

# Lung Cancer Screening & Lung Nodule Monitoring

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- **Current Principles of Lung Cancer Screening**
- **Efforts Toward Expansion and Remaining Gaps**
- **Initial Assessment of Pulmonary Nodules**
- **Nodule Management: From Follow-Up to Planning Biopsy**

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# How Lung Cancer Screening Works



Lung cancer is a significant public health issue

Globally, one fifth of all cancer-related deaths are due to lung cancer.<sup>4</sup>

Lung cancer also incurs the greatest economic burden of all cancers.<sup>5</sup>



Lung cancer has a detectable early stage of the disease, for which effective treatments are available

Most people with lung cancer are diagnosed late (stage IV), when five-year survival is <10%.<sup>6,7</sup>

If diagnosed earlier (stage I), five-year survival increases to 68–92%<sup>7</sup> as treatment (such as surgery) can be potentially curative.<sup>8</sup>



LDCT screening is recognised as a suitable test for lung cancer

When optimised, targeted LDCT screening has been shown to be **effective** and **does not lead** to a high proportion of unnecessary procedures or treatments.<sup>9-12</sup>

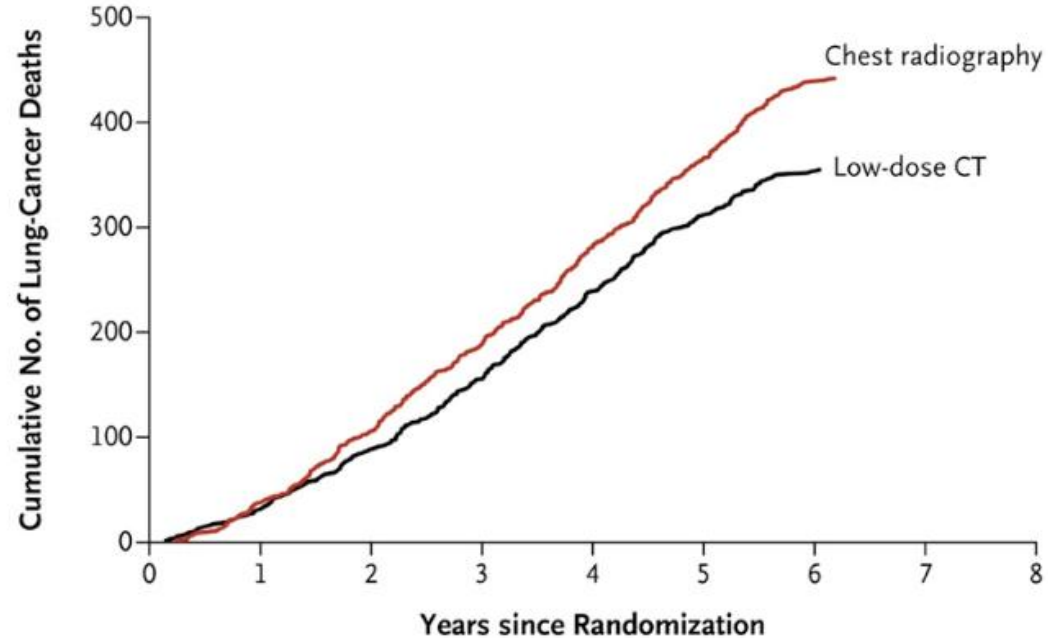


Lung cancer screening is cost-effective

LDCT screening is also potentially **more efficient** than other cancer screening programmes.<sup>13-15</sup> In other words, fewer people need to be screened to avoid one death from lung cancer than with other cancer screening programmes.

# Evidence from Randomized Controlled Trials

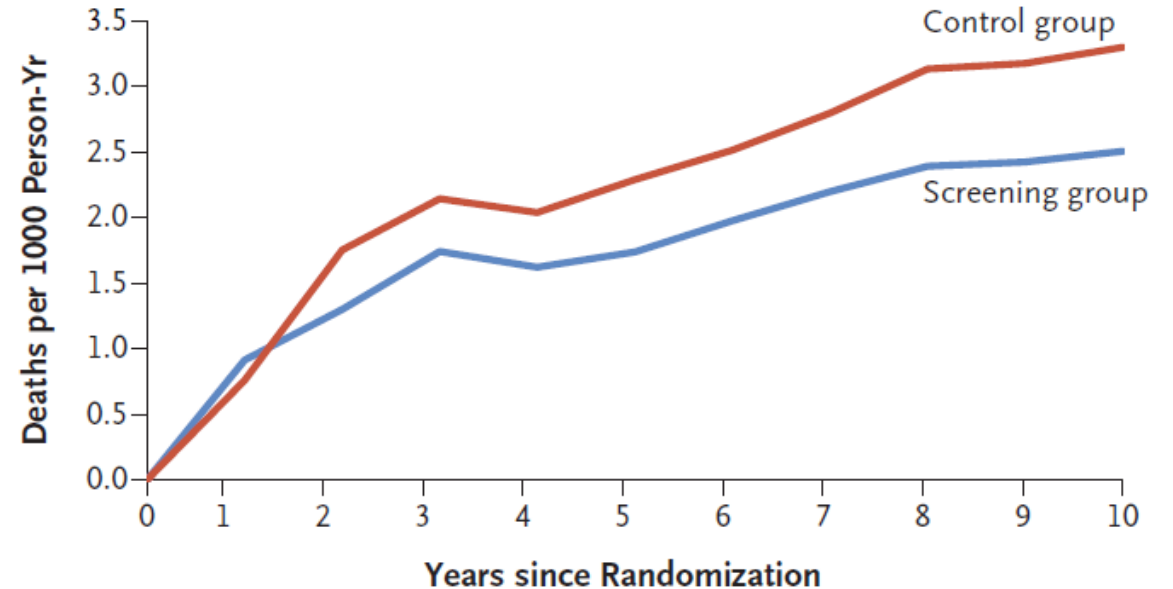
**B** Death from Lung Cancer



**<NLST trial>**

**20%** mortality reduction compared to those who were not screened with LDCT

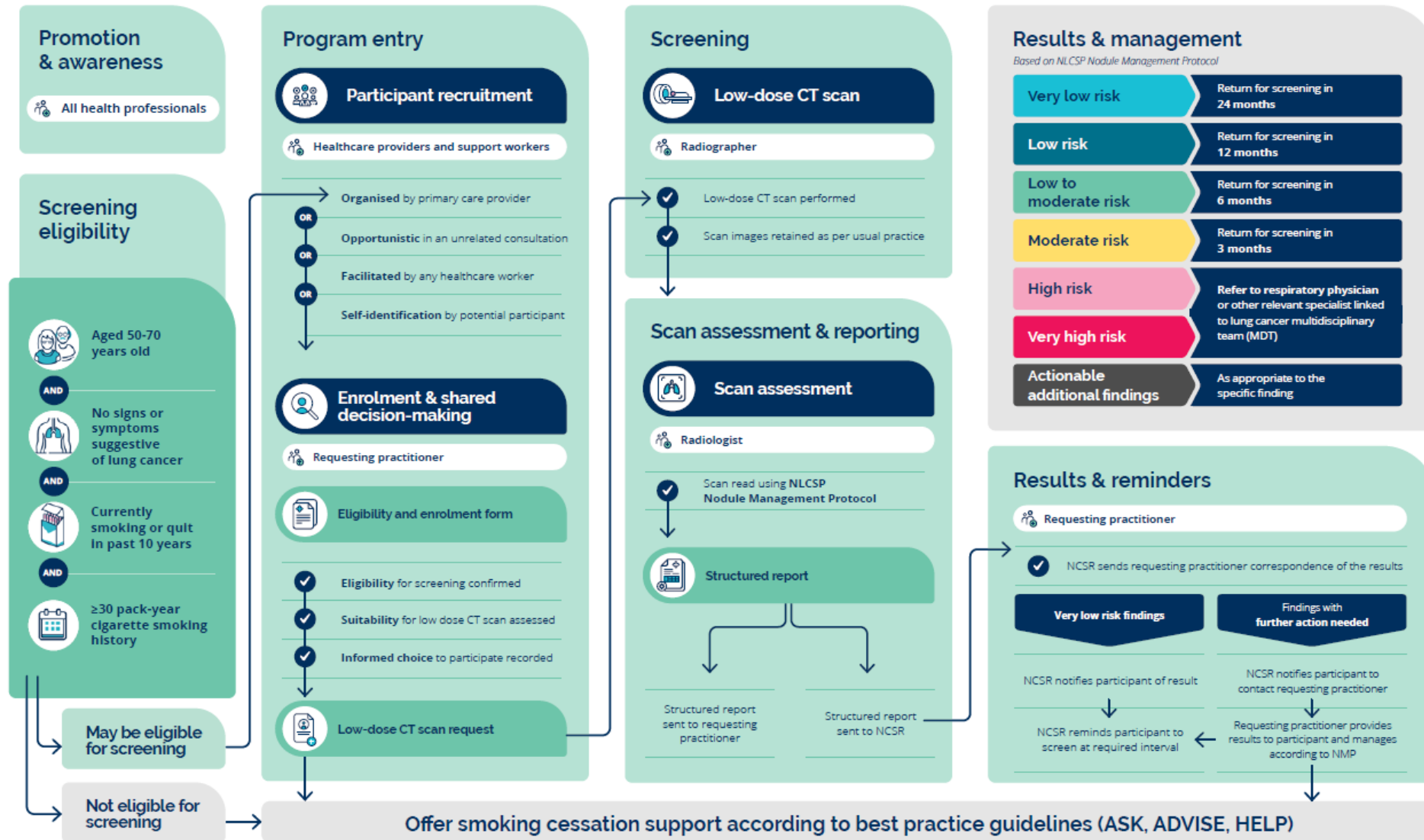
**B** Lung-Cancer Mortality



**<NELSON trial>**

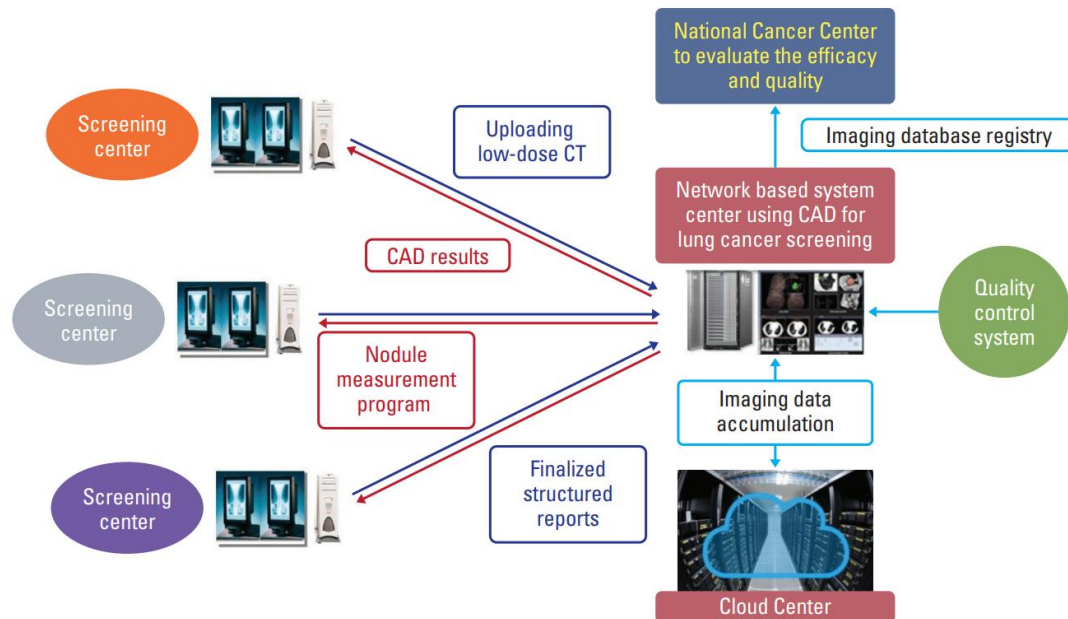
**24%** mortality reduction in men for those who underwent LDCT screening

# Roadmap of Real-World Implementation



# Korean National Lung Cancer Screening Program

	Target Population	Frequency	Test or Procedure
<b>Lung Cancer Screening</b>	Smokers aged 54-74, with $\geq 30$ PYs smoking history	Every 2 years	Low dose chest CT



**Centralized reporting aid system**

Solid nodule			Part solid nodule			Ground glass nodule		
Size	Timing/Change	Cat.	Size	Timing/Change	Cat.	Size	Timing/Change	Cat.
<6 mm	Baseline	2	<6 mm	Baseline	2	<20 mm	Baseline	2
	No change	2		No change	2		No change	2
	Growing	4A		Growing (solid <4 mm)	4A		Growing	2
	New (<4 mm)	2		Growing (solid 4-6 mm)	4B	New	2	
	New (4-6 mm)	3		New	3	$\geq 20$ mm	Baseline	3
6-8 mm	Baseline	3	$\geq 6$ mm (solid <6 mm)	Baseline	3	No change	2	
	No change	2		No change	2	Growing	2	
	Growing	4A		Growing (solid <4 mm)	4A	New	3	
	New	4A		Growing (solid 4-6 mm)	4B	<b>Other</b>		
8-15 mm	Baseline	4A	$\geq 6$ mm (solid 6-8 mm)	Baseline	4A	Endobronchial nodule	4A	
	No change	2		No change	2	Cat. 3,4+additional finding	4X	
	Growing	4B		Growing (solid <4 mm)	4A	; Consolidation, atelectasis, lymph node enlargement, other (spiculation, etc.)		
	New	4B		New (solid 4-6 mm)	4B	Other clinically significant findings	S	
$\geq 15$ mm	Baseline	4B	$\geq 8$ mm (solid $\geq 8$ mm)	Baseline	4B	Prior lung cancer	C	
	No change	2		No change	2			
	Growing	4B		Growing	4B			
	New	4B		New	4B			
<b>Category</b>	<b>Description</b>	<b>Prob.cancer</b>	<b>Manage</b>					
0	Incomplete	Not evaluable	Additional LDCT images and/or comparison to prior chest CT images					
1	Negative	< 1%	Continue annual screening with LDCT in 12 months					
2, 2b <sup>a</sup>	Benign	< 1%	Continue annual screening with LDCT in 12 months					
3	Probably benign	1-2%	Follow up LDCT in 6 months					
4A	Suspicious	5-15%	Follow up LDCT in 3 months, PET-CT may be used when there is a solid $\geq 8$ mm					
4B, X	Very suspicious	> 15%	Immediate chest CT, consider biopsy, PET-CT may be used					

**Modified Lung-RADS**

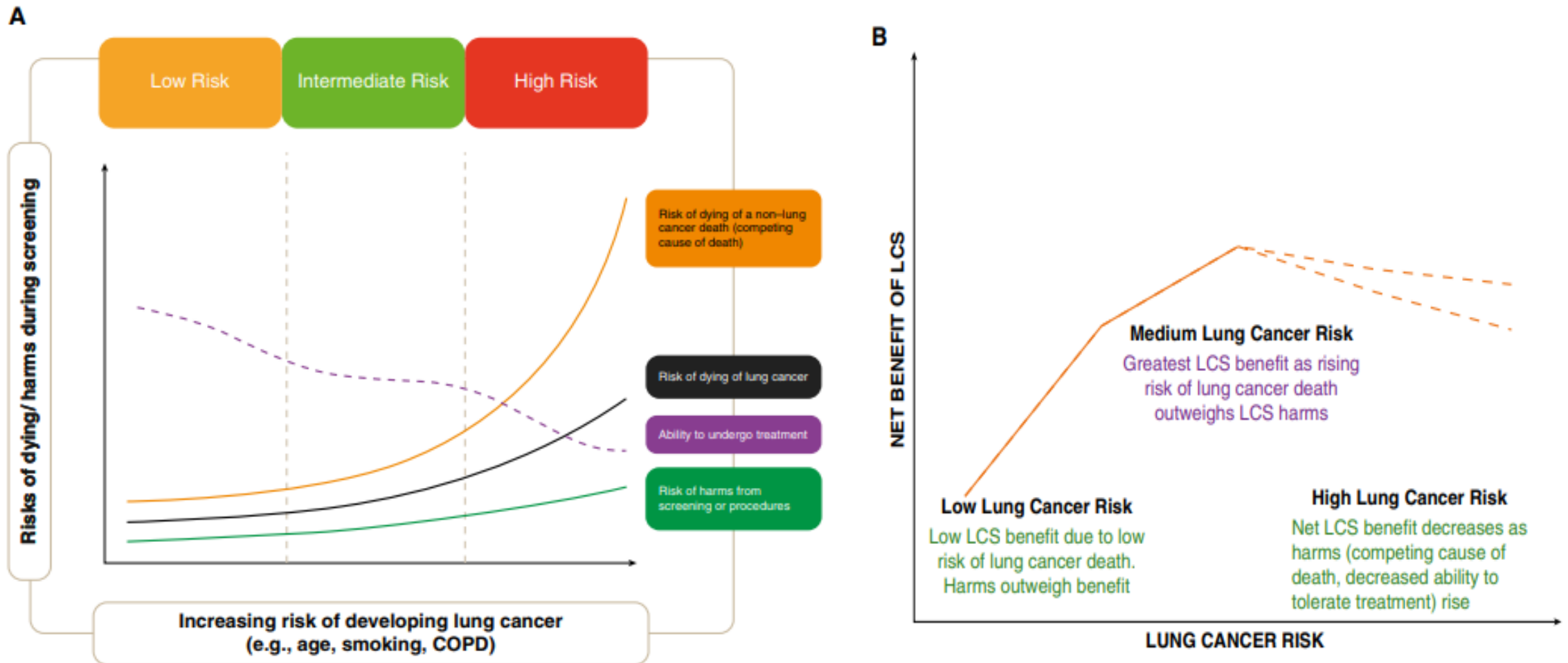
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# How to Achieve Net Benefit From Screening

- Choosing the eligibility criteria must be balanced by potential benefits and harms

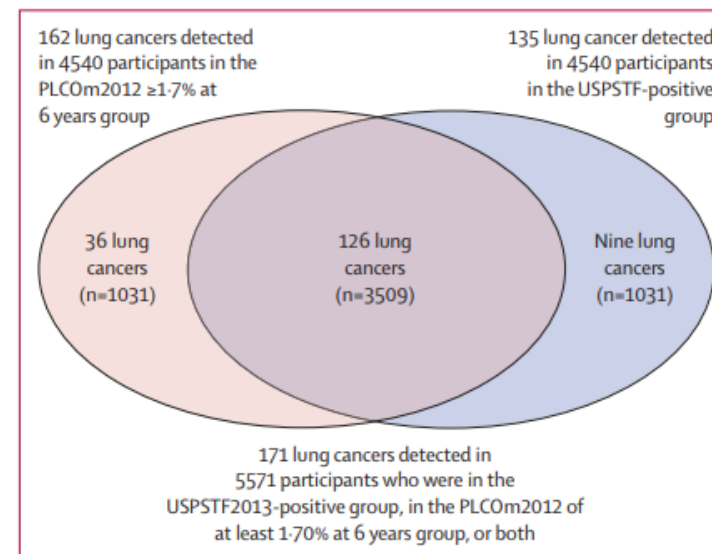


# Risk Model Based Screening

## - PLCOm2012 model: calculation of 6 year lung cancer risk

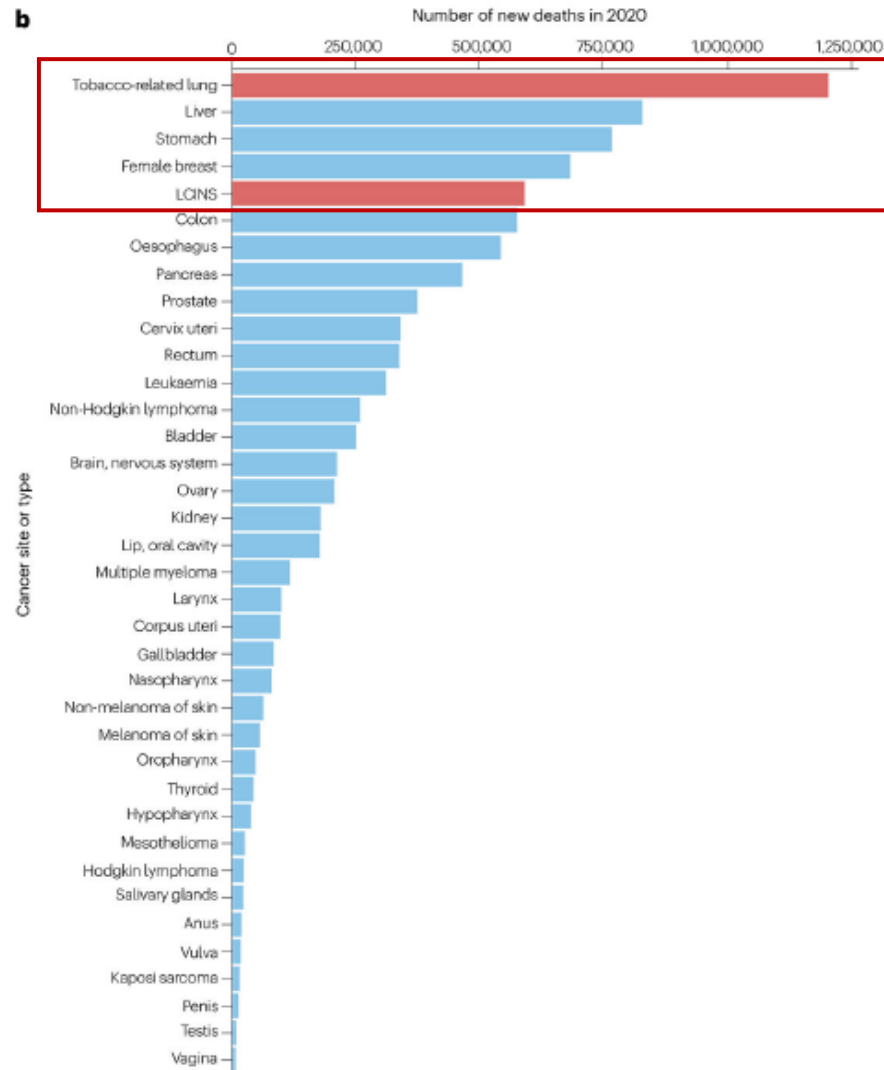
**Table 2. Modified Logistic-Regression Prediction Model (PLCO<sub>M2012</sub>) of Cancer Risk for 36,286 Control Participants Who Had Ever Smoked.\***

Variable	Odds Ratio (95% CI)	P Value	Beta Coefficient
Age, per 1-yr increase†	1.081 (1.057–1.105)	<0.001	0.0778868
Race or ethnic group‡			
White	1.000		Reference group
Black	1.484 (1.083–2.033)	0.01	0.3944778
Hispanic	0.475 (0.195–1.160)	0.10	-0.7434744
Asian	0.627 (0.332–1.185)	0.15	-0.466585
American Indian or Alaskan Native	1		0
Native Hawaiian or Pacific Islander	2.793 (0.992–7.862)	0.05	1.027152
Education, per increase of 1 level†§	0.922 (0.874–0.972)	0.003	-0.0812744
Body-mass index, per 1-unit increase†	0.973 (0.955–0.991)	0.003	-0.0274194
Chronic obstructive pulmonary disease (yes vs. no)	1.427 (1.162–1.751)	0.001	0.3553063
Personal history of cancer (yes vs. no)	1.582 (1.172–2.128)	0.003	0.4589971
Family history of lung cancer (yes vs. no)	1.799 (1.471–2.200)	<0.001	0.587185
Smoking status (current vs. former)	1.297 (1.047–1.605)	0.02	0.2597431
Smoking intensity¶			-1.822606
Duration of smoking, per 1-yr increase†	1.032 (1.014–1.051)	0.001	0.0317321
Smoking quit time, per 1-yr increase†	0.970 (0.950–0.990)	0.003	-0.0308572
Model constant			-4.532506

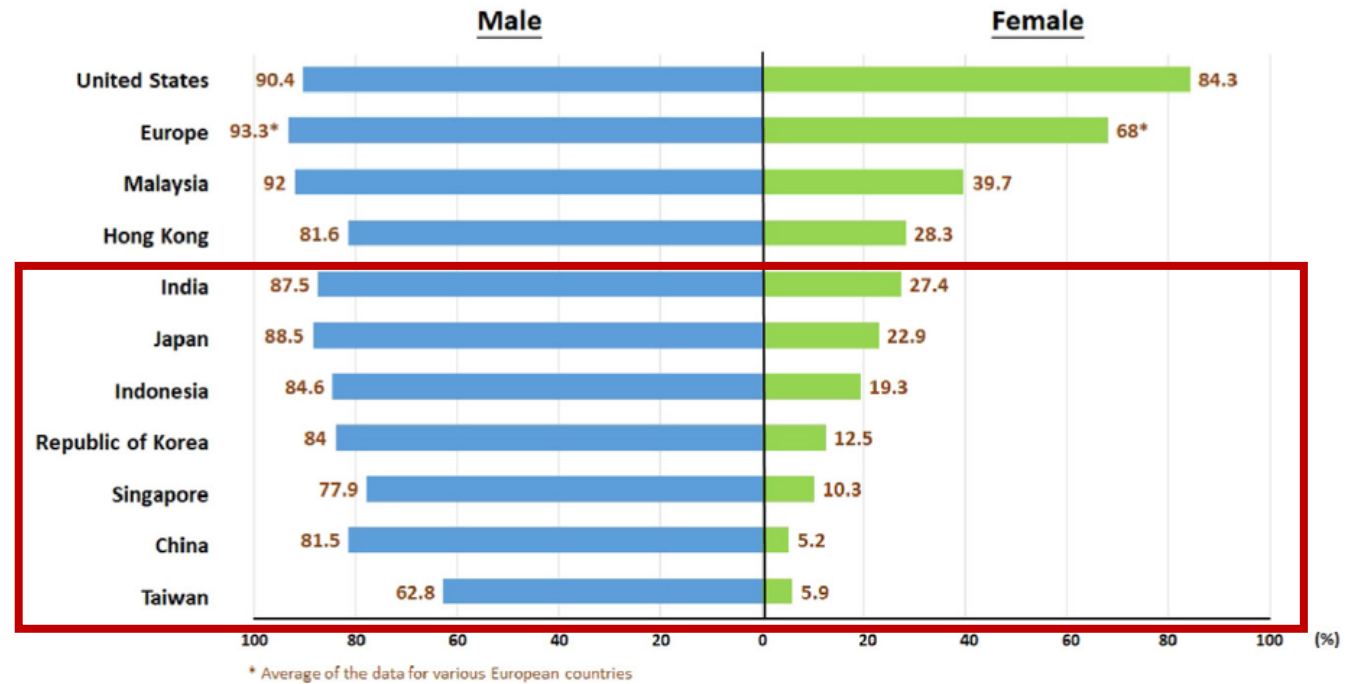


	USPSTF eligible	PLCOm2012 $\geq 1.70\%$ at 6 years	p value
<b>ILST data</b>			
Cancer detection rate*	135/177 (76.3% [69.3–82.3])	162/177 (91.5% [86.4–95.2])	$p_{McNemar}=0.0001$
Cancer detection rate†	135/171 (78.9% [72.1–84.8])	162/171 (94.7% [90.2–97.6])	$p_{McNemar}=0.0001$
Positive predictive value‡	135/4540 (2.97% [2.90–3.51])	162/4540 (3.57% [3.05–4.15])	$p=0.11$
False-negative proportion‡	42/1279 (3.28% [2.38–4.41])	15/1279 (1.17% [0.66–1.93])	$p=0.0003$
Negative predictive value	96.72%	98.83%	..

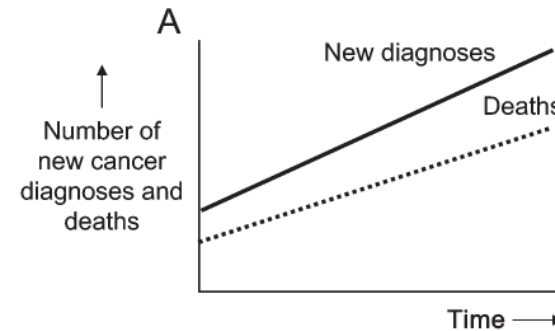
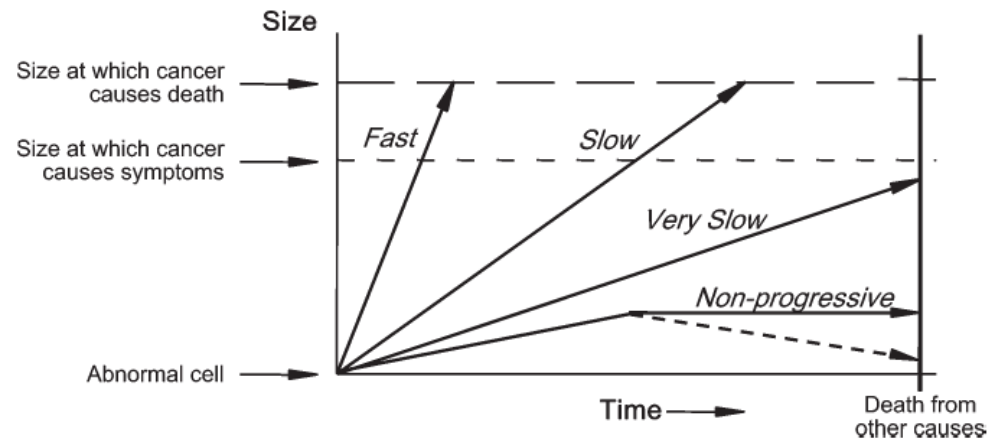
# Lung Cancer in Never-Smokers: A Distinct Disease



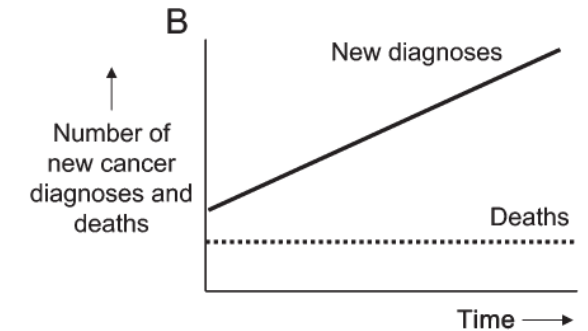
Smoking Prevalence of Lung Cancer Patients by Gender in Asia and Western Regions



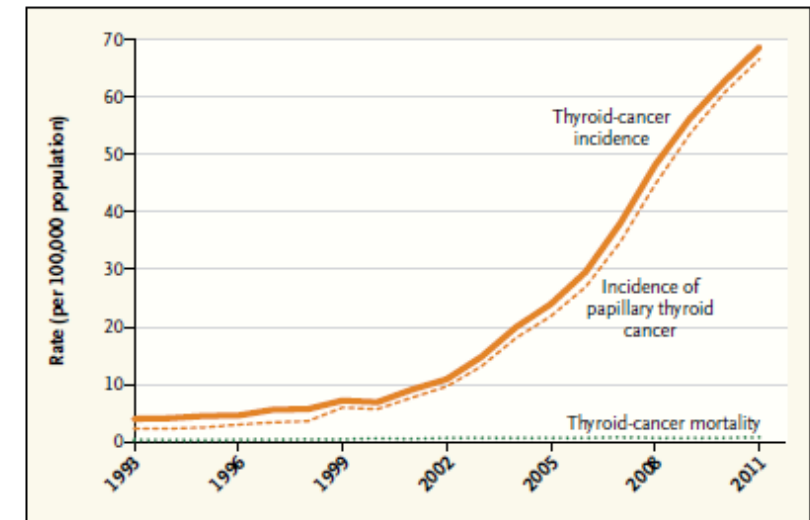
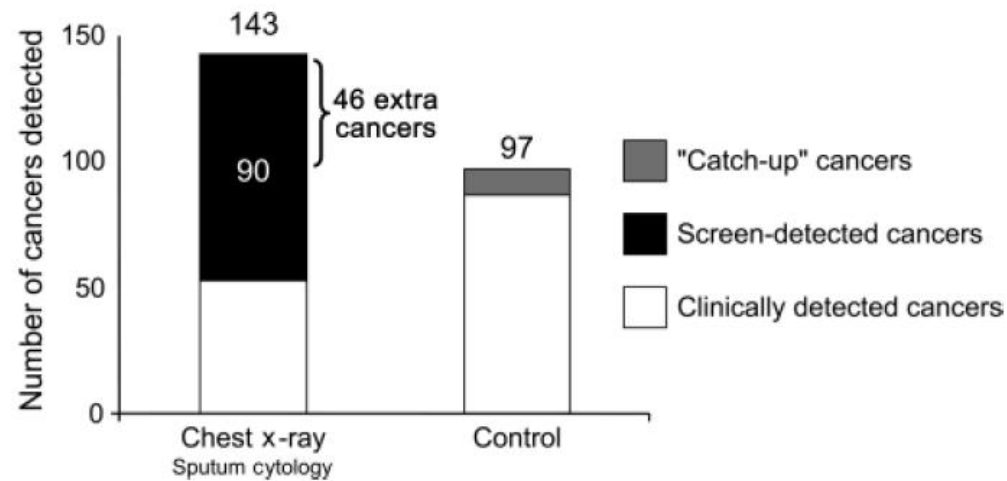
# Capturing Overdiagnosis: Available Only in A Population Level



Suggests a true increase in the amount of cancer

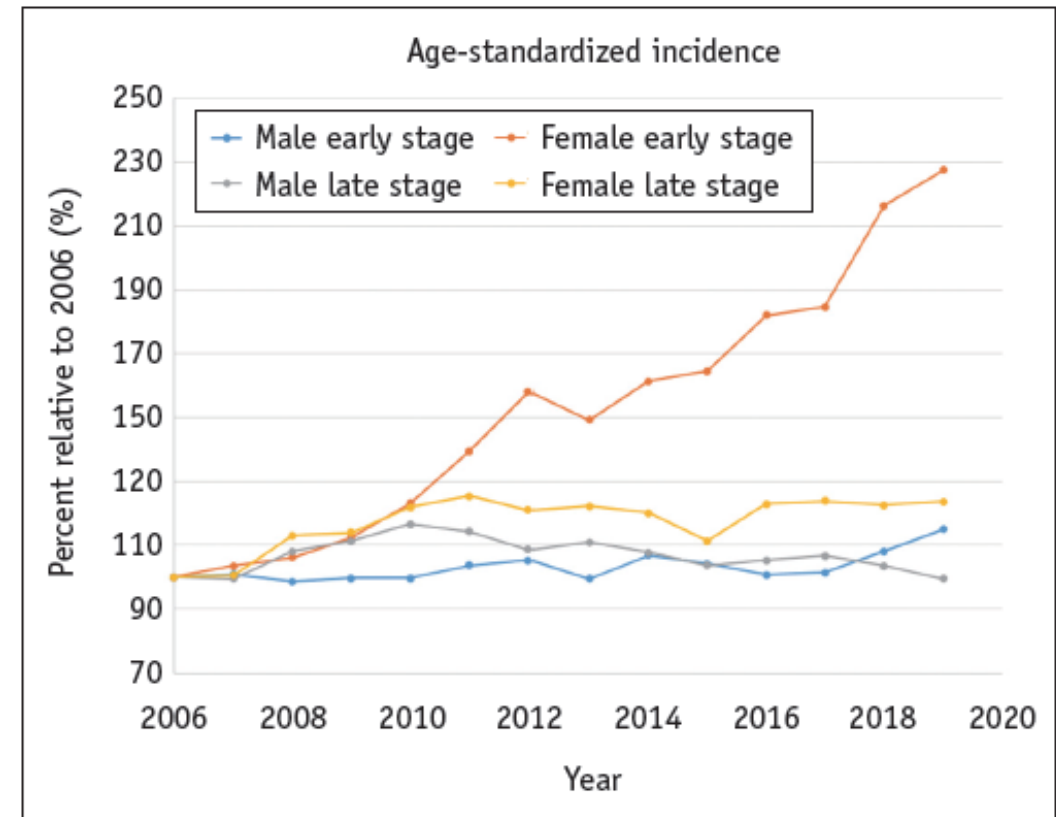
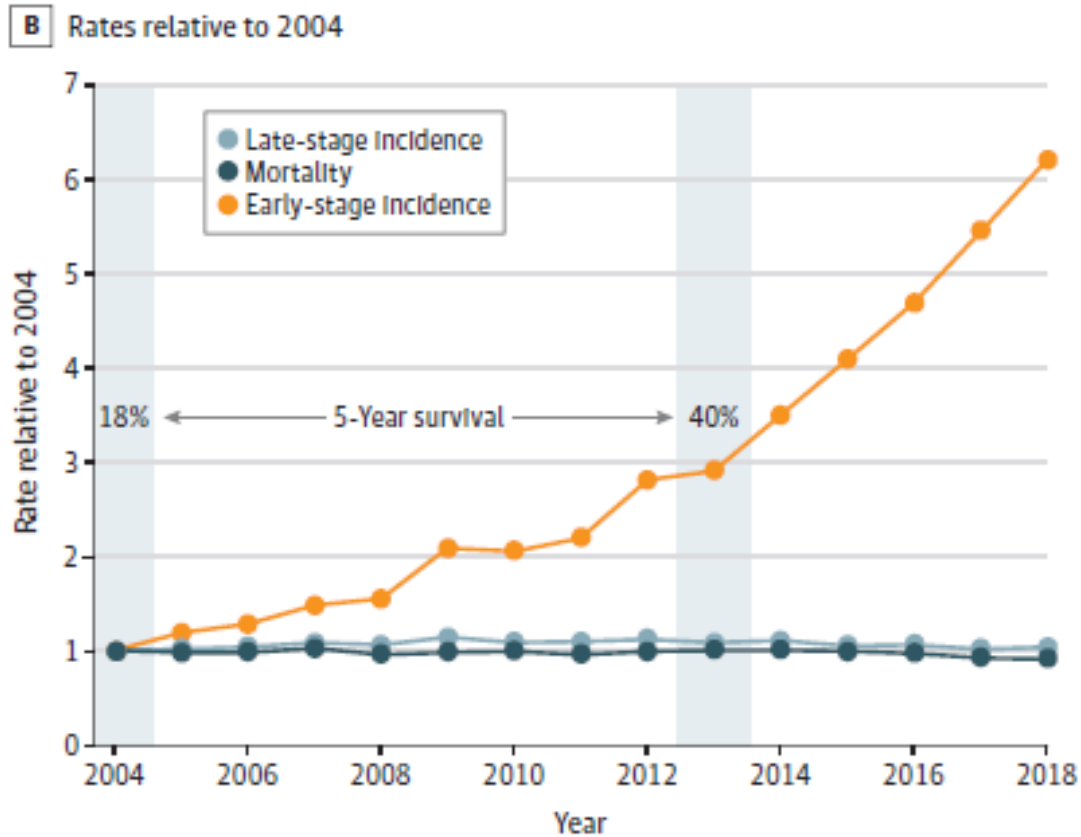


Suggests overdiagnosis of cancer



Thyroid-Cancer Incidence and Related Mortality in South Korea, 1993–2011.

# More Detection of Early Stage Disease Without Stage Shift in Asia

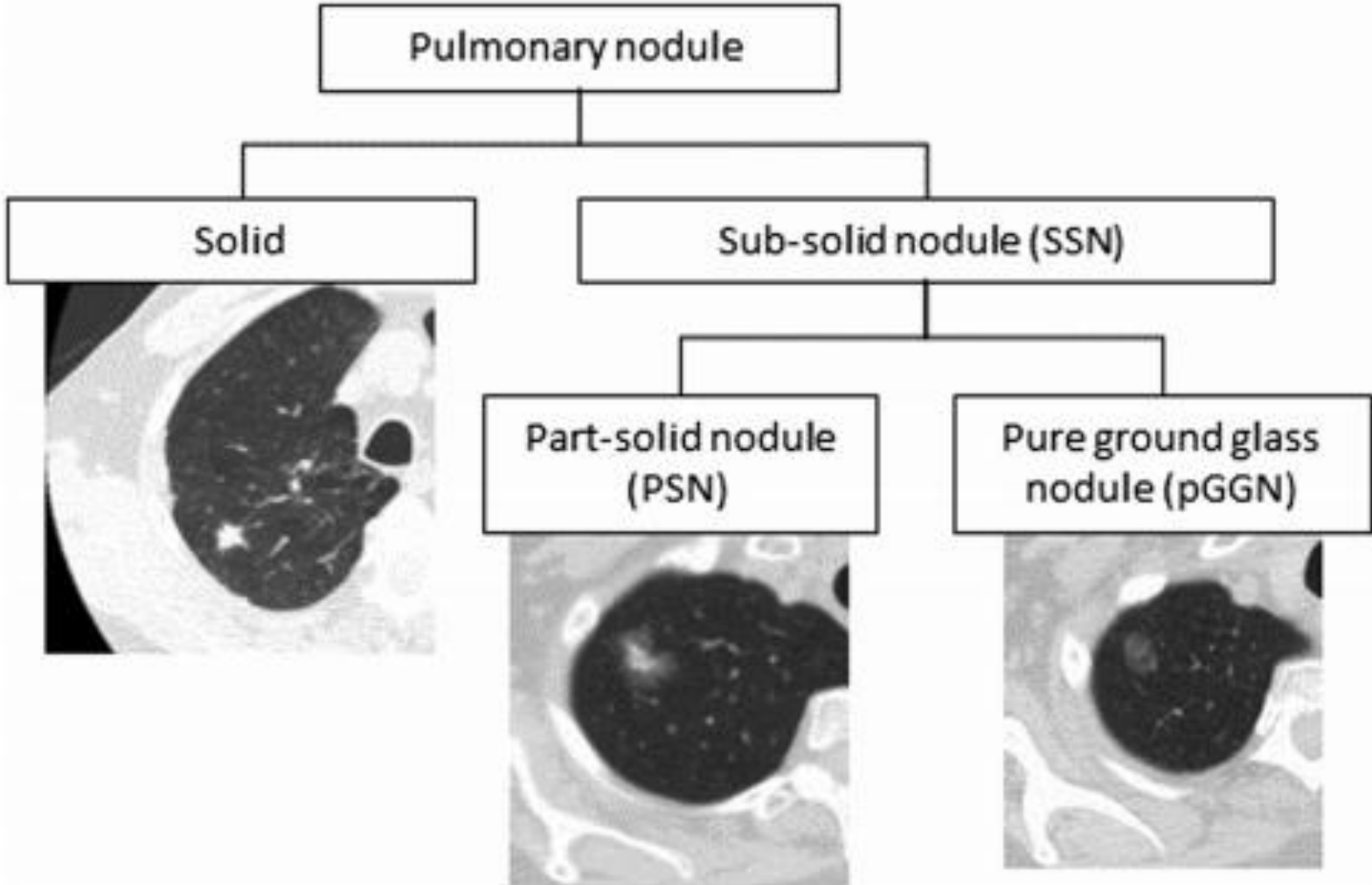


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# Classification of Pulmonary Nodules

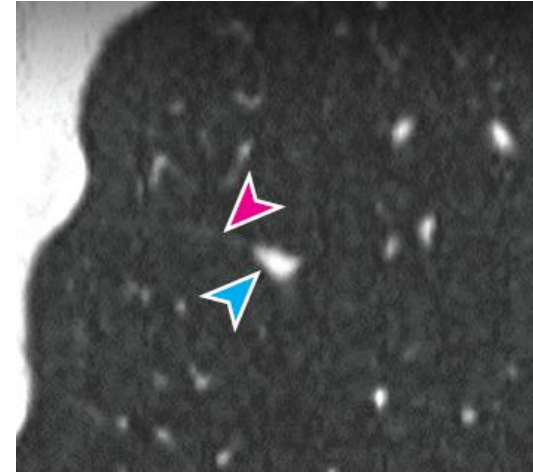


# Solid Pulmonary Nodules

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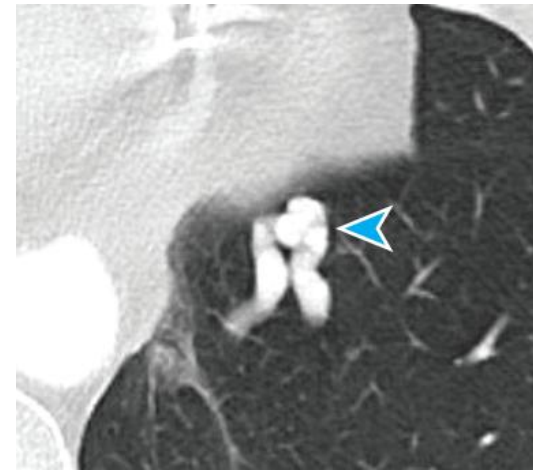
Calcified granuloma



Perifissural nodule

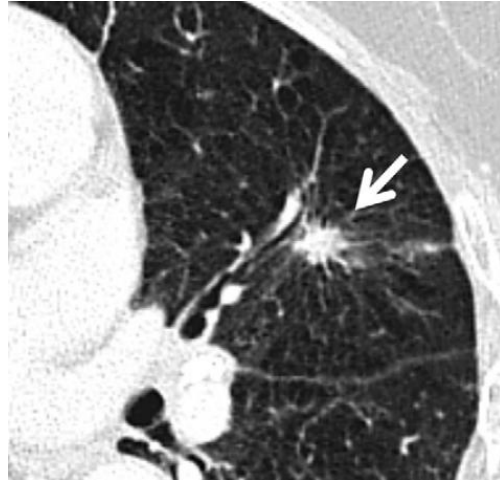


Hamartoma



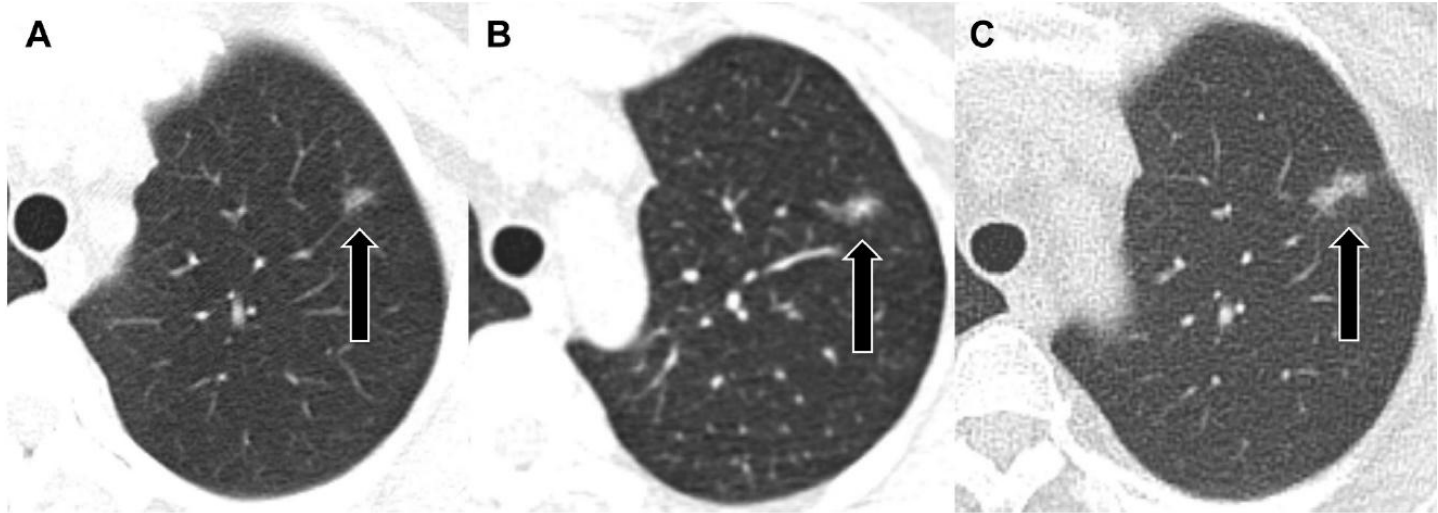
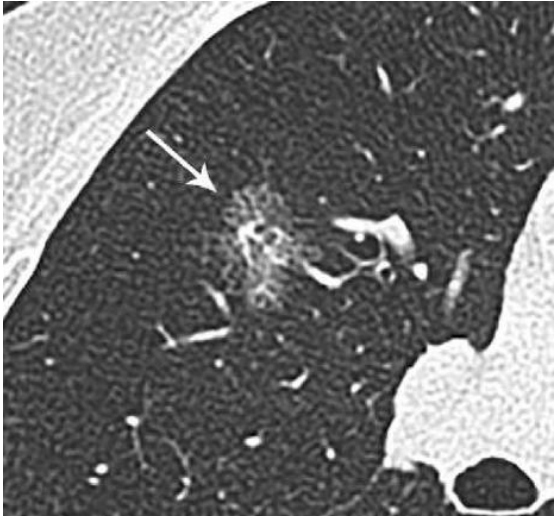
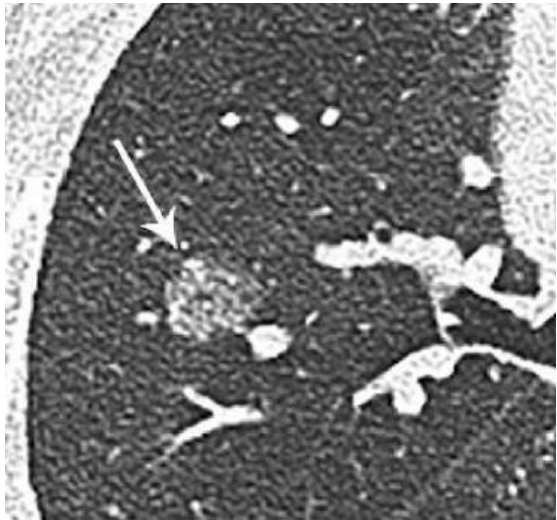
Arteriovenous malformation

# Solid Pulmonary Nodules with Malignancy Risk



Parameter	Characteristics Associated With Malignant Nodules
Growth rate	Doubling time 20-400 d (< 100 d for most solid nodules); growth rate may be slower with ground-glass and subsolid nodules (> 200 d); very rapid doubling suggests an infectious or inflammatory cause
Location	Upper lobe is a more common site for malignant nodules, although the diagnostic significance of this finding is reduced in Asia due to the high prevalence of TB
Margins	Lobulated or speculated margins are strongly associated with malignancy; notches are commonly seen in adenocarcinomas with overt invasion
Cavitation	Malignant lesions are associated with irregular, thicker walls > 15 mm thick
Size	Probability of malignancy increases with size (nodules > 2 cm are more likely to be malignant, although smaller size does not exclude malignancy)
Calcification	Punctate and eccentric (evidence of necrosis within nodule) calcification may occur with malignancy
Other features	Vascular convergence, dilated bronchus leading into the nodule

# Subsolid Pulmonary Nodules



10 years of follow-up

# Differential Considerations for Subsolid Nodules

Primary Lung Adenocarcinoma	Nonprimary Lung Adenocarcinoma Etiologies
<ul style="list-style-type: none"><li>• Atypical adenomatous hyperplasia</li></ul>	<ul style="list-style-type: none"><li>• Transient infection (eg, aspergillosis, candidiasis)</li></ul>
<ul style="list-style-type: none"><li>• Adenocarcinoma in situ</li></ul>	<ul style="list-style-type: none"><li>• Transient inflammation</li></ul>
<ul style="list-style-type: none"><li>• Minimally invasive adenocarcinoma</li></ul>	<ul style="list-style-type: none"><li>• Focal interstitial fibrosis</li></ul>
<ul style="list-style-type: none"><li>• Invasive adenocarcinoma</li></ul>	<ul style="list-style-type: none"><li>• Organizing pneumonia</li></ul>
<ul style="list-style-type: none"><li>• Mucinous adenocarcinoma</li></ul>	<ul style="list-style-type: none"><li>• Eosinophilic pneumonia</li></ul>
	<ul style="list-style-type: none"><li>• Alveolar sarcoid</li></ul>
	<ul style="list-style-type: none"><li>• Drug reaction</li></ul>
	<ul style="list-style-type: none"><li>• Vasculitis (granulomatosis with polyangiitis)</li></ul>
	<ul style="list-style-type: none"><li>• Endometriosis</li></ul>
	<ul style="list-style-type: none"><li>• Mucosa associated lymphoid tissue (MALT) and lymphoproliferative disorders</li></ul>
	<ul style="list-style-type: none"><li>• Metastatic lesions (including melanoma; renal carcinoma; breast, GI, and pancreatic adenocarcinomas)</li></ul>

# Risk Prediction for Malignancy

Risk prediction model	Mayo Clinic model <sup>17</sup>	Herder model <sup>18</sup>	VA model <sup>19</sup>	Brock University model <sup>2</sup>	Cleveland Clinic model <sup>20</sup>
Nodule detection	Incidental nodule on chest radiograph	Incidental nodule on chest radiograph and PET scan was performed for further evaluation	Incidental nodule seen on chest radiographic confirmed on CT imaging +/- PET scan	Nodules detected on LDCT as part of lung cancer screening program	Incidental nodules referred to biopsy or resection
% Of nodules that were malignant in the cohort used to develop the model	23	57	54	5.5	66.5
Model variables	Age Smoking history History of extrathoracic malignancy ≥5 y ago Nodule diameter Spiculation Upper lobe location	Mayo Clinic model + FDG-PET uptake	Age Smoking history Time since quitting smoking Nodule diameter	Age Sex Family history of lung cancer Emphysema Nodule Size Nodule type Location Nodule count	Age Smoking history Upper lobe location Solid and irregular/spiculated nodule edges Emphysema FDG-PET avidity History of cancer other than lung
Area under the curve	0.83	0.88	0.79	≥0.94	0.75-0.81 (C-index)

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# Management of Screen-Detected Nodules

- Lung-RADS 2022

Size: mean diameter

Growth: increase of >1.5 mm (2 mm<sup>3</sup>)



Lung-RADS® v2022

Release Date: November 2022

Lung-RADS	Category Descriptor	Findings	Management
0	Incomplete Estimated Population Prevalence: ~1%	Prior chest CT examination being located for comparison (see note 9)	Comparison to prior chest CT;
		Part or all of lung(s) cannot be evaluated	Additional lung cancer screening CT imaging needed;
1	Negative Estimated Population Prevalence: 39%	No lung nodules OR	1-3 month LDCT
		Nodule with benign features: • Complete, central, popcorn, or concentric ring calcifications OR • Fat-containing	
2	Benign - Based on imaging features or	Juxtapleural nodule: • < 10 mm (524 mm <sup>3</sup> ) mean diameter at baseline or now AND • Solid; smooth margins; and oval, lentiform, or triangular shape	12-month screening LDCT
		Solid nodule: • < 6 mm (< 113 mm <sup>3</sup> ) at baseline OR • New < 4 mm (< 34 mm <sup>3</sup> )	

4A	Suspicious Estimated Population Prevalence: 4%	Solid nodule: • ≥ 8 to < 15 mm (≥ 268 to < 1,767 mm <sup>3</sup> ) at baseline OR • Growing < 8 mm (< 268 mm <sup>3</sup> ) OR • New 6 to < 8 mm (113 to < 268 mm <sup>3</sup> )	3-month LDCT; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm <sup>3</sup> ) solid nodule or solid component	6-month LDCT
		Part solid nodule: • ≥ 6 mm total mean diameter (≥ 113 mm <sup>3</sup> ) with solid component ≥ 6 mm to < 8 mm (≥ 113 to < 268 mm <sup>3</sup> ) at baseline OR • New or growing < 4 mm (< 34 mm <sup>3</sup> ) solid component.		
		Airway nodule, segmental or more proximal - at baseline (see note 11)		
		Atypical pulmonary cyst: (see note 12) • Thick-walled cyst OR • Multilocular cyst at baseline OR • Thin- or thick-walled cyst that becomes multilocular		
4B	Very Suspicious Estimated Population Prevalence: 2%	Airway nodule, segmental or more proximal - stable or growing (see note 11)	Referral for further clinical evaluation	3-month LDCT; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm <sup>3</sup> ) solid nodule or solid component
		Solid nodule: • ≥ 15 mm (≥ 1,767 mm <sup>3</sup> ) at baseline OR • New or growing ≥ 8 mm (≥ 268 mm <sup>3</sup> )	Diagnostic chest CT with or without contrast;	Referral for further clinical evaluation
		Part solid nodule: • Solid component ≥ 8 mm (≥ 268 mm <sup>3</sup> ) at baseline OR • New or growing ≥ 4 mm (≥ 34 mm <sup>3</sup> ) solid component	PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm <sup>3</sup> ) solid nodule or solid component;	Diagnostic chest CT with or without contrast; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm <sup>3</sup> ) solid nodule or solid component;
		Atypical pulmonary cyst: (see note 12) • Thick-walled cyst with growing wall thickness/nodularity OR • Growing multilocular cyst (mean diameter) OR • Multilocular cyst with increased loculation or new/increased opacity (nodular, ground glass, or consolidation)	tissue sampling; and/or referral for further clinical evaluation	tissue sampling; and/or referral for further clinical evaluation
		Slow growing solid or part solid nodule that demonstrates growth over multiple screening exams (see note 8)	Management depends on clinical evaluation, patient preference, and the probability of malignancy (see note 13)	Management depends on clinical evaluation, patient preference, and the probability of malignancy (see note 13)
4X	Estimated Population Prevalence: < 1%	Category 3 or 4 nodules with additional features or imaging findings that increase suspicion for lung cancer (see note 14)		As appropriate to the specific finding

# Management of Incidental Nodules: Fleischner Society Guidelines

<b>A: Solid Nodules*</b>				
Nodule Type	Size			Comments
	<6 mm (<100 mm <sup>3</sup> )	6–8 mm (100–250 mm <sup>3</sup> )	>8 mm (>250 mm <sup>3</sup> )	
<b>Single</b>				
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	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A).
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	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
<b>Multiple</b>				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
<b>B: Subsolid Nodules*</b>				
Nodule Type	Size			Comments
	<6 mm (<100 mm <sup>3</sup> )	≥6 mm (>100 mm <sup>3</sup> )		
<b>Single</b>				
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years		In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.		In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C).
<b>Multiple</b>				
	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).		Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

# New Nodules Detected During Follow-Up: Solid

- New solid nodules detected at interval screening have a high probability of malignancy even at a small size

	Second screening round (lung cancer/ total nodules)	Third screening round (lung cancer/ total nodules)	Second and third screening rounds (lung cancer/ total nodules)	Lung cancer probability (95% CI)
New solid nodules	13/452 (3%)	35/679 (5%)	48/1131 (4%)	4.2% (3.2–5.6)
<25 mm <sup>3</sup>	1/160 (1%)	1/216 (<1%)	2/376 (1%)	0.5% (0.0–2.0)
25 to <50 mm <sup>3</sup>	3/104 (3%)	4/154 (3%)	7/258 (3%)	2.7% (1.2–5.6)
50 to <100 mm <sup>3</sup>	2/72 (3%)	4/113 (4%)	6/185 (3%)	3.2% (1.3–7.1)
100 to <200 mm <sup>3</sup>	2/46 (4%)	2/85 (2%)	4/131 (3%)	3.1% (0.9–7.8)
200 to <300 mm <sup>3</sup>	2/19 (11%)	4/31 (13%)	6/50 (12%)	12.0% (5.2–24.2)
300 to <400 mm <sup>3</sup>	0/14	2/18 (11%)	2/32 (6%)	6.3% (0.7–21.2)
400 to <500 mm <sup>3</sup>	0/8	3/20 (15%)	3/28 (11%)	10.7% (2.9–28.0)
≥500 mm <sup>3</sup>	3/29 (10%)	15/42 (36%)	18/71 (25%)	25.4% (16.6–36.6)
Cutoff values				
<27 mm <sup>3</sup>	1/180 (1%)	1/237 (<1%)	2/417 (<1%)	0.5% (0.0–1.9)
27 to <206 mm <sup>3</sup>	7/206 (3%)	10/336 (3%)	17/542 (3%)	3.1% (1.9–5.0)
≥206 mm <sup>3</sup>	5/66 (8%)	24/106 (23%)	29/172 (17%)	16.9% (12.0–23.2)

Data are n/N (%), unless otherwise specified. Exact volume measurement was not available for 89 benign nodules and two cancers, and they were not included in the calculations.

**Table 3: Volume at first detection and lung cancer probability of new solid nodules (N=1131; 1083 benign nodules and 48 lung cancer nodules)**

# New Nodules Detected During Follow-Up: Subsolid

**Frequency of Nonsolid Nodules and Diagnoses of Lung Cancer Identified in 2392 of 57 496 Participants at Baseline CT Screening according to Size of Largest Nonsolid Nodule**

Parameter	Diameter of Largest Nodule					Total
	<6 mm	6–9 mm	10–14 mm	15–30 mm	≥31 mm	
Resolved or decreased	341	177	70	39	1	628
Lung cancer	0	0	0	0	0	0
Stable or growth	1063	439	164	92	6	1764
Pathologic diagnosis						
Lung cancer	9	20	27	15	2	73
AAH, ABP*	2	3	0	0	0	5
Nonmalignant diagnosis	1	1	1	1	0	4
<b>Total</b>	<b>1404</b>	<b>616</b>	<b>234</b>	<b>131</b>	<b>7</b>	<b>2392</b>

**Frequency of Nonsolid Nodules and Diagnoses of Lung Cancer Identified in 485 of 64 677 Annual Repeat Screenings according to Size of Largest Nonsolid Nodule**

Parameter	Diameter of Largest Nodule					Total
	<6 mm	6–9 mm	10–14 mm	15–30 mm	≥31 mm	
Resolved or decreased	125	113	53	28	3	322
Lung cancer	0	0	0	0	0	0
Stable or growth	89	42	29	3	0	163
Pathologic diagnosis						
Lung cancer	2	4	5	0	0	11
AAH, ABP*	0	1	1	0	0	2
Nonmalignant diagnoses	0	1	1	0	0	2
<b>Total</b>	<b>214</b>	<b>155</b>	<b>82</b>	<b>31</b>	<b>3</b>	<b>485</b>

**Newly seen nonsolid decrease more frequently  
(322/485, 66%)**

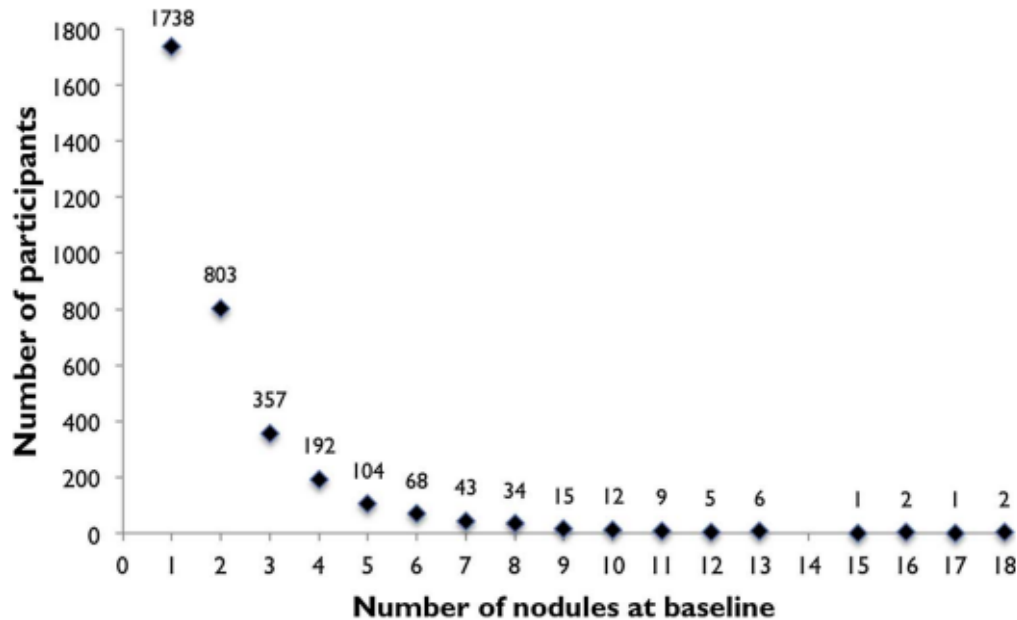
**than those seen at baseline screening**

**(628/2392, 26%)**

# Considerations for Multiple Nodules

## Data from the NELSON trial

- Among screenees with a positive nodule, 48.5% had multiple nodules
- Multiplicity did not affect lung cancer probability
- Each nodule should be assessed separately

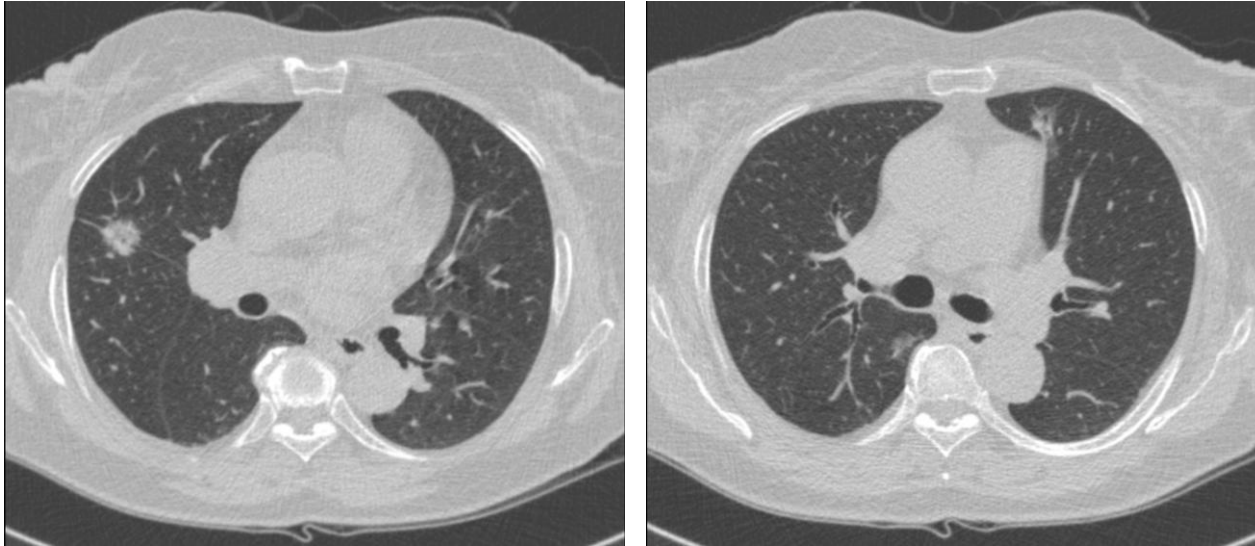


Nodule Count	Participants	Total Cancer	Lung cancer probability	95% CI	Baseline Cancer	Lung cancer probability Baseline
1 Nodule	1746	62	3.6%	2.8–4.6%	30	1.7%
2 Nodules	800	33	4.1%	2.9–5.8%	17	2.1%
3 Nodules	354	17	4.8%	2.9–7.7%	6	1.7%
4 Nodules	191	12	6.3%	3.4–11.0%	7	4.2%
> 4 Nodules	301	10	3.3%	1.7–6.2%	6	2.0%
<b>Total</b>	<b>3392</b>	<b>134</b>	<b>4.1%</b>	<b>3.4–4.8%</b>	<b>66</b>	<b>2.0%</b>

# Considerations for Multiple Subsolid Nodules

## In cases of malignancy

- Most multifocal nodules are synchronous primary adenocarcinomas
- Each nodule should be evaluated as primary lung cancer



**TABLE 3.** Summary of *EGFR* and *K-ras* Gene Combinations in the Multiple GGOs

No. of Lesion	<i>n</i>	Case No.
Identical combination ( <i>n</i> = 6)		
<i>EGFR</i> and <i>K-ras</i> wild type	6	5, 8, 9, 14, 19, 22
Different combination ( <i>n</i> = 18)		
<i>EGFR</i> exon19 del and wild type	9	1, 2, 6, 10, 12, 15, 20, 24
<i>EGFR</i> exon19 del/ <i>K-ras</i> PM (G12V) and wild type	1	13
<i>EGFR</i> exon19 del and exon 21PM(L858R)	4	4, 7, 21, 23
<i>EGFR</i> exon19 del/exon18 PM (F712L) and wild type	1	3
<i>EGFR</i> exon 21 PM (L858R) and wild type	1	18
<i>EGFR</i> exon 21 PM (L858R) and exon 18/21 PM (G724S/L861Q)	1	17
<i>K-ras</i> mutation and wild type	1	16

# Diagnostic Tissue Sampling

- **Nonsurgical biopsy**

- Transthoracic needle biopsy
- Conventional bronchoscopy and EBUS -> **Not optimal for peripheral nodules**
- Advanced image-guided bronchoscopy

- **Surgical biopsy**

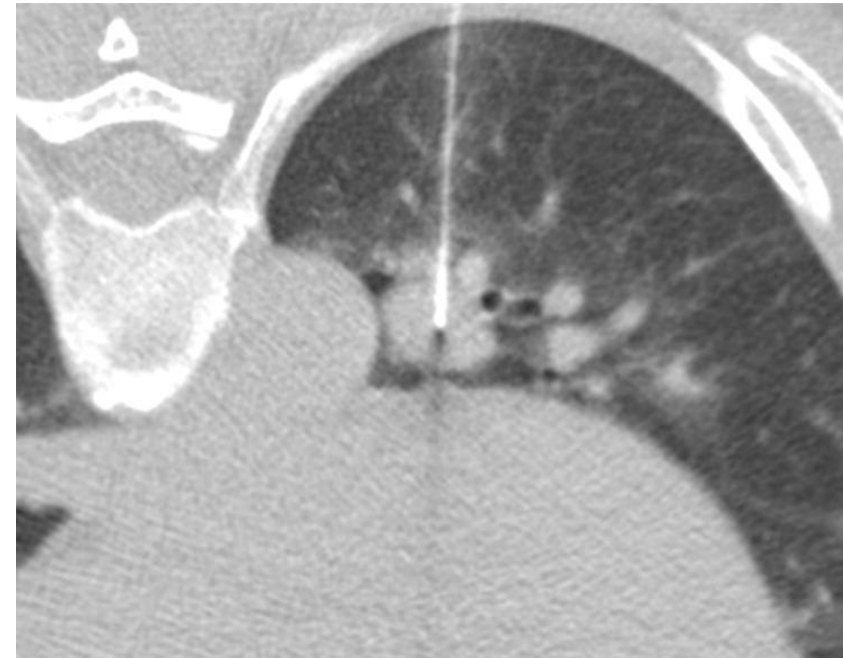
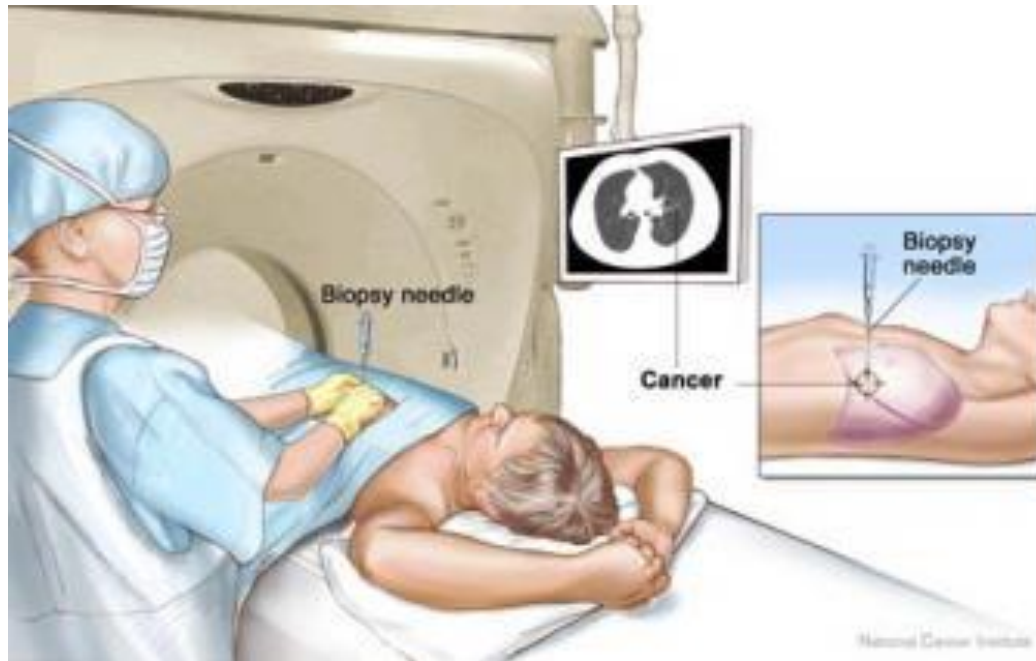
- Sublobar resection with VATS or RATS preferred

Sensitivity of flexible bronchoscopy for peripheral lung lesions

<b>All Methods:</b>		<b>&lt; 2 cm LESION</b>				<b>&gt; 2 cm LESION</b>			
<b>First Author</b>	<b>Year</b>	<b>N</b>	<b>Pos</b>	<b>Neg</b>	<b>Sens</b>	<b>N</b>	<b>Pos</b>	<b>Neg</b>	<b>Sens</b>
Gasparini <sup>110</sup>	1995	195	82	113	<b>42</b>	300	169	131	<b>56</b>
Hattori <sup>76</sup>	1971	17	13	4	<b>76</b>	182	150	32	<b>82</b>
Baaklini <sup>88</sup>	2000	16	4	12	<b>25</b>	135	93	42	<b>69</b>
Wallace <sup>122</sup>	1982	65	3	62	<b>5</b>	78	24	54	<b>31</b>
Bandoh <sup>130</sup>	2003	25	8	17	<b>32</b>	72	50	22	<b>69</b>
Radke <sup>106</sup>	1979	21	6	15	<b>29</b>	76	49	27	<b>64</b>
Naidich <sup>121</sup>	1988	15	4	11	<b>27</b>	46	26	20	<b>57</b>
Trkanjec <sup>129</sup>	2003	17	9	8	<b>53</b>	33	27	6	<b>82</b>
McDougall <sup>105</sup>	1981	9	1	8	<b>11</b>	36	21	15	<b>58</b>
Stringfield <sup>107</sup>	1977	3	1	2	<b>33</b>	26	13	13	<b>50</b>
<b>Summary</b>		<b>383</b>	<b>131</b>	<b>252</b>	<b>34</b>	<b>984</b>	<b>622</b>	<b>362</b>	<b>63</b>

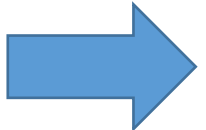
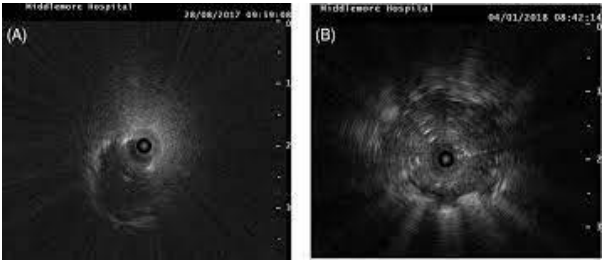
# Transthoracic Needle Biopsy

- Conducted under local anesthesia
- High diagnostic yield
- Notable rate of complications (pneumothorax rate = ~ 25%)
- Certain lesions are inaccessible



# Advanced Guided Bronchoscopy

- Lower risk of complications (pneumothorax rate <5%)
- Sequential mediastinal staging with EBUS is available



Electromagnetic Navigation Bronchoscopy

Radial EBUS

Robotic Bronchoscopy

# Paradigm Shift Towards Modern Bronchoscopy as Standard of Care

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Navigational Bronchoscopy or Transthoracic Needle Biopsy for Lung Nodules

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Randomization of 258 peripheral pulmonary lesions that can either be performed by transthoracic approach and guided bronchoscopy

Table 2. Primary and Secondary Outcomes.

Outcome	Navigational Bronchoscopy (N=121)	Transthoracic Needle Biopsy (N=113)	Difference (95% CI)*
<b>Primary outcome: diagnostic accuracy — no./total no. (%)†</b>			
Accurate	94/119 (79.0)	81/110 (73.6)	5.4 (-6.5 to 17.2)‡
Inaccurate	25/119 (21.0)	29/110 (26.4)	—
False negative	0	4/110 (3.6)	—
Initially nondiagnostic	25/119 (21.0)	25/110 (22.7)	—
Lost to follow-up	2/121 (1.7)	3/113 (2.7)	—

Table 3. Safety Outcomes.

Outcome	Navigational Bronchoscopy (N=121)	Transthoracic Needle Biopsy (N=113)	Difference (95% CI)*	P Value
<b>Any complication — no. (%)</b>				
Pneumothorax				
Any grade — no. (%)	4 (3.3)	32 (28.3)	25.0 (15.3 to 34.8)	<0.001
Grade 1 or 2‡	3 (2.5)	19 (16.8)	14.3 (6.0 to 22.6)	<0.001
Grade 3 or 4‡	1 (0.8)	13 (11.5)	10.7 (3.7 to 17.6)	<0.001
Median duration of chest tube in place (IQR) — days	1.0 (1.0 to 1.0)	1.0 (1.0 to 2.0)	0	0.65
Respiratory failure resulting in hospital admission — no. (%)	1 (0.8)	1 (0.9)	0.1 (-2.5 to 2.4)	0.96
Hemorrhage resulting in medical intervention — no. (%)	0	0	0	—
Acute coronary syndrome — no. (%)	1 (0.8)	0	0.8 (-1.6 to 3.3)	0.33

# Take home

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- **Lung cancer screening** can save lives, and efforts are focused on **expanding its reach to maximize the net benefit**
- The need for screening **never-smokers may be present**, but the **evidence of benefit** remains **insufficient**
- **Different types of nodules** can be detected in **different situations**, requiring **individualized management** and use of various guidelines
- **Invasive diagnosis** of a nodule should be guided by the **probability of malignancy**, expected **yield and safety** of testing, and **patient preferences**

***Thank you for your attention***

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