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Medical Center

Ted Yamamoto, 2011
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Lung Cancer Screening

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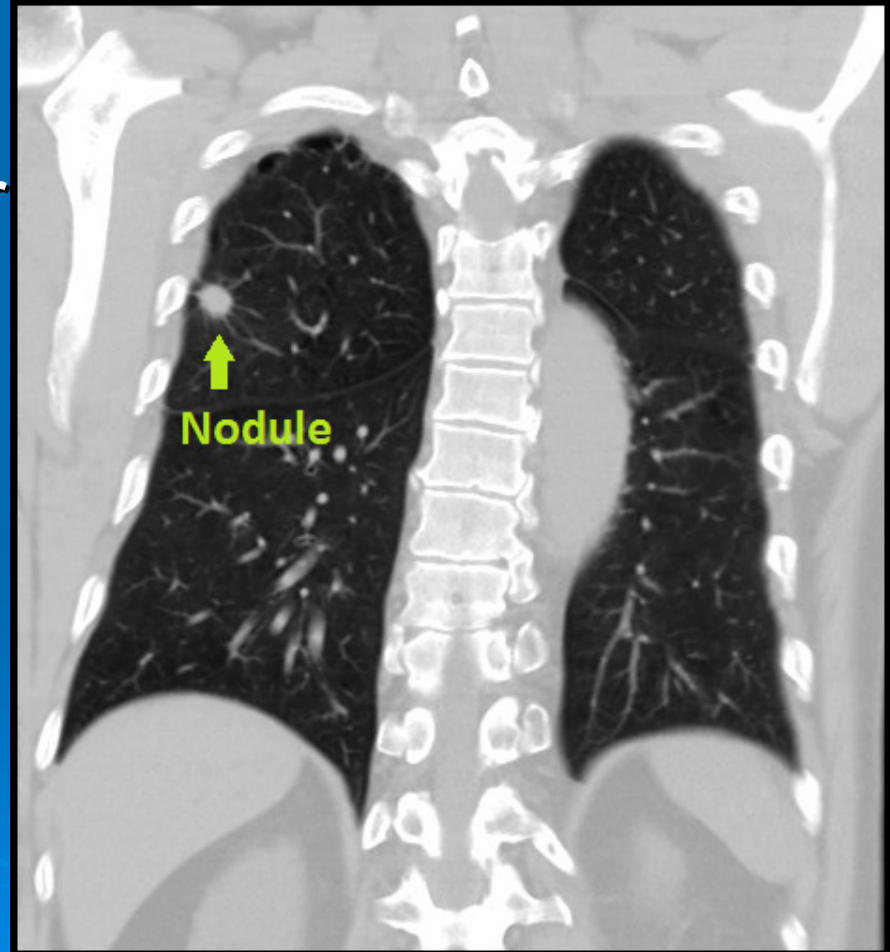
Case Presentation

- 67 year old male
- Hypertension, but otherwise healthy
- Smokes 7-8 cigarettes per day, >50 pack year history
- Here for routine health maintenance
- Should you screen for lung cancer?



Case Presentation

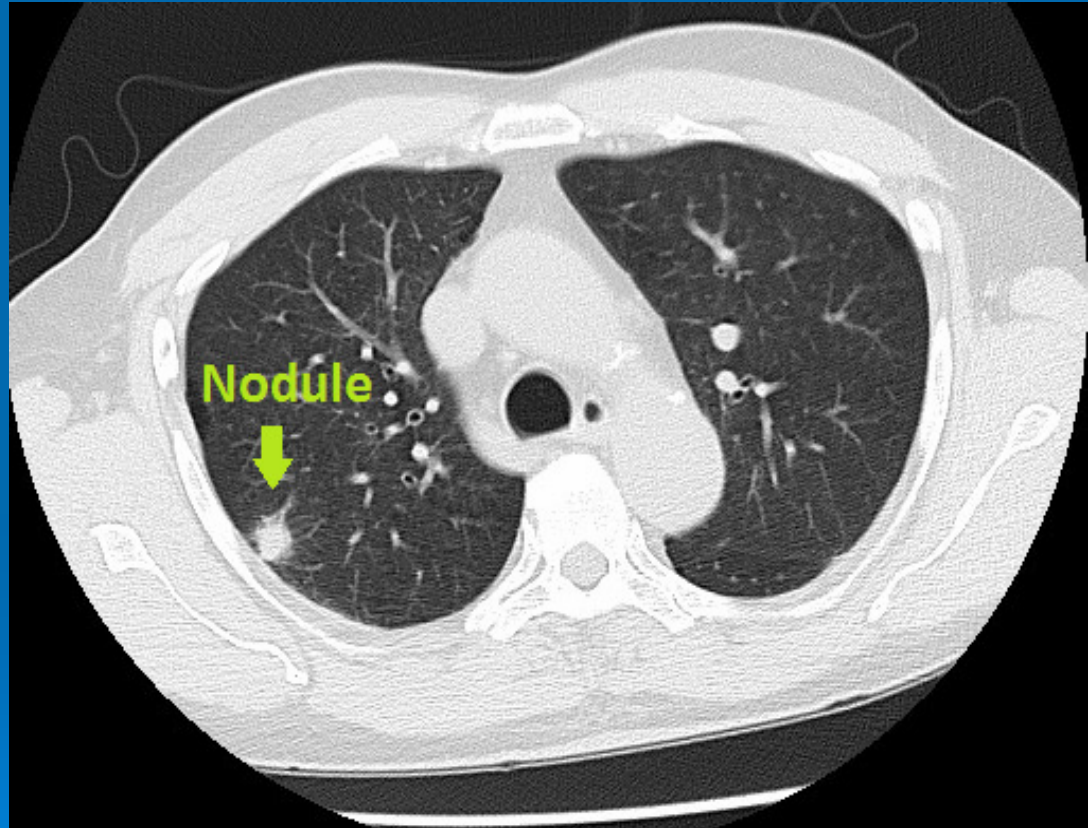
- Our patient was not screened for lung cancer
- But he developed pneumonia
- CXR raised the possibility of a **nodular lesion**
- A CT was obtained





Case Presentation

- FDG-PET showed avid uptake
- VATS right upper lobe resection
- Stage IA adenocarcinoma



PACS BIDMC, courtesy Dr. Petkovska



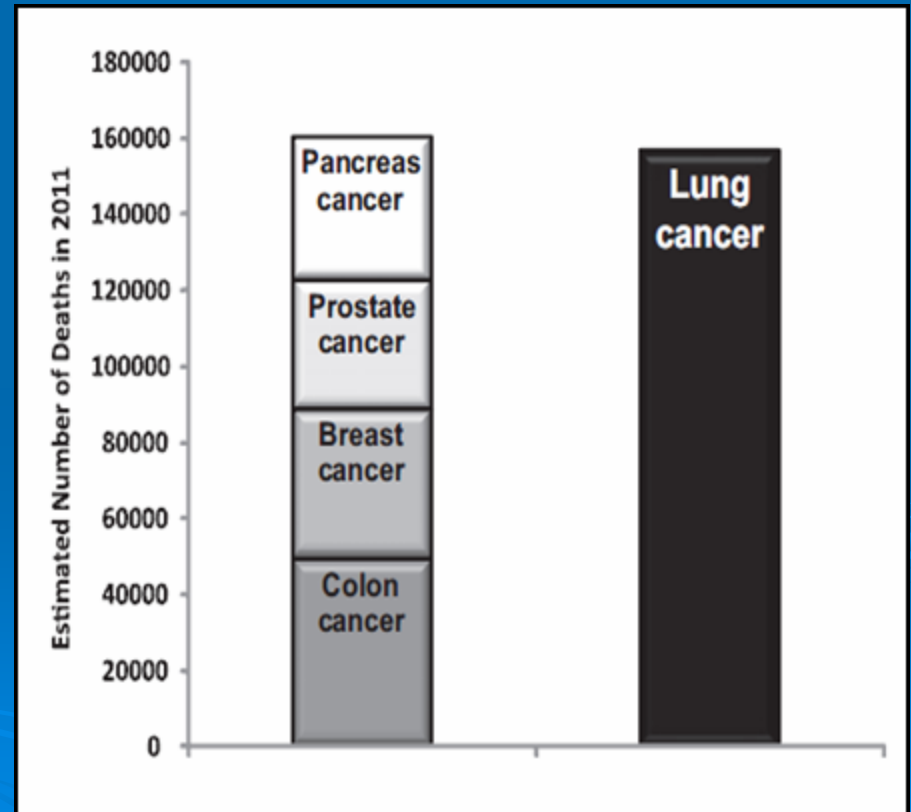
ACS recommendations

- American Cancer Society (ACS) position for early detection: “At present neither the ACS, nor any other medical/scientific organization, recommends testing for early lung cancer detection in asymptomatic individuals.”



Epidemiology

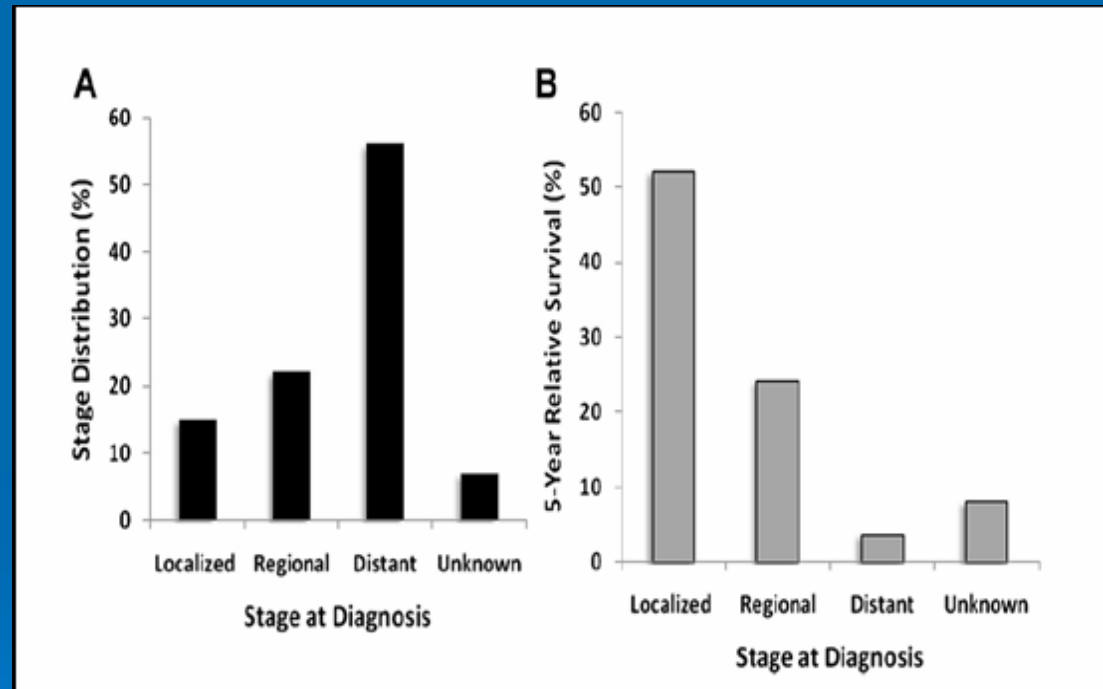
- 2nd most common cancer in the U.S.
221,000 new cases of lung cancer (2010).
- Most common cause of cancer death,
>150,000 per year





Epidemiology

- 5 year survival rate for stage I disease is 60%
- 5 year survival rate for stage IV disease is <5%
- 75% of patients have incurable locally advanced or metastatic disease by diagnosis
- 15% of patients survive >5 years



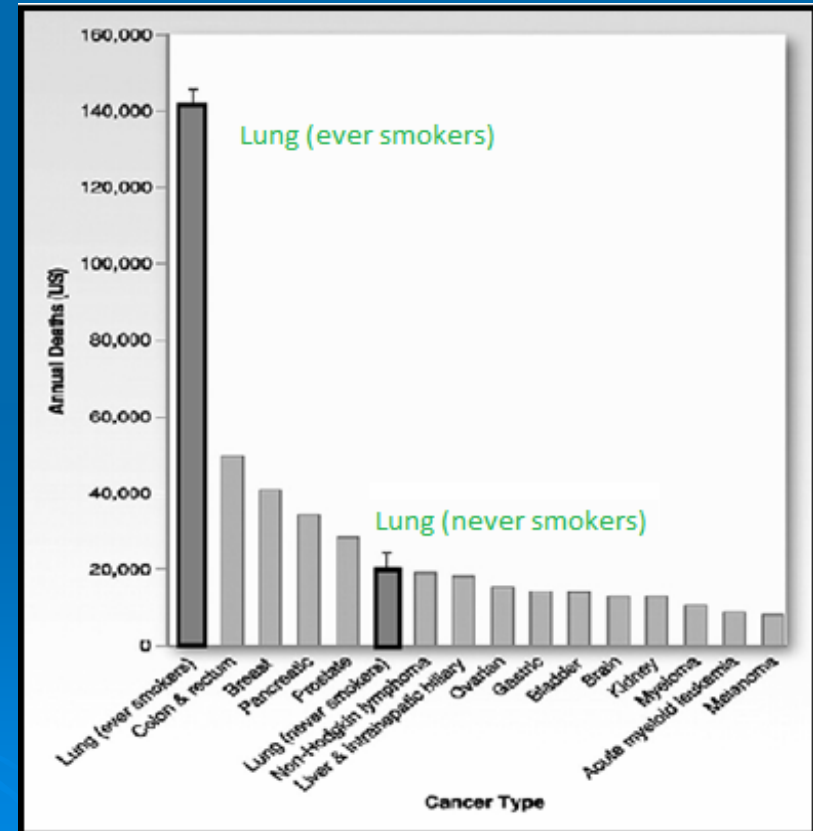
Cruz CD, Tanoue LT, Matthay RA. Lung Cancer: Epidemiology, Etiology, and Prevention. *Clin Chest Med* 2011; 32: 605-644.

- A: stage at diagnosis
- B: 5-year relative survival based on stage of diagnosis



Epidemiology

- Cigarette smoking is a major cause of lung cancer
- >80% of lung cancers occur in persons with tobacco exposure (RR 20-25, AR 85%-90%)
- 1 in 9 smokers eventually develop lung cancer
- 20.6% of Americans >18 years old smoke





Rationale for Screening

- Lung cancer is common
- Most lung cancer is diagnosed at advanced stages at which the prognosis is poor
- Early intervention save lives
- High risk cohort that we can target for screening (smokers)
- **Key point:** Given the lethality and high incidence of lung cancer, an effective screening test is needed



Screening Goals

- Detection of stage I disease
- Target high risk groups
- Decrease disease-related mortality



Screening Test Criteria

- High sensitivity (especially for early stage disease)
- High specificity (reduce false positives and number of people needing diagnostic evaluation)
- High positive predictive value
- Low cost
- Safety



Screening Modalities

- Chest radiography/Sputum
- Low dose computed tomography





Chest radiography

- Projection image
- Good resolution but poor contrast
- Fast
- Inexpensive
- Low radiation



Low Dose CT

- 3D imaging
- Good resolution and contrast
- High sensitivity
- Fast- 15 seconds during a single breath hold
- More expensive than radiograph
- Low radiation ($1/9^{\text{th}}$ radiation of conventional CT)



Early trials

- No difference in mortality rate between screened and control group
 - Used survival as an endpoint rather than mortality reduction
 - Lead-time bias- screening test appears to increase survival by detecting cancer early
 - Length-time bias- screening test may detect slow-growing tumors more often and thereby show an improvement in survival rates
 - Overdiagnosis bias- diagnoses disease that may never have caused symptoms



Radiograph & Sputum

- U.S. National Cancer Institute 1970's
 - 3 Randomized control trials in males smokers
 - Memorial Sloan-Kettering Study
 - Johns Hopkins Study
 - Mayo Lung Project
- Czechoslovakian Study
 - Randomized control trial
- No reduction in lung cancer mortality



Chest Radiograph

- Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO)
 - RCT of 155,000 subjects aged 55-74
 - Subjects randomized to standard care or annual screening with chest radiograph
 - **Findings:** Annual screening did not reduce lung cancer mortality compared with usual care



Computed Tomography

- CT screening detects more lung cancers compared with CXR but does not reduce lung cancer deaths

Table 1

Observational CT-screening studies: prevalence cancers and nodules detected

Study/Authors ^{Ref.}	No. of Participants	CT Collimation (mm)	No. of CT-Detected Lung Cancers	Surgical Stage I A/B	Number Missed on CXR	Participants with Noncalcified Nodules
Kaneko et al ¹³	1369	10	15 (1.1%)	14 (93%)	11 (73%)	588 (17%)
Sone et al ¹⁴	3967	10	19 (0.48%)	16 (84%)	15 (79%)	217 (5%)
ELCAP ¹⁵	1000	10	27 (2.7%)	23 (85%)	20 (74%)	233 (23%)
Mayo ¹⁶	1520	5	31 (2.0%)	22 (71%)	^a	782 (51%)
Diederich et al ¹⁷	817	5	12 (1.5%)	7 (58%)	^a	350 (43%)
Pastorino et al ¹⁸	1035	10	11 (1.1%)	6 (55%)	^a	199 (19%)
Nawa et al ³²	7956	10	36 (.45%)	31 (86%)	^a	2099 (26%)
McWilliams et al ²⁹	561	7 (36%) 1.25 (60%)	10 (1.8%)	7 (70%)	^a	431 (46%)
IELCAP ²⁰	31,567	1.25–10	405 (1.3)	85% ^b	^a	4186 (13%) ^c

^a CXR not performed.

^b Only pooled prevalence and incidence clinical stage information reported.

^c Not reported for nodules <5 mm.

From Midthun, DE. Screening for Lung Cancer. *Clin Chest Med.* 2011; 32: 659-668.



Low Dose CT

- National Lung Screening Trial (NLST)- Study Design
 - Largest RCT to date consisting of 53,464 subjects
 - Aged 55-74 years
 - At least 30 pack year history (if former smoker, quit within the past 15 years)
 - Randomized to undergo baseline and 2 annual screenings by either low dose CT or CXR



<http://www.cancer.gov>



Low Dose CT

- National Lung Screening Trial- Results
 - 649 cancers detected by CT screening compared with 279 cancers by CXR
 - Of lung cancers diagnosed with CT 63% were stage I and 29.8% were stage III or IV compared with 47.6%, 43.2% respectively in the CXR arm
 - 20.0% relative reduction in mortality from lung cancer with low-dose CT
 - Number needed to treat was 320



Low Dose CT

- National Lung Screening Trial- Results Cont.
- Rate of positive screening tests
 - CT- 24.2%; Radiography- 6.9%
 - 90% had further diagnostic evaluation
- False positive results
 - CT- 96.4%; Radiography- 94.5%



CT: Potential Problems

- False-positive scans
- Benign nodule resections
- Overdiagnosis
- Patient anxiety
- Radiation
- Cost

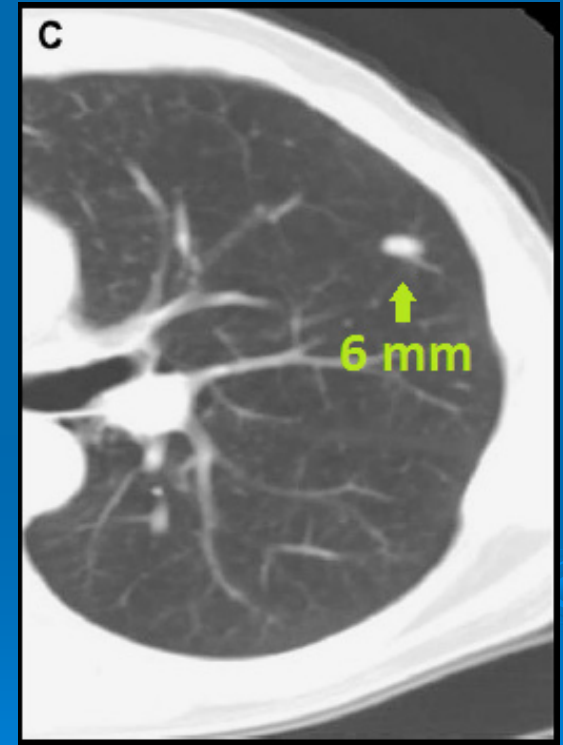
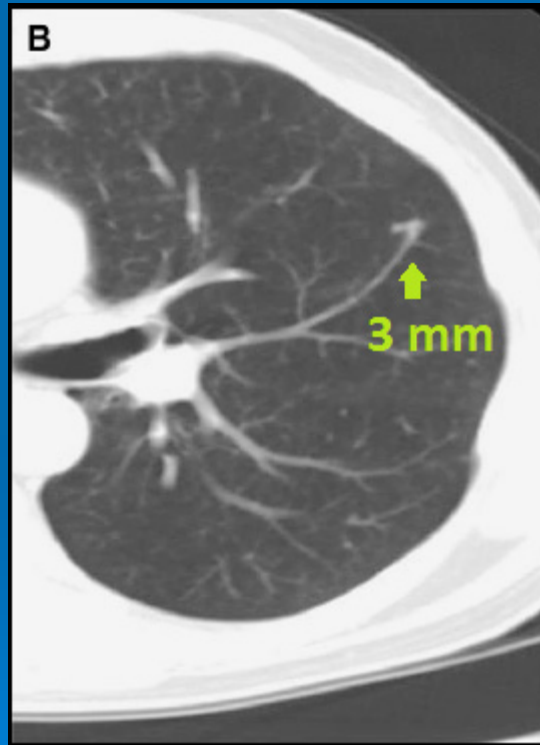
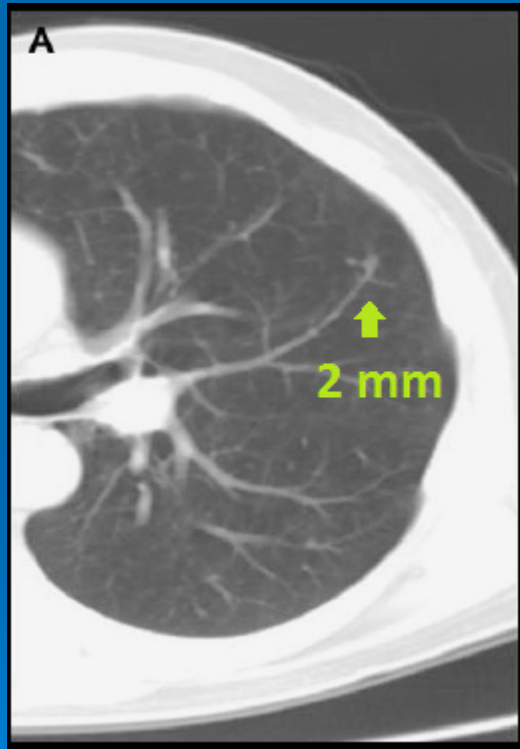


CT: Potential Problems

- High false positive rate
 - Benign nodule resection
 - Expensive diagnostic workup
- Response to high false positive rate
 - Many researchers call a scan “negative” if the largest nodule is <4-5 mm.
 - Decreases false positive rate, but increases the false negative rate
 - **Caution:** McWilliams et al. (2006) 18% of cancers were first detected when less than 4 mm



CT: Potential Problems



From Midthun, DE. Screening for Lung Cancer. *Clin Chest Med.* 2011; 32: 659-668.

Progressive growth of a **nodule** in the left upper lobe. (A) baseline (B) 1 year (C) 2 years



CT: Potential Problems

- Benign nodule resection
 - Diederich et al. 20% of resections
 - DANTE study 22% of resections
 - NLST study 27% of resections
- Overall CT-screening reports benign nodules resection rates between 15-30%
- Surgical series report benign nodules resection rates between 50-86%



CT: Potential Problems

- How can we reduce the number of benign nodules resections?
 - Careful review of old images
 - Serial examinations
 - Evaluating larger nodules with needle biopsy or PET



CT: Potential Problems

- Radiation risk
 - NLST: radiation risk from screening 55 year old smokers results in 1-3 lung cancer deaths per 10,000 screened and 0.3 new breast cancer per 10,000 women screened.
 - Highlight importance of having proven mortality benefit before implementing screening





Future

- NLST: Awaiting quality of life, smoking behavior, health care use, and cost-effectiveness of screening reports. Who will pay for screening and follow up?
- UK Lung Screen trial- RCT using CT screening, designed to determine the appropriate population to screen



Conclusions

- Lung cancer is a common and lethal disease and therefore patients would benefit from early detection and intervention.
- NLST demonstrates that low dose CT screening saves lives.
- Reports regarding cost-effectiveness are pending.
- Currently, routine screening is not recommended. In the meantime, the decision to screen for lung cancer should be evaluated on a case by case basis with discussion of the risks and benefits.
- Primary prevention is still paramount!



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