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Geographic Variation in the Use of Adjuvant Therapy among Elderly Patients with Resected Non-Small Cell Lung Cancer

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Abstract

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Objectives—The purpose of this study was to assess to what extent geographic variation in adjuvant treatment for non-small cell lung cancer (NSCLC) patients would remain, after controlling for patient and area-level characteristics.

Materials and Methods—A retrospective cohort of 18,410 Medicare beneficiaries with resected, stage I-IIIa NSCLC was identified from the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database. Adjuvant therapies were classified as adjuvant chemotherapy (ACT), postoperative radiation therapy (PORT), or no adjuvant therapy. Predicted treatment probabilities were estimated for each patient given their clinical, demographic, and area-level characteristics with multivariate logistic regression. Area Treatment Ratios were used to estimate the propensity of patients in a local area to receive an adjuvant treatment, controlling for characteristics of patients in the area. Areas were categorized as low-, mid- and high-use and mapped for two representative SEER registries.

Results—Overall, 10%, 12%, and 78% of patients received ACT, PORT and no adjuvant therapy, respectively. Age, sex, stage, type and year of surgery, and comorbidity were associated with adjuvant treatment use. Even after adjusting for patient characteristics, substantial geographic treatment variation remained. High- and low-use areas were tightly juxtaposed within and across SEER registries, often within the same county. In some local areas, patients were up to eight times more likely to receive adjuvant therapy than expected, given their characteristics. On the other hand, almost a quarter of patients lived in local areas in which patients were more than three times less likely to receive ACT than would be predicted.

Conclusion—Controlling for patient and area-level covariates did not remove geographic variation in adjuvant therapies for resected NSCLC patients. A greater proportion of patients were treated less than expected, rather than more than expected. Further research is needed to better understand its causes and potential impact on outcomes.

Keywords

non-small cell lung cancer; adjuvant therapy; geographic treatment variation; SEER-Medicare; elderly patients

1. Introduction

The standard of care for early stage non-small cell lung cancer (NSCLC) is lobectomy or pneumonectomy, followed by adjuvant chemotherapy (ACT) [1]. Although this approach has been shown to improve overall survival [2–4], the evidence is based on randomized trials that have generally excluded the old and fragile, and those with multiple comorbidities [5]. This is particularly relevant for NSCLC as the median age at diagnosis is 70 [6] and a considerable proportion of patients have poor performance status [7]. Thus, the outcome evidence associated with adjuvant treatment for elderly patients with resected NSCLC is incomplete, especially for those with comorbidities [8].

It has been argued that uncertainty regarding treatment effectiveness may give rise to treatment variation [9,10]. Indeed, geographic variation in NSCLC cancer care and treatment practices has been observed [11–23]. However, the cause of this variation is still unclear. Patient characteristics such as age, race and ethnicity, stage, comorbidities, and

socioeconomic status [11,12,20–22,24–34] have been shown to affect treatments for lung cancer patients, and differences in these characteristics across areas may contribute to the observed treatment variation. Other proposed explanations include differences in the rate of observed toxicities from cancer treatments in various geographic areas [13], proximity to a cancer-treatment center [35], geographic residence and area-level characteristics [17,22,36], and local area “tastes” for medical care measured in terms of the intensity of fee-for-service spending in Medicare beneficiaries [18]. Identifying and understanding the factors associated with geographic variation in the adjuvant treatment of NSCLC is extremely important, as withholding adjuvant treatment inappropriately can potentially jeopardize curability.

Although geographic variation in adjuvant treatment for NSCLC has been reported, and patient and area-level characteristics have been identified as potential sources of this variation, studies have not quantified to what extent these characteristics influence geographic variation in adjuvant treatments. It is possible that the observed geographic variation in treatments is driven solely by differences in patient and area-level characteristics. Whether geographic variation in treatments exists after controlling for observed patient and area-level characteristics is not known.

2. Materials and Methods

2.1 Subject Selection

Data was obtained from the United States National Cancer Institute’s Surveillance, Epidemiology, and End Results (SEER) program. SEER has collected data on cancer cases since 1973 [37]. Over time, the catchment area expanded to increase coverage of minority populations. Currently, 18 registries are included, representing about 28% of U.S. population [38]. Since 1991, SEER registry data have been linked to Medicare claims, with a match rate of about 93% [39]. The SEER-Medicare linked dataset contains information on patient demographics, tumor and clinical characteristic, healthcare utilization, and date and cause of death [39]. Although typically encrypted, this project was granted access to patient-level Zone Improvement Plan (ZIP) code data. This study was approved by our institutional review board.

These data were used to identify the study cohort, which included patients 1) with first, primary, malignant lung cancer diagnosed 1992–2007, 2) aged 66 or older at the time of diagnosis, 3) with pathologically confirmed non-small cell type, 4) diagnosed with stage I–IIIA, and 5) who underwent resection one month prior to, through six months after, diagnosis. Patients were excluded if they 1) had an unknown month of diagnosis (N=2,469), 2) were diagnosed at autopsy or death (N=224), 3) had an unreliable date of death (N=91) (i.e. had a death date in the SEER registry but not in Medicare claims or a death date before the diagnosis date), 4) lacked continuous Medicare fee-for-service Parts A and B coverage the 12 months prior to diagnosis through either death or four months after surgery, whichever occurred earlier (N=17,691), 5) died within 30 days of surgery (N=888), 6) received neoadjuvant therapy (N=714), 7) received the first course of adjuvant radiation and chemotherapy on the same day (N=97), or 8) had missing race or rural/urban location of residence (N=32). In addition, we excluded those residing in Hawaii (N=323) because

distance measures are complicated due to the fact that the state is a series of small islands. Those with invalid ZIP codes (N=20) or residing outside SEER areas were also excluded (N=335). A total of 18,410 patients were included in this study.

2.2 Measures

Type of surgery was categorized as pneumonectomy, lobectomy, or segmental/wedge and must have been received in the month prior to diagnosis through six months after diagnosis. Adjuvant therapy was defined as the first treatment received within four months of surgery and categorized into three mutually exclusive groups: ACT, PORT, and no adjuvant therapy. All treatments were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnosis and Procedure codes, Current Procedural Terminology (CPT) codes, and/or Healthcare Common Procedure Coding System (HCPCS) codes reported on the Medicare claims and are listed in Appendix Table A.1.

Patient demographic variables were gathered from the SEER data. Age was categorized into five groups: 66–70, 71–75, 76–80, 81–84, and 85 or over. Race was categorized as white, black, and other, per SEER definitions. Urban/rural codes were used to categorize patient residency with five levels: big metro, metro, urban, less urban, and rural. The following socioeconomic characteristics, measured at the census-tract level, were included: median household income, percent of people aged 25 or older with a high school education only, percent of population being white, and percent of residents living below the poverty level. These area-level variables were ranked and patients were grouped based on the quartile values.

Baseline comorbidity was determined from inpatient and outpatient Medicare claims for the year prior to NSCLC diagnosis using a modified Charlson comorbidity index [40]. Patients were characterized based on the number of non-cancer comorbidities: 0, 1, and 2 or more. Tumor stages were grouped into stage I, II, and IIIA based on American Joint Committee on Cancer (AJCC) staging 3rd edition. Variables were also created for AJCC T (T0/T1, T2, T3, and TX) and N (N0, N1, N2, and NX) stages, as these clinical indicators are important determinants of the use of adjuvant therapy even within a stage. Indicators were created for receipt of surgery in biennial periods.

2.3 Area Treatment Ratios

Area Treatment Ratios (ATRs) were used to estimate the propensity of patients in a local area to receive adjuvant treatment, controlling for characteristics of patients in the area. As such, ATRs provide an adjusted measure of a local area's "adjuvant treatment signature." The ATR method has been used successfully in previous studies of geographic treatment variation and comparative effectiveness, along with methodological papers aimed at better understanding estimates of treatment effectiveness from observational studies with unmeasured confounding [41–47]. A summary of the method is outlined below.

To calculate ATRs, "local areas" were first defined, following the approach developed by Fang et al. [48]. ZIP codes with at least one NSCLC patient were identified. For ZIP codes with fewer than 10 patients, additional patients living in the nearest ZIP codes (based on driving distance) were included until at least 10 patients were identified. This

conglomeration of ZIP codes was then deemed the “local area” for the original ZIP code. Creating local areas in this way takes into consideration population density and variation in transportation time (e.g. due to geographic features such as lakes and mountains).

For the local area surrounding each patient’s residence ZIP code, the number of patients receiving each type of adjuvant therapy was determined from the SEER-Medicare data. Predicted treatment probabilities were then estimated for each patient in our sample given their clinical, demographic and area-level characteristics based on multivariate logistic regression using the full sample. For each adjuvant therapy and local area, an ATR was calculated by dividing the actual number of patients receiving that adjuvant therapy in that local area by the sum of the predicted probabilities of receiving that adjuvant therapy in that local area. Thus, an ATR less (greater) than one, then, would indicate that patients living in that local area were less (more) apt to receive adjuvant therapy than would be predicted, given the patient and socioeconomic characteristics in that local area.

2.4 Analysis

Chi-squared tests were conducted to compare the distribution of patient and area-level characteristics across the treatments. Descriptive statistics were calculated for both the actual treatment rates and ATR values across local areas, and box plots were drawn for the ATR values. ZIP codes were characterized as low-, mid-, or high-use areas based on tertiles of ATR values, and mapped to visualize the geographic variation in adjusted treatment rates for two representative SEER registries. Patient characteristics were compared across these low-, mid-, or high-use areas with a Cochran-Armitage trend test to determine the extent that measured covariates were balanced using the ATR method. All statistical analyses were performed using SAS 9.3 (SAS Institute Inc., Cary, North Carolina) and maps were generated using Microsoft MapPoint North America 2010.

3. Results

3.1 Sample Characteristics

A total of 18,410 Medicare beneficiaries diagnosed in 1992–2007 in the SEER-Medicare linked database met study inclusion criteria. The mean (SD) age at time of diagnosis was 74.2 (5.2) and the vast majority were white (90%). Over half of the cohort had at least one comorbidity in addition to NSCLC. The most common comorbidities were chronic obstructive pulmonary disease (37%), diabetes (15%), and peripheral vascular disease (8%). Most patients (83%) received lobectomy.

3.2 Adjuvant Therapy, Unadjusted

In this sample, 10% received ACT, 12% received PORT and 78% did not receive any adjuvant therapy within four months of surgery. Actual treatment rates in local areas ranged from 0–60% for ACT, 0–64% for PORT and 18–100% for no adjuvant therapy. Although the treatment rates varied in range, interquartile ranges for the three treatments were similar. Treatment rates at the first and third quartile (Q1–Q3) were 3–15% for ACT, 6–18% for PORT and 70–86% for no adjuvant therapy.

A number of patient and area-level characteristics were associated with the use of and type of adjuvant therapy (Table 1). Similar to other studies, age, sex, stage, comorbidity, and type of surgery were associated with adjuvant therapy (all P-values<0.05). Year of surgery was also associated with type of adjuvant therapy. This is expected, as treatment guidelines changed during this time period. ACT use dramatically increased after 2003, following reports from large randomized trials of the benefit of adjuvant chemotherapy. PORT use dropped steadily throughout the study period. Greater comorbidity was negatively associated with use of any adjuvant therapy and PORT, although not for ACT. There was no association between race and use of adjuvant therapy at the 5% level (P-value=0.0552). Areal-level measures of socioeconomic status were not associated with receipt of adjuvant therapy in a clinically significant way.

3.3 Adjuvant Therapy, Adjusted

ATRs, an adjusted measure of the likelihood in which patients in that local area were to receive adjuvant therapy, were calculated for each adjuvant therapy and local area. Box plots of ATRs were plotted (Figure 1) and mean (SD, median, Q1–Q3) values for ACT, PORT, and no adjuvant therapy were 1.0 (0.9, 0.9, 0.3–1.5), 1.0 (0.8, 0.9, 0.5–1.4), and 1.0 (0.1, 1.0, 0.9–1.1), respectively. Patients at the first quantile (25%) of ATR values were 3.2 times less likely to receive ACT than would be predicted. On the other extreme, patients at the third quantile (75%) were 1.5 times more likely to receive ACT. For PORT, patients at the first quantile were 2.2 times less likely to receive adjuvant radiation and, at the 75%, 1.4 times more likely. Thus, although the right-sided tails for ATR values were long for ACT and PORT (with maximum values of 8.0 and 8.4), more patients were treated less than would be expected rather than more.

As a sensitivity analysis, ATRs were also created excluding patients with stage I disease, as the value of adjuvant chemotherapy remains controversial for these patients. The standard deviation of ATRs for ACT was smaller for the stage II-IIIa patients than the full sample, although not completely diminished (0.7 versus 0.9). Patients in the first quantile (25%) of ATR values were 1.7 times less likely to receive ACT than would be predicted, and 1.4 times more likely at the third quantile (75%). A similar pattern was seen with PORT.

3.4. Geographic Variation in Adjuvant Therapy, Adjusted

ATR values falling in the first, second, and third tertiles were 0–0.5, 0.6–1.1, 1.2–8.0 for ACT, and 0–0.6, 0.7–1.2, 1.3–8.4 for PORT. ZIP codes in the first, second, and third tertile were characterized as low-, mid-, and high-use areas, respectively, and mapped for two representative SEER regions, Iowa and Connecticut (Figure 2). These maps reveal substantial geographic variation even after adjusting for patient and area-level characteristics, given the tight juxtaposition of high- and low-use areas, within and across SEER areas. As seen in the figure, counties almost always enclosed not just multiple areas, but multiple types of areas. For example, Hartford county, located in the middle, upper side of Connecticut, included two low-use areas completely separated by two distinct high-use areas and a larger mid-use area. Over all SEER registries, patients in low-use areas were on average 7.9 times less likely to receive ACT and 5.0 times less likely to receive PORT, than in mid-use areas. In high use areas, patients were 2.0 times more likely to receive ACT and

1.8 times more likely to receive PORT. Results from Cochran-Armitage trend tests revealed that patient characteristics did not differ meaningfully across the low-, mid-, or high-use areas, suggesting that the ATR method was able to balance measured covariates (Appendix Tables A.2 and A.3).

4. Discussion

Although other studies have reported a relationship between geographic variation in adjuvant therapy and baseline patient characteristics [12,15,28] and area-level characteristics [17,36], our study is the first to assess geographic variation in adjuvant treatment after controlling for patient and area-level characteristics. In this population-based cohort, we demonstrated substantial geographic variation in the use of ACT and PORT, even after adjusting for measured covariates. For example, patients in some areas were 8.4 times more likely to receive PORT than would be predicted, given their own characteristics and characteristics of their local area. In addition to the extent of variation in terms of adjusted adjuvant treatment use, substantial variation existed geographically. High- and low-use areas were found alongside each other within and across SEER areas, often within the same county.

Even though low-, mid-, and high-use areas were constructed in such a way that patient and area-level characteristics were balanced across the areas, patients living in low-use areas were on average eight times less likely to receive ACT than patients living in mid-use areas, whereas patients in high-use areas were on average twice as likely to receive ACT. This would suggest that the variation in adjusted treatment rates were skewed towards less use, not more use. In fact, the skewness of patient-specific ATRs for ACT was 1.4, with the mass of the distribution concentrated to the left (i.e. a greater number of patients residing in areas with less than predicted ACT use). This may be clinically significant, as our model controlled for a number of patient and tumor characteristics (e.g. age, stage, comorbidity, and type of surgery) that are commonly incorporated in the treatment decision. Our results suggest that physicians across SEER areas, when faced with the “same” patient (in terms of our measured covariates), tended to treat less rather than treat more. This is in line with previous research documenting an inverse relationship between adjuvant treatment and elderly NSCLC patients [21,49].

As a sensitivity analysis, ATRs were calculated, excluding patients with stage I disease. Although the variation in ATR values for ACT and PORT were diminished, substantial variation remained, even for a subset of patients where the role of ACT was less controversial. In fact, 42% of the ACT in our sample was given to stage I patients. Thus the observed variation in ATRs for the full sample is not being driven solely by the patients for whom adjuvant therapy benefit is uncertain.

Because the measured patient and area-level characteristics were balanced by the ATR method, the observed geographic variation in treatment rates among elderly patients with NSCLC extends beyond merely differences in patient and socioeconomic characteristics across areas. Other potential factors explaining the remaining treatment variation could include variation in market access, disparity in supply-sensitive care, or variation in patients’

value for adjuvant therapy or provider belief in the value of adjuvant therapy [10,50–52]. Although our paper does not test for these factors, it does conclude that the observed variation in adjuvant therapy is not due to differences in the measured patient and area-level characteristics.

There are limitations to this study. First, this study identified adjuvant therapy as the first therapy a patient received after surgery without accounting for cases in which patients discontinued or switched treatments for reasons such as toxicity. However, we believe that this measure reflects the initial treatment decision, which is more likely to be related to patient baseline characteristics. Second, variation in chemotherapy regimen and dose was not accounted for. Therefore, if anything, our estimates of geographic variation in treatments are underestimated. Finally, there are other clinical characteristics that affect the decision to initiate adjuvant therapy but are not captured in SEER-Medicare data. These limitations are a reminder that our conclusions only apply to the patient and area-level characteristics that we were able to measure and include in the model.

5. Conclusions

There remains substantial geographic variation in the delivery of adjuvant therapies for elderly, resected NSCLC patients, even after adjusting for patient and area-level characteristics. Although withholding adjuvant treatment inappropriately can potentially jeopardize curability, the magnitude and distribution of the ATRs suggest that substantial uncertainty and discretion remains in the distribution of adjuvant therapies across these patients. The observed geographic variation begs the question of optimal treatment rates [53], and whether this variation has any effect on clinical outcomes such as toxicity-related hospitalization and survival.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ACT	adjuvant chemotherapy
AJCC	American Joint Committee on Cancer
ATR	Area Treatment Ratio

CPT	Current Procedural Terminology
HCPCS	Healthcare Common Procedure Coding System
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
PORT	postoperative radiation therapy
SEER	Surveillance, Epidemiology, and End Results

References

1. Pisters KM, Evans WK, Azzoli CG, Kris MG, Smith CA, Desch CE, Somerfield MR, Brouwers MC, Darling G, Ellis PM, Gaspar LE, Pass HI, Spigel DR, Strawn JR, Ung YC, Shepherd FA, Cancer Care O. American Society of Clinical O. Cancer Care Ontario and American Society of Clinical Oncology adjuvant chemotherapy and adjuvant radiation therapy for stages I-IIIa resectable non small-cell lung cancer guideline. *J Clin Oncol*. 2007; 25:5506–5518. [PubMed: 17954710]
2. Arriagada R, Bergman B, Dunant A, Le Chevalier T, Pignon JP, Vansteenkiste J. International Adjuvant Lung Cancer Trial Collaborative G. Cisplatin-based adjuvant chemotherapy in patients with completely resected non-small-cell lung cancer. *N Engl J Med*. 2004; 350:351–360. [PubMed: 14736927]
3. Winton T, Livingston R, Johnson D, Rigas J, Johnston M, Butts C, Cormier Y, Goss G, Incullet R, Vallieres E, Fry W, Bethune D, Ayoub J, Ding K, Seymour L, Graham B, Tsao MS, Gandara D, Kesler K, Demmy T, Shepherd F. National Cancer Institute of Canada Clinical Trials G, National Cancer Institute of the United States Intergroup JBRTI. Vinorelbine plus cisplatin vs. observation in resected non-small-cell lung cancer. *N Engl J Med*. 2005; 352:2589–2597. [PubMed: 15972865]
4. Douillard JY, Rosell R, De Lena M, Carpagnano F, Ramlau R, Gonzales-Larriba JL, Grodzki T, Pereira JR, Le Groumellec A, Lorusso V, Clary C, Torres AJ, Dahabreh J, Souquet PJ, Astudillo J, Fournel P, Artal-Cortes A, Jassem J, Koubkova L, His P, Riggi M, Hurteloup P. Adjuvant vinorelbine plus cisplatin versus observation in patients with completely resected stage IB-IIIa non-small-cell lung cancer (Adjuvant Navelbine International Trialist Association [ANITA]): a randomised controlled trial. *Lancet Oncol*. 2006; 7:719–727. [PubMed: 16945766]
5. Lewis JH, Kilgore ML, Goldman DP, Trimble EL, Kaplan R, Montello MJ, Housman MG, Escarce JJ. Participation of patients 65 years of age or older in cancer clinical trials. *J Clin Oncol*. 2003; 21:1383–1389. [PubMed: 12663731]
6. Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z. SEER Cancer Statistics Review, 1975–2011. 2013
7. Lilienbaum RC, Cashy J, Hensing TA, Young S, Cella D. Prevalence of poor performance status in lung cancer patients: implications for research. *J Thorac Oncol*. 2008; 3:125–129. [PubMed: 18303431]
8. Chrischilles EA, Pendergast JF, Kahn KL, Wallace RB, Moga DC, Harrington DP, Kiefe CI, Weeks JC, West DW, Zafar SY, Fletcher RH. Adverse events among the elderly receiving chemotherapy for advanced non-small-cell lung cancer. *J Clin Oncol*. 2010; 28:620–627. [PubMed: 20038726]
9. Wennberg J. Which rate is right? *N Engl J Med*. 1986; 314:310–311. [PubMed: 3941721]
10. Wennberg J, Gittelsohn A. Variations in medical care among small areas. *Scientific American*. 1982; 246:120–134. [PubMed: 7079718]
11. Smith TJ, Penberthy L, Desch CE, Whittemore M, Newschaffer C, Hillner BE, McClish D, Retchin SM. Differences in initial treatment patterns and outcomes of lung cancer in the elderly. *Lung Cancer*. 1995; 13:235–252. [PubMed: 8719064]
12. Potosky AL, Saxman S, Wallace RB, Lynch CF. Population variations in the initial treatment of non-small-cell lung cancer. *J Clin Oncol*. 2004; 22:3261–3268. [PubMed: 15310770]

13. Edelman MJ, Sekine I, Tamura T, Saijo N. Geographic variation in the second-line treatment of non-small cell lung cancer. *Semin Oncol*. 2006; 33:S39–44. [PubMed: 16472708]
14. Bekelman JE, Rosenzweig KE, Bach PB, Schrag D. Trends in the use of postoperative radiotherapy for resected non-small-cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2006; 66:492–499. [PubMed: 16814952]
15. Patel N, Adatia R, Mellemgaard A, Jack R, Moller H. Variation in the use of chemotherapy in lung cancer. *Br J Cancer*. 2007; 96:886–890. [PubMed: 17342091]
16. Lang K, Marciniak MD, Faries D, Stokes M, Buesching D, Earle C, Treat J, Morissette N, Thompson D. Trends and predictors of first-line chemotherapy use among elderly patients with advanced non-small cell lung cancer in the United States. *Lung Cancer*. 2009; 63:264–270. [PubMed: 18649969]
17. Myrdal G, Lamberg K, Lambe M, Stahle E, Wagenius G, Holmberg L. Regional differences in treatment and outcome in non-small cell lung cancer: a population-based study (Sweden). *Lung Cancer*. 2009; 63:16–22. [PubMed: 18571760]
18. Keating NL, Landrum MB, Lamont EB, Bozeman SR, McNeil BJ. Area-level variations in cancer care and outcomes. *Med Care*. 2012; 50:366–373. [PubMed: 22437623]
19. Ramsey SD, Howlader N, Etzioni RD, Donato B. Chemotherapy use, outcomes, and costs for older persons with advanced non-small-cell lung cancer: evidence from surveillance, epidemiology and end results-Medicare. *J Clin Oncol*. 2004; 22:4971–4978. [PubMed: 15611512]
20. Edwards BK, Brown ML, Wingo PA, Howe HL, Ward E, Ries LA, Schrag D, Jamison PM, Jemal A, Wu XC, Friedman C, Harlan L, Warren J, Anderson RN, Pickle LW. Annual report to the nation on the status of cancer, 1975–2002, featuring population-based trends in cancer treatment. *J Natl Cancer Inst*. 2005; 97:1407–1427. [PubMed: 16204691]
21. Cuffe S, Booth CM, Peng Y, Darling GE, Li G, Kong W, Mackillop WJ, Shepherd FA. Adjuvant chemotherapy for non-small-cell lung cancer in the elderly: A population-based study in Ontario, Canada. *Journal of Clinical Oncology*. 2012; 30:1813–1821. [PubMed: 22529258]
22. Mahmud SM, Reilly M, Comber H. Patterns of initial management of lung cancer in the Republic of Ireland: a population-based observational study. *Lung Cancer*. 2003; 41:57–64. [PubMed: 12826313]
23. Bach P, Cramer L, Warren J, Begg C. Racial Differences in the Treatment of Early-Stage Lung Cancer. *The New England journal of medicine*. 1999; 341:1198. [PubMed: 10519898]
24. Kankesan J, Shepherd FA, Peng Y, Darling G, Li G, Kong W, Mackillop WJ, Booth CM. Factors associated with referral to medical oncology and subsequent use of adjuvant chemotherapy for non-small-cell lung cancer: a population-based study. *Curr Oncol*. 2013; 20:30–37. [PubMed: 23443880]
25. Bach PB, Cramer LD, Warren JL, Begg CB. Racial differences in the treatment of early-stage lung cancer. *N Engl J Med*. 1999; 341:1198–1205. [PubMed: 10519898]
26. Earle CC, Venditti LN, Neumann PJ, Gelber RD, Weinstein MC, Potosky AL, Weeks JC. Who gets chemotherapy for metastatic lung cancer? *Chest*. 2000; 117:1239–1246. [PubMed: 10807806]
27. Stevens W, Stevens G, Kolbe J, Cox B. Ethnic differences in the management of lung cancer in New Zealand. *J Thorac Oncol*. 2008; 3:237–244. [PubMed: 18317065]
28. de Rijke JM, Schouten LJ, ten Velde GP, Wanders SL, Bollen EC, Lalisang RI, van Dijk JA, Kramer GW, van den Brandt PA. Influence of age, comorbidity and performance status on the choice of treatment for patients with non-small cell lung cancer; results of a population-based study. *Lung Cancer*. 2004; 46:233–245. [PubMed: 15474672]
29. Grose D, Devereux G, Brown L, Jones R, Sharma D, Selby C, Morrison DS, Docherty K, McIntosh D, Loudon G, Downer P, Nicolson M, Milroy R. Variation in comorbidity and clinical management in patients newly diagnosed with lung cancer in four Scottish centers. *J Thorac Oncol*. 2011; 6:500–509. [PubMed: 21258251]
30. Gerber DE, Rasco DW, Le P, Yan J, Dowell JE, Xie Y. Predictors and impact of second-line chemotherapy for advanced non-small cell lung cancer in the United States: real-world considerations for maintenance therapy. *J Thorac Oncol*. 2011; 6:365–371. [PubMed: 21173713]

31. Forrest LF, Adams J, Wareham H, Rubin G, White M. Socioeconomic inequalities in lung cancer treatment: systematic review and meta-analysis. *PLoS Med*. 2013; 10:e1001376. [PubMed: 23393428]
32. Forrest LF, White M, Rubin G, Adams J. The role of patient, tumour and system factors in socioeconomic inequalities in lung cancer treatment: population-based study. *Br J Cancer*. 2014; 111:608–618. [PubMed: 24918815]
33. Shavers VL, Brown ML. Racial and ethnic disparities in the receipt of cancer treatment. *Journal of the National Cancer Institute*. 2002; 94:334–357. [PubMed: 11880473]
34. Ritzwoller DP, Carroll NM, Delate T, Hornbrook MC, Kushi L, Bowles EJA, Freml JM, Huang K, Loggers ET. Patterns and predictors of first-line chemotherapy use among adults with advanced non-small cell lung cancer in the cancer research network. *Lung Cancer*. 2012; 78:245–252. [PubMed: 23022316]
35. Greenberg ER, Chute CG, Stukel T, Baron JA, Freeman DH, Yates J, Korson R. Social and economic factors in the choice of lung cancer treatment. A population-based study in two rural states. *N Engl J Med*. 1988; 318:612–617. [PubMed: 2830514]
36. Johnson AM, Hines RB, Johnson JA, Bayakly AR. Treatment and survival disparities in lung cancer: the effect of social environment and place of residence. *Lung Cancer*. 2014; 83:401–407. [PubMed: 24491311]
37. National Cancer Institute. [Accessed June 17, 2015] About the SEER registries. <http://seer.cancer.gov/registries/>
38. National Cancer Institute. [Accessed June 17, 2015] Overview of the SEER program. <http://seer.cancer.gov/about/overview.html>
39. Warren JL, Klabunde CN, Schrag D, Bach PB, Riley GF. Overview of the SEER-Medicare data: content, research applications, and generalizability to the United States elderly population. *Med Care*. 2002; 40:IV-3–18.
40. Klabunde CN, Potosky AL, Legler JM, Warren JL. Development of a comorbidity index using physician claims data. *Journal of clinical epidemiology*. 2000; 53:1258–1267. [PubMed: 11146273]
41. Brooks JM, Cook EA, Chapman CG, Kulchaitanaroaj P, Chrischilles EA, Welch S, Robinson J. Geographic variation in statin use for complex acute myocardial infarction patients: evidence of effective care? *Med Care*. 2014; 52(Suppl 3):S37–44. [PubMed: 24561757]
42. Tang Y, Brooks JM, Wetmore JB, Shireman TI. Association between higher rates of cardioprotective drug use and survival in patients on dialysis. *Res Social Adm Pharm*. 2014
43. Polgreen LA, Cook EA, Brooks JM, Tang Y, Polgreen PM. Increased statin prescribing does not lower pneumonia risk. *Clin Infect Dis*. 2015; 60:1760–1766. [PubMed: 25759433]
44. Brooks JM, Cook E, Chapman CG, Schroeder MC, EAC, Schneider KM, Kulchaitanaroaj P, Robinson J. Statin use after acute myocardial infarction by patient complexity: are the rates right? *Med Care*. 2015; 53:324–331. [PubMed: 25719431]
45. Brooks JM, Chrischilles EA, Landrum MB, Wright KB, Fang G, Winer EP, Keating NL. Survival implications associated with variation in mastectomy rates for early-staged breast cancer. *Int J Surg Oncol*. 2012; 2012:127854. [PubMed: 22928097]
46. Fang G, Brooks JM, Chrischilles EA. Comparison of instrumental variable analysis using a new instrument with risk adjustment methods to reduce confounding by indication. *Am J Epidemiol*. 2012; 175:1142–1151. [PubMed: 22510277]
47. Brooks JM, Tang Y, Chapman CG, Cook EA, Chrischilles EA. What is the effect of area size when using local area practice style as an instrument? *J Clin Epidemiol*. 2013; 66:S69–83. [PubMed: 23849157]
48. Fang G, Brooks JM, Chrischilles EA. A new method to isolate local-area practice styles in prescription use as the basis for instrumental variables in comparative effectiveness research. *Med Care*. 2010; 48:710–717. [PubMed: 20613655]
49. Highton AM, Monach J, Congleton J. Investigation and management of lung cancer in older adults. *Lung Cancer*. 2010; 69:209–212. [PubMed: 20018399]
50. Folland S, Stano M. Sources of small area variations in the use of medical care. *Journal of health economics*. 1989; 8:85–107. [PubMed: 10303558]

51. Wang J, Kuo YF, Freeman J, Goodwin JS. Increasing access to medical oncology consultation in older patients with stage II-IIIa non-small-cell lung cancer. *Med Oncol*. 2008; 25:125–132. [PubMed: 18488153]
52. Wennberg DE, Wennberg JE. Addressing variations: is there hope for the future? *Health affairs (Project Hope)*. 2003; (Suppl Web Exclusives):W3-614–617.
53. Brook RH, Lohr K, Chassin M, Koseoff J, Fink A, Solomon D. Geographic variations in the use of services: do they have any clinical significance? *Health affairs (Project Hope)*. 1984; 3:63–73. [PubMed: 6432668]

Highlights

- In our sample, 10% and 12% of patients received ACT and PORT, respectively.
- Patient and area-level characteristics were associated with adjuvant therapy use.
- Geographic variation in adjuvant therapy remained, even adjusting for covariates.
- More patients were treated less than expected, rather than more than expected.

Figure 1. Distribution of Area Treatment Ratios (ATRs) across local areas

The median ATR is shown for adjuvant chemotherapy (ACT), postoperative radiation (PORT), and no adjuvant therapy. Surrounding boxes correspond to the interquartile range and whiskers span 1.5 times the interquartile range.

Figure 2. Use of adjuvant therapy in two representative SEER registries

Area Treatment Ratios (ATRs) were calculated for each local area as an adjusted measure of the propensity of patients in that area to receive adjuvant therapy, controlling for patient and area-level characteristics. Areas were categorized as low-, mid-, and high-use based off of tertiles of ATR values.

Table 1
Patient and Area-level Characteristics by First Adjuvant Therapy Received within Four Months of Surgery

Variables	Levels	Adjuvant Therapy			Total (%) ^b (N=18,410)	P-value [*]
		ACT (%) ^a (N=1,866)	PORT (%) ^a (N=2,177)	None (%) ^a (N=14,367)		
Age	66–70	770 (13)	809 (14)	4251 (73)	5830 (32)	<0.0001
	71–75	679 (11)	768 (12)	4699 (76)	6146 (33)	
	76–80	332 (8)	445 (10)	3616 (82)	4393 (24)	
	81–84	67 (4)	117 (8)	1335 (88)	1519 (8)	
	85+	18 (3)	38 (7)	466 (89)	522 (3)	
Sex	Male	997 (11)	1233 (13)	7248 (76)	9478 (51)	<0.0001
	Female	869 (10)	944 (11)	7119 (80)	8932 (49)	
Race	White	1670 (10)	1925 (12)	12990 (78)	16585 (90)	0.0552
	Black	110 (11)	141 (14)	764 (75)	1015 (6)	
	Other	86 (11)	111 (14)	613 (76)	810 (4)	
Stage	I	786 (6)	606 (5)	12036 (90)	13428 (73)	<0.0001
	II	571 (22)	645 (25)	1362 (53)	2578 (14)	
	IIIA	509 (21)	926 (39)	969 (40)	2404 (13)	
Tumor size	T0/T1	448 (6)	460 (6)	6425 (88)	7333 (40)	<0.0001
	T2	1207 (13)	1193 (13)	6586 (73)	8986 (49)	
	T3	140 (14)	372 (38)	468 (48)	980 (5)	
	Unknown	71 (6)	152 (14)	888 (80)	1111 (6)	
Lymph nodes	N0	858 (6)	787 (6)	12100 (88)	13745 (75)	<0.0001
	N1	571 (22)	653 (25)	1349 (52)	2573 (14)	
	N2	400 (26)	616 (40)	529 (34)	1545 (8)	
	Unknown	37 (7)	121 (22)	389 (71)	547 (3)	
Pneumonectomy	No	1717 (10)	1963 (11)	13682 (79)	17362 (94)	<0.0001
	Yes	149 (14)	214 (20)	685 (65)	1048 (6)	
Lobectomy	No	304 (10)	499 (16)	2359 (75)	3162 (17)	<0.0001
	Yes	1562 (10)	1678 (11)	12008 (79)	15248 (83)	

Variables	Levels	Adjuvant Therapy			Total (%)* (N=18,410)	P-value*
		ACT (%)* (N=1,866)	PORT (%)* (N=2,177)	None (%)* (N=14,367)		
Wedge	No	1430 (11)	1571 (12)	10591 (78)	13592 (74)	0.0045
	Yes	436 (9)	606 (13)	3776 (78)	4818 (26)	
Comorbidity	0	840 (10)	1085 (14)	6141 (76)	8066 (44)	<0.0001
	1	629 (10)	701 (11)	4834 (78)	6164 (33)	
	2+	397 (10)	391 (9)	3392 (81)	4180 (23)	
	Big metro	1184 (11)	1297 (12)	8442 (77)	10923 (59)	
Urban/rural	Metro	429 (9)	560 (12)	3752 (79)	4741 (26)	0.0333
	Urban	91 (9)	129 (12)	840 (79)	1060 (6)	
	Less urban	129 (9)	155 (11)	1090 (79)	1374 (7)	
	Rural	33 (11)	36 (12)	243 (78)	312 (2)	
	1992–1993	47 (3)	353 (20)	1344 (77)	1744 (9)	
Year of surgery	1994–1995	69 (4)	346 (19)	1398 (77)	1813 (10)	<0.0001
	1996–1997	74 (4)	272 (16)	1332 (79)	1678 (9)	
	1998–1999	89 (6)	187 (13)	1131 (80)	1407 (7)	
	2000–2001	158 (6)	348 (12)	2310 (82)	2816 (15)	
	2002–2003	190 (7)	307 (11)	2419 (83)	2916 (16)	
	2004–2005	602 (20)	201 (7)	2201 (73)	3004 (16)	
	2006–2008	637 (21)	163 (5)	2232 (74)	3032 (16)	
	Quartile 1	432 (9)	520 (11)	3608 (79)	4560 (25)	
Median household income in the patient's census tract, by quintiles	Quartile 2	463 (10)	564 (12)	3566 (78)	4593 (25)	0.0103
	Quartile 3	456 (10)	578 (13)	3546 (77)	4580 (25)	
	Quartile 4	514 (11)	493 (11)	3550 (78)	4557 (25)	
	Quartile 1	490 (11)	494 (11)	3556 (78)	4540 (25)	
Percent with only high school education in the patient's census tract, by quintiles	Quartile 2	467 (10)	539 (12)	3563 (78)	4569 (25)	0.1388
	Quartile 3	474 (10)	561 (12)	3531 (77)	4566 (25)	
	Quartile 4	434 (9)	561 (12)	3620 (78)	4615 (25)	
	Quartile 1	416 (9)	555 (12)	3600 (79)	4571 (25)	
Percent white in the patient's census tract, by quintiles	Quartile 2	424 (9)	586 (13)	3571 (78)	4581 (25)	<0.0001

Variables	Levels	Adjuvant Therapy			Total (%) ^b (N=18,410)	P-value [*]
		ACT (%) ^a (N=1,866)	PORT (%) ^a (N=2,177)	None (%) ^a (N=14,367)		
Percent of residents living below the poverty level in the patient's census tract, by quintiles	Quartile 3	514 (11)	536 (12)	3511 (77)	4561 (25)	
	Quartile 4	511 (11)	478 (10)	3588 (78)	4577 (25)	
	Quartile 1	450 (12)	354 (10)	2805 (78)	3609 (25)	0.0552
	Quartile 2	464 (13)	357 (10)	2809 (77)	3630 (25)	
	Quartile 3	410 (11)	335 (9)	2911 (80)	3656 (25)	
	Quartile 4	414 (11)	396 (11)	2863 (78)	3673 (25)	

ACT = adjuvant chemotherapy, PORT = postoperative radiation therapy

^a Percentages reported are row percentages

^b Percentages reported are column percentages

^{*} P-values are based on chi-squared analyses comparing adjuvant chemotherapy (ACT), postoperative radiation therapy (PORT) and no adjuvant therapy.