In which of the following situations would the U.S. Preventive Services Task Force (USPSTF) recommend that M.B. be screened for lung cancer?

A. M.B. is 60 years of age, her diabetes is well controlled by diet, and she quit smoking 20 years ago.

B. M.B. is 60 years of age, her diabetes is well controlled by medications, and she quit smoking 10 years ago.

C. M.B. is 75 years of age, her diabetes is well controlled by medications, and she currently smokes.

D. M.B. is 78 years of age, her diabetes is poorly controlled, she has emphysema and heart failure with an ejection fraction of 30% and she currently smokes
Case 1

It is determined that M.B. should be screened for lung cancer. According to the USPSTF, which one of the following screening tests is recommended?

A. Annual chest radiography with sputum cytology.
B. Chest radiography and sputum cytology once every three years.
C. Annual low-dose computed tomography (CT).
D. Low-dose CT once every three years.
E. Annual magnetic resonance imaging.

Case 1

Based on the USPSTF’s findings, which one of the following statements about the potential benefits or harms of lung cancer screening is correct?

A. Annual screening can substantially lower lung cancer incidence in high-risk persons.
B. Annual screening can prevent a substantial number of lung cancer–related deaths in a defined population of high-risk persons.
C. Annual screening can prevent most lung cancer–related deaths.
D. There is a low likelihood of false-positive results; 95% of all positive results lead to a diagnosis of cancer.
E. Only 1% to 2% of screen-detected cancer cases are overdiagnosed.
Lung Cancer Facts

1 out of 14 people develop lung cancer.

Leading Sites of New Cancer Cases and Deaths: 2016 Estimates
Why are we here?

Prevention is the most effective strategy for reducing the burden of lung cancer

For non-preventable lung cancers,
Early detection & screening is critical

IMPROVE PATIENT CARE • SAVE LIVES

Sense of Urgency

LUNG CANCER KILLS 433 PEOPLE EVERY DAY!
Patient Cohorts

SYMPTOMATIC PATIENTS  HIGH-RISK PATIENTS

INCIDENTAL FINDINGS PATIENTS

Risk Factors

- Smoking
- Exposure to radon
- Exposure to other hazardous chemicals
  - Asbestos
  - Uranium
  - Arsenic
  - Cadmium
  - Chromium
  - Nickel
  - Some petroleum products
- Particle pollution
- Age
- Genetics: Personal or family history of lung cancer
Impact of Smoking

- Cigarette smoking is by far the most important risk factor for lung cancer
  - 80% of lung cancer deaths in women
  - 90% of lung cancer deaths in men
- Risk increases with both quantity and duration of smoking.

- Smoking
  - Cigarette smoking
  - Cigar & pipe smoking
  - Secondhand smoke
- Combined risk
  (i.e. smoking + asbestos)
- Smoking Cessation

Identifying Symptomatic Patients

- A cough that doesn't go away and gets worse over time
- A chronic cough or "smoker's cough"
- Hoarseness
- Constant chest pain
- Shortness of breath or wheezing
- Frequent lung infections such as bronchitis or pneumonia
- Coughing up blood
- Weight loss and loss of appetite
- Feeling tired or weak
- Infections such as bronchitis and pneumonia that don't go away or keep coming back
Identifying High-risk Patients

Two identifiers:

- Age 55-74
- 30-pack year Smoking History

Primary Care Provider Role

- Know the risk factors
- Counsel on smoking cessation
- Critical role in identifying:
  - Symptomatic patients
  - High-risk patients
Screening for Lung Cancer
National Lung Screening Trial (NLST)

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening
The National Lung Screening Trial Research Team*

20% fewer lung cancer deaths among 53,000 participants screened with low-dose helical (spiral) CT compared to those screened with chest X-rays.

The trial ended early due to promising results.

NLST
Study Design

53,454 persons ages 55 to 74 years at high risk* for lung cancer at 33 US medical centers

RANDOMIZE

1:1

3 annual screenings with LDCT
N = 26,722

3 annual screenings with CX-RAY
N = 26,732

*High risk for lung cancer was defined as a 30-year or more history of cigarette smoking. If the patient was a former smoker, they must have quit smoking within the last 15 years.

United States Preventive Task Force (USPSTF) Screening Recommendation

- Age 55-80
- ≥ 30 pack-year smoking history
- Current smoker or quit within the last 15 years
- Able and willing to receive treatment
- Screening should be discontinued
  - Once a person has not smoked for 15 years
  - Develops health problem(s) that substantially limits life expectancy or the ability or willingness to have curative lung surgery
Lung Screening Programs
Requirements


Chart 6.1 Must-haves for screening sites

<table>
<thead>
<tr>
<th>Follows an organized plan—a proven protocol—that is updated to include new technology and knowledge like that from NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Has a high-quality screening program with enough staff and resources</td>
</tr>
<tr>
<td>Is accredited to do CT scans by a certifying organization, such as the American College of Radiology</td>
</tr>
<tr>
<td>Has scans read by an American Board of Radiology board-certified radiologist who's an expert in lung cancer screening</td>
</tr>
<tr>
<td>Has modern multislice CT equipment that does high-quality, low-dose, and non-contrast spiral CT</td>
</tr>
<tr>
<td>Is partnered with a health center that has: 1) experience and excellence in biopsy methods; 2) board-certified pulmonologists; and 3) board-certified thoracic surgeons who are experts in lung cancer</td>
</tr>
</tbody>
</table>
Case 2

- 58 year old male presented with dyspnea and dyspnea with exertion
- 40 pack year tobacco history, still smokes
- Father had lung lung cancer, age 68
- Hypertension
- ROS: chronic productive cough
- Exam: end expiratory wheezes

Case 2 Next Steps

- Treat exacerbation COPD
- PFT’s
- Assess likelihood of lung cancer
- Manage pulmonary nodule
What are you going to tell the patient?

- A. You have a 5 mm nodule in the left lower lobe
- B. This might be cancer
- C. We want you to come back in 6 months
- D. We’ll keep an eye on it
- E. A spot on the lung is always something to worry about. I don’t want you to get frantic. We’ll just take the test as we go along…

What’s the Patient Thinking?

- What’s a nodule? A “spot”. A “shadow”
- What’s the chances that it is cancer?
- If it’s not cancer, what else are we considering?
- Is it serious?
- What should I expect? Will I be able to breathe? Will I have pain?
- How long do we watch?
Tell the Patient

• 1. Estimate the risk of cancer
• 2. Must be verbal. A letter is not satisfactory.
• 3. Avoid minimizing or dismissive language
• 4. Give this high priority, answer all the questions
• 5. Provide details of the nodule, it’s the size of a pea, etc.
• 6. Explain the evaluation or surveillance
• 7. Let the patient know what to expect and acknowledge their concerns

What is a Nodule?

• Solitary Pulmonary Nodule (SPN) is a radiographic opacity < 3 cm with at least 2/3 of its margins surrounded by lung parenchyma
• This excludes lymph nodes, atelectasis, and post-obstructive pneumonia
• Establishing the etiology of a SPN assumes critical importance
SPN

- 150,00 per year
- CT imaging: 8% to 51%
- Prevalence of malignancy: 1.1% to 12%
- Accurate and timely diagnosis is important as treatment of early stage lung cancer provides the highest chance for cure.

Clinical Evaluation: History

- History of smoking
- History of prior malignancy
- History of interstitial Lung Disease
- Residence in or travel to areas endemic with fungal pathogens
- Prior CT scan or Chest radiograph
CT Scan

- Thin sections
- 1.5 mm
- Lung and mediastinal windows
- Contrast for mediastinal structures and nodule enhancement

Growth Rate

- Malignant nodules double in 20 to 400 days
- Volume of a sphere $= \frac{4\pi r^3}{3}$
- An increase in diameter of 26% represents a doubling in volume
- Example: 4mm nodule to 5mm is almost a doubling in volume
- A solid nodule which does not change in size over 2 years is considered benign
Size Matters

• Size trumps morphology: diameter and likelihood of cancer in screened smokers

  • < 3 mm: 0.2%
  • 4 – 7 mm 2.7%
  • 8 – 30 mm 18%
  • > 30 mm 99%

  • Radiology 235:259, 2005

Benign patterns of calcifications

diffuse
central
popcorn
concentric
Indeterminate patterns of calcification

- stippled
- eccentric
- inhomogeneous calcification of irregular nodule

Findings that suggest a benign lesion

- shape: oblong, polygonal, concave margins
- edge smooth
- subpleural location (attached to the pleura)
- satellite nodules

Xu et al, Radiology 250; 264, 2009
Li et al, Radiology 233; 793, 2004
Takashima et al. AJR 2003; 180:1255
Ground Glass Opacities

- Subsolid nodule = pure GGO
- Partly solid GGN: focal nodular area of increased attenuation
- Semi-solid GGN: may represent a histologic spectrum of adenocarcinoma
- Atypical adenomatous hyperplasia → adenocarcinoma in situ → minimally invasive adenocarcinoma → lepidic predominant adenocarcinoma
5 mm, standard algorithm
PET Scan

- Combined PET-CT correlates results from 2 modalities
- Glucose analog tagged with positron-emitting isotope fluorine(FDG)
- Reveals aspects of tumor function and metabolism
- Metabolic activity quantitated using Standard Uptake Value (SUV)
  Mean value > 2.5
Pulmonary nodules: FDG-PET diagnosis
Gould et al. JAMA 2001; 285:914

- meta-analysis of 40 studies with 1474 nodules
- SUV 2.5
- sensitivity 97%; specificity 78%; accuracy 90%
Pulmonary nodules: FDG-PET diagnosis

- 625 patients
- 433 diagnosed with cancer
- false negatives:
  - » 11/23 (48%) BAC
  - » 8/234 (3%) adenocarcinoma
  - » 4/14 (29%) carcinoid
  - » 2/8 (25%) renal cell metastases

Pulmonary nodules: FDG-PET diagnosis
Nomori et al. Lung Cancer 2004; 45:19

- 136 nodules < 3 cm; 81 malignant
- all 20 < 1 cm (8 malignant) were negative on PET
- 101 solid nodules 1-3 cm (63 malignant) sensitivity 90%, specificity 71%
- 15 ground-glass nodules 1-3 cm (10 malignant) sensitivity 10%, specificity 20%
Probability of Cancer in Pulmonary Nodules

369; 10, September 5 2013

- Predictors of cancer model
  - Older age
  - Female sex
  - Family history of lung cancer
  - Emphysema
  - Larger nodule size
  - Location of nodule in the upper lobe
  - Part-solid nodule type
  - Lower nodule count
  - Spiculation
Pulmonary Nodule Risk for Cancer Predictor

Algorithmic Approach to SPN

- Review previous imaging
- Solid or subsolid
- Solid nodules < 8 mm can be followed
- Solid nodules > 8 mm need pretest probability for cancer
- Pretest probability < 5%, follow
- Pretest probability > 60% needs tissue diagnosis
- Intermediate range: PET
Where Do You Compare With Your Peers?

- Annals of the American Thoracic Society, January 2018
- An Assessment of Primary Care and Pulmonary Provider Perspectives on Lung Cancer Screening

Primary Provider Perspective On Lung Cancer Screening

- 196 participants
- 80% primary care
- 41% University or affiliated clinics
- 47% county hospital based clinics
- 74% endorsed screening effectiveness
- Key barriers: inadequate time (36%), inadequate staffing (36%), patients have too many other illnesses to address (38%)
- Decision aids were important, at point of referral, to facilitate screening
- Point-of-care referral materials may be helpful in reducing knowledge gaps and clinical burden of referral.

### Lung Cancer Screening Recommendation

<table>
<thead>
<tr>
<th>RISK CRITERIA</th>
<th>USPSTF</th>
<th>CMS</th>
<th>NCCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55-80</td>
<td>55-77</td>
<td>N/A</td>
</tr>
<tr>
<td>Pack-year Smoking History</td>
<td>≥ 30</td>
<td>≥ 30</td>
<td>≥ 30</td>
</tr>
<tr>
<td>Status</td>
<td>Current smoker or quit within the last 15 years</td>
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<td>Current smoker or quit within the last 15 years</td>
</tr>
<tr>
<td>Other</td>
<td>Able and willing to receive treatment</td>
<td>Shared decision making</td>
<td>Shared decision making</td>
</tr>
<tr>
<td>Discontinuation Guidelines</td>
<td>Age 80</td>
<td>Age 77</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td>Once a person has not smoked for 15 years</td>
<td>Develops health problem(s) that substantially limits life expectancy or the ability or willingness to have curative lung surgery</td>
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</table>
Top 5 Practice Changing Developments in Lung cancer for 2017

• Pacific Trial: huge and sustained PFS in Stage III NSCLC with maintenance durvalumab after chemoradiotherapy
• FDA approval of carboplatin/pemetrexed/pembrolizumab in non-squamous NSCLC, first approved combination of standard chemotherapy and immunotherapy
• FDA approval of broad genomic testing in advanced solid tumors, enables patients with rare but treatable targets to be identified

5 Significant Developments

• FLAURA Trial: osimertinib is now first line treatment for EGFR mutation positive advanced NSCLC
• Immunotherapy in relapsed small cell lung cancer, potential single agent therapy in a setting where existing alternative are disappointing
Questions?