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Inequalities in Lung Cancer Care of Elderly Patients with Schizophrenia: An Observational Cohort Study

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Abstract

Objective—Cancer mortality is higher in individuals with schizophrenia, a finding that may be due, in part, to inequalities in care. We evaluated gaps in lung cancer diagnosis, treatment, and survival among elderly individuals with schizophrenia.

Methods—The Surveillance, Epidemiology, and End Results (SEER) database linked to Medicare records was used to identify primary non-small cell lung cancer (NSCLC) patients ≥66 years of age. Lung cancer stage, diagnostic evaluation, and rates of stage-appropriate treatment were compared among patients with and without schizophrenia using unadjusted and multiple regression analyses. Survival was compared among groups using Kaplan-Meier methods.

Results—Of the 96,702 NSCLC patients in SEER, 1,303 (1.3%) had schizophrenia. In comparison to the general population, patients with schizophrenia were less likely to present with late-stage disease after controlling for age, sex, marital status, race/ethnicity, income, histology, and comorbidities (odds ratio [OR]: 0.82; 95% confidence interval [CI]: 0.73-0.93) and were less likely to undergo appropriate evaluation ($p<0.050$ for all comparisons). Adjusting for similar factors, patients with schizophrenia were also less likely to receive stage-appropriate treatment (OR: 0.50, 95% CI: 0.43-0.58). Survival was decreased among patients with schizophrenia (mean survival 22.3 vs. 26.3 months, $p=0.002$), however no differences were observed after controlling for treatment received ($p=0.4$).

Conclusions—Elderly patients with schizophrenia present with earlier stages of lung cancer, but are less likely to undergo diagnostic evaluation or to receive stage appropriate treatment, resulting in poorer outcomes. Efforts to increase treatment rates for elderly patients with schizophrenia may lead to improved survival in this group.

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Keywords

Schizophrenia; elderly; non-small cell lung cancer; health care disparities; cigarette smoking; health outcomes

Introduction

Schizophrenia is a chronic mental illness that affects approximately 1% of the population (1). In comparison to the general population, individuals with schizophrenia have a shorter lifespan(2), a gap that has widened in recent decades(3). After suicide, cancer is one of the leading causes of mortality among these individuals(4, 5) and a recent analysis showed that patients with schizophrenia are at a 30% increased risk of death from cancer(3). Lung cancer, the leading cause of cancer mortality in the United States (US) (6), is a disease primarily affecting older adults(7), and a significant concern for the elderly population with schizophrenia because of their increased disease burden due to high smoking rates(8). Furthermore, as the number of elderly patients with schizophrenia increases due to aging of the US population and improvement in psychotropic medications, the burden of lung cancer among these patients is expected to grow.

Evidence shows that individuals with schizophrenia are twice as likely to die from lung cancer in comparison to the general population(4). The increased burden of cancer mortality among these individuals may be a result of delayed diagnosis and suboptimal treatment(9, 10). This problem may be exacerbated among older patients who, even without significant mental illness, are often not appropriately staged or treated for lung cancer(11, 12). However, there is little data characterizing specific deficiencies in diagnosis, clinical evaluation and treatment of lung cancer that explains the poorer outcomes experienced by patients with schizophrenia. This information may provide specific targets for improvement in the care and outcomes of this vulnerable population.

Using a national cancer database linked with Medicare data, we evaluated disparities in lung cancer diagnosis, evaluation, treatment and survival in elderly patients with schizophrenia diagnosed with primary non-small cell lung cancer (NSCLC).

Methods

Study Population

We used the Surveillance, Epidemiology and End Results (SEER) database linked to Medicare claims to assemble the study cohort. The SEER registry is sponsored by the National Cancer Institute and integrates data from 17 regional cancer registries throughout the US(13). The SEER-Medicare database encompasses approximately 94% of individuals ≥65 years of age in the SEER registry(14).

Using the SEER-Medicare database, we identified individuals ≥66 years of age (so that they would have at least a year of Medicare claims available) with histologically confirmed primary NSCLC diagnosed between 1992 and 2007. Patients were excluded if their

diagnoses were established post-mortem or if they lacked part B (outpatient) coverage or were insured by a Health Maintenance Organization(15).

Diagnosis of Schizophrenia and Other Covariates

We identified patients with schizophrenia, prior to lung cancer diagnosis, using Medicare inpatient, physician, and outpatient ICD-9 codes (295.xx), which have been shown to be 90-100% reliable in validation studies(16, 17). We ascertained Medicare claims for long-term care facility use to identify institutionalized patients with schizophrenia and used records of utilization of home services to assess their functional status(11). Additional markers of disease severity included episodes of emergency department (ED) and hospital admissions for schizophrenia and diagnosis codes signifying drug or alcohol abuse(11).

Sociodemographic information, such as age, gender, race/ethnicity, marital status and estimated income was obtained from the SEER and Medicare databases. We evaluated the number of primary care visits during the year prior to lung cancer diagnosis as a measure of health care utilization. The burden of comorbid illness (other than lung cancer and schizophrenia) was evaluated using the Deyo adaptation of the Charlson comorbidity index. From SEER data, we obtained information on tumor location and histology.

Outcomes

We analyzed inequalities in lung cancer care between elderly patients with and without schizophrenia with respect to four primary outcomes: 1) stage at diagnosis; 2) diagnostic and staging evaluation; 3) stage-appropriate treatment; and 4) survival. Lung cancer stage was determined based on the most recent Tumor, Node and Metastasis staging system of the American Joint Commission on Cancer using SEER data. Patients with stage III or IV lung cancer were classified as diagnosed with advanced-stage disease. The extent of diagnostic evaluation was examined using Medicare claims. Procedures considered relevant to the diagnostic evaluation of all patients, regardless of stage, included bronchoscopy, fine needle aspiration (FNA), chest computed tomography (CT) scans, positron emission topography (PET) scans, and mediastinoscopy(18). For individuals with stage II-IV, we assessed use of brain magnetic resonance imaging (MRI). For individuals that did not undergo a PET scan, we assessed for use of an abdominal CT for all stages and bone scans for those with stage III-IV disease. Additionally, we evaluated whether patients had at least one visit with a surgeon (stage I-IIIA), a medical oncologist (stage IB-IV), and/or a radiation oncologist (unresected stage I-IIIA and stage IIIB).

Treatment with surgery and radiation therapy (RT) was ascertained from SEER and Medicare data. Administration of chemotherapy was established using Medicare data. We evaluated rates of appropriate treatment, as specified by current guidelines(19), including surgery for stages I-IIIA (followed by adjuvant chemotherapy for stage II-IIIA disease), combined chemotherapy and RT for stage IIIB disease, and chemotherapy for stage IV NSCLC. As some elderly patients may not be candidates for surgery or aggressive chemoradiation, we also evaluated the number of unresected patients with stage I-II NSCLC treated with RT or stage IIIB patients who underwent RT or chemotherapy alone.

Overall survival was determined using Medicare data. Survival time was estimated from the time of diagnosis until the date of death or last follow-up (December 31, 2009). The Institutional Review Board of Mount Sinai School of Medicine exempted this study from an ethics board approval.

Statistical Analysis

Differences in sociodemographic characteristics between patients with and without schizophrenia were evaluated using chi-square and t-tests, as appropriate. Unadjusted differences in lung cancer stage, diagnostic evaluation, and treatment were assessed using a chi-square test. We used logistic regression analysis to assess the association between these outcomes and a diagnosis of schizophrenia after controlling for age, sex, marital status, race/ethnicity, income, histology, and comorbidity status. Adjustments for cancer stage were made in the analyses assessing diagnostic evaluation or treatment. We used Kaplan-Meier methods to estimate survival among lung cancer patients with and without schizophrenia. We then stratified the cohort by use of stage-appropriate treatment, and repeated survival analyses within each strata, comparing outcomes in patients with and without schizophrenia. To assess differences in survival accounting for potential confounders, we fitted a Cox model evaluating overall survival with schizophrenia as our primary exposure of interest, adjusting for age, sex, race/ethnicity, marital status, median income in zip code area of residence, comorbidity score, tumor histology, tumor stage, and tumor site. In a second model, we further adjusted for stage-appropriate lung cancer treatment.

Analyses were performed with SPSS statistical package (IBM, Chicago, IL) using two tailed p-values.

Results

Of the 96,702 patients with NSCLC in SEER-Medicare, 1,303 (1.3%) had a diagnosis of schizophrenia. Overall, elderly lung cancer patients with schizophrenia were younger and more likely to be female, black, unmarried, and reside in areas with the lowest income quartile (Table 1). Middle lobe tumors and squamous cell histology were also more frequent among patients with schizophrenia. Additionally, individuals with schizophrenia had more visits with their PCP in the year prior to diagnosis and experienced a greater burden of comorbid illness.

Stage at Diagnosis and Evaluation

Patients with schizophrenia were more likely to be diagnosed with early-stage (I-II) lung cancer compared to the general population (34.9% vs. 30.6%, respectively; $p<0.001$; Table 2). Adjusted analysis (including number of PCP visits in the last year) also showed that patients with schizophrenia had 0.82 (95% Confidence Interval [CI]: 0.73-0.93) lower odds of being diagnosed with late-stage (III- IV) NSCLC compared with the general population.

Use of chest CT ($p=0.01$), PET scan ($p<0.001$), mediastinoscopy ($p=0.01$), abdominal CT ($p<0.001$), and bone scan ($p<0.001$) was less frequent among elderly patients with schizophrenia (Table 3). However, no significant differences were observed in the use of bronchoscopy, FNA, and brain MRI ($p>0.05$ for all comparisons). In analyses adjusting for

sociodemographics, comorbid illness, and cancer stage, bronchoscopy was also less likely to be used in the diagnostic evaluation of patients with schizophrenia (OR: 0.88; 95% CI: 0.79-0.98; Table 3). Results similar to our unadjusted analysis were observed for other diagnostic tests.

Lung cancer patients with schizophrenia were less likely to be evaluated by a surgeon (58.2% vs. 53.5%; p=0.02) or to have visited a medical oncologist (58.5% vs. 49.4%; p<0.001; Table 4). Patients with schizophrenia were 4% less likely to visit with a radiation oncologist however, this difference was not statistical significant (37.1% vs. 41.2%, p=0.06).

Analyses adjusting for year of diagnosis showed similar associations between a diagnosis of schizophrenia with disease stage and diagnostic evaluation.

Stage-appropriate Treatment

Elderly patients with schizophrenia were less likely to receive stage-appropriate NSCLC treatment compared to those without schizophrenia (38.4% vs. 49.1%, respectively; p<0.001; Table 5). When analyzed according to stage, patients with schizophrenia were less likely to undergo surgery for stages I-IIIA (p<0.001), receive combined RT and chemotherapy for stage IIIB (p<0.001) or chemotherapy for stage IV (p<0.001) NSCLC. Among stage I-II patients who were not treated with surgical resection, RT was also less frequently used among patients with schizophrenia (p=0.001). However, no differences were observed in the use of adjuvant chemotherapy for resected stage II-IIIA disease (p=0.52). Adjusted analysis showed that patients with schizophrenia had half (95% CI: 0.43-0.58) the odds of receiving stage-appropriate treatment compared with the patients without schizophrenia. Similar results were obtained when year of diagnosis was included in the model, thus controlling for potential temporal changes in the treatment of lung cancer.

Long-term care facility use (OR: 0.62; 95% CI: 0.38-0.99), and ED visits (OR: 0.59; 95% CI: 0.40-0.87) or hospitalizations (OR: 0.59; 95% CI: 0.41-0.85) for schizophrenia were significantly associated with receiving suboptimal treatment in unadjusted and adjusted analyses.

Survival

Kaplan-Meier analysis revealed that NSCLC patients with schizophrenia had significantly shorter overall survival (mean survival 22.3 vs. 26.3 months; p=0.002). After stratifying by use of stage-appropriate treatment, patients had similar survival times (mean survival 41.5 vs. 43.1 months for appropriately treated patients and 9.8 vs. 10.3 months for not appropriately treated patients with and without schizophrenia, respectively; for both comparisons p=0.4). Our Cox model also showed schizophrenia was associated with an increased hazard of death (hazard ratio [HR]: 1.07; 95% CI: 1.01-1.13), after adjustment for potential confounders except lung cancer treatment. After including stage-appropriate treatment in the model, there was no significant difference in overall survival (HR: 1.02; 95% CI: 0.96-1.09).

Discussion

The burden of lung cancer is increased in elderly patients with schizophrenia. Using a large population-based registry, we demonstrated that individuals with schizophrenia presented with earlier stages of lung cancer, but were less likely to undergo standard diagnostic evaluation or to receive stage-appropriate treatment. In addition, survival was decreased among elderly patients with schizophrenia, a finding potentially explained, in part, by differences in utilization of stage-appropriate treatment. These results show the need to assess the reasons and develop interventions to eliminate these inequalities in care, thus improving the outcomes of this vulnerable population.

Elderly cancer patients with schizophrenia are an understudied population. Both the elderly as well as individuals with mental illness are reported to receive suboptimal health care and to have poorer outcomes(12, 20-23); however, there is a paucity of information pertaining to the care of cancer in general and lung cancer specifically among elderly patients with schizophrenia. Recognition of inequalities in lung cancer care in this population is important because it will help advance necessary policy changes to promote better outcomes for these patients. Additionally, similar inequalities may exist for other cancers, highlighting the need for further research.

Elderly patients with schizophrenia in our study were more likely to present with early-stage lung cancer, a somewhat unexpected result. This finding may be due to an increased utilization of primary care services by individuals with schizophrenia, a previously reported phenomenon(24), which may be more prominent in Medicare beneficiaries. It is also possible that physicians treating patients with schizophrenia have a heightened level of suspicion for lung cancer due to increased rates of smoking in this population. Patients with schizophrenia presenting with pulmonary comorbidities may have undergone more aggressive evaluation, thus, finding cancer at an earlier stage. Another mechanism for the increase rate of early disease among patients with schizophrenia may be related to antipsychotic medication use. Several large epidemiological studies and, more recently, laboratory data suggest that antipsychotics may have an anti-cancer effect(25-28). If these data are correct, lung cancer may progress slower in patients with schizophrenia treated with antipsychotic medications, increasing the opportunities for diagnosis at an early stage. Lastly, individuals with schizophrenia in our study were more likely to have squamous cell carcinomas, a centrally located cancer that, due to compression of central airways and blood vessels, may produce symptoms and, ultimately, earlier diagnosis.

Despite an earlier stage at diagnosis, patients with schizophrenia were less likely to receive stage-appropriate diagnostic evaluation and treatment. Inequalities in disease management for individuals with mental illnesses have been reported in the literature and range from suboptimal preventative medical care (29) to poor quality management of chronic diseases and surgical interventions (30, 31). In a meta-analysis of cardiovascular disease management, patients with severe mental illnesses were less likely to receive appropriate prescriptions for cardiovascular disease or to undergo basic cardiac procedures (31). Similarly, another study showed that individuals with mental illnesses received substandard diabetic care and had more diabetic complications(30). In one study assessing the receipt of

coronary artery bypass graft surgery among patients in New York State, individuals with any mental disorder were more likely to be treated by a low-quality surgeon(32). Our results extend these findings to the treatment of lung cancer, an important cause of death in this population.

The reasons for these disparities in the care of patients with schizophrenia are complex and not well understood. One potential explanation may be related to difficulties for patients in navigating the health system(33, 34). Lung cancer treatment requires patients to make specialist appointments, schedule and complete multiple diagnostic tests, and, for radiation and chemotherapy, attend multiple treatment sessions. These tasks can be overwhelming, particularly for patients with schizophrenia, who may experience varying levels of cognitive dysfunction. If indeed this is a major barrier for appropriate lung cancer care, future initiatives may evaluate the effectiveness of patient navigators, who have been found to effectively address racial disparities in cancer care(35).

Another reason for these inequalities may be that individuals with schizophrenia were unable to consent or less likely adhere to diagnostic tests and lung cancer treatments. This barrier may be related to difficulties understanding treatments and outcomes. We found that the severity of schizophrenia was significantly associated with receiving suboptimal treatment, suggesting that more impaired patients are at particular risk for undertreatment. In addition, it is possible that providers may contribute to these inequalities because of uncertainty about the impact of lung cancer treatments on the outcomes of patients with schizophrenia that have, in general, a reduced life expectancy.

Our analysis has some strengths and limitations that are worth mentioning. Our study was limited to elderly patients, thus these findings may not be generalizable to younger populations. However, lung cancer is predominantly a disease of older adults, and elderly patients with schizophrenia are an understudied population. We were unable to evaluate the smoking history of study patients due to lack of data on tobacco use in the SEER-Medicare database. The number of years of tobacco consumption is an important indicator of lung cancer survival among the schizophrenic population. However, more than 90% of all lung cancer patients have a history of smoking(36), potentially attenuating differences in smoking patterns among patients with schizophrenia compared to the general population. Given the relatively rare treatment of nicotine dependence in patients with severe mental illness compared to the general population, exploring the impact of smoking status and cessation should be considered in future studies(37). We were also unable to identify the underlying reasons for suboptimal evaluation and treatment of patients with schizophrenia, as this data is not available in the SEER-Medicare database. However, use of the SEER-Medicare data allowed us to evaluate the patterns of care for a large, nationally representative cohort of lung cancer patients with schizophrenia. One study that analyzed lung cancer treatment among 29 patients with schizophrenia found that treatment decisions were not based solely on whether the patient had schizophrenia but rather a combination of the patients' comorbidity status and mental capacity(38). This finding, while promising, should be analyzed in a larger patient population.

In summary, our study provides evidence of considerable inequalities in the lung cancer care received by elderly patients with schizophrenia, a finding that translates into worse survival of these vulnerable individuals. Future explorations into the underlying reasons for this disparity are necessary to improve lung cancer care and outcomes in for these patients.

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Abbreviations

NSCLC	Non-small cell lung cancer
SEER	Surveillance Epidemiology and End-Results
ICD-9	International Classification of Disease, Ninth Edition
FNA	Fine needle aspiration
CT	Computed tomography
PET	Positron emission topography
MRI	Magnetic resonance imaging
PCP	Primary care provider
ED	Emergency department
RT	Radiation Therapy

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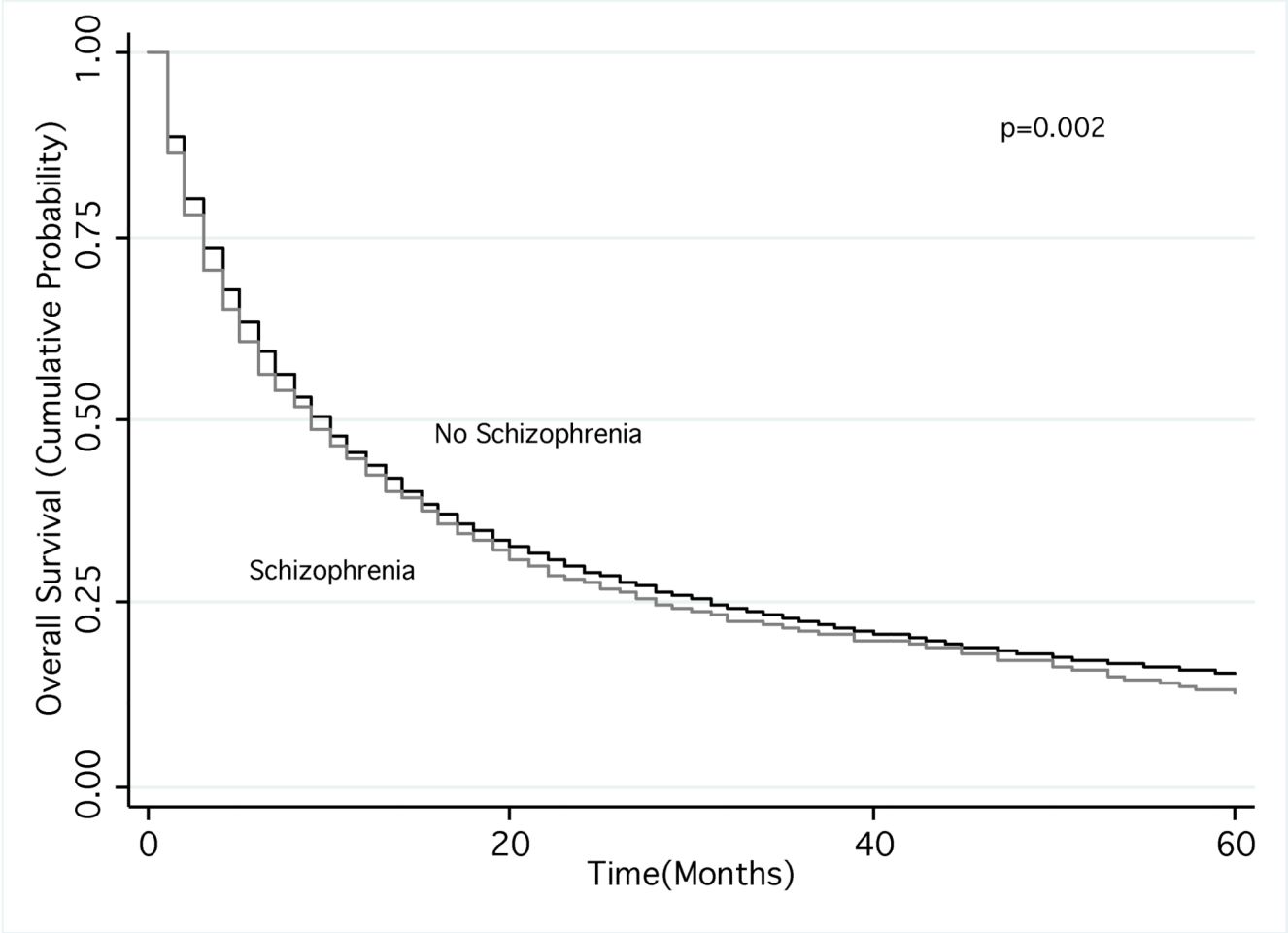

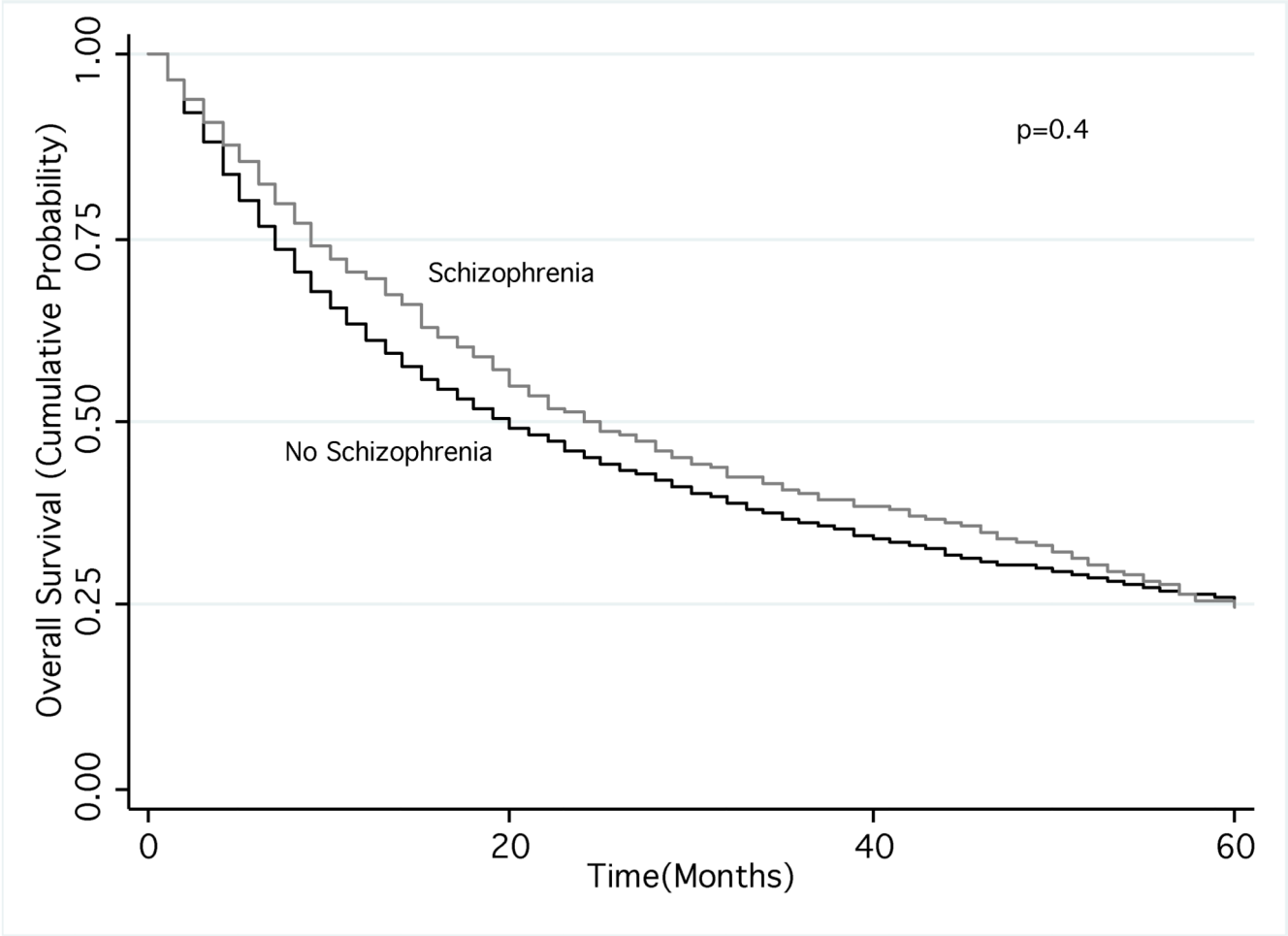

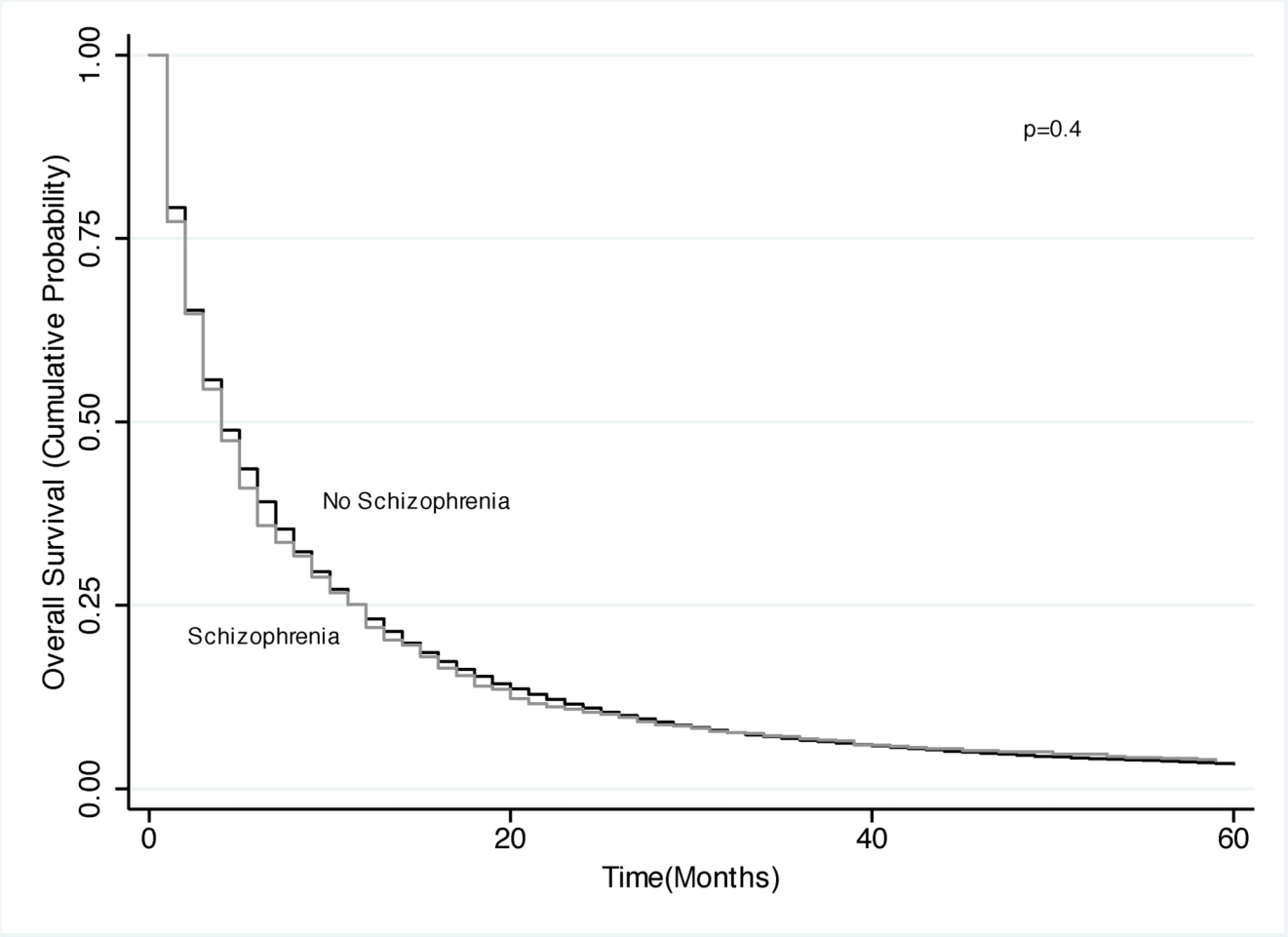

Figure 1.

Table 1

Characteristics of Study Patients

	No Schizophrenia N = 95,399	Schizophrenia N = 1,303
Age, years, mean (SD)	75.1 (6.1)	73.9 (5.6)
Female, N (%)	43,080 (45.2)	720 (55.3)
Marital Status, N (%)	50,555 (53.0)	346 (26.6)
Race/Ethnicity, N (%)		
White	79,615 (83.4)	965 (74.1)
Black	7,881 (8.3)	240 (18.4)
Hispanic	3,203 (3.4)	54 (4.1)
Other	4,700 (4.9)	44 (3.4)
Income Quartiles, N (%)		
Quartile 1 (Lowest)	23,992 (25.2)	443 (34.0)
Quartile 2	23,849 (25.0)	317 (24.3)
Quartile 3	23,762 (24.9)	320 (24.6)
Quartile 4 (Highest)	23,693 (24.9)	222 (17.1)
Histology, N (%)		
Adenocarcinoma	45,832 (48.0)	540 (41.5)
Squamous Cell	30,603 (32.1)	520 (39.9)
Large Cell	6,569 (6.9)	85 (6.5)
Other	12,395 (13.0)	158 (12.1)
Tumor Location, N (%)		
Upper Lobe	47,291 (49.6)	643 (49.4)
Middle Lobe	3,779 (4.0)	73 (5.6)
Lower Lobe	25,375 (26.6)	325 (24.9)
Other	18,954 (19.9)	262 (20.1)
Total PCP[1] **visits in year prior to diagnosis**, mean (SD)	6.2 (6.4)	8.3 (7.9)
Comorbidity Score, N (%)		
≤1.0	36,346 (38.0)	314 (24.1)
1.0 – 2.0	26,969 (28.3)	382 (29.3)
2.0 – 4.0	21,611 (22.7)	365 (28.0)
≥4.0	10,473 (11.0)	242 (18.6)

[1]PCP=primary care provider

Table 2

Stage at Diagnosis of Patients with and without Schizophrenia

Stage	No Schizophrenia N (%)	Schizophrenia N (%)	P-value[1]
I	24,899 (26.1)	398 (30.5)	**<0.001**
II	4,292 (4.5)	57 (4.4)	
III	29,501 (30.9)	423 (32.5)	
IV	35,596 (37.3)	413 (31.7)	
Unstaged	1,111 (1.2)	12 (0.9)	

[1] **Chi-square test**

Table 3

Diagnostic Evaluation of Patients with and without Schizophrenia

Test	No Schizophrenia N (%)	Schizophrenia N (%)	Test Use among Patients with Schizophrenia	
			Unadjusted[2] OR[1] (95% CI)	Adjusted[3] OR (95% CI)
All Stages:				
Bronchoscopy	47,895 (50.2)	631 (48.4)	0.93 (0.84-1.04)	0.88 (0.79-0.98)
Fine Needle Aspiration	39,677 (41.6)	542 (41.6)	1.00 (0.90-1.12)	1.01 (0.90-1.13)
Positron Emission Test	11,428 (12.0)	111 (8.5)	0.68 (0.56-0.83)	0.68 (0.56-0.83)
Chest Computed Tomography	80,640 (84.5)	1,069 (82.0)	0.84 (0.73-0.96)	0.84 (0.73-0.98)
Mediastinoscopy	7,658 (8.0)	77 (5.9)	0.72 (0.57-0.91)	0.75 (0.59-0.95)
Stage II-IV:				
Brain Magnetic Resonance Imaging	144 (0.2)	≤11 (0.2)	1.08 (0.27-4.36)	1.00 (0.25-4.06)
If no PET:				
Abdominal Computed Tomography	32,054 (38.2)	373 (31.3)	0.74 (0.65-0.83)	0.78 (0.69-0.88)
Bone Scan (stages III-IV)	28,625 (49.1)	316 (41.2)	0.73 (0.63-0.84)	0.74 (0.64-0.86)

[1] OR = odds ratio

[2] Logistic regression model, unadjusted

[3] Logistic regression model, adjusted for age, gender, marital status, race/ethnicity, income, histology, comorbidities, and stage

Table 4

Cancer Specialist Visits among Patients with and without Schizophrenia

Specialist	No Schizophrenia N (%)	Schizophrenia N (%)	Specialist Visit among Patients with Schizophrenia	
			Unadjusted[2] OR[1] (95% CI)	Adjusted[3] OR (95% CI)
Surgeon	22,729 (58.2)	319 (53.5)	0.83 (0.70-0.97)	0.98 (0.74-1.04)
Medical Oncologist	42,727 (58.5)	462 (49.4)	0.69 (0.61-0.79)	0.73 (0.64-0.83)
Radiation Oncologist	14,234 (41.2)	202 (37.1)	0.84 (0.71-1.00)	0.80 (0.67-0.96)

[1] OR = odds ratio

[2] Logistic regression model, unadjusted

[3] Logistic regression model, adjusted for age, gender, marital status, race/ethnicity, income, histology, comorbidities, and stage

Table 5

Stage-Appropriate Treatment among Patients with and without Schizophrenia

Stage	No Schizophrenia N (%)	Schizophrenia N (%)	Treatment among Patients with Schizophrenia	
			Unadjusted[2] OR[1] (95% CI)	Adjusted[3] OR (95% CI)
All Stages	45,365 (49.1)	484 (38.4)	0.65 (0.58-0.73)	0.50 (0.43-0.58)
Stage I-IIIA				
Surgery	23,519 (60.5)	313 (53.0)	0.73 (0.62-0.86)	0.82 (0.68-0.98)
Resected Stage II-IIIA				
Adjuvant Chemotherapy	1,132 (17.7)	≤ 11 (14.9)	0.81 (0.43-1.54)	0.84 (0.44-1.62)
Unresected Stage I-II				
Radiation Therapy	5,261 (62.7)	84 (51.5)	0.63 (0.46-0.86)	0.62 (0.45-0.85)
Stage IIIB				
Radiation and Chemotherapy	4,225 (22.2)	27 (10.2)	0.39 (0.26-0.60)	0.39 (0.26-0.58)
Radiation or Chemotherapy	7,689 (40.4)	91 (34.5)		
Neither	7,106 (37.4)	146 (55.3)		
Stage IV				
Chemotherapy	12,981 (36.5)	70 (16.9)	0.36 (0.28-0.48)	0.39 (0.30-0.50)

[1] OR = odds ratio

[2] Logistic regression model, unadjusted

[3] Logistic regression model, adjusted for age, gender, marital status, race/ethnicity, income, histology, and comorbidities