Predictors of Unplanned Hospitalizations in Patients With Nonmetastatic Lung Cancer During Chemotherapy

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Fessele and Hayat provided the statistical support and analysis. Fessele completed the data collection. All authors contributed to the conceptualization and design and the manuscript preparation.

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Purpose/Objectives: To determine predictors of unplanned hospitalizations in patients with lung cancer to receive chemotherapy in the outpatient setting and examine the potential financial burden of these events.

Design: Retrospective, longitudinal cohort study.

Setting: The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER)–Medicare linked database.

Sample: Of 104,388 incident cases of lung cancer diagnosed from 2005–2009, 2,457 cases of patients with lung cancer who received outpatient chemotherapy were identified. Patients were aged 66 years or older at diagnosis, had uninterrupted Medicare Part A and B coverage with no health maintenance organization enrollment, and received IV chemotherapy at least once.

Methods: Generalized estimating equations was used.

Main Research Variables: Patient age, sex, race, marital status, degree of residential urbanization, median income, education level, stage, receipt of radiation therapy, and comorbidities.

Findings: Younger age, non-White race, lower education, higher income, receipt of radiation therapy, and lack of preexisting comorbidity were significant predictors of the likelihood of an initial unplanned hospitalization for lung cancer. Non-White race, receipt of radiation therapy, and comorbidity were factors associated with an increased number of hospitalizations.

Conclusions: Unplanned hospitalizations are frequent, disruptive, and costly. This article defines areas for further exploration to identify patients at high risk for unexpected complications.

Implications for Nursing: This article represents a foundation for development of risk models to enable nursing evaluation of patient risk for chemotherapy treatment interruption and unplanned hospitalization.

Unplanned hospitalizations in patients receiving chemotherapy for nonmetastatic cancer disrupt potentially curative treatment regimens, significantly affect quality of life, and are costly to the patient and healthcare system. Efforts to identify patients at risk of requiring unexpected care are needed to prevent negative outcomes and improve care quality and value. Lung cancer is the second most commonly diagnosed cancer in Americans, with an average age of 70 years at presentation, and the leading cause of cancer deaths (American Cancer Society, 2016). Treatment typically includes combinations of surgical resection, chemotherapy, radiation therapy, targeted agents, and biotherapy, depending on histology, stage, and molecular characteristics. Extensive research has focused on identification of factors associated with increased risk of readmission postsurgery in this population (Hu, McMurry, Isbell, Stukenborg, & Kozower, 2014; McDevitt et al., 2013;

Puri et al., 2015; Stitzenberg, Chang, Smith, & Nielsen, 2015), but less is known about predictors of hospitalizations occurring during chemotherapy.

Objectives

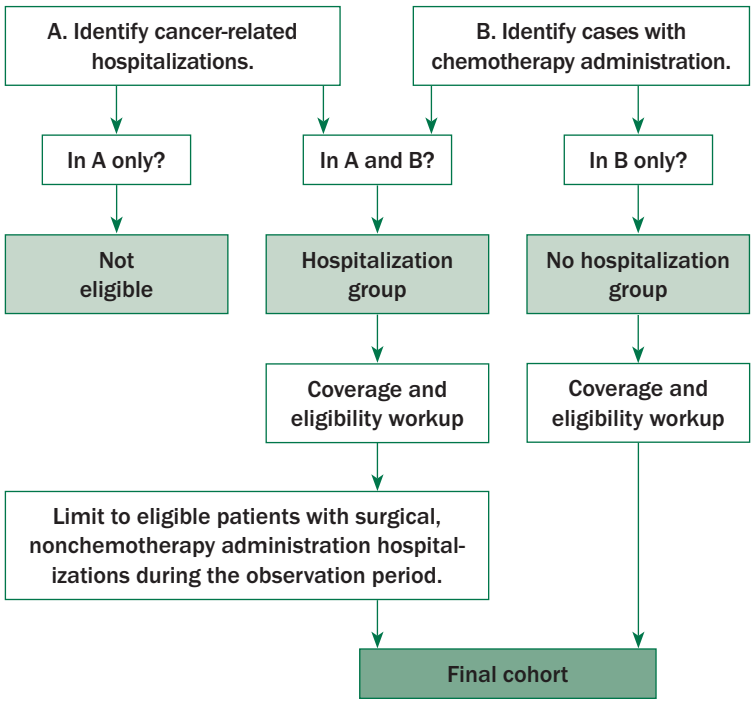
This study examined a cohort of patients with nonmetastatic lung cancer who received outpatient chemotherapy in the National Cancer Institute's (NCI's) Surveillance, Epidemiology, and End Results (SEER)–Medicare database. It was part of a larger project in which colorectal and lung cancer data were simultaneously obtained from the NCI SEER–Medicare linked database and then analyzed in parallel using the same methods to determine predictors of the initial, as well as repeated, unplanned hospitalizations. These tumor types were selected based on two main criteria: First, standard treatment for these solid tumors typically involves an initial surgical resection followed by a period of ambulatory chemotherapy administration with no planned inpatient component, and second, a review of the literature indicated the most frequent rates of hospital admission in these groups (González et al., 2005; Grant, Ferrell, Rivera, & Lee, 1995; Hassett et al., 2011; Weaver et al., 2006). An exploratory aim examined the potential financial burden of these events. The colorectal data analysis is published elsewhere (Fessele, Hayat, Mayer, & Atkins, 2016).

Chemotherapy for patients with solid tumors, such as those with lung cancer, is intended to be administered and managed on an outpatient basis; however, because of crises related to disease progression, intractable symptoms, or toxicity associated with anticancer treatment, some patients will require hospital admission. The patient-specific (demographic or clinical) or setting-of-care–related factors associated with an initial hospitalization, or the characteristics of those patients repeatedly admitted for management of severe symptoms during cancer treatment, are not well understood, particularly among older adults who are poorly represented among clinical trial data (Zulman et al., 2011). The current study uses a large, population-based database that is nationally representative to overcome this limitation in a population of older adults (Warren, Klabunde, Schrag, Bach, & Riley, 2002).

The problem of readmission, in which a patient returns to the hospital after an initial "index" stay, is a well-defined phenomenon (Jencks, Williams, & Coleman, 2009). An initial unplanned hospitalization, defined for the purpose of this study as an event in which a patient is scheduled to receive all treatment in the ambulatory setting but experiences a crisis that requires inpatient care, is distinct from readmission, which is conditional on a prior related or unrelated hospitalization (Fessele & Atkins, 2012; Jencks et al., 2009; Mulder, Tzeng, & Vecchioni, 2012).

Patients with lung cancer frequently visit the emergency department and hospital for unplanned care (Mayer, Travers, Wyss, Leak, & Waller, 2011). Most of the literature identified focused on patients with metastatic disease who received chemotherapy where surgical resection of the presenting tumor was not possible, and the admissions frequently related to symptoms of disease burden or progression (Elkin, O'Neill, Atoria, O'Reilly, & Bach, 2015; Hurria et al., 2011; Zauderer, Sima, Korc-Grodzicki, Kris, & Krug, 2013). The current authors were unable to locate data addressing unplanned hospitalizations specific to the population of patients with nonmetastatic lung cancer receiving chemotherapy, which is concerning because the treatment intent in this population may be cure or long-term remission.

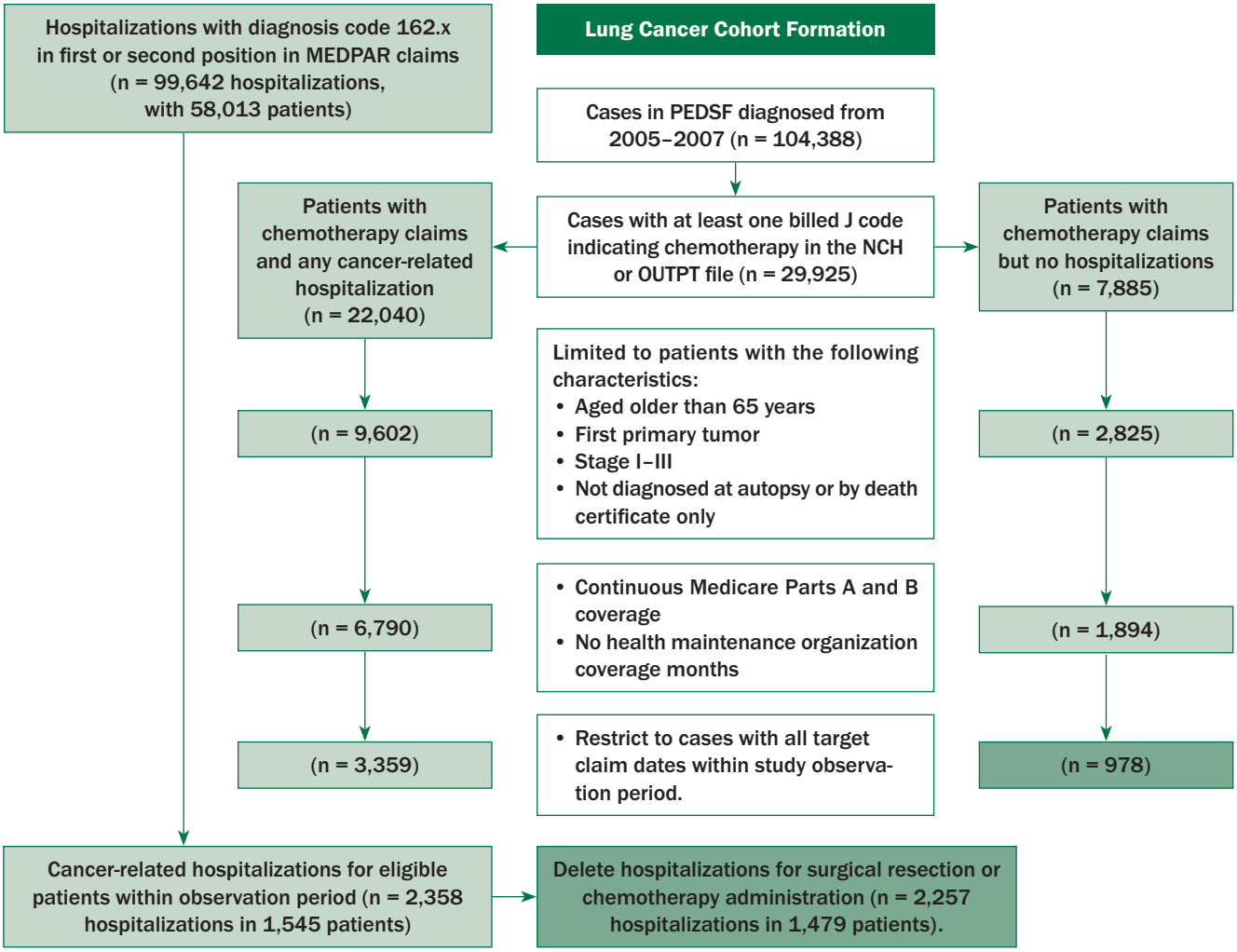
FIGURE 1. Study Cohort Design



Methods

Data Source

The SEER–Medicare database links Centers for Medicare and Medicaid Services (CMS) claims data with information from the NCI's SEER Program to produce research-grade administrative and clinical data that represent a longitudinal view across settings of care at



MEDPAR—Medicare provider analysis and review; NCH—national carrier history; OUTPT—outpatient; PEDSF—patient entitlement and diagnosis summary file

FIGURE 2. Formation of the Lung Cancer Cohort

the individual patient level (Warren et al., 2002). The SEER Program, implemented in 1973, collects data on newly diagnosed cancer cases across 17 registries within the United States, representing about 28% of all cases nationally (NCI, n.d.). For each primary malignancy, SEER data record cancer stage, histology, initial radiation or surgical interventions (because of the variations in and complexity of chemotherapy options, the record will indicate whether a patient received chemotherapy as part of the initial treatment but not the regimen received), patient demographics, and survival.

About 93% of those aged older than 65 years in the United States are covered by Medicare (U.S. Department of Health and Human Services, 2014), which is comprised of different benefits or "parts." Hospitalization, hospice, skilled nursing facility, and home health costs are covered under Part A benefits. Part B, an optional benefit elected by about 96% of covered beneficiaries, provides coverage for outpatient services. Optional Parts C and D offer CMS-managed health maintenance organization (HMO) plans and benefits for prescription medications, respectively (CMS, 2014).

The SEER–Medicare database includes a number of file types joined by a unique patient identifier. Information from the SEER registry informs the patient entitlement and diagnosis summary file (PEDSF). Medicare Part A claims data generate the Medicare provider analysis and review (MEDPAR) file. The national carrier history (NCH) and outpatient (OUTPT) files list claims for physician, advanced practice nurse, physician assistant, and other provider visits, as well as treatments administered in the ambulatory setting. OUTPT data are specific to hospital-based outpatient facilities.

The current study was reviewed by the Rutgers University Institutional Review Board prior to its start. The project was found to be nonhuman subject research and authorized to proceed.

Study Population

Eligible patients in the SEER–Medicare database had stage I–III non-small cell lung cancer diagnosed from 2005–2007, with claims data followed longitudinally through 2009. In addition, they were aged 66 years or older at the time of cancer diagnosis and had continuous Medicare Parts A and B coverage as the primary payer without an HMO component for at least 12 months prior to a subsequent initial cancer diagnosis to permit identification of comorbidities. The cohort was then limited to include those cases in which at least one billed claim for a chemotherapy drug existed prior to the initial and subsequent unplanned hospitalizations (see Figure 1). As a population-based study, no sampling was conducted.

Main Research Variables

Patient age, sex, race, marital status, degree of residential urbanization, median income, educational level, stage, receipt of radiation therapy, and comorbidities were studied and considered as potential predictors. Demographic and cancer diagnostic information was obtained from the PEDSF file. Patients who received chemotherapy were identified by searching the multiyear ambulatory claims files (NCH and OUTPT) for observations with a Healthcare Common Procedure Coding System (HCPCS) value containing a J9 code that designates chemotherapy agents (Lamont et al., 2005). Cancer-related hospitalizations were identified by searching the multiyear hospital claims file (MEDPAR) for the tumor type of interest in either the first or second position of 10 possible International Classification of Diseases, Ninth Revision, Clinical Modification diagnostic codes assigned to the admission (Mayer et al., 2011). When a patient identification number was located in the "received chemotherapy" and "had a cancer-related hospitalization" files, that case was assigned to the hospitalized group. When a case was found only in the received chemotherapy file, that patient was assigned to the no hospitalization group (n = 978).

The file of all cancer-related hospitalizations was then restricted to include only admissions associated with dates within the hospitalization observation period (date of first chemotherapy administration plus one day through date of last chemotherapy administration plus 30 days) for the eligible patient cases. The remaining observations formed the final hospitalization group for analysis (see Figure 2). Hospitalized and nonhospitalized cases underwent weighted preexisting comorbidity analysis using the NCI combined index to identify noncancer conditions treated in the 365 days prior to the cancer diagnosis date (Klabunde, Legler, Warren, Baldwin, & Schrag, 2007).

To obtain a general estimation of potential financial burden associated with these unplanned hospitalizations, the MEDPAR file was examined to calculate the total charges (in U.S. dollars) submitted by the hospital for each admission through use of the Medicare total charge variable TOTCHRGS. The variable REIMBAMT captured the amount the hospital was paid for each of the MEDPAR file unplanned hospitalizations. No additional adjustments or calculations, such as cost-to-charge ratios, were conducted as part of this study.

Statistical Analysis

Patient cases were included from the 16 NCI SEER registries that contributed complete data at the time. Consistent with previous reports that illustrated the importance of including geography at the SEER registry level as a variable (Du, Osborne, & Goodwin, 2002; Nurgalieva, Liu, & Du, 2009), the 16 registries were grouped into four SEER regions (see Table 1) to facilitate analysis. The NCI combined index (Klabunde et al., 2007) was used to produce a weighted comorbidity score for each case. This method evolved from the inpatient-developed Charlson Comorbidity Index (Charlson, Pompei, Ales, & MacKenzie, 1987) to enable use with hospital and outpatient administrative data. Claims data are examined to detect whether any of 14 noncancer conditions are present; a coefficient estimate for two-year noncancer mortality is then applied to obtain a weighted score (Klabunde, Potosky, Legler, & Warren, 2000).

To properly account for geographical differences and the resulting within-region correlations that may occur, advanced statistical modeling techniques were used. Generalized estimating equations (GEE), a statistical modeling technique that builds on generalized linear modeling to correctly adjust standard error estimates and account for within-region correlated data, was employed (Liang & Zeger, 1986).

To examine the demographic and clinical factors predictive of initial unplanned hospitalizations within the defined study period, a binary hospitalized/not hospitalized outcome was used with a binomial distribution and logit link to predict the probability of the event as a function of linear predictors in a manner similar to logistic regression. However, the variance of the binary response was adjusted for the likelihood that cases from the same region are more similar. Results were interpreted in terms of odds ratios (ORs), giving the likelihood of hospitalization versus not for each independent variable.

To explore factors that predict the number of unplanned hospitalizations, the dependent variable was defined as the number of hospitalizations in the defined study period, conditional on at least one

TABLE 1. Characteristics by Cohort

Characteristic	Hospitalized (N = 1,479)			Nonhospitalized (N = 978)		
	$\bar{X}$	SD	Range	$\bar{X}$	SD	Range
Age at diagnosis (years)	76.2	5	66–92	77.5	5.1	66–95
Education (%)[a]	19.6	12.9	0.8–77	18.5	12.3	0–69.9
Income ($)[b]	44,661.50	–	8,324–200,008	44,434	–	7,000–200,008
Characteristic		**n**	**%[c]**		**n**	**%[c]**
Chemotherapy[d]						
Platin		1,283	87		805	82
Taxane		943	64		537	55
Gemcitabine		417	28		195	20
Pemetrexed		320	22		135	14
Topoisomerases		369	25		241	25
Monoclonal antibodies		209	14		134	14
Vinca alkaloids		138	9		69	7
Comorbidity score[e, f]						
0		1,149	78		443	45
1		149	10		323	33
2		86	6		135	14
3 or greater		95	6		77	8
Disease stage						
I		108	7		57	6
II		895	61		549	56
III		242	16		229	23
Unknown[g]		234	16		143	15
Married						
Yes		799	54		510	52
Race						
White		1,320	89		905	93
Radiation treatment						
External beam		718	50		484	52
None (includes refused)		711	50		453	48
SEER registry region[h]						
New Jersey		268	18		125	13
West		487	33		407	42
South		370	25		217	22
Mid/Northeast		354	24		229	23
Sex						
Female		656	44		468	48
Urbanization						
Big metro		823	56		483	49
Metro/urban		486	33		408	42
Less urban/rural		170	11		86	9

[a] Census tract percentage of non-high school graduates
[b] Census tract median income
[c] Percentages based on column totals
[d] Patients generally received more than one drug class during the study period.
[e] National Cancer Institute combined index
[f] The range (pre-recode) of comorbidities for hospitalized and nonhospitalized patients was 0–7 and 0–9, respectively.
[g] Not missing
[h] West consists of California, Hawaii, and Seattle. South consists of Kentucky, Louisiana, and Georgia. Mid/Northeast consists of Connecticut, Iowa, Michigan, New Mexico, and Utah.
SEER—Surveillance, Epidemiology, and End Results

recorded hospitalization. A GEE model with a Poisson distribution and log link was used to predict the number of hospitalizations occurring among those patients with one or more admissions. Results were interpreted through the use of incidence rates (Rothman, 2002).

DATA step programming in SAS®, version 9.3, was used to perform data management, integration, and manipulation. Statistical modeling was completed with the PROC GENMOD procedure. After assessing the characteristics and frequency distributions of the independent variables, bivariate models were fit

to assess the association between each independent variable and the dependent variable. A nominal level of significance of 0.05 was used initially, followed by model-building steps retaining independent variables with statistical results at the alpha of 0.15 level. Advanced statistical modeling was then performed. After considering independent variables that were known to be associated with hospitalization and including them in each model by default regardless of statistical significance, statistical results (p values) and the QIC (quasi-likelihood under the independence model criterion) goodness-of-fit statistic were used throughout to determine the best final models (Pan, 2001). See Tables 2 and 3 for the results of this modeling.

Results

The cohort consisted of 2,457 patients. Most (54%) were male, and about 9% were of a self-reported non-White race, with a mean age of about 77 years. The hospitalized group comprised 60% of the cohort (n = 1,479), and experienced a mean of 1.5 hospitalizations per patient (SD = 0.9, range = 1–9). Participants experienced 2,257 unplanned hospitalizations, with a median length of stay of four days (range = 1–432 days); the total charges billed for the unplanned hospitalizations identified in this study equaled $74,187,751. The median Medicare charge and payment per hospitalization were $31,036 and $8,633, respectively.

The characteristics of the hospitalized and nonhospitalized patients were similar, with the exception of comorbidity score. The hospitalized group had a significantly higher proportion of patients with no preexisting comorbidity than the nonhospitalized group in this cohort (χ^2 = 300.31, degrees of freedom [df] = 3, p < 0.0001).

Initial Unplanned Hospitalization

For each year of increasing age, the likelihood of hospitalization decreased by 5.4% (OR = 0.95, 95% confidence interval [CI] [0.94, 0.97], p < 0.0001). Comorbidity was significant in the multivariate model; after controlling for other factors, compared with a weighted NCI combined index score of 0 (which indicates no comorbidities), patients with one or more comorbidities had a decreased likelihood of hospitalization. Compared with patients who had no comorbidities, those with a weighted score of 1 had an 82% decreased likelihood of hospitalization (OR = 0.18, 95% CI [0.15, 0.21], p < 0.0001). In patients with a weighted score of 2, the likelihood of hospitalization decreased by 76% (OR = 0.24, 95% CI [0.16, 0.35], p < 0.0001) and by 55% for those patients with a weighted score of 3 or higher (OR = 0.45, 95% CI [0.32, 0.65], p < 0.0001).

Non-White patients experienced an increased likelihood of hospitalization (59%) as compared to Whites (OR = 1.59, 95% CI [1.14, 2.22], p = 0.0066). After controlling for other factors, for each 10% increment decrease in census tract level rate of high school completion, the likelihood of hospitalization increased by 9.8% (OR = 1.1, 95% CI [1.03, 1.17], p = 0.0068). For each $10,000 increment increase in census tract level median income, the likelihood of hospitalization increased by 8.3% (OR = 1.08, 95% CI [1.01, 1.16], p = 0.02). The influence of degree of urbanization as a predictive factor is complex. Compared to patients living in an area designated as completely rural (defined by Census 2000 data as an urban population of less than 20,000), those in areas with an urban population of 20,000 to 1 million (metro/urban) have a 41% decreased likelihood of hospitalization (OR = 0.59, 95% CI [0.43, 0.82], p = 0.0015). However, living in metro areas of 1 million or more (big metro) did not significantly affect the likelihood of an initial unplanned hospitalization (OR = 0.77, 95% CI [0.51, 1.17], p = 0.2234).

Number of Unplanned Hospitalizations

Controlling for clustered SEER registry, education, and median income, cases designated in the SEER record with a non-White race had 1.08 times the number of unplanned hospitalizations as compared to Whites (estimate = 1.08, 95% CI [1, 1.16], p = 0.042). After controlling for other factors, patients who received radiation therapy had 1.4 times the number of repeated hospitalizations compared to those who did not undergo that treatment (estimate = 1.04, 95% CI [1, 1.07], p = 0.017), and those with a comorbidity score of 1 had 1.15 times the number of repeated hospitalizations as compared to those with a score of 0 (estimate = 1.15, 95% CI [1.07, 1.24], p = 0.0002). As compared to those patients living in a completely rural area, those in a metro/urban area had 0.9 times the number of hospitalizations (estimate = 0.9, 95% CI [0.83, 0.99], p = 0.0122).

Discussion

This study illustrates that unplanned hospitalizations are frequently and repeatedly experienced by patients with nonmetastatic lung cancer in the SEER–Medicare database and that these result in significant Medicare charges. The authors found that younger age, non-White race, lower high school graduation rate, higher median income in the census tract of residence, residence outside of an urban area, receipt of radiation therapy, and lower comorbidity scores were significant predictors of the likelihood of initial unplanned hospitalizations. Non-White race, receipt of radiation therapy, residence outside of an

urban area, and comorbidity were associated with the number of hospitalizations experienced.

Numerous sources have noted the impact of comorbidities on the patient's ability to tolerate anticancer treatments and on the natural history of the cancer process itself (Geraci, Escalante, Freeman, & Goodwin, 2005; Gross, McAvay, Guo, & Tinetti, 2007; Hernandez et al., 2009; Janssen-Heijnen et al., 2005; Lemmens et al., 2005). In this lung cancer cohort, a mixed set of observations was noted. After controlling for other factors in the model, as compared to patients with a weighted score of 0 (indicating no comorbidities), the OR for likelihood of initial hospitalization for scores of 1, 2, or 3 or higher was 0.18, 0.24, and 0.45, respectively, which is not the trend that was expected. Among the ultimately eligible cases, significant differences existed in the comorbidity scoring categories between the hospitalized and nonhospitalized groups; the latter appeared to present at the time of cancer diagnosis with more preexisting illnesses, which may have contributed to these unexpected results.

In this lung cancer cohort and in the previously published colorectal cancer cohort, age was a statistically significant predictor related to the incidence of initial unplanned hospitalization but not in regard to the number of hospitalizations experienced. Each year of additional age was associated with a 4.7% decrease in the likelihood of initial unplanned hospitalization. This may appear to be a counterintuitive result, but a bias toward offering less aggressive anticancer treatments to patients based on their chronologic age is evident in the literature (Hurria et al., 2008; Sargent et al., 2001; Sundararajan et al., 2002) and could contribute to the appearance of fewer severe toxicities leading to hospitalization. In addition, although the specific drugs administered could be precisely identified through billing data, the exact dose could not because the unit of measurement is at the billed vial size rather than indicative of true milligram per meter squared dosing.

Taken together, these unexpected trends (younger chronologic age and lower weighted comorbidity scores were associated with increased likelihood of unplanned hospitalization) support the need for further study investigating whether more aggressive therapy is offered preferentially to this group and the related outcomes, including ability to tolerate full courses of therapy at intended doses. Hurria et al. (2016) validated a scoring algorithm to predict

TABLE 2. Initial Unplanned Hospitalization in Lung Cancer Treatment: GEE Prediction Models (N = 1,479)

	Unadjusted (Bivariate) Models			Adjusted (Multivariate) Model[a]		
Predictor	**OR**	**95% CI**	**p**	**OR**	**95% CI**	**p**
Age (years)	0.95	[0.94, 0.97]	< 0.0001	0.95	[0.94, 0.97]	< 0.0001
Comorbidity[b]						
0	1	–	–	–	–	–
1	0.18	[0.15, 0.22]	< 0.0001	0.18	[0.15, 0.21]	< 0.0001
2	0.25	[0.17, 0.35]	< 0.0001	0.24	[0.16, 0.35]	< 0.0001
3 or more	0.46	[0.34, 0.66]	< 0.0001	0.45	[0.32, 0.65]	< 0.0001
Education (%)[c]						
Non-HS graduates	1.05	[1.03, 1.07]	< 0.0001	1.1	[1.03, 1.17]	0.0068
HS graduates	1	–	–	–	–	–
Income (median)[c]	1.02	[0.96, 1.07]	0.5369	1.08	[1.01, 1.16]	0.02
Marital status						
Married	0.93	[0.76, 1.13]	0.4484	–	–	–
Not married	1	–	–	–	–	–
Race						
Non-White	1.48	[1.07, 2.06]	0.0182	1.59	[1.14, 2.22]	0.0066
White	1	–	–	–	–	–
Radiation therapy						
Yes	0.95	[0.85, 1.05]	0.3127	0.89	[0.79, 1.01]	0.0691
No	1	–	–	–	–	–
Sex						
Female	0.87	[0.75, 1.01]	0.0598	–	–	–
Male	1	–	–	–	–	–
Urbanization						
Big metro	0.86	[0.58, 1.28]	0.4634	0.77	[0.51, 1.17]	0.2234
Metro/urban	0.6	[0.46, 0.78]	0.0001	0.59	[0.43, 0.82]	0.0015
Less urban/rural	1	–	–	–	–	–

[a] Quasi-likelihood under independence model = 2,849.601
[b] National Cancer Institute combined index
[c] Census tract data
CI—confidence interval; GEE—generalized estimating equations; HS—high school; OR—odds ratio

the likelihood of chemotherapy-related toxicity in older adults. Among other components, including age, hemoglobin level, cancer type, and multiple functional assessment questions, the planned number of chemotherapy drugs and intended dose were significant factors in the model. Future work to compare chemotherapy doses planned versus those actually delivered, explored in the context of the patient's physiologic age, including factors such as organ function and physical performance status, is needed.

Although less than 10% of the lung cancer and colorectal cancer cohorts were non-White, race was a significant predictor of unplanned hospitalizations in both studies; other SEER–Medicare analyses have shown mixed results (Du et al., 2002; Nurgalieva et al., 2009). Various socioeconomic variables (e.g., education, income, and degree of urbanization) were also statistically significant factors across the lung cohort, and further investigation is needed to understand their impact.

Limitations

Notable limitations are associated with the use of administrative and claims data, including the unavoidable time lapse that exists between data collection, curation, and linkage by SEER and Medicare administrators and analysis and publication by investigators. The authors believe that study design using demographic and clinical variables, such as those in this work, remain relevant despite data aging.

An additional limitation of the analysis is related to unavailability of complete disease staging data. Although stage IV or metastatic disease was excluded from this study, escalating stage of disease has been implicated in increasing the risk of unplanned hospitalization in this population in other studies (Hassett et al., 2011; Hassett, O'Malley, Pakes, Newhouse, & Earle, 2006; Nurgalieva et al., 2009). Cancer stage was unable to be retained in this analysis because, in about 30% of the cases examined, SEER staging value at diagnosis was entered by the local registry as unknown, not missing. The proportion of cases in which the diagnostic stage was coded as unknown was significantly higher in the nonhospitalized groups (χ^2 = 25.82, df = 1, p < 0.0001). Most cancer registries reside within a hospital setting where direct access to documents verifying the staging workup are available, providing a possible

TABLE 3. Number of Unplanned Hospitalizations in Lung Cancer: GEE Prediction Models (N = 1,479)

	Unadjusted (Bivariate) Models			Adjusted (Multivariate) Model[a]		
Predictor	**Multiplier**	**95% CI**	**p**	**Multiplier**	**95% CI**	**p**
Age (years)	0.99	[0.98, 1]	0.1997	–	–	–
Comorbidity[b]						
0	1	–	–	–	–	–
1	1.15	[1.07, 1.24]	0.0003	1.15	[1.07, 1.24]	0.0002
2	1.01	[0.98, 1.04]	0.4666	1.01	[0.97, 1.04]	0.6757
3 or more	0.96	[0.92, 1.01]	0.1446	0.96	[0.92, 1.01]	0.1309
Education (%)[c]						
Non-HS graduates	1.01	[0.99, 1.02]	0.1776	0.99	[0.99, 1.01]	0.8199
HS graduates	1	–	–	–	–	–
Income (median)[c]	0.99	[0.98, 1.01]	0.3691	0.99	[0.97, 1.02]	0.9443
Marital status						
Married	1	[0.96, 1.04]	0.9768	–	–	–
Not married	1	–	–	–	–	–
Race						
Non-White	1.09	[1, 1.17]	0.0337	1.08	[1, 1.16]	0.042
White	1	–	–	–	–	–
Radiation therapy						
Yes	1.04	[1.02, 1.07]	0.0002	1.04	[1, 1.07]	0.017
No	1	–	–	–	–	–
Sex						
Female	1.02	[0.95, 1.11]	0.5321	–	–	–
Male	1	–	–	–	–	–
Urbanization[c]						
Big metro	0.93	[0.85, 1.02]	0.157	0.93	[0.82, 1.06]	0.2832
Metro/urban	0.9	[0.86, 0.95]	0.0001	0.9	[0.83, 0.98]	0.0122
Less urban/rural	1	–	–	–	–	–

[a] Quasi-likelihood under independence model = 4,527.808
[b] National Cancer Institute combined index
[c] Census tract data
Note. There were 2,257 hospitalizations ($\bar{X}$ = 1.53, SD = 0.92, range = 1–9). The outcome was a count variable.
CI—confidence interval; GEE—generalized estimating equations; HS—high school

explanation for the higher rate of SEER diagnostic classification among those patients in the hospitalized group.

This study was not designed to examine how the timing of chemotherapy administration or specific regimens were associated with unplanned hospitalizations, and the authors hope to undertake this more complex but more informative type of analysis in future work. In addition, more advanced exploration of financial factors, such as cost-to-charge ratios and direct versus indirect costs, should be included in next steps to more fully describe the impact of these potentially avoidable hospitalizations on the healthcare system and the patient.

Implications for Nursing

The availability of a large-scale, NCI-managed dataset, such as SEER–Medicare, offers many advantages for nursing inquiry, although claims data are limited by nature and do not offer the same opportunities to capture factors critical to clinical outcomes (e.g., performance or psychosocial status); they also do not inform subtleties of the clinical situation that would be available in the narrative or other clinician documentation in an electronic health record. Until more robust, integrated, and easily accessible data sources become available to the research community, this study provides a first step toward the identification of patients at elevated risk of unplanned hospitalizations. The ability to recognize high-risk individuals prior to treatment initiation shifts nursing care from a reactive paradigm to one where additional proactive, tailored nursing education, supportive care, and monitoring may enable more patients to remain on potentially curative therapies without experiencing toxicity-related interruptions. Future work that includes additional clinical variables, such as performance status and chemotherapy timing, dosing, and relationship to symptom incidence and management, is needed.

Conclusion

Patients receiving chemotherapy for nonmetastatic lung cancer may be at high risk for experiencing costly unplanned hospitalizations during the course of therapy, but identifying those most likely to be admitted prior to treatment administration remains challenging. More work is needed to identify predictors of negative outcomes, such as treatment interruption, that can be proactively used by nurses to assess risk and tailor monitoring and symptom management planning, particularly in populations with early-stage disease where the treatment intent is cure or long-term cancer control.

Knowledge Translation

- Variables key to nursing inquiry in large datasets (e.g., patient performance status, symptom incidence and severity) are frequently lacking and limit the ability to include them in predictor modeling; advocacy by nurses to ensure inclusion in electronic health record–derived and other databases as structured fields will facilitate future knowledge generation.
- More research is required to understand the impact of specific comorbidities on patterns of adverse events among older adults receiving chemotherapy.
- Further work is needed to identify socioeconomic variables in administrative and claims data that are meaningful at the population level to reveal patterns of risk and potential healthcare disparities.

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References

American Cancer Society. (2016). *About non-small cell lung cancer*. Retrieved from https://www.cancer.org/content/dam/CRC/PDF/Public/8703.00.pdf

Centers for Medicare and Medicaid Services. (2014). Medicare and Medicaid statistical supplement: 2011 edition. Retrieved from https://www.cms.gov/Research-Statistics-Data-and-Systems/Statistics-Trends-and-Reports/MedicareMedicaidStatSupp/2011.html

Charlson, M.E., Pompei, P., Ales, K.L., & MacKenzie, C.R. (1987). A new method of classifying prognostic comorbidity in longitudinal studies: Development and validation. *Journal of Chronic Diseases, 40,* 373–383. doi:10.1016/0021-9681(87)90171-8

Du, X.L., Osborne, C., & Goodwin, J.S. (2002). Population-based assessment of hospitalizations for toxicity from chemotherapy in older women with breast cancer. *Journal of Clinical Oncology, 20,* 4636–4642. doi:10.1200/JCO.2002.05.088

Elkin, E.B., O'Neill, C., Atoria, C.L., O'Reilly, E.M., & Bach, P. (2015). The impact of chemotherapy on hospitalizations and emergency care in older adults with advanced cancer [Abstract 6545]. *Journal of Clinical Oncology, 33*(Suppl.), 6545.

Fessele, K., & Atkins, R. (2012). Unplanned hospitalizations for adverse events during outpatient chemotherapy: Conceptual and methodological delineation during analysis of a large, oncology-focused administrative dataset [Abstract 1423803]. *Oncology Nursing Forum, 39,* E511–E547. doi:10.1188/12.ONF.E511-E547

Fessele, K.L., Hayat, M.J., Mayer, D.K., & Atkins, R.L. (2016). Factors associated with unplanned hospitalizations among patients with nonmetastatic colorectal cancers intended for treatment in the ambulatory setting. *Nursing Research, 65,* 24–34. doi:10.1097/NNR.0000000000000134

Geraci, J.M., Escalante, C.P., Freeman, J.L., & Goodwin, J.S. (2005). Comorbid disease and cancer: The need for more relevant conceptual models in health services research. *Journal of Clinical Oncology, 23,* 7399–7404. doi:10.1200/JCO.2004.00.9753

González, J.R., Fernandez, E., Moreno, V., Ribes, J., Peris, M., Navarro, M., . . . Borràs, J.M. (2005). Sex differences in hospital readmission among colorectal cancer patients. *Journal of Epidemiology and Community Health, 59,* 506–511. doi:10.1136/jech.2004.028902

Grant, M., Ferrell, B.R., Rivera, L.M., & Lee, J. (1995). Unscheduled readmissions for uncontrolled symptoms. A health care challenge for nurses. *Nursing Clinics of North America, 30,* 673–682.

Gross, C.P., McAvay, G.J., Guo, Z., & Tinetti, M.E. (2007). The impact of chronic illnesses on the use and effectiveness of adjuvant chemotherapy for colon cancer. *Cancer, 109,* 2410–2419. doi:10.1002/cncr.22726

Hassett, M.J., O'Malley, A.J., Pakes, J.R., Newhouse, J.P., & Earle, C.C. (2006). Frequency and cost of chemotherapy-related serious adverse effects in a population sample of women with breast cancer. *Journal of the National Cancer Institute, 98,* 1108–1117. doi:10.1093/jnci/djj305

Hassett, M.J., Rao, S.R., Brozovic, S., Stahl, J.E., Schwartz, J.H., Maloney, B., & Jacobson, J.O. (2011). Chemotherapy-related hospitalization among community cancer center patients. *Oncologist, 16,* 378–387. doi:10.1634/theoncologist.2010-0354

Hernandez, C., Jansa, M., Vidal, M., Nuñez, M., Bertran, M.J., Garcia-Aymerich, J., & Roca, J. (2009). The burden of chronic disorders on hospital admissions prompts the need for new modalities of care: A cross-sectional analysis in a tertiary hospital. *QJM, 102,* 193–202. doi:10.1093/qjmed/hcn172

Hu, Y., McMurry, T.L., Isbell, J.M., Stukenborg, G.J., & Kozower, B.D. (2014). Readmission after lung cancer resection is associated with a 6-fold increase in 90-day postoperative mortality. *Journal of Thoracic and Cardiovascular Surgery, 148,* 2261–2267. doi:10.1016/j.jtcvs.2014.04.026

Hurria, A., Mohile, S., Gajra, A., Klepin, H., Muss, H., Chapman, A., . . . Tew, W.P. (2016). Validation of a prediction tool for chemotherapy toxicity in older adults with cancer. *Journal of Clinical Oncology, 34,* 2366–2371. doi:10.1200/JCO.2015.65.4327

Hurria, A., Togawa, K., Mohile, S.G., Owusu, C., Klepin, H.D., Gross, C.P., . . . Tew, W.P. (2011). Predicting chemotherapy toxicity in older adults with cancer: A prospective multicenter study. *Journal of Clinical Oncology, 29,* 3457–3465. doi:10.1200/JCO.2011.34.7625

Hurria, A., Wong, F.L., Villaluna, D., Bhatia, S., Chung, C.T., Mortimer, J., . . . Naeim, A. (2008). Role of age and health in treatment recommendations for older adults with breast cancer: The perspective of oncologists and primary care providers. *Journal of Clinical Oncology, 26,* 5386–5392. doi:10.1200/JCO.2008.17.6891

Janssen-Heijnen, M.L., Houterman, S., Lemmens, V.E., Louwman, M.W., Maas, H.A., & Coebergh, J.W. (2005). Prognostic impact of increasing age and co-morbidity in cancer patients: A population-based approach. *Critical Reviews in Oncology/Hematology, 55,* 231–240. doi:10.1016/j.critrevonc.2005.04.008

Jencks, S.F., Williams, M.V., & Coleman, E.A. (2009). Rehospitalizations among patients in the Medicare Fee-for-Service Program. *New England Journal of Medicine, 360,* 1418–1428. doi:10.1056/NEJMsa0803563

Klabunde, C.N., Legler, J.M., Warren, J.L., Baldwin, L.-M., & Schrag, D. (2007). A refined comorbidity measurement algorithm for claims-based studies of breast, prostate, colorectal, and lung cancer patients. *Annals of Epidemiology, 17,* 584–590. doi:10.1016/j.annepidem.2007.03.011

Klabunde, C.N., Potosky, A.L., Legler, J.M., & Warren, J.L. (2000). Development of a comorbidity index using physician claims data. *Journal of Clinical Epidemiology, 53,* 1258–1267. doi:10.1016/s0895-4356(00)00256-0

Lamont, E.B., Herndon, J.E., II, Weeks, J.C., Henderson, I.C., Lilenbaum, R., Schilsky, R.L., & Christakis, N.A. (2005). Criterion validity of Medicare chemotherapy claims in cancer and leukemia Group B breast and lung cancer trial participants. *Journal of the National Cancer Institute, 97,* 1080–1083. doi:10.1093/jnci/dji189

Lemmens, V.E., Janssen-Heijnen, M.L., Verheij, C.D., Houterman, S., Repelaer van Driel, O.J., & Coebergh, J.W. (2005). Co-morbidity leads to altered treatment and worse survival of elderly patients with colorectal cancer. *British Journal of Surgery, 92,* 615–623. doi:10.1002/bjs.4913

Liang, K.-Y., & Zeger, S.L. (1986). Longitudinal data analysis using generalized linear models. *Biometrika, 73,* 13–22. doi:10.1093/biomet/73.1.13

Mayer, D.K., Travers, D., Wyss, A., Leak, A., & Waller, A. (2011). Why do patients with cancer visit emergency departments? Results of a 2008 population study in North Carolina. *Journal of Clinical Oncology, 29,* 2683–2688. doi:10.1200/JCO.2010.34.2816

McDevitt, J., Kelly, M., Comber, H., Kelleher, T., Dwane, F., & Sharp, L. (2013). A population-based study of hospital length of stay and emergency readmission following surgery for non-small-cell lung cancer. *European Journal of Cardio-Thoracic Surgery, 44,* E253–E259. doi:10.1093/ejcts/ezt389

Mulder, B.J., Tzeng, H.-M., & Vecchioni, N.D. (2012). Preventing avoidable rehospitalizations by understanding the characteristics of "frequent fliers." *Journal of Nursing Care Quality, 27,* 77–82. doi:10.1097/NCQ.0b013e318229fddc

National Cancer Institute. (n.d.). Overview of the SEER Program. Retrieved from http://seer.cancer.gov/about/overview.html

Nurgalieva, Z., Liu, C.-C., & Du, X.L. (2009). Risk of hospitalizations associated with adverse effects of chemotherapy in a large community-based cohort of elderly women with ovarian cancer. *International Journal of Gynecological Cancer, 19,* 1314–1321. doi:10.1111/IGC.0b013e3181b7662d

Pan, W. (2001). Akaike's information criterion in generalized estimating equations. *Biometrics, 57,* 120–125. doi:10.1111/j.0006-341x.2001.00120.x

Puri, V., Patel, A.P., Crabtree, T.D., Bell, J.M., Broderick, S.R., Kreisel, D., . . . Meyers, B.F. (2015). Unexpected readmission after lung cancer surgery: A benign event? *Journal of Thoracic and Cardiovascular Surgery, 150,* 1496–1505. doi:10.1016/j.jtcvs.2015.08.067

Rothman, K.J. (2002). *Epidemiology: An introduction*. New York, NY: Oxford University Press.

Sargent, D.J., Goldberg, R.M., Jacobson, S.D., Macdonald, J.S., Labianca, R., Haller, D.G., . . . Francini, G. (2001). A pooled analysis of adjuvant chemotherapy for resected colon cancer in elderly patients. *New England Journal of Medicine, 345,* 1091–1097. doi:10.1056/NEJMoa010957

Stitzenberg, K.B., Chang, Y., Smith, A.B., & Nielsen, M.E. (2015). Exploring the burden of inpatient readmissions after major cancer surgery. *Journal of Clinical Oncology, 33,* 455–464. doi:10.1200/JCO.2014.55.5938

Sundararajan, V., Mitra, N., Jacobson, J.S., Grann, V.R., Heitjan, D.F., & Neugut, A.I. (2002). Survival associated with 5-fluorouracil-based adjuvant chemotherapy among elderly patients with node-positive colon cancer. *Annals of Internal Medicine, 136,* 349–357. doi:10.7326/0003-4819-136-5-200203050-00007

U.S. Department of Health and Human Services. (2014). *A profile of older Americans: 2014*. Retrieved from https://www.acl.gov/sites/default/files/Aging%20and%20Disability%20in%20America/2014-Profile.pdf

Warren, J.L., Klabunde, C.N., Schrag, D., Bach, P.B., & Riley, G.F. (2002). Overview of the SEER-Medicare data—Content, research applications, and generalizability to the United States elderly population. *Medical Care, 40*(Suppl.), IV3–IV18.

Weaver, C., Schiech, L., Held-Warmkessel, J., Kedziera, P., Haney, E., DiLullo, G., . . . Barsevick, A. (2006). Risk for unplanned hospital readmission of patients with cancer: Results of a retrospective medical record review [Online exclusive]. *Oncology Nursing Forum, 33,* E44–E52. doi:10.1188/06.ONF.E44-E52

Zauderer, M.G., Sima, C.S., Korc-Grodzicki, B., Kris, M.G., & Krug, L.M. (2013). Toxicity of initial chemotherapy in older patients with lung cancers. *Journal of Geriatric Oncology, 4,* 64–70.

Zulman, D.M., Sussman, J.B., Chen, X., Cigolle, C.T., Blaum, C.S., & Hayward, R.A. (2011). Examining the evidence: A systematic review of the inclusion and analysis of older adults in randomized controlled trials. *Journal of General Internal Medicine, 26,* 783–790. doi:10.1007/s11606-010-1629-x