries.

METHODS

This was a cross-sectional, multi-center study. Before study initiation, this study received ethics approval from Maharaj Nakorn Chiang Mai Hospital and Naresuan University. The recommendations of the Declaration of Helsinki for biomedical research involving human patients were also followed.

Subjects

We prospectively enrolled 150 patients with lung cancer from the oncology unit at Maharaj Nakorn Chiang Mai Hospital. Subjects were 18 years of age or older, could read and understand Thai, had pathological diagnosed lung cancer, and had completed a planned treatment cycle of chemotherapy or radiotherapy.

In parallel, we prospectively enrolled 150 subjects from the general public in urban and suburban areas of Phitsanulok. A uniform distribution of general public respondents' age was sought. Respondents were required to be at least 18 years of age and had never been diagnosed with lung cancer. After attainment of written informed consent, subjects were enrolled into the study and interviewed by trained interviewers.

Health State Vignettes

Health state vignettes, or hypothetical health states, were developed for evaluation and rating by respondents. Common symptoms and side effects associated with advanced disease and treatment were identified through the literature and presented to two oncologists and three oncology nurses. Factors were selected based on being common within Thai patients and their ability to affect health state utility and QOL, based on their experience. Following the development of the vignettes, they were subsequently assessed with the clinical team for face

and content validity, who were encouraged to suggest changes to better reflect realistic health states. Following clinical review, the vignettes were pilot tested with twenty subjects from the general public using a visual analogue scale (VAS) to ascertain their level of comprehension and to assess language issues. Six different vignettes were developed to represent two primary factors; lung cancer status and side effect severity. Lung cancer status reflected three groups within a cancer population: (i) responders (complete or partial response) to treatment, (ii) stable disease (disease under control with cancer treatment), and (iii) progression of disease (cancer progressed; however, symptoms may be relieved by palliative medication). Side effects were grouped as moderate or severe. Moderate side effects were defined as nausea/vomiting, diarrhea, and tiredness. Severe side effects included significant symptoms such as anemia, febrile neutropenia, and severe mouth ulcers. The six vignettes were then paired for evaluation (Supplementary Figure 1).

Questionnaires

Questionnaires contained three sections: socio-demographic data, respondents' health status/utility, and a structured WTP interview.

Socio-Demographic and Clinical Data. Respondents provided data on age, educational attainment, employment and marital status, monthly household income, health insurance type, household assets, and other demographic information. Clinical data extracted from clinical charts included cancer stage, Eastern Cooperative Oncology Group (ECOG) performance status, and experience of side effects.

Health Status/Utility. All respondents completed the EuroQol 5-Dimension Questionnaire (EQ-5D) to assess their health state preference, or utility, upon study entry. The EQ-5D used the Thai EQ-5D index scoring of Tongsiri (6). Utilities range from 1, "perfect health" to 0, "death" to negative values representing health states the person considers worse than death. The general public respondents were asked to assess their current health state utility by means of a time-trade-off (TTO) exercise. This was not done with patients for ethical concerns.

Patients also completed the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core-30 and Lung Cancer-13 to assess their current QOL (7). All of the EORTC scales and single-item measures range in score from 0 to 100, with higher scores representing higher response level.

Next, each respondent was randomly provided two vignettes to rate. Respondents rated each vignette using the VAS and the general public respondents also rated each vignette with the TTO.

Willingness to Pay. Willingness to pay was assessed by evaluating the respondent's WTP to improve their health from the worse vignette of the pair to the better vignette. Willingness to pay

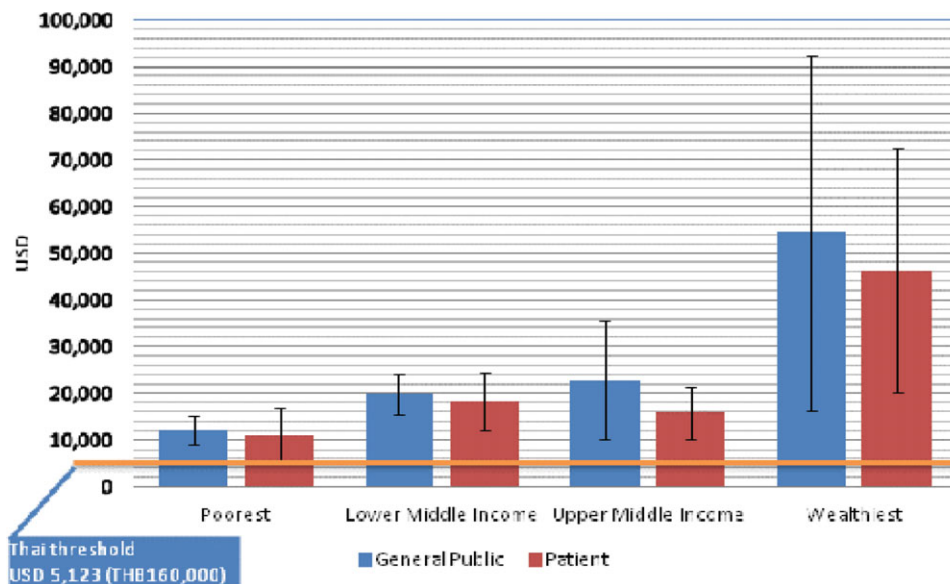


Figure 1. Willingness to pay/quality-adjusted life-year by wealth category and respondent.

amounts were elicited using a consumption-based approach, assuming that the treatment would not be covered by insurance or any government healthcare scheme, and, therefore, the full cost would be borne by the patient (8). Respondents were asked to consider their household monthly income when responding. The bidding game approach comprised of asking the respondent if he/she would be willing to pay the starting amount for a treatment that would restore them to the better health state. If he/she declined to pay this amount, he/she was then asked if they would be willing to pay a lower amount. Those who were willing to pay the initial amount were subsequently asked if they would be willing to pay a higher amount. The bidding continued until they reached their maximal WTP. This was then followed by an open ended question to elicit and confirm their maximal WTP. The starting bid was USD 960 (THB 30,000) which has been benchmarked just below 0.2 GDP per capita in Thailand for 2011.

Statistical Analysis

Descriptive statistics were conducted for all demographic and medical characteristics, health status and WTP variables. Due to income disparities, a wealth index was calculated using twelve household assets collected during the study, based on the continuous parameters reported by Srisuchart (9).

WTP, health state utility, and WTP/QALY estimates were compared between patients and the general population. WTP/QALY was estimated by dividing the WTP amount to move between health states by the differences in utility between the two vignettes. Differences in WTP estimates across populations were assessed with a generalized linear model. As WTP estimates are often skewed, the model was also conducted on the natural log of WTP to account for skewness. Respondents' ra-

tionale for their WTP level was also summarized to understand the drivers for their decision.

Several subgroup analyses were conducted to better understand the WTP and utility responses, including evaluation by age group (<60 years versus 60+ years), ECOG status (0 or 1 versus 2+) and insurance status. A multivariable regression model was used to evaluate the factors most important to patient WTP, including all the QOL scales, age group, gender, education level, occupation, wealth group, insurance type, marital status, family status, and ECOG performance status. Factors were retained/dropped at the 0.15 level.

RESULTS

A total of 300 respondents were recruited into this study. The general population respondents were wealthier, had higher education, and younger (Table 1). The majority of lung cancer patients had an ECOG Performance score of 0 or 1 despite being in mostly stage 3 and 4 (96.7 percent). Respondents' current health state utility was higher in the general population than patients (Table 1), with a larger difference seen on the EQ-5D.

Patients experienced decrements across all domains of their QOL, as measured by the EORTC QLQ-C30, with the greatest impact on their overall QOL being rated as 67.7 of 100. Among the symptom scales, fatigue demonstrated the greatest impact (38.8) followed by pain (29.9). In addition, financial difficulties was found to be burdensome (30.9). The bothersome lung cancer specific symptoms were alopecia (33.8), peripheral neuropathy (31.3), dyspnea (31.2), and coughing (30.4).

Respondent WTP/QALY, measured with improvements in the VAS, was consistently higher among the general public across all wealth groups (Figure 1). The range of WTP/QALY across wealth groups was USD 11,093 (THB 346,425) to USD

Table 1. Respondent Characteristics

	Patient (n = 150)	General population (n = 150)
Age; mean years (SD)	60.9 (10.40)	44.4 (14.36)
Male (%)	52%	48%
Wealth index category		
Poorest	56 (37.33%)	22 (14.67%)
Lower middle income	42 (28.00%)	30 (20.00%)
Upper middle income	28 (18.67%)	47 (31.33%)
Wealthiest	24 (16.00%)	51 (34.00%)
Education		
None	15 (10.00%)	5 (3.33%)
Elementary school	100 (66.67%)	44 (29.33%)
High school	19 (12.67%)	26 (17.33%)
Bachelor or higher	16 (10.67%)	75 (50.00%)
Occupation		
Agriculture	27 (18.00%)	9 (6.00%)
Worker, business, company employee	23 (15.33%)	70 (46.67%)
Government officer, Officer of state of Enterprise	19 (12.67%)	40 (26.67%)
Student	–	19 (12.67%)
Retired, Unemployed, Housewife, Other	81 (54.00%)	12 (8.00%)
ECOG Performance Score		
ECOG 0 or 1	129 (86.00%)	–
ECOG 2+	21 (14.00%)	–
Health Insurance		
UC & SS	101 (67.33%)	104 (69.33 %)
CSMBS & State of Enterprise	47 (31.33%)	35 (23.33 %)
Out of pocket & others	2 (1.33%)	11 (7.33 %)
Income (USD [THB])		
Household income; mean (SD)	USD 698 (1,237) [THB 21,786 (38,644)]	USD 2,245 (13,017) [THB 70,115 (406,509)]
Monthly income; mean (SD)	USD 200 (506) [THB 6,237 (15,793)]	USD 584 (1,381) [THB 18,236 (43,124)]
Current health state utility		
VAS (max = 100) ; mean (SD)	73.45 (15.59)	78.37 (12.55)
EQ-5D (max = 1.0) ; mean (SD)	0.67 (0.30)	0.78 (0.17)

UC, Universal coverage; SS, Social Security; CSMBS, Civil servant benefit scheme; ECOG, Eastern Cooperative Oncology Group; VAS, Visual Analog Scale; EQ-5D, EuroQol 5-Dimension questionnaire; SD, standard deviation.

54,432 (THB 1,699,911), and was found to increase with wealth. Using the natural log of WTP/QALY to account for the skewed data, wealth categories were significantly different ($p < .05$ for all comparisons). Each wealth category also reported a greater WTP/QALY than the current Thai threshold of USD 5,123 (THB 160,000), based on 1.2-times GNI (gross national income) per capita (10).

Whether or not patients and the general public displayed different preferences and WTP were explored (Supplementary Table 1). The utility differences between vignettes ranged between 0.03 and 0.18 for patients and 0.12 and 0.17 for the general public. Mean WTP/QALY ranged from USD -4,647 to USD 43,020 (THB -145,119 to THB 1,343,512) for patients and USD -2,291 to USD 66,944 (THB -71,562 to THB 2,090,686) for the general public. Negative values occurred when a

Table 2. Regression Parameter Estimates

Parameter	Model 1: WTP		Model 2: LN(WTP)	
	Estimate	p-value	Estimate	p-Value
Intercept	− 45174	0.6477	10.44064	<.0001
Global Health Status/QOL	− 1973.49104	0.0516	− 0.01552	0.0274
Financial Difficulties	− 1031.69168	0.0555	− 0.01225	0.0064
Dysphagia	2569.36198	0.0022	−	−
Pain in chest	− 1336.5093	0.0572	−	−
Education	36542	0.0722	−	−
Health insurance categories (collapsed)	151477	<.0001	0.93630	0.0008
ECOG (0 or 1 and 2+)	114728	0.0207	−	−
Social functioning	−	−	− 0.00985	0.0987
Diarrhea	−	−	− 0.01673	0.0393
Occupation	−	−	− 0.03976	0.1079
Wealth Index Category	−	−	0.52506	<.0001
R ²	0.2950		0.4273	
AdjR ²	0.2597		0.3974	

respondent rated the better health state worse (resulting in a negative utility). The differences in utility assigned to each vignette pair between the general public and patients ranged between 0.0103 and 0.1309.

Respondents were asked for their rationale for their selected WTP level. Patients based their payments on their expectations of recovering (70.7 percent) and to relieve symptoms (16.0 percent). The general public also based their payments on the relief of symptoms (32.0 percent; disregarding ability to pay which had 47.3 percent responding) followed by the desire to live longer (18.0 percent).

A multivariable stepwise regression was conducted to evaluate the patient parameters associated with their WTP. The model was able to explain 25.97 percent of the variance in the data after adjusting for the number of variables in the model, finding several significant associations. WTP was significantly associated with the patient's ECOG performance status, health insurance, and EORTC Dysphagia score (Table 2). Given the skewness of WTP data, the same model was run on the log transformed WTP. The log model performed better and was able to explain 39.74 percent of the variance after adjusting for the number of variables. The log transformed WTP was significantly associated with the patient's EORTC overall quality of life score, EORTC financial difficulties score, health insurance, EORTC diarrhea score and level of wealth. Therefore, as income and educational attainment increases, the patient is willing to pay more for a treatment that will improve their health status.

DISCUSSION

This study focused on the value society places on effective newer therapies, with a comparison of patients and the general public. In countries with universal healthcare coverage, where the public funds its own healthcare insurance, accounting for societal willingness to pay is important. In this study, both patients with advanced lung cancer and the general public were recruited to evaluate hypothetical health state vignettes in an effort to standardize the response stimulus. A uniform distribution of ages from the general public was recruited to ensure each age group was represented. However, as lung cancer usually affects older adults, the patients recruited into this study were older. The poorest patients and general public were willing to pay more than twice the threshold for acceptability (1.2-times GNI/capita; USD 5,123/QALY (THB 160,000/QALY). This increased significantly by wealth category up to approximately 10 times the threshold for the wealthiest respondents.

Patients had advanced lung cancer with decrements across all domains of their QOL. However, despite financial difficulties being reported as one of the most bothersome effects of lung cancer, patients consistently reported a WTP/QALY significantly greater than the existing cost-effectiveness threshold.

Several limitations should be considered in interpreting these results. First, QALY gains were assessed by means of VAS rather than a true utility measure. Although the VAS does not incorporate any trade nor risk, it would not be ethical to ask subjects currently undergoing treatment to trade life or risk death for a more effective treatment. Additionally, for older

patients with less education, the VAS is a convenient tool for them to understand compared with other methods of measuring utility. Second, patients were both older and had experience with the symptoms and severity levels of lung cancer. The experiences they have had may have influenced their utility assessment with respect to the severity of these health states, as noted by the general public usually stating the differences between vignettes being greater than that rated by patients. To evaluate if older subjects in general valued the health states differently, we examine the data by age group and respondent type. In both age categories, the general public found greater mean differences in vignettes as compared to patients. The median differences in the older population were the same, although the sample size for the general population was small ($n = 31$). (data not shown)

The use of rigid cost per QALY thresholds, for example at 1-times GDP in some countries or 1.2-times GNI/capita of USD 5,123/QALY (THB 160,000/QALY) in Thailand, makes it difficult for oncology therapies to be considered cost-effective for the government funding into universal coverage. Thus, it may inhibit patient access to effective treatment and eventually result in economic burden to patient or their family.

Both payers and patients have expressed concerns about the high costs of new, effective healthcare technologies. The access to targeted oncology therapies appears to be an issue in most developing countries in Asia but there are no formal arrangements from the payer side to improve access in those countries (11). Although public health insurance has been established in many settings in this region, incremental cost-effectiveness ratio (ICER) appears to be the key condition for reimbursement decisions. Lim et al. reported that there was significant association between reimbursement decision in the oncology drugs with a demonstrated lower ICER (12). As the cost-effectiveness threshold in most countries is not very flexible, risk sharing schemes between manufacturers and government have become an important solution to improve access to innovative anti-cancer drugs. Recently, South Korea arranged risk-sharing schemes for expensive targeted oncology drugs whose cost-effectiveness remains elusive (13). Nevertheless, such an arrangement is not widely established in most Asian countries. As a result, patients under universal coverage, including Thailand, may not be able to access effective lung cancer treatment and eventually pay out-of-pocket to receive such care. However, the results from our study found that both patients and general public respondents were willing to pay for effective treatment that would help them recover from the disease at a rate 2–10 times GDP. It may also reflect that there is still unmet need for an effective cancer drug in Thailand and other developing countries.

CONCLUSION

The current study highlights the value patients and general public place on effective therapies that help them recover from their disease. In the example of Thailand, it was demonstrated

that across all wealth levels, WTP for health improvements as measured by QALY was greater than the current threshold set by the government for cost-effective treatment; currently set at 1.2-times GNI for Thailand, or USD 5,123 (THB 160,000). Using arbitrary thresholds may lead to limited access to effective new therapies as less wealthy patients will not be able to afford these treatments, thereby foregoing potential beneficial improvements. A better understanding of society's WTP for treatment should be considered when deciding whether to include newer healthcare technologies into universal coverage and a more flexible approach to the cost per QALY threshold or using a weighted methodology for WTP or QALYs when assessing oncology therapy would allow for better access to effective therapies that subjects clearly state they want.

SUPPLEMENTARY MATERIAL

Supplementary Figure 1

Supplementary Table 1

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CONFLICTS OF INTEREST

ST, RS, NC, and UP received funding for their participation in the study design, recruitment of patients and general population, interpretation of analysis and manuscript development. BC was employed with Adelphi Values at the time of this study, a healthcare consulting firm who conducted this study. ST and JL were employees of Pfizer (Thailand) at the time of this study and were the sponsors. The sponsors did not influence the study design, vignette development or conduct of the study and analysis. No other conflicts exist.

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