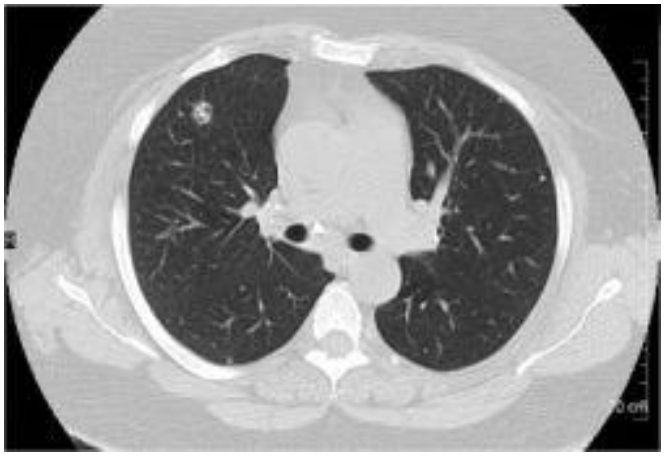
Screening for Lung Cancer: New Guidelines, Old Problems



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

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

The National Lung Screening Trial Research Team*

Robert Schilz DO, PhD
Associate Professor of Medicine
Interim Chief of the Division of Pulmonary, Critical Care and Sleep Medicine
University Hospitals Case Medical Center

Answer Key for Media – Delete for final set

- Question #1 – Answer is 4 (none of the above)
- Question #2 – Answer is 1 (A and C are correct)
- Question #3 – Answer is 3 (CT scan in 3-6 months)

Pretest Question #1:
Which of the following is/are true?

A. The incidence of fatal lung cancer is increasing
B. The incidence of teen smoking incidence is increasing
C. 5 year survival once lung cancer has been diagnosed has improved in the last 10 years
D. Second hand smoke is the second most important risk factor for lung cancer in the United States.

1) A and C
2) B and D
3) A, B and C
4) None are correct
5) All are correct

Pretest Question #2:

Which of the following is/are true regarding the current recommendations for lung cancer screening?

A. Patients < 55 years old should not be screened
B. The threshold for smoking risk is 25 pk/years
C. Patients that have quit > 15 years should not be screened
D. Expected nodules on screened populations are < 15%

1) A and C
2) B and D
3) A, B and C
4) None are correct
5) All are correct

Pretest Question #3:

Which of the following is the best test to order for an 7 mm nodule in a person with low-intermediate lung cancer risk?

A. PET scanning
B. CT guided transthoracic needle biopsy
C. CT scan in 3-6 months
D. Video Assisted Thoracoscopic (VATS) Biopsy
E. EMN guided bronchoscopic biopsy

Disclosures

- No disclosures relevant to this topic

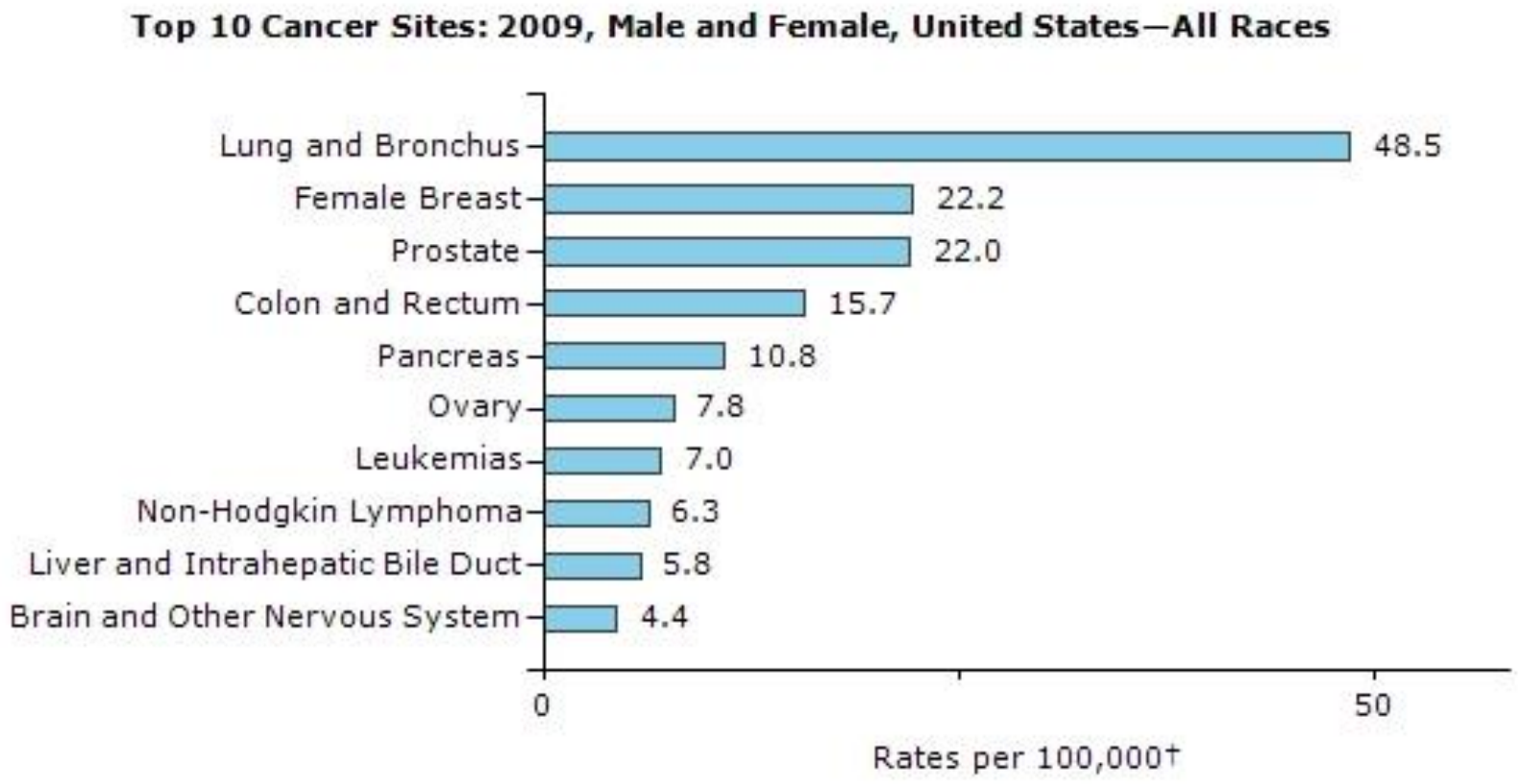
Objectives

- At the end of the lecture, the participants should be able to:
  - Identify current trends in lung cancer mortality
  - Understand common risk factors for lung cancer
  - Discuss current lung cancer screening recommendations
  - Understand potential negative impacts of screening
    - Incidence of benign findings
    - Consequence of diagnostic procedures
  - Outline a practical work up of pulmonary nodules that occur outside of screening as incidental findings utilizing current cancer diagnosis and treatment guidelines

Section 1

EPIDEMIOLOGY OF LUNG CANCER

US Age Adjusted Cancer Death Rates



U.S. Cancer Statistics Working Group. *United States Cancer Statistics: 1999–2009 Incidence and Mortality Web-based Report*. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2013

The Lifetime Probability of Developing Cancer for Men, 2007-2009*

Site	Risk
All sites†	1 in 2
Prostate	1 in 6
Lung and bronchus	1 in 13
Colon and rectum	1 in 19
Urinary bladder‡	1 in 26
Melanoma §	1 in 35
Non-Hodgkin lymphoma	1 in 43
Kidney	1 in 49
Leukemia	1 in 63
Oral Cavity	1 in 66
Stomach	1 in 92

* For those free of cancer at beginning of age interval.

† All sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.

‡ Includes invasive and in situ cancer cases

§ Statistic for white men.

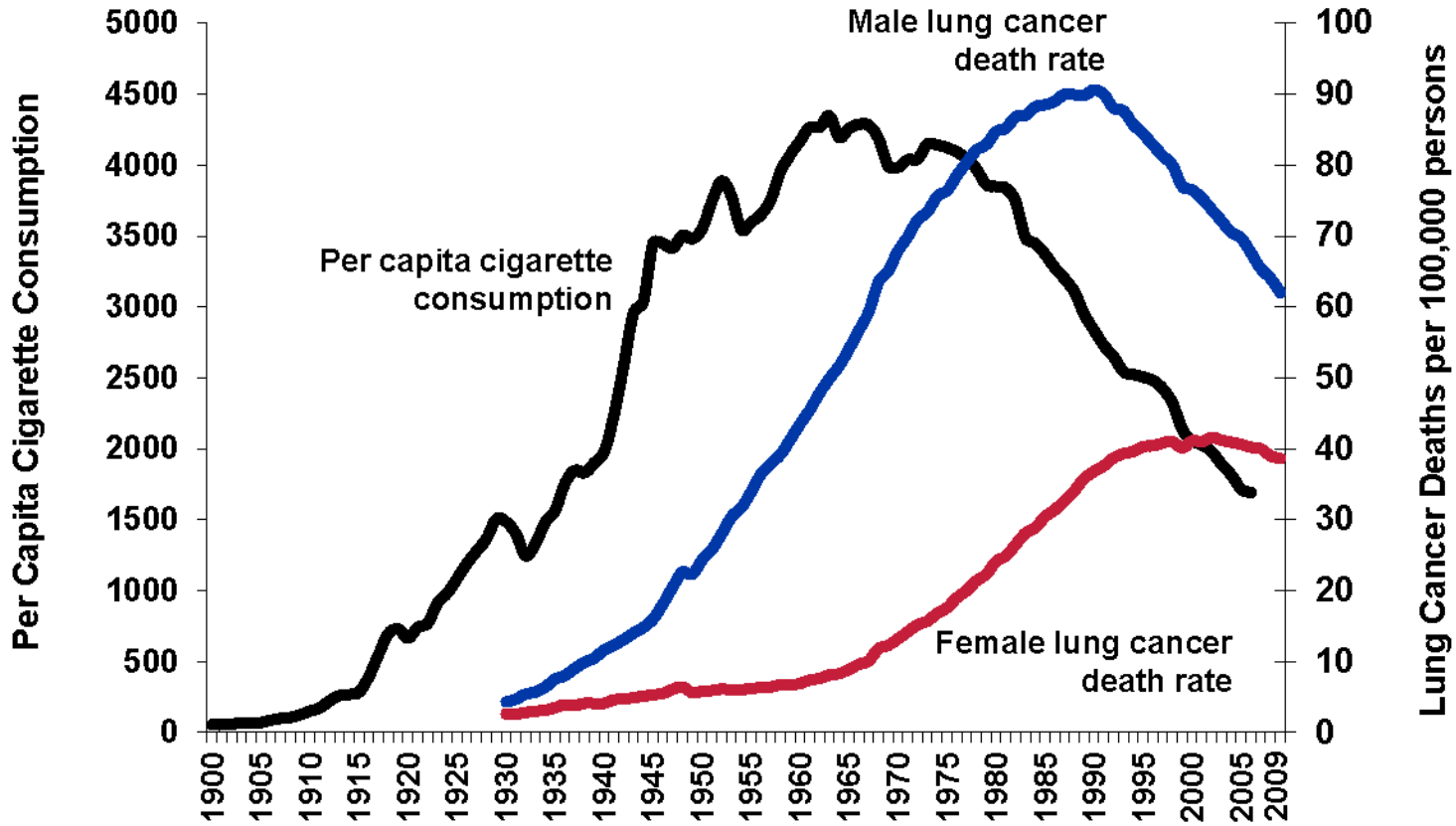
Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.6.1 Statistical Research and Applications Branch, National Cancer Institute, 2012.

The Lifetime Probability of Developing Cancer for Women, 2007-2009*

Site	Risk
All sites†	1 in 3
Breast	1 in 8
Lung & bronchus	1 in 16
Colon & rectum	1 in 21
Uterine corpus	1 in 38
Non-Hodgkin lymphoma	1 in 52
Urinary bladder‡	1 in 87
Melanoma §	1 in 54
Ovary	1 in 72
Pancreas	1 in 69
Uterine cervix	1 in 147

* For those free of cancer at beginning of age interval.
† All sites exclude basal and squamous cell skin cancers and in situ cancers except urinary bladder.
‡ Includes invasive and in situ cancer cases
§ Statistic for white women.
Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.6.1 Statistical Research and Applications Branch, National Cancer Institute, 2012.

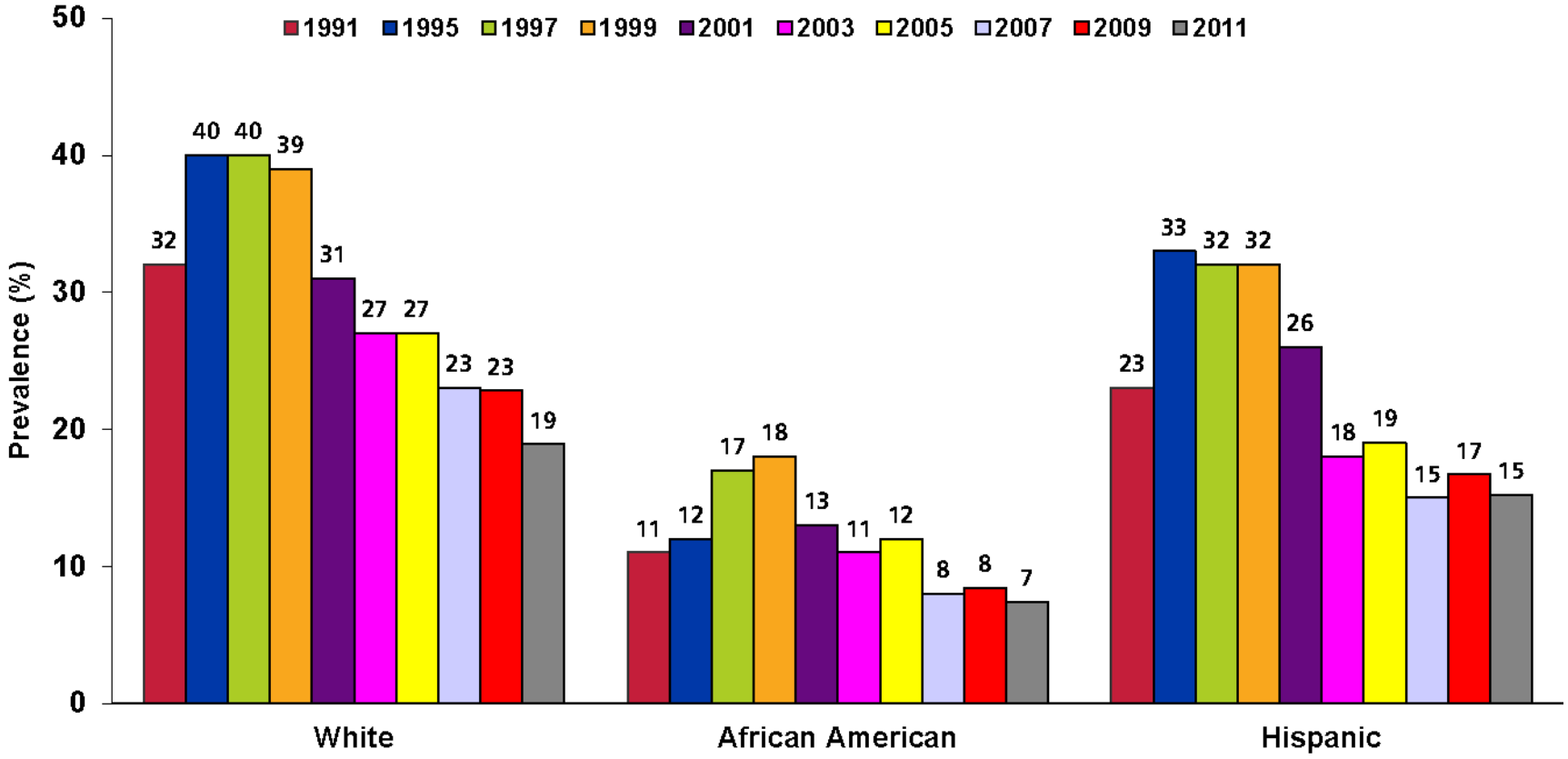
Trends in Tobacco Use and Lung Cancer Death Rates* in the US



*Age-adjusted to 2000 US standard population.

Source: Death rates: US Mortality Data, 1960-2009, US Mortality Volumes, 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention. Cigarette consumption: US Department of Agriculture, 1900-2007.

Trends in Cigarette Smoking* among Female High School Students, US, 1991-2011



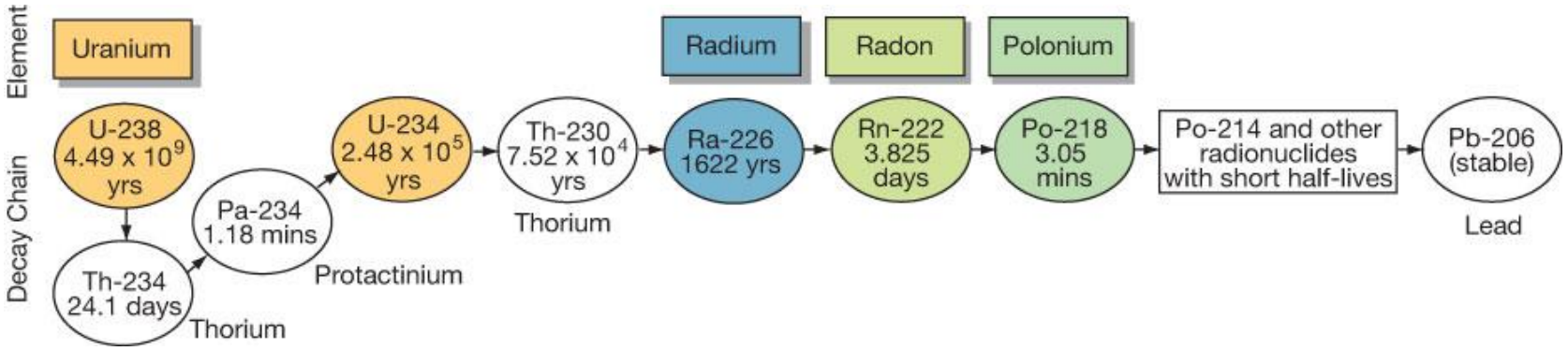
*Smoked cigarettes on one or more of the 30 days preceding the survey. Whites and African Americans are non-Hispanic.

Source: Youth Risk Behavior Surveillance System, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 2012.

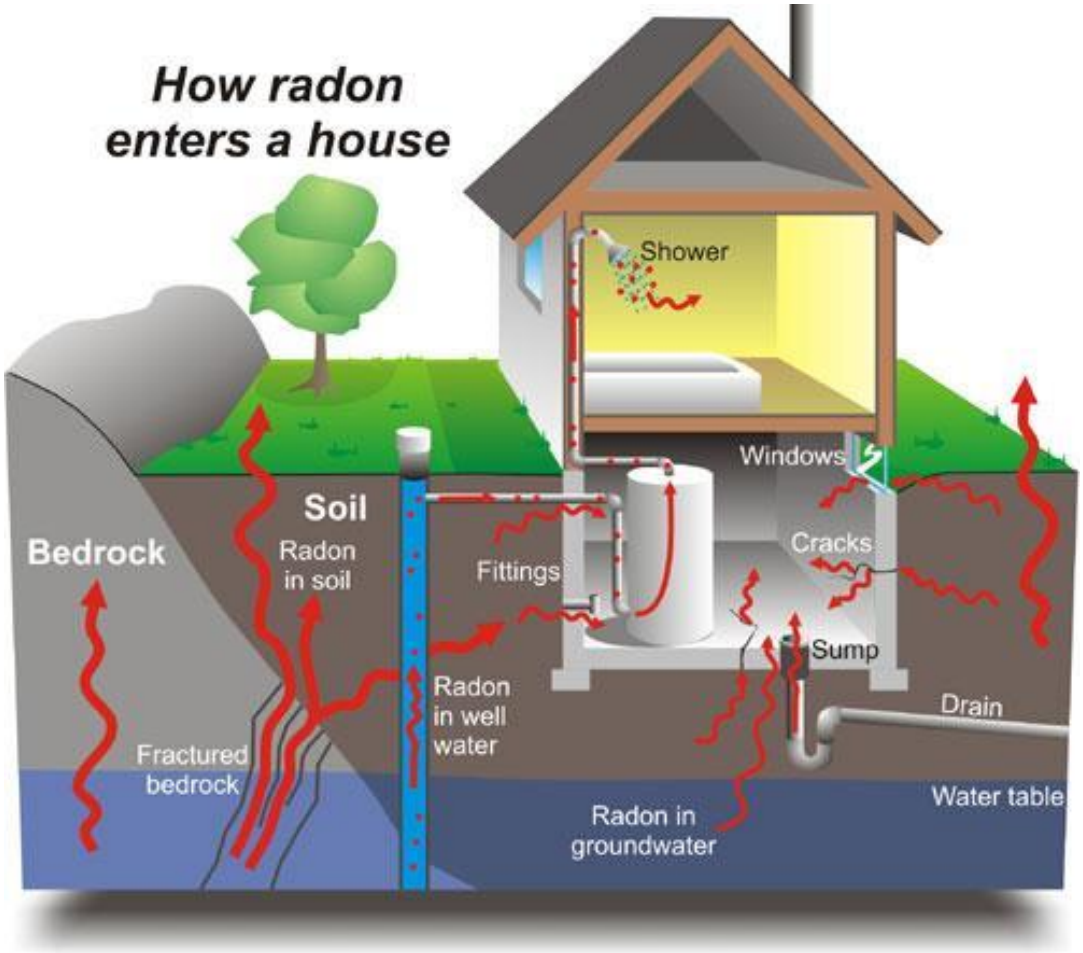
Risk Factors for Lung Cancer

- Smoking (87-90% of All US Cases)
- Radon (10-16%)
- Occupational Exposures
  - Asbestos, coal smoke, soot, diesel fumes, silica
  - Arsenic, beryllium, cadmium, cobalt, nickel
  - Painting (1.4 RR increase)
- Family History / Genetic Susceptibility
  - 15q24 susceptibility locus (Amos et al., 2008; Hung et al., 2008)
  - T790M mutations, which occur in the epidermal growth factor receptor kinase (Jackman et al. Clin Cancer Res 2009.15:5267-5273)
- Second Hand Smoke (1%) (RR estimates from 1.15 -1.29)
- COPD and IPF

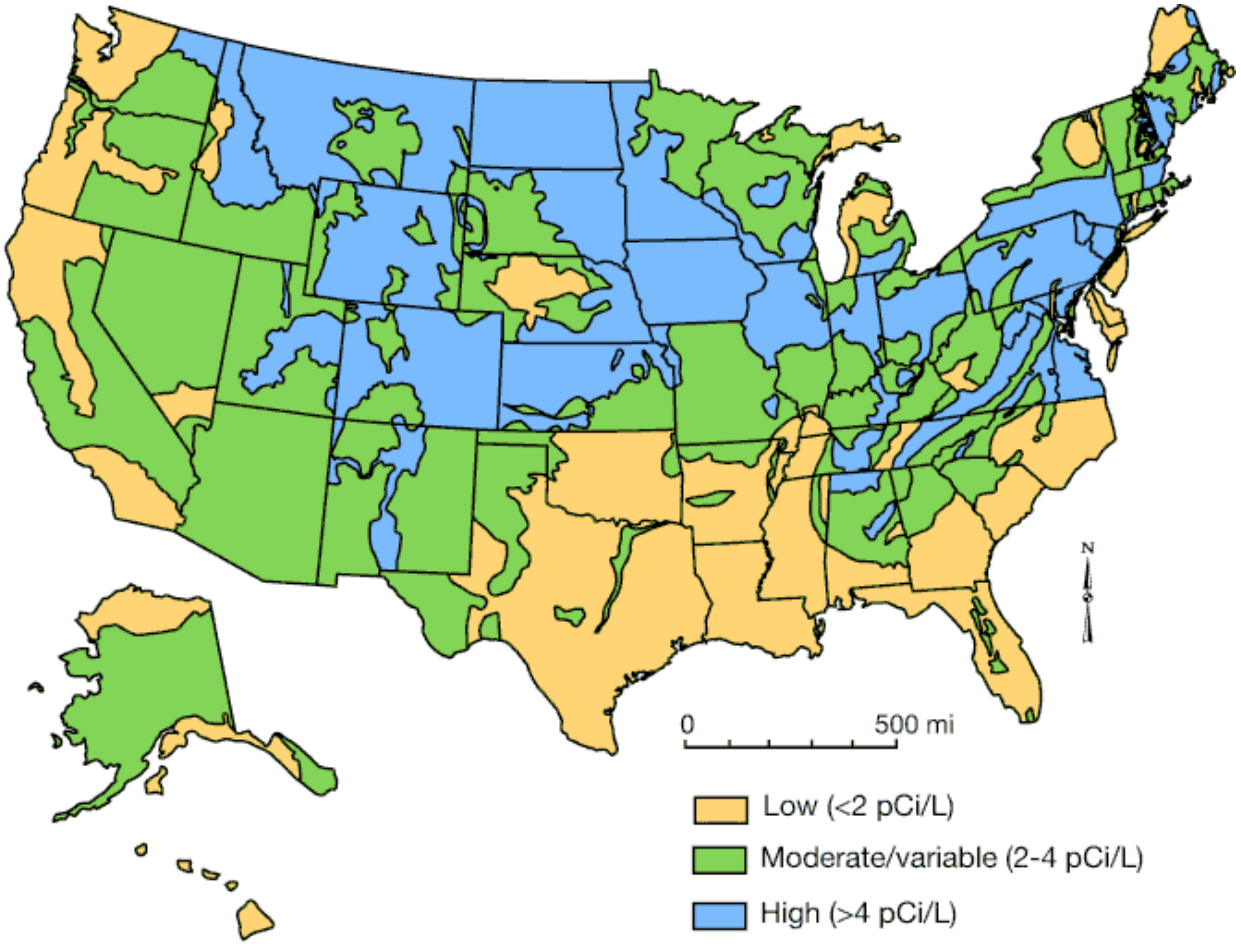
Radon Facts



- Radon is odorless and colorless
- Comes from natural decay of uranium
- Radon per se does not pose significant direct effects but decays to stable lead and other radioactive particles that attach easily to dust particles and deposit in lungs
- Alpha radiation then causes DNA damage etc.


How radon enters a house
Shower
Windows
Soil
Bedrock
Radon in soil
Fittings
Cracks
Sump
Drain
Radon in well water
Fractured bedrock
Water table
Radon in groundwater

Estimated Radon Potential Based on Geological Survey



Information from US Geological Survey, 1996

Radon Risk in Non-Smokers*

Radon Level	If 1,000 people who never smoked were exposed to this level over a lifetime*...	The risk of cancer from radon exposure compares to**...	WHAT TO DO:
20 pCi/L	About 36 people could get lung cancer	35 times the risk of drowning	Fix your home
10 pCi/L	About 18 people could get lung cancer	20 times the risk of dying in a home fire	Fix your home
8 pCi/L	About 15 people could get lung cancer	4 times the risk of dying in a fall	Fix your home
4 pCi/L	About 7 people could get lung cancer	The risk of dying in a car crash	Fix your home
2 pCi/L	About 4 person could get lung cancer	The risk of dying from poison	Consider fixing between 2 and 4 pCi/L
1.3 pCi/L	About 2 people could get lung cancer	(Average indoor radon level)	(Reducing radon levels below 2 pCi/L is difficult.)
0.4 pCi/L		(Average outdoor radon level)	

*Estimated Risk in Smokers is approximately 7-10 fold higher
Lifetime risk of lung cancer deaths from EPA Assessment of Risks from Radon in Homes (EPA 402-R-03-003)

Trends in Five-year Relative Cancer Survival Rates (%), 1975-2008

Site	1975-1977	1987-1989	2002-2008
All sites	49	56	68
Breast (female)	75	84	90
Colon	51	61	65
Leukemia	34	43	58
Lung & bronchus	12	13	17
Melanoma	82	88	93
Non-Hodgkin lymphoma	47	51	71
Ovary	36	38	43
Pancreas	2	4	6
Prostate	68	83	100
Rectum	48	58	68
Urinary bladder	73	79	80

5-year relative survival rates based on patients diagnosed from 2002 to 2008, all followed through 2009.
Source: *SEER Cancer Statistics Review 1975-2009 (*SEER 9 registries), National Cancer Institute, 2012.

Summary and Implication of Lung Cancer Demographics

- Lung cancer is the number one cancer killer in the US for both men and women
- Primary US risk factor is smoking
- Overall incidence of lung cancer decreasing likely due to decreased smoking in previous decades
- *Mortality once diagnosed is not changed*
- Screening of at risk populations should be important if effective

Section 2

NATIONAL LUNG SCREENING TRIAL

General Statements about Screening

- Purpose is to prevent the development of advanced stage disease and death in asymptomatic individuals
- Disease-specific mortality is gold standard for evaluation of screening efficacy
- Screening effectiveness is best described using absolute risk reduction

Computed Tomography Scanning in the Chest

320 Detector CT Scanner

Current CT Use

- Uncontrasted CT
  - Nodules
  - Lung Disease
- CT Pulmonary Angiogram
- Cardiac CT
  - Calcium Scoring
  - Angiography
- Screening?

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

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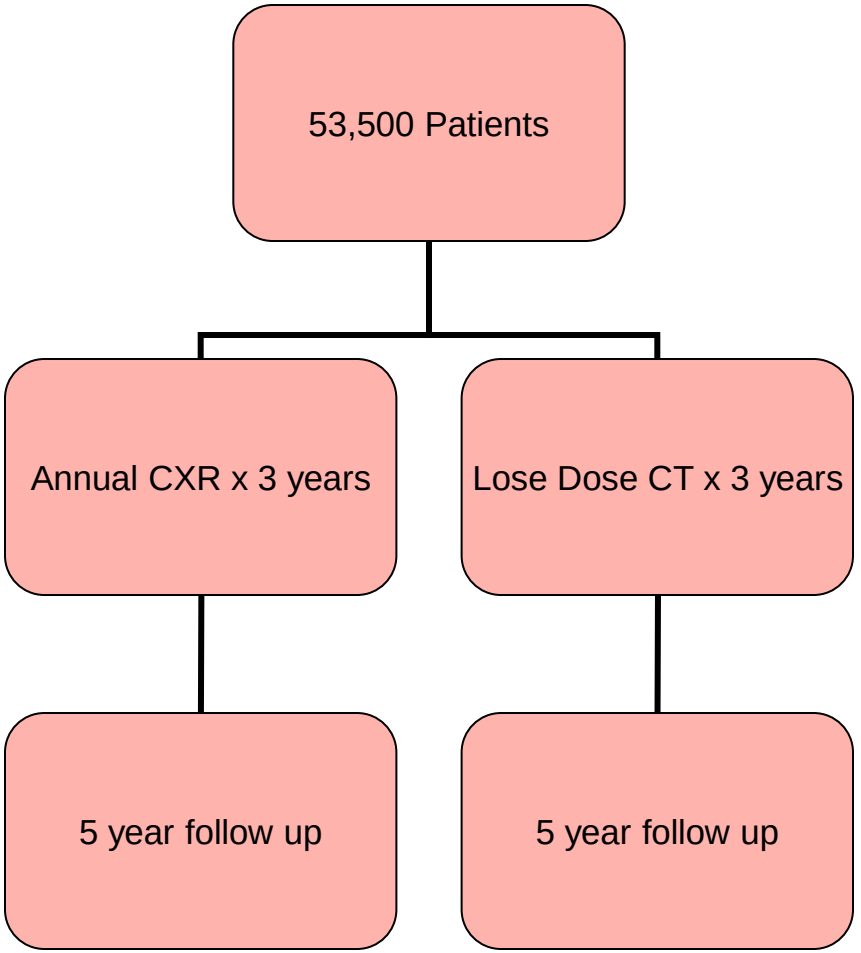
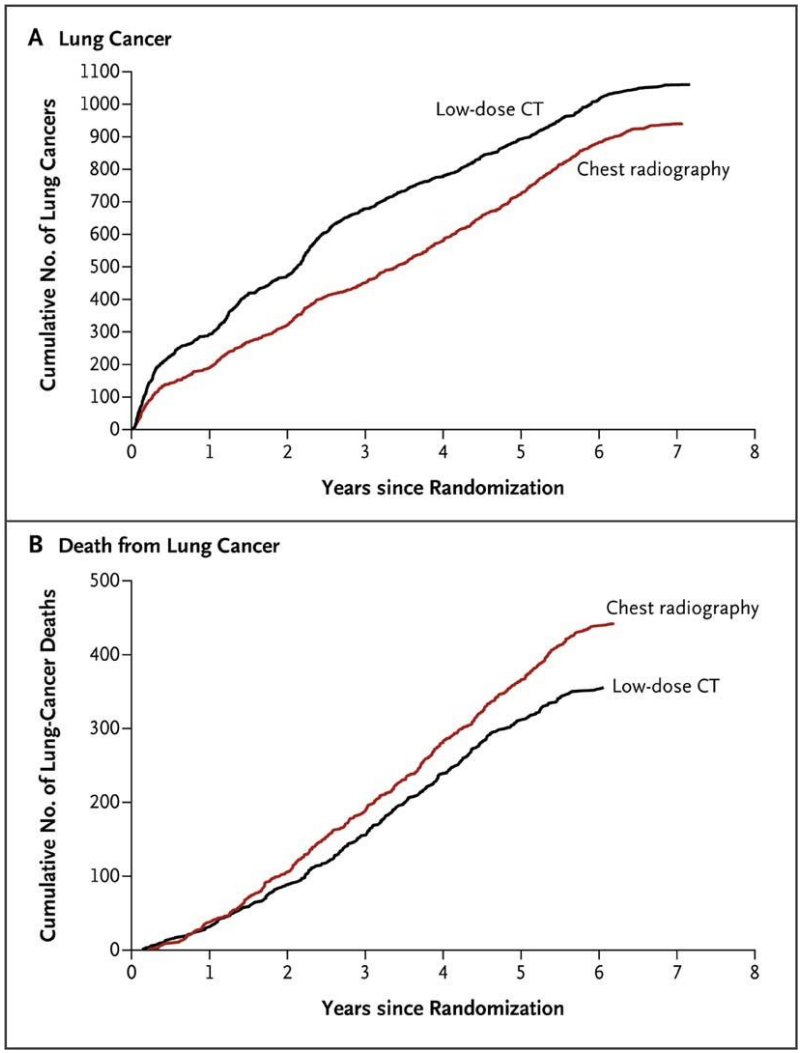
National Lung Screening Trial (NCI 2010)

- Utility of low dose CT screening for detection of lung cancer
- High risk patients for lung cancer
  - Current or previous smoker
  - >30 pack/year history
- Results
  - 354 vs 442 deaths from lung cancer
  - 20% reduction in lung cancer deaths in CT
- Caveats
  - **Cost**
  - **False (+) consequences**
  - **Radiation effects**



The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

Cumulative Numbers of Lung Cancers and of Deaths from Lung Cancer in the National Lung Screening Trial



The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

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

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)							
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)
Histologic type								
Bronchioloalveolar carcinoma	95/646 (14.7)	1/44 (2.3)	14/358 (3.9)	110/1048 (10.5)	13/276 (4.7)	1/135 (0.7)	21/520 (4.0)	35/931 (3.8)
Adenocarcinoma	258/646 (39.9)	8/44 (18.2)	114/358 (31.8)	380/1048 (36.3)	112/276 (40.6)	37/135 (27.4)	179/520 (34.4)	328/931 (35.2)
Squamous-cell carcinoma	136/646 (21.1)	13/44 (29.5)	94/358 (26.3)	243/1048 (23.2)	70/276 (25.4)	24/135 (17.8)	112/520 (21.5)	206/931 (22.1)
Large-cell carcinoma	28/646 (4.3)	3/44 (6.8)	10/358 (2.8)	41/1048 (3.9)	12/276 (4.3)	10/135 (7.4)	21/520 (4.0)	43/931 (4.6)
Non–small-cell carcinoma or other§	75/646 (11.6)	4/44 (9.1)	52/358 (14.5)	131/1048 (12.5)	40/276 (14.5)	30/135 (22.2)	88/520 (16.9)	158/931 (17.0)
Small-cell carcinoma	49/646 (7.6)	15/44 (34.1)	73/358 (20.4)	137/1048 (13.1)	28/276 (10.1)	32/135 (23.7)	99/520 (19.0)	159/931 (17.1)
Carcinoid	5/646 (0.8)	0	1/358 (0.3)	6/1048 (0.6)	1/276 (0.4)	1/135 (0.7)	0	2/931 (0.2)

* The denominators represent only cancers with a known stage or known histologic type. The stage was not known in the case of 14 cancers after a positive screening test and 6 after no screening in the low-dose CT group and in the case of 4 cancers after a positive screening test, 2 after a negative screening test, and 6 after no screening in the radiography group. The histologic type was not known for 3 cancers after a positive screening test and 9 after no screening in the low-dose CT group and for 3 cancers after a positive screening test, 2 after a negative screening test, and 5 after no screening in the radiography group.

† Negative screening tests included tests that revealed either minor or clinically significant abnormalities that were not suspicious for lung cancer.

‡ The 892 lung cancers in participants with no screening test included 35 in participants who were never screened, 802 that were diagnosed during the post-screening period, and 55 in participants who were due for a screening test.

§ The 289 lung cancers in this category (in the two groups combined) included 28 adenosquamous carcinomas, 6 sarcomatoid carcinomas, 55 unclassified carcinomas, 1 anaplastic-type carcinoma, 1 carcinosarcoma, and 198 coded only as "non–small-cell carcinoma."

The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

Complications after the Most Invasive Screening-Related Diagnostic Evaluation Procedure, According to Lung-Cancer Status.

Table 4. Complications after the Most Invasive Screening-Related Diagnostic Evaluation Procedure, According to Lung-Cancer Status.*

Complication	Lung Cancer Confirmed					Lung Cancer Not Confirmed				
	Thoracotomy, Thoracoscopy, or Mediastinoscopy	Bron-choscopy	Needle Biopsy	No Invasive Procedure	Total	Thoracotomy, Thoracoscopy, or Mediastinoscopy	Bronchoscopy	Needle Biopsy	No Invasive Procedure	Total
	number (percent)					*number (percent)*				
Low-dose CT group										
Positive screening results for which diagnostic information was complete	509 (100.0)	76 (100.0)	33 (100.0)	31 (100.0)	649 (100.0	164 (100.0)	227 (100.0)	66 (100.0)	16,596 (100.0)	17,053 (100.0)
No complication	344 (67.6)	69 (90.8)	26 (78.8)	26 (83.9)	465 (71.6)	138 (84.1)	216 (95.2)	59 (89.4)	16,579 (99.9)	16,992 (99.6)
At least one complication	165 (32.4)	7 (9.2)	7 (21.2)	5 (16.1)	184 (28.4)	26 (15.9)	11 (4.8)	7 (10.6)	17 (0.1)	61 (0.4)
Most severe complication classified as major	71 (13.9)	2 (2.6)	0	2 (6.5)	75 (11.6)	9 (5.5)	2 (0.9)	0	1 (<0.1)	12 (0.1)
Most severe complication classified as intermediate	81 (15.9)	5 (6.6)	7 (21.2)	2 (6.5)	95 (14.6)	13 (7.9)	9 (4.0)	6 (9.1)	16 (0.1)	44 (0.3)
Most severe complication classified as minor	13 (2.6)	0	0	1 (3.2)	14 (2.2)	4 (2.4)	0	1 (1.5)	0	5 (<0.1)
Death within 60 days after most invasive diagnostic procedure†	5 (1.0)	4 (5.3)	1 (3.0)	0	10 (1.5)	2 (1.2)	4 (1.8)	0	5 (<0.1)	11 (0.1)
Radiography group										
Positive screening results for which diagnostic information was complete	189 (100.0)	46 (100.0)	29 (100.0)	15 (100.0)	279 (100.0	45 (100.0)	46 (100.0)	24 (100.0)	4,559 (100.0)	4,674 (100.0)
No complication	130 (68.8)	42 (91.3)	28 (96.6)	14 (93.3)	214 (76.7)	38 (84.4)	46 (100.0)	23 (95.8)	4,551 (99.8)	4,658 (99.7)
At least one complication	59 (31.2)	4 (8.7)	1 (3.4)	1 (6.7)	65 (23.3)	7 (15.6)	0	1 (4.2)	8 (0.2)	16 (0.3)
Most severe complication classified as major	22 (11.6)	1 (2.2)	0	1 (6.7)	24 (8.6)	1 (2.2)	0	0	3 (0.1)	4 (0.1)
Most severe complication classified as intermediate	32 (16.9)	2 (4.3)	1 (3.4)	0	35 (12.5)	6 (13.3)	0	1 (4.2)	2 (<0.1)	9 (0.2)
Most severe complication classified as minor	5 (2.6)	1 (2.2)	0	0	6 (2.2)	0	0	0	3 (0.1)	3 (0.1)
Death within 60 days after most invasive diagnostic procedure†	4 (2.1)	5 (10.9)	1 (3.4)	1 (6.7)	11 (3.9)	0	0	0	3 (0.1)	3 (0.1)

* In the case of multiple evaluation procedures of the same type, the earliest is included. Complications that occurred before the most invasive procedure are not included. Participants could have up to three positive screening tests and therefore may be included up to three times in any row. Columns of procedures are arranged in decreasing order of invasiveness. In the case of the first procedure column, thoracotomy was considered to be more invasive than thoracoscopy, which was considered to be more invasive than mediastinoscopy.

† For patients who did not undergo an invasive procedure, deaths were included if they occurred within 60 days after the positive screening result.

The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

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

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)
Positive screening results with complete diagnostic follow-up information	7049 (100.0)	6740 (100.0)	3913 (100.0)	17,702 (100.0)	2348 (100.0)	1456 (100.0)	1149 (100.0)	4953 (100.0)
Any diagnostic follow-up	6369 (90.4)	3866 (57.4)	2522 (64.5)	12,757 (72.1)	2176 (92.7)	1078 (74.0)	957 (83.3)	4211 (85.0)
Clinical procedure	5089 (72.2)	3190 (47.3)	2151 (55.0)	10,430 (58.9)	1414 (60.2)	723 (49.7)	658 (57.3)	2795 (56.4)
Imaging examination	5717 (81.1)	2520 (37.4)	2009 (51.3)	10,246 (57.9)	2010 (85.6)	968 (66.5)	906 (78.9)	3884 (78.4)
Chest radiography	1284 (18.2)	613 (9.1)	650 (16.6)	2,547 (14.4)	867 (36.9)	381 (26.2)	365 (31.8)	1613 (32.6)
Chest CT	5153 (73.1)	2046 (30.4)	1608 (41.1)	8,807 (49.8)	1546 (65.8)	745 (51.2)	712 (62.0)	3003 (60.6)
FDG PET or FDG PET–CT	728 (10.3)	350 (5.2)	393 (10.0)	1,471 (8.3)	179 (7.6)	105 (7.2)	113 (9.8)	397 (8.0)
Percutaneous cytologic examination or biopsy	155 (2.2)	74 (1.1)	93 (2.4)	322 (1.8)	83 (3.5)	37 (2.5)	52 (4.5)	172 (3.5)
Transthoracic	120 (1.7)	60 (0.9)	74 (1.9)	254 (1.4)	67 (2.9)	31 (2.1)	43 (3.7)	141 (2.8)
Extrathoracic	39 (0.6)	17 (0.3)	24 (0.6)	80 (0.5)	20 (0.9)	6 (0.4)	13 (1.1)	39 (0.8)
Bronchoscopy	306 (4.3)	178 (2.6)	187 (4.8)	671 (3.8)	107 (4.6)	56 (3.8)	62 (5.4)	225 (4.5)
With neither biopsy nor cytologic testing	126 (1.8)	95 (1.4)	99 (2.5)	320 (1.8)	45 (1.9)	19 (1.3)	32 (2.8)	96 (1.9)
With biopsy or cytologic testing	194 (2.8)	95 (1.4)	102 (2.6)	391 (2.2)	74 (3.2)	40 (2.7)	36 (3.1)	150 (3.0)
Surgical procedure	297 (4.2)	197 (2.9)	219 (5.6)	713 (4.0)	121 (5.2)	51 (3.5)	67 (5.8)	239 (4.8)
Mediastinoscopy or mediastinotomy	60 (0.9)	32 (0.5)	25 (0.6)	117 (0.7)	22 (0.9)	12 (0.8)	21 (1.8)	55 (1.1)
Thoracoscopy	82 (1.2)	56 (0.8)	96 (2.5)	234 (1.3)	22 (0.9)	11 (0.8)	20 (1.7)	53 (1.1)
Thoracotomy	197 (2.8)	148 (2.2)	164 (4.2)	509 (2.9)	96 (4.1)	44 (3.0)	44 (3.8)	184 (3.7)
Other procedures	168 (2.4)	96 (1.4)	63 (1.6)	327 (1.8)	55 (2.3)	33 (2.3)	34 (3.0)	122 (2.5)

* 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 positron-emission 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).

24% of surgical procedures yielded a benign result

The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

Additional Findings and Implications in National Lung Screening Trial

Additional Findings	Implications
39.1% of the LDCT group had at least 1 positive finding	Significant potential burden of workup and liability
24% of surgical procedures yielded a benign result	Non-trivial “unnecessary” procedures
367/1060 cancers in the LDCT group were diagnosed either after the screening period or in patients missing screening.	Do additional years of screening need to be done?
Number needed to screen to prevent 1 death was 320	Can this change/cost?

The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

Current Recommendations for Lung Cancer Screening*

- WHO?
  - "Current or former smokers ages 55-74 in good health"
  - "with at least a 30 pack-year history"
- WHAT?
  - Low dose helical CT (LDCT)
  - Organized screening program that has experience in LDCT
- HOW and WHERE?
  - ***Clinicians with access to high-volume, high quality lung cancer screening and treatment centers*** should initiate a discussion about lung cancer screening with apparently healthy patients ages 55-74 who have at least a 30 pack-year smoking history, and who currently smoke or have quit within the past 15 years.
  - A process of informed and shared decision making with a clinician related to the potential benefits, limitations, and harms associated with screening for lung cancer with LDCT should occur before any decision is made to initiate lung cancer screening.
  - Smoking cessation counseling remains a high priority for clinical attention in discussions with current smokers, who should be informed of their continuing risk of lung cancer.
  - ***Screening should not be viewed as an alternative to smoking cessation***

*(American College of Chest Physicians, American Society of Clinical Oncology, the American Thoracic Society, the National Comprehensive Cancer Network (NCCN) and the American Lung Association)

Section 3

IMPLEMENTATION OF GUIDELINES

Lung Cancer Screening in Primary Care

Indentify

- Age 55-74
- > 30 pk/year
- Active Smoker or quit < 15 years

Counsel

- Likelihood of (+) study – high likelihood of false (+)
- Need for follow-up
- Likely with procedures
- Risk imaging

Refer

- Multidisciplinary lung cancer screening program
- Low dose CT protocol
- Have full range of diagnostic and therapeutic options

AMA Review of Current Evidence Leading to Guidelines: Summary of Additional Concerns

- For individuals who have accumulated fewer than 30 pack-years of smoking or are either younger than 55 years or older than 74 years, or individuals who quit smoking more than 15 years ago, and for individuals with severe comorbidities that would preclude potentially curative treatment, limit life expectancy, or both, we suggest that CT screening should not be performed.
- Counseling should include a complete description of potential benefits and harms (as outlined in the full guideline text) so the individual can decide whether to undergo LDCT screening.
- The fear and anxiety that patients can experience once there is even a slight suspicion of lung cancer highlights the need for careful education of LDCT participants and the need for carefully worded scan interpretations.
- Screening should be conducted in a center similar to those where the NLST was conducted, with multidisciplinary coordinated care and a comprehensive process for screening, image interpretation, management of findings, and evaluation and treatment of potential cancers.

JAMA. 2012;307(22):2418-2429. doi:10.1001/jama.2012.5521

CHEST

From: Evaluation of Individuals With Pulmonary Nodules: When Is It Lung Cancer?Evaluation of Individuals With Pulmonary Nodules: Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Chest. 2013;143(5_suppl):e93S-e120S. doi:10.1378/chest.12-2351

	Potential Benefits		Potential Harms	
Procedure	Outcome	% Frequency	Outcome	% Frequency
Surgical wedge resection	• Prompt, definitive diagnosis	96-100	• Physical complications	5
	• Avoid inconvenience and potential complications of nonsurgical biopsy, if malignant		Persistent air leak	3-5
			Pneumonia	1-8
			Death	0.5
	• Reassurance if specific benign diagnosis established		• Worsened lung function (short term)	Varies
	• Proceed to lobectomy if frozen section reveals malignancy		• Unnecessary surgery if nodule turns out to be benign disease	Varies
	• Acquisition of tissue for molecular testing		• Uncertain benefits of surgery if very-slow-growing tumor	
Bronchoscopy with biopsy	• Definitive preoperative cancer diagnosis in many cases		• Physical complications	
			Bleeding	2-5
	Fluoroscope-guided	~ 30	Any pneumothorax	2-4
	EBUS, ENB ± VBN guided	60-90	Death	<<1
	• Reassurance if specific benign diagnosis established		• May still require surgery if biopsy result is nondiagnostic or shows cancer	
	• Acquisition of tissue for molecular testing		• False negative biopsy results	30-70
			• False positive biopsy results	Rare
CT scan-guided needle lung biopsy	• Definitive preoperative cancer diagnosis in many cases		• Physical complications	
			Bleeding	1
	≤ 15 mm	~ 70-80	Any pneumothorax	15
	> 15 mm	~ 90	Pneumothorax needing chest tube	6-7
			Death	<<1
	• Reassurance if specific benign diagnosis established		• May still require surgery if biopsy is non-diagnostic or shows cancer	
	• Acquisition of tissue for molecular testing		• False negative	10-30
			• False positive	Rare
Radiologic surveillance (serial CT ± PET scans)	• Avoid physical complications		• Radiation exposure	
	• Discovering other incidental findings that are clinically important		• Other incidental findings that prompt evaluation but turn out to be of little clinical significance	
			• Psychologic toll of uncertainty	
			(eg, moderate to severe distress)	24
			• Overdiagnosis of indolent cancers	
			• Delayed cancer diagnosis and treatment, with uncertain effect on outcomes	
No further evaluation	• Avoid physical complications		• Psychologic toll of uncertainty	
	• Avoid radiation exposure		• Delayed or missed cancer diagnosis	
	• Avoid overdiagnosis of indolent cancers that do not need treatment			

[Section 4.3] Balance sheet of pros and cons of alternatives for evaluation and management of pulmonary nodule. EBUS = endobronchial ultrasound; ENB = electromagnetic navigation bronchoscopy; VBN = virtual bronchoscopy navigation.

Comparison of Radiography Doses

Study	Radiation Amt.	Comparable Background Exposure	Common Risk* Comparators
Radiography-Chest	0.1 mSv	10 days	Smoking 9 cigarettes, driving 23 miles
Computed Tomography (CT) -Chest Low Dose	1.5 mSv	6 months	
Computed Tomography (CT)-Chest	7 -10 mSv	2 years	

Projected Number of Future Cancers That Could Be Related to CT Scans Performed in the United States in 2007, According to CT Scan Type

Table 2. Projected Number of Future Cancers That Could Be Related to CT Scans Performed in the United States in 2007, According to CT Scan Type[a]

		No. of Cancers					
		Females		Males		Total	
Type of CT Scan	No. of Scans,[b] Millions (%)	Mean (95% UL)	%	Mean (95% UL)	%	Mean (95% UL)	%
Head	18.7 (33)	1900 (500-4400)	11	2100 (600-4300)	19	4000 (1100-8700)	14
Chest	7.1 (12)	3100 (1400-6100)	17	1000 (500-2000)	9	4100 (1900-8100)	14
Cervical spine	1.8 (3)	700 (200-1700)	4	300 (100-600)	3	1000 (300-2300)	3
Thoracic spine	0.3 (<1)	200 (80-300)	1	50 (20-100)	<1	250 (10-400)	1
Lumbar spine	2.2 (4)	700 (300-1600)	4	500 (200-1100)	5	1200 (400-2700)	4
Abdomen/pelvis	18.3 (32)	8500 (4200-15 000)	47	5500 (2600-9600)	50	14 000 (6900-25 000)	48
CTA chest	2.3 (4)	2200 (1100-4200)	12	500 (200-900)	5	2700 (1300-5000)	9
CTA other[c]	1.6 (3)	400 (200-900)	2	500 (200-1100)	5	900 (300-1900)	3
Whole body	0.3 (<1)	300 (100-500)	2	100 (50-200)	1	400 (200-600)	1
Colonography	0.2 (<1)	70 (30-120)	<1	50 (20-100)	<1	120 (60-200)	<1
Calcium scoring	0.6 (1)	150 (70-300)	1	30 (10-60)	<1	180 (80-400)	<1
Other[d]	3.5 (6)	10 (3-20)	<1	20 (1-80)	<1	30 (4-100)	<1
Total[e]	56.9 (100)	18 000 (9000-28 000)	100	11 000 (6000-16 000)	100	29 000 (15 000-45 000)	100

Abbreviations: CT, computed tomographic; CTA, CT angiography; UL, uncertainty limits.
[a] The numbers are presented to a maximum of 2 significant figures.
[b] Excluding CT scans with a diagnosis code of cancer or that were performed in the last 5 years of life.
[c] Abdomen, pelvis, and head.
[d] Primarily extremity CT scans and bone mineral density.
[e] Totals are not equal to the sum for males and females because of rounding.

Berrington de Gonzalez, A. et al. Arch Intern Med 2009;169:2071-2077.

From: Screening for Lung CancerScreening for Lung Cancer: Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Chest. 2013;143(5_suppl):e78S-e92S. doi:10.1378/chest.12-2350

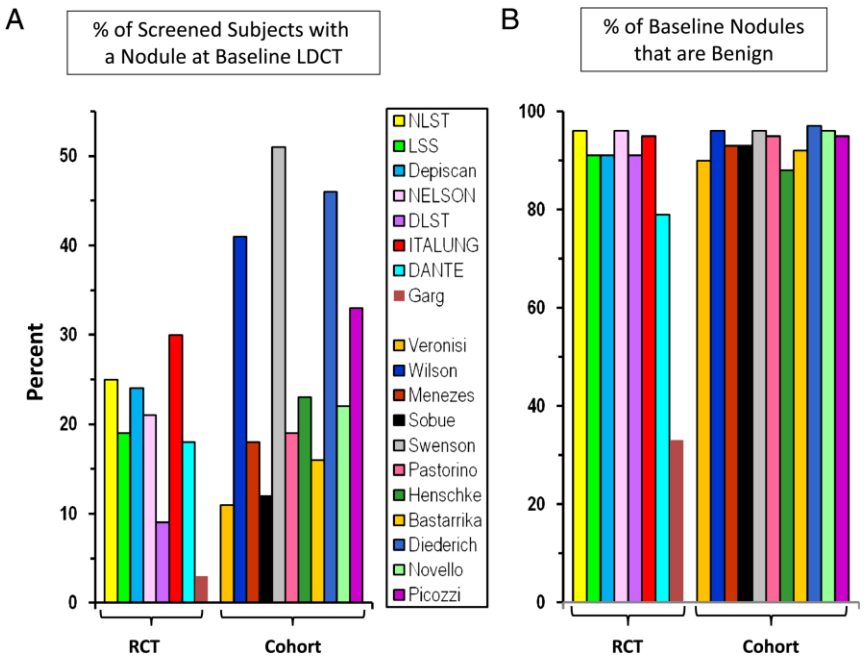
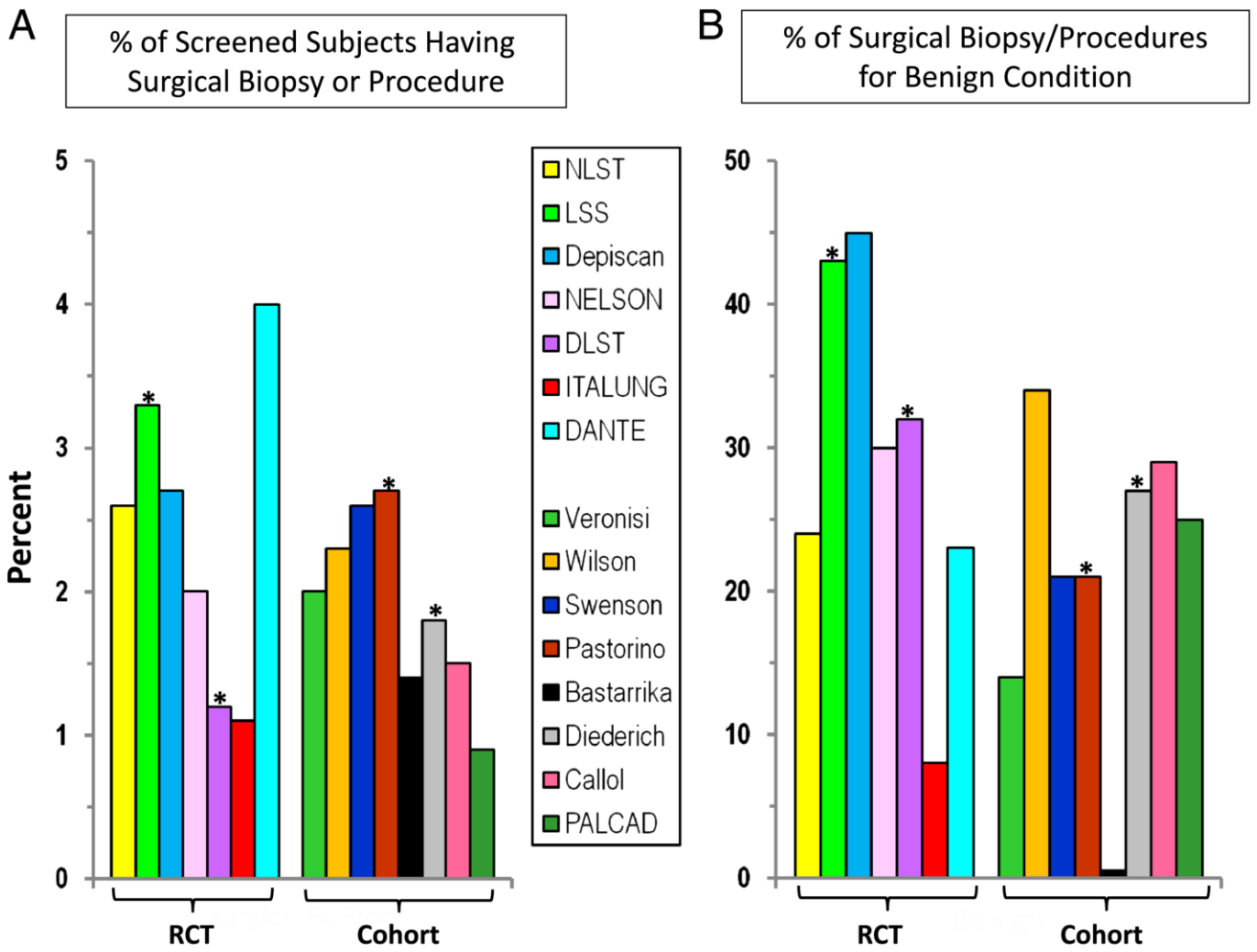


Figure Legend:

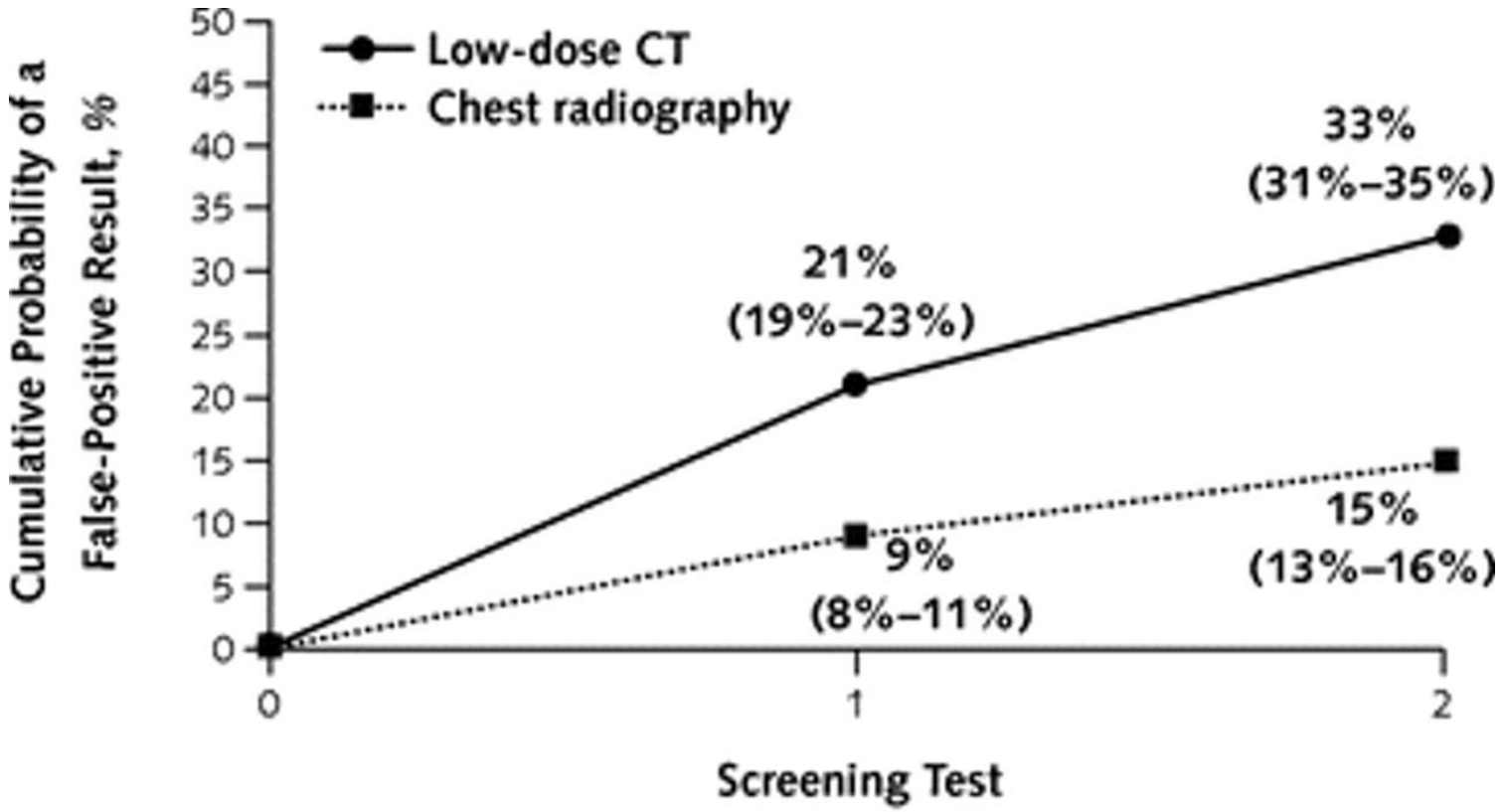
[Section 3.3] Frequency of screening participants with a nodule detected on baseline LDCT scan and percentage of nodules eventually proven to be benign in LDCT studies. A, Percentage of all participants screened with LDCT imaging who had a nodule detected at baseline screening. B, Percentage of patients with a lesion identified at baseline LDCT screening that was eventually found to be benign. Cohort = single-arm cohort studies of LDCT; DANTE = Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays Trial; DLST = Danish Lung Cancer Screening Trial; LDCT = low-dose CT; LSS = Lung Screening Study; NELSON = Dutch Belgian Randomised Lung Cancer Screening Trial; RCT = randomized controlled trial. See Figure 1 legend for expansion of other abbreviation.

Frequency of patients undergoing a surgical biopsy or procedure and percentage of such surgical biopsies or procedures done for a benign lesion in LDCT studies



Chest. 2013;143(5_suppl):e78S-e92S. doi:10.1378/chest.12-2350

Cumulative probability (95% CI) of a false-positive result for a person who participated in a lung cancer screening program over several years.The cumulative probability is for the first false-positive result received from a number of tests done.



Participants at risk, *n*		
Low-dose CT	1610	1114
Chest radiography	1580	1183

Croswell J M et al. Ann Intern Med 2010;152:505-512

Section 4

BEYOND THE GUIDELINES

Diagnosis and Management of Lung Cancer, 3rd edition: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Chest **May 2013; 143(5_suppl): 1S-512S**

Management algorithm for individuals with solid nodules measuring 8 to 30 mm in diameter

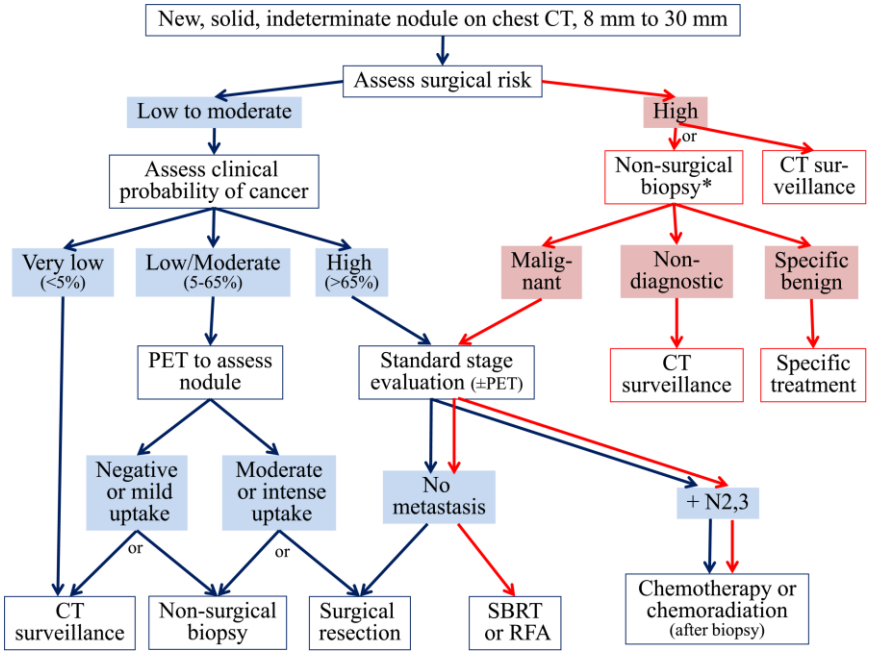


Figure Legend:

[Sections 4.0, 4.3] Management algorithm for individuals with solid nodules measuring 8 to 30 mm in diameter. Branches indicate steps in the algorithm following nonsurgical biopsy. *Among individuals at high risk for surgical complications, we recommend either CT scan surveillance (when the clinical probability of malignancy is low to moderate) or nonsurgical biopsy (when the clinical probability of malignancy is moderate to high). RFA = radiofrequency ablation; SBRT = stereotactic body radiotherapy.

Chest. 2013;143(5_suppl):e93S-e120S. doi:10.1378/chest.12-2351

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Chest. 2013;143(5_suppl):e93S-e120S. doi:10.1378/chest.12-2351

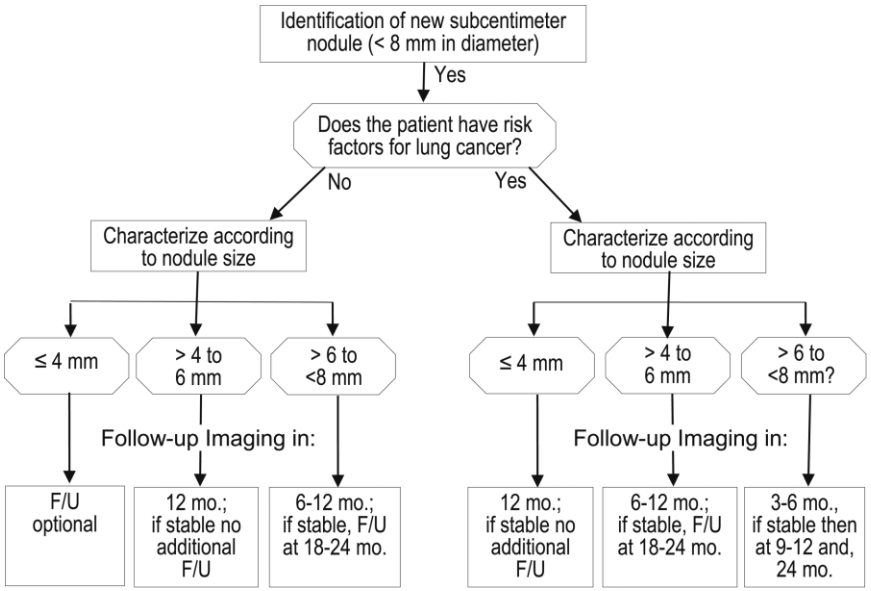

Figure Legend:

[Section 5.2] Management algorithm for individuals with solid nodules measuring < 8 mm in diameter. F/U =follow-up.

Components of a CT scan screening program as proposed by major organizations.

Components Recommended	ACCP LC III article[83]	Multi-society[a] guideline[2]	ACS[84]	IASLC[85]	AATS[86]	NCCN[59]	STS[87]
Multispecialty program	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Careful participant selection	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Participant Education/Counseling	Yes	Yes	Yes	-	-	Yes	Yes
Smoking cessation	Yes	Yes	Yes	Yes	Yes	Yes	Yes
CT with quality controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Defined process for scan interpretation	Yes	Yes	Yes	Yes	-	-	Yes
Defined intervention algorithm	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Quality metrics	Yes	Yes	-	Yes	-	-	Yes
Registry/data collection	Yes	Yes	-	Yes	Yes	-	Yes
Ongoing research participation	Yes	Yes	-	Yes	Yes	-	Yes
Video-Assisted Thoracic Surgery	Yes	-	-	Yes	Yes	-	Yes
Demonstration Project needed	Yes	Yes	-	Yes	-	-	-

ACS = American Cancer Society; ASCO = American Society of Clinical Oncologists; ATS = American Thoracic Society; IASLC = International Association for the Study of Lung Cancer; LC III = Lung Cancer Guidelines (3rd ed); NCCN = National Comprehensive Cancer Network.

[a]ACCP, ASCO, and ATS.

Chest. 2013;143(5_suppl):e78S-e92S. doi:10.1378/chest.12-2350

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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		-	-	+++	++++

Figure Legend:

[Section 4.0] Factors that influence choice between evaluation and management alternatives for indeterminate, solid nodules ≥ 8 to 30 mm in diameter. VATS = video-assisted thoracoscopic surgery.

From: Evaluation of Individuals With Pulmonary Nodules: When Is It Lung Cancer?Evaluation of Individuals With Pulmonary Nodules: Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Chest. 2013;143(5_suppl):e93S-e120S. doi:10.1378/chest.12-2351

Assessment Criteria	Probability of Malignancy		
	Low (< 5%)	Intermediate (5%- 65%)	High (> 65%)
Clinical factors alone (determined by clinical judgment and/or use of validated model)[a]	Young, less smoking, no prior cancer, smaller nodule size, regular margins, and/or non-upper-lobe location	Mixture of low and high probability features	Older, heavy smoking, prior cancer, larger size, irregular/spiculated margins, and/or upper-lobe location
FDG-PET scan results	Low-moderate clinical probability and low FDG-PET activity	Weak or moderate FDG-PET scan activity	Intensely hypermetabolic nodule
Nonsurgical biopsy results (bronchoscopy or TTNA)	Specific benign diagnosis	Nondiagnostic	Suspicious for malignancy
CT scan surveillance	Resolution or near-complete resolution, progressive or persistent decrease in size,[b] or no growth over ≥2 y (solid nodule) or ≥ 3-5 y (subsolid nodule)	NA	Clear evidence of growth

Figure Legend:

[Section 4.1] Assessment of the probability of malignancy. FDG = fluorodeoxyglucose; NA = not applicable; TTNA = transthoracic needle aspiration.

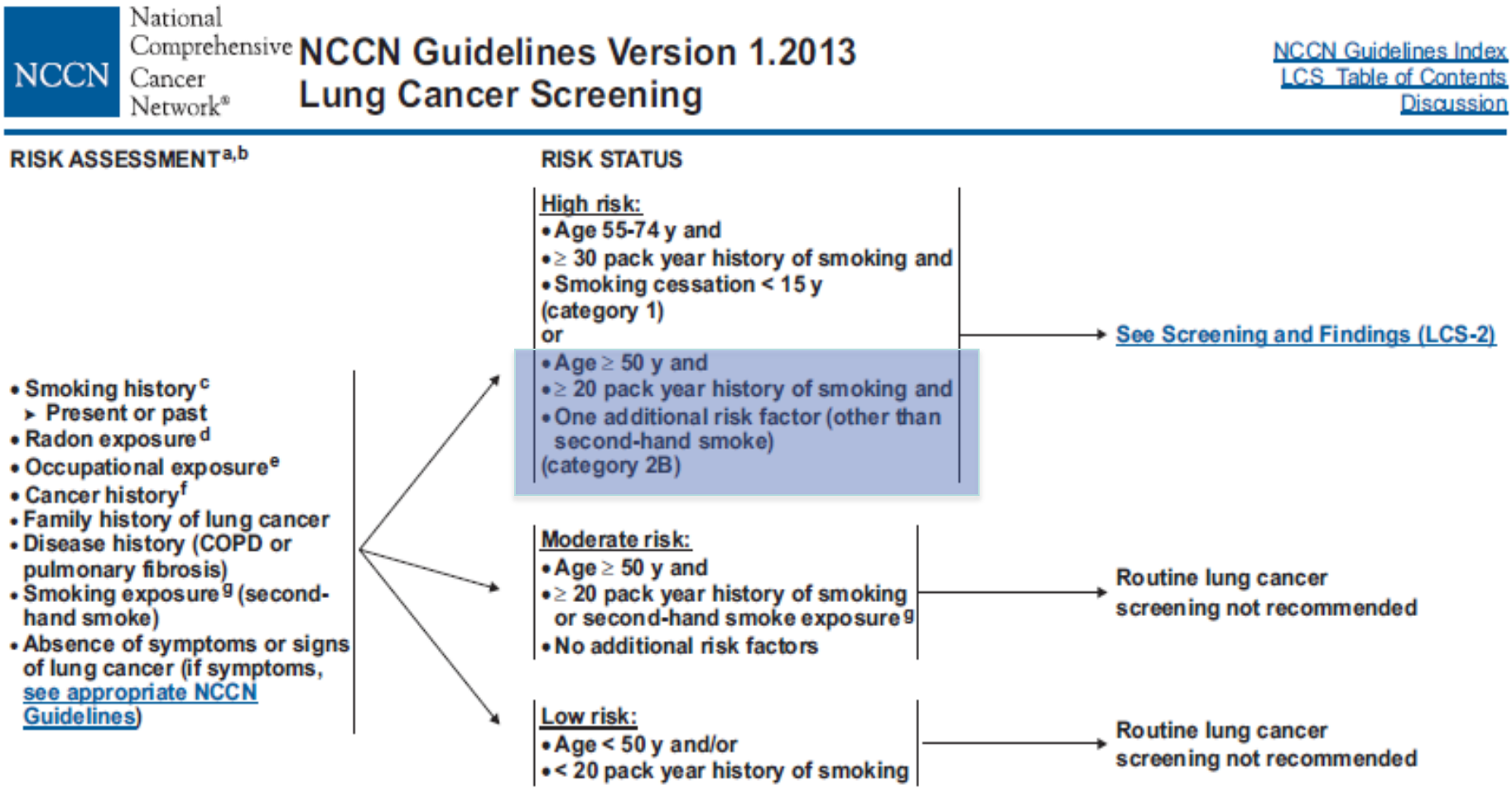
[a]In three studies, independent risk factors for malignancy included older age, current or former smoking, history of extrathoracic cancer > 5 y prior to nodule detection, larger nodule diameter, spiculated margins, and upper-lobe location[26]; older age, current or former smoking, shorter time since quitting smoking, and larger nodule diameter[27]; and high serum C-reactive protein level, high serum carcinoembryonic antigen level, absence of calcification, spiculation, and CT scan bronchus sign.[28] In another study, the combination of smooth or lobulated borders, irregular shape, and solid attenuation had a negative predictive value of 86%.[29]

[b]Approximately 20% of observed cancers have decreased in size at least at some point during the observation period.

Section 5

Additional Considerations and Confusions – Another Guideline !

NCCN Guidelines



Summary 1

- Epidemiology
  - Lung cancer remains #1 cancer killer in men and women
  - Cigarette smoking remains primary risk in spite of decreasing adult smoking
  - Radon exposure may be a significant issue for some in Ohio
  - Genetic predispositions are being evaluated

Summary 2

Lung Cancer Screening Recommendations (ACCP, AMA, ASCO, ATS)

- 55-74 years of age
- > 30 pk/year smoker either active or quit < 15 years
- Low dose chest CT screening protocol
- At least 3 successive years (stay tuned for more)
- Centers with multidisciplinary screening programs similar to study sites
- Counselling regarding false positives, procedures, anxiety and follow-up

Summary

Lung Cancer Screening Recommendations (NCCN) extend previous to:

- 50-55 years of age *and*:
- > 20 pk/year smoker *and:*
- One additional risk factor for lung cancer (not second-hand smoking)
  - Radon, asbestos, coal smoke, soot, diesel fumes, silica, arsenic, beryllium, cadmium, cobalt, nickel, irradiation
  - COPD or IPF
  - Family History
  - Select previous cancers (Head/neck, SCLCA)

Questions

Pretest Question #1:
Which of the following is/are true?

A. The incidence of fatal lung cancer is increasing
B. The incidence of teen smoking incidence is increasing
C. 5 year survival once lung cancer has been diagnosed has improved in the last 10 years
D. Second hand smoke is the second most important risk factor for lung cancer in the United States.

1) A and C
2) B and D
3) A, B and C
4) None are correct
5) All are correct

Pretest Question #2:

Which of the following is/are true regarding the current recommendations for lung cancer screening?

A. Patients < 55 years old should not be screened
B. The threshold for smoking risk is 25 pk/years
C. Patients that have quit > 15 years should not be screened
D. Expected nodules on screened populations are < 15%

1) A and C
2) B and D
3) A, B and C
4) None are correct
5) All are correct

Pretest Question #3:

Which of the following is/are true?

A. Screening CXR for lung cancer saves lives
B. Screening CXR for lung cancer detects early stage cancer
C. CT scanning of patients at high risk for lung cancer is recommended
D. CXR should be performed at intake if not available for nursing home residents

1) A and C
2) B and D
3) A, B and C
4) None are correct
5) All are correct