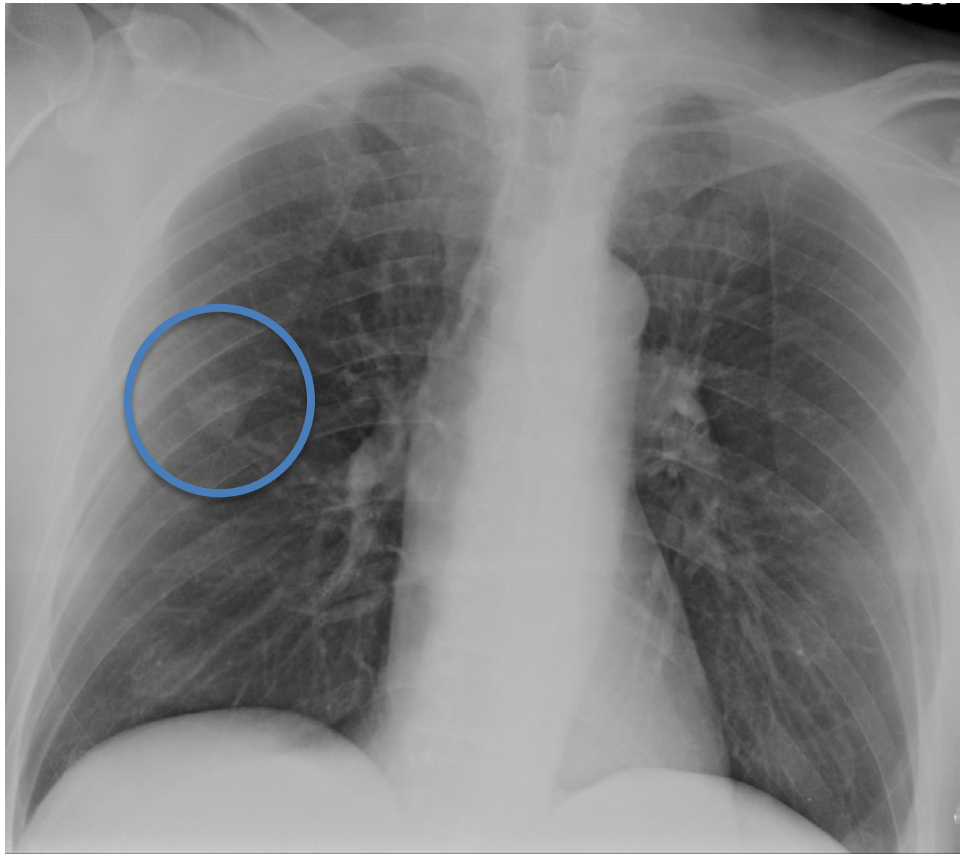
Pulmonary Nodules

Michael Morris, MD

Case

- 45 year old healthy male
  - Smokes ‘socially’
  - Normal physical exam
- Pre-employment screening
  - remote +PPD
  - screening CXR → “nodular opacity”



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1. Follow-up CXR
2. Chest CT without contrast
3. Chest CT with contrast
4. PET/CT scan
5. Unsure→refer to pulmonary

Case

- 45 year old healthy male
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  - Chest CT →“1 cm nodule”

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  - Normal physical exam
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  - screening CXR → “nodular opacity”
  - Chest CT →“1 cm nodule”

1. No further imaging
2. Follow with CXR
3. Follow with chest CT
4. PET/CT
5. Percuatenous biopsy
6. Unsure→refer to pulmonary

Overview

1. Imaging basics for nodules
2. Features of a solitary nodule
   - Type
   - Size
   - Patient at risk for cancer?
3. Management of solitary nodules
   - Incidental
   - Screening
4. Not Covered
   - Multiple nodules

Pulmonary nodule

- Imaging finding without physical exam correlate
- Incidence ~150,000/year
- Expected to increase with CT screening for lung ca

Ost et al NEJM 2003
http://tobacco.stanford.edu/

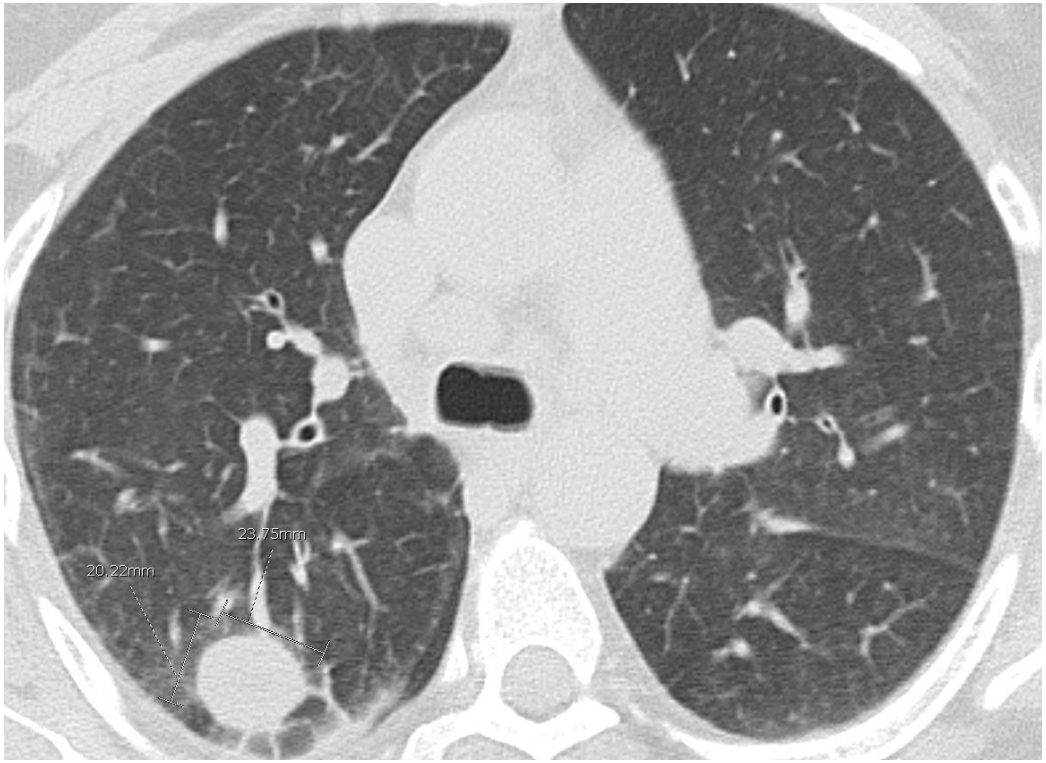
Pulmonary nodule

- DDx
  - Infectious
  - Cancer
  - Everything else
    - AVM
    - Necrobiotic
    - Amyloid
    - Infacrt
    - Etc.

http://tobacco.stanford.edu/

Definition

- Nodule
  - opacity <3cm surrounded by lung
  - NOT lymph nodes, atelectasis, pna



- Mass
  - “ ” >3cm
  - Usually bad
    - adenoca>squamous>met

“Danger” Zones on CXR

1. Apex
2. Hila
3. Lung periphery
4. Behind ribs

“Danger” Zones on CXR

1. Apex
2. Hila
3. Lung periphery
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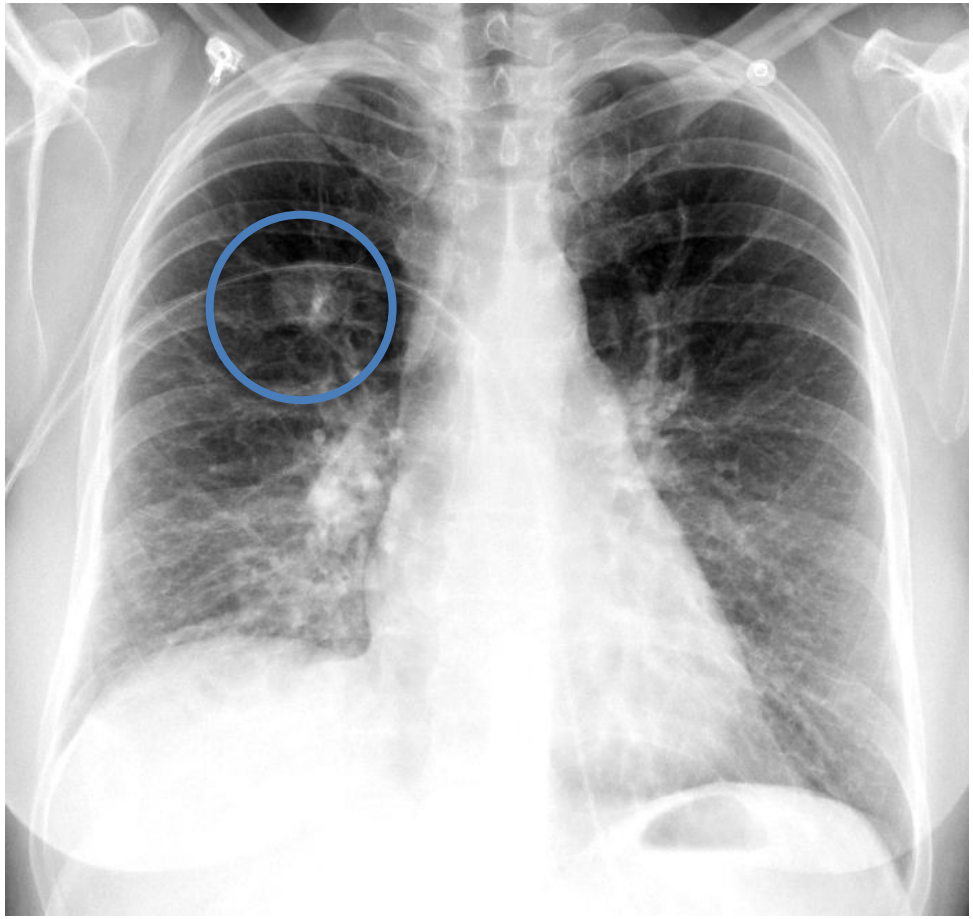
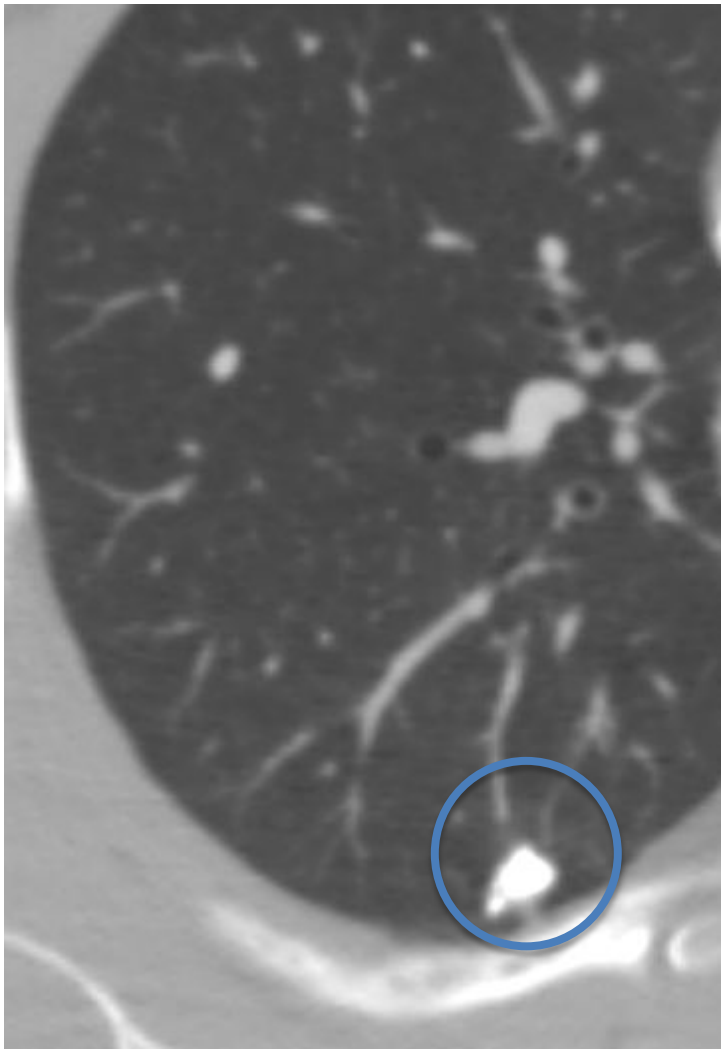


Imaging Features of Nodules

- Usually benign
  - Coarse calcification
  - Fat containing
- Everything else
  - Spiculated
  - Cavitary
  - Circumscribed
  - Upper or lower
  - Peripheral or central



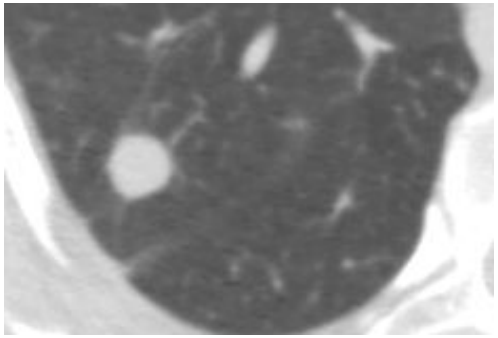
Nodule management - Rule #1

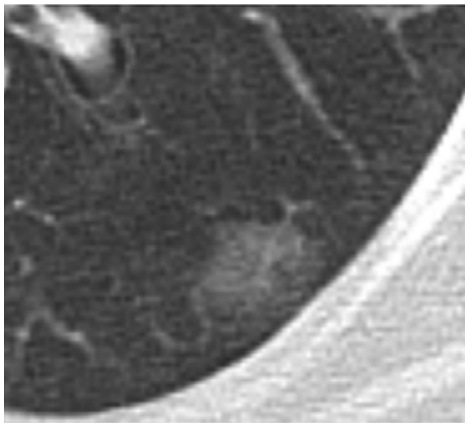
- Compare with old films
  - 2+ years stability is good*

- If seen on CXR and no old fims→chest CT without contrast

Imaging Features

- Type
  1. Solid
  2. Ground glass
  3. Part solid
- Size

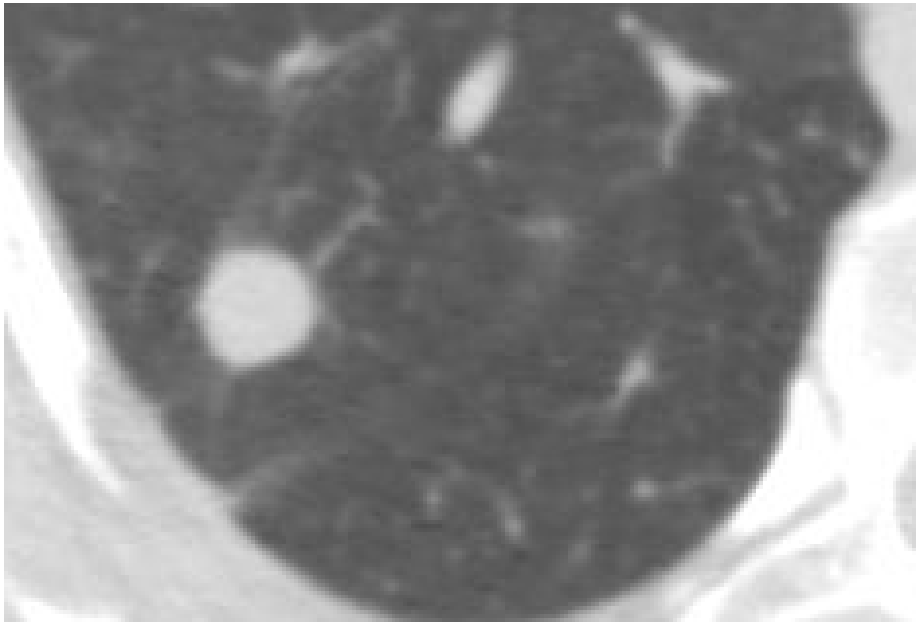




- Patient risk for cancer?

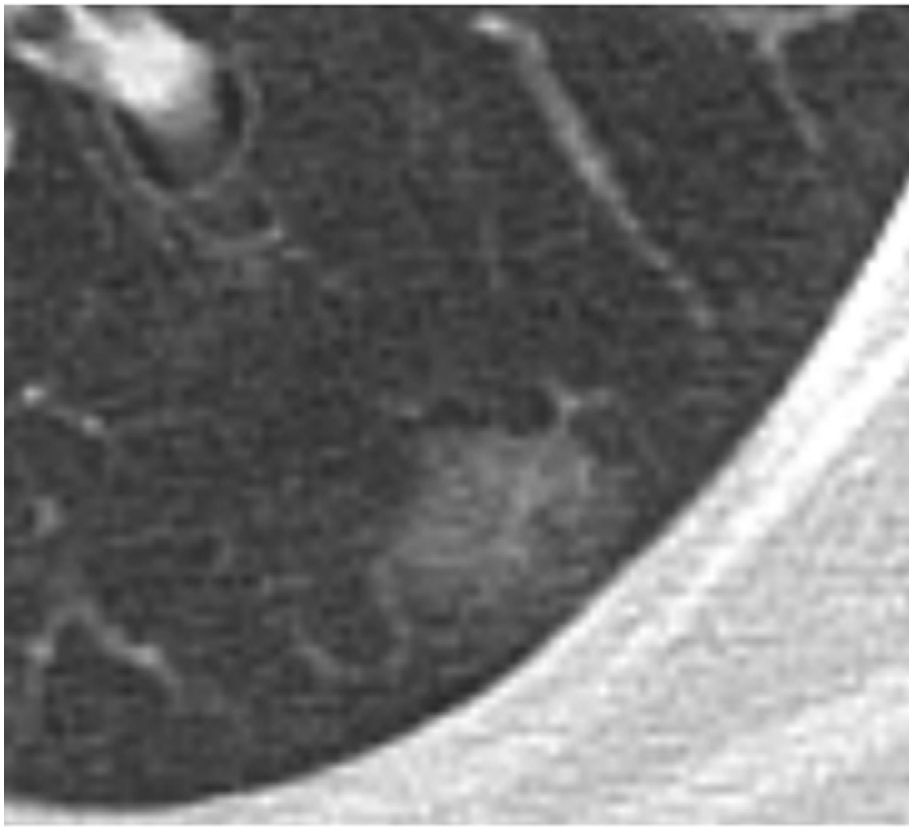
Imaging Features

- Solid
  - Obscures lung parenchyma
  - Ddx: infxn, cancer, granuloma
  - Double time: ~30-400 days
- Ground glass
- Part solid



Imaging Features

- Solid
- Ground glass
  - Area of incr attenuation, but underlying lung still seen
  - Ddx: infxn, AAH, AIS
  - Double time: ~600-900 days
- Part solid

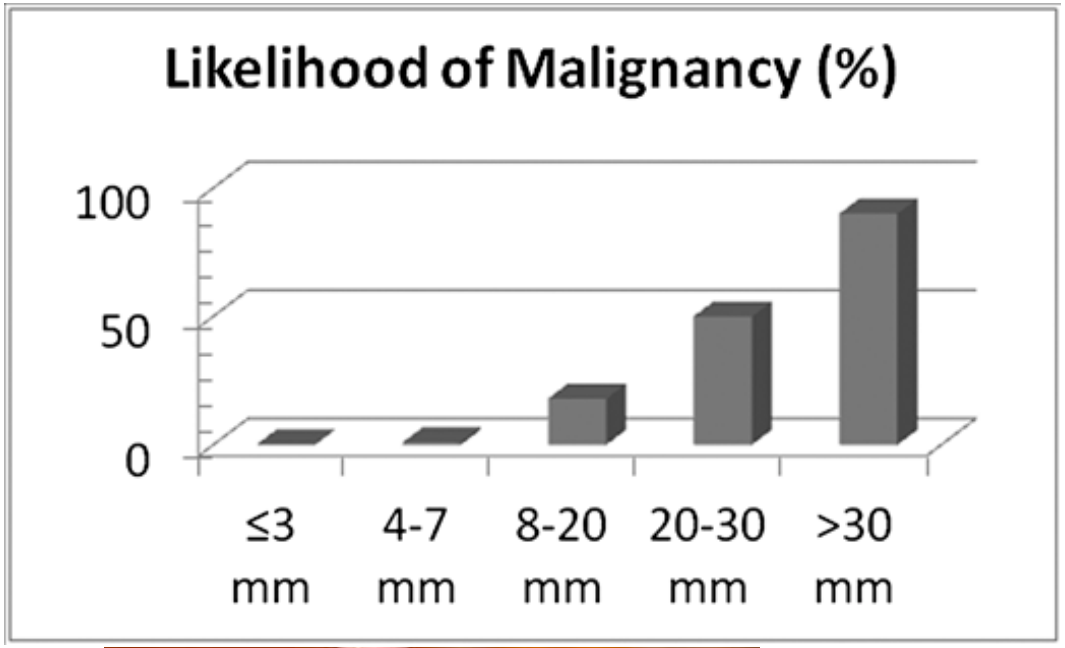


Imaging Features

- Solid
- Ground glass
- Part solid
  - Combination of above
  - Ddx: infxn, MIA, AdenoCa
  - Double time: ~300-500 days

Imaging Features

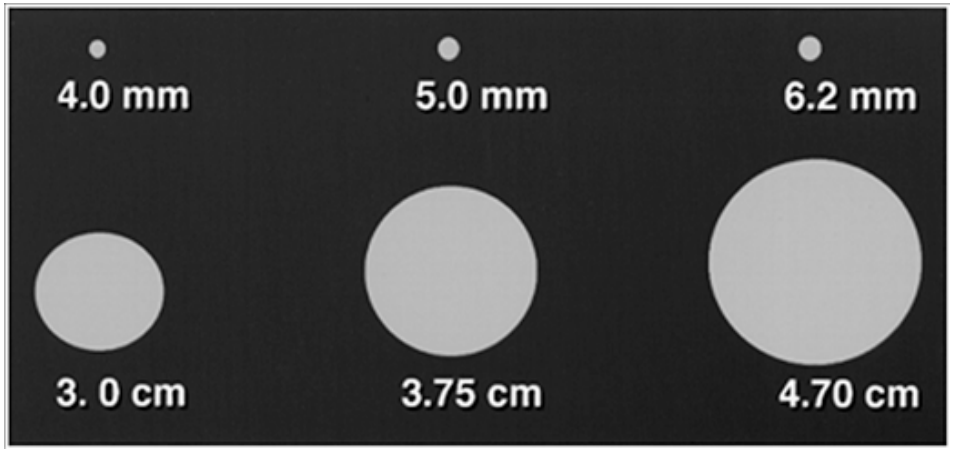
- Type
  - Solid
  - Groundglass
  - Part solid
- Size
  - Bigger is worser
  - >8mm
- Risk for cancer?

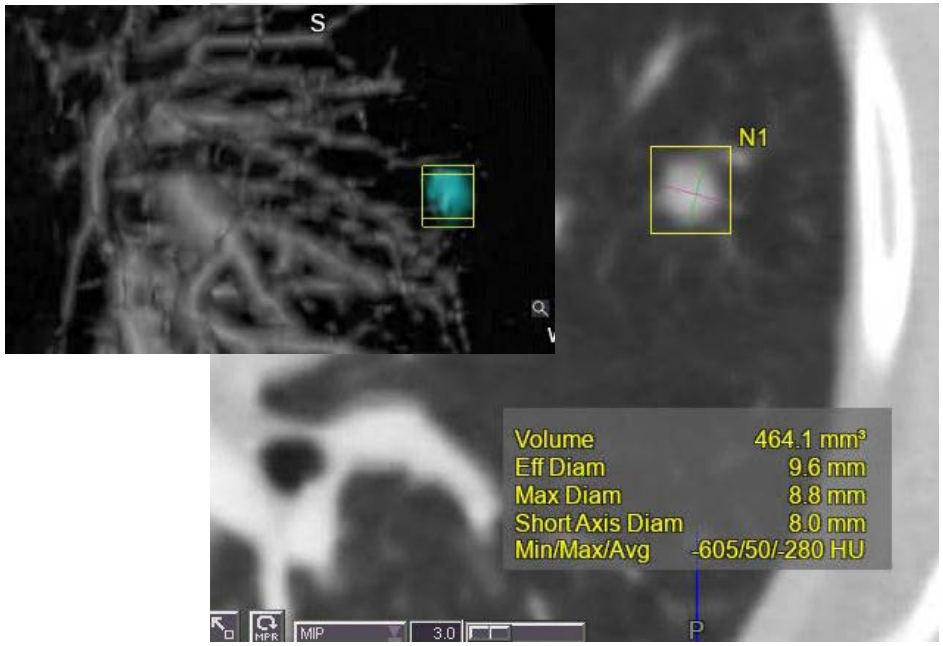


Patel el al Chest 2013

Measurement error

- 2x volume = 26% incr diameter
  - Sphere volume $4\pi r^3/3$
- Volumetric assessment better smaller diameters
- Best bet→same person for serial measurements





Patel el al Chest 2013

Patient Factors

- Type
  - Solid
  - Groundglass
  - Part solid
- Size
  - >8mm?
- Patient risk for cancer
  - Use models or clinical judgment

Table 1—Calculation of Probability of Malignancy

Source/Reference	Factors Taken Into Consideration to Determine the Probability of Malignancy
www.chestx-ray.com	1. Age
	2. Smoking (ever vs never and pack-y)
	3. Hemoptysis
	4. History of prior malignancy
	5. Nodule diameter
	6. Location
	7. Edge characteristics
	8. Growth rate
	9. Cavity wall thickness
	10. Calcification
	11. Contrast enhancement on CT scan > 15 HU
	12. PET scan
Swensen et al[6]	1. Age
	2. Smoking history (ever vs never)
	3. History of previous malignancy > 5 y ago
	4. Presence of spiculation
	5. Upper lobe location
Gould et al[7]	1. Age
	2. Smoking history (ever vs never)
	3. Nodule diameter
	4. Time since quitting smoking

HU = Hounsfield unit.

Patel et al Chest 2013

Case

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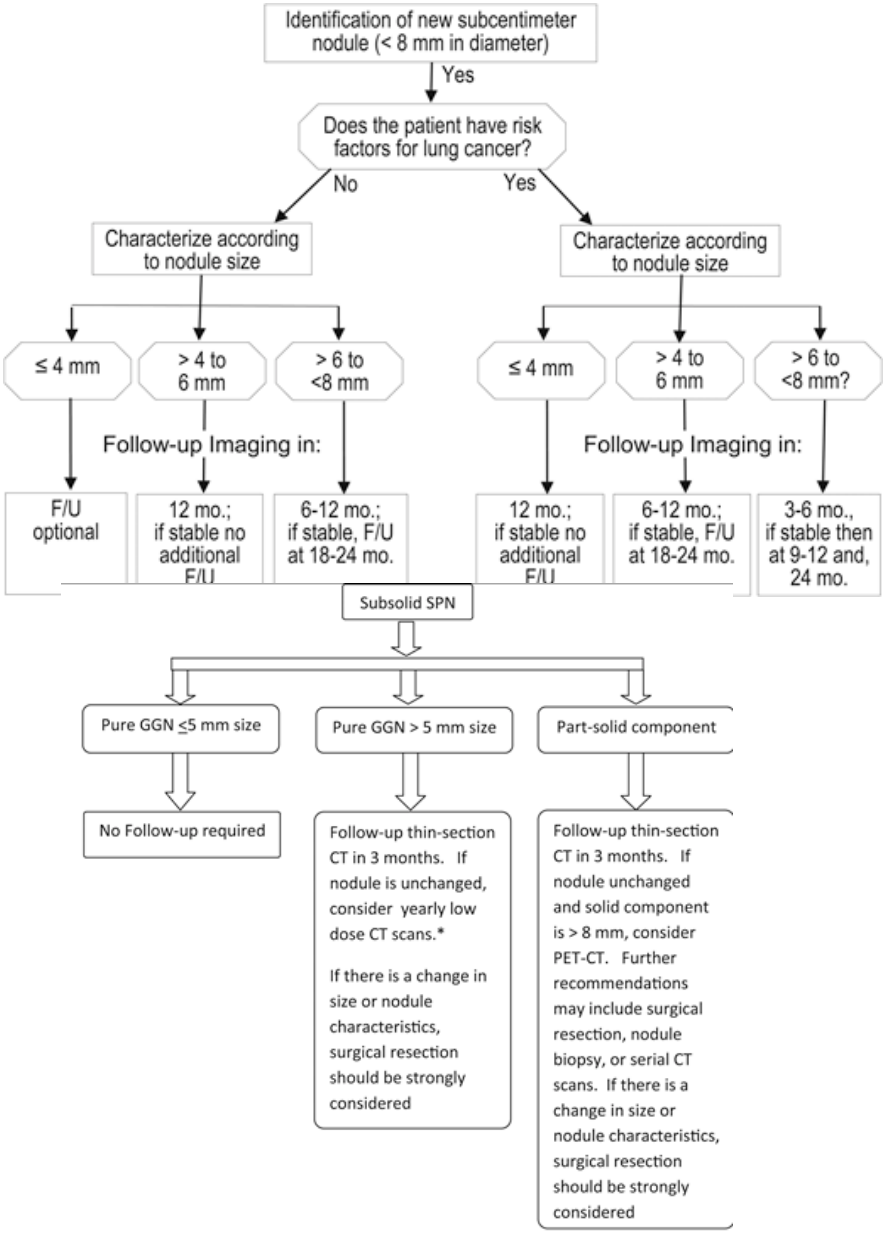
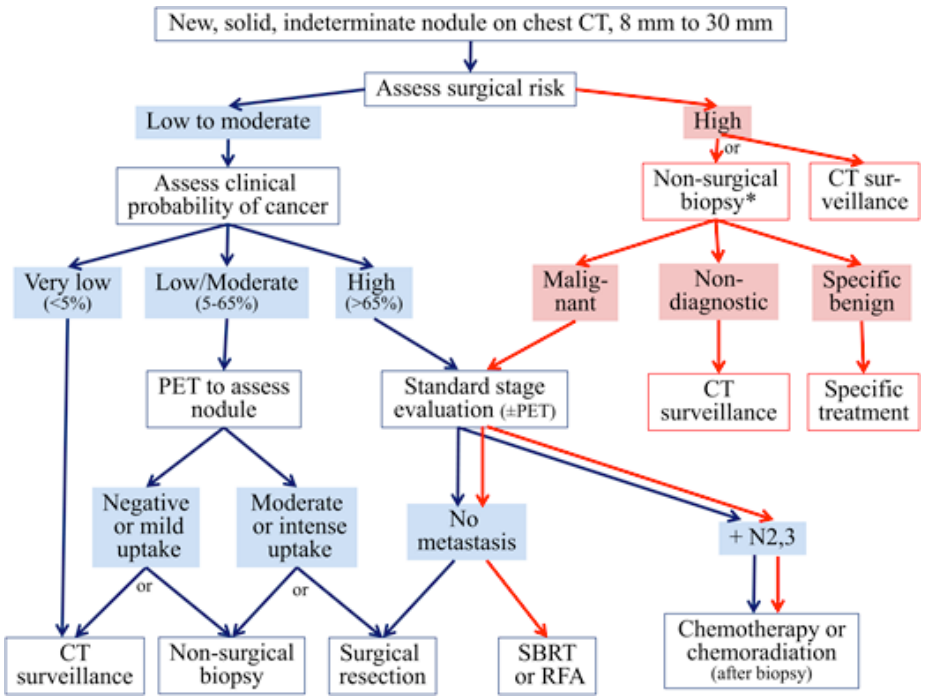
  - Chest CT →1 cm nodule

Nodule Management ???





Gould et al Chest 2013
Naidich et al Radiology 2013
MacMahon et al Radiology 2005

Case

- Type
  - Solid
  - Ground glass
  - Part solid
- Size
  - >8mm? --YES
- Risk for cancer
  - Intermediate

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  - Solid
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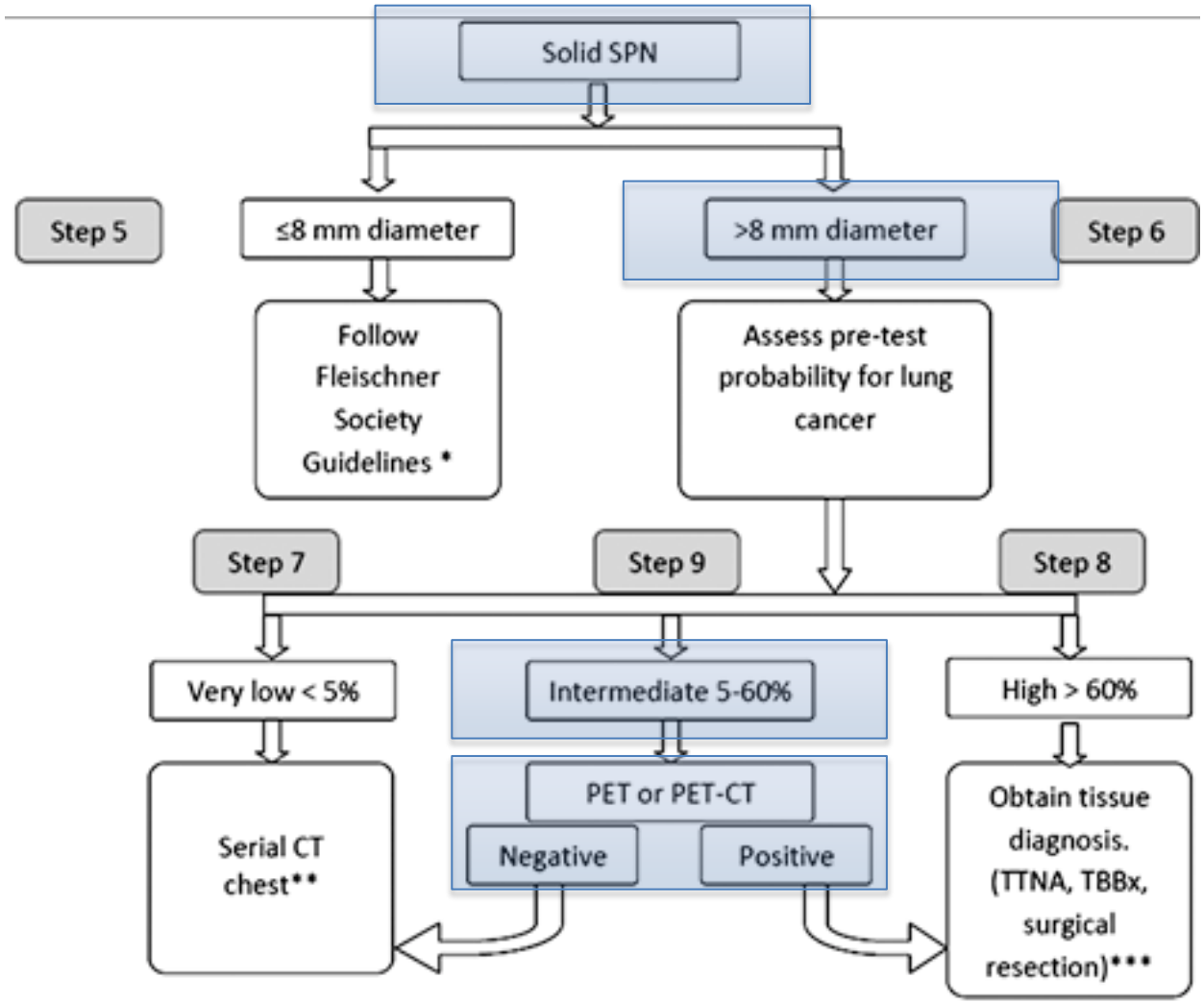
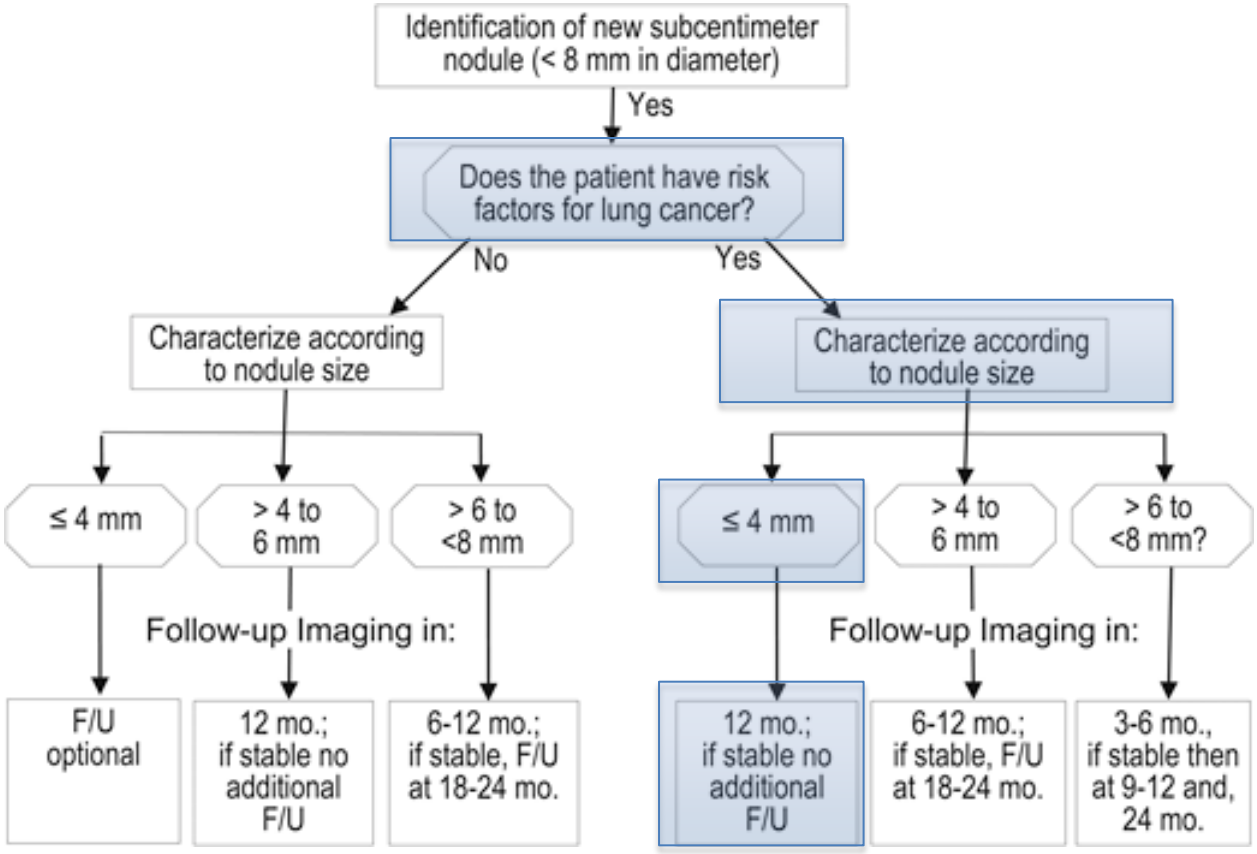


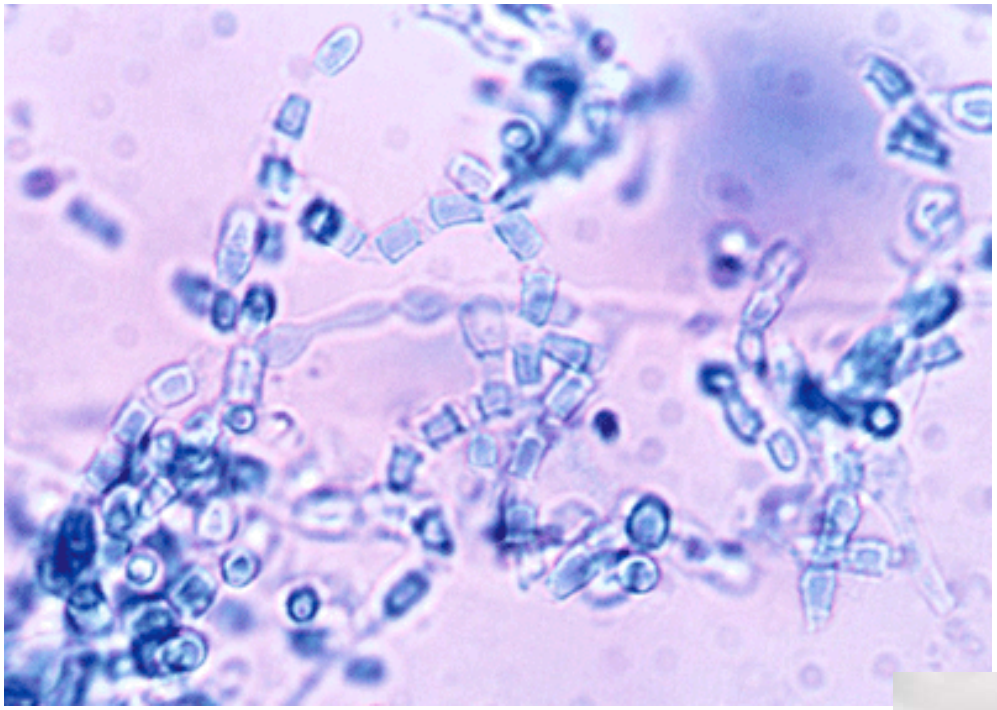
Gould et al Chest 2013
MacMahon et al Radiology 2005

Case

- Type
  - Solid
  - Ground glass
  - Part solid
- Size
  - 4mm
- Risk for cancer
  - Intermediate

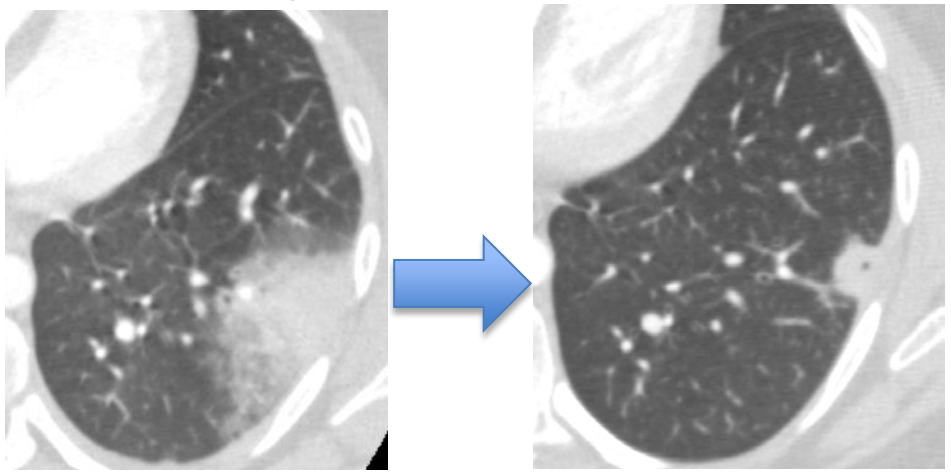


Gould et al Chest 2013
MacMahon et al Radiology 2005



Coccidiomycosis

- Common cause of pulmonary nodules in endemic regions
  - Solid or cavitary
  - Usually >8mm



- Specificity of PET is significantly lower in endemic regions

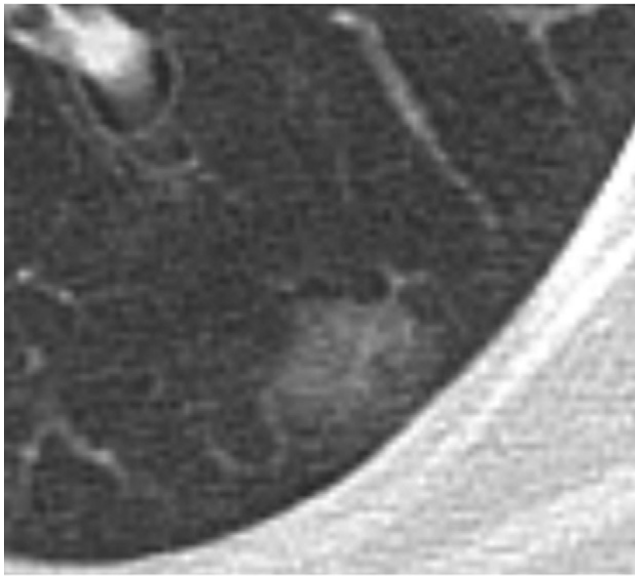
Research

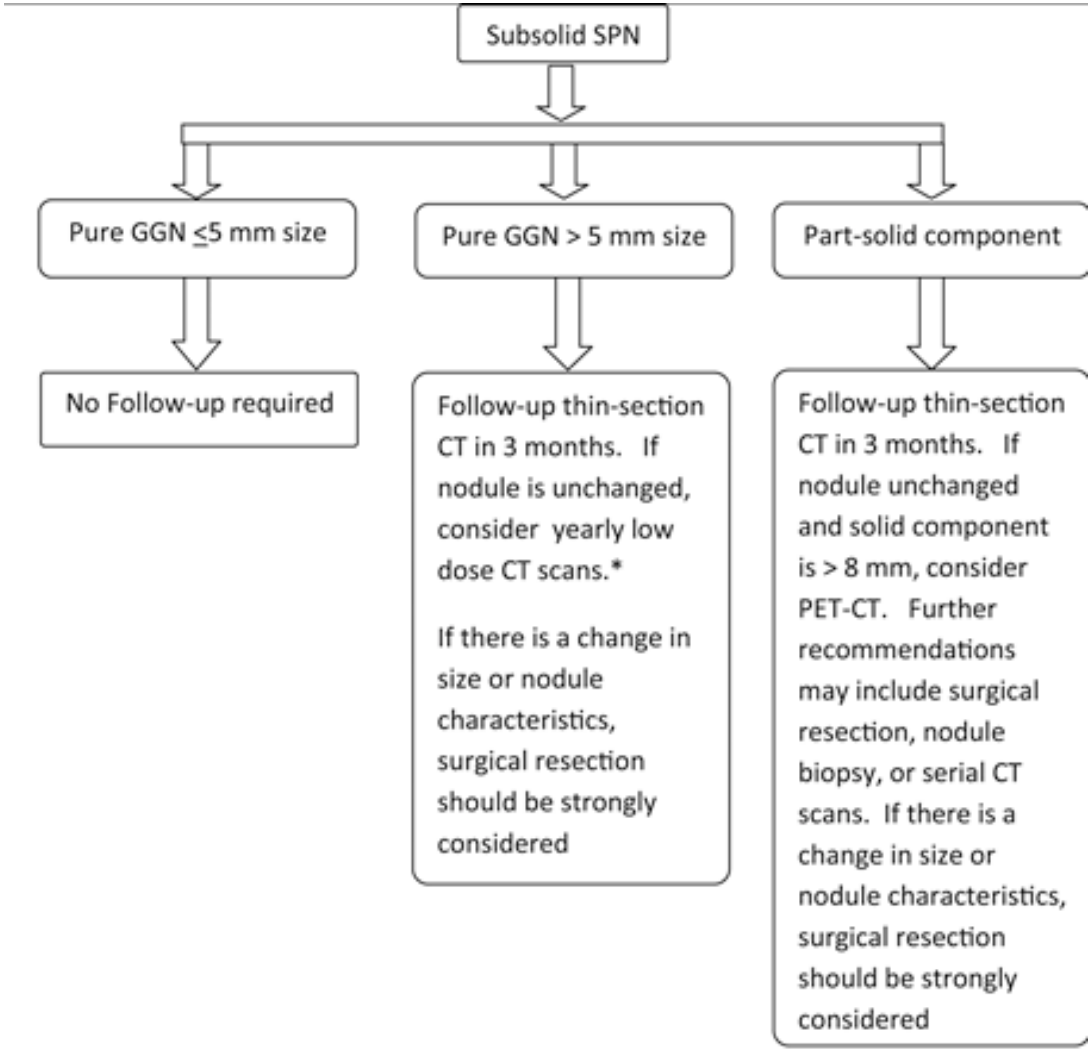
Original Investigation

Accuracy of FDG-PET to Diagnose Lung Cancer in Areas With Infectious Lung Disease
A Meta-analysis

Deppen et al JAMA 2014

Subsolid Nodules

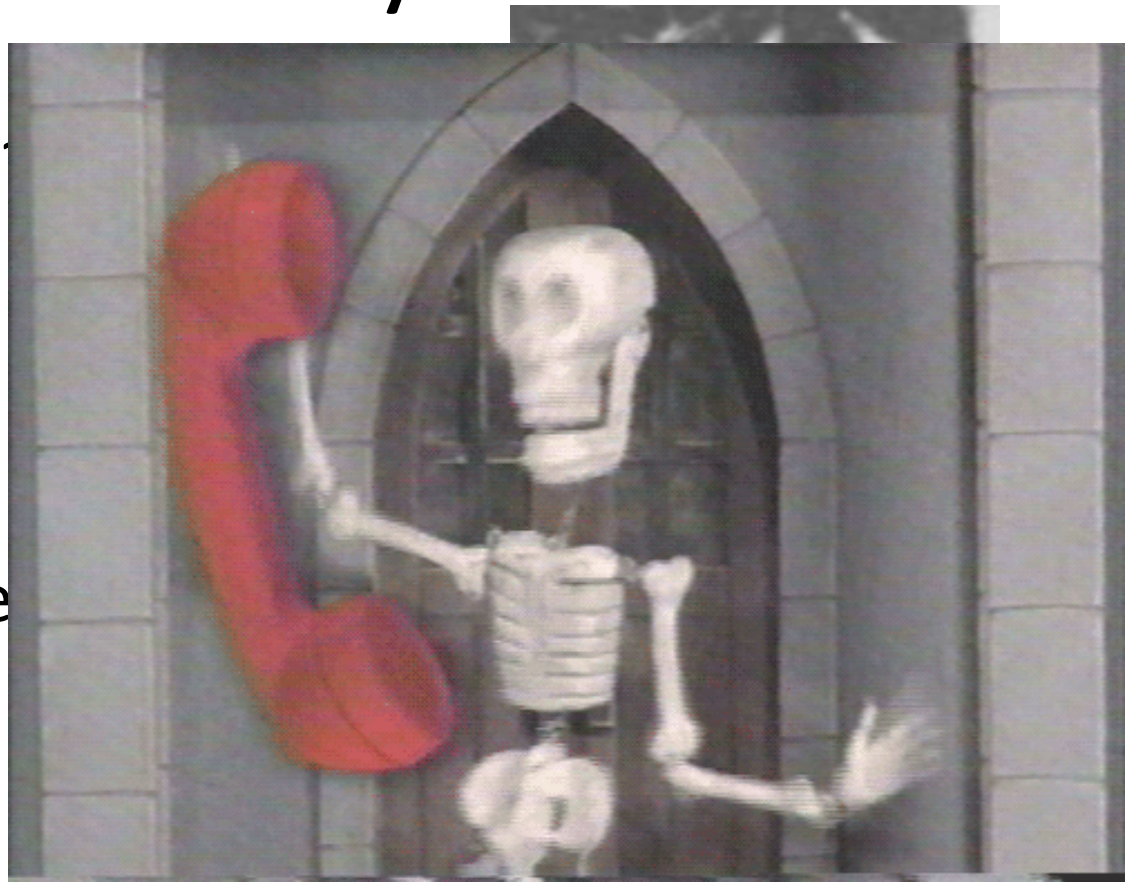




Gould et al Chest 2013
Naidich et al Radiology 2013

Summary

- Old films for stability
- Type
- Size (≤ 4 OR >8mm)
- Risk factors for cance
- Is it Cocci?
- Call your friendly radiologist



Case

- 55 year old male female comes to your office for annual exam
- 30 pack year smoker
- Still smokes ½ pack/day

- Should I get screened for lung cancer?

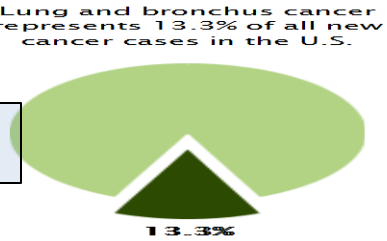
1. No
2. Yes, chest xray
3. Yes, chest CT
4. Unknown→ refer to pulmonary

Number of New Cases and Deaths

How Common Is This Cancer?

Compared to other cancers, lung and bronchus cancer is fairly common.

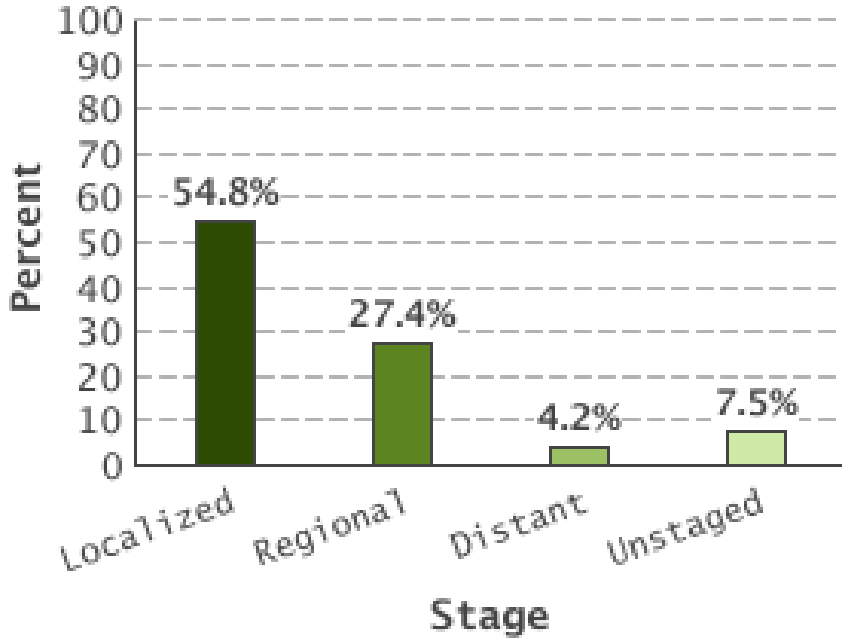
	Common Types of Cancer	Estimated New Cases 2015	Estimated Deaths 2015
1.	Breast Cancer (Female)	231,840	40,290
2.	**Lung and Bronchus Cancer**	**221,200**	**158,040**
3.	Prostate Cancer	220,800	27,540
4.	Colon and Rectum Cancer	132,700	49,700
5.	Bladder Cancer	74,000	16,000
6.	Melanoma of the Skin	73,870	9,940
7.	Non-Hodgkin Lymphoma	71,850	19,790
8.	Thyroid Cancer	62,450	1,950
9.	Kidney and Renal Pelvis Cancer	61,560	14,080
10.	Endometrial Cancer	54,870	10,170



In 2015, it is estimated that there will be 221,200 new cases of lung and bronchus cancer and an estimated 158,040 people will die of this disease.

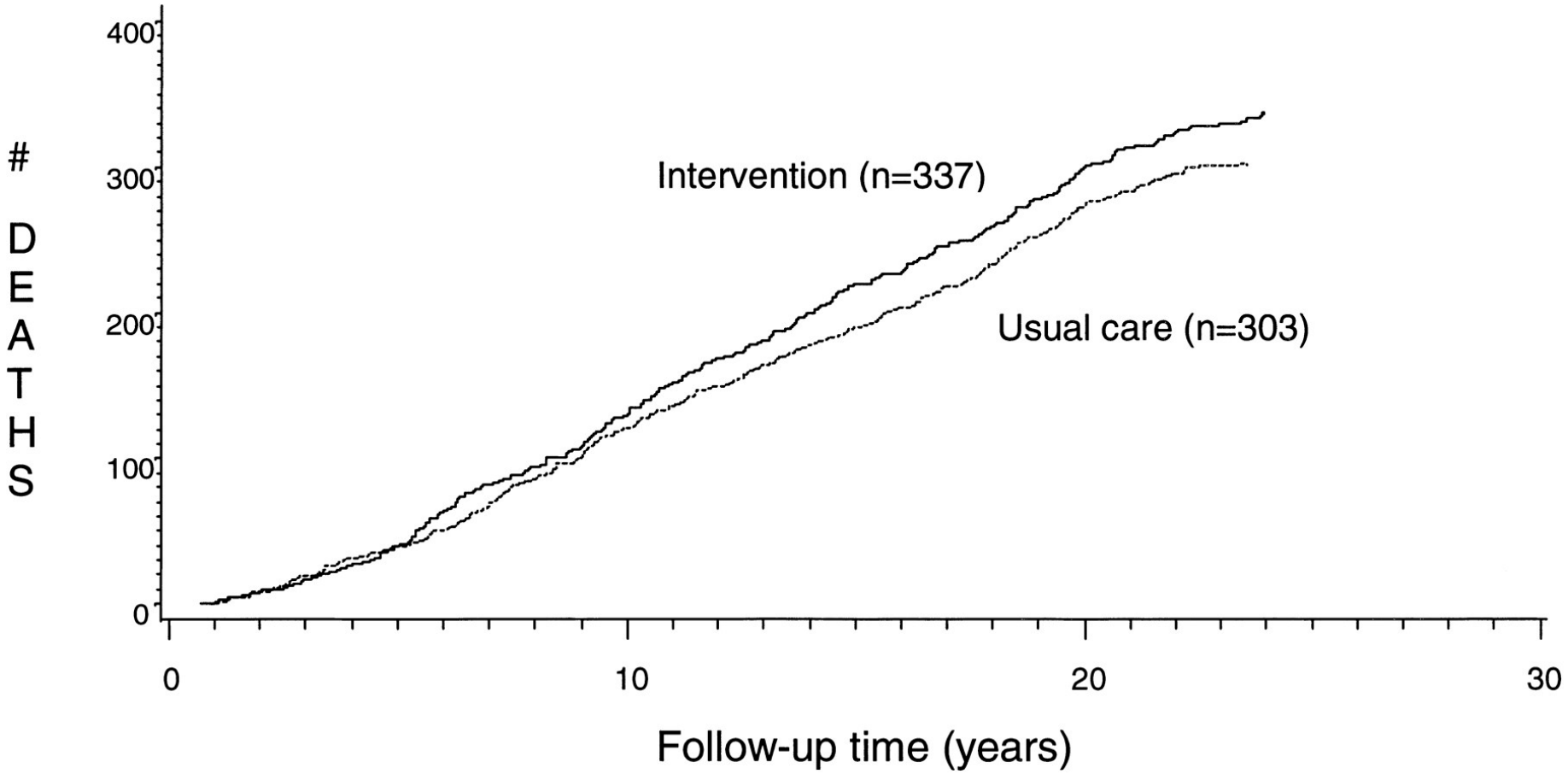
How to reduce lung cancer mortality?

1. Environmental
   - Stop smoking!
2. Better treatment
3. Screening?
   - earlier stage = better survival



http://seer.cancer.gov

Chest X-Ray Screening



Marcus et al JNCI. 2000 92(16):1308-16

UPRIGHT

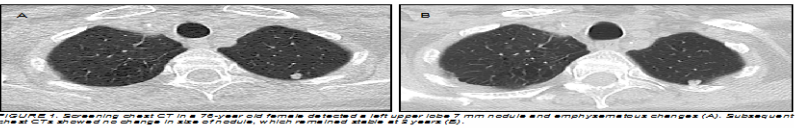


FIGURE 1. Screening chest CT in a 76-year-old female detected a left upper lobe 7 mm nodule and emphysematous changes (A). Subsequent chest CTs showed no change in size of nodule, which remained stable at 3 years (B).

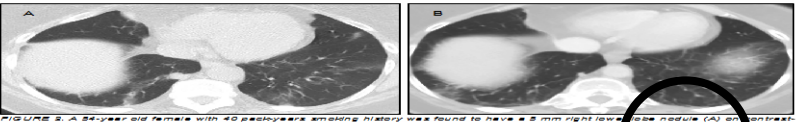
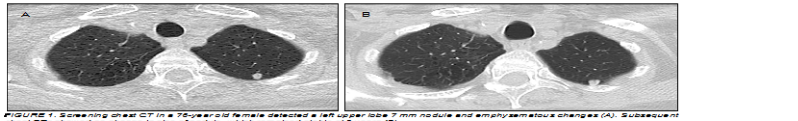


FIGURE 2. A 64-year-old female with 40 pack-years smoking history was found to have a 5 mm right lower lobe nodule (A) on contrast-enhanced CT and then lost to follow-up. A chest CT performed 4 years later demonstrated interval growth of the nodule to 10 mm (B). Metastatic adenocarcinoma was found on mediastinoscopy.

participants undergoing invasive follow up for false-positive results.[3]

The rigorous methodology and large size of the NLST set it apart from most prior randomized studies, which have had inconclusive or conflicting results. This methodology has been reviewed and largely accepted by the medical community, and has given rise to a series of corollary studies. One area of particular interest has been whether to broaden the restrictive enrollment criteria (55- to 74-year-old smokers and nonsmokers with a smoking history of 30 pack-years or greater) and how to make screening more accessible outside of large urban subspecialty medical centers. The focus on large academic centers likely contributed to the power of LDCT to detect early lung cancer and the minimization of risks of invasive follow up.

A number of societies with interest in lung cancer screening have published guidelines recommending LDCT screening in certain instances, for the most part employing the NLST inclusion criteria as a reference. In July 2013, the USPSTF, which previously regarded the evidence regarding LDCT lung screening as insufficient, upgraded its recommendation to a grade B recommendation ("There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial"), concluding that "strong evidence shows that LDCT screening can reduce lung cancer and all-cause mortality."[1] Specifically, the USPSTF recommendations are for LDCT screening in individuals between 55 and 79 years of age who have a 30-pack-year history of smoking or have quit in the past 15 years. The Affordable Care Act mandates that private insurers cover low-dose lung cancer screening based on the USPSTF recommendations. In February 2015, a national coverage determination (NCD) of CMS, whose beneficiaries are typically 65 years or older, recommended CT screening for adults between 55–77 years of age who have a 30 pack-year history of smoking and who are current smokers or have quit smoking in the past 15 years.[4]



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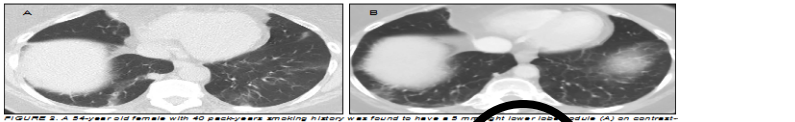

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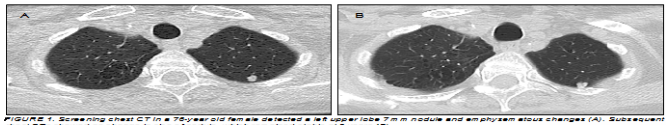
Folllow-up

LUNG CANCER SCREENING



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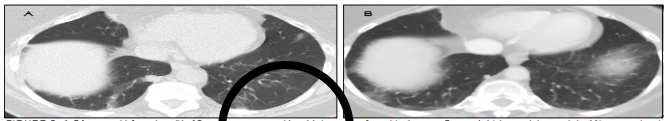

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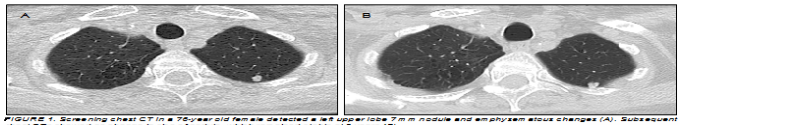

FIGURE 1. Screening chest CT in a 76-year-old female detected a left upper lobe 7 mm nodule and emphysematous changes (A). Subsequent chest CTs showed no change in size of nodule, which remained stable at 3 years (B).

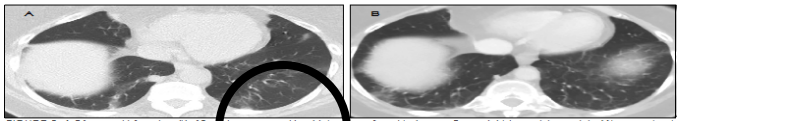

FIGURE 2. A 64-year-old female with 40 pack-years smoking history was found to have a 5 mm right lower lobe nodule (A) on contrast-enhanced CT and then lost to follow-up. A chest CT performed 4 years later demonstrated interval growth of the nodule to 10 mm (B). Metastatic adenocarcinoma was found on mediastinoscopy.

participants undergoing invasive follow up for false-positive results.[3]

The rigorous methodology and large size of the NLST set it apart from most prior randomized studies, which have had inconclusive or conflicting results. This methodology has been reviewed and largely accepted by the medical community, and has given rise to a series of corollary studies. One area of particular interest has been whether to broaden the restrictive enrollment criteria (55- to 74-year-old smokers and nonsmokers with a smoking history of 30 pack-years or greater) and how to make screening more accessible outside of large urban subspecialty medical centers. The focus on large academic centers likely contributed to the power of LDCT to detect early lung cancer and the minimization of risks of invasive follow up.

A number of societies with interest in lung cancer screening have published guidelines recommending LDCT screening in certain instances, for the most part employing the NLST inclusion criteria as a reference. In July 2013, the USPSTF, which previously regarded the evidence regarding LDCT lung screening as insufficient, upgraded its recommendation to a grade B recommendation ("There is high certainty that the net benefit is moderate or there is moderate certainty that the net benefit is moderate to substantial"), concluding that "strong evidence shows that LDCT screening can reduce lung cancer and all-cause mortality."[1] Specifically, the USPSTF recommendations are for LDCT screening in individuals between 55 and 79 years of age who have a 30-pack-year history of smoking or have quit in the past 15 years. The Affordable Care Act mandates that private insurers cover low-dose lung cancer screening based on the USPSTF recommendations. In February 2015, a national coverage determination (NCD) of CMS, whose beneficiaries are typically 65 years or older, recommended CT screening for adults between 55–77 years of age who have a 30 pack-year history of smoking and who are current smokers or have quit smoking in the past 15 years.[4]

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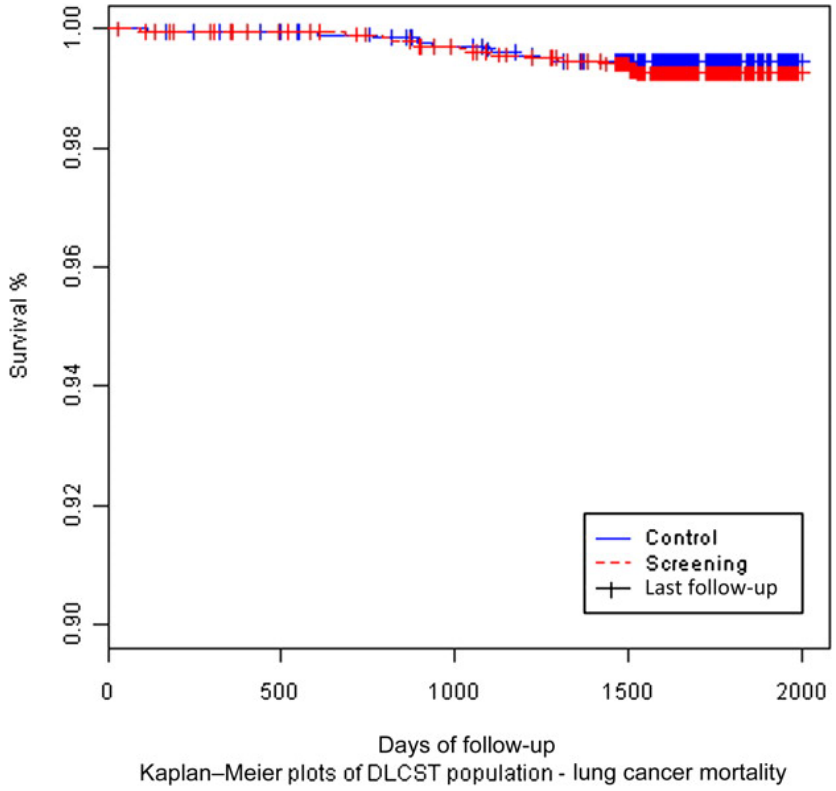
Chest CT Screening

- DANTE trial
  - 2472 participants
  - CXR vs CT
- DLST
  - 4104 participants
  - CT vs no screen



Saghir et al Thorax 2012 67(4):296-30
Infante et al AJRCCM 2009 180(5):445-45

Chest CT Screening

- NLST
  - 53,454 participants
    - 55-74 year old

      AND
    - 30 pack year smoker
    - Non-smoker if quit <15 yrs
  - CT or CXR x 3yrs
  - + CT if >4mm nodule

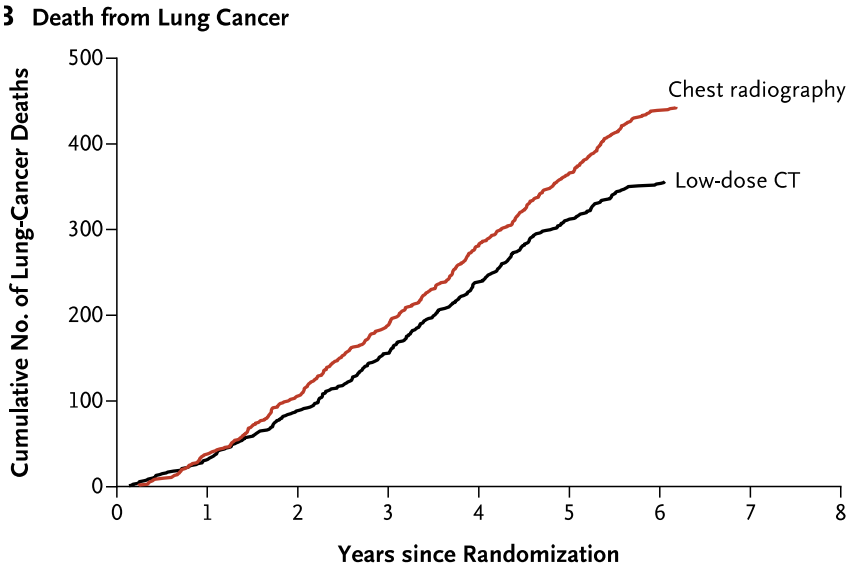
Table 1. Selected Baseline Characteristics of the Study Participants.*

Characteristic	Low-Dose CT Group (N=26,722)	Radiography Group (N=26,732)
	number (percent)	
Age at randomization		
<55 yr†	2 (<0.1)	4 (<0.1)
55–59 yr	11,440 (42.8)	11,420 (42.7)
60–64 yr	8,170 (30.6)	8,198 (30.7)
65–69 yr	4,756 (17.8)	4,762 (17.8)
70–74 yr	2,353 (8.8)	2,345 (8.8)
≥75 yr†	1 (<0.1)	3 (<0.1)
Sex		
Male	15,770 (59.0)	15,762 (59.0)
Female	10,952 (41.0)	10,970 (41.0)
Race or ethnic group‡		
White	24,289 (90.9)	24,260 (90.8)
Black	1,195 (4.5)	1,181 (4.4)
Asian	559 (2.1)	536 (2.0)
American Indian or Alaska Native	92 (0.3)	98 (0.4)
Native Hawaiian or other Pacific Islander	91 (0.3)	102 (0.4)
More than one race or ethnic group	333 (1.2)	346 (1.3)
Data missing	163 (0.6)	209 (0.8)
Hispanic ethnic group‡		
Hispanic or Latino	479 (1.8)	456 (1.7)
Neither Hispanic nor Latino	26,079 (97.6)	26,039 (97.4)
Data missing	164 (0.6)	237 (0.9)
Smoking status		
Current	12,862 (48.1)	12,900 (48.3)
Former	13,860 (51.9)	13,832 (51.7)

NEJM 2011 365(5): 395-409

Chest CT Screening

- NLST
  - 20% decrease in lung cancer mortality
  - 6.7% reduction in overall mortality
- NELSON
  - 15,822 participants
  - Final results 1-2 yrs



NEJM 2011 365(5): 395-409

Chest CT Screening

U.S. Preventive Services TASK FORCE

SCREENING FOR LUNG CANCER
CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Asymptomatic adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit smoking within the past 15 years
Recommendation	Screen annually for lung cancer with low-dose computed tomography. Discontinue screening when the patient has not smoked for 15 years. Grade: B

Risk Assessment	Age, total cumulative exposure to tobacco smoke, and years since quitting smoking are the most important risk factors for lung cancer. Other risk factors include specific occupational exposures, radon exposure, family history, and history of pulmonary fibrosis or chronic obstructive lung disease.
Screening Tests	Low-dose computed tomography has high sensitivity and acceptable specificity for detecting lung cancer in high-risk persons and is the only currently recommended screening test for lung cancer.
Treatment	Non–small cell lung cancer is treated with surgical resection when possible and also with radiation and chemotherapy.
Balance of Benefits and Harms	Annual screening for lung cancer with low-dose computed tomography is of moderate net benefit in asymptomatic persons who are at high risk for lung cancer based on age, total cumulative exposure to tobacco smoke, and years since quitting smoking.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on counseling and interventions to prevent tobacco use and tobacco-caused disease. These recommendations are available at http://www.uspreventiveservicestaskforce.org/.

For a summary of the evidence systematically reviewed in making this recommendation, the full recommendation statement, and supporting documents, please go to http://www.uspreventiveservicestaskforce.org/.

NEJM 2011 365(5): 395-409

Benefits of Screening vs **"Harms" of Screening**

Benefits of Screening

- 20% mortality reduction*
  - If 1000 patients screened
  - Absolute decrease 17 → 14

→

- **Very big benefits, few people**

"Harms" of Screening

NEJM 2014; 371:1793-1802
JAMA Int Med. 2014;174:269-74
Ann Intern Med. 2015;162:485-91

Benefits of Screening

- 20% mortality reduction*
  - If 1000 patients screened
  - Absolute decrease 17 → 14

→ **Very big benefits, few people**

"Harms" of Screening

- False Positives
  - ~26% recalled
    - 3.8% lung cancer
    - (4→6mm = ~13% recall)
- Radiation exposure
  - Max 30 CXR equivalent
- Cost
  - $81,000/QALY

→ **Small harms, many people**

→ **Small harms, many people**

NEJM 2014; 371:1793-1802
JAMA Int Med. 2014;174:269-74
Ann Intern Med. 2015;162:485-91

Benefits of Screening

- 20% mortality reduction*

→ Very big benefits, few people

"Harms" of Screening

- False Positives
- Radiation exposure
- Cost

→ Small harms, many people

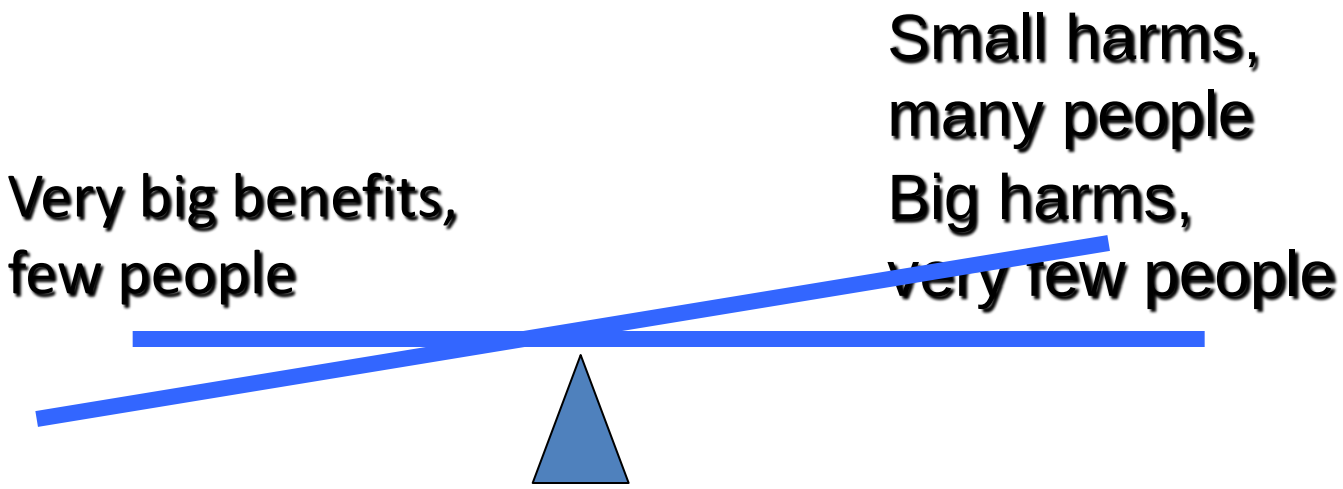
- Overdiagnosis
  - ~10-20% with cancer rx unnecessarily

→ Big harms, very few people

NEJM 2014; 371:1793-1802
JAMA Int Med. 2014;174:269-74
Ann Intern Med. 2015;162:485-91

- When to start screening?
  - 55-74 year old
  - 30 pack year smoker
  - Non-smoker if quit <15 yrs
- Screening frequency?
  - Yearly

- What's next?
  - Await NELSON trial results
  - Encourage smoking cessation
    - CT influence to quit?
  - Novel biomarkers (e.g. circulating DNA)



THANK YOU

THANK YOU

Lung Cancer Screening

- Screening CXR
  - no benefit (Mayo Lung Project)
- Screening chest CT
  - 20% reduction in lung cancer deaths (NLST)
    - (20/1000→17/1000)
    - Age 55-74
    - 30 pack-year smoker
    - Quit <15 yrs ago
  - "NELSON" trial ongoing

NEJM 2011

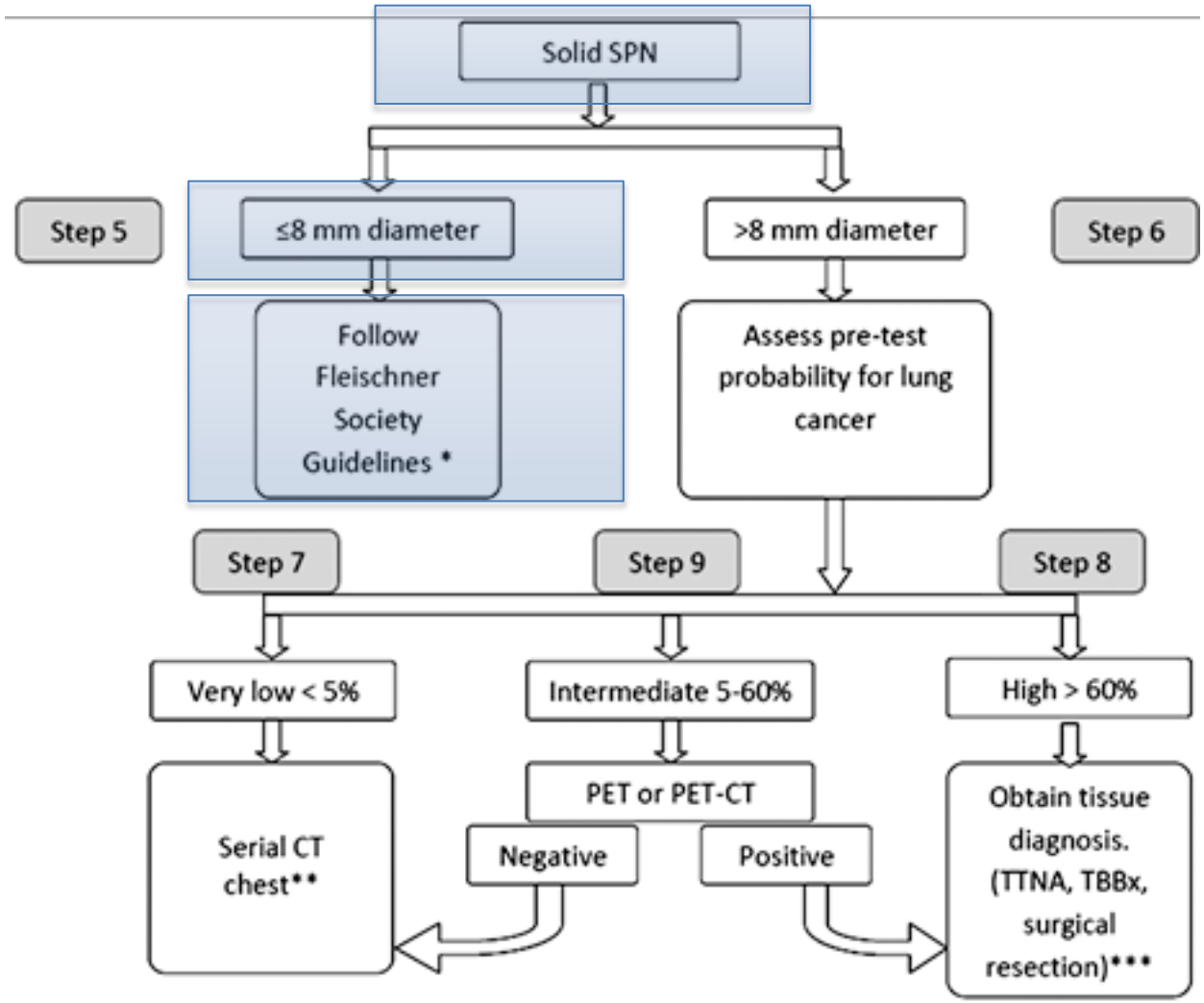
Case 1

- 60 year old healthy male for annual exam
  - 20 pack -year smoker
- Normal physical exam
  - Lungs clear to ascultation
  - No weight loss or type B sx
- Should I get screened for lung cancer?

1. No data to support screening
2. Chest X-ray
3. Chest CT without contrast
4. Chest CT with contrast
5. Unsure→refer to pulmonary

Case

- Type
  - Solid
  - Ground glass
  - Part solid
- Size
  - 6mm
- Risk for cancer
  - Intermediate



Gould et al Chest 2013
MacMahon et al Radiology 2005

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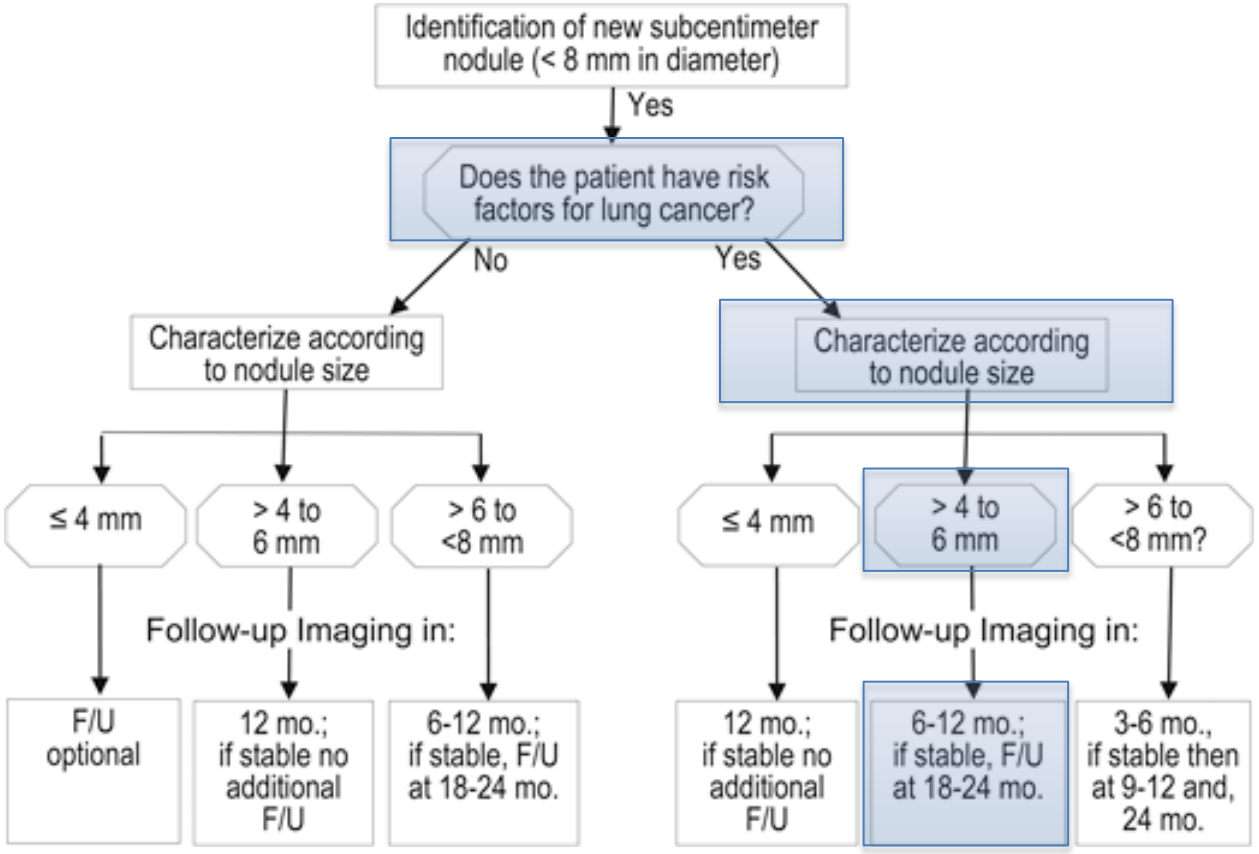

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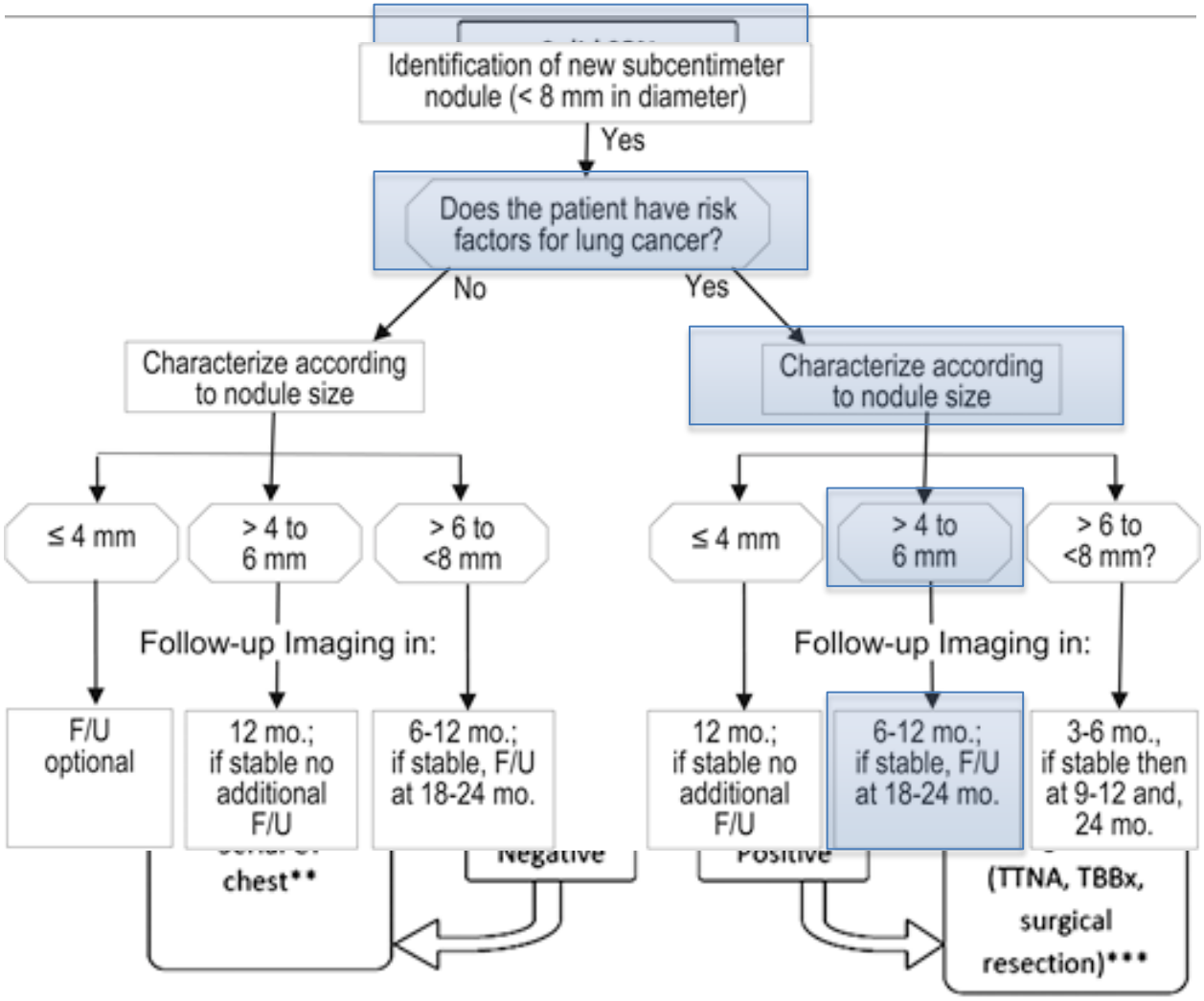
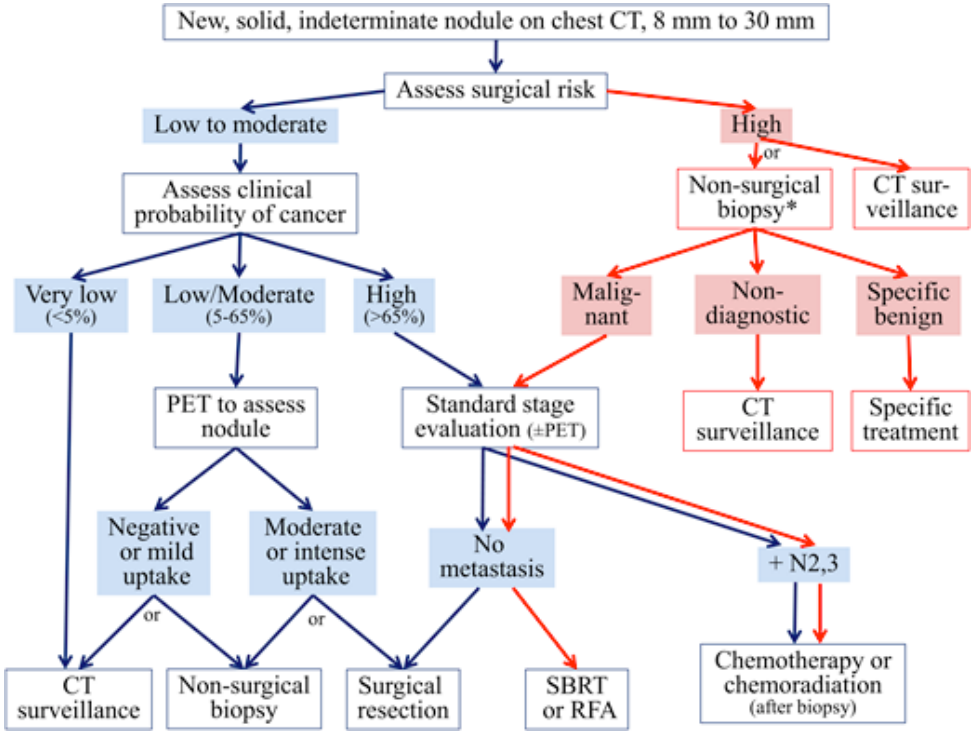
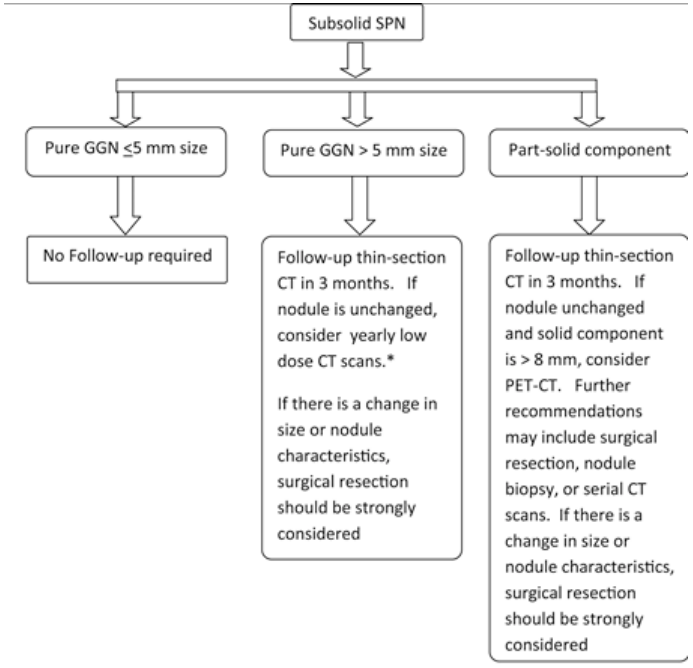


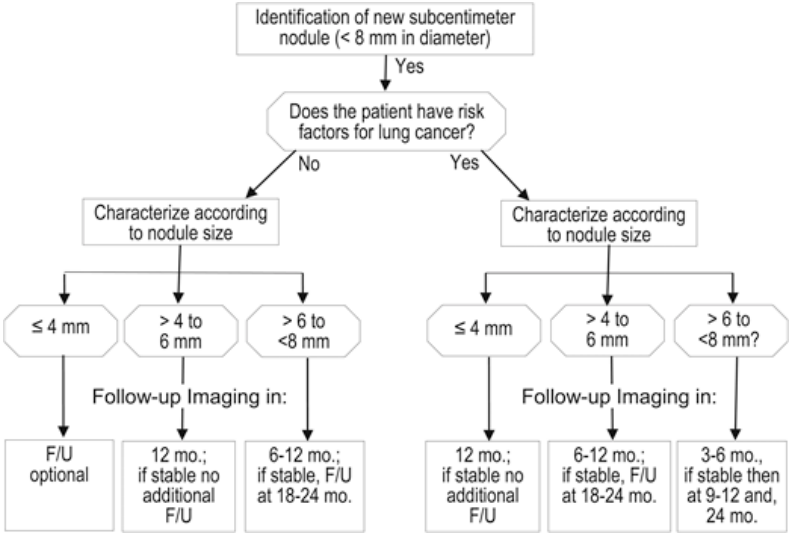
Gould et al Chest 2013
MacMahon et al Radiology 2005

Nodule Management ???





Nodule Type	Management Recommendations	Additional Remarks
Solitary pure GGNs		
≤5 mm	No CT follow-up required	Obtain contiguous 1-mm-thick sections to confirm that nodule is truly a pure GGN
>5 mm	Initial follow-up CT at 3 months to confirm persistence then annual surveillance CT for a minimum of 3 years	FDG PET is of limited value, potentially misleading, and therefore not recommended
Solitary part-solid nodules	Initial follow-up CT at 3 months to confirm persistence. If persistent and solid component <5 mm, then yearly surveillance CT for a minimum of 3 years. If persistent and solid component ≥5 mm, then biopsy or surgical resection	Consider PET/CT for part-solid nodules >10 mm



Gould et al Chest 2013
Naidich et al Radiology 2013
MacMahon et al Radiology 2005