Online Data Supplement for

Factors That Influence Physician Decision-making for Indeterminate Pulmonary Nodules

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Supplemental Methods

Survey Instrument Design
Standard conjoint analysis methodology was used to design, implement and analyze the web-based survey. The five main steps included defining attributes, assigning attribute levels, creating scenarios, obtaining preference data, and estimating model parameters. The first task required identification of key clinical factors that influence the decision to pursue invasive testing for indeterminate pulmonary nodules, as well as to identify clinically meaningful ranges for each of the variables. This was accomplished via a review of medical literature, and interviews with 16 pulmonologists and thoracic surgeons who manage patients with pulmonary nodules. The survey instrument was piloted with 6 pulmonologists to verify understanding of the case scenarios and iteratively refined.

Details of Survey Instrument Administration
The survey was administered between October 4, 2012 and October 22, 2012 to pulmonary physicians. The median time to completion was 25 minutes. The following additional information is included below: survey sections that assessed physician eligibility and practice characteristics, and information regarding the hypothetical blood test provided to respondents. This is followed by a summary of the discrete choice experiment that was completed by respondents. This includes the definitions provided as well as the attributes and their levels.

1. **Text of Physician Eligibility Verification**

Thank you for agreeing to participate in the survey. Before you begin, please verify your eligibility by answering the following questions:

EV1: Please select the option that most closely describes your specialty.
- □ Primary Care *(Exclude)*
- □ Thoracic Surgery *(Exclude)*
- □ Pulmonologist *(Target 150)*
- □ Other *(Exclude)*

EV2: In what state are you located?

Northeast *(Target 25)*	Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont
Midwest *(Target 25)*	Indiana, Illinois, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin
South Atlantic *(Target 25)*	Delaware, District of Columbia, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia
South Central *(Target 25)*	Alabama, Arkansas, Kentucky, Louisiana, Mississippi, Oklahoma, Tennessee, Texas
Mountain *(Target 25)*	Arizona, Colorado, Idaho, Montana, New Mexico, Nevada, Utah, Wyoming
Pacific *(Target 25)*	Alaska, California, Hawaii, Oregon, Washington

EV3: Are you board certified or board eligible?
- □ Yes
- □ No *(Exclude)*

EV4: How many years have you been in practice? _____year(s)
> *If >3 and <26 – CONTINUE*
> *If <3 or >26 – EXCLUDE*

EV5: What percentage of your time is spent performing direct clinical care (versus research or administrative duties)? _____%
> *If >75% - CONTINUE*
> *If <75% - EXCLUDE*

EV6: Approximately how many patients do you see per month? _____patients
> *If >50 - CONTINUE*
> *If <50 - EXCLUDE*

EV7: Pulmonary nodules are small, approximately spherical, circumscribed piece of abnormal tissue found in the lung. They are often identified incidentally on chest radiographs or CT scans. Of the [EV6 response] patients you see per month, approximately how many patients have pulmonary nodules?
> _____patients
> *If >10 – CONTINUE*
> *IF <10 – EXCLUDE*

EV8: Of the [EV7 response] patients with nodules you see per month, approximately how many patients have newly identified nodules?
> _____patients
> *If >5 – CONTINUE*
> *If <5 – EXCLUDE*

EV9: Of the [EV8 response] patients with newly identified pulmonary nodules, what percent of patients' nodules fall into each of the following size categories? Please stratify your responses by nodule size. *Should add up to 100%*

<4mm	4-7mm	8-15mm	16-20mm	>20mm	Total
(n)%	(n)%	(n)%	(n)%	(n)%	100%

> *If %8-15mm + %16-20mm = 0 – EXCLUDE*

EV10: Have you received money for work associated with the development of diagnostic products for lung nodules?
- ☐ Yes *(Exclude)*
- ☐ No

2. **Text of Physician Introduction**

Welcome

We have confirmed your eligibility. The purpose of this survey is to learn from your insights regarding current diagnostic and treatment approaches for non-small cell lung cancer (NSCLC) in patients with indeterminate pulmonary nodules. In addition, we hope to learn about your preferences regarding a novel diagnostic test for determining the risk of non-small cell lung cancer in patients with indeterminate pulmonary nodules.

Once you have completed the survey, please allow time for us to process your honoraria. You must fully complete the survey to receive the honoraria.

The survey is confidential and should take about 20 minutes. *[We will use the physician feedback to adjust the survey as necessary.]*

We recommend you finish the survey in one sitting.

You can return to a previous page in the survey (unless otherwise noted), but you may lose the data you have already entered on the page you are currently viewing. To review questions, use the "back" buttons in the survey itself, not arrows in your browser. Do not open the survey in multiple windows.

Should you encounter any problems in completing the survey, please e-mail Aneesh Kapur at akapur@bostonhealthcare.com.

Thank you for your time and opinions.

3. Assessment of Practice Description

The following questions are design to let us gain a better understanding of your current practice and how you approach clinical decision-making for patients with lung nodules.

1. How many physicians are in your practice? _____
2. How many pulmonologists are in your practice? _____

Q3a. Which of the following best describes the primary hospital(s) to which your practice refers patients? [Select one or more and enter approximate # of beds at the institution]

- □ Community (non-teaching) Hospital (Size _____ beds)
- □ Community Teaching Hospital (Size _____ beds)
- □ Academic Medical Center (Size _____ beds)
- □ Other_____*[Text entry]*

Q4a. Over what size range do you, personally, view pulmonary nodules as "indeterminate"?

- □ _____mm - _____ mm *[Text entry]*
- □ There is no specific size range where I view nodules as "indeterminate"

- What defines an indeterminate nodule for you? _____ *[Text entry]*

Q4. For patients with indeterminate lung nodules, which of the following patient characteristics have the greatest impact on your assessment of the risk for NSCLC. (Rank from 1-10 with 1 being the most impactful, 10 being the least impactful) *Program so options are presented in random order.*

- ____ Smoking history (# pack years)
- ____ Smoking status (never, former, current)
- ____ Nodule size
- ____ Nodule opacity
- ____ Nodule edge morphology (e.g. speculated or smooth)
- ____ Nodule location
- ____ Age
- ____ Family history of lung cancer/lung disease
- ____ Patient history of lung cancer/lung disease
- ____ Occupational exposure to lung cancer causative agents

MQ5a_Q5b. What nodule size do you use as a threshold, if any, for determining whether a patient should undergo either of the following?

Q5a. …a minor invasive procedure such as Biopsy/FNA or Bronchoscopy?

- □ _____mm *Program so values cannot include decimals (i.e., cm) >0 and <50.*
- □ I do not have a specific size threshold

Q5b. …a major invasive procedure such as Thoracoscopy/VATS or Thoracotomy?

- □ _____mm *Program so values cannot include decimals (i.e., cm) >0 and <50.*
- □ I do not have a specific size threshold

*The following 3 questions aim to better understand the population of patients with newly identified pulmonary nodules **between 8-20 mm in size**.*

Q6. What is the typical age distribution of your patients with newly identified indeterminate pulmonary nodules between 8-20 mm? *Should add up to 100%*

Age Distribution	% of Patients, Lung Nodule Size (8-20mm)
<40	(n)%
40 to 50	(n)%
51 to 60	(n)%
61 to 70	(n)%
71 to 80	(n)%
>80	(n)%
Total	100%

Q7. What is the typical smoking status of your patients with newly identified indeterminate pulmonary nodules between 8-20 mm? *Should add up to 100%*

Smoking History	% of Patients, Lung Nodule Size (8-20mm)
0 pack years (<100 cigarettes lifetime)	(n)%
1-20 pack years	(n)%
21-30 pack years	(n)%
> 30 pack years	(n)%
Total	100%

Q8. For patients with newly identified indeterminate pulmonary nodules between 8-20 mm, what percent of the time do you use or refer patients for each diagnostic procedure below? (More than one procedure can be used for each nodule work-up and thus numbers are not expected to sum to 100%) [Aim 3: Characterize current use of invasive procedures]

Procedure	% of Patients, Lung Nodule Size (8-20mm)
CT Scan	(n)%
PET	(n)%
Biopsy/FNA	(n)%
Bronchoscopy	(n)%
Thoracoscopy/VATS	(n)%
Thoracotomy	(n)%

Q9a. Which of the following best describes your practice's access to PET imaging?
- □ We offer PET imaging within our practice
- □ We have a financial relationship with an independent diagnostic testing facility where PET imaging is offered
- □ We refer patients to an independent diagnostic testing facility where PET imaging is offered
- □ We refer patients to hospital where PET imaging is offered
- □ Other_____*[Text entry]*

4. Information on Hypothetical Diagnostic Test Provided to Respondents

Please review the description of the following test. As you continue taking the survey, you will be able to click on a link to refer back to this product description.

Overview	• The lung nodule test is a non-invasive diagnostic test based on the analysis of multiple proteins circulating in the blood (specifically the plasma component) to assess the likelihood of non-small cell lung cancer (NSCLC) for a new pulmonary nodule identified radiographically in a patient who presents for clinical evaluation
Test Description	• Target proteins present in the plasma sample are analyzed by mass spectroscopy, which identifies and quantifies biological compounds based on their molecular spectra • The relative expression levels of the specific target proteins are used to generate a score that reflects the clinical likelihood of NSCLC for the patient's lung nodule
Clinical Use	• The lung nodule test has been developed to address the specific clinical need of the difficult-to-manage, indeterminate subgroup of pulmonary nodules • The clinical value of the lung nodule test focuses on achieving an earlier diagnosis by enabling the physician to refine the clinical assessment of the likelihood of malignancy based on test results (in conjunction with other clinical factors) • The test is intended to be used on patients who already have radiographic evidence of a new lung nodule and prior to using invasive diagnostic options
Predictive Value	• The test score will classify patients as low risk, high risk, or indeterminate risk with a correlated confidence interval • The target negative predictive value (NPV) for the "rule out" test is 95%, meaning that a low risk test score indicates that the patient's lung nodule has a 95 out of 100 likelihood of being benign, in contrast to a 5 out of 100 chance of being malignant • The positive predictive value (PPV) of 50% means that a high risk test score indicates that the patient's lung nodule has a 50% likelihood of being benign
Test Validation	• The clinical development of the test involves studies that evaluate the test's performance, including sensitivity, specificity, PPV and NPV, on the target population of patients who present with radiographic evidence of an indeterminate pulmonary nodule • A prospective, multi-center study is in progress with a target enrollment of ~1,600 subjects and a target accuracy of 90%±5%, 95% CI
Availability	• Assume this test has been on the market for 1 year • Assume price is not an issue

5. Discrete Choice Experiment and Conjoint Analysis

Information provided to Respondents

Next, we are going to present several case studies, and based on your assessment of the clinical information, ask that you i) formulate an assessment of risk for NSCLC and ii) make a recommendation for the next diagnostic step for each patient based on your risk assessment. In addition to clinical risk factors in the previous exercise, each scenario will include a 'test result' attribute, which will be the result of the non-invasive lung nodule test that is the subject of this survey. For each case, there will be a result designated as either: 'no test performed', 'low risk test result', 'high risk test result', or "indeterminate test result."

Again, we understand that this can be a bit tedious, but please pay close attention and answer as you believe you would act in clinical practice. This will help ensure the test is optimized for the patients where it is needed most.

You will see 5 screens with 4 patients per screen.
You are able to click on the link to refer back to the test description as necessary.

6. Example of 20 Case Scenarios Presented to Single Respondent

An otherwise asymptomatic patient, who is a surgical canidate, presents with a newly identified pulmonary nodule with the following clinical data:

	Patient 1	Patient 2	Patient 3	Patient 4
Age	53 years old	44 years old	71 years old	62 years old
Smoking History	12 pack years	0 pack years	12 pack years	36 pack years
Nodule Size	14 mm	6 mm	18 mm	18 mm
Test Result	Low risk	Indeterminate risk	High risk	No test performed

For each patient, what would you recommend?

What would you recommend?	○ Non-invasive monitoring only	○ Non-invasive monitoring only	○ Non-invasive monitoring only	○ Non-invasive monitoring only
	○ Minor invasive procedure	○ Minor invasive procedure	○ Minor invasive procedure	○ Minor invasive procedure
	○ Major invasive procedure	○ Major invasive procedure	○ Major invasive procedure	○ Major invasive procedure

An otherwise asymptomatic patient, who is a surgical canidate, presents with a newly identified pulmonary nodule with the following clinical data:

	Patient 1	Patient 2	Patient 3	Patient 4
Age	53 years old	71 years old	62 years old	44 years old
Smoking History	24 pack years	36 pack years	24 pack years	12 pack years
Nodule Size	10 mm	18 mm	6 mm	22 mm
Test Result	Low risk	High risk	Indeterminate risk	No test performed

For each patient, what would you recommend?

What would you recommend?	Patient 1	Patient 2	Patient 3	Patient 4
	○ Non-invasive monitoring only	○ Non-invasive monitoring only	○ Non-invasive monitoring only	○ Non-invasive monitoring only
	○ Minor invasive procedure	○ Minor invasive procedure	○ Minor invasive procedure	○ Minor invasive procedure
	○ Major invasive procedure	○ Major invasive procedure	○ Major invasive procedure	○ Major invasive procedure

An otherwise asymptomatic patient, who is a surgical canidate, presents with a newly identified pulmonary nodule with the following clinical data:

	Patient 1	Patient 2	Patient 3	Patient 4
Age	71 years old	44 years old	53 years old	80 years old
Smoking History	0 pack years	36 pack years	24 pack years	12 pack years
Nodule Size	22 mm	6 mm	10 mm	14 mm
Test Result	Indeterminate risk	Low risk	No test performed	High risk

For each patient, what would you recommend?

What would you recommend?	Patient 1	Patient 2	Patient 3	Patient 4
	○ Non-invasive monitoring only	○ Non-invasive monitoring only	○ Non-invasive monitoring only	○ Non-invasive monitoring only
	○ Minor invasive procedure	○ Minor invasive procedure	○ Minor invasive procedure	○ Minor invasive procedure
	○ Major invasive procedure	○ Major invasive procedure	○ Major invasive procedure	○ Major invasive procedure

An otherwise asymptomatic patient, who is a surgical canidate, presents with a newly identified pulmonary nodule with the following clinical data:

	Patient 1	Patient 2	Patient 3	Patient 4
Age	71 years old	62 years old	53 years old	53 years old
Smoking History	12 pack years	24 pack years	0 pack years	24 pack years
Nodule Size	6 mm	18 mm	10 mm	10 mm
Test Result	No test performed	Low risk	High risk	Low risk

For each patient, what would you recommend?

What would you recommend?	Patient 1	Patient 2	Patient 3	Patient 4
	◯ Non-invasive monitoring only	◯ Non-invasive monitoring only	◯ Non-invasive monitoring only	◯ Non-invasive monitoring only
	◯ Minor invasive procedure	◯ Minor invasive procedure	◯ Minor invasive procedure	◯ Minor invasive procedure
	◯ Major invasive procedure	◯ Major invasive procedure	◯ Major invasive procedure	◯ Major invasive procedure

An otherwise asymptomatic patient, who is a surgical canidate, presents with a newly identified pulmonary nodule with the following clinical data:

	Patient 1	Patient 2	Patient 3	Patient 4
Age	53 years old	71 years old	80 years old	44 years old
Smoking History	36 pack years	12 pack years	0 pack years	24 pack years
Nodule Size	22 mm	18 mm	18 mm	14 mm
Test Result	Low risk	High risk	No test performed	High risk

For each patient, what would you recommend?

What would you recommend?	Patient 1	Patient 2	Patient 3	Patient 4
	◯ Non-invasive monitoring only	◯ Non-invasive monitoring only	◯ Non-invasive monitoring only	◯ Non-invasive monitoring only
	◯ Minor invasive procedure	◯ Minor invasive procedure	◯ Minor invasive procedure	◯ Minor invasive procedure
	◯ Major invasive procedure	◯ Major invasive procedure	◯ Major invasive procedure	◯ Major invasive procedure

7.   Fixed Cases Presented to Respondents

There were two holdout cases that were asked twice for each respondent to assess internal consistency

	Case 1	Case 2
Age	71 years old	53 years old
Smoking history	12 pack years	24 pack years
Nodule Size	18 mm	10 mm
Test result	High risk	Low risk

8.   Definitions Provided to Respondents

Non-invasive monitoring: CT scan, PET scan
Minor invasive procedure: Biopsy/FNA, Bronchoscopy
Major invasive procedure: Thoracoscopy/VATS, Thoracotomy