Economic Value of Bronchoscopy Technologies that Improves Sensitivity for Malignancy for Peripheral Pulmonary Lesions

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Abstract

Rationale: Although previous studies have assessed the clinical or economic value of specific technologies, the economic value of improving sensitivity for malignancy in lung cancer diagnoses broadly across technologies is unclear.

Objectives: To identify the economic value of improving sensitivity of bronchoscopy biopsy for the diagnosis of lung cancer.

Methods: A decision analytic model was developed to quantify the economic value of increased sensitivity for malignancy for bronchoscopy biopsy of peripheral pulmonary lesions. Primary clinical outcomes included time to diagnosis and survival. Economic outcomes included *1*) net monetary benefit (NMB), defined as the health benefits measured in quality-adjusted life-years (QALYs) times willingness to pay ($100,000/QALY) net of changes in medical costs; and *2*) incremental cost-effectiveness ratio. A decision tree modeling framework with two Markov module branches was developed. The two Markov modules corresponded to patients with cancer who were *1*) diagnosed and treated or *2*) undiagnosed and remained untreated. Outcomes were measured from a U.S. payer perspective over 30 years.

Results: Improving sensitivity for malignancy by 10 percentage points decreased average time to diagnosis for patients with lung cancer by 0.85 month (4 wk) and increased survival by 0.36 year (19 wk) because of faster treatment initiation. Overall health outcomes improved by 0.20 QALYs per patient. Cost increased by $6,727 per patient primarily through increased treatment costs among those diagnosed with cancer. Increasing sensitivity for malignancy by 10 percentage points improved NMB by $8,729 over 30 years (incremental cost-effectiveness ratio of $34,052), driven largely by improved sensitivity to early-stage cancer (stage-specific NMB, I/II, $19,805; III, $2,101; IV, −$1,438). Forty-two percent of overall NMB ($3,668) accrued within 5 years of biopsy. The relationship between change in sensitivity and NMB was approximately linear (1% vs. 10% sensitivity improvement corresponded to NMB of $885 vs. $8,729). The model was most sensitive to cancer treatment efficacy and follow-up time after a negative result.

Conclusions: Increasing sensitivity of malignancy by 10 percentage points resulted in a $8,729 improvement in net economic value. Health systems can use this information when making decisions regarding the value of new bronchoscopy technologies.

Keywords: bronchoscopy; sensitivity for malignancy; economics; economic value

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Early diagnosis is vital for effective lung cancer management. In 2021, the U.S. Preventive Services Task Force revised 2013 lung cancer screening guidelines, lowering age eligibility from 55 to 50 and pack-year history from 30 to 20 and increasing the estimated population eligibility for screening by 53.7%. In addition, over 1.5 million pulmonary lesions are incidentally identified each year (1–4). As a result, the use of minimally invasive biopsy techniques for evaluating pulmonary lesions is expected to increase.

Minimally invasive biopsy approaches for sampling of peripheral lesions vary in sensitivity for malignancy and safety outcomes. Currently, computed tomography (CT)-guided transthoracic needle biopsy, a widely used minimally invasive biopsy method, has a sensitivity for malignancy of approximately 90% (5). However, approximately one-quarter of patients who undergo CT-guided transthoracic needle biopsy experience complications such as pneumothorax (23.3%), hemorrhage (3.6%), and air embolism (0.02%), with some patients requiring additional interventions for management (6). Some lesions may also be inaccessible via a transthoracic approach because of anatomy or patient risk factors.

An alternative methodology for biopsy of peripheral pulmonary lesions is bronchoscopy. Although conventional bronchoscopy has demonstrated diagnostic sensitivity (60–76% sensitivity for malignancy) (7, 8), recent innovation in the bronchoscopy field (e.g., real-time ultrasound, advanced navigation platforms, advanced imaging modalities [9]) now allows targeting peripheral lesions with greater accuracy while preserving patient safety. Furthermore, robotics enhances maneuverability and improves reach into the periphery and stability to increase sensitivity for malignancy (10–13). Bronchoscopy allows mediastinal staging, sampling of multiple lesions, and a reduced risk of complications.

The diagnosis of peripheral pulmonary lesions with bronchoscopy involves a complex decision-making process in which clinicians consider factors such as the likelihood of establishing a diagnosis, complications, diagnosis time, staging, cost, nodal metastasis risk, and mortality. Previous studies evaluated that the most cost-effective diagnostic strategy for lung cancer depends on lesion stage, location, and type of biopsy (14). Other studies have assessed the economic value between bronchoscopy and traditional CT-guided biopsy (15, 16); however, little is known about the economic outcomes of increased test sensitivity when diagnosing patients with suspected lung cancer. The purpose of this study was to quantify the health and economic value of improved sensitivity for malignancy for bronchoscopic procedures targeting peripheral pulmonary lesions to inform health care decision makers on decisions related to diagnostic technologies for health systems.

Methods

Model Overview and Decision Context

A decision-tree model of patients who undergo bronchoscopy as the initial procedure for lung cancer diagnosis (Figure 1) was developed. The target population for the model consisted of a hypothetical cohort of 1,000 patients with peripheral pulmonary lesions suspected of being malignant who required a biopsy and were deemed candidates for a bronchoscopic procedure following previous studies (14). The population excludes patients who received a rapid on-site diagnosis from lymph node sampling that precludes the need for a peripheral biopsy. The model population had a 67% prevalence of cancer and incorporated lesion factors such as size, location, and patient history, consistent with large-scale bronchoscopy studies (17, 18).

The simulated model contained two submodels: one for patients with lesions that are not malignant (noncancer submodel) and another for patients whose lesions are malignant (cancer submodel). The intervention was a hypothetical increase of sensitivity for malignancy of 10%, hereinafter referred to as the high-sensitivity group. Baseline sensitivity for malignancy was assumed to be 70%, hereinafter referred to as the low-sensitivity group. This model did not consider changes in bronchoscopy cost as sensitivity increases, because the aim of this study was to quantify the economic value of improved sensitivity for malignancy, regardless of any specific bronchoscopy technology. As such, the utility of this model is to support the evaluation of future bronchoscopy technologies. The final model was conducted in Microsoft Excel 365 and followed Consolidated Health Economic Evaluation Reporting Standards guidelines (19).

At index, bronchoscopy results were either malignant or nonmalignant on the basis of test sensitivity. Patients diagnosed with malignancy (true positive) in the model had their disease progress based on a first-order Markov chain with a 1-month cycle length, which is defined by three severity stages of lung cancer—stage I/II (localized), stage III (regional), and stage IV (distant)—and death and the transition probabilities between stages, hereafter referred to as the long-term outcomes model.

Patients with nonmalignant histopathologic results were classified as either true negative and exited the model or false negative and entered the delayed-diagnosis model. The model assumes that improvements in sensitivity for malignancy did not affect detection of other (i.e., nonmalignant) diseases, thus keeping costs and outcomes for true-negative lung cancer patients unchanged. Patients with a false-negative result (undiagnosed) were either sent to immediate follow-up biopsy or surveillance until diagnosis. Specificity was assumed to be 100%. Undiagnosed patients with lung cancer remained untreated, and their lung cancer progressed until diagnosed through a follow-up biopsy, hereafter referred to as the delayed-diagnosis model. Delays in follow-up biopsy within the immediate follow-up, surveillance, and lost-to-follow-up arms were 1, 6, and 24 months, respectively, from index bronchoscopy. Subsequent procedures included both nonsurgical (bronchoscopy or transthoracic needle aspiration) and surgical biopsies (video-assisted thoracic surgery or thoracotomy; *see* Table E1 in the data supplement) (20, 21).

Outcomes were estimated from a U.S. payer perspective over 30 years. Clinical outcomes assessed included *1*) time until a biopsy correctly confirms malignancy (i.e., time to diagnosis) and *2*) distribution of cancer stage at diagnosis and patient survival (i.e., life-years gained). Health gains were quantified on the basis of quality-adjusted life-years (QALYs) and monetized assuming a willingness to pay (WTP) of $100,000 per QALY (22). Costs included initial bronchoscopy procedure (assumed to be equal between both sensitivity groups), follow-up diagnostic procedures, related adverse events, cancer treatment costs, and all other lifetime medical costs. Treatment value was assessed using net monetary benefit (NMB) and incremental cost-effectiveness ratio (ICER). NMB is a

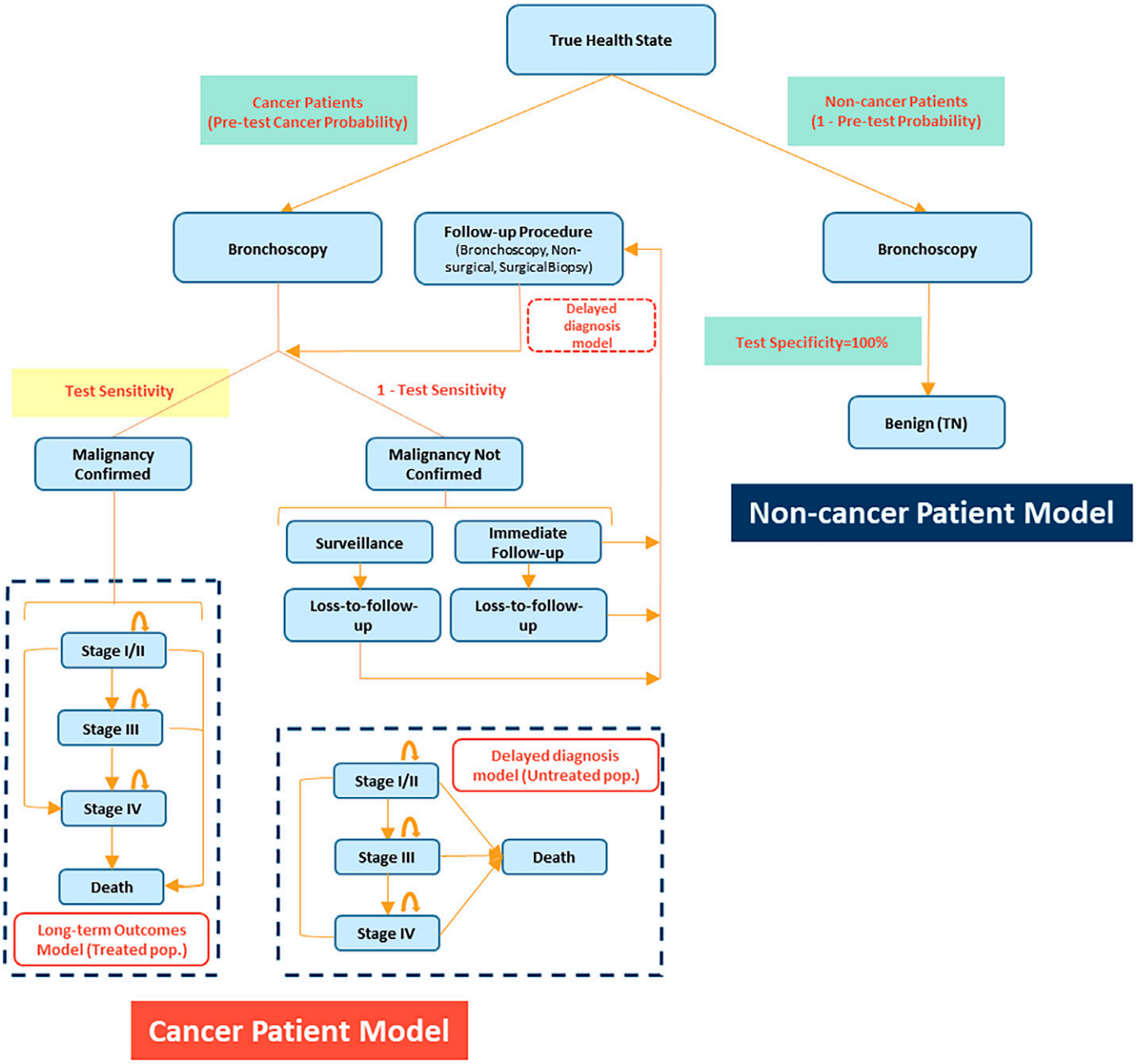

Figure 1. Model structure.

summary statistic that measures the value of an intervention in monetary terms at a specified WTP threshold for a unit of benefit (e.g., QALY). More precisely, NMB is defined as the incremental health benefit times the WTP, net of incremental costs. NMB measures the difference between alternative interventions, so a positive NMB indicates that an intervention is cost-effective compared with the alternative at the given WTP threshold, whereas a negative NMB indicates that costs exceed benefits. Conceptually, ICER is similar to NMB, but it is a ratio rather than additive. The discount rate used was 3% (23).

Stage-specific NMB was determined by calculating NMB when 100% of the population had stage I/II, III, or IV lung cancer. With this information, one can calculate the NMB of increased sensitivity in other populations using the following equation: (Economic value stage I/II × Cancer prevalence × % stage I/II) + (Economic value stage III × Cancer prevalence × % stage III) + (Economic value stage IV × Cancer prevalence × % stage IV).

Model Inputs

Model inputs were composed of *1*) clinical inputs including the efficacy, safety, and use of procedures and treatments; *2*) transition probabilities for long-term and delayed-diagnosis models; *3*) utility inputs for

health-related quality-of-life measurements; and *4*) financial inputs, including costs of procedures and treatments (Tables 1 and E1).

Clinical Inputs

The test sensitivities for follow-up bronchoscopies were 70% and 80% for the baseline (low sensitivity) and intervention (high sensitivity) groups, respectively; test sensitivities for follow-up transthoracic needle aspiration and surgical biopsies were 90% and 100%, respectively (21). Among those requiring a follow-up biopsy after bronchoscopy, the model assumed 25.0% received another bronchoscopy, 43.0% transthoracic needle aspiration, 18.4% thoracotomy, and 13.6% video-assisted thoracic surgery (20, 21). Diagnostic procedure safety was identified by reported occurrence rates of adverse events (i.e., pneumothorax, hemorrhage, and mechanical ventilation for nonsurgical procedures and pneumonia and empyema additionally for surgical procedures) (24).

Transition Probabilities

In the long-term outcomes model, the distribution for the stage at diagnosis was parameterized from the largest prospective study on bronchoscopy (25). For this model, we used the 1-, 3-, 5-, and 10-year lung cancer survival rates for localized disease (stage I/II), regional (stage III), and distant (for stage IV) from 2022 Surveillance, Epidemiology, and End Results Program data (26). Assuming that transitioning to later stage or death followed a Poisson process for each stage, we analytically derived survival for 1–12, 13–36, 37–60, and 61–360 months on the basis of 1-, 3-, 5-, and 10-year survival rates, respectively. A numerical approach was used to derive transition probabilities from a lower cancer stage to a higher stage or all-cause mortality. Survival functions of patients in stages I/II, III, and IV are shown in Figure E1.

For the delayed-diagnosis model, monthly transition probabilities of the undiagnosed/untreated patients with lung cancer were derived from literature that calibrated the quarterly hazard rate of natural progression for untreated lung cancer, assuming exponential survival (27). These transition probabilities approximate the accelerated progression of more advanced stages of lung cancer from lack of treatment. To validate the accuracy of progression and mortality rates for the delay period, we compared the model's estimated effects of early diagnosis on mortality with the efficacy estimates of low-dose CT screening on the long-term mortality rate of lung cancer from the NLST (National Lung Screening Trial) (Appendix E1) (28).

Utility Inputs for Health-related Quality-of-Life Measurements

Health-related quality-of-life estimates were measured using two components: quality of life by cancer stage and adverse events. Quality-of-life estimates by cancer stage were drawn from a meta-analysis of lung cancer utility (29, 30). Additive impacts from adverse events were based on disutilities of empyema, hemorrhage, mechanical ventilation, pneumonia, and pneumothorax (15, 24, 29, 31–37).

Financial Inputs

Healthcare costs were assumed to be impacted by changes in sensitivity for malignancy through two pathways. The first comprised costs increased from additional biopsies and surveillance needed when the initial biopsy did not confirm malignancy, which included costs for CT scans, physician office visits (38, 39), biopsy, and related adverse events (24). Biopsy-related and adverse event costs were identified by calculating the weighted average of median costs for each biopsy modality between inpatient and outpatient settings (24). The second comprised costs increased resulting from delayed diagnosis: If cancer diagnosis was delayed, patients were more likely to be diagnosed at a later stage of lung cancer when cancer treatment costs are higher. Monthly medical costs of treated patients at each stage were derived using lung cancer stage-specific time to death calculated from Surveillance, Epidemiology, and End Results data and total medical cost of patients with lung cancer measured by stage at diagnosis (26, 40). Monthly medical costs of undiagnosed/untreated patients were calculated by total medical costs of patients with lung cancer net of lung cancer treatment costs (40). Costs were inflated to 2022 U.S. dollars (41).

Sensitivity and Scenario Analyses

One-way sensitivity analysis (i.e., adjusted model parameters by $\pm$10%) was performed to evaluate model robustness. Scenario analyses were conducted to consider the interaction between sensitivity for malignancy with follow-up time, different distribution of immediate follow-up, surveillance, loss to follow-up, and changes in surgery use for any follow-up biopsies. This study also calculated the economic impacts at WTP thresholds of \$50,000, \$100,000 (baseline), \$150,000, and \$200,000 per QALY (22). Last, we conducted a societal perspective analysis based on nonmedical out of cost, caregiver burden, and productivity loss (Table E6). Two-way sensitivity analyses were developed on the three most impactful parameters from the one-way sensitivity analysis (Appendix E2).

Results

Base Case Analysis Results

Increasing sensitivity for malignancy of bronchoscopy from 70% to 80% reduced time to diagnosis by 0.85 months (4 wk) compared with the low-sensitivity group (1.61 vs. 2.46 mo or 7 vs. 11 wk; Table 2). This resulted in a higher proportion of patients diagnosed at an earlier cancer stage for the high-sensitivity group relative to the low-sensitivity group (62.96% vs. 61.68% in stages I/II, 18.08% vs. 18.68% in stage III, and 18.95% vs. 19.65% in stage IV) (Table 2).

Because of earlier diagnosis and treatment, patients in the high-sensitivity group had higher rates of lung cancer diagnosis and reduced mortality relative to those in the low-sensitivity group (Figure E2). Life-year gains of the high-sensitivity group were 0.36 year (10.89 vs. 10.53 for the high- and low-sensitivity groups, respectively), or 19 weeks (Table 2). Patients with cancer in the high-sensitivity group also spent more time in treatment than those in the low-sensitivity group: 0.40 year (10.82 vs. 10.42), or 20 weeks. Moreover, the high-sensitivity group spent 0.04 fewer years (0.07 vs. 0.11, or 2 wk) remaining untreated than the low-sensitivity group. A reduction of approximately one unnecessary diagnostic procedure per 12 patients was achieved (1.16 vs. 1.24 procedures per patient).

When considering survival, quality of life, and adverse events, higher sensitivity for malignancy improved health outcomes. Specifically, total discounted QALYs of patients with cancer were higher in the high-sensitivity group (5.99) than in the low-sensitivity group (5.79) by 0.20 QALYs (Table 2). The largest health gains were due to an increased share of patients receiving cancer treatment earlier (5.94 vs. 5.72; difference = 0.22). A negligible proportion of

Table 1. Table of model inputs

Category	Parameter	Value	Source
Clinical input	Pretest prevalence of lung cancer	67%	Folch *et al.* (25)
	Test sensitivity		
	Initial biopsy		
	Baseline (low sensitivity)	70%	Assumption
	Intervention (high sensitivity)	80%	Assumption
	Follow-up biopsy		
	Bronchoscopy		
	Baseline	70%	Assumption
	Intervention	80%	Assumption
	TTNA	90%	DiBardino *et al.* (5)
	Surgical biopsy	100%	Feller-Kopman *et al.* (21)
	Noncancer disease	100%	Assumption
	Biopsy use		
	First biopsy		
	Bronchoscopy	100%	Assumption
	TTNA	0%	Assumption
	Follow-up biopsy		
	Bronchoscopy	25%	Zhang *et al.* (20)
	TTNA	43%	Zhang *et al.* (20)
	Surgery	32%	Zhang *et al.* (20)
	Thoracotomy	58%	Feller-Kopman *et al.* (21)
	VATS	42%	Feller-Kopman *et al.* (21)
	Distribution of follow-up conditional on false negatives		
	Surveillance (benign)	50%	Assumption
	Loss to follow-up conditional on surveillance (benign)	10%	Assumption
	Immediate follow-up (nondiagnostic)	50%	Assumption
	Loss to follow-up conditional on immediate follow-up (nondiagnostic)	10%	Assumption
	Distribution of lung cancer stages at diagnosis		
	Stage I/II	0.6527	Folch *et al.* (25)
	Stage III	0.1702	Folch *et al.* (25)
	Stage IV	0.1772	Folch *et al.* (25)
	Monthly survival rates		
	1–12 mo		
	Stage I/II	0.889	Author's calculations based on NIH SEER (2019)
	Stage III	0.771	Author's calculations based on NIH SEER (2019)
	Stage IV	0.381	Author's calculations based on NIH SEER (2019)
	13–36 mo		
	Stage I/II	0.952	Author's calculations based on NIH SEER (2019)
	Stage III	0.816	Author's calculations based on NIH SEER (2019)
	Stage IV	0.660	Author's calculations based on NIH SEER (2019)
	37–60 mo		
	Stage I/II	0.952	Author's calculations based on NIH SEER (2019)
	Stage III	0.905	Author's calculations based on NIH SEER (2019)
	Stage IV	0.829	Author's calculations based on NIH SEER (2019)
	61–360 mo		
	Stage I/II	0.964	Author's calculations based on NIH SEER (2019)
	Stage III	0.937	Author's calculations based on NIH SEER (2019)
	Stage IV	0.907	Author's calculations based on NIH SEER (2019)
	Monthly transition probability (delay-period model)		
	Stage I/II to stage III	5.08%	Hofer *et al.* (27)
	Stage I/II to stage IV	3.74%	Hofer *et al.* (27)
	Stage I/II to stage death	4.86%	Hofer *et al.* (27)
	Stage III to stage IV	5.11%	Hofer *et al.* (27)
	Stage III to death	5.37%	Hofer *et al.* (27)
	Stage IV to death	11.12%	Hofer *et al.* (27)

(*Continued*)

Table 1. (*Continued*)

Category	Parameter	Value	Source
Utility	Quality of life without cancer	0.867	Szende *et al.* (30)
	Baseline quality of life by lung cancer stage		
	Stage I/II	0.825	Sturza (29)
	Stage III	0.772	Sturza (29)
	Stage IV	0.573	Sturza (29)
	Disutility by indeterminate test results	−0.0033	Toumazis *et al.* (37)
Cost	Biopsy (including adverse event costs)		
	Bronchoscopy	$6,684	Calculated using Chiu *et al.* (24)
	TTNA	$2,756	Calculated using Chiu *et al.* (24)
	Surgery	$32,247	Calculated using Chiu *et al.* (24)
	Physician visits (including screening counseling)	$173	CMS, ACR
	Monthly treatment cost for patients with lung cancer		
	Long-term outcomes model (diagnosed patients)		
	Stage I/II	$1,771	Calculated using Sheehan *et al.* (40)
	Stage III	$3,740	Calculated using Sheehan *et al.* (40)
	Stage IV	$5,880	Calculated using Sheehan *et al.* (40)
	Delayed-period model (undiagnosed patients)		
	Stage I/II	$896	Calculated using Sheehan *et al.* (40)
	Stage III	$630	Calculated using Sheehan *et al.* (40)
	Stage IV	$760	Calculated using Sheehan *et al.* (40)

Definition of abbreviations: NIH SEER = National Institute of Health Surveillance, Epidemiology, and End Results Program; TTNA = transthoracic needle aspiration; VATS = video-assisted thoracoscopic surgery.

the health improvements was explained by a reduced number of biopsy-related adverse events: <0.01 increase in QALY. Conversely, the high-sensitivity group obtained 0.03 lower QALYs than the low-sensitivity group before cancer diagnosis (0.08 vs. 0.05). The discounted QALY gains when including all patients with and without cancer was 0.13 QALYs (4.01 vs. 3.88).

Although earlier diagnosis of cancer from increased sensitivity for malignancy decreased average monthly cost among patients with cancer ($2,235 vs. $2,257 for the high- and low-sensitivity groups, respectively), total lifetime costs were higher in the high-sensitivity group than in the low-sensitivity group by $6,727 ($291,964 vs. $285,237) because patients lived longer

Table 2. Base case model results

Model Output	Low-Sensitivity Group	High-Sensitivity Group
Time to diagnosis, mo	2.47	1.61
Distribution of cancer stage at diagnosis		
Stage I/II	61.68%	62.96%
Stage III	18.68%	18.08%
Stage IV	19.65%	18.95%
Health outcomes among lung cancer patients		
Years that a patient receives treatment	10.42	10.82
Years that a patient remained untreated	0.11	0.07
Life-years	10.53	10.89
Number of biopsies per patient with cancer	1.24	1.16
QALYs per lung cancer patients		
QALYs accrued after lung cancer diagnosis	5.72	5.94
QALYs before lung cancer diagnosis	0.08	0.05
Biopsy-associated QALYs	−0.0022	−0.0018
Total	5.79	5.99
Costs per patient with lung cancer		
Medical costs accrued after lung cancer diagnosis	$274,299	$282,505
Biopsy-associated costs	$9,878	$8,765
Medical cost before lung cancer	$1,060	$694
Total	$285,237	$291,964
Net monetary benefit	$8,729	
Incremental cost-effectiveness ratio	$34,052	

Definition of abbreviation: QALY = quality-adjusted life-year.

and received treatment longer (Table 2). Increased cost due to longer duration of lung cancer treatment—largely due to increased life expectancy—explained more than 90% of the total costs for both groups ($282,505 vs. $274,299; difference of $8,206). These costs were partly offset by reduced biopsy costs ($8,765 vs. $9,878; difference of −$1,113) and reduced medical costs for undiagnosed patients with lung cancer ($694 vs. $1,060; difference of −$366). For all patients who did and did not have cancer, total discounted costs were $4,507 higher for the high-sensitivity group than for the low-sensitivity group ($195,616 vs. $191,109).

Increasing test sensitivity for malignancy from 70% to 80% generated a positive economic value, NMB of $8,729, corresponding to the ICER of $34,052 per QALY (Tables 2 and E2). About 40% of the value (NMB of $3,668) was realized within 5 years of the initial bronchoscopy (Figure E3). Increasing test sensitivity from 70% to 71% led to an NMB of $885, or approximately one-tenth of increasing sensitivity for malignancy by 10% (Tables E2 and E3).

The stage-specific NMB values of increasing test sensitivity from 70% to 80% when 100% of patients had stage I/II, III, or IV disease were $19,805, $2,101, and −$1,438, respectively (Table 3). The overall NMB of the base case model, $8,729, was obtained by taking a weighted average of the stage-specific NMBs using the prevalence (67%) and cancer stage distribution as weights (i.e., [$19,805 × 67% × 65.27%] + [$2,101 × 67% × 17.02%] + [−$1,438 × 67% × 17.72%]). The NMB for any population can be calculated, provided that the prevalence of cancer and the stage distribution is known, using the stage-specific NMB as shown.

Sensitivity and Scenario Analysis Results

Our results were robust through a variety of sensitivity and scenario analyses. The economic value results were most sensitive to variations in the utility of stage I/II lung cancer (NMB of [$7,786, $9,672]), the stage I/II transition probabilities of the long-term outcomes model ([$7,917, $9,655]), and those of the delay-period model ([$8,083, $9,323]) (Figure 2).

Among the three scenario types, longer delays in follow-up made the value of improved sensitivity for malignancy higher (Table E4 and Figure 3). Delaying immediate follow-up from 1 to 3 months or surveillance from 6 to 12 months increased the value of higher sensitivity for malignancy (NMB of $10,288 and $10,717 for scenarios 1a and 1b). Higher sensitivity was particularly valuable when patients were likely to be lost to follow-up after a false-negative index bronchoscopy (scenario 2c, $22,242) but less valuable when all patients had an immediate follow-up biopsy within 1 month (scenario 2a, $3,635).

Increased sensitivity for malignancy continued to be a cost-effective solution, even after adjusting the WTP threshold. The 30-year NMB values when the WTP threshold was changed to $50,000, $150,000, and $200,000 per QALY were $2,111, $15,347, and $21,965, respectively (Table E5). The base case model showed that increased sensitivity continues to provide economic benefit at the societal perspective (NMB = $9,344; Table E6) (42, 43).

Discussion

This study quantified the economic value of increasing sensitivity for malignancy for bronchoscopy biopsy procedures in diagnosing lung cancer. The model estimated that patients with lung cancer benefit from increases in sensitivity for malignancy by reducing time to treatment by 0.85 month (4 wk) and increasing the proportion of patients diagnosed at stage I/II by 1.28%. Increasing sensitivity for malignancy improved health outcomes (5.99 vs. 5.79 QALYs for the high- and low-sensitivity groups, respectively) but increased cost ($291,964 vs. $285,237) in large part due to patients with lung cancer being diagnosed and treated more rapidly and living longer. As a result, when sensitivity for malignancy increased by 10 percentage points, the NMB was $8,729, assuming a WTP of $100,000 per QALY, and the ICER was $34,052. In other words, the value of health benefits from a 10–percentage point increase in sensitivity for malignancy was $8,729 higher per patient than the costs.

Although this study estimated the economic value of increased sensitivity of malignancy using the distribution of cancer stage from the NAVIGATE (Clinical Evaluation of superDimension Navigation System for Electromagnetic Navigation Bronchoscopy) trial, the stage-specific NMB results from this study can be used to calculate the NMB of increased sensitivity in other populations, provided the prevalence

Table 3. Stage-specific economic value when all patients have malignancy and all are at same stage

All Patients Begin in Stage	Stage-Specific NMB (A)	Prevalence of Lung Cancer (B)	Stage-Specific NMB at Given Prevalence (C = A × B)	Lung Cancer Distribution (D)	NMB of Base Case Population (A) × (B) × (D)
I/II	$19,805	67%	$13,269	65.27%	$8,729*
III	$2,101	67%	$1,408	17.02%	
IV	−$1,438	67%	−$963	17.72%	

Definition of abbreviation: NMB = net monetary benefit.
For a population with a prevalence of cancer (B) and a stage distribution (D), we can calculate the NMB as shown. The stage-specific NMB (A) is the NMB if all patients have the stage of disease shown on the left. If the prevalence of cancer was 67%, as shown in (B), but that was the only stage of cancer present, then the NMB is shown in column (C). In column (D) is the stage distribution used in the base case scenario. Multiplying column (A) × (B) × (D) for each stage and summing the three different stages provides the NMB for the entire population. In the base case that is shown above, that is $8,729. The stage-specific NMB can be used to calculate the NMB for any population, provided the prevalence of cancer is known and the stage distribution of the cancers is specified.
*Cross product of columns (C) and (D) do not match NMB exactly because of rounding. Column (D) does not add up to 100% exactly because of rounding.

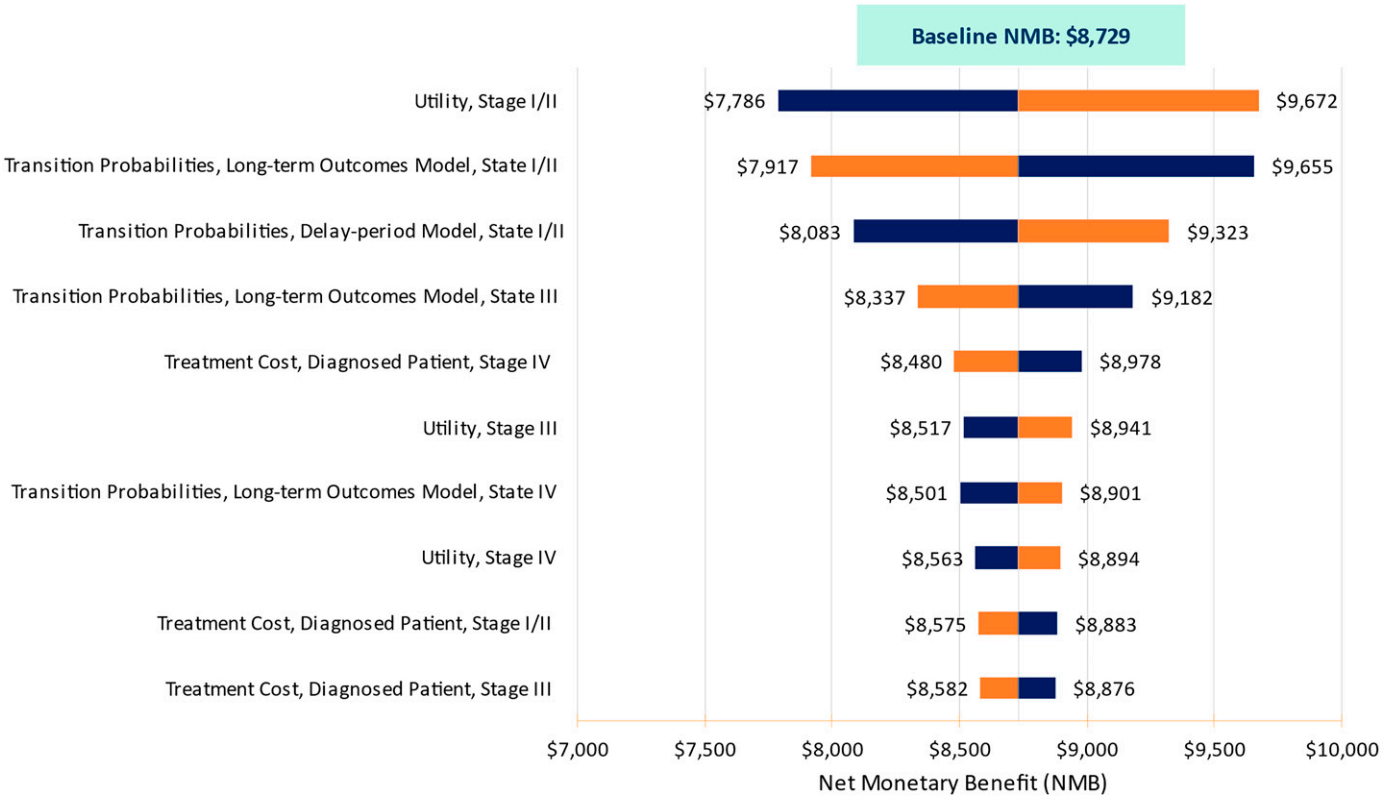

Figure 2. Sensitivity analysis tornado diagram. NMB = net monetary benefit.

and stage distribution of lung cancer is known (Table 3). Appendix E3 provides sample calculations using the NLST study population (28).

The scenario analysis revealed that the value of improved sensitivity for malignancy varies, depending on patient follow-up protocols. When physician discretion, budget limitations, or social determinants of health lead to less frequent follow-up or cause patients not to return for follow-up visits (20), the value of improved sensitivity for malignancy for lung cancer diagnosis increases. Conversely, the value of improved sensitivity for malignancy declines with more rapid follow-up, because false-negative or nondiagnostic results can be identified more rapidly. Pairing advanced diagnostic technologies with prompt outreach for follow-up visits would improve health and economic outcomes.

Limitations

This study has several limitations. Although the model aimed to quantify the benefit of increased sensitivity for malignancy in bronchoscopy for patients with peripheral lesions, if applied to a similar population that received endobronchial ultrasound without rapid on-site evaluation (38% among patients with lung cancer undergoing endobronchial ultrasound) (44), the model would overestimate the NMB, because some patients receiving a nondiagnostic peripheral biopsy would be diagnosed by lymph node biopsy, and no treatment delay would ensue. Second, the model assumed immediate treatment upon diagnosis, whereas in practice, there may be delays between diagnosis and treatment (45). Third, the model assumes the population is similar to the NAVIGATE population and that increased sensitivity for malignancy did not change stage distribution or prevalence among those who underwent a bronchoscopy. This might not be true in the future. However, using stage-specific NMBs calculated in Table 3 can address this, provided that prevalence and stage distribution are accurately specified. Fourth, the model does not consider potential correlations between cancer stage and the probability of immediate follow-up biopsies versus surveillance after a negative test result. For instance, negative results would be suspicious to physicians among patients with larger lesions; surveillance would only be likely for small lesions (e.g., $<$1 cm) more likely to be stage I if malignant. The model assumes surveillance would be equally likely in patients with across stages. Moreover, loss to follow-up was assumed to be equally likely among groups, but it is probable that patients who are asymptomatic with earlier stage disease would be much more likely to be lost to follow-up than patients who are symptomatic with stage III/IV disease. Fifth, we do not account for benefits from new therapies. Although external validation was performed comparing the proportional effect with the effect observed in the NLST study (Appendix E1) (28), in practice, the benefits of improved sensitivity for malignancy may vary because new immunotherapy and other agents have improved lung cancer survival in recent years (46). Sixth, this model does not account for overdiagnosis of lung cancer. If there is more overdiagnosis due to lung cancer screening, then the impact of improved sensitivity would be mitigated for those patients (47). A specificity of 100% was also assumed due to bronchoscopy having nearly 100% specificity and previously

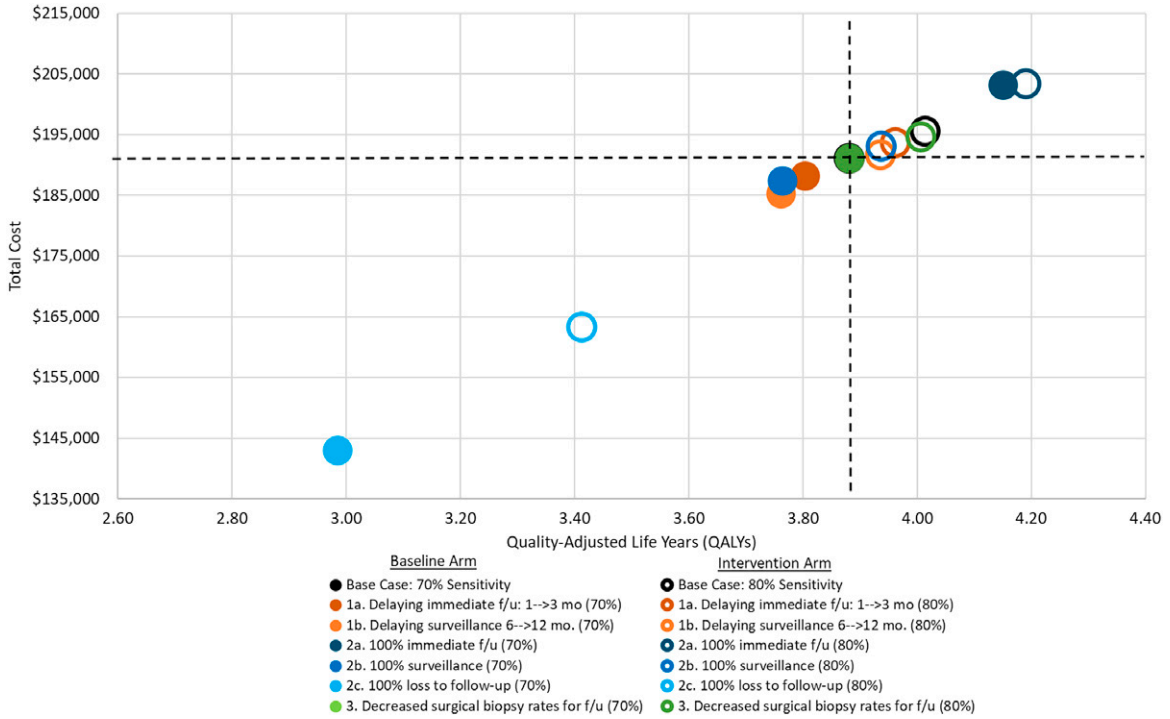

Figure 3. Total cost and quality-adjusted life-years (QALYs) for each scenario. The intersecting dashed black lines outline the cost-effectiveness quadrants relative to the base case scenario with 70% sensitivity. Points in the upper left quadrant relative to this are more costly and less effective. Points in the lower left quadrant are less costly but less effective. Points in the lower right quadrant are less costly and more effective. Points in the upper right quadrant are more costly but also more effective. Relative to the base case scenario with 70% sensitivity, all scenarios in this analysis fall into either the upper right quadrant (more costly but more effective) or in the lower left quadrant (less costly but less effective). Overall, the single best scenario in terms of QALYs is scenario 2a, with 100% immediate follow-up and 80% sensitivity (darker blue hollow dot). Note that compared with the base cases scenario, most of the improvement in QALYs is due to the 100% immediate follow-up. If sensitivity remains at 70% but we change to 100% immediate follow-up, QALYs improve from 3.88 per patient screened in the base case to 4.15, whereas costs increase from $191,109 to $203,060 (incremental cost-effectiveness ratio = $44,359).

published models assumed 100% specificity (17, 21, 48, 49). Next, because of the limited evidence from the literature, follow-up time intervals were estimated from clinical experience of three pulmonologists from different U.S. medical institutions. Moreover, this study does not explicitly consider lesion size. However, lesion size is implicitly addressed through cancer stage because lesion size and stage are closely associated with each other. Last, this study does not discuss the economic benefit of improving accuracy in nonmalignant diseases; in practice, however, more advanced bronchoscopy technologies that improve sensitivity for malignancy are also likely to improve diagnosis of certain other diseases, and thus this model likely provides a conservative estimate of economic value.

Conclusions

In summary, increasing sensitivity for malignancy resulted in meaningful health economic benefits. Specifically, $8,729 of health economic value is generated when increasing sensitivity for malignancy from 70% to 80%. Improved sensitivity for malignancy through advanced bronchoscopy technologies coupled with interventions to stratify the risk of patients with nondiagnostic bronchoscopy results and expedite follow-up biopsy time can maximize patient outcomes and generate economic value for payers and health systems. ■

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