Incidental Pulmonary Nodules

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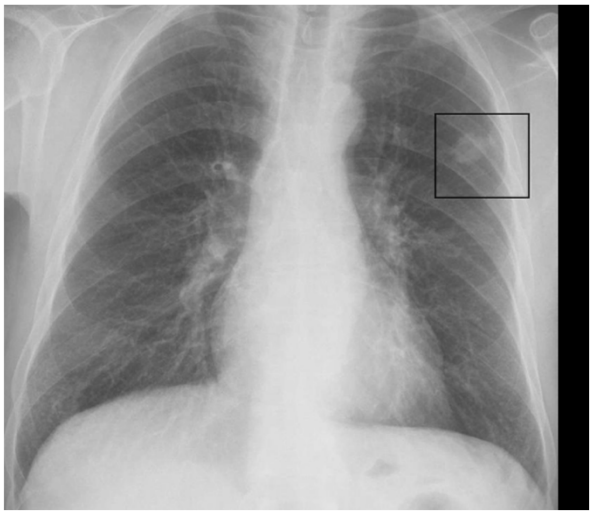
What is a (Solitary) Pulmonary Nodule?

- Nodule: A rounded opacity, well or poorly defined, measuring up to 3 cm in diameter
- Mass: >3 cm
- Micronodule: 0-5 mm
- Often are *incidentally* found
  - Pre-operative chest X-rays
  - CT pulmonary venograms (atrial fibrillation pre-ablation)
  - **In the Emergency Department**
    - Abdominal CT scans (kidney stones, abdominal pain)
    - Chest CT scans (pulmonary embolism evaluation)
    - OFTEN reported at the end of the CT report; OFTEN forgotten!

2



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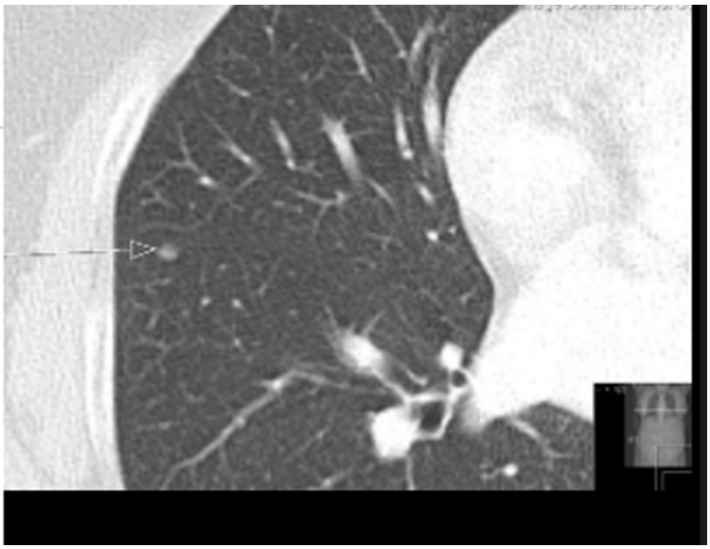


4

Epidemiology

- 2010 Adult population: 234.5 million
- Estimate of Chest CT scans: 4.8 million
  In adults per year
- Estimate of lung nodules: 1.57 million per year
- New lung cancer diagnosis (within 2 years): 63, 000
- Approx 72,000 of 224,210 lung cancer cases in 2014 in the US were ≤ 30mm

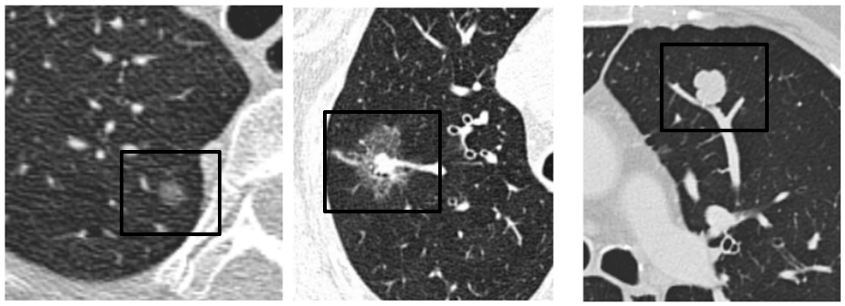
Roughly 4% of lung nodules turned out to be malignant

Etiology of Pulmonary Nodules

- Benign >>>>> Malignant
  - Benign etiologies:
    - Fungal infection (acute, chronic, or remote)
    - Benign neoplasms (ie hamartoma)
    - Vascular pathology (pulmonary arteriovenous malformation)
    - Inflammatory nodules (sarcoidosis, rheumatoid arthritis, vasculitis)
    - 'Other' (intrapulmonary lymph node, mucoid impaction, rounded atelectasis)
  - Malignant etiologies:
    - Bronchogenic carcinoma (ie primary lung cancer)
    - Metastatic cancer (breast, testicular, germ cell, melanoma, sarcoma, renal cell)
    - Carcinoid tumors

6

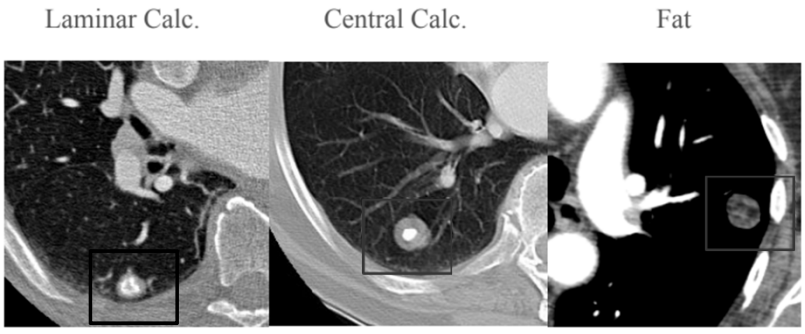
Nodule Textures



7

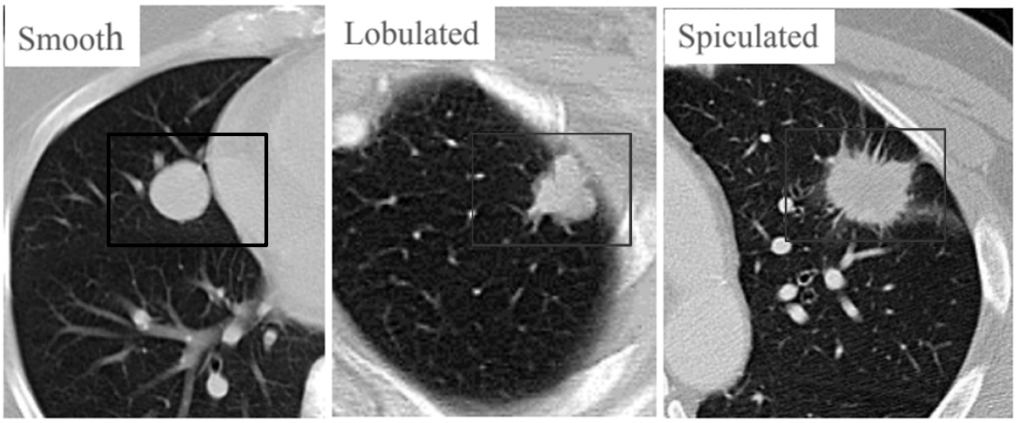
Nodule Attenuation

Benign Features



8

Nodule Margins



9

Why is the Solitary Pulmonary nodule Important?

- Malignant nodules represent a potentially curable form of lung cancer
- 5 year survival for patients with malignant SPN 65%-80%
- 5 year survival for unselected patients with lung cancer 17%

Mountain CF. Chest 1997;111:1710 Ginsberg et al. J Thorac Cardiovasc Surg 1983;86:654 Inoue et al. J Thorac Cardiovasc Surg 1998;116:407

Current Models used to Predict Cancer in Nodules

Six independent predictors of malignancy in SPN

- **Patient characteristics:**
  - Age
  - Smoking status
  - History of extrathoracic malignancy
- **Nodule characteristics:**
  - Diameter
  - Borders
  - Location

George Box: "All models are wrong but some are useful"
Swensen et al. Arch Intern Med 1997;157:849

CT Size matters

Size	% malignant
<4 mm	0%
4-7 mm	0.8%
8-20 mm	22%
>20 mm	63%

Swensen et al. AJRCCM 2002;165:508-13.

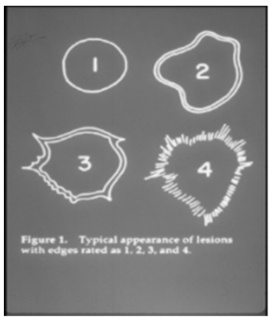


Figure 1. Typical appearance of lesions with edges rated as 1, 2, 3, and 4.

CT: Edge Characteristics

Border type	LR
1. Smooth	0.2
2. Lobulated	0.5
3. Spiculated	5.0
4. Corona radiata	14

Siegelman et al. Radiology 1986;160:307

Risk prediction calculators

Model	Population	Number	Validation	Prevalence of malignancy	Comments
Mayo	Incidental nodules Single institution	629 patients	210 patients	23%	Useful for incidental nodules
Brock	Pan canadian multicenter screening trial	1871 patients 7008 nodules	1090 patients 5021 nodules	5.5%	Useful for screen detected nodules
Herder	Single institution Cohort referred for PET	106	None	57%	Additive to mayo

Solitary Pulmonary Nodule (SPN) Malignancy Risk Score (Mayo Clinic Model)

Predicts malignancy risk in solitary lung nodules on chest x-ray.

INSTRUCTIONS

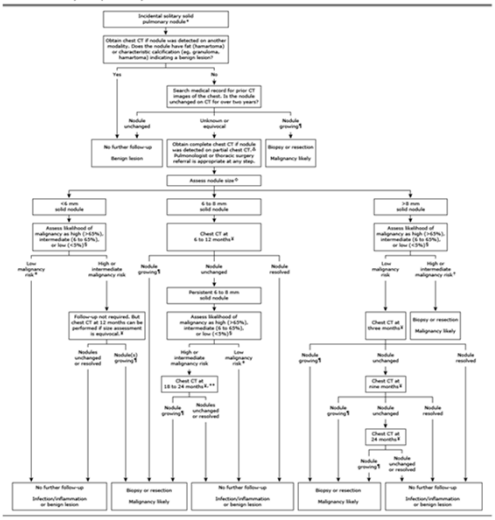
Do not use in patients with prior lung cancer diagnosis or with history of extrathoracic cancer diagnosed within 5 years of nodule presentation.

When to Use

- Patients with solitary lung nodule on chest x-ray.
- Do not use in patients with prior lung cancer diagnosis or with history of extrathoracic cancer diagnosed within 5 years of nodule presentation.

Age		years
Nodule diameter		mm
Current or former smoker	**No** 0	Yes +1
Extrathoracic cancer diagnosis ≥5 years prior	**No** 0	Yes +1
Upper lobe location of tumor	**No** 0	Yes +1
Nodule spiculation	**No** 0	Yes +1
FDG-PET Optional, if performed	**PET not performed**	
	No uptake	
	Faint uptake	
	Moderate uptake	
	Intense uptake	

Incidental solitary solid pulmonary nodule evaluation



Algorithm applies to asymptomatic, immunocompetent adults, age >35 years without malignancy that is actively under treatment or follow-up. It is not designed for use in other populations or in those undergoing lung cancer screening. The clinician is expected to use his or her independent medical judgment in the context of individual circumstances and patient preferences to make adjustments, as necessary. Chest CT should be performed without contrast as contiguous thin (ie, 1 mm) images on a helical scanner using low radiation dose techniques.

CT: computed tomography; FDG: fluorodeoxyglucose; PET: positron emission tomography.

* Nodule is a well-defined opacity completely surrounded by lung parenchyma measuring <30 mm in longest dimension.

¶ Growth is defined as >2 mm increase in overall size.

Δ If the chest CT reveals findings relevant to nodule diagnosis (eg, other nodules or masses, mediastinal lymphadenopathy, or findings of pulmonary inflammation or infection), subsequent workup should be based on these findings.

◊ Nodule size is defined as the average of long and short axes in axial cross-section.

§ Likelihood of malignancy assessed either clinically or by quantitative predictive models.

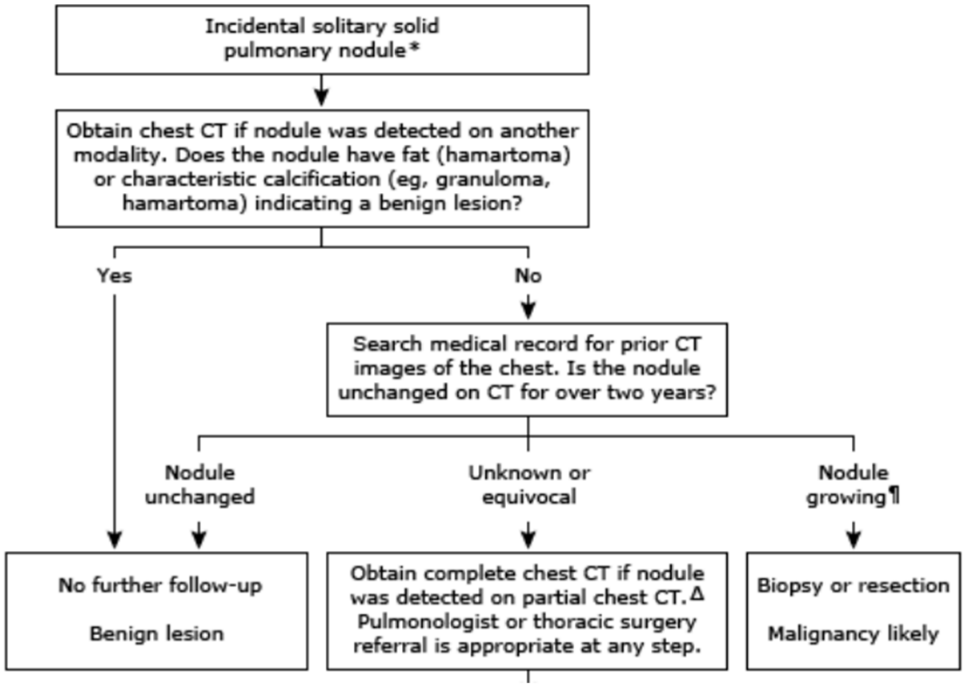
‡ Timing of chest CT is relative to the date of the initial nodule detection.

‡ Another chest CT at 18 to 24 months is an option if stability of nodules is equivocal.

† FDG PET/CT is an option in patients at intermediate cancer risk or those considered high medical risk for biopsy. FDG-avid nodules proceed to tissue sampling. FDG-nonavid nodules are triaged to annual CT surveillance.

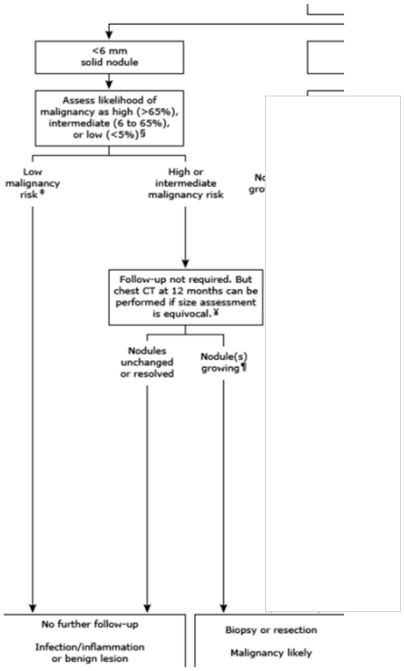
** Follow-up interval should be the same or longer than the preceding one that showed no nodule growth. In addition, longer interval is needed to demonstrate unequivocal growth for smaller nodules.

UpToDate®



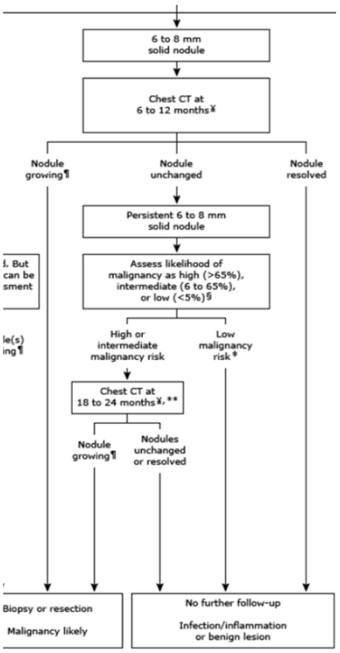
17

Less than 6 mm



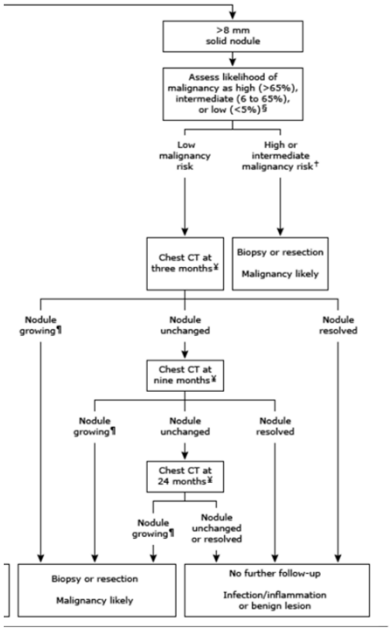
18

6-8 mm



19

Greater than 8 mm



20

Summary of Fleischner Guidelines for SOLID, SOLITARY Nodules

	<6 mm (<100 mm^3)	6-8 mm (100-250 mm^3)	>8 mm (>250 mm^3)
Single			
Low Risk	No routine follow-up	CT at 6-12 months, then consider CT at 18-24 months	Consider CT at 3 months, PET/CT, or tissue sampling
High Risk	Optional CT at 12 months	CT at 6-12 months, then CT at 18-24 months	Consider CT at 3 months, PET/CT, or tissue sampling

21

Fleischner Criteria Exclusions?

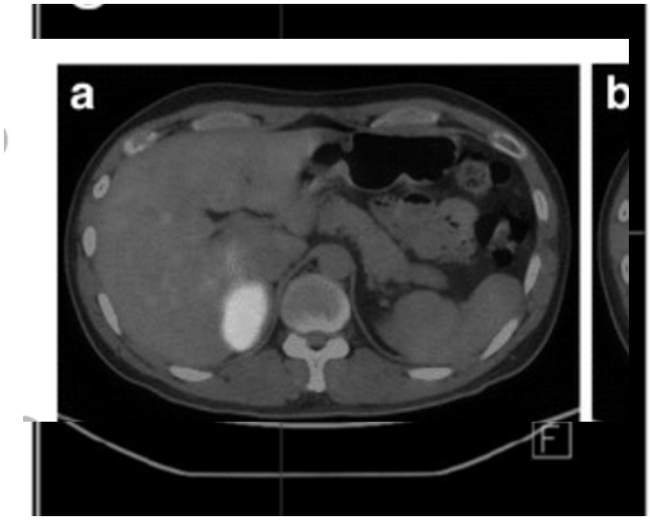
- Exclusions:
  - Patients with unexplained fever
  - Patients with known or suspected metastases
  - Patients <35 years of age
  - Lung cancer screening (use LUNG-RADS)

Management

- CT scan surveillance
  - NON-contrast, THIN cuts, LOW-dose radiation CT scan is preferred
  - If any interval growth, likely will need to proceed to PET scan, biopsy, resection, etc

Management

- Positron emission tomography (PET) scan
  - Measures the 'metabolic activity' of nodules
    - Nodule/lesion can be 'PET-avid' if malignant, infectious, or inflammatory (like sarcoidosis)
  - Typically reserved for SOLID nodules GREATER than 8 mm (or even 10 mm)
    - High false negative rates in nodules < 8 mm or pure subsolid (ground glass) nodules
  - Can be helpful to determine best site to biopsy (ie diagnose AND stage simultaneously)



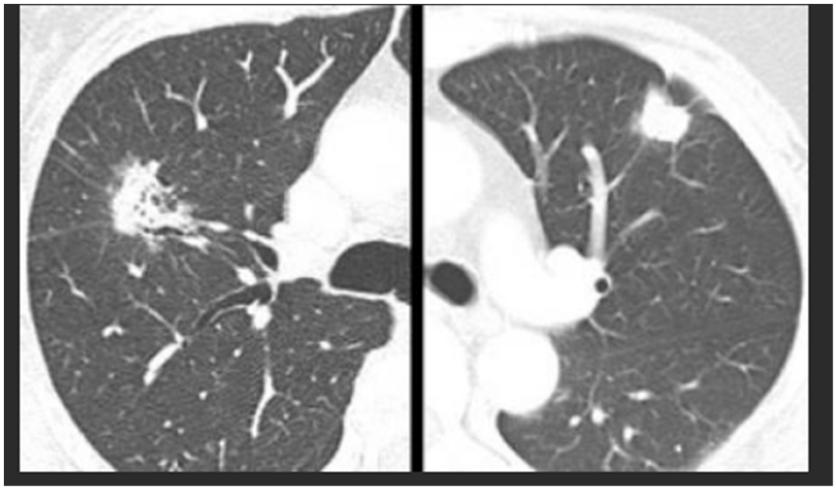
Management

- Biopsy
  - Bronchoscopic biopsy
    - Endobronchial Ultrasound (EBUS) Transbronchial Needle Aspiration (TBNA)
      - Useful for centrally-located lesions and if adenopathy present
    - Electromagnetic Navigational bronchoscopic biopsies
      - Useful for peripherally-located nodules that may not be amenable to transthoracic needle biopsy
  - Transthoracic needle biopsy (ie 'CT-guided' biopsy)
  - Depends on size of nodule, presence of other 'biopsyable' sites (ie lymph nodes), location of nodule (ie peripheral vs central)

Bronchoscopic vs CT-guided Biopsies

- Bronchoscopic biopsies (EBUS or navigational bronchoscopy)
  - Require at least moderate sedation (though often performed under general anesthesia)
  - 1-3 hours in duration
  - Minimal risks
    - Most risk is from anesthesia itself
    - Low rates of bleeding and pneumothoraces
- Transthoracic needle biopsies
  - Relatively quick procedures done using local anesthetic
  - Comparably higher risks of bleeding and pneumothoraces

Navigational Bronchoscopy



CT-guided biopsy

Management

- Biopsy via surgical resection
  - Theoretically can be diagnostic *and* curative
  - Reserved for:
    - Nodules with high pre-test probability for cancer
      - Enlarging, > 1 cm, spiculated, high-risk patient (ie smokers)
    - NO evidence of concerning adenopathy or distant metastatic lesions (ie would diagnose but NOT stage)
    - Patients that are good surgical candidates
  - In *theory*, can proceed directly from CT scan to surgical resection (without a PET scan *or* a biopsy)
    - In *practice*, PET scans are usually obtained to evaluate for:
      - A) PET-avidity in the nodule itself
      - B) ensure there are no other PET-avid lesions

Next Steps?

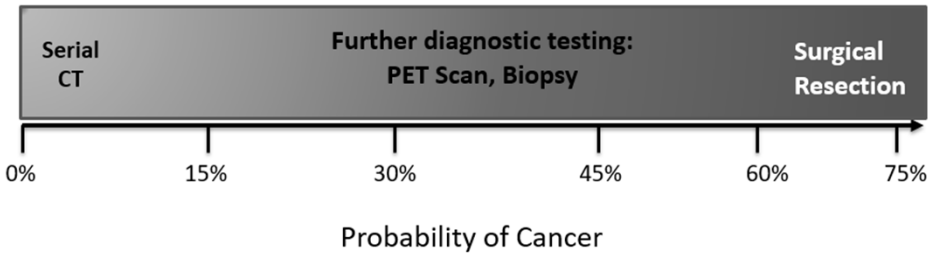


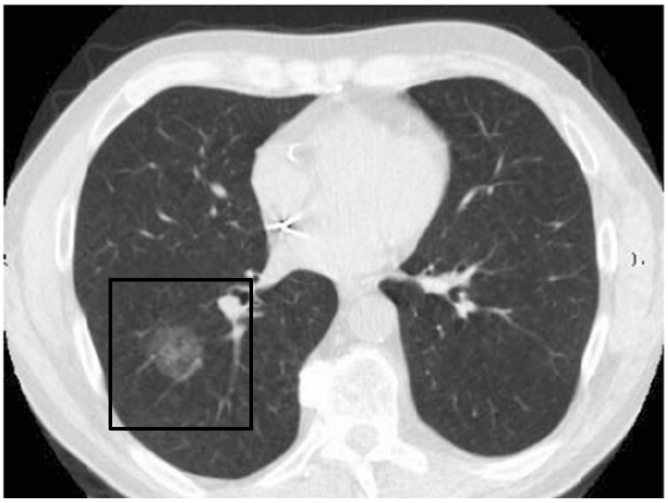
FIGURE 2. [Section 4.0] Factors that influence choice between evaluation and management alternatives for indeterminate, solid nodules ≥ 8 to 30 mm in diameter.

Factor	Level	CT Scan Surveillance	PET Imaging	Nonsurgical Biopsy	VATS Wedge Resection
Clinical probability of lung cancer	Very low (< 5%)	++++	-	-	-
	Low-moderate	+	+++	++	+
	High (< 65%)	-	(± staging)	++	++++
Surgical risk	Low	++	++	++	+++
	High	++	+++	++	-
Biopsy risk	Low	-	++	+++	+++
	High	++	+++	-	+
High suspicion of active infection or inflammation		-	-	++++	++
Values and preferences	Desires certainty	-	+	+++	++++
	Risk averse to procedure-related complications	++++	+++	++	-
Poor adherence with follow-up		-	-	+++	++++

VATS = video-assisted thoracoscopic surgery.

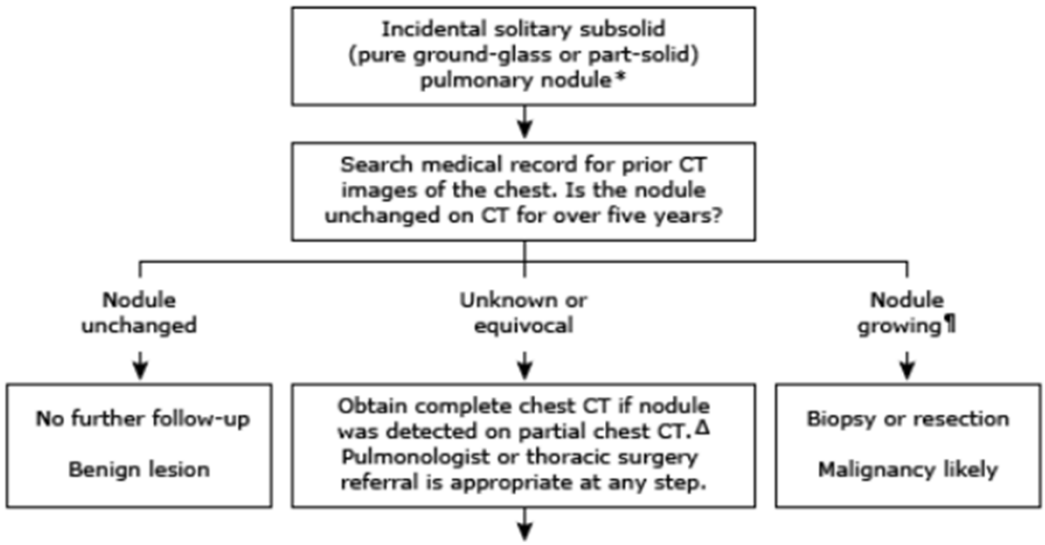
Gould M, CHEST 2013

'Ground Glass' Nodules



32

Incidental Solitary Subsolid Pulmonary Nodules ('ground glass')



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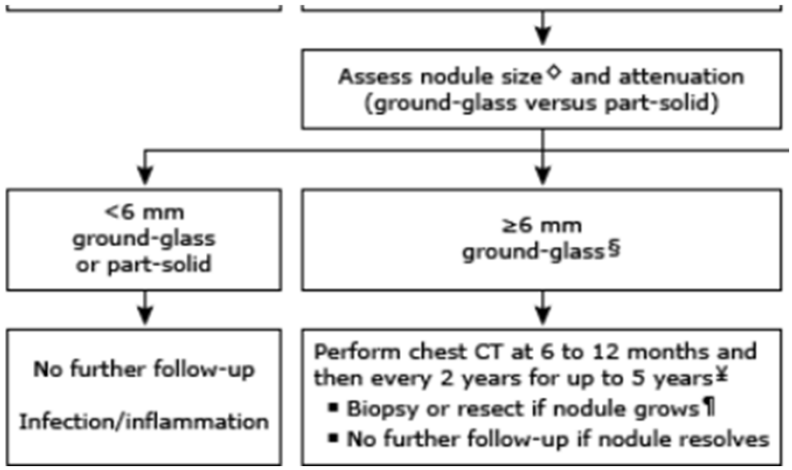

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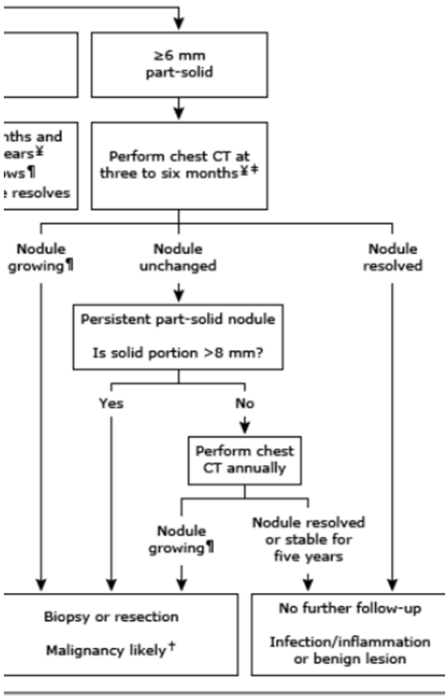
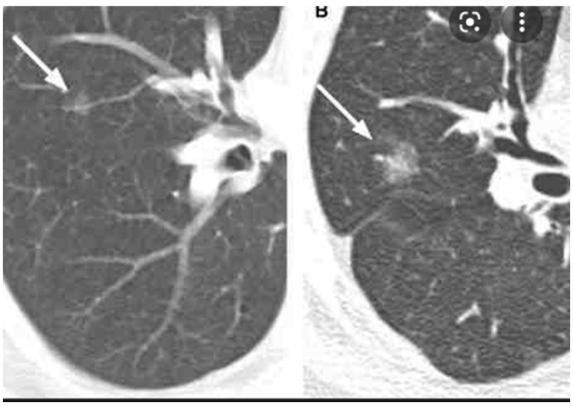


35

Enlarging Ground Glass Nodules



36

Management of Enlarging Ground Glass Nodules

- Malignant until proven otherwise
  - Adenocarcinoma 'in situ' (formerly known as 'bronchoalveolar carcinoma')
- PET scan vs percutaneous/transthoracic biopsy vs surgical resection
  - Compared to solid nodules, there are higher rates of false negatives with PET scans and percutaneous biopsies for ground glass nodules
    - Slow rate of growth, so not particularly metabolic active (false negative on PET scan)
    - Lesion is not solid, so needle biopsy may not be representative
  - 'if in doubt, cut it out' → referral to thoracic surgery

37

Take Home Points

- Always be on the lookout for incidental pulmonary nodules
  - CT scans (both CT chest angiography as well as CT abdomen) in the ER
  - CT pulmonary venograms (often obtained in the management of atrial fibrillation)
- 1st step is ALWAYS to look for prior imaging
- Use caution if/when ordering PET scans (particularly with ground glass nodules and nodules < 1 cm)
  - High rates of false positives AND false negatives
- Fine line between wanting to 'cure'/not wanting to 'miss' an early cancer and surgically resecting a benign lesion
- If ANY concern, can refer to pulmonary or thoracic surgery

38

Lung Cancer Screening

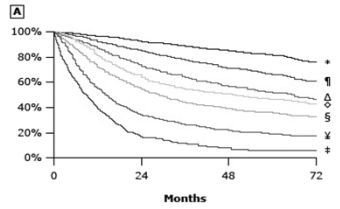
39

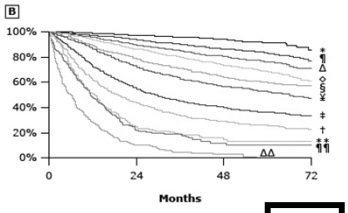
Why Do We Need Screening?

- Lung cancer is the leading cause of cancer-related death among men and women
- Worldwide → 1.6 million deaths due to lung cancer annually
- United States → 234,000 new cases of lung cancer diagnosed yearly
  - 154,000 lung cancer-associated deaths annually
- Clinical outcome for non-small cell lung cancer is directly related to stage at the time of diagnosis
  - Estimated that 75% of patients with lung cancer present with symptoms due to advanced local/metastatic disease no longer amenable to curative surgery
  - 5 year survival rates average 18% for all individuals with lung cancer

40

Overall survival by clinical stage according to the seventh edition (A) and the eighth edition (B) groupings using the entire database available for the eighth edition





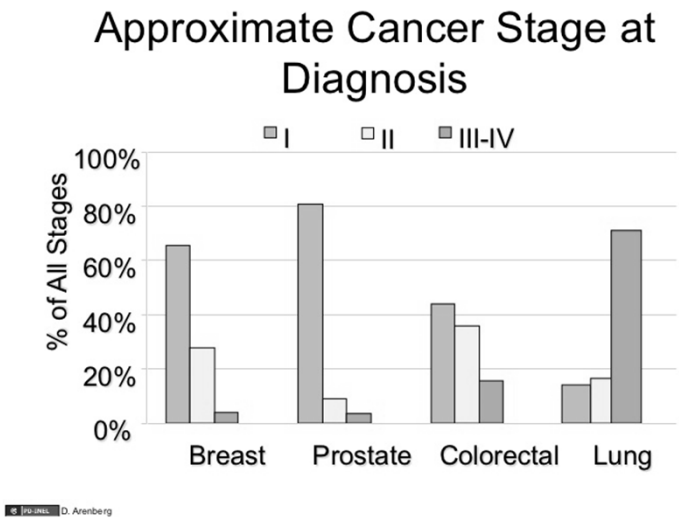
7th edition	Events / N	MST	24 month	60 month
* IA	1119 / 6303	NR	93%	82%
¶ IB	768 / 2492	NR	85%	66%
Δ IIA	424 / 1008	66.0	74%	52%
◇ IIB	382 / 824	49.0	64%	47%
§ IIIA	2139 / 3344	29.0	55%	36%
¥ IIIB	2101 / 2624	14.1	34%	19%
‡ IV	664 / 882	8.8	17%	6%

8th edition	Events / N	MST	24 month	60 month
* IA1	68 / 781	NR	97%	92%
¶ IA2	505 / 3105	NR	94%	83%
Δ IA3	546 / 2417	NR	90%	77%
◇ IB	560 / 1928	NR	87%	68%
§ IIA	215 / 585	NR	79%	60%
¥ IIB	605 / 1453	66.0	72%	53%
‡ IIIA	2052 / 3200	29.3	55%	36%
† IIIB	1551 / 2140	19.0	44%	26%
** IIIC	831 / 986	12.6	24%	13%
¶¶ IVA	336 / 484	11.5	23%	10%
ΔΔ IVB	328 / 398	6.0	10%	0%

Overall survival by clinical stage according to the seventh edition (A) and the eighth edition (B) groupings using the entire database available for the eighth edition. Survival is weighted by type of database submission: registry versus other.

N: number of patients; MST: median survival time; NR: not reached.

Reproduced from: Goldstraw P, Chansky K, Crowley J, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. J Thorac Oncol 2016; 11:39. Illustration used with the permission of Elsevier Inc. All rights reserved.



42

Pros and Cons of Screening

- Potential benefits of lung cancer screening:
  - Early detection (early stage) → potential curative surgical resection → increased survival (decreased morbidity and mortality)
  - ? Increased smoking cessation rates
- Potential 'harms' of lung cancer screening:
  - Consequences of evaluating normal findings:
    - High risk procedures (biopsy, surgery) for likely benign nodules
    - Incidental findings → asymptomatic emphysema, coronary artery disease, thyroid nodules
  - Radiation exposure (though we use 'low dose' radiation chest CTs for screening)
  - Patient 'distress' → presence of nodules (likely benign) may cause anxiety related to fear of having lung cancer

43

What's the Best Way to Screen for Lung Cancer?

Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening

The National Lung Screening Trial Research Team*

44

- Roughly 54,000 patients at 'high risk' for lung cancer were randomly assigned to undergo three annual screenings with either:
  - Low-dose chest CT
  - Chest radiograph
- Inclusion criteria:
  - Age 55 to 74 years
  - At least a 30 pack year smoking history
  - If former smoker, had to have quit within the previous 15 years
- Excluded if:
  - Previous diagnosis of lung cancer
  - Had undergone chest CT within previous 18 months
  - Any symptoms present (hemoptysis and weight loss)

45

Table 2. Results of Three Rounds of Screening.*

Screening Round			Low-Dose CT				Chest Radiography	
	Total No. Screened	Positive Result	Clinically Significant Abnormality Not Suspicious for Lung Cancer	No or Minor Abnormality	Total No. Screened	Positive Result	Clinically Significant Abnormality Not Suspicious for Lung Cancer	No or Minor Abnormality
			no. (% of screened)				*no. (% of screened)*	
T0	26,309	7191 (27.3)	2695 (10.2)	16,423 (62.4)	26,035	2387 (9.2)	785 (3.0)	22,863 (87.8)
T1	24,715	6901 (27.9)	1519 (6.1)	16,295 (65.9)	24,089	1482 (6.2)	429 (1.8)	22,178 (92.1)
T2	24,102	4054 (16.8)	1408 (5.8)	18,640 (77.3)	23,346	1174 (5.0)	361 (1.5)	21,811 (93.4)

Rate of positive screening:
CT group: 24.2%
CXR group: 6.9%

* The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. Results of screening tests that were technically inadequate (7 in the low-dose CT group and 26 in the radiography group, across the three screening rounds) are not included in this table. A screening test with low-dose CT was considered to be positive if it revealed a nodule at least 4 mm in any diameter or other abnormalities that were suspicious for lung cancer. A screening test with chest radiography was considered to be positive if it revealed a nodule or mass of any size or other abnormalities suspicious for lung cancer.

Source: N Engl J Med 2011;365:395-409.

'False positive' rates:
CT group: 96.4%
CXR group: 94.5%

Table 3. Diagnostic Follow-up of Positive Screening Results in the Three Screening Rounds.*

Variable	Low-Dose CT				Chest Radiography			
	T0	T1	T2	Total	T0	T1	T2	Total
				number (percent)				
Total positive tests	7191 (100.0)	6901 (100.0)	4054 (100.0)	18,146 (100.0)	2387 (100.0)	1482 (100.0)	1174 (100.0)	5043 (100.0)
Lung cancer confirmed	270 (3.8)	168 (2.4)	211 (5.2)	649 (3.6)	136 (5.7)	65 (4.4)	78 (6.6)	279 (5.5)
Lung cancer not confirmed†	6921 (96.2)	6733 (97.6)	3843 (94.8)	17,497 (96.4)	2251 (94.3)	1417 (95.6)	1096 (93.4)	4764 (94.5)

The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. FDG PET denotes ^{18}F-fluorodeoxyglucose positronemission tomography.

† Positive tests with incomplete information on diagnostic follow-up are included in this category (142 at T0, 161 at T1, and 141 at T2 in the low-dose CT group and 39 at T0, 26 at T1, and 25 at T2 in the radiography group).

47

Source: N Engl J Med 2011;365:395-409.

screenings,97+% of patients did NOT require ANY invasive procedures!

Complication	Lung Cancer Confirmed				
	Thoracotomy, Thoracoscopy, or Mediastinoscopy	Bronchoscopy	Needle Biopsy number (percent)	No Invasive Procedure	Total
Low-dose CT group					
Positive screening results for which diagnostic information was complete	164 (100.0)	227 (100.0)	66 (100.0)	16,596 (100.0)	17,053 (100.0)
No complication	138 (84.1)	216 (95.2)	59 (89.4)	16,579 (99.9)	16,992 (99.6)

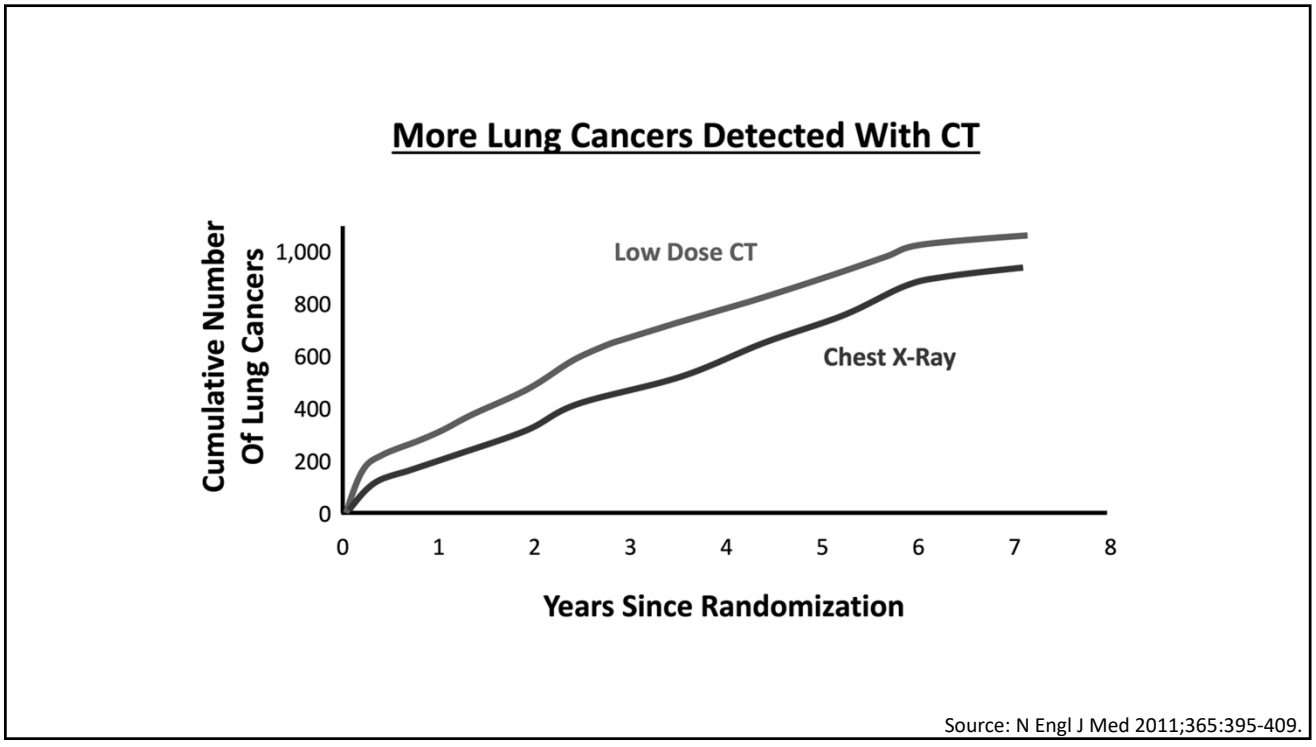
48

Source: N Engl J Med 2011;365:395-409.

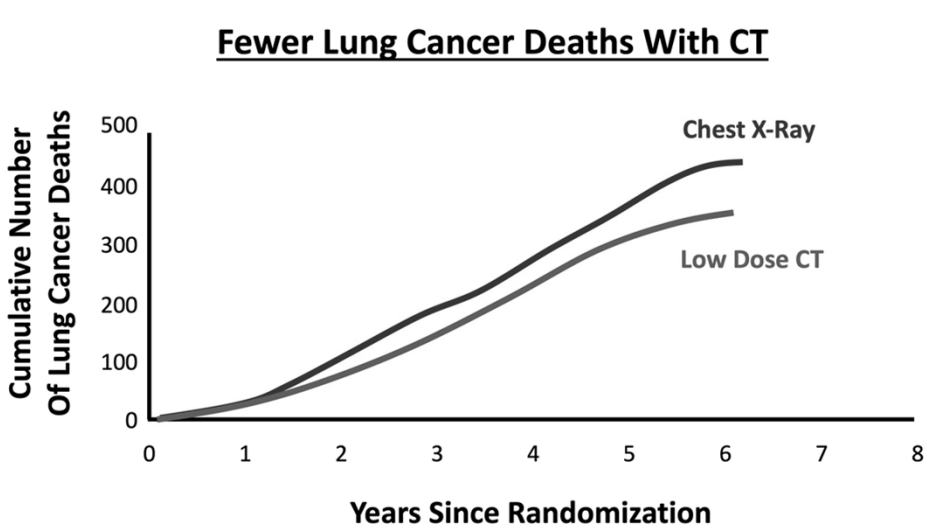
Table 5. Stage and Histologic Type of Lung Cancers in the Two Screening Groups, According to the Result of Screening.*

Stage and Histologic Type	Low-Dose CT				Chest Radiography			
	Positive Screening Test (N=649)	Negative Screening Test (N=44)†	No Screening Test (N=367)‡	Total (N=1060)	Positive Screening Test (N=279)	Negative Screening Test (N=137)†	No Screening Test (N=525)‡	Total (N=941)
				number/total number (percent)		*no. (% of screened)*		
Stage								
IA	329/635 (51.8)	5/44 (11.4)	82/361 (22.7)	416/1040 (40.0)	90/275 (32.7)	16/135 (11.9)	90/519 (17.3)	196/929 (21.1)
IB	71/635 (11.2)	2/44 (4.5)	31/361 (8.6)	104/1040 (10.0)	41/275 (14.9)	6/135 (4.4)	46/519 (8.9)	93/929 (10.0)
IIA	26/635 (4.1)	2/44 (4.5)	7/361 (1.9)	35/1040 (3.4)	14/275 (5.1)	2/135 (1.5)	16/519 (3.1)	32/929 (3.4)
IIB	20/635 (3.1)	3/44 (6.8)	15/361 (4.2)	38/1040 (3.7)	11/275 (4.0)	6/135 (4.4)	25/519 (4.8)	42/929 (4.5)
IIIA	59/635 (9.3)	3/44 (6.8)	37/361 (10.2)	99/1040 (9.5)	35/275 (12.7)	21/135 (15.6)	53/519 (10.2)	109/929 (11.7)
IIIB	49/635 (7.7)	15/44 (34.1)	58/361 (16.1)	122/1040 (11.7)	27/275 (9.8)	24/135 (17.8)	71/519 (13.7)	122/929 (13.1)
IV	81/635 (12.8)	14/44 (31.8)	131/361 (36.3)	226/1040 (21.7)	57/275 (20.7)	60/135 (44.4)	218/519 (42.0)	335/929 (36.1)

Source: N Engl J Med 2011;365:395-409.



Source: N Engl J Med 2011;365:395-409.



Relative reduction in the rate of death from lung cancer with low-dose CT screening of 20%!!!

Number needed to screen with LDCT to prevent one death from lung cancer was 320

Source: N Engl J Med 2011;365:395-409.

Lung Cancer Screening

Intermittent CT screening (baseline, 1 year, 3 years, 5.5 years) vs NO screening

The NEW ENGLAND JOURNAL of MEDICINE
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Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial

H.J. de Koning, C.M. van der Aalst, P.A. de Jong, E.T. Scholten, K. Nackaerts, M.A. Heuvelmans, J.-W.J. Lammers, C. Weenink, U. Yousaf-Khan, N. Horeweg, S. van 't Westeinde, M. Prokop, W.P. Mali, F.A.A. Mohamed Hoesein, P.M.A. van Ooijen, J.G.J.V. Aerts, M.A. den Bakker, E. Thunnissen, J. Verschakelen, R. Vliegenthart, J.E. Walter, K. ten Haaf, H.J.M. Groen, and M. Oudkerk

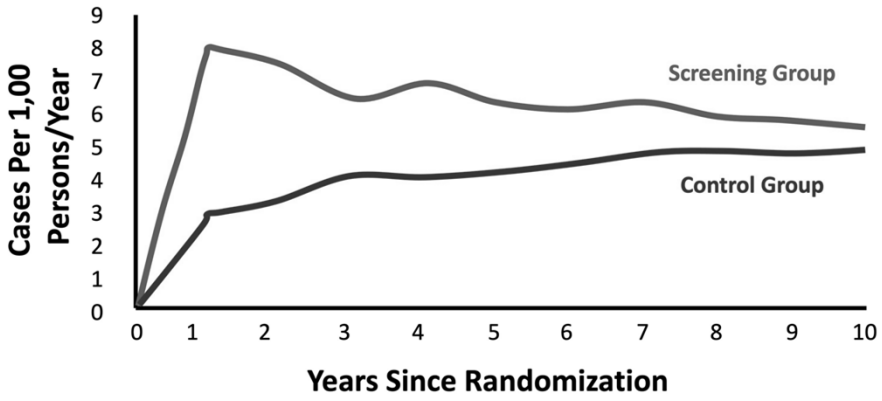
52

Table 3. Lung-Cancer Stage and Histologic Type of All First-Detected Lung Cancers in Male Participants at 10 Years of Follow-up or on December 31, 2015.*

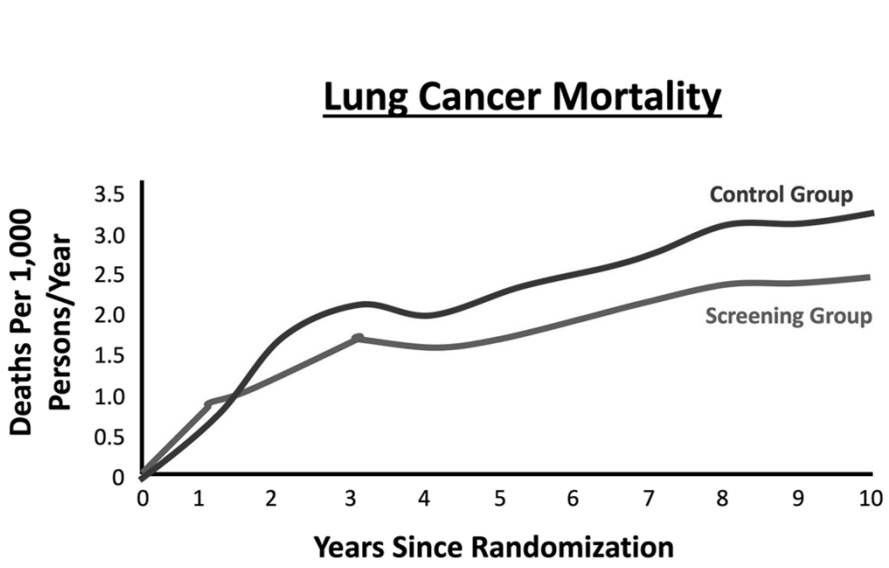
Variable	Screening Group				Control Group
	Screening-Detected Lung Cancer (N=203)†	Non–Screening-Detected Lung Cancer (N=141)	Any Lung Cancer (N=344)		Any Lung Cancer (N=304)
	number of participants (percent)				
Stage					
IA	95 (46.8)	10 (7.1)	105 (30.5)		21 (6.9)
IB	24 (11.8)	10 (7.1)	34 (9.9)		20 (6.6)
IIA	8 (3.9)	4 (2.8)	12 (3.5)		13 (4.3)
IIB	11 (5.4)	6 (4.3)	17 (4.9)		17 (5.6)
IIIA	20 (9.9)	14 (9.9)	34 (9.9)		43 (14.1)
IIIB	13 (6.4)	14 (9.9)	27 (7.8)		34 (11.2)
IV	19 (9.4)	73 (51.8)	92 (26.7)		139 (45.7)

53

Source: N Engl J Med 2020;382:503-13



Source: N Engl J Med 2020;382:503-13



Death rate (from lung cancer):

CT group: 2.50 deaths per 1000 person-years

Control group: 3.30 deaths per 1000 person-years
(p = 0.01)

Potential 26% relative risk reduction in males and up to 61% in females!

Source: N Engl J Med 2020;382:503-13

Cost to Patient?

Out of pocket cost for annual LCS? → $400-600
Cost of pack per day smoking over a year? → $2300

- Medicare Part B covers an annual lung cancer screening and LDCT scan (at 100%) if all of the following apply:
  - Age 55 to 77 years
  - Currently smoke or quit within the past 15 years
  - 30 pack year smoking history
  - No signs/symptoms of lung cancer
  - Receive the screening/LDCT at a Medicare-approved radiology facility
- Before the 1st screening, patient MUST have a shared decision-making conversation with ordering physician (risks/benefits)
  - Ordering physician will also provide counseling on smoking risks/smoking cessation services (when appropriate)

56

Cost Effectiveness of Lung Cancer Screening

- Milliman actuarial studies from 2010-14:
  - In terms of cost per life-year saved:
    - Colonoscopy → $12,000-$26,000
    - Mammography → $31,000-$51,000
    - Pap smears → $50,000-$75,000
    - LDCT for lung cancer screening → $12,000-$26,000
      - well below the $100,000 threshold experts consider to be a reasonable value

57

Is the False Positive Rate too High?

- Majority of 'false positives' on screening CT scans do NOT result in an invasive procedure
  - For example:
    - A 4 mm nodule found on initial LCS would be considered a false positive if stable/resolved on repeat imaging at the 12 month interval
- False positive rate likely greatly exaggerated…

58

Table 1. Summary of Lung-RADS Classification*

Lung-RADS Category	Baseline Screening	Subsequent Screening
1	No nodules; nodules with calcification	No nodules; nodules with calcification
2	Solid/part solid: <6 mm GGN: <20 mm –	Solid/part solid: <6 mm GGN: <20 mm or unchanged/slowly growing Category 3-4 nodules unchanged at ≥3 mo
3	Solid: ≥6 to <8 mm Part solid: ≥6 mm with solid component <6 mm GGN: ≥20 mm	Solid: New ≥4 to <6 mm Part solid: New <6 mm GGN: New ≥20 mm
4A	Solid: ≥8 to <15 mm Part solid: ≥8 mm with solid component ≥6 and <8 mm	Solid: Growing <8 mm or new ≥6 and <8 mm Part solid: ≥6 mm with new or growing solid component <4 mm
4B	Solid: ≥15 mm Part solid: Solid component ≥8 mm	Solid: New or growing and ≥8 mm Part solid: ≥6 mm with new or growing solid component ≥4 mm
4X	Category 3 or 4 nodules with additional features: imaging findings	Category 3 or 4 nodules with additional features: imaging findings

Table 4. Sensitivity, Specificity, PPV, and NPV in the Lung-RADS and Original NLST Readings: Baseline and After Baseline*

Variable	Lung-RADS at Baseline		NLST at Baseline	
	Percentage (95% CI)	*n/N*	Percentage (95% CI)	*n/N*
Sensitivity	84.90 (80.80-89.00)	248/292	93.50 (90.70-96.30)	273/292
False-positive result rate†	12.80 (12.40-13.20)	3343/26 090	26.60 (26.10-27.10)	6939/26 090
PPV	6.90 (6.10-7.70)	248/3591	3.80 (3.30-4.20)	273/7236
NPV	99.81 (99.75-99.86)	22 747/22 791	99.90 (99.86-99.94)	19 200/19 219

NLST = National Lung Screening Trial; NPV = negative predictive value; PPV = positive predictive value.
* Totals of 22 screening results at baseline and 28 after baseline with cancer absent were positive in Lung-RADS and had nodule characteristics meeting the positive screening criteria but were nonetheless reported as negative screening results in the NLST. Otherwise, all screening results that were positive according to the Lung-RADS criteria were also positive according to the NLST criteria.
† 1 minus the specificity rate.

59

Radiation Over-Exposure?

Table 1. Comparison of mean effective radiation dose

Chest X-ray:	0.1 mSv
Low dose chest CT:	1.5 mSv (1.0 mSv at Holy Name)
Routine chest CT:	7.0 mSv (5.0 mSv at Holy Name)
Mammography:	0.4 mSv
Natural Background Radiation:	3.0 mSv/year (1.5 mSv/year more in Colorado)
Transcontinental Flight:	0.03 mSv

60

Lung Cancer Screening Uptake in the U.S.

- 'Lung Cancer Screening with Low-Dose Computed Tomography in the United States – 2010 to 2015' (*JAMA Oncology, 2017*)
  - According to 2010 National Health Interview Survey (NHIS), only 2-4% of high-risk smokers received LDCT for cancer screening in the previous year
  - This study examined whether the 2013 USPSTF recommendation for screening had made a meaningful difference

61

Table 1. Prevalence of LDCT Testing for Lung Cancer in the Past Year Among Screening-Eligible and Noneligible Smokers: National Health Interview Survey, 2010 and 2015[a]

Characteristic	Total		2010		2015		P Value[c]
	No. (%)	(95% CI)	No. (%)	(95% CI)	No. (%)	(95% CI)	
Screening-eligible smokers (n = 2167)							
Weighted No. receiving LDCT[d]			276 700		262 700		
Weighted No. eligible for LDCT			8 456 800		6 819 500		
Total	2167 (3.5)	(2.6-4.8)	1036 (3.3)	(2.3-4.7)	1131 (3.9)	(2.4-6.2)	.60
Smoking history							
Former, ≥30 PY, quit ≤15 years ago	1020 (4.2)	(2.7-6.5)	491 (4.0)	(2.6-6.1)	529 (4.6)[e]	(2.1-9.4)[e]	.76
Current, ≥30 PY	1147 (2.9)	(1.8-4.5)	545 (2.6)[e]	(1.4-4.9)[e]	602 (3.2)	(1.8-5.6)	.64
Age, y							
55-64	1119 (2.3)	(1.5-3.6)	554 (2.8)[e]	(1.6-5.1)[e]	565 (1.7)	(1.0-3.1)	
65-80	1048 (5.0)	(3.3-7.6)	482 (3.8)	(2.4-6.0)	566 (6.6)[e]	(3.6-11.9)[e]	
Sex							
Male	1245 (3.8)	(2.6-5.4)	597 (3.8)	(2.5-5.9)	648 (3.8)	(2.2-6.3)	
Female	922 (3.2)[e]	(1.7-5.7)[e]	439 (2.5)[e]	(1.2-5.0)[e]	483 (4.0)[e]	(1.6-9.5)[e]	
BMI							
<25	688 (5.6)	(3.4-9.3)	320 (4.4)[e]	(2.4-8.0)[e]	368 (7.2)[e]	(3.3-14.7)[e]	
≥25	1400 (2.6)	(1.8-3.7)	673 (2.7)	(1.7-4.3)	727 (2.5)	(1.5-4.2)	
Usual place for medical care							
Yes	1965 (3.9)	(2.9-5.3)	934 (3.6)	(2.5-5.2)	1031 (4.3)	(2.6-6.9)	.60
No	202 (0.2)[e]	(0.0-1.2)[e]	102[e,f]		100 (0.4)[e]	(0.1-2.6)[e]	[f]
Visited PCP in past year							
Yes	1726 (4.3)	(3.1-5.9)	813 (4.1)	(2.9-5.9)	913 (4.5)	(2.7-7.4)	.78
No	440 (0.6)	(0.2-1.8)	223[f]		217 (1.4)	(0.5-4.1)	[f]
Insurance type							
Uninsured or Medicaid	1230 (4.2)	(2.8-6.3)	586 (3.2)	(2.0-5.1)	644 (5.5)[e]	(3.0-9.9)[e]	.20
Medicare, private, or other	937 (2.8)	(1.7-4.4)	450 (3.4)	(1.9-6.1)	487 (2.0)[e]	(1.1-3.6)[e]	.20
Race[g]							
White	1787 (3.5)	(2.5-5.0)	833 (3.1)	(2.0-4.6)	954 (4.1)	(2.4-6.9)	.39
Nonwhite	380 (3.5)	(2.0-6.2)	203 (4.7)[e]	(2.3-9.5)[e]	177 (2.1)[e]	(1.0-4.6)[e]	.18
Education level							
<High school or high school graduate	1216 (3.4)	(2.4-4.9)	613 (2.6)	(1.6-4.1)	603 (4.6)	(2.9-7.3)	.08
Some college or college graduate	946 (3.7)	(2.2-6.2)	420 (4.3)	(2.5-7.3)	526 (3.0)[e]	(1.1-8.3)[e]	.51

Pre-guidelines screening rates? 3.3%

Post-guidelines screening rates? 3.9%

62

Table 1. Prevalence of LDCT Testing for Lung Cancer in the Past Year Among Screening-Eligible and Noneligible Smokers, National Health Interview Surveys 2010 and 2015[a,b] (continued)

Characteristic	Total No. (%)	Total (95% CI)	2010 No. (%)	2010 (95% CI)	2015 No. (%)	2015 (95% CI)	P Value[c]
Income, $							
<35 000	1130 (3.9)	(2.8-5.3)	543 (3.9)	(2.5-6.1)	587 (3.8)	(2.3-6.2)	.97
≥35 000	926 (3.3)	(2.0-5.4)	446 (2.8)	(1.5-5.0)	480 (3.9)[e]	(1.8-8.1)[e]	.51
Family history of lung cancer							
Yes	362 (4.5)[e]	(2.4-8.2)[e]	161 (4.8)[e]	(2.0-10.8)[e]	201 (4.1)[e]	(2.1-8.0)[e]	.75
No	1709 (3.3)	(2.3-4.8)	812 (2.8)	(1.9-4.4)	897 (3.9)	(2.1-6.9)	
Attempted to quit smoking in the past 12 months[h]							
Yes	363 (4.1)[e]	(2.1-8.0)[e]	164 (3.3)[e]	(1.2-8.8)[e]	199 (5.1)[e]	(2.1-12.3)[e]	
No	784 (2.3)	(1.3-3.9)	381 (2.3)[e]	(1.0-5.2)[e]	403 (2.2)[e]	(1.1-4.3)[e]	
Ever diagnosed with emphysema							
Yes	321 (8.9)	(5.8-13.4)	169 (9.6)	(5.8-15.5)	152 (7.9)[e]	(3.8-15.8)[e]	
No	1844 (2.6)	(1.7-3.9)	866 (2.0)	(1.2-3.4)	978 (3.2)[e]	(1.7-5.9)[e]	
Ever diagnosed with bronchitis							
Yes	272 (11.2)	(6.4-18.8)	135 (11.5)	(6.5-19.7)	137 (10.7)[e]	(3.6-27.7)[e]	
No	1895 (2.4)	(1.7-3.5)	901 (2.1)	(1.3-3.3)	994 (2.9)	(1.8-4.6)	
Ever diagnosed with asthma							
Yes	327 (6.2)	(3.7-10.1)	184 (8.0)	(4.4-14.0)	143 (3.2)[e]	(1.3-7.3)[e]	.08
No	1838 (3.1)	(2.1-4.5)	851 (2.3)	(1.5-3.7)	987 (4.0)	(2.3-6.7)	.16
Noneligible smokers (n = 6632)[i]							
Total	6632 (2.4)	(1.9-2.9)	2632 (2.0)	(1.5-2.9)	3989 (2.7)	(2.1-3.6)	.12
Former, <30 PY, quit ≤15 years ago	932 (2.3)	(1.3-4.1)	378 (3.1)	(1.5-6.3)	554 (1.7)	(0.7-4.4)	.36
Former, ≥30 PY, quit >15 years ago	740 (4.0)	(2.5-6.2)	339 (2.5)	(1.1-5.4)	401 (5.8)	(2.9-11.3)	.17
Former, <30 PY, quit ≥15 years ago	3334 (1.6)	(1.2-2.3)	1255 (1.5)	(0.9-2.5)	2079 (1.7)	(1.2-2.6)	.68
Current, <30 PY	1626 (3.3)	(2.3-4.6)	671 (2.0)	(1.2-3.5)	955 (4.4)	(2.8-6.6)	.04

Screening rate for ELIGIBLE patients in 2015? 3.9%

Screening rate for INELIGIBLE patients in 2015? 2.7%!

63

LDCT screens performed in 2016 compared to eligible smokers per USPSTF criteria.

U.S. Census Region	No. of Accredited Centers	Estimated Eligible Smokers	LDCT Screens	Rate (%)
Northeast	404	1,152,141	40,105	3.5
Midwest	497	2,020,045	38,931	1.9
South	663	3,072,095	47,966	1.6
West	232	1,368,694	14,080	1.0
Total	**1796**	**7,612,975**	**141,260**	**1.9**

64

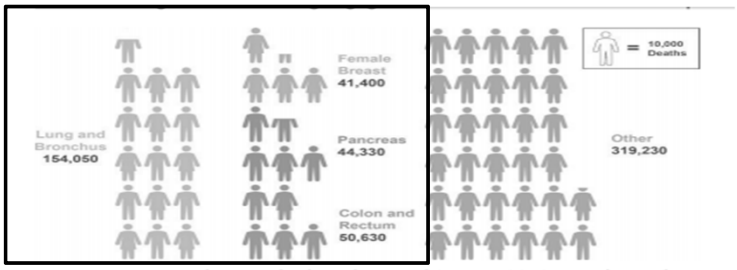


Figure 1: Estimated cancer deaths in the United States in 2018 according to the Surveillance, Epidemiology, and End Results Program (1).

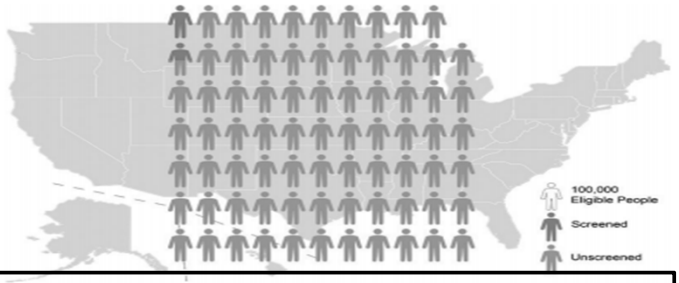


Figure 2: Lung cancer screening rate in the United States in 2016. A 2018 analysis reported that of an estimated 7.6 million eligible smokers, 141 260 underwent screening in 2016 (7).

65

Why Is Uptake So Poor?

- 'Knowledge of, Attitudes Toward, and Use of Low-Dose Computed Tomography for Lung Cancer Screening Among Physicians' (*Cancer, Aug 2016*)

66

TABLE 1. Family Physicians' Knowledg and Practice Patterns Regarding Low-puted Tomography Screening

Knowledge	
Is a CT machine available within a 20-min radius of pr	
Yes	
No	
Not sure	
Does this CT machine offer low-dose CT screening for	
Yes	
No	
Not sure	
How often sho	
Every 6 mo	
Every year	
Every 2 y	
Every 3 y	
Does Medicar	
Yes	
No	
Not sure	

Attitudes	No. (%)
I have the time needed to stay abreast of current cancer screening guidelines.	
Agree	44 (59)
Disagree	31 (41)
Perceived benefits of LDCT screening (check all that apply)	
It reduces lung cancer mortality.	33 (41)
It increases the chances of finding lung cancer at an earlier stage.	79 (98)
Perceived risks of LDCT screening (check all that apply)	
Positive screening rarely results in a lung cancer diagnosis.	20 (24)
Psychological stress or anxiety for the patient	44 (52)
It may lead to unnecessary diagnostic procedures.	74 (88)
Exposure to radiation increases cancer risk.	42 (50)

Practice patterns	
Which best describes your practice st	
I recommend screening to patients of risks and benefits.	
I discuss risks and benefits and the screening.	
I discuss risks and benefits and then let the patient decide whether to be screened.	41 (51)
I discuss risks and benefits and then recommend against screening.	3 (4)
I do not discuss risks and benefits or recommend screening.	16 (20)
I recommend against screening.	3 (4)
How often do you discuss the risks and benefits of LDCT screening with patients at high risk for lung cancer?	
Always	4 (5)
Frequently	10 (13)
Sometimes	19 (24)
Infrequently	25 (31)
Never	22 (28)
Did any of your patients ask if they could/should be screened in the past year?	
Yes	44 (52)
No	41 (48)

Practice patterns	No. (%)
What is the number of patients who asked if they could/should be screened in the last 12 mo?	
1	5 (12)
2–4	8 (19)
5–10	18 (43)
>10	6 (14)
Other[c]	3 (7)
What is the number of patients who were referred for LDCT screening in the last 12 mo?	
0	41 (47)
1	10 (11)
2–4	14 (16)
5–10	13 (15)
>10	8 (9)
If a patient recommended for LDCT screening initially declines, I still encourage him/her to get screened.	
Agree	29 (37)
Disagree	50 (63)

67

Guidelines for lung cancer screening

Organization	Recommendation	Year
American Academy of Family Physicians	Concludes that evidence is insufficient to recommend for or against low-dose CT scan screening in persons at high risk for lung cancer based on age and smoking history.	2013
American Association of Thoracic Surgery	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 79 years with 30 pack-year history of smoking and current smoker or quit within past 15 years) or age 50 with cumulative risk >5% over next five years.	2012

Population	Recommendation	Grade
Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

	with a 20 pack-year history of smoking with one additional risk factor.	
US Preventive Services Task Force	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 80 years with a 30 pack-year history of smoking and current smoker or quit within past 15 years). Discontinue when person has not smoked for 15 years or if limited life expectancy.	2013

CT: computed tomography.

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Barriers to LCS

- Patients:
  - Unawareness of screening programs
  - Fear of cancer diagnosis
  - Cost concerns
  - Access to screening/imaging sites
- Physicians/providers:
  - Unfamiliarity with screening guidelines/insurance coverage
  - Insufficient time/knowledge to conduct shared-decision making
  - Lack of guidance for managing lung cancer screening results
  - Skepticism about benefits of screening
  - Concerns over 'false positive' rates

69

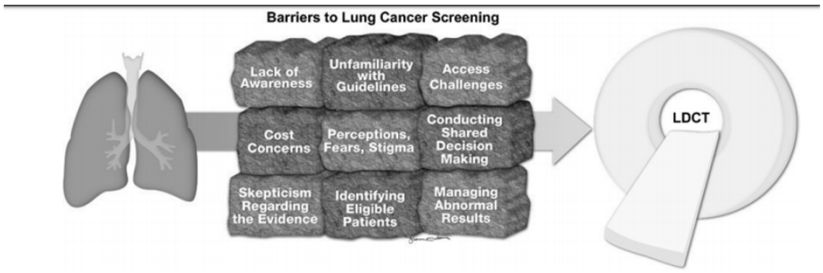

Figure 3: Barriers to lung cancer screening encountered by patients and referring providers. LDCT = low-dose CT.

70

How to Improve Screening Uptake?

Evidence-based Interventions Recommended by the Community Preventive Services Task Force for Breast, Cervical, and Colorectal Cancer

Intervention	Description*
Patient-oriented interventions	
One-on-one education	Telephone or in-person education to discuss indications for, benefits of, and ways to overcome barriers to screening
Client reminders	Text or telephone reminders that screening is due or overdue
Small media	Videos, printed materials (eg, brochures, pamphlets, newsletters), possibly tailored to specific people based on individual assessment
Increasing provider delivery	
Provider assessment and feedback	Evaluate and inform provider regarding performance in offering and/or delivering screening
Provider reminder and recall systems	Inform provider that patients are due or overdue for a cancer screening test

* Descriptions of interventions are summarized from references 65 and 90–92.

71

Summary/Key Points

- Early detection is great, but PREVENTION will always be better! (ie smoking cessation)
- New USPSTF guidelines are a great step in the right direction to expand the screening pool, but we need insurance companies to buy in!
- Remember, lung cancer screening is ANNUAL (and basically life-long until patient no longer meets criteria), not a ‘one and done’ venture
- Be persistent! Empower your patients!

72

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73