Effect of Insurance Type on Stage at Presentation, Surgical Approach, Tumor Recurrence and Cancer-Specific Survival in Resectable Non-Small Lung Cancer Patients

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Purpose: The aim of this study was to identify the association between Thailand’s insurance types and stage at presentation, surgical approach, tumor recurrence and cancer-specific survival in resectable non-small cell lung cancer (NSCLC) patients in northern Thailand.

Patients and Methods: Medical records of patients with NSCLC who underwent pulmonary resection at Chiang Mai University Hospital from January 2007 through December 2015 were retrospectively reviewed. Patients were divided into two groups: patients with the Universal Coverage Scheme (UCS) or Social Security Scheme (SSS) and patients with the Civil Servant Medical Benefit Scheme (CSMBS) or private insurance (PI). Patient characteristics were assessed. The primary outcome was cancer-specific survival while the secondary outcome was tumor recurrence. Cox’s regression and matching propensity score analysis was used to analyze data.

Results: This study included 583 patients: 344 with UCS or SSS and 239 with CSMBS or PI. Patients with UCS or SSS were more likely to be active smokers, have a lower percent predicted FEV1, present with higher-stage tumors and worse differentiated tumors, present with tumor necrosis, and undergo an open surgical approach than those with CSMBS or PI. At multivariable analysis of all patients cohort, there were no significant differences in terms of early stage at presentation (adjusted odds ratio (ORadj) = 0.94, 95% confidence interval (CI) = 0.65–1.37), undergoing lobectomy (ORadj = 0.59, 95% CI = 0.24–1.46), and recurrent-free survival (adjusted hazard ratio (HRadj) = 1.20, 95% CI = 0.88–1.65) between groups (UCS/SSS versus CSMBS/PI). However, patients with UCS or SSS had shorter cancer-specific survival (HRadj = 1.61, 95% CI = 1.22–2.15). The results from the propensity score matched patient cohort were not different from those analyses on the full patient cohort.

Conclusion: Thai insurance types have an effect on cancer-specific survival. The Thai government should recognize the importance of these differences, and further multi-center studies with a larger sample size are warranted to confirm this result.

Keywords: Universal Coverage Scheme, Social Security Scheme, Civil Servant Medical Benefit Scheme, cancer death, coverage, pulmonary resection

Introduction

Lung cancer remains an important public health problem and is the leading cause of cancer-related death worldwide. In 2012, 1.6 million patients died of lung cancer1 and lung cancer was the second most common cause of cancer death in Thailand.2

In the same year, the National Cancer Institute of Thailand reported that lung cancer...
was the most common cancer diagnosed in male Thai patients (16.6%) and the fourth most common cancer diagnosed in female Thai patients (6.6%). If left untreated, the 5-year survival of lung cancer patients is only 6%. However, research has identified a significant difference in recurrence and survival rate between resectable stages (IA-IIIA) of Non-small cell lung cancer (NSCLC) after complete oncologic resection, and in the five-year survival of stage I (70%) and stage III (38%) resectable NSCLC patients.4

According to current guidelines, pre-treatment investigation of NSCLC requires advanced procedures such as an endobronchial ultrasound (EBUS), esophageal ultrasound and positron emission tomography-computed tomography (PET-CT), as well as high-cost drugs, targeted drugs and immunotherapy, which can increase the overall cost of treatment. Despite these recommendations, some of these procedures and drugs are not included in certain health-care insurance programs and are not eligible for reimbursement.

Currently, three public health insurance programs are available for the Thai population, including the Civil Servant Medical Benefit Scheme (CSMBS; 9%), the Social Security Scheme (SSS; 16%), and the Universal Coverage Scheme (UCS; 75%).5 Private health insurance (PI) is another health insurance program that everyone can apply for depending on the plan they choose and the cost they can afford. Overall, the benefits package of CSMBS is slightly higher than those of UCS and SSS (Table 1). For example, CSMBS covers high-cost drugs, targeted drugs and immunotherapy as well as high-cost procedures (EBUS, PET-CT), while UCS and SSS do not. Private health insurance coverage varies by company and depends on patient age and the type of plan they choose (local, international, basic coverage, etc.).

Previous studies have demonstrated that insurance type is significantly associated with surgical outcomes, stage of disease at diagnosis, tumor recurrence and survival,6–9 while some studies have not reported these differences.10,11 Although the insurance types available in each country are different, the association between higher coverage and better outcomes has been consistently observed.12 To our knowledge, this is the first study to report on the impact of insurance type on NSCLC outcomes in the Thai population. The aim of this study was to determine the effect of insurance type on stage at presentation, surgical procedure, tumor recurrence and cancer-specific survival in resectable NSCLC.

### Table 1 Characteristics of Thailand's Health Insurance Programs

| Insurance Types | Characteristics |
|-----------------|-----------------|
| **A. CSMBS (9%)** | Government employees plus dependents including parents, spouses and up to two children aged <20 years |
| **B. SSS (16%)** | Private sector employees, excluding dependents |
| **B. UCS (75%)** | The rest of population not covered by SSS and CSMBS |

**Note:** Data from Health Insurance System Research Office (HISRO) (2012), Nonthaburi, Thailand.4

**Abbreviations:** CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; DRG, diagnosis-related groups.

### Patients and Methods

#### Patient Selection, Treatments and Outcomes

Adult patients (age ≥18 years) with NSCLC who underwent pulmonary resection (either curative or palliative...
Surgical Stage at presentation

Results of the MI analysis were then estimated according to the 8th edition of the TNM classification for lung cancer issued by the International Association for the Study of Lung Cancer (IASLC).² Stage at presentation was categorized into 3 groups: localized (stage I), regional (stage II or III), and distant (stage IV), as previously described by Walker et al.⁸

After discharge, follow-up was performed at 2 weeks and at 1–2 months with a chest x-ray and physical examination, and then every 3 months for the first 2 years, and then every 6 months with a CT scan. When tumor recurrence was suspected, diagnostic procedures were performed to confirm the diagnosis either with cytology or diagnostic radiology. Patients received chemotherapy and/or radiotherapy according to their performance status and tumor status. The regimens of chemotherapy included cisplatin, carboplatin, vinorelbine, vinorelbine, gemcitabine, docetaxel, pemetrexed and targeted therapy (erlotinib, gefitinib, crizotinib) depending on molecular testing and insurance coverage. Overall survival and recurrence-free survival were calculated from the date of surgery to the most recent follow-up contact or to the date of death, and from the date of first tumor diagnosis to either local recurrence or distant metastasis, respectively.

This study was reviewed and approved by the Institutional Review Board of Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand with Study Code: SUR-2561-05572/Research ID: 5572, and approval ID 238/2018. Patient consent to review their medical records was not required by the Institutional Review Board of the Faculty of Medicine, Chiang Mai University. This study was considered exempt as de-identified data for all analyses. Individual-level data was not used, and all data was kept confidential and in compliance with the Declaration of Helsinki.

Statistical Analysis

Categorical variables were presented as frequencies and proportions; continuous variables were presented as mean ± standard deviation (SD) or median ± interquartile range (IQR). Fisher exact tests were used for comparing categorical data, and unpaired Student’s t-test or Wilcoxon rank-sum tests were performed for continuous variables. Multiple imputations (MI) with a multivariate normal equation were performed for any variables with at least 10% missing values.¹⁴ Results of the MI analysis were then compared to the results from a complete-case analysis. Cox proportional hazards models were used to examine the impact of insurance type on recurrence and cancer-specific survival. Logistic regressions were performed to assess associations of insurance type with tumor stage at presentation, surgical procedure (lobectomy versus sublobar resection), and surgical approaches (VATS versus open thoracotomy). Any prognostic factors with a p value <0.1 in

Patients underwent wedge resection, segmentectomy, lobectomy and pneumonectomy. The indication for sublobar resection (wedge resection or segmentectomy) was made according to the American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.¹³ Surgical approaches included open thoracotomy and video-assisted thoracoscopic surgery (VATS). Systematic mediastinal lymph node dissection (SLND) or sampling (SLNS) was performed in all cases. Lymph node ratio was calculated as the proportion of positive dissected lymph node divided by the total amount of dissected lymph nodes. Tumor staging was reviewed according to the 8th edition of the TNM classification for lung cancer issued by the International Association for the Study of Lung Cancer (IASLC).² Stage at presentation was categorized into 3 groups; localized (stage I), regional (stage II or III), and distant (stage IV), as previously described by Walker et al.⁸

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the univariable analyses, in addition to other potential clinical confounders associated with stage at presentation, surgical procedures or approaches, tumor recurrence, and cancer-specific survival, were adjusted for in the multivariable Cox proportional hazards model. Multicollinearity of independent factors was tested before performing multivariable analysis. One-to-one propensity score matching was also performed. Logistic regression was used to calculate a propensity score, which evaluates confounding by indication and/or baseline covariates between two insurance groups. The variables included in the propensity score matching model were age, gender, body mass index (BMI), smoking status, comorbid disease, stage of disease, intratumoral lymphatic invasion, intratumoral vessel invasion, visceral pleural invasion, and tumor necrosis. A standardized mean difference (SMD) between groups for all covariates is shown in Table 2. The primary and secondary outcomes for propensity score matched patient cohort were analyzed by multivariable Cox’s regression analysis and logistic regression analysis as appropriate. The statistical analysis was completed in STATA (Release 15.1, 2018; StataCorp, CS, TX, USA), with p < 0.05 indicating a statistically significant difference.

**Results**

**Patient Characteristics**

There were 583 patients diagnosed with resectable NSCLC included in this study; 334 with UCS or SSS and 239 with CSMBS or PI. Patients with UCS or SSS were younger, more likely to be active smokers, had lower BMI, lower percent predicted forced expiratory volume in 1 minute (FEV1), more advanced stage of disease, poorer cell differentiation, were less likely to have hypertension and dyslipidemia, and were more likely to have tumor necrosis (Table 2). There were no statistically significant differences in gender, number of pack-years of smoking, having chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), history of malignancy, preoperative ECG, ejection fraction, cell types, intratumoral lymphatic and vascular invasion, and having visceral pleural invasion between the two groups. After matching, 224 patients were included in both groups, and almost all covariates were balanced between two groups (Table 2). A standardized mean difference (SMD) of almost all covariates between the two groups after matching was less than 0.2.

**Stage at Diagnosis**

More patients with CSMB or PI presented with localized disease than did those with UCS or SSS (Figure 1). After adjusting for age, gender, smoking status, and clinical presentation, the adjusted odds ratio of localized disease (early stage) at presentation for UCS or SSS group compared to CSMBS or PI group were 0.94 (95% CI = 0.65–1.37, \( p = 0.762 \)) for the full patient cohort and 0.95 (95% CI = 0.63–1.42, \( p = 0.796 \)) for the propensity score matched patient cohort.

**Surgical Procedures**

The percentage of patients undergoing lobectomy between those with UCS or SSS and CSMBS or PI were 82.1% and 73.5%, respectively (\( p = 0.041 \)) (Table 3). However, after adjusting by age, gender, percent predicted FEV1, comorbid diseases, tumor diameter, and stage of disease, this difference was not statistically significant. The adjusted odds ratio of lobectomy for UCS or SSS group compared to CSMBS or PI group was 0.59 (95% CI = 0.24–1.46, \( p = 0.251 \)) for the full patient cohort and 0.50 (95% CI = 0.19–1.32, \( p = 0.160 \)) for the propensity score matched patient cohort (Table 4). There was no significant difference in terms of the type of mediastinal lymph node evaluation between the two groups.

**Surgical Approaches**

The percentage of patients undergoing VATS approach between those with UCS or SSS and CSMBS or PI were 22.3% and 14.6%, respectively (\( p = 0.020 \)) (Table 3). However, after adjusting by age, gender, percent predicted FEV1, comorbid diseases, tumor diameter, and stage of disease, this difference was not statistically significant. The adjusted odds ratio of VATS approach for UCS or SSS group compared to CSMBS or PI group was 0.99 (95% CI = 0.36–2.72, \( p = 0.989 \)) for the full patient cohort and 0.82 (95% CI = 0.26–2.55, \( p = 0.729 \)) for the propensity score matched patient cohort (Table 4).

**Perioperative Outcomes**

There were no significant differences in post-operative complications such as pneumonia, re-intubation, arrhythmias, atelectasis, acute renal failure with hemodialysis and air leakage between the two insurance groups. Length of hospital stay was comparable between the two groups, and the median time was 7 days (IQR=5–10 days). Operative time was longer in patients with UCS or SSS (149.8±54.3 minutes versus 138.8±50.1 minutes, respectively; \( p = 0.015 \)). Median
Table 2: Patient Characteristics Before and After Propensity Score Matching According to Insurance Coverage

| Variable                          | Before Propensity Score Matching (Full Patient Cohort) | After Propensity Score Matching (Propensity Score Matched Patient Cohort) | p-value | SMD | p-value | SMD |
|-----------------------------------|----------------------------------------------------------|--------------------------------------------------------------------------|---------|-----|---------|-----|
|                                   | UCS or SSS N=144                                         | CSMBS or PI N=239                                                        |         |     |         |     |
| Age (years), Mean ± SD            | 61.10±10.70                                              | 64.28±9.80                                                               | <0.001  | 0.310 | 63.9±10.0 | 62.9±10.6 | 0.316 | 0.098 |
| Gender, n (%)                     |                                                          |                                                                          |         |     |         |     |
| Female                            | 140 (40.7)                                               | 99 (41.4)                                                                | 0.864   | 0.015 | 95 (42.4) | 86 (38.4) | 0.441 | 0.082 |
| Male                              | 204 (59.3)                                               | 140 (58.6)                                                               |         |     |         |     |
| BMI (kg/m²), Mean ± SD            | 20.7±3.6                                                 | 22.3±3.9                                                                | <0.001  | 0.420 | 22.0±3.8 | 21.4±3.5 | 0.099 | 0.167 |
| Smoking status, n (%)             |                                                          |                                                                          |         |     |         |     |
| Non-smokers                       | 60 (17.4)                                                | 74 (31.0)                                                                |         |     | 49 (21.9) | 68 (30.4) |         |       |
| Active smoker or ex-smokers       | 248 (72.1)                                               | 145 (60.7)                                                               |         |     | 145 (64.7) | 139 (62.1) |         |       |
| Passive smoking                   | 11 (3.2)                                                 | 3 (1.3)                                                                  |         |     | 10 (4.5)  | 3 (1.3)   |         |       |
| Unknown                           | 25 (7.3)                                                 | 17 (7.1)                                                                 |         |     | 20 (8.9)  | 14 (6.2)  |         |       |
| Pack-year, Median (IQR)           | 25 (12–41.3)                                             | 24 (10.5–40)                                                            | 0.559   | −0.189 | 24 (10.8–40) | 30 (15–50) | 0.103 | −0.317 |
| Comorbid Disease, n (%)           |                                                          |                                                                          |         |     |         |     |
| COPD                              | 48 (14.0)                                                | 39 (16.3)                                                                | 0.479   | 0.066 | 38 (17)   | 32 (14.3) | 0.516 | 0.074 |
| Diabetic mellitus                 | 41 (11.9)                                                | 27 (11.3)                                                                | 0.896   | 0.019 | 26 (11.6) | 33 (14.7) | 0.402 | 0.093 |
| Hypertension                      | 115 (33.4)                                               | 111 (46.4)                                                               | 0.002   | 0.268 | 98 (43.8) | 92 (41.1) | 0.633 | 0.054 |
| Dyslipidemia                      | 50 (14.5)                                                | 63 (26.4)                                                                | 0.001   | 0.296 | 53 (23.7) | 41 (18.3) | 0.202 | 0.132 |
| History of other malignancy       | 16 (4.7)                                                 | 20 (8.4)                                                                 | 0.080   | 0.151 | 16 (7.1)  | 14 (6.3)  | 0.850 | 0.036 |
| Pulmonary Function Test           |                                                          |                                                                          |         |     |         |     |
| Percent predicted FEV1, Mean ± SD | 77.0±21.9                                                | 84.2±22.9                                                                | 0.036   | 0.322 | 84.6±23.0 | 79.8±22.2 | 0.212 | 0.212 |
| Preoperative PaO₂, Mean ± SD      | 127.9±52.9                                               | 120.3±49.2                                                               | 0.609   | −0.149 | 120.1±49.7 | 123.6±52.1 | 0.832 | −0.069 |
| Preoperative PaCO₂, Mean ± SD     | 49.4±29.9                                                | 39.9±12.8                                                                | 0.198   | −0.409 | 41.6±12.2 | 47.5±16.2 | 0.217 | −0.412 |
| Preoperative ECG, n (%)           |                                                          |                                                                          | 0.106   | 0.234 |          |       |
| Normal                            | 233 (67.7)                                               | 176 (73.6)                                                               |         |     | 166 (74.10) | 151 (67.4) | 0.146 | 0.247 |
| ST-T segment abnormality          | 28 (8.1)                                                 | 17 (7.1)                                                                 |         |     | 16 (7.1)  | 19 (8.5)  |         |       |
| Bundle branch block               | 11 (3.2)                                                 | 13 (5.4)                                                                 |         |     | 13 (5.8)  | 8 (3.6)   |         |       |
| Arrhythmias                       | 8 (2.3)                                                  | 6 (2.5)                                                                  |         |     | 6 (2.7)   | 6 (2.7)   |         |       |
| Non-specific abnormality          | 64 (18.6)                                                | 27 (11.3)                                                                |         |     | 23 (10.3) | 40 (17.9) |         |       |
| Ejection fraction (%), Mean ± SD   | 64.4±10.0                                                | 67.6±7.4                                                                 | 0.159   | 0.367 | 67.6±7.5  | 64.4±10.2 | 0.199 | 0.364 |
| Cell types, n (%)                 |                                                          |                                                                          | 0.272   | 0.251 |          |       |
| Adenocarcinoma                    | 215 (62.5)                                               | 167 (60.4)                                                               |         |     | 156 (69.6) | 151 (67.4) | 0.952 | 0.053 |
| Squamous cell carcinoma           | 87 (25.3)                                                | 45 (18.8)                                                                |         |     | 43 (19.2) | 45 (20.1) |         |       |
| Large cell carcinoma              | 10 (2.9)                                                 | 6 (2.5)                                                                  |         |     | 5 (2.2)   | 6 (2.7)   |         |       |
| Other*                            | 32 (9.3)                                                 | 21 (8.8)                                                                 |         |     | 20 (8.9)  | 22 (9.8)  |         |       |
| Tumor staging (8th IASLC edition) |                                                          |                                                                          | 0.016   | 0.381 | 0.016    | 0.381    | 0.642 | 0.252 |
| IA1                               | 6 (1.7)                                                  | 8 (3.4)                                                                  |         |     | 8 (3.6)   | 5 (2.2)   |         |       |
| IA2                               | 18 (5.2)                                                 | 29 (12.1)                                                                |         |     | 23 (10.3) | 13 (5.8)  |         |       |
| IA3                               | 41 (11.9)                                                | 26 (10.9)                                                                |         |     | 24 (10.7) | 25 (11.2) |         |       |
| IB                                | 46 (13.4)                                                | 28 (11.7)                                                                |         |     | 28 (12.5) | 33 (14.7) |         |       |
| IIA                               | 25 (7.3)                                                 | 11 (4.6)                                                                 |         |     | 11 (4.9)  | 16 (7.1)  |         |       |
| IIB                               | 67 (19.5)                                                | 43 (18.0)                                                                |         |     | 41 (18.3) | 48 (21.4) |         |       |
| IIIA                              | 92 (26.7)                                                | 61 (25.5)                                                                |         |     | 59 (26.3) | 55 (24.6) |         |       |
| IIIB                              | 32 (9.3)                                                 | 11 (4.6)                                                                 |         |     | 11 (4.9)  | 15 (6.7)  |         |       |
| IIC                               | 1 (0.3)                                                  | 2 (0.8)                                                                  |         |     | 2 (0.9)   | 1 (0.5)   |         |       |
| IVA                               | 16 (4.7)                                                 | 20 (8.4)                                                                 |         |     | 17 (7.6)  | 13 (5.8)  |         |       |

(Continued)
Table 2 (Continued).

| Variable                                                      | Before Propensity Score Matching (Full Patient Cohort) | After Propensity Score Matching (Propensity Score Matched Patient Cohort) |
|---------------------------------------------------------------|--------------------------------------------------------|------------------------------------------------------------------------|
|                                                               | UCS or SSS N=344                                       | CSMBS or PI N=239                                                      |
|                                                               | p-value SMD                                           | p-value SMD                                                           |
| Cell differentiation, n (%)                                   |                                                       |                                                                       |
| Well differentiation                                          | 88 (29.8)                                             | 73 (41.2)                                                             |
| Moderately differentiation                                   | 128 (43.4)                                            | 69 (39.0)                                                             |
| Poorly differentiation                                        | 70 (23.7)                                             | 30 (17.0)                                                             |
| Undifferentiation                                             | 9 (3.1)                                               | 5 (2.8)                                                               |
| Intratumoral lymphatic invasion, n (%)                       | 249 (72.4)                                            | 164 (73.2)                                                            |
| Intratumoral vascular invasion, n (%)                        | 132 (38.4)                                            | 89 (39.7)                                                             |
| Visceral pleural invasion, n (%)                             | 64 (18.6)                                             | 40 (17.9)                                                             |
| Tumor necrosis, n (%)                                         | 119 (34.6)                                            | 47 (21.0)                                                             |
| Propensity score, Mean±SD                                    | 0.65±0.16                                             | 0.57±0.12                                                             |

| Notes: Other cell types included mucoepidermoid carcinoma, adenoid cystic carcinoma, carcinoid tumor, adenocarcinoma, and neuroendocrine tumor; Abbreviations: SD, standard deviation; BMI, body mass index; IQR, interquartile range; FEV1, forced expiratory volume in 1 second; PaCO2, partial pressure of carbon dioxide (mmHg); PaO2, partial pressure of oxygen (mmHg); ECG, electrocardiogram; ST-T, the interval between ventricular depolarization and repolarization from electrocardiogram; CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; PI, private health insurance; COPD, chronic obstructive pulmonary disease; SMD, standard mean difference.

Tumor Recurrence and Cancer-Specific Survival

In the univariable analysis for tumor recurrence, 36 patients (6.2%) diagnosed with stage IVA who were treated with palliative resection due to tumor complications such as obstructive pneumonitis or hemoptysis were excluded for analysis (Table 2). Although tumor recurrence rate was similar between both groups, time to recurrence was significantly shorter in the UCS or SSS group (16.4 months [IQR=6.3–45.7 months] versus 21.7 months [IQR=8.6–50.2 months], respectively; p = 0.013) for the full patient cohort, but not different for the propensity score matched patient cohort (Table 3). Cancer-specific mortality rate was higher in the UCS or SSS group for both patient cohorts (63.9% - 219 patients versus 50.6% - 121 patients; p = 0.002 for the full patient cohort and 62.1%-139 patients versus 50.9%-114 patients; p=0.018 for the propensity score matched patient cohort) (Table 3). In multivariable analyses using multivariable Cox’s regression analysis adjusted by age, gender, comorbid disease, smoking status, cell differentiation, cell type, visceral pleural invasion, intratumoral blood vessel invasion, intratumoral lymphatic invasion, perineural invasion, tumor necrosis, tumor stage, surgical approaches, surgical procedures, type of lymph node dissection, tumor recurrence, and chemotherapy (including targeted therapy or immunotherapy), insurance type was not associated with tumor recurrence; the adjusted hazard ratio for tumor recurrence of UCS or SSS group compared to CSMBS or PI group was 1.20 (95% CI=0.88–1.65, p=0.241) for the full patient cohort and 1.11 (95% CI=0.78–1.59, p=0.554) for the propensity score matched patient cohort. However, insurance type was associated with cancer-specific survival; the adjusted hazard ratio for cancer-specific mortality of UCS

Figure 1 Proportion of patients presenting with localized, regional, or distant diseases according to insurance status (p = 0.034). Stage I disease was considered localized, stage II to III disease was considered regional, and stage IV disease was considered distant.

Abbreviations: CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; PI, private insurance.
Table 3 Treatment and Post-Operative Outcomes Between Two Patient Cohort According to Insurance Coverage.

| Variable                                           | Full Patient Cohort | Propensity Score Matched Patient Cohort |
|----------------------------------------------------|---------------------|----------------------------------------|
|                                                    | UCS or SSS N=344    | CSMB or PI N=239                       | UCS or SSS N=224 | CSMB or PI N=224 |
| Surgical Procedure, n (%)                          | 44 (12.9)           | 52 (21.9)                              | 46 (20.6)       | 34 (15.2)        |
| Wedge resection                                     | 10 (2.9)            | 6 (2.5)                                | 6 (2.7)         | 5 (2.2)          |
| Segmentectomy                                       | 280 (82.1)          | 175 (73.5)                             | 168 (74.9)      | 181 (80.8)       |
| Lobectomy                                           | 7 (2.1)             | 5 (2.1)                                | 4 (1.8)         | 4 (1.8)          |
| Surgical Approach, n (%)                           | 292 (85.4)          | 185 (77.7)                             | 179 (79.8)      | 189 (84.3)       |
| Mediastinal lymph node evaluation, n (%)            | 50 (14.6)           | 53 (22.3)                              | 45 (20.2)       | 35 (15.7)        |
| Lymp node sampling                                  | 48 (16.1)           | 31 (15.5)                              | 33 (14.7)       | 34 (15.2)        |
| Systematic lymph node dissection                    | 251 (83.9)          | 169 (84.5)                             | 29 (13.0)       | 30 (13.4)        |
| Lymp node ratio, Median (IQR)                       | 0.2 (0.1–0.4)       | 0.2 (0.1–0.4)                          | 162 (72.3)      | 160 (71.4)       |
| Chemotherapy, n (%)                                 | 165 (48.0)          | 121 (50.6)                             | 113 (50.5)      | 109 (48.7)       |
| No chemotherapy                                     | 147 (42.7)          | 105 (43.9)                             | 87 (39.0)       | 87 (40.2)        |
| Neoadjuvant therapy or induction therapy            | 32 (9.3)            | 13 (5.4)                               | 98 (43.7)       | 95 (42.4)        |
| Operative time (minutes), Mean ± SD                 | 149.8±54.3          | 138.8±50.1                             | 13 (5.8)        | 20 (8.9)         |
| Estimated blood loss (mL), Median (IQR)             | 200 (100–300)       | 100 (100–200)                          | 144±53.9       | 139±50.0         |
| ICU stay (hours), Median (IQR)                      | 36.2 (17.8–69.3)    | 37.2 (18.4–68.2)                       | 200 (100–300)   | 100 (100–200)    |
| Immediate extubation after surgery, n (%)           | 283 (82.3)          | 215 (90.0)                             | 0 (0–17.2)      | 0 (0–0)          |
| In-hospital mortality, n (%)                        | 8 (2.3)             | 3 (1.3)                                | 188 (83.9)      | 201 (89.7)       |
| Postoperative complications, n (%)                  | 13 (3.8)            | 6 (2.5)                                | 10 (4.5)        | 5 (2.2)          |
| Pneumonia                                           | 11 (3.2)            | 4 (1.7)                                | 8 (3.6)         | 3 (1.3)          |
| Re-intubation                                       | 7 (2.0)             | 7 (2.9)                                | 4 (1.8)         | 7 (3.1)          |
| Arrhythmias                                         | 10 (2.9)            | 5 (2.1)                                | 7 (3.1)         | 5 (2.2)          |
| Air leakage                                         | 32 (9.3)            | 14 (5.9)                               | 17 (7.6)        | 14 (6.2)         |
| Acute renal failure with hemodialysis needed        | 2 (0.6)             | 2 (0.8)                                | 2 (0.9)         | 2 (0.9)          |
| Acute pulmonary embolism                           | 1 (0.3)             | 0                                      | 1.000           | 0                |
| Chylothorax                                         | 3 (0.9)             | 3 (1.3)                                | 0               | 0                |
| Other minor complications                          | 31 (9.0)            | 15 (6.3)                               | 8 (3.9)         | 13 (5.8)         |
| Composite major complications                      | 43 (12.5)           | 25 (10.5)                              | 25 (11.2)       | 23 (10.3)        |
| Length of hospital stay (days), Median (IQR)        | 5 (7–10)            | 5 (7–10)                               | 7 (5–9)         | 7 (5–10)         |
| Tumor recurrence, n (%)                             | 145 (44.2)          | 100 (45.7)                             | 93 (44.1)       | 93 (44.9)        |
| Recurrence time (months), Median (IQR)              | 16.4 (6.3–45.7)     | 21.7 (8.6–50.2)                        | 11.5 (5.3–21.2) | 14.2 (6.4–22.9)  |
| Cancer-specific mortality, n (%)                    | 219 (63.9)          | 121 (50.6)                             | 139 (62.1)      | 145 (60.9)       |
| Follow-up time (months), median (IQR)               | 26.5 (10.0–55.9)    | 34.6 (17.2–61.3)                       | 30.0 (11.1–56.3)| 34.5 (16.5–61.0) |

Notes: a Targeted therapy and immunotherapy were not used as induction therapy or adjuvant setting. b Excluded stage IV disease.

Abbreviations: ICU, intensive care unit; IQR, interquartile range; CSMB, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; PI, private health insurance

or SSS group compared to CSMB or PI group was 1.61 (95% CI = 1.22–2.15, p=0.001) for the full patient cohort and 1.48 (95% CI=1.08–2.03, p=0.027 for the propensity score matched patient cohort) (Table 4). Kaplan–Meier curves illustrating the recurrent-free survival and cancer-specific survival between insurance types for the full patient cohort are shown in Figure 2 and Kaplan–Meier curves illustrating the cancer-specific survival between insurance types for propensity score matched patient cohort is shown in Supplement Figure A.
In summary, the results from the propensity score matched patient cohort analysis were not different from the full patient cohort analysis.

Discussion
This study evaluated the association between health insurance, stage at presentation, surgical treatment and outcomes among a group of NSCLC patients in northern Thailand. Currently, UCS or SSS coverage is provided for 75% of the Thai population while CSMBS is provided for government officials and provides coverage after retirement. Additionally, PI is provided for all patients who are willing to pay for non-government health insurance.

This analysis revealed differences between the two groups on the full patient cohort analysis; UCS or SSS patients were younger and had lower mean BMI than those with CSMBS or PI. However, BMI values in both groups were within the “normal” range. CSMBS or PI patients had more comorbid diseases such as COPD, hypertension and dyslipidemia. This may relate to the older age of CSMBS or PI patients (64.28±9.80 years vs 61.10±10.70 years, p<0.001). There were a greater number of active- and former smoking patients in the UCS or SSS group than in the CSMBS or PI group, and this may explain why percent predicted FEV1 in the UCS or SSS group was lower compared to the CSMBS or PI group.

Consistent with previous research, the most common cancer type observed here was adenocarcinoma (65.52%), followed by squamous cell carcinoma (22.64%). Variability in stage at presentation, tumor aggressiveness, mean recurrence time and overall survival among insurance types has been documented among lung cancer patients.

Table 4 Differences in Outcomes and Surgical Procedure/Approach for UCS or SSI Vs CSMBS or PI Between Two Patient Cohort

| Outcome Variable               | Full Patient Cohort | Propensity Score Matched Patient Cohort |
|-------------------------------|---------------------|----------------------------------------|
|                               | Estimate            | 95% CI       | p-value    | Estimate            | 95% CI       | p-value    |
| Tumor recurrence              | 1.20a               | 0.88–1.65    | 0.241      | 1.11a               | 0.78–1.59    | 0.554      |
| Cancer-specific mortality     | 1.6a                | 1.22–2.15    | 0.001      | 1.48a               | 1.08–2.03    | 0.027      |
| Early stage at presentation   | 0.94b               | 0.65–1.37    | 0.762      | 0.95b               | 0.63–1.42    | 0.796      |
| Lobectomy procedure           | 0.59c               | 0.24–1.46    | 0.251      | 0.50c               | 0.19–1.32    | 0.160      |
| VATS approach                 | 0.99c               | 0.36–2.72    | 0.989      | 0.82c               | 0.26–2.55    | 0.729      |

Notes: aAdjusted hazard ratio analyzed by Cox’s proportion hazard model adjusted by age, gender, comorbid disease, smoking status, cell differentiation, cell type, visceral pleural invasion, intratumoral blood vessel invasion, intratumoral lymphatic invasion, perineural invasion, tumor necrosis, tumor stage, surgical approach, surgical procedures, type of lymph node dissection, tumor recurrence, and chemotherapy (included targeted therapy or immunotherapy). Patients with stage IV were excluded in multivariable analysis model for tumor recurrence.

bAdjusted odds ratio analyzed by logistic regression analysis adjusting for age, gender, smoking status and clinical presentations (hemoptysis, chronic cough, significant weight loss, poor appetite, chest pain, and dyspnea on exertion).

cAdjusted odds ratio analyzed by logistic regression analysis adjusting for age, gender, % predicted FEV1, comorbid diseases, smoking status, tumor diameter, and stage of disease.

Abbreviations: CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; PI, private health insurance; CI, confidence interval; VATS, video-assisted thoracoscopic surgery.

Figure 2 Kaplan–Meier curves illustrating (A) recurrent-free survival (p = 0.538) (excluded stage IV disease) and (B) cancer-specific survival (p=0.001) between insurance types (CSMBS, Civil Servant Medical Benefit Scheme; SSS, Social Security Scheme; UCS, Universal Coverage Scheme; PI, private insurance).
patients. Here, we observed that the proportion of patients who presented with localized disease was higher in the CSMBS or PI group in univariable analyses, but this difference was not significant after adjusting for other confounding factors. Previous studies have demonstrated that both patients with insurance that provides less medical coverage and patients with no insurance were associated with more advanced disease at presentation and poorer long-term outcomes. These studies also reported that insurance status was associated with a shorter cancer-specific survival and an average time to recurrence. A systematic review of 23 articles stated that American patients with Medicaid or no insurance had a higher stage-specific and overall mortality rate. There were several reasons that survival might be impacted by insurance status. First, lung cancer survival depends on disease stage and treatment type; for example, chemotherapy regimen and targeted therapy are associated with a higher cancer-specific survival. Second, in terms of access to medical service, most UCS or SSS patients reside in rural areas in northern Thailand. In general, lower education, lower socioeconomic status, and transit burden of this population result in reduced access to medical care, delays in proper management of their cancer, and loss to follow-up care. Previous studies from other countries have found that insurance type effects accessing medical care. Third, insurance type can be a limitation to diagnostic workup and treatment; high-cost invasive and non-invasive procedures such as EBUS, PET-CT scans, some chemotherapy regimen (high-cost drug), targeted therapy and immunotherapy are not covered by UCS or SSS. Therefore, patients with UCS or SSS have to pay out of pocket for these services and cannot receive reimbursement. In reality, most of these patients cannot make these payments. Instead, patients with UCS or SSS are treated with low-cost chemotherapy regimens instead of targeted therapy or high-cost drug regimens. Even though targeted and immunotherapy data were not available in this dataset and not included in the multivariable analysis model, these therapies were only used in patients with CSMBS/PI depended on molecular testing. This study found that Thai insurance affected on cancer-specific survival. Patients with UCS or SSS were more likely to have shorter survival than those with CSMBS or PI, both on the full patient cohort analysis and on the propensity score matched patient cohort analysis.

This study found that insurance type was not associated with surgical procedures or surgical approaches in multivariable models. The proportion of patients who underwent a VATS approach was lower in the UCS or SSS group. Before 2009, the stapler devices used were not covered by UCS or SSS but covered by CSMBS or PI with a co-payment. After 2009, these devices were covered by all insurance types. We also found that the operative time and intra-operative blood loss were greater in UCS or SSS group, which may be a consequence in the operative approach. The proportion of open thoracotomy was higher in UCS or SSS group. VATS approach can minimize operative time and intra-operative blood loss as shown in many previous studies.

This study has limitations including its retrospective nature and the possibility of selection bias. All patients were fit for surgery, so patients treated with chemotherapy or radiotherapy alone were not included. Although the UCS, SSS, and CSMBS coverage were developed by the Thai government and available to use in all areas of Thailand, Chang Mai University Hospital is a single-tertiary care center that may not represent the heterogeneity in lung cancer treatment found in other institutes. Similarly, the patient population of northern Thailand patients may be different from other areas. Therefore, results of this study may not be generalizable to all other areas in Thailand. Other causes of death such as trauma were not included in the dataset; therefore, we cannot analyze overall survival. Because the median follow-up time is only 30 months, this study presented only the short-term results of NSCLC patients who received primary surgery as their first treatment. Further studies with longer follow-up time are warranted to confirm the results.

Finally, there are some unknown prognostic factors such as socioeconomic, lifestyle, occupational or other patient characteristics, as well as treatments including targeted therapy, immunotherapy and radiotherapy that are associated with tumor recurrence or cancer-specific survival that were not included in the multivariable analysis model, as they could not be incorporated from this data.

Conclusions
Thai NSCLC patients with UCS or SSS coverage were more likely to have shorter cancer-specific survival than those with CSMBS or PI. Differences in coverage provided by each insurance type, especially in terms of pre-operative investigation, chemotherapy regimens, targeted therapy and immunotherapy may be associated with cancer-specific survival of these patients. The Thai government should recognize the importance of these differences.
and further multi-center studies with a larger sample size are warranted to confirm this result.

Disclosure

The authors report no conflicts of interest in this work. An abstract of this paper was presented at the 19th World Conference on Lung Cancer (WCLC) as a poster presentation. The poster's abstract was published in 'Poster Abstracts' in the Journal of Thoracic Oncology (https://www.jto.org/article/S1556-0864(18)32428-6/fulltext).

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