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Complication Rates and Downstream Medical Costs Associated With Invasive Diagnostic Procedures for Lung Abnormalities in the Community Setting

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IMPORTANCE The Centers for Medicare & Medicaid Services added lung cancer screening with low-dose computed tomography (LDCT) as a Medicare preventive service benefit in 2015 following findings from the National Lung Screening Trial (NLST) that showed a 16% reduction in lung cancer mortality associated with LDCT. A challenge in developing and promoting a national lung cancer screening program is the high false-positive rate of LDCT because abnormal findings from thoracic imaging often trigger subsequent invasive diagnostic procedures and could lead to postprocedural complications.

OBJECTIVE To determine the complication rates and downstream medical costs associated with invasive diagnostic procedures performed for identification of lung abnormalities in the community setting.

DESIGN, SETTING, AND PARTICIPANTS A retrospective cohort study of non–protocol-driven community practices captured in MarketScan Commercial Claims & Encounters and Medicare supplemental databases was conducted. A nationally representative sample of 344 510 patients aged 55 to 77 years who underwent invasive diagnostic procedures between 2008 and 2013 was included.

MAIN OUTCOMES AND MEASURES One-year complication rates were calculated for 4 groups of invasive diagnostic procedures. The complication rates and costs were further stratified by age group.

RESULTS Of the 344 510 individuals aged 55 to 77 years included in the study, 174 702 comprised the study group (109 363 [62.6%] women) and 169 808 served as the control group (106 007 [62.4%] women). The estimated complication rate was 22.2% (95% CI, 21.7%-22.7%) for individuals in the young age group and 23.8% (95% CI, 23.0%-24.6%) for those in the Medicare group; the rates were approximately twice as high as those reported in the NLST (9.8% and 8.5%, respectively). The mean incremental complication costs were $6320 (95% CI, $5863-$6777) for minor complications to $56 845 (95% CI, $47 953-$65 737) for major complications.

CONCLUSIONS AND RELEVANCE The rates of complications after invasive diagnostic procedures were higher than the rates reported in clinical trials. Physicians and patients should be aware of the potential risks of subsequent adverse events and their high downstream costs in the shared decision-making process.

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Supplemental content

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Lung cancer is the leading cause of cancer-related deaths in the United States. Despite advances in cancer treatment, the 5-year survival rate of advanced-stage lung cancer has remained low at only 16%.[1] Lung cancer is diagnosed at advanced stages in approximately 70% of the patients, making the development of effective screening strategies for lung cancer a public health priority nationwide. Efforts to establish an effective screening strategy for lung cancer had not been successful until the landmark National Lung Screening Trial (NLST). Published in 2011, the NLST demonstrated the efficacy of low-dose computed tomography (LDCT), reporting a 20% reduction in lung cancer–related death compared with chest radiography.[2] Analyses with more mature data report an approximately 16% reduction in lung cancer mortality.[3] Following the release of the NLST results, many professional societies issued guidelines recommending LDCT for individuals at high risk for lung cancer.[4-10]

Success of the NLST trial was somewhat shadowed by the high false-positive rate associated with LDCT. At a 23.3% false-positive rate across 3 rounds of screening, screening experts are concerned that the 8.5% to 9.8% complication rate from invasive diagnostic procedures reported in the NLST for those who experienced false-positive results associated with LDCT could translate to substantial harms and financial burden when lung cancer screening programs are implemented in the United States.[11] This concern is heightened because the participants in the NLST tended to be healthier than the screening-eligible population in the United States. A recent analysis of Surveillance, Epidemiology, and End Results (SEER)-Medicare data showed that the mortality benefit from screening demonstrated by the NLST would likely diminish among elderly patients with significant comorbid conditions.[12] Another concern is that most procedures used to evaluate abnormal findings in the NLST may have been performed at the participating sites, although this process was not required in the trial protocol. Because of the better health status of the trial participants and the observation that many NLST sites were high-volume facilities with proficiency in patient care,[13-19] we hypothesized that the rates of complications after invasive diagnostic procedures observed among the screening-eligible general population would likely be higher than those reported in the NLST.

Using ages 55 to 77 years, which is the age eligibility criterion specified in the Decision Memo for Screening for Lung Cancer with Low-Dose Computed Tomography issued by the Centers for Medicare & Medicaid Services[20] as the targeted age range for the lung cancer screening, we tested our hypothesis by estimating the complication rate associated with common invasive diagnostic procedures in community settings. To understand the potential financial outcome of the higher complication rates outside the trial setting, we also estimated the associated downstream costs.

Key Points

Question What are the complication rates and downstream medical costs associated with invasive diagnostic procedures for lung abnormalities in the community setting?

Findings In this cohort study of 344 510 patients in national databases, the estimated complication rate was 22.2% for individuals in the younger age group (55-64 years) and 23.8% for those in the Medicare group (65-77 years). The complication costs varied by patient age and complication type, ranging from $6320 to $56 845.

Meaning Shared decision-making communications between physicians and patients on lung cancer screening should include a discussion on the risks of subsequent adverse events and downstream costs associated with invasive diagnostic procedures.

Methods

Data

We used the 2008-2013 Truven MarketScan claims databases to identify a study cohort representative of the community practice setting. MarketScan data are from one of the largest US-based proprietary claims databases, covering nearly 240 million unique patients since 1995 and widely used in medical and health services research.[21-24] MarketScan databases capture medical information on the full continuum of care in all settings, including inpatient and outpatient services and outpatient prescription drugs. Patient-level details can be linked via unique identifiers for consistency across services. The MarketScan Commercial Claims and Encounters database provides claims data for current employees and their spouses and dependents (age, ≤64 years), and the Coordination of Benefits database provides claims for Medicare-eligible retirees (age, ≥65 years) carrying supplemental insurance offered by their prior employers. Our study was considered exempt from review by the institutional review board at The University of Texas MD Anderson Cancer Center because of the use of deidentified data.

Invasive Diagnostic Procedures and Postprocedural Complications

The NLST protocol categorized 23 invasive diagnostic procedures into 4 groups[2]: cytology or needle biopsy, bronchoscopy, thoracic surgery, and others (eTable 1 in the Supplement). The NLST reported 43 complications classified as minor, intermediate, or major (eTable 2 in the Supplement).[2] The clinicians on our research team mapped each of the diagnostic procedures and complications reported in the NLST to *International Classification of Diseases, Ninth Revision* (*ICD-9*) diagnosis and procedure codes as well as Healthcare Common Procedure Coding System (HCPCS) codes so that we could identify them from claims data. In determining an individual's diagnostic procedure group, those who underwent more than 1 procedure for lung abnormality were categorized on the basis of the most invasive procedure.

Ascertainment of Study Cohort

The study cohort consisted of individuals aged 55 to 77 years, consistent with the Centers for Medicare & Medicaid Services age eligibility criterion for lung cancer screening with LDCT.[20] Smoking status was not included because such information is unavailable in the claims databases. We further limited the cohort to individuals who had undergone invasive diagnostic procedures but did not have a diagnosis code indicative of lung

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cancer 12 months before and after these procedures. Because the period of our data was before February 5, 2015, the date that the billing codes for lung cancer screening with LDCT (HCPCS code G0297) became effective, our case cohort was not individuals who underwent invasive diagnostic procedures following a positive finding from LDCT but rather those who received the types of invasive procedures reported in the NLST to assess lung abnormalities.

In addition, we restricted our analysis to individuals who had continuous insurance coverage during the 12 months before and 12 months after the date of the index invasive procedure. By using complete, 12-month claims data before the index date, we calculated Charlson comorbidity index scores with the modified algorithm by Klabunde et al.[25] The score was grouped as 0 for no comorbidity, 1 for mild, and 2 or higher for moderate to severe. We then extracted the following information from the MarketScan databases: year of procedure, age, sex, and state of residence.

Complications Attributable to Invasive Diagnostic Procedures

An analytical challenge for our study was that complications listed in the NLST report were not necessarily a result of the invasive diagnostic procedures; the complications could have developed for other reasons. To derive complications that were likely associated with the invasive procedures, we used an incremental approach by constructing a matched control cohort that did not undergo these invasive procedures between January 1, 2008, and December 31, 2013, compared the complication rates between the study and control cohorts, and attributed the differences in complication rates to the invasive procedures. Using a matched-control cohort to compute the attributable risks or costs associated with specific causes has been widely applied in oncology health services research.[26-28]

We assigned January 1 in the year of the index procedure received by the matched individuals in the study cohort as the pseudo-index date for individuals in the control cohort. The control group was required to have 1 year of insurance coverage before the pseudo-index date to calculate the comorbidity score and 1 year after the pseudo-index date to identify complication events. For both the study and control cohorts from the same year of data, we constructed the control cohort by conducting 1:1 propensity score matching by age, sex, state, and comorbidity.[29] The balance between the study and control cohorts was tested using standardized differences.[30]

After stratifying individuals in the study cohort by the type of invasive diagnostic procedure, we further classified the study cohort into 4 age groups (55-59, 60-64, 65-69, and 70-77 years) within each procedural type, creating a total of 16 subgroups. Within each subgroup, we identified complication events that occurred within the 1-year observation window and calculated the gross rate of complications of each complication category by dividing the total number of individuals with complications in the corresponding category by the total number of individuals in that subgroup. Because some complications can be the trigger of these invasive procedures, we searched claims within 1 month prior to the invasive procedure date and, if the same diagnosis code used to determine complication was found within this 1-month time window, we did not consider that downstream event to be a complication. For the control group, we calculated the gross rate of complications of each category with age stratification. For each subgroup, we calculated the rate of complications attributable to invasive procedures by subtracting the gross rate of the control cohort from that of the study cohort.

Cost Analysis

Among individuals who experienced postprocedural complications, we estimated the 1-year complication costs by aggregating insurance payments and out-of-pocket expenditures for inpatient, outpatient, and physician services rendered on the dates for which an *ICD-9* diagnosis, procedure, or HCPCS code was indicated for complications. We also estimated the mean procedure costs for each invasive diagnostic procedure group. All costs were normalized to 2017 US dollars by using the Consumer Price Index medical care component.[31]

Statistical Analysis

In addition to reporting complication rates and costs by 16 subgroups stratified by age group and type of procedure, we collapsed age strata from 4 to 2 groups (younger [age 55-64 years] vs Medicare [age 65-77 years]) so that the complications rates estimated from our study can be directly compared with the age-stratified complication rates reported from the NLST.[11] Differences between individuals grouped on the basis of the 4 types of invasive diagnostic procedures, demographics, and comorbidities were analyzed using Pearson χ^2 tests. A P value ≤.05, based on a 2-tailed test, was considered statistically significant. All analyses were conducted using the statistical software SAS, version 9.4 (SAS Institute Inc).

Results

Patient Characteristics

We identified 174 702 individuals (109 363 [62.6%] women) who underwent 1 of the invasive diagnostic procedures documented in the NLST for the overall cohort, and 169 808 individuals (106 007 [62.4%] women) for the control group after matching. Selected demographic and clinical characteristics of study patients and the matched controls are presented in **Table 1**.

Of the patients in the study cohort who were identified as having undergone an invasive diagnostic procedure, 44 319 (26.1%) had a cytology test or biopsy, 43 437 (25.6%) had a bronchoscopy, 9161 (5.4%) underwent thoracic surgery, and 72 891 (42.9%) underwent other procedures. Further data are reported in **Table 2**.

Postprocedural Complications

After adjustment (by taking into account the differences in complication rates between the study and control cohorts for the corresponding age groups), individuals in the younger age group had a lower rate of complications than those in the Medicare group (22.2%; 95% CI, 21.7%-22.7% vs 23.8%; 95% CI, 23.0%-24.6%). Compared with the complication rates re-

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Table 1. Descriptive Statistics of the Population Samples

Characteristic	Younger Age Group (n = 222 740)			Medicare Age Group (n = 116 876)		
	Study Cohort, No. (%) (n = 111 370)	Matched Cohort, No. (%) (n = 111 370)	Standardized Difference[a]	Study Cohort, No. (%) (n = 58 438)	Matched Cohort, No. (%) (n = 58 438)	Standardized Difference[a]
Year						
2008	13 820 (12.4)	13 727 (12.3)	0.0030	1219 (2.1)	1284 (2.2)	0.0249
2009	18 844 (16.9)	18 858 (16.9)		10 365 (17.7)	10 191 (17.4)	
2010	21 422 (19.2)	21 402 (19.2)		10 963 (18.8)	10 816 (18.5)	
2011	22 725 (20.4)	22 760 (20.4)		11 525 (19.7)	11 343 (19.4)	
2012	17 815 (16.0)	17 883 (16.1)		11 171 (19.1)	11 046 (18.9)	
2013	16 744 (15.0)	16 740 (15.0)		13 195 (22.6)	13 758 (23.5)	
Age, y						
55-59	60 469 (54.3)	60 469 (54.3)	0.0001			0.0001
60-64	50 901 (45.7)	50 901 (45.7)				
65-69				20 217 (34.6)	20 249 (34.7)	
70-77				38 221 (65.4)	38 189 (65.4)	
Sex						
Male	40 788 (36.6)	40 767 (36.6)	0.0004	23 012 (39.4)	23 034 (39.4)	0.0008
Female	70 582 (63.4)	70 603 (63.4)		35 426 (60.6)	35 404 (60.6)	
Census division[b]						
Pacific	15 434 (13.9)	15 436 (13.9)	0.0038	8868 (15.5)	8775 (15.3)	0.0120
New England	6412 (5.8)	6383 (5.7)		3315 (5.8)	3313 (5.8)	
Middle Atlantic	12 804 (11.5)	12 709 (11.4)		7532 (13.2)	7732 (13.5)	
Northeast central	23 255 (20.9)	23 224 (20.9)		15 692 (27.4)	15 649 (27.4)	
Northwest central	5071 (4.6)	5075 (4.6)		2662 (4.7)	2689 (4.7)	
South Atlantic	22 455 (20.2)	22 510 (20.2)		9033 (15.8)	8930 (15.6)	
Southeast central	8237 (7.4)	8268 (7.4)		2694 (4.7)	2697 (4.7)	
Southwest central	11 810 (10.6)	11 881 (10.7)		4192 (7.3)	4182 (7.3)	
Mountain	5892 (5.3)	5884 (5.3)		3215 (5.6)	3254 (5.7)	
Comorbidity[c]						
0	82 364 (74.0)	82 012 (73.6)	0.0093	36 012 (61.6)	35 872 (61.4)	0.0051
1	21 308 (19.1)	21 416 (19.2)		14 210 (24.3)	14 274 (24.4)	
2+	7698 (6.9)	7942 (7.1)		8216 (14.1)	8292 (14.2)	

[a] Standardized difference measures the balance in baseline covariates between 2 groups, and a value less than 0.10 suggests the study cohort and control cohort are well balanced.

[b] We used state to match the study cohort and control cohort, and we collapsed the states into census division to improve the readability of the table.

[c] Charlson comorbidity index scores were grouped as 0 for no comorbidity, 1 for mild, and 2 or higher for moderate to severe.

ported in the NLST (9.8% and 8.5%), the complication rates found in our study were approximately 2 times higher for the younger age group and the Medicare group (**Figure 1**A).[11] The comparison by procedure type showed that the complication rates were higher in our cohort (18.7% after needle biopsy, 36.1% after bronchoscopy, and 51.7% after thoracic surgery) than those reported in the NLST (Figure 1B). The detailed complication rates by age group and procedure type are reported in **Table 3**. Among these, for patients in the age range of 65 to 69 years who underwent bronchoscopy, the rate of minor complications was 23.6% (95% CI, 22.0%-25.4%); intermediate, 33.6% (31.3%-36.0%); and major, 13.6% (12.3%-14.9%), respectively.

Cost Analysis

Table 3 also lists the costs of complications stratified by the level of complication and type of diagnostic procedure. Complication costs varied based on the type of procedure as well as the level of complication. Among these, for patients between ages 65 and 69 years, the cost of a minor complication associated with bronchoscopy was $5573 (95% CI, $3637-$7508); intermediate, $19 470 ($9859-$29 081); and major, $57 893 (95% CI, $37 899-$77 888). The cost of procedures was lower for biopsy ($312-$374) and bronchoscopy ($855-$1063) than for thoracic surgery ($5957-$9670) (**Figure 2**A). Managing postprocedural complications incurred higher costs than the diagnostic procedures, ranging from $6320 (95% CI, $5863-$6777) for minor complications to $56 845 (95% CI, $47 953-$65 737) for major complications (Figure 2B).

Discussion

This study estimated the rates and costs of complications associated with invasive diagnostic procedures that are likely to be received by individuals who have positive findings from tho-

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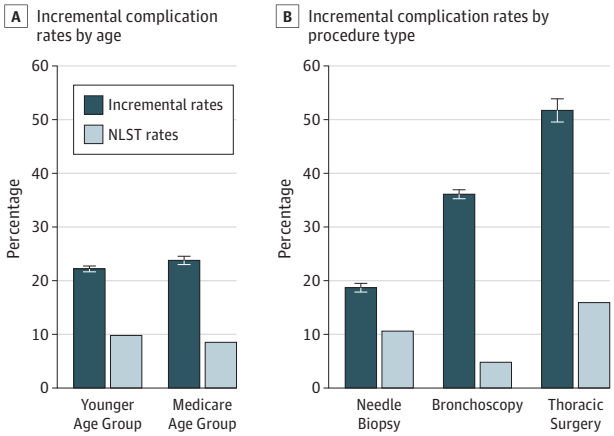
Table 2. Descriptive Statistics of the Study Sample, by Invasive Diagnostic Procedure

Characteristic	Total, No.	Cytology/Needle Biopsy, No. (%) (n = 44 319)	Bronchoscopy, No. (%) (n = 43 437)	Thoracic Surgery, No. (%) (n = 9161)	Other, No. (%) (n = 72 891)	*P* Value
Year						
2008	15 011	4063 (27.1)	3221 (21.5)	878 (5.8)	6849 (45.6)	<.001
2009	29 049	7541 (26.0)	7660 (26.4)	1682 (5.8)	12 166 (41.9)	
2010	32 218	8487 (26.3)	8357 (25.9)	1848 (5.7)	13 526 (42.0)	
2011	34 103	8836 (25.9)	8692 (25.5)	1762 (5.2)	14 813 (43.4)	
2012	28 929	7554 (26.1)	7268 (25.1)	1501 (5.2)	12 606 (43.6)	
2013	30 498	7838 (25.7)	8239 (27.0)	1490 (4.9)	12 931 (42.4)	
Age, y						
55-59	60 469	18 214 (30.1)	12 833 (21.2)	3156 (5.2)	26 266 (43.4)	<.001
60-64	50 901	13 296 (26.1)	12 008 (23.6)	2745 (5.4)	22 852 (44.9)	
65-69	20 249	4695 (23.2)	5935 (29.3)	1175 (5.8)	8444 (41.7)	
70-77	38 189	8114 (21.2)	12 661 (33.2)	2085 (5.5)	15 329 (40.1)	
Sex						
Male	63 801	21 211 (33.2)	21 449 (33.6)	4759 (7.5)	16 382 (25.7)	<.001
Female	106 007	23 108 (21.8)	21 988 (20.7)	4402 (4.2)	56 509 (53.3)	
Geographic division						
Pacific	24 211	6939 (28.7)	5193 (21.4)	1184 (4.9)	10 895 (45.0)	<.001
New England	9696	2867 (29.6)	1887 (19.5)	618 (6.4)	4324 (44.6)	
Middle Atlantic	20 441	5051 (24.7)	4610 (22.6)	1310 (6.4)	9470 (46.3)	
Northeast central	38 873	9487 (24.4)	10 966 (28.2)	2161 (5.6)	16 259 (41.8)	
Northwest central	7764	1977 (25.5)	1951 (25.1)	453 (5.8)	3383 (43.6)	
South Atlantic	31 440	7726 (24.6)	8866 (28.2)	1529 (4.9)	13 319 (42.4)	
Southeast central	10 965	2522 (23.0)	3352 (30.6)	588 (5.4)	4503 (41.1)	
Southwest central	16 063	4793 (29.8)	4113 (25.6)	794 (4.9)	6363 (39.6)	
Mountain	9138	2708 (29.6)	2105 (23.0)	464 (5.1)	3861 (42.3)	
Comorbidity						
0	117 884	30 377 (25.8)	22 943 (19.5)	5771 (4.9)	58 793 (49.9)	<.001
1	35 690	9349 (26.2)	13 223 (37.0)	2331 (6.5)	10 787 (30.2)	
≥2	16 234	4593 (28.3)	7271 (44.8)	1059 (6.5)	3311 (20.4)	

racic imaging examination. We found that, compared with the rate of complications reported in the NLST, the rate was twice as high in the younger and Medicare age groups, even after adjustment for the underlying rate in the control cohort. In addition, the overall rate of complications in the elderly group was higher than that in younger individuals. For certain complications, such as those associated with surgical diagnosis, the costs can be as high as $56 200.

Although the NLST demonstrated the effectiveness of lung cancer screening, whether a similar magnitude of mortality benefit will be realized outside the trial setting remains uncertain; a similar concern has been raised about complication rates from diagnostic procedures. Tanner and colleagues[12] reported that, compared with NLST participants who had stage I non-small cell lung cancer, the 5-year all-cause mortality was comparable for an NLST-eligible cohort extracted from SEER-Medicare data but was worse for elderly patients with stage 1 non-small cell lung cancer who had significant comorbidities or did not undergo surgery. The authors concluded that the benefit of screening could be weakened among sicker elderly patients owing to the competing risk of death. This conclusion was not drawn from non-small cell lung cancer patients who had been screened for lung cancer with LDCT as the analysis used 1998 to 2010 SEER-Medicare data; instead, the authors made their inference by contrasting the characteristics between patients in the NLST and those in the general elderly population captured by SEER-Medicare data.

Figure 1. Incremental Complication Rates From Invasive Diagnostic Procedures After False-Positive Screening Results



A, Incremental complication rates in the younger age group (55-64 years) and the Medicare age group (65-77 years), with the complication rates reported in the National Lung Screening Trial (NLST) for comparison.[11] B, Incremental complication rates stratified by the procedure type, with the complication rates reported in the NLST for comparison.[2]

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Table 3. Incremental Complication Rates and Complication Costs Stratified by Procedure Type and Age Group

Procedure and Age Group, y	Rate (95% CI)				Cost (95% CI)		
	Incremental Complication Rate, %[a]				Complication Cost, $		
	Any	Minor	Intermediate	Major	Minor	Intermediate	Major
Cytology/needle biopsy							
All patients	18.7 (17.9-19.5)	13.6 (13.1-14.1)	13.9 (13.1-14.6)	4.0 (3.6-4.3)	9501 (8804-10 197)	15 252 (14 125-16 379)	38 633 (33 861-43 405)
55-59	15.8 (14.6-17.0)	11.0 (10.3-11.7)	11.6 (10.6-12.6)	2.6 (2.2-3.0)	10 177 (9076-11 278)	17 860 (15 264-20 457)	49 062 (35 854-62 270)
60-64	18.7 (17.3-20.2)	13.5 (12.6-14.4)	13.6 (12.3-14.8)	4.0 (3.4-4.5)	12 154 (10 172-14 136)	17 517 (15 093-19 940)	51 816 (40 084-63 547)
65-69	21.6 (19.1-24.2)	15.6 (13.9-17.2)	16.8 (14.5-19.1)	4.7 (3.6-5.9)	7159 (5881-8436)	12 757 (10 334-15 180)	44 135 (30 127-58 143)
70-77	23.5 (21.3-25.6)	18.7 (17.3-20.1)	18.0 (16.1-19.8)	6.6 (5.5-7.7)	7494 (6575-8412)	12 290 (10 791-13 789)	23 050 (19 169-26 932)
Bronchoscopy							
All patients	36.0 (35.1-36.9)	24.0 (23.3-24.6)	32.1 (31.2-32.9)	13.4 (12.9-13.9)	7478 (6617-8340)	18 985 (16 266-21 703)	60 838 (50 490-71 187)
55-59	37.7 (36.0-39.3)	24.0 (22.9-25.1)	32.2 (30.7-33.7)	12.7 (12.0-13.5)	7542 (6004-9080)	20 810 (16 355-25 266)	86 046 (53 021-119 070)
60-64	36.7 (35.0-38.5)	24.6 (23.4-25.7)	32.4 (30.8-34.0)	13.7 (12.9-14.6)	9795 (7735-11 854)	22 776 (16 082-29 470)	57 410 (36 612-78 207)
65-69	37.0 (34.5-39.7)	23.6 (22.0-25.4)	33.6 (31.3-36.0)	13.6 (12.3-14.9)	5573 (3637-7508)	19 470 (9859-29 081)	57 893 (37 899-77 888)
70-77	33.2 (31.3-35.0)	23.5 (22.3-24.7)	30.9 (29.2-32.5)	13.6 (12.5-14.6)	6441 (5063-7819)	14 368 (11 810-16 926)	52 071 (38 268-65 874)
Surgical							
All patients	51.7 (49.6-53.9)	46.5 (11.8-12.5)	41.3 (39.6-43.0)	11.3 (10.3-12.2)	10 634 (9129-12 139)	24 841 (22 129-27 552)	63 034 (52 038-74 031)
55-59	54.6 (51.1-58.1)	46.1 (43.4-48.8)	42.4 (39.3-45.5)	10.1 (8.7-11.4)	12 805 (9323-16 287)	27 796 (22 311-33 281)	78 283 (52 313-104 252)
60-64	53.1 (49.3-56.9)	47.8 (44.8-50.8)	41.4 (38.0-44.8)	11.3 (9.7-12.9)	10 564 (8445-12 682)	25 198 (20 592-29 804)	75 015 (51 572-98 458)
65-69	49.0 (43.5-55.7)	45.5 (41.0-50.2)	39.1 (33.9-44.5)	13.7 (10.7-16.7)	10 788 (5600-15 976)	21 420 (15 031-27 809)	46 544 (27 351-65 738)
70-77	47.3 (42.3-51.6)	46.2 (42.5-49.7)	40.8 (36.5-44.8)	11.8 (9.3-14.2)	8008 (6409-9607)	22 532 (17 317-27 746)	52 926 (34 691-71 162)
Other							
All patients	13.7 (13.1-14.3)	12.1 (11.8-12.5)	6.3 (5.8-6.8)	2.8 (2.6-3.0)	6255 (5905-6606)	10 942 (10 069-11 815)	31 444 (26 971-35 917)
55-59	14.4 (13.4-15.3)	12.5 (11.9-13.1)	6.1 (5.3-6.9)	3.2 (2.9-3.5)	7115 (6502-7729)	11 877 (10 023-13 730)	40 616 (29 680-51 551)
60-64	13.9 (12.9-15.0)	12.4 (11.7-13.0)	6.1 (5.2-7.0)	3.0 (2.7-3.4)	6571 (5942-7199)	13 882 (11 910-15 853)	42 854 (31 400-54 309)
65-69	13.6 (11.8-15.4)	11.9 (10.8-13.1)	6.4 (4.8-7.9)	3.1 (2.4-3.8)	6009 (4752-7265)	9416 (7608-11 224)	23 020 (16 944-29 097)
70-77	12.2 (10.8-13.6)	11.2 (10.3-12.1)	6.8 (5.6-8.0)	1.8 (1.2-2.4)	4975 (4406-5543)	7973 (6853-9093)	20 251 (14 896-25 606)

[a] The percentages are the incremental rates of complication levels (minor, intermediate, and major) in each age group between the study and control cohorts. For example, in the cytology/needle biopsy section, 13.6 in the cell corresponding to the minor incremental complication rate column and all patients row means that, among all individuals between ages 55 and 77 years who underwent cytology or needle biopsy, the adjusted rate (calculated using the incremental approach) of minor complications was 13.6%. The type of complications are not mutually exclusive, so 1 patient can have more than 1 type/level of complication.

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We followed a similar approach by analyzing complication rates and the associated costs among individuals who had undergone the types of invasive diagnostic procedures likely to be experienced by those who have positive findings identified on LDCT screening. Although our study cohort predated the implementation of lung cancer screening with LDCT, findings from our analysis contribute to the literature by informing policymakers and clinical communities of the potential magnitude of complication rates and the financial burden, at the population level, as the uptake of LDCT is extended to individuals in the general population who meet the screening eligibility criteria.

The complications associated with invasive diagnostic procedures played a role at a meeting that the Medicare Evidence Development & Coverage Advisory Committee convened to discuss Medicare coverage of lung cancer screening.[32] Several experts at the meeting expressed concerns that complication rates in settings outside the NLST could be higher than those reported in the NLST. Our findings echoed this concern, showing that the rates of postprocedural complications were more than twice the rates in the NLST (22.2% vs 9.8% among individuals younger than 65 years and 23.8% vs 8.5% among those 65 years or older).[11] Another concern voiced at the above meeting was variations in the quality of care across facilities that performed the follow-up diagnostic procedures. This concern is corroborated; the rates of postprocedural complications identified in our study and others showed considerable variation associated with various thoracic procedures.[33-38]

Many factors may have contributed to the wide variation in postprocedural complication rates across studies, such as quality standards, physician proficiency, and clinical infrastructure among community practices in performing diagnostic procedures subsequent to a positive finding. These variations will induce uncertainty regarding the harms of lung cancer screening programs in patients with positive findings determined on LDCT. Therefore, further studies are needed to determine factors that affect the quality of diagnostic procedures. Identifying factors that differentiate between practices with high vs low rates of complications will provide an opportunity to design interventions to lower the risk of postprocedural complications following positive LDCT findings and thereby reduce the physical, psychological, and financial burden associated with lung cancer screening.

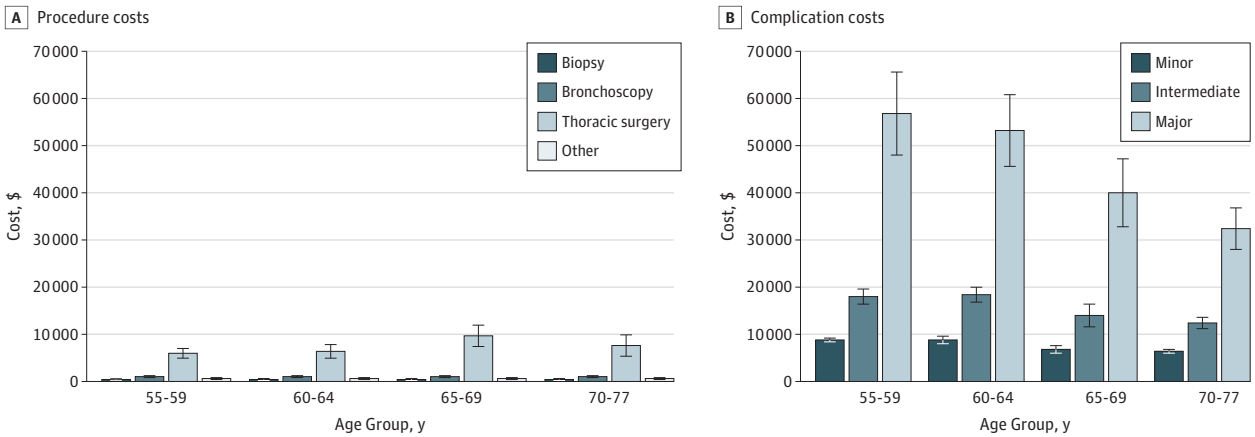
The financial burden of postprocedural complications can be great, as our data indicate that considerable costs are associated with the invasive diagnostic procedures and postprocedural complications. Although none of the costs reported in our study should be directly interpreted as costs associated with lung cancer screening, 2 implications can be drawn from our study for future research on the costs and cost-effectiveness of lung cancer screening. First, studies estimating costs associated with lung cancer screening programs should use complication rates observed in community-based clinical practices. Studies that use rates from clinical trials would likely underestimate the real cost; our study showed that the complication rates were higher in community settings than those reported in clinical trials. Second, our findings suggest that age is associated with the clinical and economic outcomes. The positive association between age and complication rates (and consequently costs) implies that future research using age-stratified analyses should yield more accurate estimates of costs and cost-effectiveness.

Limitations

Our study has limitations. We analyzed insurance claims data to estimate rates of complications occurring after invasive diagnostic procedures for lung abnormalities. To avoid overestimating the rates of complications, we applied an incremental approach by constructing a matched control cohort. Although this approach allows a more conservative assessment of postprocedural complication rates, its application to claims data has limitations.

First, our study may have underestimated minor complications because they are less likely to be coded and recorded in administrative data. Second, even with the use of an incremental

Figure 2. Procedure Costs and Complication Costs



A, Procedure costs stratified by age group and invasive diagnostic procedure group. B, Complication costs stratified by age group and complication type.

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approach by including a matched control cohort, this method was unlikely to subtract all medical problems that were not related to the invasive procedures in claims data. Third, MarketScan databases do not report information on the dates and causes of deaths; therefore, we were unable to evaluate whether the mortality rates associated with invasive diagnostic procedures were also higher in the community setting compared with the rate reported in the NLST. Fourth, we were not able to determine the extent to which the higher complication rates observed in community settings were owing to lower quality of care in these facilities, less experienced physicians performing these procedures, or unmeasured patient-level factors.

Fifth, as the data used in our study predated the acceptance of LDCT lung cancer screening by payers and the medical community, our study did not assess complication rates among individuals who met the screening eligibility criteria and had received LDCT. Individuals who underwent invasive procedures captured in our study likely either had a lung nodule noted as an incidental finding on imaging or a symptom indicating lung abnormality that prompted further investigations. Sixth, in claims data, it is difficult to determine whether medical events subsequent to an invasive diagnostic procedure were caused by the procedure, so the complication rates estimated in our study are more suggestive than conclusive. Seventh, some unobserved patient-level factors, such as smoking history, were not matched between the study and control cohorts owing to lack of data availability.

Conclusions

The complication rates associated with invasive diagnostic procedures for lung abnormalities estimated from the general population indicate that complication rates from diagnostic procedures subsequent to lung cancer screening in the real-world setting are likely to be significantly higher than those reported from clinical trials. As the number of individuals seeking lung cancer screening with LDCT increases, so too will the number of individuals undergoing invasive diagnostic procedures as a result of abnormal findings.[39] Results from this study, while tentative, emphasize the importance of including the risks of subsequent adverse events and downstream costs in the shared decision-making communications between physicians and patients.

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Concept and design: Huo, Shih.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Huo, Shih.
Critical revision of the manuscript for important intellectual content: All authors.
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