

Incidental Pulmonary Nodules

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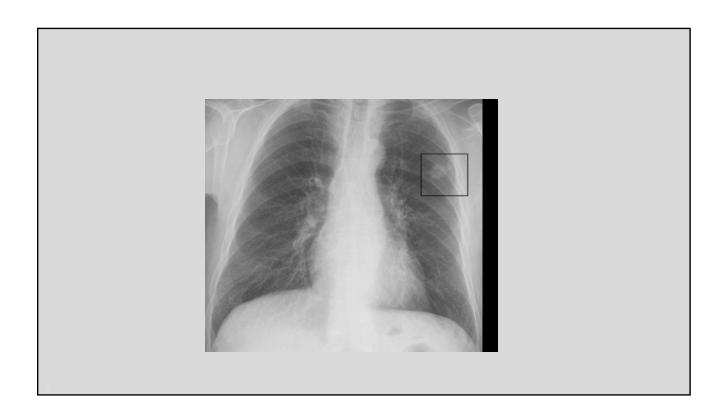
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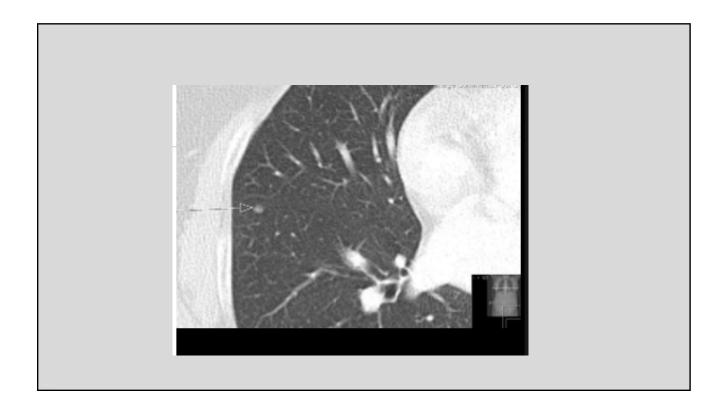
MedNet21
Center for Continuing Medical Education

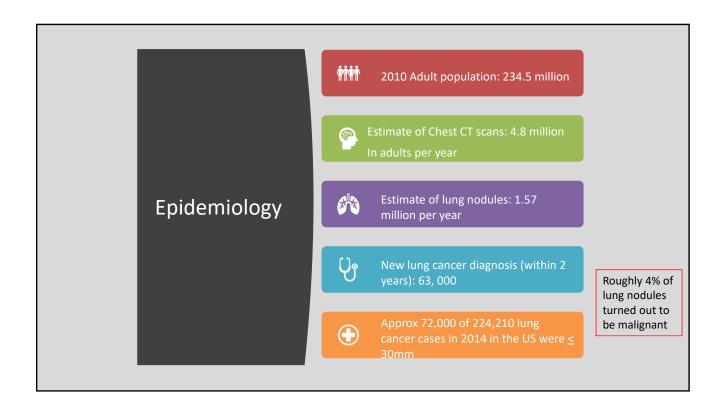


What is a (Solitary) Pulmonary Nodule?

- 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!

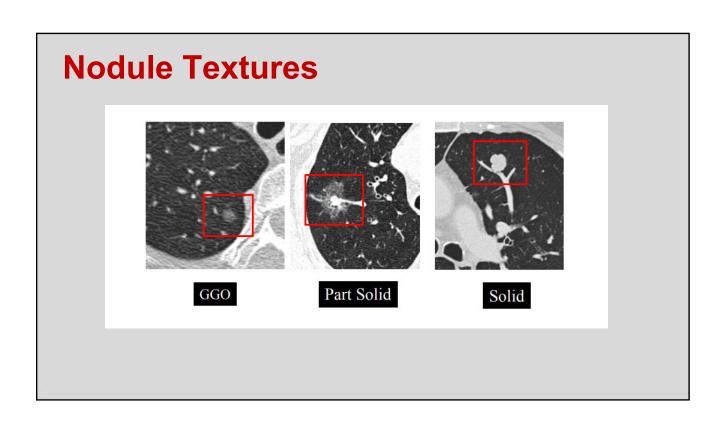


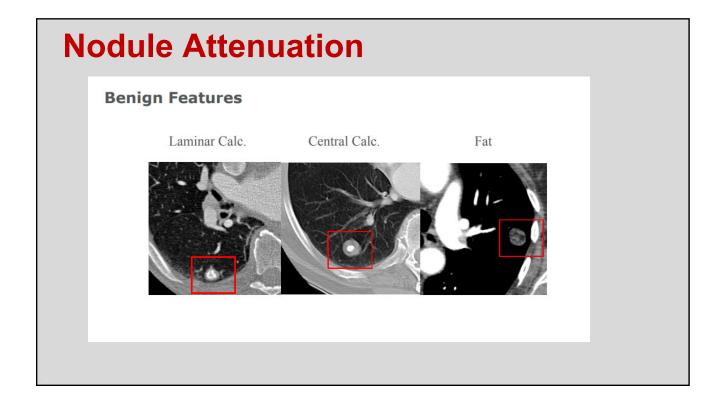




Etiology of Pulmonary Nodules

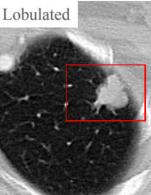
- Benign >>>> Malignant
 - Benign etiologies:
 - Fungal infection (acute, chronic, or remote)
 - Benign neoplasms (ie hamartoma)
 - Vascular pathology (pulmonary arteriovenous malformation)
 - Inflammatory nodules (sarcoidosis, rheumatoid arthritis, vasculitis)
 - 'Other' (intrapulmonary lymph node,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

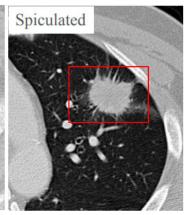




Nodule Margins







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

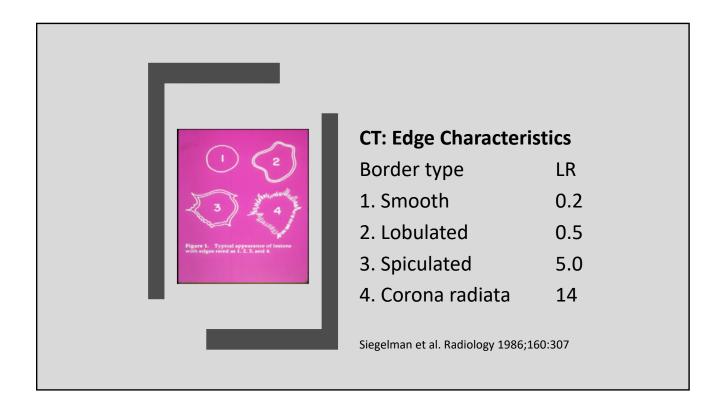
 <4 mm</td>
 0%

 4-7 mm
 0.8%

 8-20 mm
 22%

 >20 mm
 63%

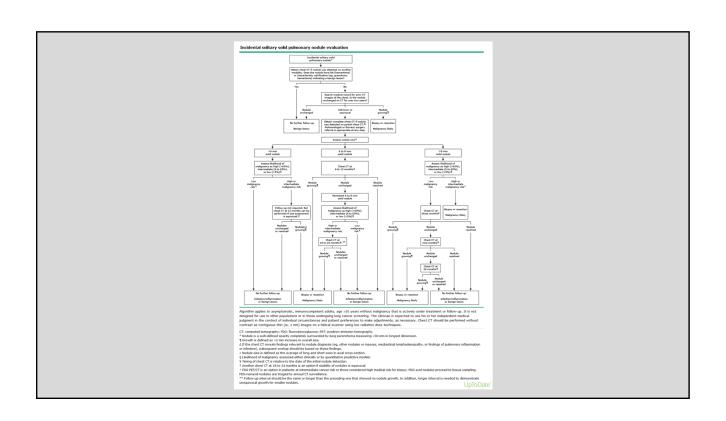
Swensen et al. AJRCCM 2002;165:508-13.

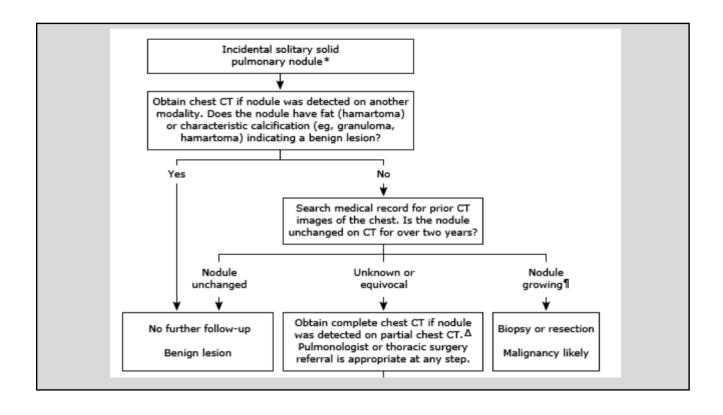


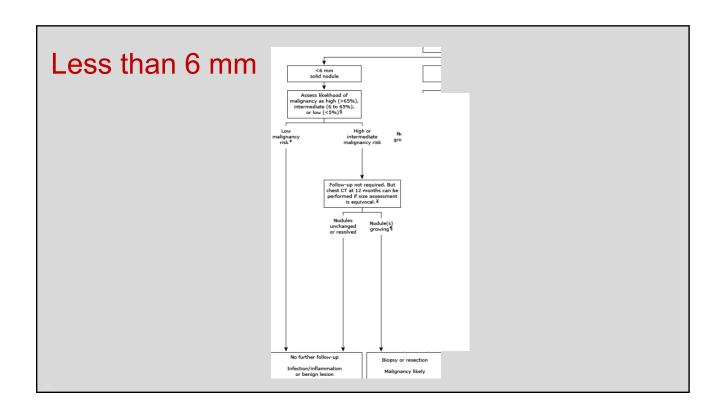
Risk prediction calculators

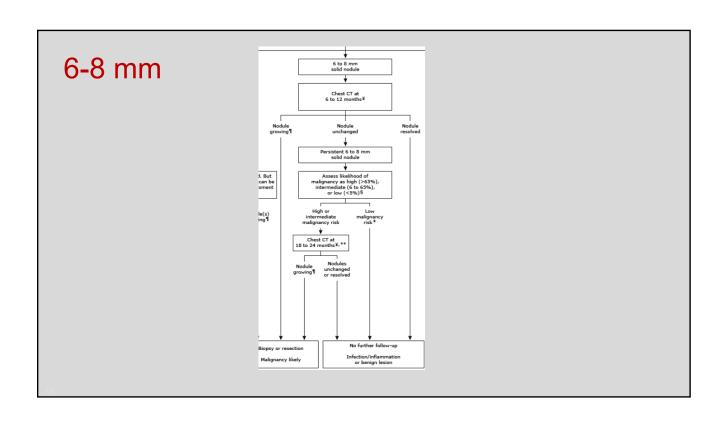
MayoIncidental nodules Single institution629 patients210 patients23%Useful for incidental nodulesBrockPan canadian multicenter screening trial1871 patients 7008 nodules1090 patients 5021 nodules5.5%Useful for screen detected nodulesHerderSingle institution Cohort referred for PET106None57%Additive to mayo	Model	Population	Number	Validation	Prevalence of malignancy	Comments
multicenter screening trial 7008 nodules 5021 nodules screen detected nodules Herder Single institution Cohort referred for 106 None 57% Additive to mayo	Mayo		629 patients	210 patients	23%	incidental
Cohort referred for mayo	Brock	multicenter			5.5%	screen detected
	Herder	Cohort referred for	106	None	57%	

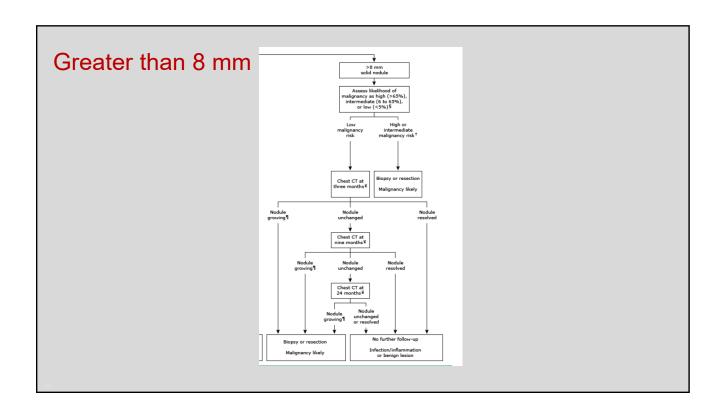
Solitary Pulmonary I Malignancy Risk Sco Predicts malignancy risk in solitary lung nodul INSTRUCTIONS Do not use in patients with prior lung cance cancer diagnosed within 5 years of nodule p	es on chest x-ray. diagnosis or with history of extrath	
When	to Use 🔨	
Patients with solitary lung nodule on che Do not use in patients with prior lung car cancer diagnosed within 5 years of nodul	cer diagnosis or with history of extr	athoracic
Age		year
Nodule diameter		mr
Current or former smoker	No 0 Ye	9s +1
Extrathoracic cancer diagnosis ≥5 years prior	No 0 Ye	9s +1
Upper lobe location of tumor	No 0 Ye	9s +1
Nodule spiculation	No 0 Ye	9s +1
FDG-PET Optional, if performed	PET not performed	
	No uptake Faint uptake	
	Moderate uptake	
	Intense uptake	











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					

Fleischner Criteria Exclusions?

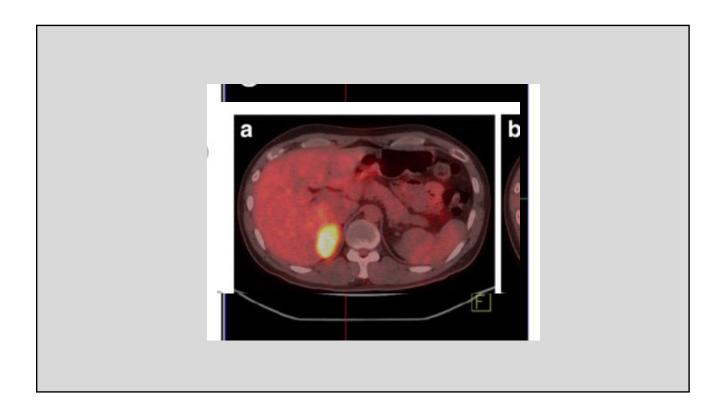
- Exclusions:
 - Patients with unexplained fever
 - Patients with known or suspected metastases
 - Patients <35 years of age</p>
 - Lung cancer screening (use LUNG-RADS)

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)

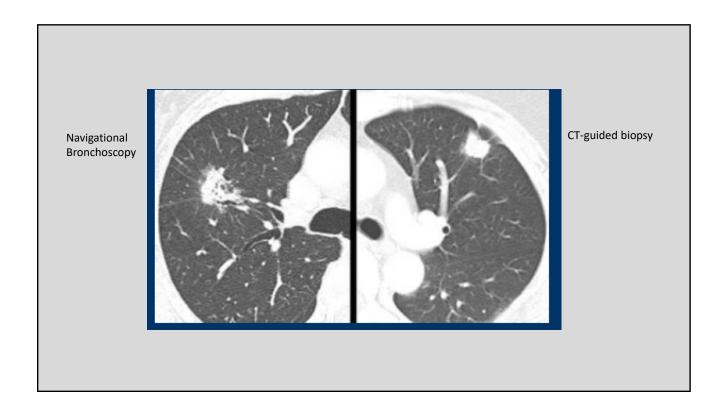


Management

- 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



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

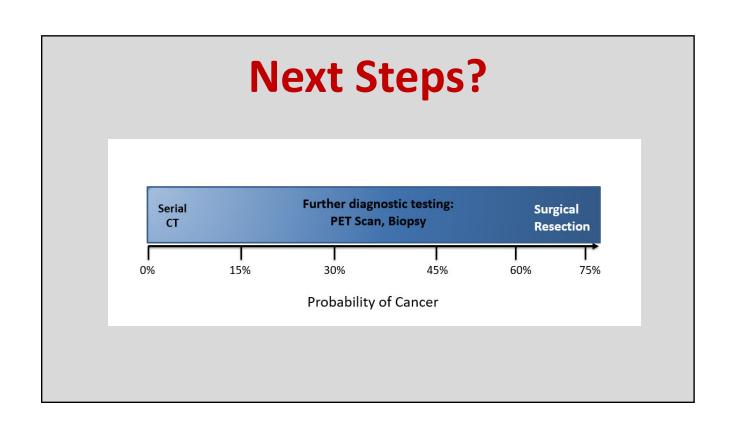


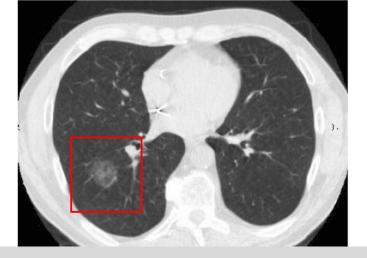
Figure 2. [Section 4.0] Factors that influence choice between evaluation and management alternatives for indeterminate, solid nodules ≥ 8 to 30 mm in diameter.

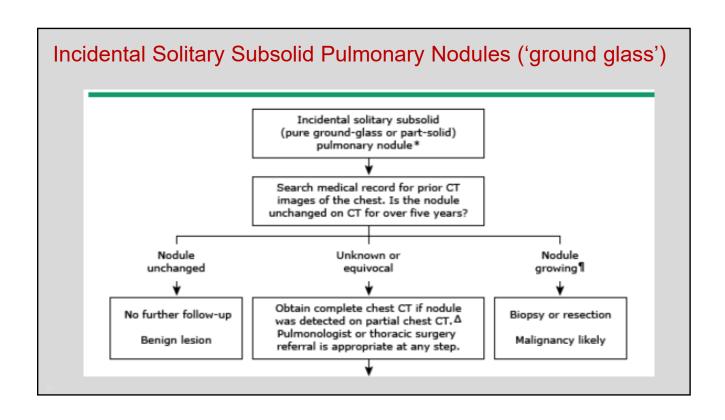
Factor	Level	CT Scan Surveillance	PET Imaging	Nonsurgical Biopsy	VATS Wedge Resection
Sun Tro de Districtorio	Very low (< 5%)	++++	_	-	-
Clinical probability of lung cancer	Low-moderate	+	+++	++	+
of lung cancer	High (< 65%)	-	(± staging)	++	++++
Samuel and the	Low	++	++	++	+++
Surgical risk	High	++	+++	++	
	Low	-5	++	+++	+++
Biopsy risk	High	++	+++	S#3	+
High suspicion of active	infection or inflammation	-	- 4	++++	++
	Desires certainty	-	+	+++	++++
Values and preferences	Risk averse to procedure- related complications	++++	+++	++	
Poor adherence with foll	ow-up	-	-	+++	++++

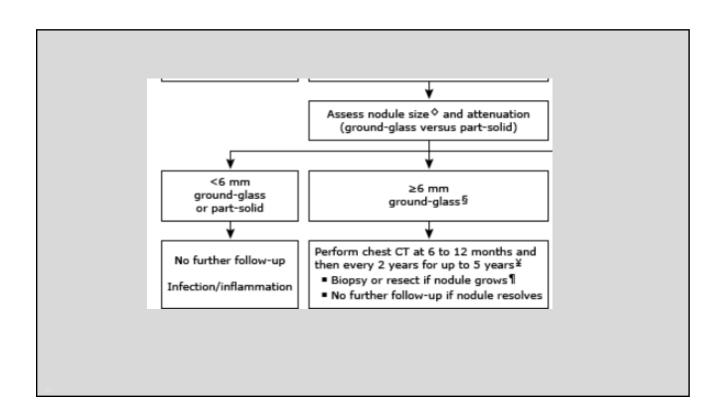
VATS = video-assisted thoracoscopic surgery.

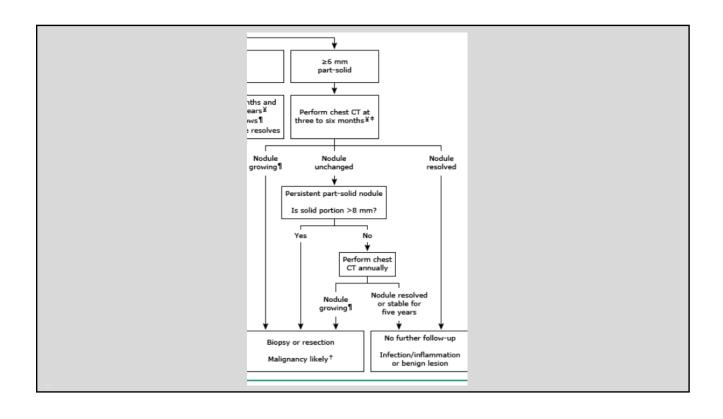
Gould M, CHEST 2013

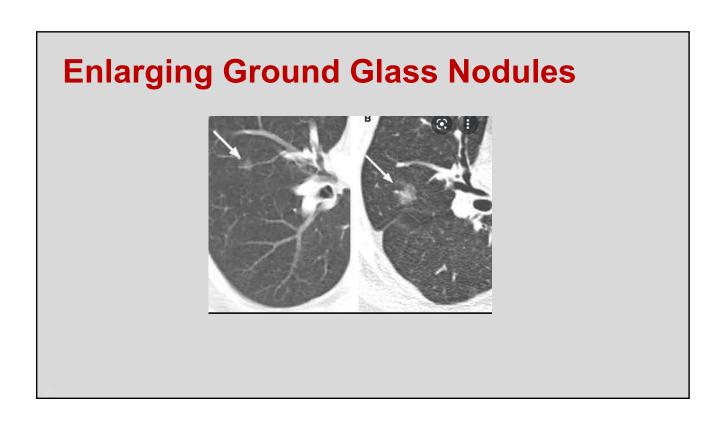
'Ground Glass' Nodules











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

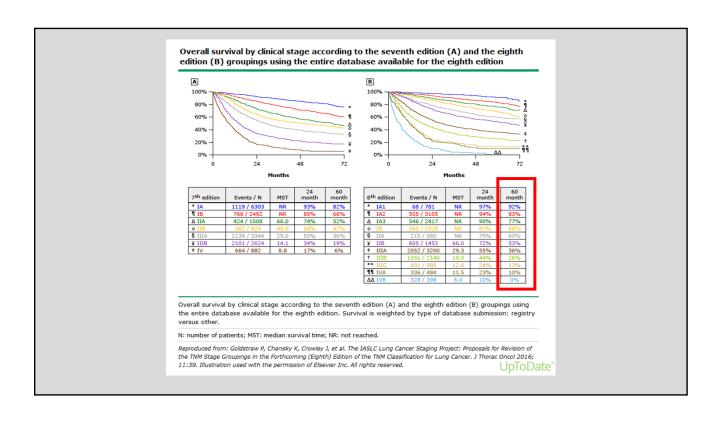
Take Home Points

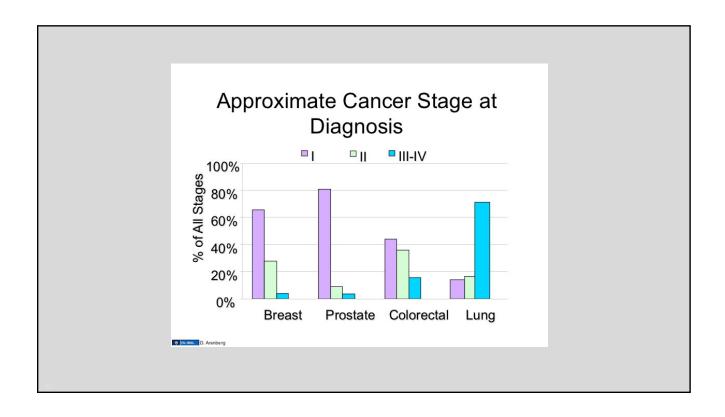
- Always be on the lookout for incidental pulmonary nodules
 - CT scans (both CT chest angiography as well as CT abdomen) in the ER
 - CT pulmonary venograms (often obtained in the management of atrial fibrillation)
- 1st step is ALWAYS to look for prior imaging
- Use caution if/when ordering PET scans (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

Lung Cancer Screening

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





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

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

The NEW ENGLAND
JOURNAL of MEDICINE

ESTABLISHED IN 18

AUGUST 4, 2011

VOL. 365 NO. 5

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

The National Lung Screening Trial Research Team*

- 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)

Table 2. Re	sults of Th	ree 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 Rate of po CT group: CXR grou		Positive Result ening:	Clinically Significant Abnormality Not Suspicious for Lung Cancer	No or Minor Abnormality
			no. (% of screened)	OXIT GIOU	p. 0.570		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)

^{*} 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-D	ose CT			Chest Ra	adiography	
	ТО	T1	T2	Total	ТО	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

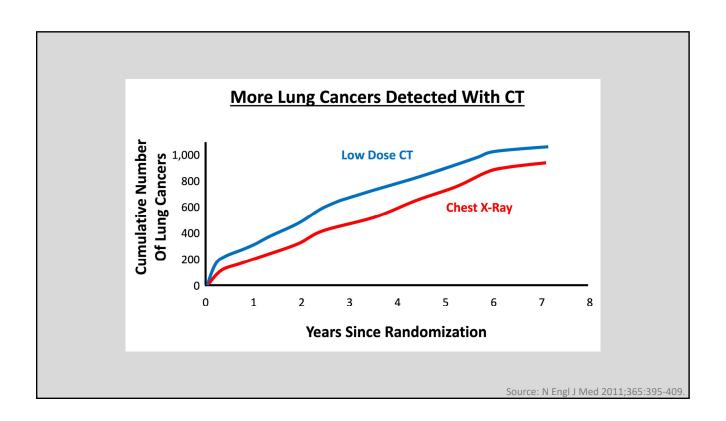
the Hostitive tests with incomplete information on diagnostic follow-up are included in this category (142 at T0, 161 at T1, and 141 at T2 in the low-dose CT group and 39 at T0, 26 at T1, and 25 at T2 in the radiography group).

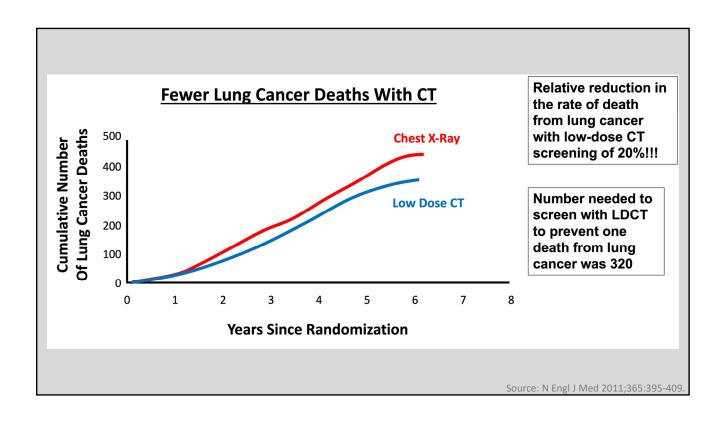
Source: N Engl J Med 2011:365:395-44

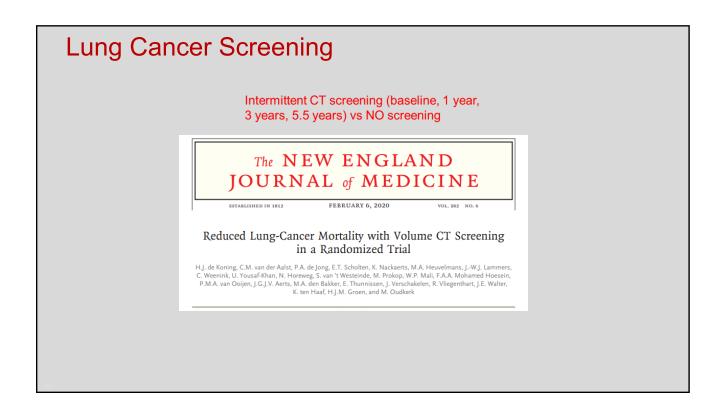
Source: N Engl J Med 2011;365:395-409.

		proce	edures!	vasive	
Complication		L	ung Cancer Confir	med	
	Thoracotomy, Thoracoscopy, or Mediastinoscopy	Bronchosc opy	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)
					ed 2011;365:395-40

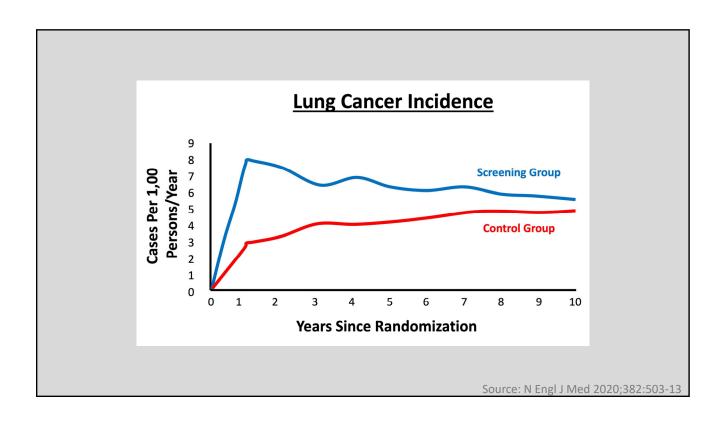
Table 5. Stag	ge and Histo	· ,.	Lung Cancers in	n the Two Scr	eening Group	s, According to the		creening.*
Histologic Type							-3	
	Positive Screenin g Test (N=649)	Negative Screening Test (N=44)†	No Screening Test (N=367)‡	Total (N=1060)	Positive Screening Test (N=279)	Negative Screening Test (N=137)†	No Screening Test (N=525)‡	Total (N=941)
				number/to	tal number cent)	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 201	1;365:395-409

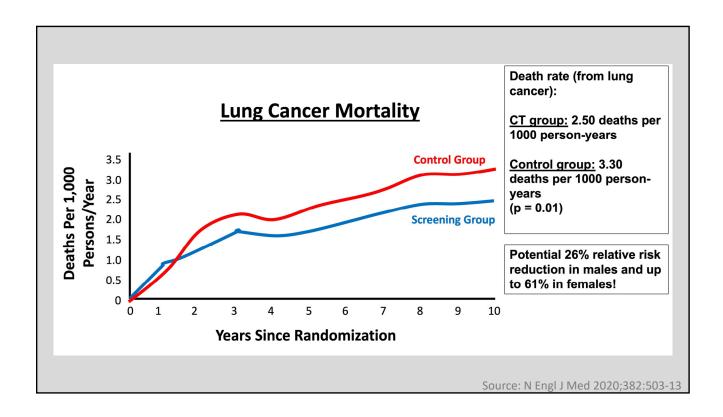






Variable		Screening Group		Control Group
	Screening- Detected Lung Cancer (N=203)†	Non–Screening-Detected Lung Cancer (N=141)	Any Lung Cancer (N=344)	Any Lung Cance (N=304)
		number of participa	ints (percent)	
Stage				
IA	95 (46.8)	10 (7.1)	105 (30.5)	21 (6.9)
IB	24 (11.8)	10 (7.1)	34 (9.9)	20 (6.6)
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)





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 decisionmaking conversation with ordering physician (risks/benefits)
 - Ordering physician will also provide counseling on smoking risks/smoking cessation services (when appropriate)

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 \rightarrow \$50,000-\$75,000
 - LDCT for lung cancer screening \rightarrow \$12,000-\$26,000
 - well below the \$100,000 threshold experts consider to be a reasonable value

Is the False Positive Rate too High?

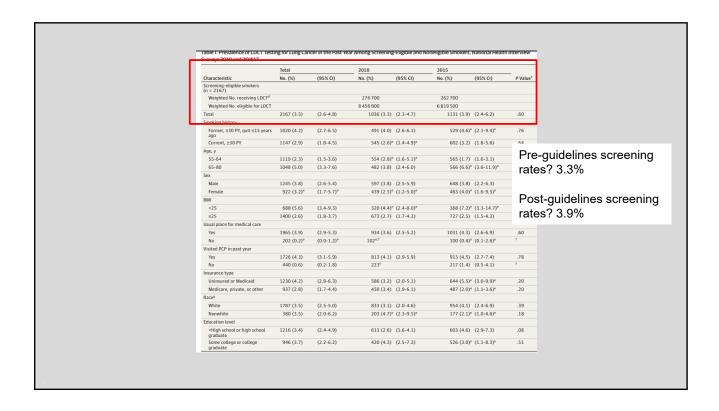
- Majority of 'false positives' on screening CT scans do NOT result in an invasive procedure
 - For example:
 - A 4 mm nodule found on initial LCS would be considered a false positive if stable/resolved on repeat imaging at the 12 month interval
- False positive rate likely greatly exaggerated...

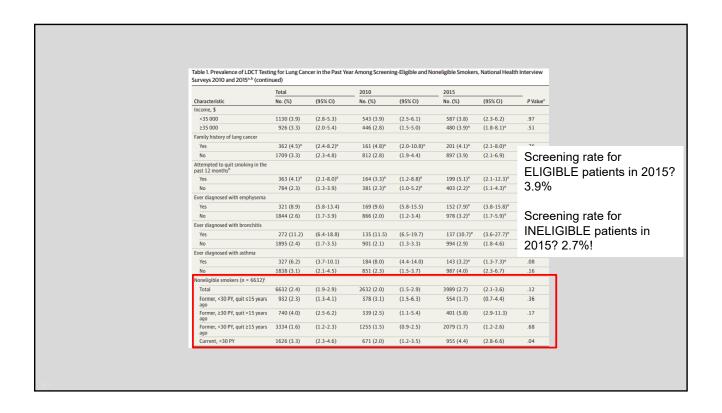
No nodules; no Solid/part solid GGN: <20 mm	odules with calcification		nodules; nodules with calcification	
	d: <6 mm			
			lid/part solid: <6 mm	
GGIV. VZG IIIIII			GN: <20 mm or unchanged/slowly gro stegory 3-4 nodules unchanged at ≥3 :	
Solid: ≥6 to <8	mm			110
Part solid: ≥6 r	nm with solid component <6 mm	Pa	rt solid: New <6 mm	
				olia component <4 mi
				olid component ≥4 mr
vity, Specific				2.0000 8.000 800
	1000 -000000000000000000000000000000000			
				n/N
t cotob				273/292 6939/26 090
t rate [6.90 (6.10-7.70)	248/3591	3.80 (3.30-4.20)	2/3//236
	99.81 (99.75-99.86)	22 747/22 791	99.90 (99.86-99.94)	19 200/19 219
	Part solid: ≥6 r GGN: ≥20 mm Solid: ≥8 to <1 Part solid: ≥8 to Solid: ≥15 mm Part solid: Solid: Catecony 3 or vity, Specific	GGN: ≥20 mm Part solid: ≥8 mm with solid component ≥6 and Solid: ≥15 mm Part solid: ≥8 mm with solid component ≥6 and Solid: ≥15 mm Category 3 or 4 needules with additional feature vity, Specificity, PPV, and NPV in the Lun Lung-RADS at Percentage (95% CI) 84 90 (80 80 -89 00) 1 72 80 (12.40 -13.20) 870 (8.10 -7.70) 978 21 (97.27 -97.8)	Solid: 26 to <8 mm	Solid: 26 to <8 mm

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

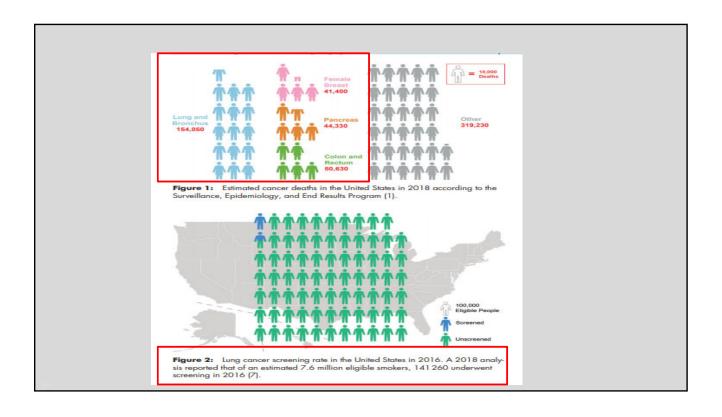
Lung Cancer Screening Uptake in the U.S.

- '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



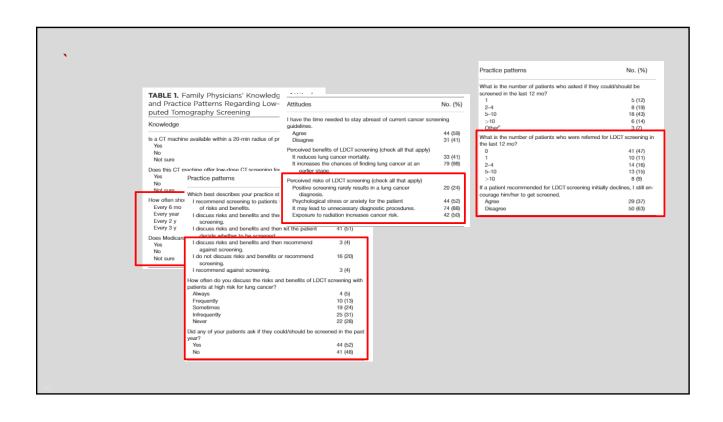


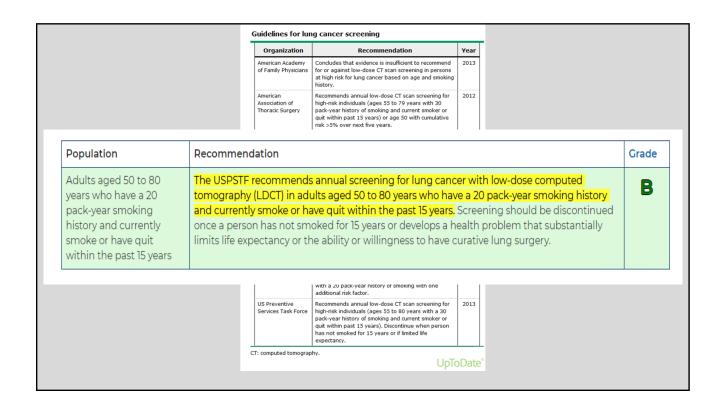
LDCT screens performed in 2016 compared to eligible smokers per USPSTF criteria. U.S. Census No. of Accredited **Estimated Eligible** LDCT Rate Smokers Region Centers Screens (%) Northeast 404 1,152,141 40,105 3.5 Midwest 2,020,045 38,931 1.9 497 South 663 3,072,095 47,966 1.6 West 14,080 232 1,368,694 1.0 7,612,975 Total 1796 141,260 1.9 © 2018 by American Society of Clinical Oncology



Why Is Uptake So Poor?

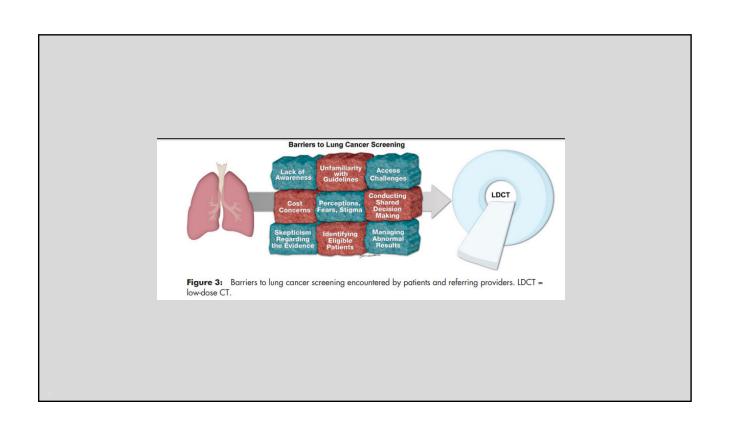
 'Knowledge of, Attitudes Toward, and Use of Low-Dose Computed Tomography for Lung Cancer Screening Among Physicians' (Cancer, Aug 2016)





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



How to Improve Screening Uptake?

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 or 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

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!

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