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To cite this article: Shweta Shah, Christopher M. Blanchette, Joseph C. Coyle, Marc Kowalkowski, Susan T. Arthur & Reuben Howden (2018) Healthcare utilization and costs associated with COPD among SEER-Medicare beneficiaries with NSCLC, Journal of Medical Economics, 21:9, 861-868, DOI: [10.1080/13696998.2018.1484370](https://doi.org/10.1080/13696998.2018.1484370)

To link to this article: <https://doi.org/10.1080/13696998.2018.1484370>



Published online: 02 Jul 2018.



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ORIGINAL RESEARCH



Healthcare utilization and costs associated with COPD among SEER-Medicare beneficiaries with NSCLC

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ABSTRACT

Aim: To estimate the healthcare utilization and costs in elderly lung cancer patients with and without pre-existing chronic obstructive pulmonary disease (COPD).

Methods: Using Surveillance, Epidemiology and End Results (SEER)-Medicare data, this study identified patients with lung cancer between 2006–2010, at least 66 years of age, and continuously enrolled in Medicare Parts A and B in the 12 months prior to cancer diagnosis. The diagnosis of pre-existing COPD in lung cancer patients was identified using ICD-9 codes. Healthcare utilization and costs were categorized as inpatient hospitalizations, skilled nursing facility (SNF) use, physician office visits, ER visits, and outpatient encounters for every stage of lung cancer. The adjusted analysis was performed using a generalized linear model for healthcare costs and a negative binomial model for healthcare utilization.

Results: Inpatient admissions in the COPD group increased for each stage of non-small cell lung cancer (NSCLC) compared to the non-COPD group per 100 person-months (Stage I: 14.67 vs 9.49 stays, $p < .0001$; Stage II: 14.13 vs 10.78 stays, $p < .0001$; Stage III: 28.31 vs 18.91 stays, $p < .0001$; Stage IV: 49.5 vs 31.24 stays, $p < .0001$). A similar trend was observed for outpatient visits, with an increase in utilization among the COPD group (Stage I: 1136.04 vs 796 visits, $p < .0001$; Stage II: 1325.12 vs 983.26 visits, $p < .0001$; Stage III: 2025.47 vs 1656.64 visits, $p < .0001$; Stage IV: 2825.73 vs 2422.26 visits, $p < .0001$). Total direct costs per person-month in patients with pre-existing COPD were significantly higher than the non-COPD group across all services (\$54,799.16 vs \$41,862.91). Outpatient visits represented the largest cost category across all services in both groups, with higher costs among the COPD group (\$41,203 vs \$31,140.08).

Conclusion: Healthcare utilization and costs among lung cancer patients with pre-existing COPD was ~2–3-times higher than the non-COPD group.

ARTICLE HISTORY

Received 24 February 2018
Revised 3 May 2018
Accepted 19 May 2018

KEYWORDS

Lung neoplasms; COPD; economic burden; claims; health resource utilization

JEL CLASSIFICATION CODES

C55; I19

Introduction

Lung cancer and chronic obstructive pulmonary disease (COPD) are among the leading causes of morbidity and mortality worldwide. According to the Global Burden of Disease Study 2013, lung cancer and COPD are among the leading causes of years of life lost globally, especially in developed and high-income countries¹. Lung cancer accounts for 27% of all cancer deaths, with more deaths from lung cancer than from colon, prostate, and breast cancer together^{2,3}. It is estimated that, by 2030, it will continue to be the leading cause of cancer death, due to the diagnosis being made at an advanced stage⁴. About two out of three people diagnosed with lung cancer are 65 or older, while less than 2% are younger than 45. Five-year survival rates are low compared to other common cancers, at 16.3%. About 80% of lung cancers are non-small cell lung cancers (NSCLC)¹. COPD is the third leading cause of death in the US, after cancer and heart disease. In 2010, COPD accounted for 134,676 deaths in the US⁵. In 2011, an estimated 11.8 million adults had been

diagnosed with COPD⁶. This number could be even higher, because COPD is often an under-diagnosed disease⁷.

Studies have suggested that the risk for lung cancer increased in proportion to the degree of airway obstruction⁸. Reduction of forced expiratory volume (FEV1) to ~90% of predicted value significantly increased the risk for lung cancer by 1.30-fold in men and by 2.64-fold in women⁹. In addition to the irreversible airflow obstruction that characterizes the disease, COPD has also been found to be an important risk factor for lung cancer, independent of age and cigarette smoking¹⁰. They may share the same genetic predispositions and environmental risk factors. Genetic studies have identified that the deficiency of alpha1 antitrypsin (AATD), caused by mutations in the SERPINA1 gene, may lead to protein degradation and increased inflammation, leading to an increased risk of COPD¹¹. A common feature among lung cancer patients with COPD is an increased resistance to pro-apoptotic stimuli¹². This might increase the population of lung epithelial cells from which tumors could arise¹³. Moreover, chronic inflammation among patients with COPD

may activate the proteins that promote lung cancer growth and deactivate the proteins required for DNA repair¹⁴. In COPD cohort studies, the incidence ratios for lung cancer ranged from 4.2–16.7 per 1,000 person-years^{15,16}. Furthermore, Powell *et al.*¹⁷ reported that 23% of lung cancer cases had a prior diagnosis of COPD, compared with only 6% of controls.

Lung cancer and COPD take a heavy toll on the US economy, and pose significant health and economic burdens on society. According to the National Institutes of Health, the total direct medical cost of cancer in the US was \$124.6 billion in 2010. It is estimated that ~\$12.6 billion are spent in the country on lung cancer treatment alone. Lost productivity due to early death from cancer lead to an additional \$134.8 billion in 2005, of which \$36.1 billion was caused by lung cancer¹⁸. Previous estimates of COPD related medical costs in the US have indicated high costs incurred by patients, with \$37.2 billion in 2004 and \$42.6 billion in 2007¹⁹. According to the National Heart Lung and Blood Institute, the national projected annual cost for COPD in 2010 was \$49.9 billion. This includes \$29.5 billion in direct healthcare expenditures, \$8.0 billion in indirect morbidity costs, and \$12.4 billion in indirect mortality costs²⁰. Ford *et al.*²¹ estimated the total national medical costs attributable to COPD at \$32.1 billion dollars annually. Absenteeism costs were \$3.9 billion, accounting for a total burden of \$36 billion in COPD-attributable costs. Moreover, 18% of the medical costs were paid for by private insurance, 51% by Medicare, and 25% by Medicaid. The study also projected a rise in medical costs from \$32.1 billion in 2010 to \$49 billion by 2020²¹.

As the median age of diagnosis of lung cancer patients is high (71 years), the cost is largely incurred by the US Medicare system. Despite this burden and its expected future trend, limited data exists comparing healthcare resource use and costs in elderly patients with NSCLC with pre-existing COPD. Most existing cost studies focus on NSCLC alone^{22–24} or on all lung cancers combined^{25–27}. Existing cost studies have primarily focused on estimations of chemotherapy use and costs^{28–30}, with little information presented regarding broader health resource utilization and costs for other service categories for every stage of lung cancer. Moreover, most cost-related studies fail to account for censoring, and present overall mean values which may not be a true reflection of costs.

To address these information needs, the current study employs retrospective analysis of the linked Surveillance, Epidemiology and End Results (SEER)-Medicare database to examine healthcare utilization and costs in elderly NSCLC patients with and without pre-existing COPD for every stage of lung cancer

Methods

Data source

The SEER-Medicare database consists of the linkage of two large population-based sources of data that provide detailed information about Medicare beneficiaries with cancer. The

SEER program collects information on incident cases of cancer, including patient demographics, date of diagnosis, and data about the cancer (e.g. histology, stage, and grade). The SEER program covers ~28% of the US population³¹.

Medicare is the primary health insurer for 97% of the US population 65 years and older. Medicare claims data account for all services provided by Medicare, from a person's program eligibility to their death. The claims data are divided into multiple files, of which three were used for data acquisition. The Medicare Provider Analysis and Review (MEDPAR) file includes all Part A short stay, long stay, and skilled nursing facility bills. The Carrier Claims (or National Claims History (NCH)) file includes all Part B non-institutional provider claims (e.g. physicians, nurse practitioners' ambulance providers, etc.). The Outpatient file includes claims from institutional outpatient providers (e.g. hospital outpatient departments, rural health clinics, etc.)³².

The linkage of the SEER data with the Medicare data entails matching incident cancer cases reported in the SEER data with a master file of Medicare enrollment³³. The linkage of these two data sources results in a unique population-based source of information that can be used for an array of epidemiological and health services research. One of the advantages of using this data over commercial claims databases is that this data contains complete claims histories of its population (≥ 65 years), as compared to incomplete medical histories of those ≥ 65 -year-old patients in a commercial database that are not enrolled in a Medicare risk plan³³.

Study population

Patients were eligible for inclusion in the study if diagnosed with first primary lung cancer between January 1, 2005 and December 31, 2010, at least 66 years of age, and continuously enrolled in Medicare Parts A and B in the 12 months prior to diagnosis. Patients were excluded if their date of death was recorded prior to or the same month as diagnosis, if they were diagnosed by autopsy, death certificate, or in an unknown month, and if they were enrolled in a health maintenance organization (HMO) at any time during the 12 months prior to diagnosis (because complete claims data were unavailable for these patients).

Study variables

NSCLC diagnosis was based on the International Classification of Disease for Oncology (3rd edition, ICD-O-3) histology codes in the SEER data. Tumor stage was classified according to the sixth edition of the American Joint Commission on Cancer manual for patients diagnosed between 2005 and 2010. The diagnosis of pre-existing COPD in lung cancer patients was identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes (491 [chronic bronchitis], 492 [emphysema], 496 [chronic airway obstruction, not elsewhere classified]) before cancer diagnosis date through the Medicare claim files. These codes were chosen, based on support from previous literature, as successful identifiers of COPD³⁴.

A Charlson Comorbidity Index (CCI) score was calculated from the Medicare claim files to obtain a measure of patients' overall comorbidity burden. The CCI included 15 non-cancer categories of comorbidities, as defined by ICD-9-CM diagnosis codes, with associated weights corresponding to the severity of the condition of interest³⁵. Because the objective of the CCI score was to evaluate underlying comorbidity burden independent of cancer and COPD, ICD-9-CM diagnosis codes for cancer and COPD were excluded from the CCI calculation for this study.

Statistical analysis

Descriptive statistics (i.e. counts, frequencies, averages) were used to summarize demographic and clinical characteristics by pre-existing COPD status (COPD vs Non-COPD). Differences between groups were assessed using Chi-square test for categorical and *t*-tests for continuous variables. We assessed healthcare utilization and costs for the COPD and non-COPD group stratified by stage of NSCLC. Resource utilization and costs were examined by the major service sector in which they occurred, and represent the claims for services incurred within the associated service location (i.e. inpatient, skilled nursing facility, emergency department, outpatient hospital, and office visits). Person-month analyses were used for reporting healthcare utilization and costs.

Person-months were summed across the study period (60 months) and for all patients who were alive and diagnosed with NSCLC and used as the denominator. The numerator was the total utilization of a service in the same period. The result of the numerator to denominator ratio was the utilization of a service per 100 person-months (PM). Costs were calculated as cost of a service per person-month as well as cumulative cost of all services per person-month by stage of NSCLC. Cost data represented the actual paid (i.e. reimbursed by Medicare) amounts for health services. The adjusted analyses were performed controlling for demographic (age, sex, race) and clinical (tumor grade and comorbidity score) factors using a negative binomial model for count of healthcare events and a generalized linear, gamma distribution, log-linked model for costs. *T*-tests were used to determine differences between groups.

Statistical significance was set at $p \leq .05$. SAS 9.4 (SAS Institute Inc, Cary, NC) was used for all data analyses. The conduct of this study was approved by the National Cancer Institute and the Institutional Review Board at the University of North Carolina at Charlotte.

Results

We identified 66,963 lung cancer patients. Of these, 22,497 (33.60%) had COPD before lung cancer diagnosis. Patients differed statistically ($p < .001$) across all demographic characteristics between pre-existing COPD and non-COPD lung cancer patients (Table 1). The mean age of pre-existing COPD patients (75 years) was similar to non-COPD patients. The majority of patients in the COPD (51.68%) and non-COPD

(51.08%) group were males. Caucasians accounted for the greatest proportion of lung cancer patients in both groups (90.74% and 86.46%, respectively), followed by African-Americans (6.71% and 8.30%). The most common comorbid conditions among COPD and non-COPD groups were congestive heart failure (11.50% and 8.61%), diabetes mellitus (10.47% and 11.71%), peripheral vascular disease (6.19% and 4.53%), and cerebrovascular disease (4.45% and 5.09%). The comorbidity status of both groups, measured by the CCI, was statistically significant. Approximately 96% of patients accounted for a CCI score of less than 3 in the COPD and non-COPD groups.

Nearly all COPD and non-COPD patients (~99%) had invasive tumors. Approximately 22% of COPD patients had poorly differentiated tumor grade, compared with 21% of patients in the non-COPD group. Among COPD patients, 36.34% had stage IV lung cancer, compared with 44.25% in the non-COPD group.

Patients with pre-existing COPD had significantly higher healthcare utilization and subsequent costs across all stages of NSCLC (Tables 2 and 3). After adjusting for covariates, utilization and costs rose appreciably in the COPD group (Table 3). Among hospitalizations, inpatient admissions in the COPD group increased for each stage of NSCLC compared to the non-COPD group (Stage I: 14.67 admissions per 100 PM vs 9.49 admissions per 100 PM, $p < .0001$; Stage II: 14.13 admissions per 100 PM vs 10.78 admissions per 100 PM, $p < .0001$; Stage III: 28.31 admissions per 100 PM vs 18.91 admissions per 100 PM, $p < .0001$; Stage IV: 49.5 admissions per 100 PM vs 31.24 per 100 PM, $p < .0001$). Among physician office visits, the utilization per 100 person-months increased more than 3-times in the COPD group among stages III and IV NSCLC. Overall, there were marked differences between the COPD and non-COPD groups, with higher utilization among COPD patients (Stage I: 927.36 visits per 100 PM vs 230.75 visits per 100 PM, $p < .0001$; Stage II: 988.95 visits per 100 PM vs 241.05 visits per 100 PM, $p < .0001$; Stage III: 1453.49 visits per 100 PM vs 387.28 visits per 100 PM, $p < .0001$; Stage IV: 2,311.94 visits per 100 PM vs 681.84 visits per 100 PM, $p < .0001$). A similar trend was observed for outpatient visits, with an increase in utilization among the COPD group (Stage I: 1,136.04 visits per 100 PM vs 796 visits per 100 PM, $p < .0001$; Stage II: 1,325.12 visits per 100 PM vs 983.26 visits per 100 PM, $p < .0001$; Stage III: 2,025.47 visits per 100 PM vs 1,656.64 visits per 100 PM, $p < .0001$; Stage IV: 2,825.73 visits per 100 PM vs 2,422.26 visits per 100 PM, $p < .0001$). For stage I and II NSCLC, the use of ER services were almost 2-times higher in the COPD group, in contrast with the non-COPD group (Stage I: 20.41 visits per 100 PM vs 9.78 visits per 100 PM, $p < .0001$; Stage II: 24.25 visits per 100 PM vs 13.59 visits per 100 PM, $p < .0001$; Stage III: 56.58 visits per 100 PM vs 33.26 visits per 100 PM, $p < .0001$).

Total direct costs in patients with pre-existing COPD were significantly higher than the non-COPD group across all services (\$54,799.16 per PM vs \$41,862.91 per PM). The subsequent hospitalization costs across all stages were also significantly higher in the COPD group compared to the non-COPD group (\$8,629.77 per PM vs \$5,879 per PM, $p < .0001$).

Table 1. Characteristics of NSCLC patients with and without COPD.

| Covariate | COPD (%) | No COPD (%) | Total (%) | p value |
|------------------------------|----------------|----------------|----------------|---------|
| No of patients | 22,497 (33.60) | 44,466 (66.40) | 66,963 | |
| Sex | | | | .1463 |
| Males | 11,626 (51.68) | 22,715 (51.08) | 34,341 (51.28) | |
| Females | 10,871 (48.32) | 21,751 (48.92) | 32,622 (48.72) | |
| Race | | | | <.0001 |
| White | 20,414 (90.74) | 38,447 (86.46) | 58,861 (87.90) | |
| Black | 1,510 (6.71) | 3,692 (8.30) | 5,202 (7.77) | |
| American Indian | 65 (0.29) | 126 (0.28) | 191 (0.29) | |
| Asian | 472 (2.09) | 2,128 (4.79) | 2,600 (3.88) | |
| Other | 36 (0.16) | 73 (0.16) | 109 (0.16) | |
| Age Mean (SD) | 74.73 (6.39) | 75.42 (6.94) | | <.0001 |
| Age Group (years) | | | | <.0001 |
| 66–69 | 4,887 (21.72) | 9,461 (21.28) | 14,348 (21.43) | |
| 70–73 | 4,731 (21.03) | 8,429 (18.96) | 13,160 (19.65) | |
| 74–79 | 6,586 (29.28) | 12,389 (27.86) | 18,975 (28.34) | |
| 80+ | 6,293 (27.97) | 14,187 (31.91) | 20,480 (30.58) | |
| Comorbidities | | | | |
| Myocardial Infarction | 802 (3.56) | 1,878 (4.22) | 2,680 (4.0) | <.0001 |
| Congestive Heart Failure | 2,587 (11.50) | 3,829 (8.61) | 6,416 (9.58) | <.0001 |
| Peripheral Vascular Disease | 1,393 (6.19) | 2,014 (4.53) | 3,407 (5.09) | <.0001 |
| Cerebrovascular Disease | 1,002 (4.45) | 2,263 (5.09) | 3,265 (4.88) | .0003 |
| Dementia | 214 (0.95) | 650 (1.46) | 864 (1.29) | <.0001 |
| Asthma | 468 (2.08) | 1,287 (2.98) | 1,755 (2.62) | <.0001 |
| Connective Tissue Disease | 306 (1.36) | 643 (1.45) | 949 (1.42) | .3746 |
| Peptic Ulcer | 196 (0.87) | 419 (0.94) | 615 (0.92) | .3625 |
| Mild Liver Disease | 184 (0.82) | 529 (1.19) | 713 (1.06) | <.0001 |
| Diabetes Mellitus | 2,355 (10.47) | 5,207 (11.71) | 7,562 (11.29) | <.0001 |
| Diabetes with complications | 187 (0.83) | 366 (0.82) | 553 (0.83) | <.9127 |
| Hemiplegia | 73 (0.32) | 373 (0.84) | 446 (0.67) | <.0001 |
| Renal Disease | 837 (3.72) | 1,713 (3.85) | 2,550 (3.81) | .3997 |
| Severe Liver Disease | 34 (0.15) | 130 (0.29) | 164 (0.24) | .0005 |
| Charlson's Comorbidity Score | | | | .016 |
| 0–2 | 21,545 (95.77) | 42,785 (96.22) | 64,330 (96.07) | |
| 3–5 | 932 (4.14) | 1,650 (3.71) | 2,582 (3.86) | |
| >5 | 20 (0.09) | 31 (0.07) | 51 (0.08) | |
| Tumor grade | | | | <.0001 |
| Well differentiated | 716 (3.18) | 1,847 (4.15) | 2,563 (3.83) | |
| Moderately differentiated | 3,093 (13.75) | 6,122 (13.77) | 9,215 (13.76) | |
| Poorly differentiated | 5,007 (22.26) | 9,665 (21.74) | 14,672 (21.91) | |
| Undifferentiated | 1,127 (5.01) | 2,126 (4.78) | 3,253 (4.86) | |
| Unknown | 12,554 (55.80) | 24,706 (55.56) | 37,260 (55.64) | |
| Stage (TNM) | | | | <.0001 |
| Stage I | 4,835 (21.49) | 7,184 (16.16) | 12,019 (17.95) | |
| Stage II | 1,123 (4.99) | 2,282 (5.13) | 3,405 (5.08) | |
| Stage IIIA | 1,977 (8.79) | 3,417 (7.68) | 5,394 (8.06) | |
| Stage IIIB | 3,338 (14.84) | 6,680 (15.02) | 10,018 (14.96) | |
| Stage IV | 8,176 (36.34) | 19,675 (44.25) | 27,851 (41.59) | |
| Unknown | 3,048 (13.55) | 5,228 (11.76) | 8,276 (12.36) | |

Among COPD patients, the proportion of costs attributed to physician office visits were highest among stages III and IV NSCLC as reflected by healthcare utilization, compared to their non-COPD counterparts (Stage I: \$468.39 per PM vs \$105.90 per PM, $p < .0001$; Stage II: \$517.40 per PM vs \$120.42 per PM, $p < .0001$; Stage III: \$762.63 per PM vs \$195.68 per PM, $p < .0001$; Stage IV: \$1,169.49 per PM vs \$336.39 per PM, $p < .0001$).

Outpatient visits represented the largest cost category across all services in both groups, with higher costs among the COPD group (\$41,203 per PM and \$31,140.08 per PM). The healthcare costs attributable to ER visits differed by stage of NSCLC, with higher costs among the COPD group in contrast with the non-COPD group (Stage I: \$71.69 per PM vs \$36.66 per PM, $p < .0001$; Stage II: \$77.70 per PM vs \$45.55 per PM, $p < .0001$; Stage III: \$116.48 per PM vs \$76.20 per PM, $p < .0001$; Stage IV: \$199.71 per PM vs \$131.03 per PM, $p < .0001$).

Discussion

This study reported healthcare utilization and costs by COPD status for each stage of NSCLC in a large population-based sample of lung cancer patients in the US. Overall, healthcare utilization and costs showed a consistent stage gradient; patients with a higher stage of NSCLC had higher healthcare utilization and costs in the COPD and non-COPD groups, even after adjustment. Based on COPD status, there was a significant trend towards higher utilization and costs among patients with pre-existing COPD. Overall, increased resource use and cost in the COPD group persisted after confounder adjustment, indicating that baseline patient characteristics (age, race, sex) and clinical characteristics (tumor grade and comorbid conditions) may influence subsequent resource use and costs.

Studies have indicated several potential factors for higher inpatient admissions among COPD patients. Chronic mucus

Table 2. Unadjusted healthcare utilization and costs among NSCLC patients with and without pre-existing COPD.

| Service | COPD-status | Lung cancer stage | PM | Utilization per 100 PM | Cost per PM | Utilization difference per 100 PM | Cost difference |
|------------------|-------------|-------------------|---------|------------------------|-------------|-----------------------------------|-----------------|
| Admissions | Non-COPD | I | 196,188 | 7.71 | \$988.82 | | |
| | | II | 52,978 | 8.69 | \$1,071.27 | | |
| | | III | 122,982 | 15.19 | \$1,697.22 | | |
| | | IV | 132,628 | 25.00 | \$2,607.27 | | |
| | COPD | I | 111,039 | 11.73 | \$1,229.49 | 4.02* | \$240.68* |
| | | II | 22,298 | 11.29 | \$1,174.14 | 2.60* | \$102.87* |
| | | III | 58,810 | 22.44 | \$2,205.70 | 7.25* | \$508.48* |
| | | IV | 50,791 | 39.23 | \$3,820.70 | 14.23* | \$1,213.42* |
| SNF | Non-COPD | I | 196,188 | 1.01 | \$83.15 | | |
| | | II | 52,978 | 0.98 | \$74.79 | | |
| | | III | 122,982 | 2.10 | \$167.82 | | |
| | | IV | 132,628 | 3.85 | \$284.29 | | |
| | COPD | I | 111,039 | 2.19 | \$171.96 | 1.18* | \$88.80* |
| | | II | 22,298 | 2.05 | \$161.22 | 1.07 | \$86.43 |
| | | III | 58,810 | 4.17 | \$308.41 | 2.07 | \$140.60 |
| | | IV | 50,791 | 7.43 | \$540.15 | 3.58* | \$255.87* |
| Physician-Visits | Non-COPD | I | 196,188 | 168.76 | \$106.57 | | |
| | | II | 52,978 | 189.87 | \$129.51 | | |
| | | III | 122,982 | 314.46 | \$201.39 | | |
| | | IV | 132,628 | 541.56 | \$338.56 | | |
| | COPD | I | 111,039 | 745.27 | \$463.86 | 576.51* | \$357.30* |
| | | II | 22,298 | 818.16 | \$528.64 | 628.29* | \$399.13* |
| | | III | 58,810 | 1,222.79 | \$764.80 | 908.33* | \$563.41* |
| | | IV | 50,791 | 1,863.74 | \$1,143.63 | 1,322.18* | \$805.07* |
| ER-Visits | Non-COPD | I | 196,188 | 8.08 | \$35.19 | | |
| | | II | 52,978 | 8.72 | \$36.59 | | |
| | | III | 122,982 | 15.59 | \$67.07 | | |
| | | IV | 132,628 | 25.85 | \$109.46 | | |
| | COPD | I | 111,039 | 14.25 | \$61.54 | 6.17 | \$26.35 |
| | | II | 22,298 | 15.71 | \$73.08 | 6.99* | \$36.49* |
| | | III | 58,810 | 23.42 | \$105.27 | 7.83* | \$38.20* |
| | | IV | 50,791 | 39.37 | \$171.96 | 13.52* | \$62.50* |
| Outpatient | Non-COPD | I | 196,188 | 506.92 | \$4,409.26 | | |
| | | II | 52,978 | 600.89 | \$6,540.81 | | |
| | | III | 122,982 | 1,026.58 | \$11,520.51 | | |
| | | IV | 132,628 | 1,469.50 | \$15,647.92 | | |
| | COPD | I | 111,039 | 658.45 | \$5,127.05 | 151.53* | \$717.80* |
| | | II | 22,298 | 767.86 | \$7,032.49 | 166.97* | \$491.69* |
| | | III | 58,810 | 1,193.58 | \$11,141.92 | 167.00* | -\$378.59* |
| | | IV | 50,791 | 1,668.95 | \$13,793.35 | 199.45* | -\$1854.57* |

* $p < 0.05$.

Abbreviations. PM, person-months; SNF, skilled nursing facility; ER, emergency room.

hypersecretion, use of anticholinergics, older age, poor health-related quality-of-life, and comorbidities were associated with hospitalizations^{36–38}. Four studies showed that lower forced expiratory volume 1 (FEV1) was associated with higher risk of COPD related admissions^{37,39–41}. Miravittles *et al.*³⁶ suggested that FEV1 impairment may explain part of the risk of frequent exacerbations and hospital admissions. Several studies highlighted the association between older age and shorter time to first readmission and increased risk of hospitalization^{38,42,43}. This may be related to the higher degree of disability and comorbidity in the older population. Patients who habitually fail to seek therapy for their exacerbations have worse health-related quality-of-life and are more likely to be hospitalized for the management of an exacerbation⁴⁴. Lau *et al.*³⁸ found that comorbid conditions such as coronary artery disease, left ventricular failure, and diabetes mellitus were significant risk factors for hospital admissions.

Our study found that emergency room (ER) visits were 2-times higher among COPD patients in early stages of NSCLC. Previous studies have found that dyspnea, neutropenic fever, respiratory tract infections, and chronic lung disease were most common causes of ER visits among stages

I/II NSCLC patients^{45,47}. Due to the increasing use of chemotherapy regimens in the outpatient setting, emergency physicians have frequently encountered complications secondary to treatment-induced febrile neutropenia⁴⁷. Kumbhare *et al.*⁴⁸ reported that extremes of body mass index (BMI) among COPD patients were associated with higher ER visits. COPD patients exhibit significant weight loss, due to the increased energy requirements associated with labored breathing⁴⁹. Low BMI is shown to be associated with emergency care needs^{50,51}.

Our findings of higher costs and utilization of physician and outpatient services among the COPD group is consistent with published literature. According to Verbrugge and Patrick⁵², COPD is a major cause of chronic disability and a leading reason for visits to office-based physicians. Mapel *et al.*⁵³ showed that COPD patients had significantly higher utilization in outpatient and physician services, including outpatient surgery in office or hospital, radiology, and laboratory use. A large difference in utilization was seen in respiratory care services, with 27.9% of COPD patients using pulmonary services compared with 2.4% of non-COPD patients. Moreover, the average number of primary care visits for COPD patients was 54% higher than the non-COPD group⁵³.

Table 3. Adjusted healthcare utilization and costs among NSCLC patients with and without pre-existing COPD.

| Service | COPD-status | Lung cancer stage | PM | Utilization per 100 PM | Cost per PM | Utilization difference per 100 PM | Cost difference |
|------------------|-------------|-------------------|---------|------------------------|-------------|-----------------------------------|-----------------|
| Admissions | Non-COPD | I | 196,188 | 9.49 | 836.61 | | |
| | | II | 52,978 | 10.78 | 946.31 | | |
| | | III | 122,982 | 18.91 | 1,558.66 | | |
| | | IV | 132,628 | 31.24 | 2,537.42 | | |
| | COPD | I | 111,039 | 14.67 | 1,235.86 | 5.18* | \$399.35* |
| | | II | 22,298 | 14.13 | 1,193.67 | 3.35* | \$247.37* |
| | | III | 58,810 | 28.31 | 2,274.88 | 9.40* | \$716.22* |
| | | IV | 50,791 | 49.50 | 3,925.36 | 18.26* | \$1,387.95* |
| SNF | Non-COPD | I | 196,188 | 1.23 | 104.10 | | |
| | | II | 52,978 | 1.20 | 103.11 | | |
| | | III | 122,982 | 2.59 | 208.31 | | |
| | | IV | 132,628 | 4.78 | 380.49 | | |
| | COPD | I | 111,039 | 2.73 | 225.36 | 1.50* | \$121.26* |
| | | II | 22,298 | 2.56 | 214.12 | 1.36 | \$111.01 |
| | | III | 58,810 | 5.24 | 412.34 | 2.65 | \$204.03 |
| | | IV | 50,791 | 9.34 | 730.26 | 4.56 | \$349.77* |
| Physician-Visits | Non-COPD | I | 196,188 | 230.75 | 105.90 | | |
| | | II | 52,978 | 241.05 | 120.42 | | |
| | | III | 122,982 | 387.28 | 195.68 | | |
| | | IV | 132,628 | 681.84 | 336.39 | | |
| | COPD | I | 111,039 | 927.36 | 468.39 | 696.61* | \$362.49* |
| | | II | 22,298 | 988.95 | 517.40 | 747.90* | \$396.97* |
| | | III | 58,810 | 1,453.49 | 762.63 | 1,066.21* | \$566.95* |
| | | IV | 50,791 | 2,311.94 | 1,169.49 | 1,630.10* | \$833.09* |
| ER-Visits | Non-COPD | I | 196,188 | 9.78 | 36.66 | | |
| | | II | 52,978 | 13.59 | 45.55 | | |
| | | III | 122,982 | 19.73 | 76.20 | | |
| | | IV | 132,628 | 33.26 | 131.03 | | |
| | COPD | I | 111,039 | 20.41 | 71.69 | 10.63* | \$35.04* |
| | | II | 22,298 | 24.25 | 77.70 | 10.66* | \$32.15* |
| | | III | 58,810 | 31.85 | 116.48 | 12.12* | \$40.28* |
| | | IV | 50,791 | 56.58 | 199.71 | 23.32* | \$68.68* |
| Outpatient | Non-COPD | I | 196,188 | 796.00 | 4,660.00 | | |
| | | II | 52,978 | 983.26 | 5,745.64 | | |
| | | III | 122,982 | 1,656.64 | 9,708.94 | | |
| | | IV | 132,628 | 2,422.26 | 14,025.50 | | |
| | COPD | I | 111,039 | 1,136.04 | 6,202.37 | 340.04* | \$1,524.36* |
| | | II | 22,298 | 1,325.12 | 7,486.42 | 341.86* | \$1,740.78* |
| | | III | 58,810 | 2,025.47 | 11,493.13 | 368.83* | \$1,784.19* |
| | | IV | 50,791 | 2,825.73 | 16,021.90 | 403.47* | \$1,996.39* |

* $p < 0.05$.

Abbreviations. PM, person-months; SNF, skilled nursing facility; ER, emergency room.

We observed a general trend of increasing costs across the COPD and non-COPD groups with an increase in stage of NSCLC. In contrast, Cipriano *et al.*⁵⁴ found that patients diagnosed with stages I/II NSCLC followed a pattern of higher costs in the 6-month period after diagnosis followed by lower costs in the subsequent post-diagnosis period. This may be explained by the differences in the definitions of phases of care over which cost of cancer was calculated by Cipriano *et al.*⁵⁴ (pre-diagnosis, staging, initial, continuing, and terminal) vs costs of cancer care stratified by stage of cancer diagnosis in the current study. Relative costs among patients with advanced stage disease at cancer diagnosis were significantly higher than for localized stage in our study and are consistent with the trends of increasing use of aggressive care near the end of life in lung cancer.

Healthcare costs in all service areas were significantly higher in the COPD group, as reflected by healthcare utilization. In our study, outpatient costs for COPD patients were highest across all service categories compared to non-COPD patients. These results were similar to the findings reported by Mapel *et al.*⁵³, in which costs for outpatient services for COPD patients were significantly higher than inpatient costs.

Our study had several important strengths. The population-based data used in the analysis included large numbers of NSCLC patients with Medicare coverage. We were able to evaluate the trajectory of care that NSCLC patients received across multiple care settings. The comprehensiveness of these data provided a detailed picture of resource use and costs across all stages of NSCLC. Person-month analyses were employed as patients had varying lengths of follow-up in our study. Person-month estimates enabled us to limit our analysis to only those patients who were "at risk" of receiving a specific type of care. We used a consistent denominator expressed in terms of person-months to quantify costs for the specific stage of cancer. Due to person-time analyses, we could not summarize costs across all stages of cancer for grand total costs. Per 100 PM were used to standardize our cost-estimates, resulting in a more accurate estimate of service use and costs than if we had included all patients.

Our study also had several limitations. We used administrative data to capture patients' treatment. Administrative data do not include information about non-covered services or patients' treatment choices. Pharmaceuticals (over the counter or prescription) were not included in our estimates, as the study period for our study had incomplete claims for

Medicare Part D. As the field of oncology typically has a rapidly evolving landscape, the issue of capturing most current data has always been a constant challenge. Due to the time-lag associated with SEER-Medicare data availability, the most current data available during study initiation period (2014) was from 2006–2010. Other limitations of the analysis include those common to analyses of SEER-Medicare data⁵⁵, such as omission of patients less than 65 years old, patients enrolled in HMOs, and an inability to identify individuals, such as veterans, for whom Medicare may have incomplete claims data.

Conclusions

The current study characterized health resource utilization patterns and costs in NSCLC patients with and without pre-existing COPD. Healthcare utilization and costs among lung cancer patients with pre-existing COPD was ~2–3-times higher than the non-COPD group. Patients with pre-existing COPD imposed a substantial direct cost burden on Medicare. The results of this study may be helpful in identifying cost-drivers and evaluate changes in practice patterns for cost containment within the lung cancer landscape.

Transparency

Declaration of funding

No external funding.

Declaration of financial/other relationships

The authors have no conflicts to declare and no financial relationships relevant to this article to disclose. JME peer reviewers on this manuscript have no relevant financial or other relationships to disclose.

Acknowledgements

None declared.

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