

Lung Cancer Screening

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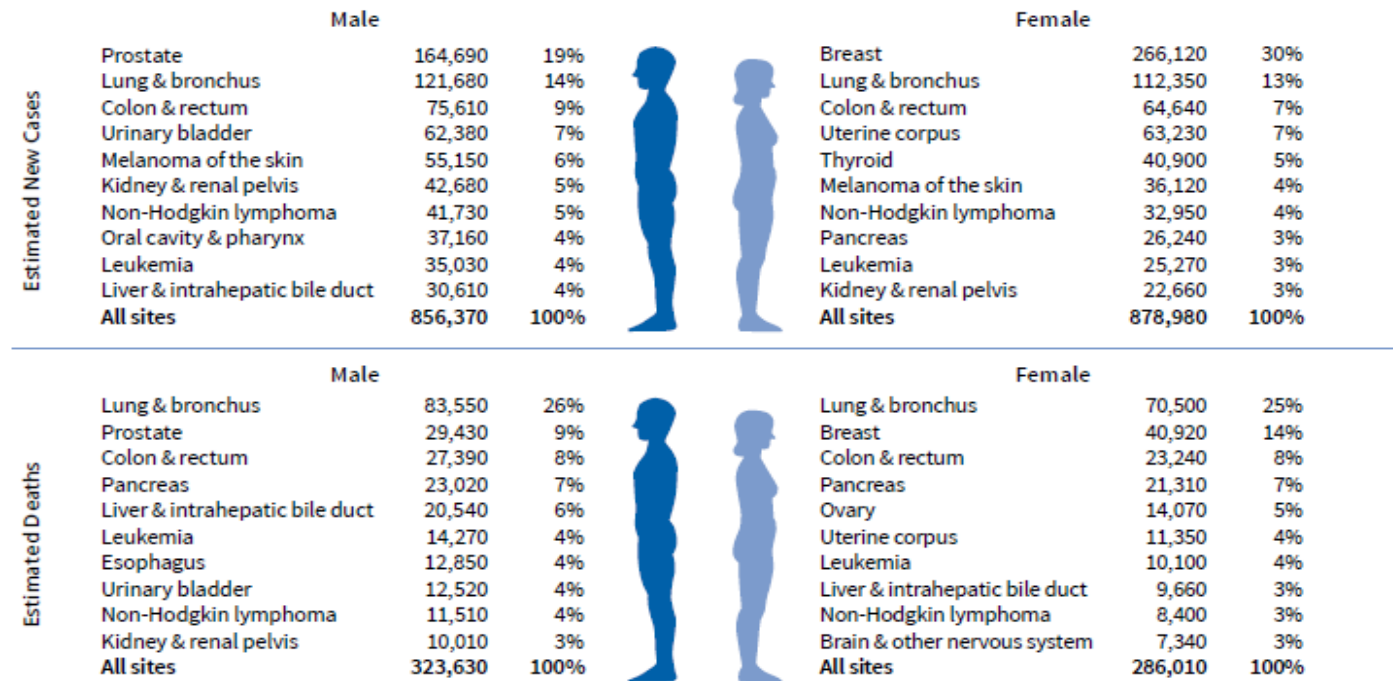
February 10, 2018

Disclosures

- * I have no financially relevant disclosures related to this presentation today.
- * I am a paid consultant for Nuvaira

Lung Cancer

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2018 Estimates



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Ranking is based on modeled projections and may differ from the most recent observed data.

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Lung Cancer

Table 8. Five-year Relative Survival Rates* (%) by Stage at Diagnosis, US, 2007-2013

	All stages	Local	Regional	Distant		All stages	Local	Regional	Distant
Breast (female)	90	99	85	27	Oral cavity & pharynx	65	84	64	39
Colon & rectum	65	90	71	14	Ovary	47	93	73	29
Colon	64	91	72	14	Pancreas	8	32	12	3
Rectum	67	88	70	15	Prostate	99	>99	>99	30
Esophagus	19	43	23	5	Stomach	31	67	31	5
Kidney†	74	93	67	12	Testis	95	99	96	73
Larynx	61	77	45	34	Thyroid	98	>99	98	56
Liver‡	18	31	11	3	Urinary bladder§	77	70	35	5
Lung & bronchus	18	56	29	5	Uterine cervix	67	92	57	17
Melanoma of the skin	92	99	63	20	Uterine corpus	81	95	69	16

*Rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 18 areas from 2007-2013, all followed through 2014. †Includes renal pelvis. ‡Includes intrahepatic bile duct. §Rate for in situ cases is 96%.

Local: an invasive malignant cancer confined entirely to the organ of origin. **Regional:** a malignant cancer that 1) has extended beyond the limits of the organ of origin directly into surrounding organs or tissues; 2) involves regional lymph nodes; or 3) has both regional extension and involvement of regional lymph nodes. **Distant:** a malignant cancer that has spread to parts of the body remote from the primary tumor either by direct extension or by discontinuous metastasis to distant organs, tissues, or via the lymphatic system to distant lymph nodes.

Source: Howlader N, Noone AM, Krapcho M, et al. (eds). SEER Cancer Statistics Review, 1975-2014, National Cancer Institute, Bethesda, MD, http://seer.cancer.gov/csr/1975_2014/, based on November 2016 SEER data submission, posted to the SEER website April 2017.

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Table 7. Trends in 5-year Relative Survival Rates* (%) by Race, US, 1975-2013

	All races			White			Black		
	1975-77	1987-89	2007-13	1975-77	1987-89	2007-13	1975-77	1987-89	2007-13
All sites	49	55	69	50	57	70	39	43	63
Brain & other nervous system	23	29	35	22	28	33	25	32	42
Breast (female)	75	84	91	76	85	92	62	71	83
Colon & rectum	50	60	66	50	60	67	45	52	59
Colon	51	60	65	51	61	67	45	52	56
Rectum	48	58	69	48	59	69	44	52	66
Esophagus	5	9	21	6	11	22	4	7	12
Hodgkin lymphoma	72	79	88	72	80	89	70	72	85
Kidney & renal pelvis	50	57	75	50	57	75	49	55	76
Larynx	66	66	63	67	67	65	58	56	50
Leukemia	34	43	64	35	44	65	33	35	58
Liver & intrahepatic bile duct	3	5	19	3	6	18	2	3	14
Lung & bronchus	12	13	20	12	13	20	11	11	17
Melanoma of the skin	82	88	94	82	88	94	57†	79†	69
Myeloma	25	27	51	24	27	51	29	30	52
Non-Hodgkin lymphoma	47	51	73	47	51	74	49	46	67
Oral cavity & pharynx	53	54	68	54	56	69	36	34	49
Ovary	36	38	47	35	38	46	41	34	39
Pancreas	3	4	9	3	3	9	2	6	8
Prostate	68	83	99	69	84	>99	61	71	97
Stomach	15	20	31	14	18	30	16	19	31
Testis	83	95	97	83	96	97	73†‡	88†	92
Thyroid	92	94	98	92	94	98	90	92	97
Urinary bladder	72	79	78	73	80	79	50	63	65
Uterine cervix	69	70	69	70	73	71	65	57	58
Uterine corpus	87	82	83	88	84	85	60	57	65

*Rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 9 areas from 1975 to 77, 1987 to 89, and 2007 to 2013, all followed through 2014. †The standard error is between 5 and 10 percentage points. ‡Survival rate is for cases diagnosed from 1978 to 1980.

NOTE: This table provides historical trends based on the 9 oldest SEER registries. Contemporary survival rates presented throughout this report and in Table 8 (page 21) may differ because they are based on more complete population coverage.

Source: Howlader N, Noone AM, Krapcho M, et al. (eds). *SEER Cancer Statistics Review, 1975-2014*, National Cancer Institute, Bethesda, MD, www.seer.cancer.gov/csr/1975_2014/, based on November 2016 SEER data submission, posted to the SEER website April 2017.

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National Lung Screening Trial

Aberle DR et al for the National Lung Screening Trial
Research Team. N Engl J Med 2011; 365: 395-409.

Intervention

- * Low dose CT scan of chest (26,722) vs. conventional chest radiography (26, 732)
- * Three yearly screening periods between August 2002 and September 2007, with follow up through December 31, 2009
- * Median duration of follow up 6.5 years, maximum duration of follow up 7.4 years.
- * Positive screening test defined as lung nodule greater than or equal to 4 mm on low dose CT or any nodule identified by chest radiography.

Entry Criteria

Inclusion Criteria

- * Ages 55-74
- * 30 pack year tobacco history
- * Currently smoking or quit within the last 15 years

Exclusion Criteria

- * Prior diagnosis of lung cancer
- * Prior CT scan within the last 18 months
- * Hemoptysis
- * Unexplained 15 lb weight loss in the last year

Results

Table 2. Results of Three Rounds of Screening.*

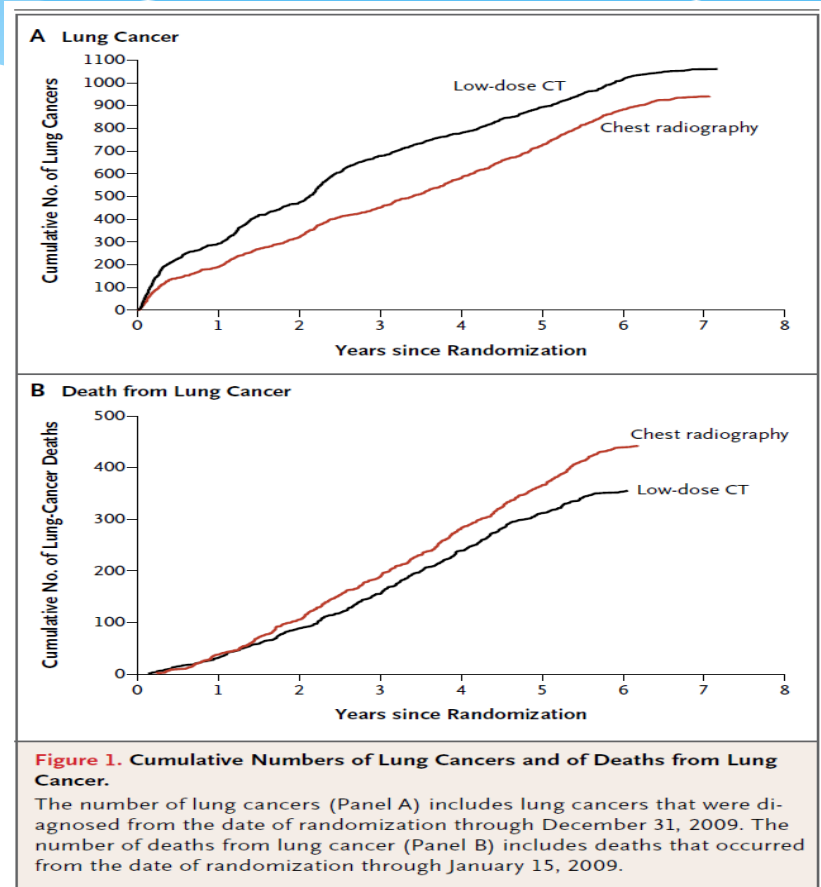
Screening Round	Low-Dose CT				Chest Radiography			
	Total No. Screened	Positive Result	Clinically Significant Abnormality Not Suspicious for Lung Cancer		Total No. Screened	Positive Result	Clinically Significant Abnormality Not Suspicious for Lung Cancer	
			No or Minor Abnormality	no. (% of screened)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

Results

- * Primary Endpoint Of Death Due To Lung Cancer
 - * 247 deaths per 100,000 person years in the low dose CT group compared to 309 deaths per 100,000 person years in the chest radiography group.
 - * **20% relative risk reduction for lung cancer related mortality**
 - * **Number needed to screen with low dose CT to prevent one lung cancer death is 320**

Results

- * Secondary endpoints
 - * **6.7% reduction in all cause mortality**
 - * 645 lung cancers were diagnosed per 100,000 person years in the low dose CT group vs 572 lung cancers per 100,000 person years in the chest radiograph group



Results

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."

Adverse Events

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

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)	

Current Lung Cancer Screening Recommendations

United States Preventive Services Task Force

- * Age 55-80
- * Asymptomatic
- * 30 pack year tobacco history
- * Actively smoking or quit within the last 15 years
- * Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

Centers for Medicare and Medicaid Services

- * Age 55-77
- * Asymptomatic
- * 30 pack year tobacco history
- * Actively smoking or quit within the last 15 years
- * Lung cancer screening counseling and shared decision making visit

Current Practice Implementation Issues

- * Patient selection
- * Appropriate lung cancer screening counseling and shared decision making visit
 - * Emphasis on false positive rate
 - * Emphasis on risk of radiation exposure
 - * Emphasis on smoking cessation
- * Standardization of low dose CT reporting and follow up – Lung RADS Criteria
- * Identification and management of significant incidental findings – coronary artery calcification and non-pulmonary malignancies

Patient Selection

- * Be sure patient fulfills lung cancer screening criteria
 - * Assess for significant limiting comorbidities
- * Assess for alternative protocol CT scans of the chest which have been performed in the last year to avoid unnecessary screening CT scans
- * Ensure routine screening scans are not ordered within one year of each other
- * Be sure to order low dose CT protocol!

Lung Cancer Screening Counseling and Shared Decision Making

- * Emphasize the increased false positive rate based on current size criteria alone
 - * In the NLST, 24.2% of all CT screens were positive, with 96.4% of those positive tests a false positive
 - * Lung cancer probability at two years was no different in individuals with lung nodules less than 5 mm compared to those without nodules.¹

1. Horeweg N et al. Lancet Oncol 2014; 15: 1332-41.

Risk Of Radiation Exposure

TABLE 1: Estimated Doses for Common Radiologic Examinations

Radiologic Examination	Effective Dose (mSv)	Range (mSv)
Chest radiography (2 view)	0.1	0.05–0.24
Mammography	0.4	0.1–0.7
Head CT	2	0.9–4.0
Neck CT	4	0.7–9.0
Standard chest CT	8	4.0–18.0
Low-dose chest CT	1.5	Variable
Coronary CT angiography	15	7–39
Abdominal CT	10	3.5–25
Pelvic CT	8	3.3–10
Multiphase abdominopelvic CT	31	6–90
Spine CT	8	1.5–10
CT colonography	10	4.0–13.2
Whole-body CT	12	7–13.5

Note—Estimated doses were derived from previous studies [1, 12, 13, 15, 21, 25, 78].

Risk Of Radiation Exposure

Table 3 | Number of lung cancers detected after 10 years of CT screening and number of estimated lung and major cancers associated with radiation exposure, according to age and sex of COSMOS trial participants

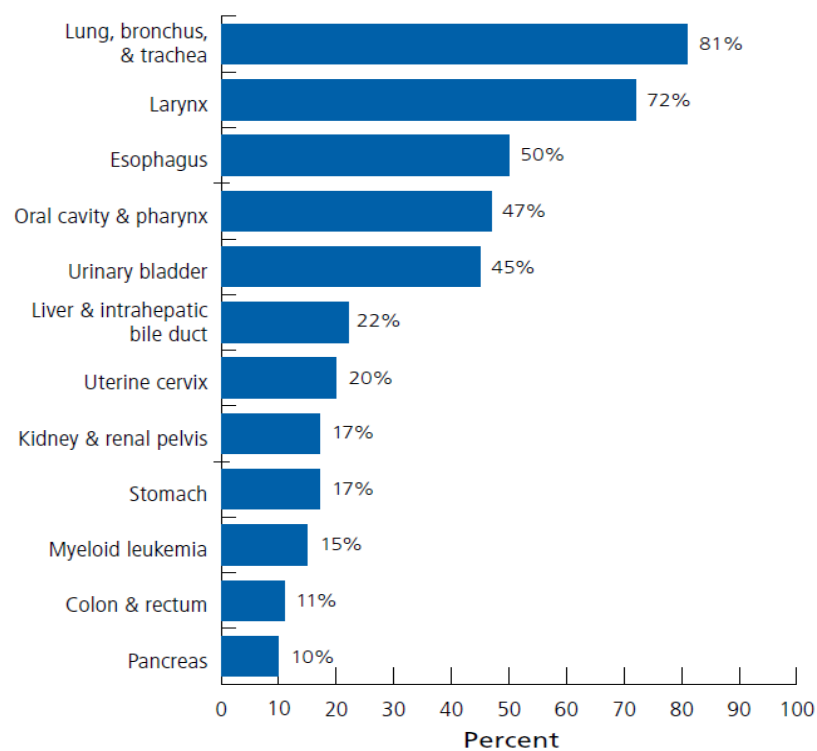
Participant age and sex at start of screening	No of participants	No of lung cancers detected	No of estimated radiation induced lung cancers (LAR/10 000)	No of estimated radiation induced major cancers* (LAR/10 000)
50-54				
Male	1153	35 (1 in 33)	0.24 (2.1)	0.43 (3.7)
Female	606	19 (1 in 32)	0.33 (5.5)	0.49 (8.1)
55-59				
Male	1114	56 (1 in 20)	0.21 (1.9)	0.38 (3.4)
Female	611	31 (1 in 20)	0.31 (5.1)	0.44 (7.2)
60-64				
Male	716	54 (1 in 13)	0.12 (1.7)	0.22 (3.0)
Female	345	13 (1 in 27)	0.16 (4.5)	0.21 (6.2)
≥65				
Male	456	41 (1 in 11)	0.07 (1.4)	0.12 (2.6)
Female	202	10 (1 in 20)	0.08 (3.8)	0.10 (5.1)
All ages, both sexes	5203	259 detected	1.5 induced	2.4 induced

LAR=lifetime attributable risk.

*Cumulative LAR for cancers of the stomach, colon, liver, lung, bladder, thyroid, breast, ovaries, uterus, or leukaemia.

Smoking Cessation

Figure 4. Proportion of Cancer Deaths Attributable to Cigarette Smoking in Adults 30 Years and Older, US, 2014



Source: Islami F, Goding Sauer A, Miller KD, et al. *CA Cancer J Clin.* Nov 2017.

Smoking Cessation

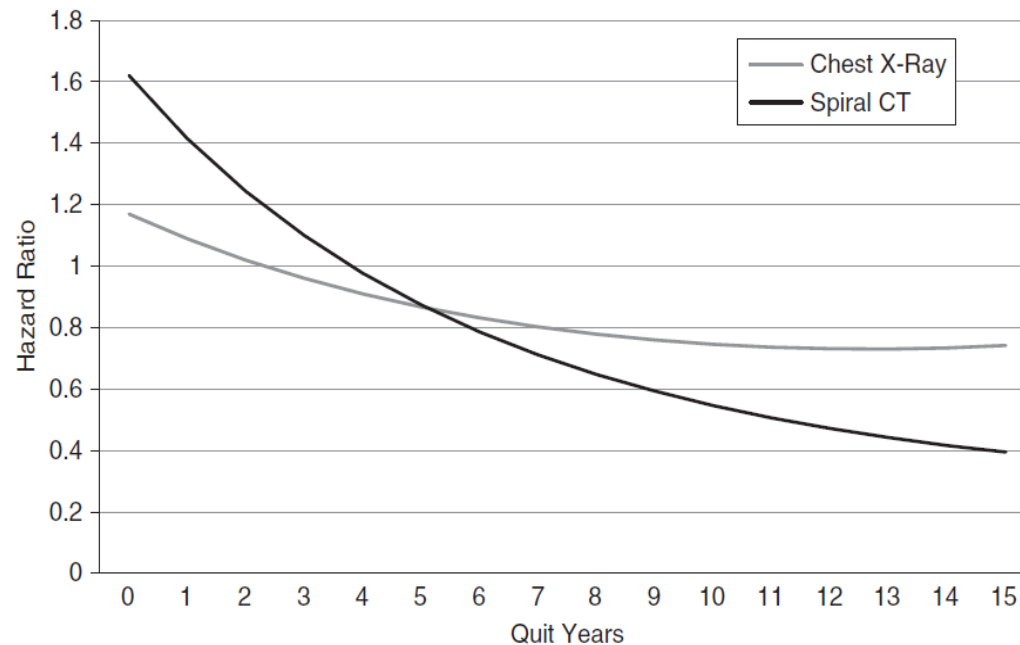


Figure 2. Adjusted hazard ratios for lung cancer-specific mortality; quit-years by screening arm for former smokers. CT = computed tomography.

Lung CT Screening Reporting and Data System (Lung-RADS)

Lung-RADS Version 1.0 Assessment Categories Release date: April 28, 2014

Category	Category Descriptor	Category	Findings	Management	Probability of Malignancy	Estimated Population Prevalence
Incomplete	-	0	prior chest CT examination(s) being located for comparison part or all of lungs cannot be evaluated	Additional lung cancer screening CT images and/or comparison to prior chest CT examinations is needed	n/a	1%
Negative	No nodules and definitely benign nodules	1	no lung nodules nodule(s) with specific calcifications: complete, central, popcorn, concentric rings and fat containing nodules	Continue annual screening with LDCT in 12 months	< 1%	90%
Benign Appearance or Behavior	Nodules with a very low likelihood of becoming a clinically active cancer due to size or lack of growth	2	solid nodule(s): < 6 mm new < 4 mm			
			part solid nodule(s): < 6 mm total diameter on baseline screening			
			non solid nodule(s) (GGN): < 20 mm OR ≥ 20 mm and unchanged or slowly growing			
			category 3 or 4 nodules unchanged for ≥ 3 months			
Probably Benign	Probably benign finding(s) - short term follow up suggested; includes nodules with a low likelihood of becoming a clinically active cancer	3	solid nodule(s): ≥ 6 to < 8 mm at baseline OR new 4 mm to < 6 mm	6 month LDCT	1-2%	5%
			part solid nodule(s): ≥ 6 mm total diameter with solid component < 6 mm OR new < 6 mm total diameter			
			non solid nodule(s) (GGN) ≥ 20 mm on baseline CT or new			
			solid nodule(s): ≥ 8 to < 15 mm at baseline OR growing < 8 mm OR new 6 to < 8 mm			
Suspicious	Findings for which additional diagnostic testing and/or tissue sampling is recommended	4A	part solid nodule(s): ≥ 6 mm with solid component ≥ 6 mm to < 8 mm OR with a new or growing < 4 mm solid component	3 month LDCT; PET/CT may be used when there is a ≥ 8 mm solid component	5-15%	2%
			endobronchial nodule			
		4B	solid nodule(s): ≥ 15 mm OR new or growing, and ≥ 8 mm	chest CT with or without contrast, PET/CT and/or tissue sampling depending on the *probability of malignancy and comorbidities. PET/CT may be used when there is a ≥ 8 mm solid component.	> 15%	2%
			part solid nodule(s) with: a solid component ≥ 8 mm OR a new or growing ≥ 4 mm solid component			
		4X	Category 3 or 4 nodules with additional features or imaging findings that increases the suspicion of malignancy			
Other	Clinically Significant or Potentially Clinically Significant Findings (non lung cancer)	S	modifier - may add on to category 0-4 coding	As appropriate to the specific finding	n/a	10%
Prior Lung Cancer	Modifier for patients with a prior diagnosis of lung cancer who return to screening	C	modifier - may add on to category 0-4 coding	-	-	-

Lung-RADS

*Table 1. Summary of Lung-RADS Classification**

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

GGN = ground-glass nodule.

* Size is the average diameter rounded to the nearest whole number. Growth is a size increase >1.5 mm.

Lung-RADS vs NLST

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

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

NLST = National Lung Screening Trial; NPV = negative predictive value; PPV = positive predictive value.

* Totals of 22 screening results at baseline and 28 after baseline with cancer absent were positive in Lung-RADS and had nodule characteristics meeting the positive screening criteria but were nonetheless reported as negative screening results in the NLST. Otherwise, all screening results that were positive according to the Lung-RADS criteria were also positive according to the NLST criteria.

† 1 minus the specificity rate.

Table 4-Continued

Lung-RADS After Baseline		NLST After Baseline	
Percentage (95% CI)	n/N	Percentage (95% CI)	n/N
78.60 (74.60-82.60)	315/401	93.80 (91.40-96.10)	376/401
5.30 (5.10-5.50)	2543/48 197	21.80 (21.40-22.20)	10 512/48 197
11.00 (9.90-12.20)	315/2858	3.50 (3.10-3.80)	376/10 888
99.81 (99.77-99.85)	45 654/45 740	99.93 (99.90-99.96)	37 685/37 710

Lung-RADS vs NLST

Table 5. NLST True- and False-Positive Screening Results and Diagnostic Procedures Missed or Avoided With Lung-RADS*

Variable	Baseline	After Baseline	All
NLST true-positive† cases of cancer missed with Lung-RADS‡	25 (9.2)	61 (16.2)	86 (13.3)
NLST false-positive results avoided with Lung-RADS			
All§	3618 (52.1)	7997 (76.1)	11 615 (66.6)
With invasive procedures	60 (23.4)	57 (23.3)	117 (23.4)
Chest CTs avoided after false-positive results¶	3557 (50.5)	2150 (45.5)	5707 (48.5)

Significant Incidental Findings

Table 7. Cause of Death on the Death Certificate, According to Screening Group.*

Cause of Death	Low-Dose CT Group	Radiography Group	Total
		<i>number/total number (percent)</i>	
Neoplasm of bronchus and lung†	427/1865 (22.9)	503/1991 (25.3)	930/3856 (24.1)
Other neoplasm	416/1865 (22.3)	442/1991 (22.2)	858/3856 (22.3)
Cardiovascular illness	486/1865 (26.1)	470/1991 (23.6)	956/3856 (24.8)
Respiratory illness	175/1865 (9.4)	226/1991 (11.4)	401/3856 (10.4)
Complications of medical or surgical care	12/1865 (0.6)	7/1991 (0.4)	19/3856 (0.5)
Other	349/1865 (18.7)	343/1991 (17.2)	692/3856 (17.9)

Aberle DR et al for the National Lung Screening Trial Research Team. N Engl J Med 2011; 365: 395-409.

Significant Incidental Findings

Table 1. Extrapulmonary findings by abnormality code

	Total Number of Unique Participants Having at Least One Occurrence of the Abnormality Code	Prevalence of the Abnormality Code
Significant cardiovascular abnormality	1,378	8.0%
Other potentially significant abnormality above the diaphragm	1,255	7.3%
Other potentially significant abnormality below the diaphragm	1,311	7.6%
Other minor abnormality noted	9,152	52.9%
All incidental abnormalities	10,166	58.7%

Table 2. Extrapulmonary findings with free-text descriptions by organ location

Organ Location	Study Participants (n = 17,309) With at Least One Incidental Abnormality With a Free-Text Description	
	All	Potentially Significant*
Total	4,428 (25.6%)	2,376 (13.7%)
Cardiovascular	2,625 (15.2%)	1,477 (8.5%)
Thyroid	221 (1.3%)	100 (0.6%)
Adrenal	419 (2.4%)	207 (1.2%)
Renal	780 (4.5%)	407 (2.4%)
Hepatobiliary	1,064 (6.1%)	369 (2.1%)

Coronary Artery Calcification

Table 3

Association between CAC and Time to CHD Death for Each of Three Scoring Methods

CAC Category	CAC Scoring Method 1	CAC Scoring Method 2	CAC Scoring Method 3
Scoring method 1 score of none, scoring method 2 score of 0, or scoring method 3 score of 0			
Selection-weighted absolute event rates for CHD death*	18/2819 (0.6)	18/2799 (0.6)	20/2909 (0.7)
Model-based hazard ratios			
Univariate model	1	1	1
Multivariate model	1	1	1
Scoring method 1 score of mild, scoring method 2 score of 1–5, or scoring method 3 score of 1–100			
Selection-weighted absolute event rates for CHD death*	64/4069 (1.6)	52/3985 (1.3)	27/2664 (1.0)
Model-based hazard ratios			
Univariate model	2.48 (1.55, 4.55)	2.03 (1.27, 3.66)	1.46 (0.84, 2.66)
Multivariate model	2.09 (1.30, 4.16)	1.72 (1.05, 3.34)	1.27 (0.69, 2.53)
Scoring method 1 score of moderate, scoring method 2 score of 6–11, or scoring method 3 score of 101–1000			
Selection-weighted absolute event rates for CHD death*	40/1233 (3.2)	58/1349 (4.3)	82/2731 (3.0)
Model-based hazard ratios			
Univariate model	5.18 (2.97, 9.69)	6.88 (4.15, 12.75)	4.53 (2.96, 8.13)
Multivariate model	3.86 (2.02, 8.20)	5.11 (2.92, 10.94)	3.57 (2.14, 7.48)
Scoring method 1 score of heavy, scoring method 2 score of 12–30, or scoring method 3 score of >1000			
Selection-weighted absolute event rates for CHD death*	49/909 (5.4)	43/897 (4.8)	42/726 (5.8)
Model-based hazard ratios			
Univariate model	9.04 (5.56, 16.87)	8.11 (4.85, 15.19)	9.11 (5.34, 16.76)
Multivariate model	6.95 (3.73, 15.67)	6.10 (3.19, 14.05)	6.63 (3.57, 14.97)

Chiles et al for the National Lung Screening Trial. Radiology 2015; 276: 82-90.

Coronary Artery Calcification

Ordinal CAC Score	Agatston Score	Recommendation
0	0	Probability of CHD is low. Reassure
1-3	1-100	Probability of CHD is low to moderate; Discuss guidelines for primary prevention.
4-12	> 100	Probability of CHD is moderately high. Consult with a preventive cardiologist for counseling about risk factor modification, and for higher values, for risk factor modification, exercise testing, or pharmacological stress testing

Non-pulmonary Malignancies

Table 3. Potentially significant extrapulmonary findings and extrapulmonary malignancies diagnosed during screening

	Thyroid	Adrenal	Kidney	Liver
Total malignancies during screening	14	0	45	8
(B) Participants with potentially significant findings	100	207	407	369
(A) Participants with malignancy during screening and potentially significant findings	7	0	11	0
Ratio of A to B	1:14		1:37	

Future Directions

- * Optimization of the patient population to be screened – use of lung cancer screening prediction models
- * Identification of the optimal frequency of lung cancer screening
- * Reduction in false positive lung cancer screens and improvements in nodule management protocols - use of lung nodule volume and volume doubling time criteria over manually determined diameters