

Lung Cancer and CT Screening

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February 17th, 2012

Goals

- ◆ Understand the **Societal impact of Lung Cancer**
- ◆ Identify **Risk Factors** for Lung Cancer
- ◆ List **Diagnostic Tests** Available for Lung Cancer
- ◆ Understand the **Staging for Lung Cancer**
- ◆ Understand the history and current recommendations on **Lung Cancer Screening**

Disclaimer

I have **NO** personal financial relationship with any manufacturer of products or services that will be discussed in this lecture.

US Epidemiology 2011

Estimated New Cases*

Male

Female

Prostate
240,890 (29%)

Breast
230,480 (30%)

Lung & bronchus
115,060 (14%)

Lung & bronchus
106,070 (14%)

Colon & rectum
71,850 (9%)

Colon & rectum
69,360 (9%)

Urinary bladder
52,020 (6%)

Uterine corpus
46,470 (6%)

Melanoma of the skin
40,010 (5%)

Thyroid
36,550 (5%)

Kidney & renal pelvis
37,120 (5%)

Non-Hodgkin lymphoma
30,300 (4%)

Non-Hodgkin lymphoma
36,060 (4%)

Melanoma of the skin
30,220 (4%)

Oral cavity & pharynx
27,710 (3%)

Kidney & renal pelvis
23,800 (3%)

Leukemia
25,320 (3%)

Ovary
21,990 (3%)

Pancreas
22,050 (3%)

Pancreas
21,980 (3%)

All sites
822,300 (100%)

All sites
774,370 (100%)

- ◆ **215,020 new cases**
 - ◆ **115,060 in men**
 - ◆ **106,070 in women**
 - ◆ **Accounts for 14% of all new cancer cases**
 - ◆ **Average age at diagnosis is 71**
 - ◆ **Lifetime risk is 1 in 13 for men and 1 in 16 for women**

US Epidemiology 2011

Estimated Deaths

Male

Lung & bronchus
85,600 (28%)

Prostate

33,720 (11%)

Colon & rectum
25,250 (8%)

Pancreas

19,360 (6%)

Liver & intrahepatic bile duct
13,260 (4%)

Leukemia

12,740 (4%)

Esophagus

11,910 (4%)

Urinary bladder

10,670 (4%)

Non-Hodgkin lymphoma
9,750 (3%)

Kidney & renal pelvis
8,270 (3%)

All sites

300,430 (100%)

Female

Lung & bronchus
71,340 (26%)

Breast

39,520 (15%)

Colon & rectum
24,130 (9%)

Pancreas

18,300 (7%)

Ovary

15,460 (6%)

Non-Hodgkin lymphoma

9,570 (4%)

Leukemia

9,040 (3%)

Uterine corpus

8,120 (3%)

Liver & intrahepatic bile duct
6,330 (2%)

Brain & other nervous system
5,670 (2%)

All sites

271,520 (100%)

- ◆ **156,940 deaths**
 - ◆ **85,600 men**
 - ◆ **71,340 women**
 - ◆ **Accounts for 27% of all cancer deaths**

Lung cancer is the leading cause of cancer death for both men and women

More people die of **Lung** cancer than
of **Colon**, **Breast**, and **Prostate**
cancers **COMBINED!**

Lung Cancer Deaths in 2008
156,940 deaths

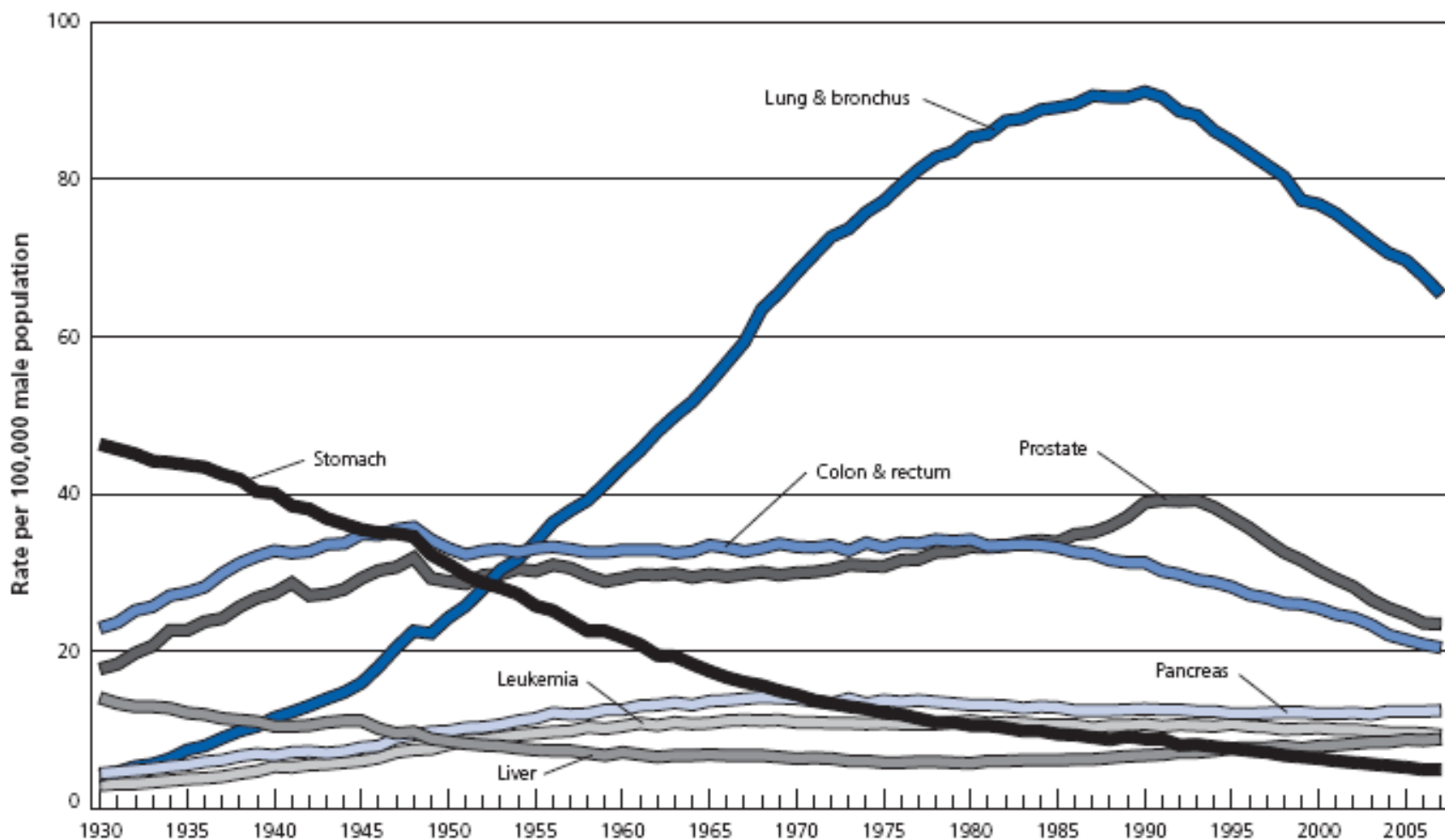
Colon Cancer Deaths = 49,380

Breast Cancer Deaths = 39,520

Prostate Cancer Deaths = 33,720

Combined Cancer Deaths = 122,620

Age-adjusted Cancer Death Rates,* Males by Site, US, 1930-2007

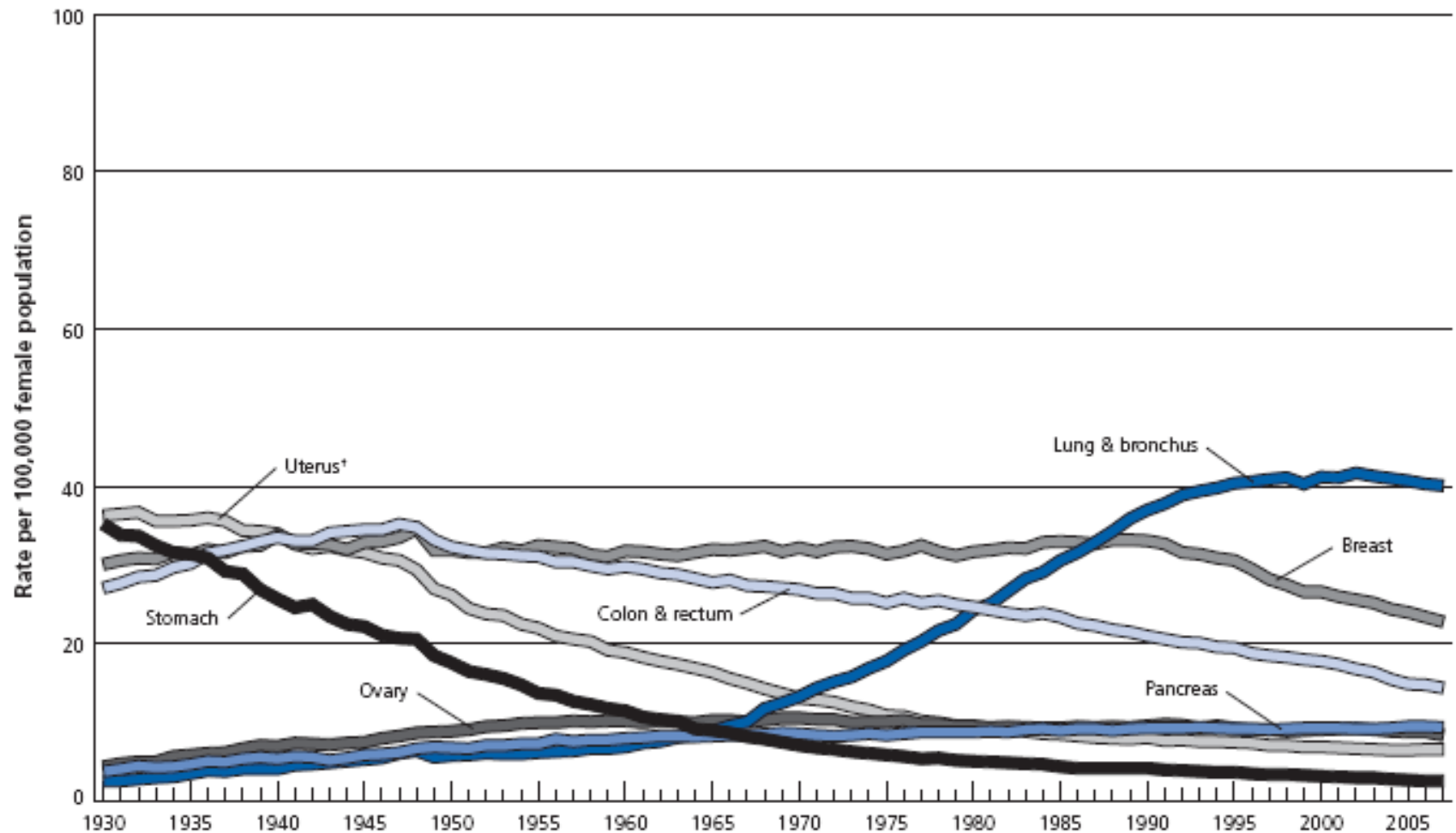


*Per 100,000, age adjusted to the 2000 US standard population.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, and colon and rectum are affected by these changes.

Source: US Mortality Data, 1960 to 2007, US Mortality Volumes, 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

Age-adjusted Cancer Death Rates, * Females by Site, US, 1930-2007



*Per 100,000, age adjusted to the 2000 US standard population.

Note: Due to changes in ICD coding, numerator information has changed over time. Rates for cancer of the liver, lung and bronchus, and colon and rectum are affected by these changes.

Source: US Mortality Data, 1960 to 2007, US Mortality Volumes, 1930 to 1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

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Lung Cancer Survival Rates

Table 1. Changes in 5-Year Survival, Mortality, and Incidence for 20 Solid Tumors

Primary Site	5-Year Survival, %		Absolute Increase in 5-Year Survival, %	% Change (1950-1996)	
	1950-1954	1989-1995		Mortality	Incidence
Prostate	43	93	50	10	190
Melanoma	49	88	39	161	453
Testis	57	96	39	-73	106
Bladder	53	82	29	-35	51
Kidney	34	61	27	37	126
Breast	60	86	26	-8	55
Colon	41	62	21	-21	12
Rectum	40	60	20	-67	-27
Ovary	30	50	20	-2	3
Thyroid	80	95	15	-48	142
Larynx	52	66	14	-14	38
Uterus	72	86	14	-67	0
Cervix	59	71	12	-76	-79
Oral cavity	46	56	10	-37	-38
Esophagus	4	13	9	22	-8
Brain	21	20	9	45	68
Lung	6	14	8	259	249
Stomach	12	19	7	-80	-78
Liver	1	6	5	34	140
Pancreas	1	4	3	16	9

Trends in 5-year Relative Survival Rates* (%) by Race and Year of Diagnosis, US, 1975-2006

	All races			White			African American		
	1975-77	1984-86	1999-2006	1975-77	1984-86	1999-2006	1975-77	1984-86	1999-2006
All sites	50	54	68 [†]	51	55	69 [†]	40	41	59 [†]
Brain	24	29	36 [†]	23	28	35 [†]	27	32	41 [†]
Breast (female)	75	79	90 [†]	76	81	91 [†]	62	65	78 [†]
Colon	52	59	66 [†]	52	60	67 [†]	47	50	55 [†]
Esophagus	5	10	19 [†]	6	11	20 [†]	3	9	13 [†]
Hodgkin lymphoma	74	80	87 [†]	74	80	88 [†]	71	75	82 [†]
Kidney	51	56	70 [†]	51	56	70 [†]	50	54	67 [†]
Larynx	67	66	63 [†]	68	68	65	59	53	49 [†]
Leukemia	36	42	55 [†]	36	43	56 [†]	34	34	47 [†]
Liver & bile duct	4	6	14 [†]	4	6	14 [†]	2	5	10 [†]
Lung & bronchus	13	13	16 [†]	13	14	17 [†]	12	11	13 [†]
Melanoma of the skin	83	87	93 [†]	83	87	93 [†]	60 [‡]	70 [§]	74 [‡]
Myeloma	26	29	39 [†]	26	27	39 [†]	31	32	38 [†]
Non-Hodgkin lymphoma	48	53	69 [†]	49	54	71 [†]	49	48	60 [†]
Oral cavity & pharynx	53	55	63 [†]	55	57	65 [†]	36	36	45 [†]
Ovary	37	40	45 [†]	37	39	45 [†]	43	41	37
Pancreas	3	3	6 [†]	3	3	6 [†]	2	5	5 [†]
Prostate	69	76	100 [†]	70	78	100 [†]	61	66	97 [†]
Rectum	49	57	69 [†]	50	58	70 [†]	45	46	60 [†]
Stomach	16	18	27 [†]	15	18	26 [†]	16	20	26 [†]
Testis	83	93	96 [†]	83	93	97 [†]	73 ^{‡#}	87 [‡]	87
Thyroid	93	94	97 [†]	93	94	98 [†]	91	90	95
Urinary bladder	74	78	81 [†]	75	79	82 [†]	51	61	66 [†]
Uterine cervix	70	68	71	71	70	73	65	59	64
Uterine corpus	88	84	84 [†]	89	85	86 [†]	61	58	61

* Survival rates are adjusted for normal life expectancy and are based on cases diagnosed in the SEER 9 areas from 1975-77, 1984-86, 1999 to 2006, and followed through 2007. † The difference in rates between 1975-1977 and 1999-2006 is statistically significant ($p < 0.05$). ‡ The standard error of the survival rate is between 5 and 10 percentage points. § The standard error of the survival rate is greater than 10 percentage points. # Survival rate is for 1978-1980.

Source: Altekruse SF, Kosary CL, Krapcho M, et al (eds.). *SEER Cancer Statistics Review, 1975-2007*, National Cancer Institute, Bethesda, MD, seer.cancer.gov/csr/1975_2007/, 2010.

Worldwide Lung Cancer

- ◆ Over **1.6 million** new cases of Lung cancer in 2008
- ◆ Accounts for **13%** of total cancer diagnoses
- ◆ Accounts for **18%** of total cancer Deaths

- ◆ More than **1.4 million** people died from Lung cancer in 2008

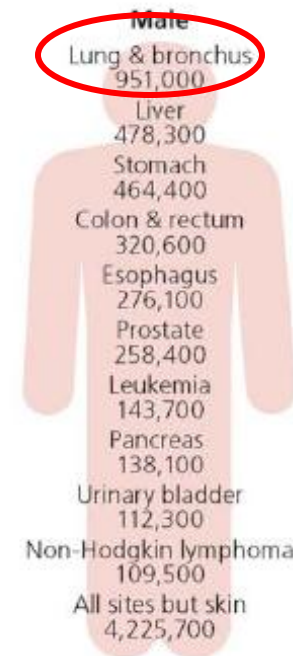
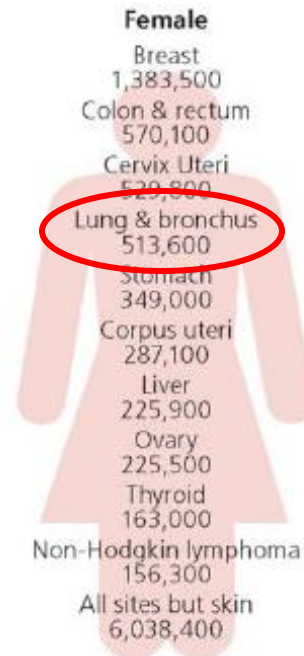
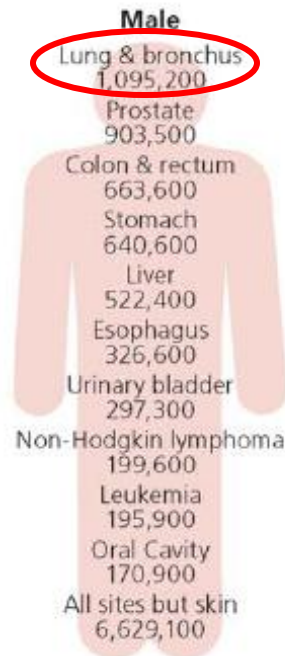
- ◆ Leading cause of cancer death in Men
- ◆ Second leading cause of cancer death in Women

Worldwide Lung Cancer

Estimated New Cases

Estimated Deaths

Worldwide



Risk Factors

- ◆ **Smoking**
 - ◆ Responsible for **87%** of Lung Cancer Deaths Annually
 - ◆ Latent period of 20-25 years
 - ◆ Dose related
 - ◆ (9-10 fold risk average smoker, **20 fold risk for heavy smoker**)
 - ◆ Smoking *reduces the lifespan of average American by 14 years*
- ◆ **Secondhand smoke**
 - ◆ Non-smoking spouses who live with a smoker have a **20-30%** greater risk
- ◆ **Air pollution**
 - ◆ *Worldwide, 5% of deaths from Lung cancer may be due to air pollution*
- ◆ **Asbestos Exposure**
 - ◆ Synergy with Tobacco (**50-90 times the risk** of cancer)

Risk Factors

♦ Race / Ethnicity

- ♦ African Americans have similar rate of smoking as Whites (20% vs 22% in 2004); yet
 - ♦ **Black men are 50% more likely to develop lung cancer**
 - ♦ **30% more likely to die from lung cancer than White men**
- ♦ Hispanics smoke less (15% in 2004) than Whites or African Americans
 - ♦ **50% lower lung cancer rate than Whites**
 - ♦ **60% lower lung cancer rate than African Americans**
- ♦ High school students **smoking** trend is alarming: data from 2004
 - ♦ **Hispanics 26.2%**
 - ♦ **African Americans 17.1%**
 - ♦ **Whites 31.5%**

Risk Factors

- ♦ Race and Gender Trends (SEER database)

SubGroup	Incidence/100,000	Death/100,000
White Men	79.4	78.1
White Women	51.9	41.5
African American Men	120.4	107
African American Women	54.8	40
Asian American Men	62.1	40.9
Asian American Women	28.4	19.1
Hispanic Men	46.1	40.7
Hispanic Women	24.4	15.1
American Indian Men	45.6	52.9
American Indian Women	23.4	26.2

C-STATS Report

Age-adjusted lung cancer mortality rates

MORTALITY (*age-adjusted*)

	<u>Number of cases</u>	<u>Rate</u>
◆ NAPA	78	50.4
◆ SOLANO	198	54.0
◆ SONOMA	229	45.6
◆ STATEWIDE	13,168	40.4

Sign and Symptoms

- ◆ **Cough (that does not resolve)** 29-87%
- ◆ **Hemoptysis** 9-57%
- ◆ **Pleuritic chest pain** 6-60%
- ◆ **Shortness of Breath / Dyspnea** 3-58%

- ◆ **ASYMPTOMATIC**
 - ◆ **All patients with Lung cancer** 5-20%
 - ◆ **Patients detected screening programs** 60%

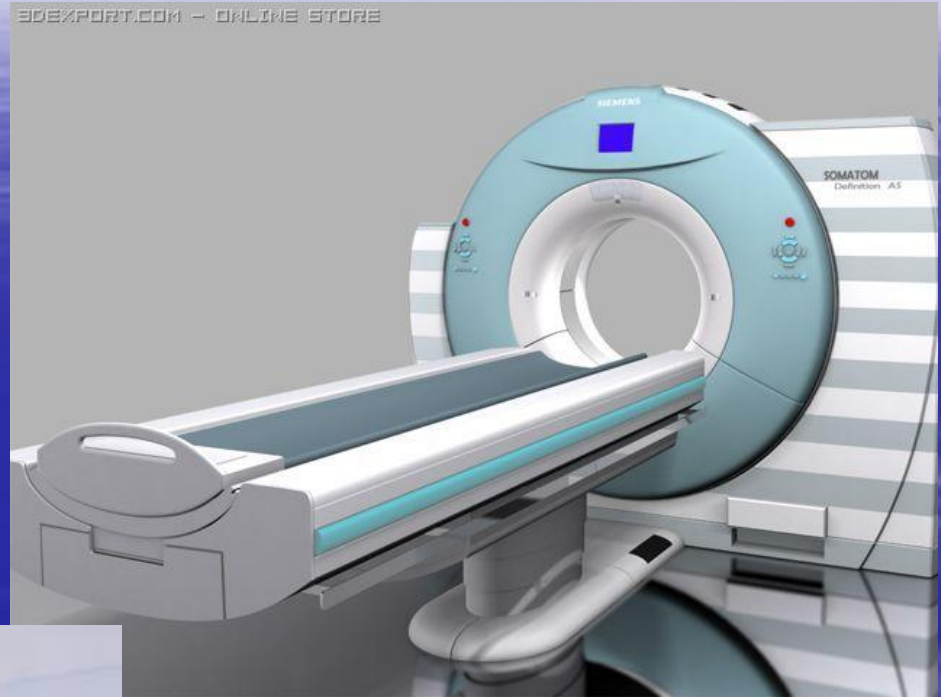
Diagnosis - Imaging

Chest X ray

CT scan

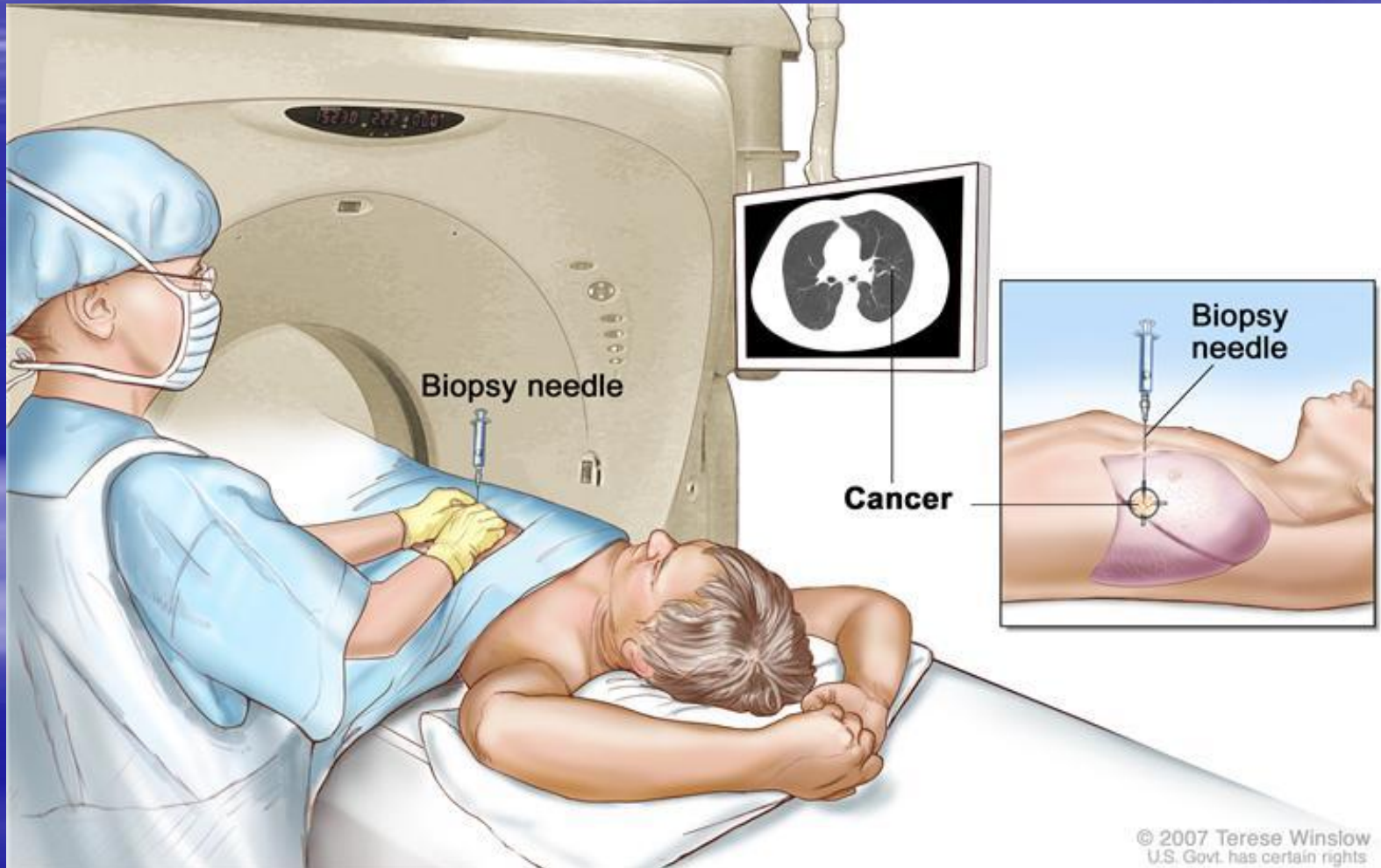
PET Scan

PET and CT scan combined

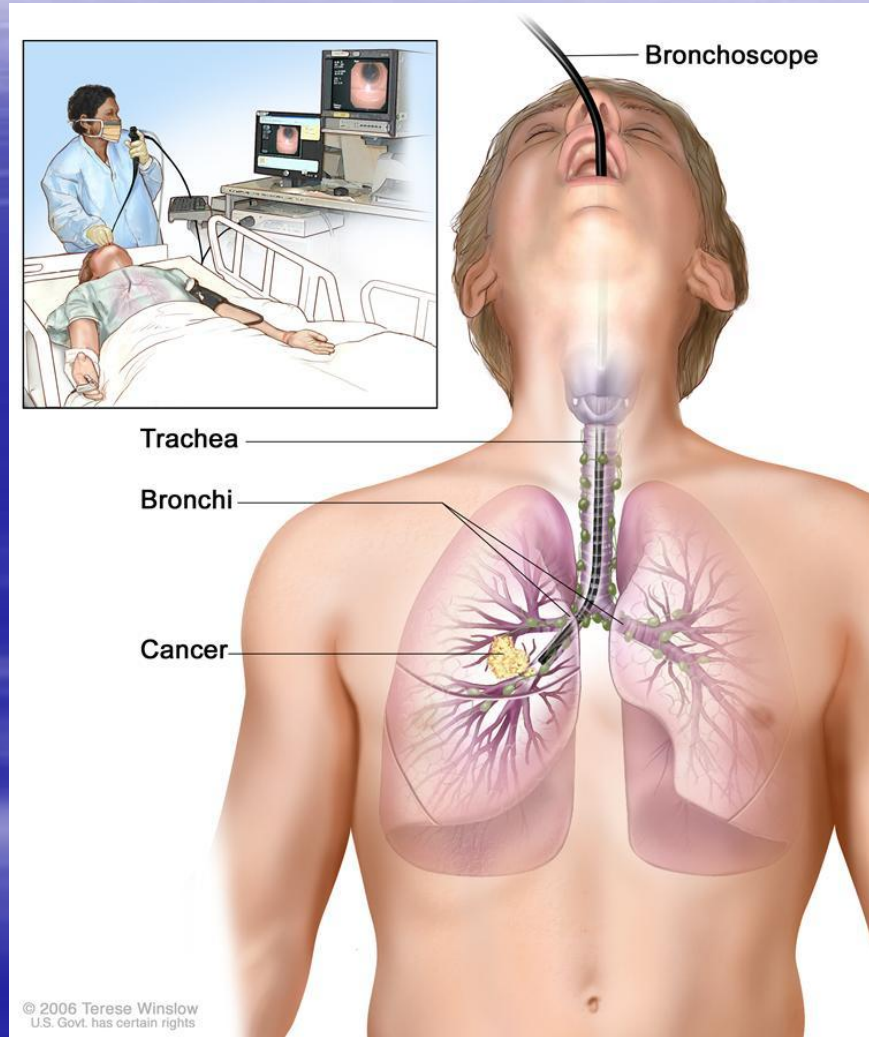
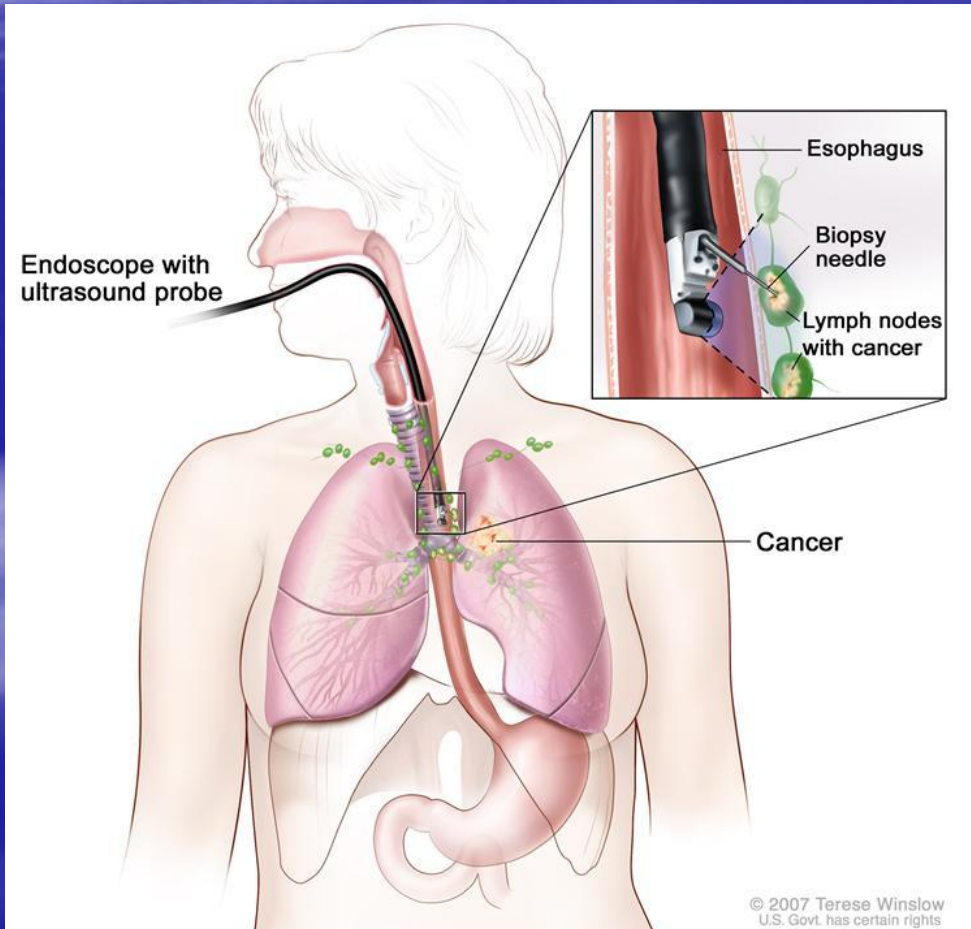


Fine Needle Aspiration

- ◆ Pneumothorax risk requiring CT placement



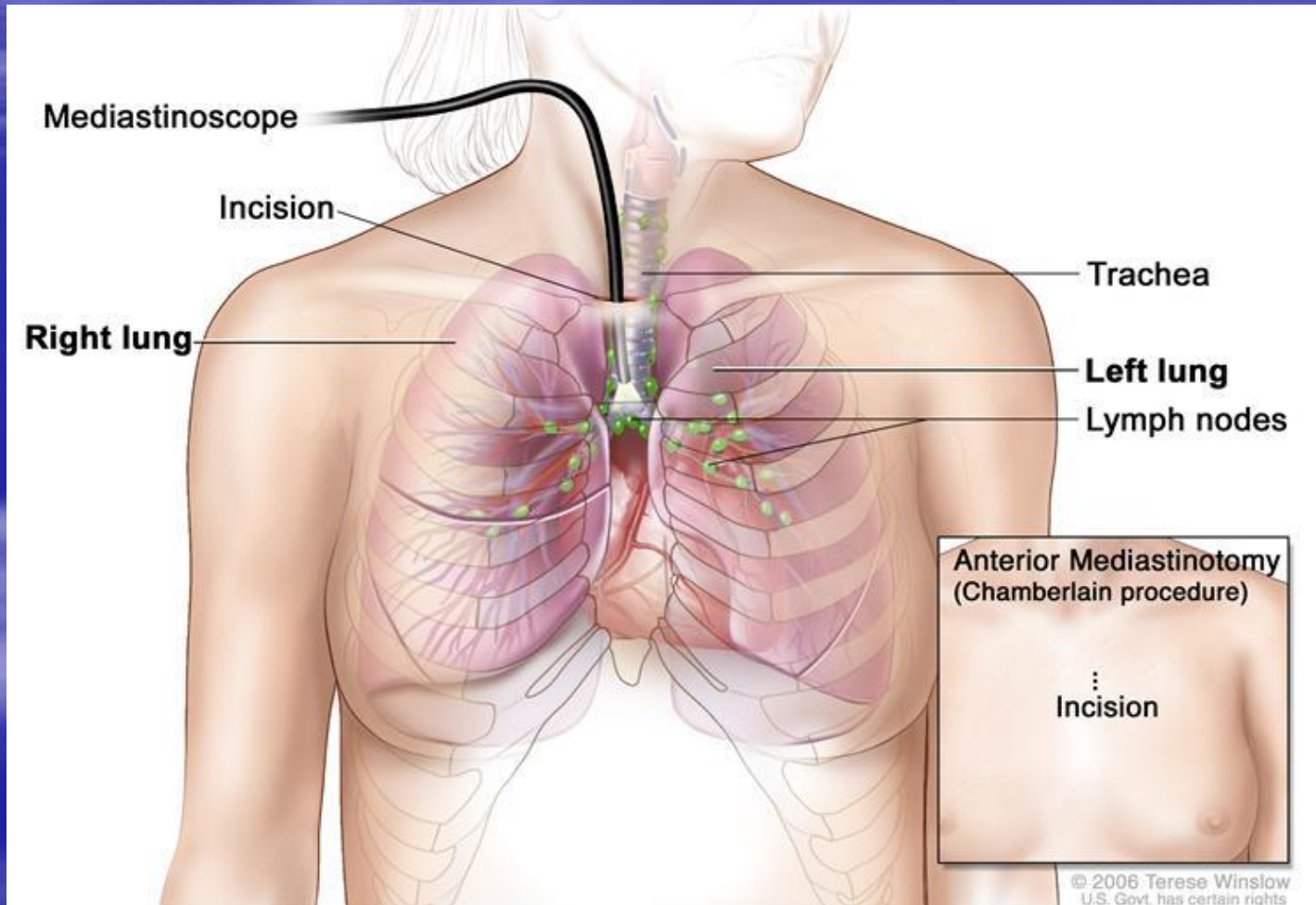
Bronchoscopy with Endoscopic / Endobronchial Ultrasound



Thoracentesis

Mediastinoscopy

Thoracoscopy



Pathology

WHO Classification (1999) for NSCLC (80% of Lung CA)

- ◆ **Squamous Cell Carcinoma (30%)**
 - ◆ Most commonly in Men
 - ◆ Tends to spread Locally and usually central lesions
 - ◆ Related to Smoking
- ◆ **Adenocarcinoma (30-50%)**
 - ◆ Most commonly in Women and Non-smokers, but Smoking is risk factor
 - ◆ Usually peripheral lesions
 - ◆ Metastasize early
 - ◆ **Bronchoalveolar Carcinoma (BAC) is a subtype**
- ◆ **Large Cell Carcinoma (10-25%)**
 - ◆ Undifferentiated, primitive cells
 - ◆ Metastasize early
 - ◆ Usually peripheral lesions
- ◆ **Carcinoid tumor (3-5%)**

Staging

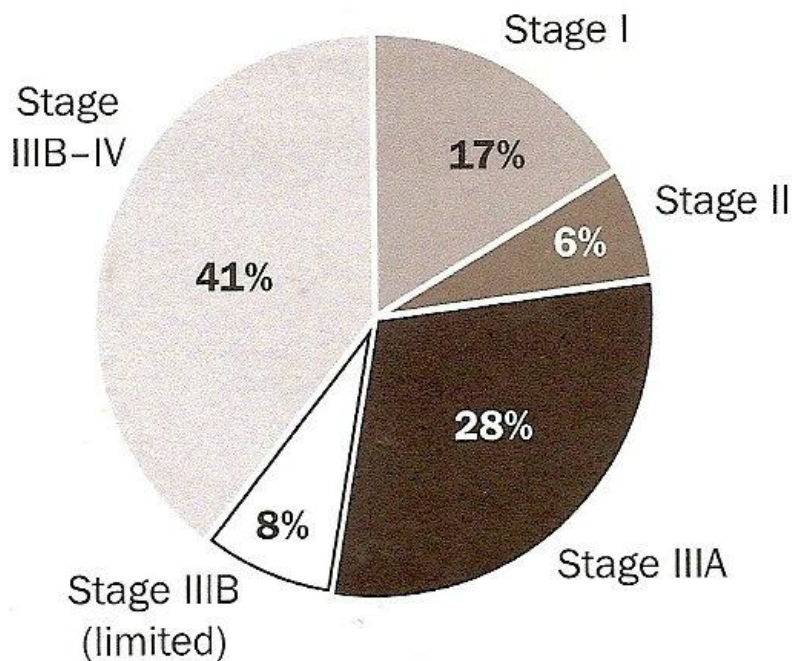
TNM Definitions

- ◆ **T Stage**
 - ◆ Size of the Primary Tumor
 - ◆ Adjacent structures invaded into by Tumor
- ◆ **N Stage**
 - ◆ Nodal disease involvement
- ◆ **M Stage**
 - ◆ Metastatic disease involvement

T and M		N0	N1	N2	N3
6 th Ed TNM	7 th Ed TNM	Stage	Stage	Stage	Stage
T1 (<2cm)	T1a	IA	IIA	IIIA	IIIB
T1 (2-3cm)	T1b	IA	IIA	IIIA	IIIB
T2 (<5cm)	T2a	IB	IIA (IB)	IIIA	IIIB
T2 (5-7cm)	T2b	IIA (IB)	IIB	IIIA	IIIB
T2 (>7cm)	T3	IIB (IB)	IIIA (IB)	IIIA	IIIB
T3 invasion	T3	IIB	IIIA	IIIA	IIIB
T4 (same lobe nodules)	T3	IIB (IIIB)	IIIA (IIIB)	IIIA (IIIB)	IIIB
T4 (extension)	T4	IIIA (IIIB)	IIIA (IIIB)	IIIB	IIIB
M1 (ipsilat lung)	T4	IIIA (IV)	IIIA (IV)	IIIB (IV)	IIIB (IV)
T4 (pleural effusion)	M1a	IV (IIIB)	IV (IIIB)	IV (IIIB)	IV (IIIB)
M1 (contralat lung)	M1a	IV	IV	IV	IV
M1 (distant)	M1b	IV	IV	IV	IV

Staging

NSCLC Incidence by Stage
US Population, 2006



Disease and Stage	Annual Incidence	1-Year Survival	5-Year Survival
NSCLC	140,000	—	17%
I	24,000	90%	70%
II	9,000	80%	40%
IIIA	42,000	70%	20%
IIIB (limited)	11,000	50%	4%
IIIB-IV	57,000	35%	3%

Screening

Chest Xray and/or Sputum Cytology

Benefits

Based on Fair evidence
Screening does **NOT** reduce mortality from lung cancer

Harms

Based on Solid evidence
Screening would lead to false-positives and unnecessary invasive procedures and treatments

Studies:

- ◆ Philadelphia Pulmonary Neoplasm Research Project
- ◆ Veterans Administration study
- ◆ South London Lung Cancer Study
- ◆ North London Lung Cancer Study
- ◆ Kaiser Foundation Health Plan multiphasic screening trial
- ◆ Czechoslovak Study
- ◆ German Democratic Republic Study
- ◆ Japan Study
- ◆ Mayo Lung Project
- ◆ Johns Hopkins Study
- ◆ Memorial Sloan-Kettering Study

CXR /Sputum cytology NOT helpful

	MSKCC	Hopkins	Mayo	Czech
Accrual	1974-1982	1973-1982	1971-1983	1976-1980
Screened	N=4968	5226	4618	3172
Protocol	Annual CXR, sputum Q4m	Annual CXR, sputum Q4m	CXR & sputum Q4m	CXR & sputum Q6m
Cancers at baseline	30	39	NA	NA
Cancers at screen	114	194	206	39
Lung cancer mortality (per 1000 person-years)	2.7	3.4	3.2	3.6
Control	N= 5072	5161	4593	3174
Protocol	Annual CXR	Annual CXR	Annual CXR & sputum	CXR & sputum Q3y
Cancers at baseline	23	40	NA	NA
Cancers at screen	121	202	160	27
Lung cancer mortality (per 1000 person-years)	2.7	3.8	3.0	2.6

Low-Dose Helical CT Scan (LDCT)

Benefits

Evidence is inadequate to determine whether screening reduces mortality from lung cancer

Harms

Based on Solid evidence
Screening would lead to false-positives and unnecessary invasive procedures and treatments

Studies:

- ◆ Early Lung Cancer Action Project (ELCAP)
- ◆ Mayo Clinic Study
- ◆ University of Munster study
- ◆ Shinshu University study
- ◆ Anti-Lung Cancer Association (ALCA)

Low-dose CT Screening Trials

	Mayo Clinic Study	Shinshu University	Early Lung Cancer Action Project (ELCAP)	Anti-Lung Cancer Association (ALCA)	University of Munster
Prevalence					
N	1520	5483	1000	1611	817
Abnormal CT	51%	35%	23%	11.5%	43%
# cancers on CXR	NA	1	7	5	NA
# cancers on CT	26	19	27	14	11
Stage I NSCLC	79%	84%	85%	71%	64%
Incidence					
N	1438	4781	1184	1180	
# cancers on CT	10	37	7	19	
Stage 1 NSCLC	67%	86%	82%	79%	
Interval cancers not detected on screening CT	2	NA	2	3	

CT-screening vs. Mammography

	Breast cancer detection in women ≥ 40	Lung cancer detection in people ≥ 40
Baseline screening	0.6 - 1.0%	1.3%
Annual screening	0.2 - 0.4%	0.3%

Henschke et al. NEJM 2006; 355



National Lung Screening Trial

The **National Lung Screening Trial (NLST)** is a **lung cancer screening** trial sponsored by the National Cancer Institute (NCI).

Launched in 2002, NLST compared: low-dose helical computed tomography (CT) and standard chest X-ray. **53,456 current and former heavy smokers ages 55 to 74 with at least a 30 pack year history** were enrolled and **randomized** to compare the effects on mortality.

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

The National Lung Screening Trial Research Team*

Methods

- ◆ **Randomized Trial** conducted by the Lung Screening Trial, National Cancer Institute Division of Cancer Prevention, and the American College of Radiology Imaging Network
- ◆ **33** Participating Medical Institutions
- ◆ Timeline
 - ◆ Enrolled patients August 2002 to September 2004
 - ◆ Screening from August 2002 to September 2007
 - ◆ Patients followed thru December 31, 2009

Study Group and Screening Center	Location	Accrual No.
NLST-ACRIN		
Beth Israel Deaconess Medical Center*†	Boston	629
Brigham and Women's Hospital†	Boston	540
Brown University, Rhode Island Hospital*†	Providence	827
The Cancer Institute of New Jersey*†	New Brunswick	88
Dartmouth-Hitchcock Medical Center*†	Lebanon	575
Emory University	Atlanta	1231
Jewish Hospital Rudd Heart and Lung Institute*†	Louisville	1971
Johns Hopkins University*†	Baltimore	1670
Mayo Clinic, Jacksonville*†	Jacksonville	288
Mayo Clinic, Rochester*†	Rochester	1183
Medical University of South Carolina	Charleston	578
Moffitt Cancer Center*†	Tampa	787
Northwestern University	Chicago	426
Ochsner Medical Center	New Orleans	504
St. Elizabeth Health Center*†	Youngstown	1046
University of California, Los Angeles*†	Los Angeles	1587
University of California, San Diego*†	San Diego	155
University of Iowa	Iowa City	1154
University of Michigan Medical Center*†	Ann Arbor	857
University of Pennsylvania	Philadelphia	386
University of Texas M.D. Anderson Cancer Center*†	Houston	782
Vanderbilt University	Nashville	465
Wake Forest University*†	Winston-Salem	1113
NLST/ACRIN total		18842

NLST-LSS

Georgetown University Medical Center	Washington	1827
Henry Ford Health System	Detroit	3395
Marshfield Clinic Research Foundation	Marshfield	2520
Pacific Health Research & Education Institute [‡]	Honolulu	2359
University of Alabama at Birmingham	Birmingham	5052
University of Colorado Denver	Aurora	3743
University of Minnesota School of Public Health	Minneapolis	6618
University of Pittsburgh Medical Center	Pittsburgh	2177
University of Utah Health Sciences Center	Salt Lake City	3159
Washington University School of Medicine	St Louis	3764
NLST/LSS total		34614
NLST total		53456

Methods

◆ Inclusion Criteria

- ◆ Age 55 – 74 years
- ◆ History of Cigarette Smoking of at least 30 pack years
- ◆ If former smokers, had quit within the previous 15 years

◆ Exclusion Criteria

- ◆ Prior diagnosis of Lung Cancer
- ◆ Prior Chest CT scan within 18 months of enrollment
- ◆ Hemoptysis within the previous year
- ◆ Unexplained Weight loss of more than 15 lbs within the previous year

◆ Patients Enrolled

- ◆ 53,454 total
- ◆ 26,722 randomized to screening CT scan
- ◆ 26,732 randomized to screening with chest radiography

Methods

◆ Screening

- ◆ Three screenings (T0, T1, T2) at 1-year intervals with T0 being done soon after randomization
- ◆ Patients diagnosed during the study with lung cancer were not offered any more screening studies
- ◆ Low Dose CT scan meant a reduced dose of 1.5mSv

◆ Radiologist Interpretation

- ◆ Images interpreted first in isolation, then in comparison to historical images, and then in comparison to NLST prior screening images.
- ◆ Positive “suspicious” lesions: any non calcified nodule greater than 4mm on CT, or any non calcified nodule or mass on CXR, adenopathy, or pleural effusion.
- ◆ Clinically significant abnormalities other than lung cancer were also noted.

Results

Table 1. Selected Baseline Characteristics of the Study Participants.*

Characteristic	Low-Dose CT Group (N = 26,722)	Radiography Group (N = 26,732)
	number (percent)	
Age at randomization		
<55 yr†	2 (<0.1)	4 (<0.1)
55–59 yr	11,440 (42.8)	11,420 (42.7)
60–64 yr	8,170 (30.6)	8,198 (30.7)
65–69 yr	4,756 (17.8)	4,762 (17.8)
70–74 yr	2,353 (8.8)	2,345 (8.8)
≥75 yr†	1 (<0.1)	3 (<0.1)
Sex		
Male	15,770 (59.0)	15,762 (59.0)
Female	10,952 (41.0)	10,970 (41.0)
Race or ethnic group‡		
White	24,289 (90.9)	24,260 (90.8)
Black	1,195 (4.5)	1,181 (4.4)
Asian	559 (2.1)	536 (2.0)
American Indian or Alaska Native	92 (0.3)	98 (0.4)
Native Hawaiian or other Pacific Islander	91 (0.3)	102 (0.4)
More than one race or ethnic group	333 (1.2)	346 (1.3)
Data missing	163 (0.6)	209 (0.8)
Hispanic ethnic group‡		
Hispanic or Latino	479 (1.8)	456 (1.7)
Neither Hispanic nor Latino	26,079 (97.6)	26,039 (97.4)
Data missing	164 (0.6)	237 (0.9)
Smoking status		
Current	12,862 (48.1)	12,900 (48.3)
Former	13,860 (51.9)	13,832 (51.7)

- ◆ Thru Dec 31, 2009:
 - ◆ 97% followup in CT scan arm
 - ◆ 96% followup in the radiograph arm
- ◆ Mean Duration of followup = 6.5 years

Table 2. Results of Three Rounds of Screening.*

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

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
	<i>number (percent)</i>							
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)

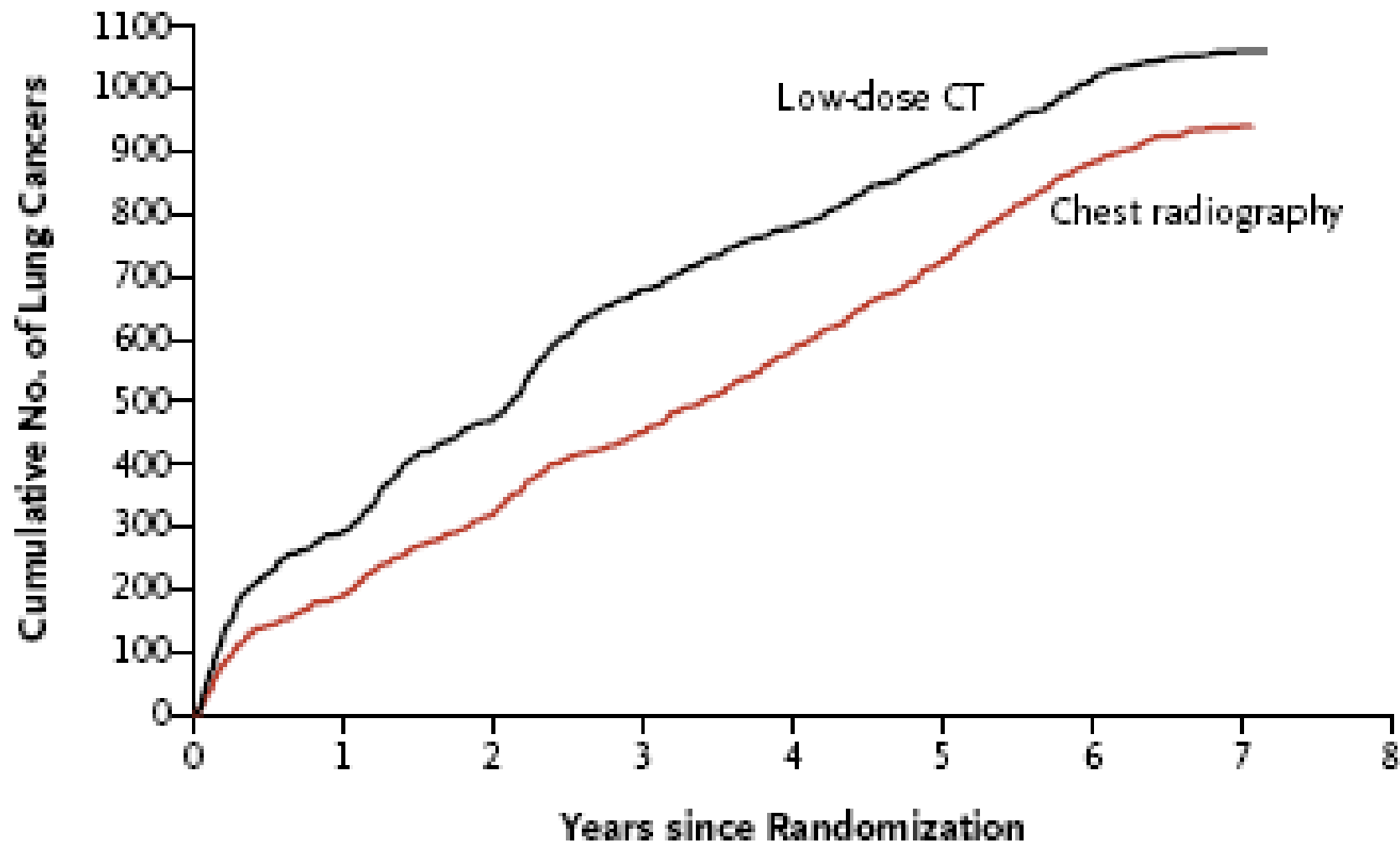
Table 4. Complications after the Most Invasive Screening-Related Diagnostic Evaluation Procedure, According to Lung-Cancer Status.*

Complication	Lung Cancer Confirmed				Total
	Thoracotomy, Thoracoscopy, or Mediastinoscopy	Bron- choscopy	Needle Biopsy	No Invasive Procedure	
	<i>number (percent)</i>				
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)
No complication	344 (67.6)	69 (90.8)	26 (78.8)	26 (83.9)	465 (71.6)
At least one complication	165 (32.4)	7 (9.2)	7 (21.2)	5 (16.1)	184 (28.4)
Most severe complication classified as major	71 (13.9)	2 (2.6)	0	2 (6.5)	75 (11.6)
Most severe complication classified as intermediate	81 (15.9)	5 (6.6)	7 (21.2)	2 (6.5)	95 (14.6)
Most severe complication classified as minor	13 (2.6)	0	0	1 (3.2)	14 (2.2)
Death within 60 days after most invasive diagnostic procedure†	5 (1.0)	4 (5.3)	1 (3.0)	0	10 (1.5)
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)
No complication	130 (68.8)	42 (91.3)	28 (96.6)	14 (93.3)	214 (76.7)
At least one complication	59 (31.2)	4 (8.7)	1 (3.4)	1 (6.7)	65 (23.3)
Most severe complication classified as major	22 (11.6)	1 (2.2)	0	1 (6.7)	24 (8.6)
Most severe complication classified as intermediate	32 (16.9)	2 (4.3)	1 (3.4)	0	35 (12.5)
Most severe complication classified as minor	5 (2.6)	1 (2.2)	0	0	6 (2.2)
Death within 60 days after most invasive diagnostic procedure†	4 (2.1)	5 (10.9)	1 (3.4)	1 (6.7)	11 (3.9)

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)
	<i>number/total number (percent)</i>							
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)

A Lung Cancer



B Death from Lung Cancer

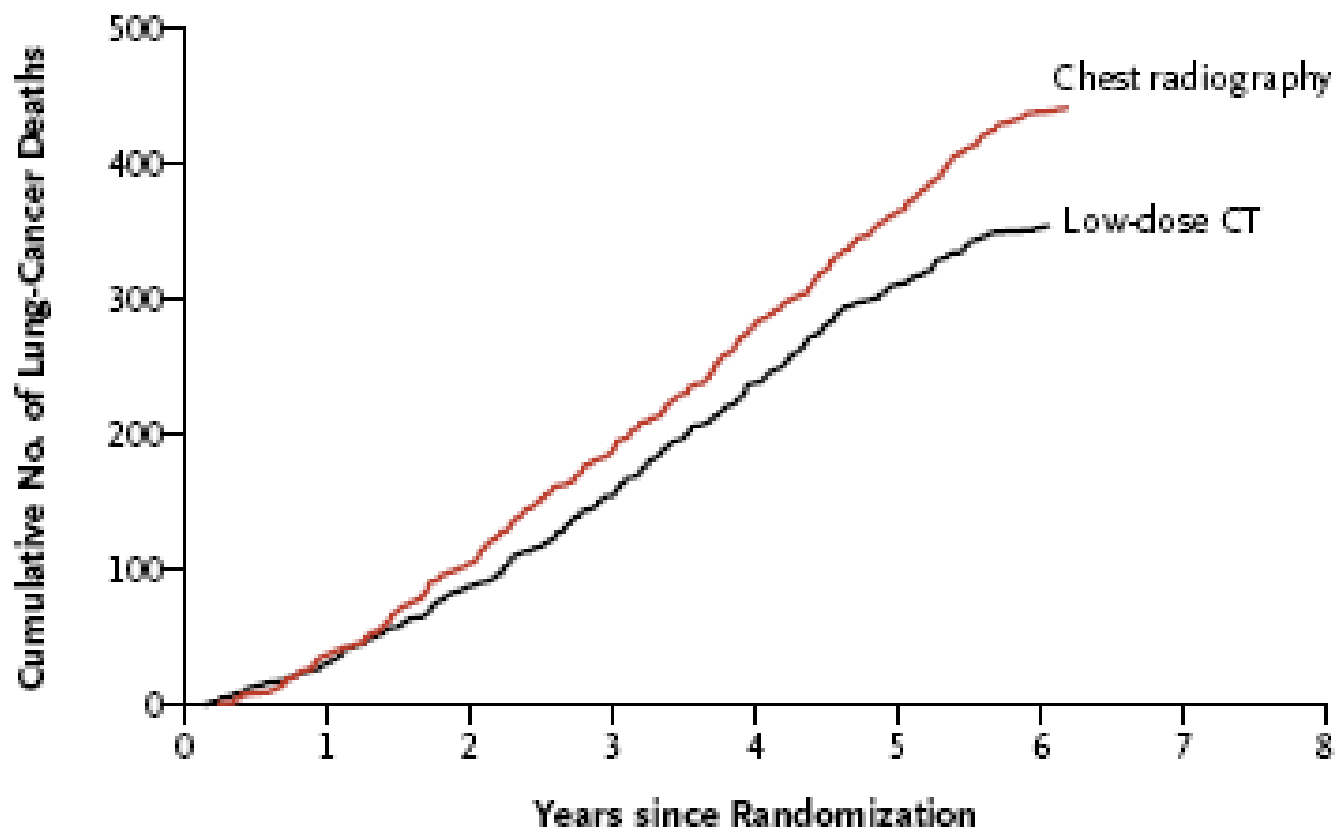


Figure 1. Cumulative Numbers of Lung Cancers and of Deaths from Lung Cancer.

The number of lung cancers (Panel A) includes lung cancers that were diagnosed from the date of randomization through December 31, 2009. The number of deaths from lung cancer (Panel B) includes deaths that occurred from the date of randomization through January 15, 2009.

♦ **LUNG CANCER** Mortality Results

♦ CT scan:	356 deaths	247/100,000
♦ Radiography:	443 deaths	309/100,000

RELATIVE REDUCTION IN THE RATE OF DEATH FROM LUNG CANCER WITH LOW DOSE CT SCREENING OF 20% (P= 0.004)

♦ **OVERALL** Mortality Results

- ♦ CT scan: 1877 deaths
- ♦ Radiography: 2000 deaths

RELATIVE REDUCTION IN THE RATE OF DEATH FROM ANY CAUSE WITH LOW DOSE CT SCREENING OF 6.7% (P= 0.02)

LIMITATIONS

- ◆ NLST was conducted at medical institutions recognized for expertise in radiology and diagnosis / treatment of cancer.

Possibility that community facilities will be less prepared to undertake screening program and its associated care.

(ie Surgical mortality 1% in the NLST vs US average of 4%)

- ◆ **Two potential harmful effects:**
 - ◆ **OVERDIAGNOSIS:** detection of cancers that never would have become symptomatic
 - ◆ **RADIATION INDUCED CANCERS:** Cannot be measured directly, is a long term phenomenon, and must be assessed in the future.

OTHER THOUGHTS

- ◆ Scanners used today versus in the NLST are technologically more advanced. This difference may mean a **larger reduction in lung cancer death rate** than seen in the NLST.
- ◆ Of course, this may mean **more false positive results** and potential interventions and complications related to those results.
- ◆ Currently, only **7 million** Americans would meet eligibility for the NLST → of the **over 94 million former or current smokers** in the United States. Also, many more Americans with **second-hand exposure to smoke** or other risk factors.



National Lung Screening Trial

Results:

20% reduction in lung cancer mortality with low-dose helical CT scan versus standard CXR

An **additional 7% reduction** in all cause mortality with low-dose helical CT scan

Translation:

156,940 Lung cancer deaths x 20.0% reduced

= 31,388 Lives Saved per year

(additional 10, 515 Lives Saved per year)

What do you do for these patients?

- ◆ **For symptomatic at-risk patients:**
 - ◆ CT scan of the Chest
 - ◆ Further Workup as Indicated
- ◆ **For asymptomatic patients who are at-risk:**
 - ◆ Low Dose Screening CT scan!

Who is Doing Screening CT?

- ◆ **CALIFORNIA:**
 - ◆ CEDAR SINAI, LOS ANGELES
 - ◆ *JOHN MUIR, WALNUT CREEK*
 - ◆ *UCSF, SAN FRANCISCO*
- ◆ YALE, NEW HAVEN
- ◆ NATIONAL JEWISH, DENVER
- ◆ UNIVERSITY COLORADO, DENVER
- ◆ MOFFITT CANCER CENTER, TAMPA
- ◆ UNIVERSITY OF MIAMI, MIAMI
- ◆ EMORY UNIVERSITY, ATLANTA
- ◆ **NORTHWESTERN MEMORIAL, CHICAGO**
- ◆ RUSH, CHICAGO
- ◆ JOHNS HOPKINS, BALTIMORE
- ◆ **BRIGHAM AND WOMEN'S HOSPITAL, BOSTON**

Who is Doing Screening CT?

- ◆ UNIVERSITY MICHIGAN, ANN ARBOR
- ◆ MAYO CLINIC, ROCHESTER
- ◆ MEMORIAL SLOAN KETTERING, NEW YORK
- ◆ WAKE FOREST, WINSTON-SALEM

- ◆ UNIVERSITY HOSPITAL SIEDMAN CANCER CENTER, CLEVELAND
 - ◆ **99\$ SCREENING CT SCAN OFFERED**

- ◆ TEMPLE UNIVERSITY, PHILADELPHIA
- ◆ THOMAS JEFFERSON UNIVERSITY, PHILADELPHIA
- ◆ MD ANDERSON, HOUSTON
- ◆ GEORGETOWN UNIVERSITY, WASHINGTON DC

- ◆ *Queen of the Valley Medical Center, NAPA ???*
- ◆ *Santa Rosa Memorial Hospital, Santa Rosa ???*

Questions?

Thank You

