

## **Incidental Pulmonary Nodules**

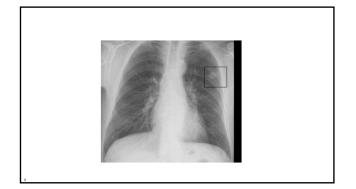
Michael Wert, MD
Assistant Professor - Clinical
Department of Internal Medicine
Division of Pulmonary, Critical Care, and Sleep Medicine
The Ohio State University Wexner Medical Center

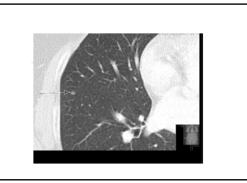
MedNet21

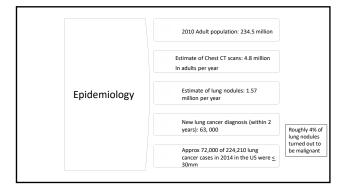


## What is a (Solitary) Pulmonary Nodule?

- 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!

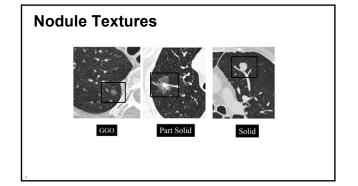


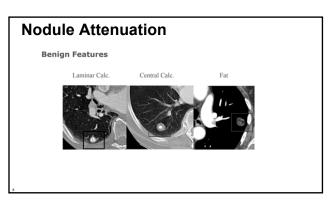


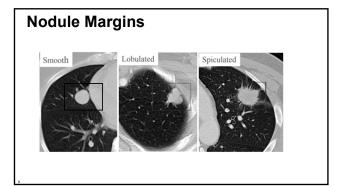


# **Etiology of Pulmonary Nodules**

- 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







Why is the Solitary Pulmonary nodule Important?

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

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

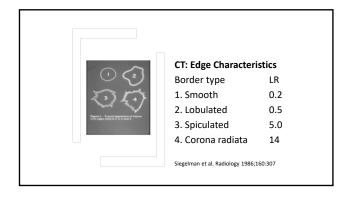
Borders

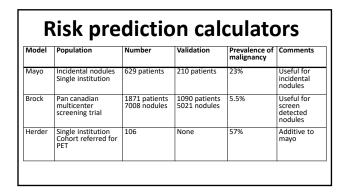
Location

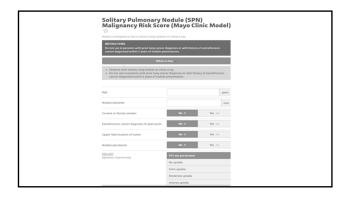
George Box: "All models are wrong but some are useful" Swensen et al. Arch Intern Med 1997;157:849

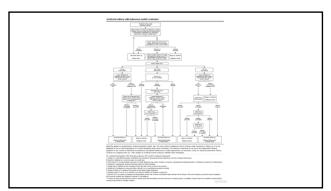
**CT Size** matters Size % malignant <4 mm 4-7 mm 0.8% 8-20 mm 22% >20 mm

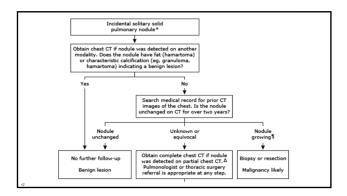
Swensen et al. AJRCCM 2002;165:508-13.

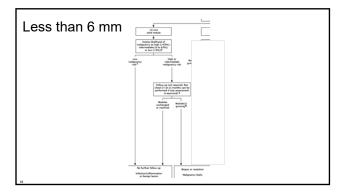


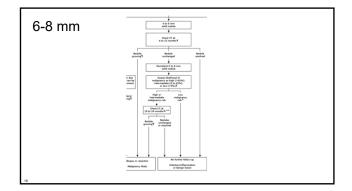


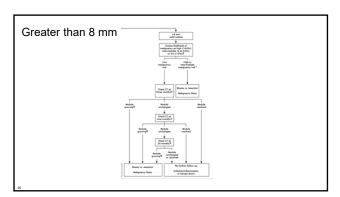












#### Summary of Fleischner Guidelines for SOLID, SOLITARY Nodules

	<6 mm (<100 mm³)	6-8 mm (100- 250 mm <sup>3</sup> )	>8 mm (>250 mm <sup>3</sup> )
	S	ingle	
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?**

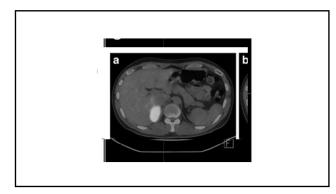
- Exclusions:
  - Patients with unexplained fever
  - -Patients with known or suspected metastases
  - Patients <35 years of age
  - Lung cancer screening (use LUNG-RADS)

# 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)

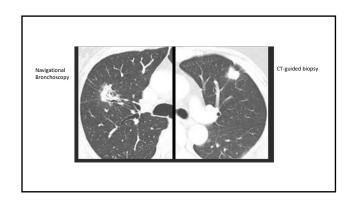


# Management

- 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

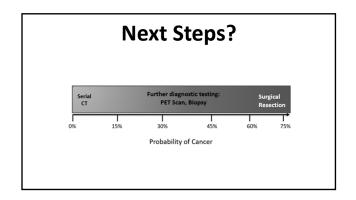
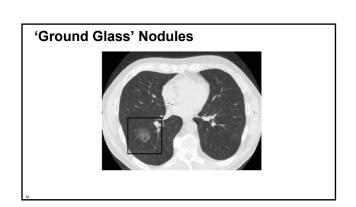


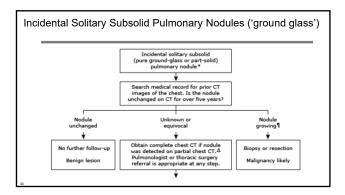
FIGURE 2. [Section 4.0] Factors that influence choice between evaluation and management alternatives for indeterminate, solid nodules ≥ 8 to 30 mm in diameter.

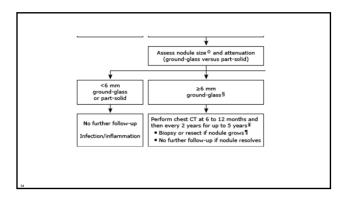
Factor	Level	CT Scan Surveillance	PET Imaging	Nonsurgical Biopsy	VATS Wedge Resection
	Very low (< 5%)	++++	-	-	-
Clinical probability of lung cancer	Low-moderate	+	+++	++	+
	High (< 65%)		(± staging)	++	++++
	Low	++	++	++	+++
Surgical risk	High	++	+++	++	
	Low		++	+++	+++
Biopsy risk	High	++	+++	-	+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

VATS = video-assisted thoracoscopic surgery.

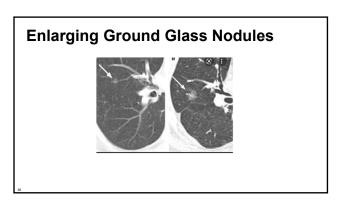
Gould M, CHEST 2013











#### **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
  - 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**

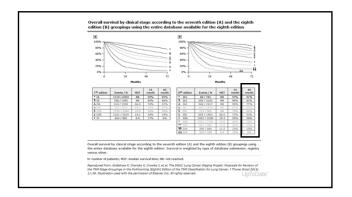
- Always be on the lookout for incidental pulmonary nodules
  - CT scans (both CT chest angiography as well as CT abdomen) in
  - CT pulmonary venograms (often obtained in the management of atrial fibrillation)
- 1st step is ALWAYS to look for prior imaging
- Use caution if/when ordering PET scans (particularly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

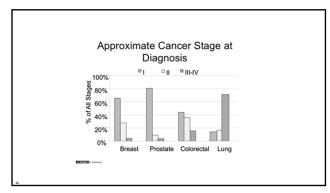
  • High rates of false positives AND false negatives
- Fine line between wanting to 'cure'/not wanting to 'miss' an early cancer and surgically resecting a benign lesion
- If ANY concern, can refer to pulmonary or thoracic surgery

# **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 DOUBLE ADDITIONS OF THE PROPERTY WITH LOW-Dose Computed Tomographic Screening The Material Long Concern Mortality with Low-Dose Computed Tomographic Screening

- 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)

Screening			Low-Dose CT				Chest	
Round							Radiography	
	Total No. Screened	Positive Result	Clinically Significant Abnormality Not	No or Minor Abnormality	Total No. Screened	Positive Result	Clinically Significant Abnormality Not	No or Minor Abnormality
			Suspicious for Lung Cancer	CT group		ening:	Suspicious for Lung Cancer	
			no. (% of screened)	CXR grou	p: 6.9%		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)

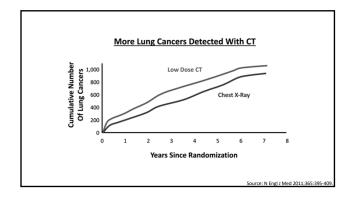
			CT gro	positive' rate up: 96.4% roup: 94.5%	s:			
Table 3. Diag	nostic Follo		sitive Screen	ing Results i	n the Three S		ounds.*	
variable		LOW-D	ose C i			Chest Ra	adiography	
	T0	T1	T2	Total	T0	T1	T2	Total
				number (percent)				
Total positive tests	7191 (100.0)	6901 (100.0)	4054 (100.0)	18,146 (100.0)	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)

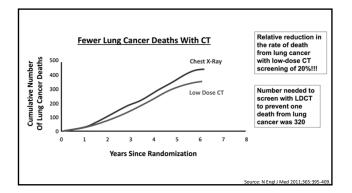
The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. FDG PET denotes "Ffluorodeoxyglucose positronemission
tomography.

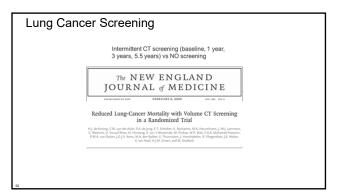
1 Positive tests with incomplete information on diagnostic follow-up are included in this category (142 at T0, 161 at T1, and 141 at T2 in the low-dose
CT group and 38 at T0, 28 at T1, and 25
4) (21 the the addocapity group).

Complication	Lung Cancer Confirmed							
	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)			

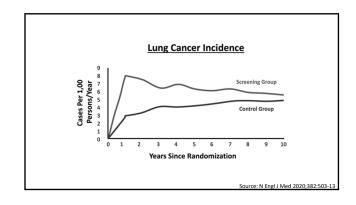
8		Low-	Dose CT		Chest Radiography				
	Positive Screenin g Test (N=649)	Negative Screening Test (N=44)†	No Screening Test (N=367)‡	Total (N=1060)	Positive Screening Test (N=279)	Negative Screening Test (N=137)†	No Screening Test (N=525)‡	Total (N=941	
					tal number cent)	no. (% of screened)			
Stage									
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)	196/92 (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	
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)	122/92 (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)	335/92 (36.1)	

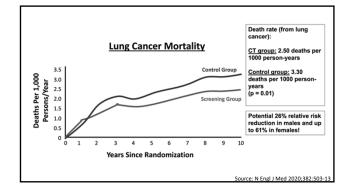






Variable		Screening Group	Control Gro	
	Screening- Detected Lung Cancer (N=203)†	Non–Screening-Detected Lung Cancer (N=141)	Any Lung Cancer (N=344)	Any Lung Cano (N=304)
		number of participa	nts (percent)	
Stage				
IA	95 (46.8)	10 (7.1)	105 (30.5)	21 (6.9)
IB	24 (11.8)	10 (7.1)	34 (9.9)	20 (6.6)
IIA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

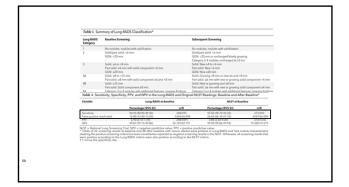
  - 30 pack year smoking history
     No signs/symptoms of lung cancer
  - Receive the screening/LDCT at a Medicare-approved radiology facility
  - Before the 1<sup>st</sup> screening, patient MUST have a shared decision-making conversation with ordering physician (risks/benefits)
    - Ordering physician will also provide counseling on smoking risks/smoking cessation services (when appropriate)

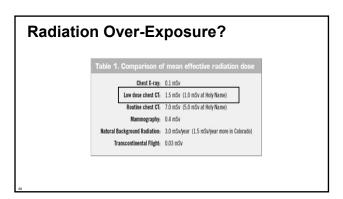
#### **Cost Effectiveness of Lung Cancer Screening**

- 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

#### Is the False Positive Rate too High?

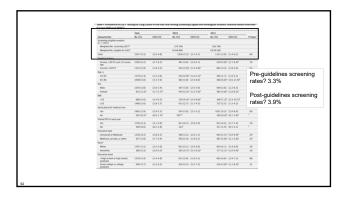
- Majority of 'false positives' on screening CT scans do NOT result in an invasive procedure
  - For example:
  - A 4 mm nodule found on initial LCS would be considered a false positive if stable/resolved on repeat imaging at the 12 month interval
- False positive rate likely greatly exaggerated...

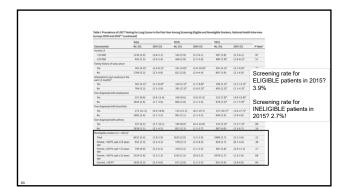


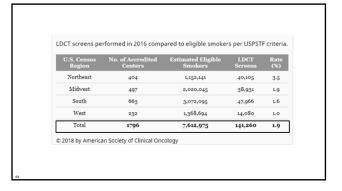


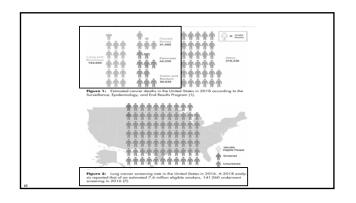
#### Lung Cancer Screening Uptake in the U.S.

- '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



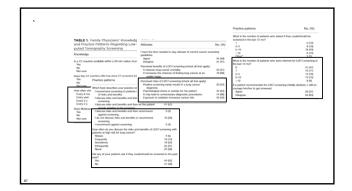


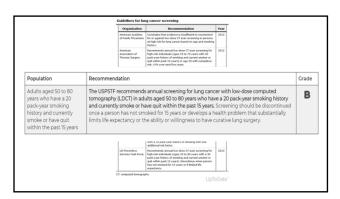




# Why Is Uptake So Poor?

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



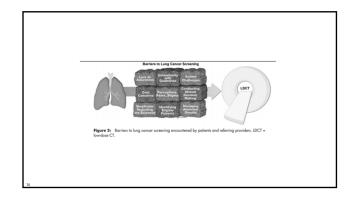


#### **Barriers to LCS**

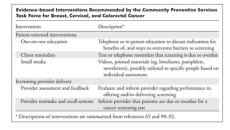
- Patients:
  - Unawareness of screening programs
  - Fear of cancer diagnosis
  - Cost concerns
- Access to screening/imaging sites
- Physicians/providers:

  - Unfamiliarity with screening guidelines/insurance coverage
     Insufficient time/knowledge to conduct shared-decision
  - Lack of guidance for managing lung cancer screening results
     Skepticism about benefits of screening

  - Concerns over 'false positive' rates



#### How to Improve Screening Uptake?



## **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!

#### References

- NLST Research Team. Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening. N Engl J Med 2011; 365:395-409
- Jemal A, Fedewa SA. Lung Cancer Screening with Low-Dose Computed Tomography in the United States 2010 to 2015. JAMA Oncol 2017. Sept 1:3(9):1278-1281
- Oncol 2017; Sept 13;8(9):127e-12o1

  Ril A, et al. Cyvaluating Lung Garoer Screening Uptake, Outcomes, and Costs in the United States: Challenges with Existing Data and Recommendations for Improvement. JMCI J Matl Cancer Inst 2019; 111(4): 9);225.

  Pirasky, et al. Performance of Lung-AROS in the National Lung Screening Trial. Ann Intern Med. 2015; 162:485-91

  Koning HJ, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med 2020;382:503-13