Natural History and Epidemiology of Lung Cancer

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DIALOGUE FOR ACTION
ON CANCER SCREENING

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Natural History and the Epidemiology of Lung Cancer

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Dignity Health™
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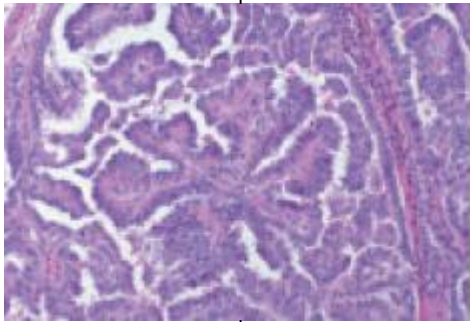Medical Center

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Disease Characteristics for Screening

- Prevalent

- Serious

- Defined risk factors

- Stage-dependent survival

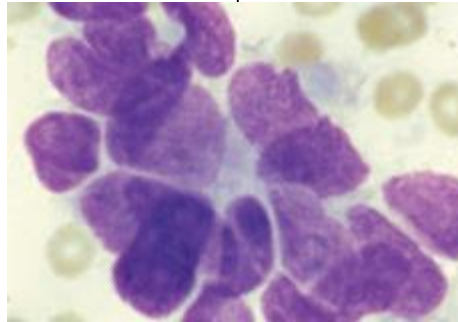- Established detection method

- Defined premalignant lesions

Primary Cancers of the Lung
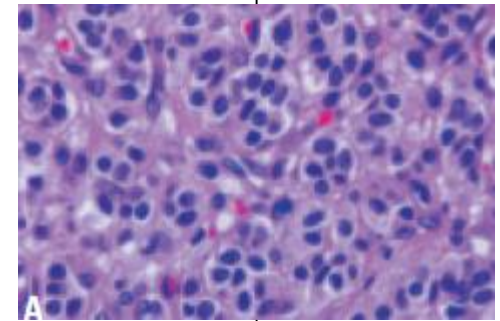
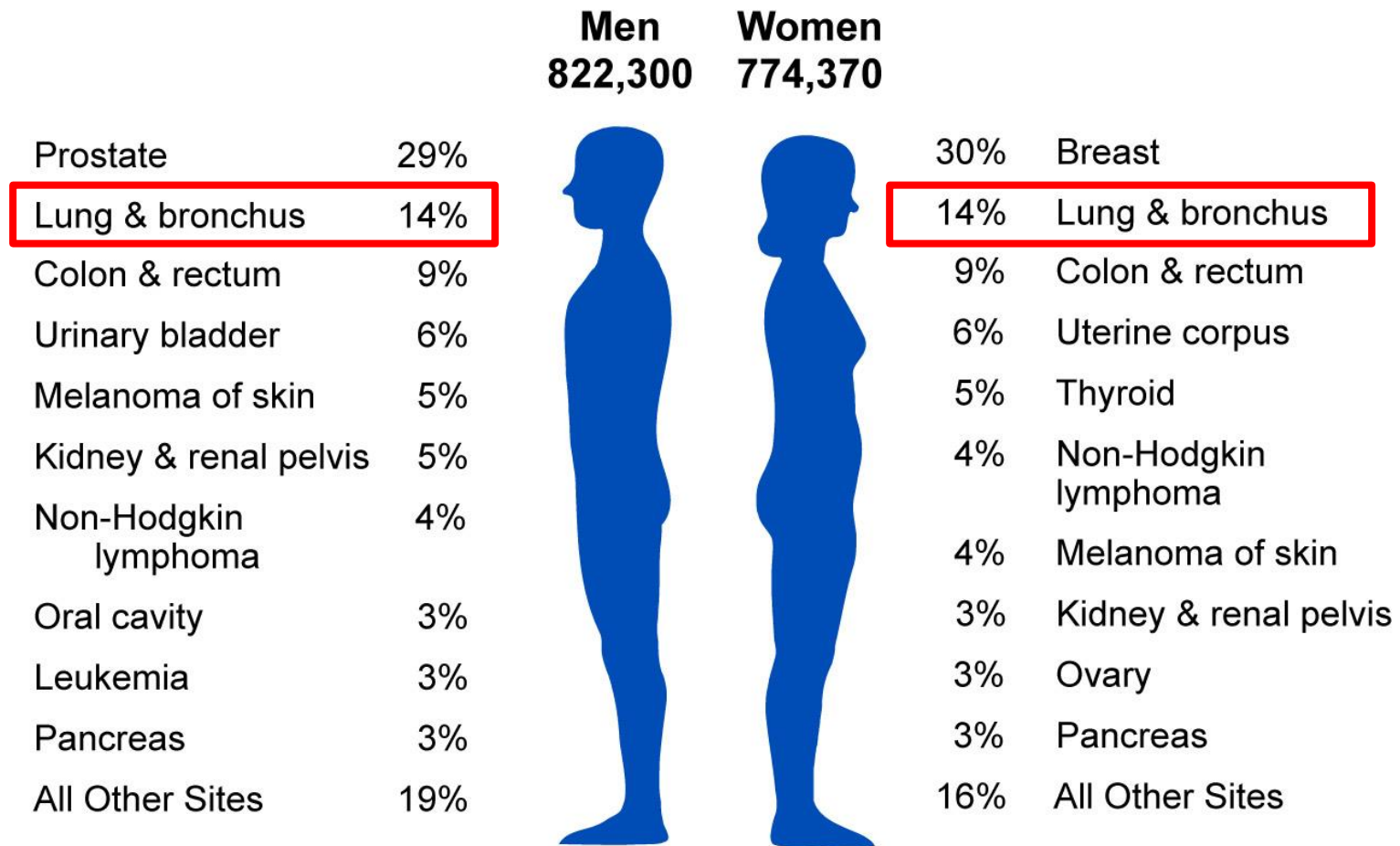| Non-Small Cell Lung Cancer	Small Cell Lung Cancer	Carcinoid
85% of cancers Typically aggressive Surgery or Chemotherapy	15% of cancers Typically very aggressive Chemotherapy	Typically very indolent Surgery

2011 Estimated US Cancer Cases
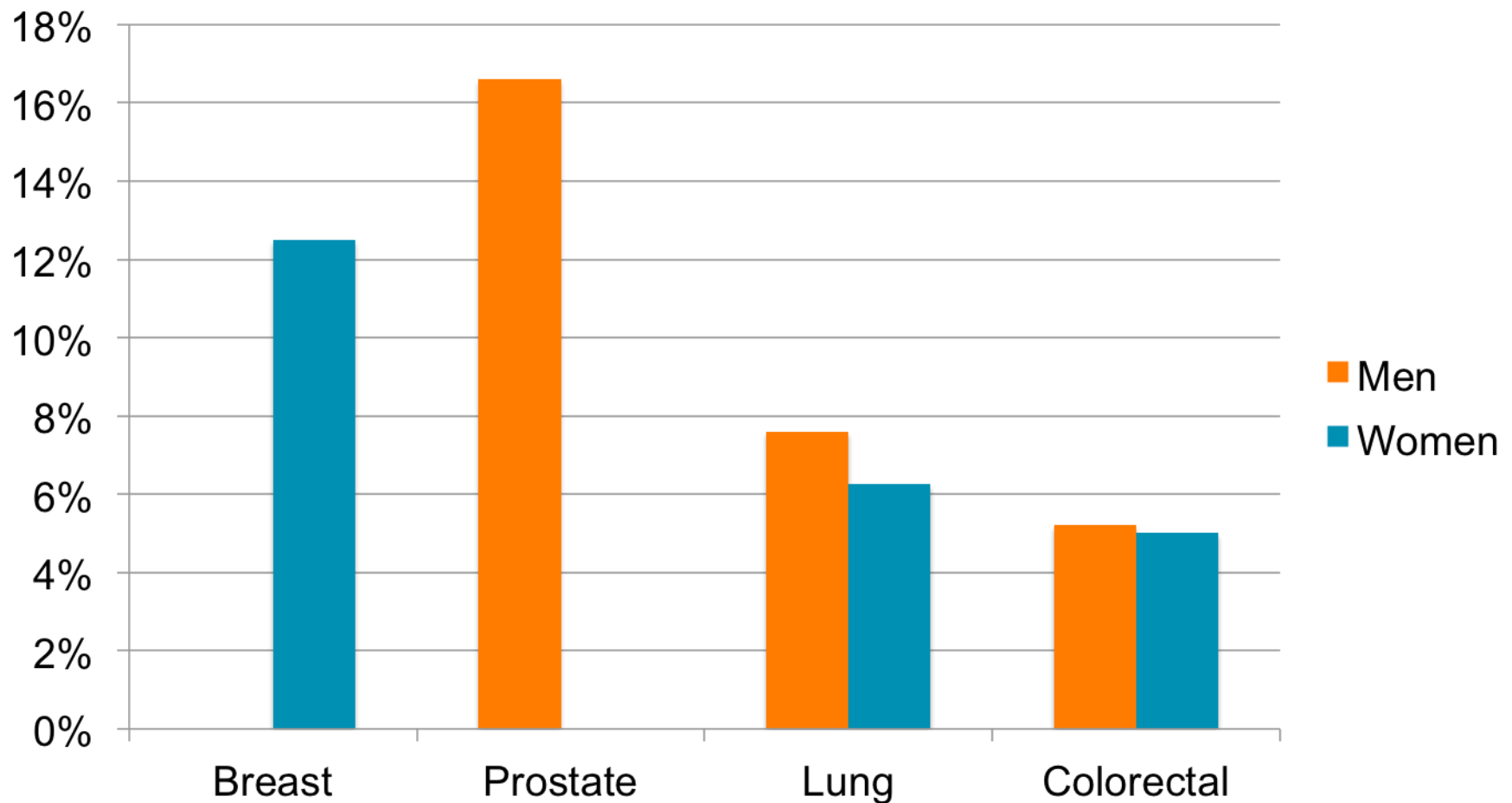
Men
822,300

Women
774,370

Prostate	29%		30%	Breast
Lung & bronchus	14%		14%	Lung & bronchus
Colon & rectum	9%		9%	Colon & rectum
Urinary bladder	6%		6%	Uterine corpus
Melanoma of skin	5%		5%	Thyroid
Kidney & renal pelvis	5%		4%	Non-Hodgkin lymphoma
Non-Hodgkin lymphoma	4%		4%	Melanoma of skin
Oral cavity	3%		3%	Kidney & renal pelvis
Leukemia	3%		3%	Ovary
Pancreas	3%		3%	Pancreas
All Other Sites	19%		16%	All Other Sites

Source: American Cancer Society, 2011

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*excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder

Lifetime Probability of Developing Cancer 2005-2007

Source: DevCan: Probability of Developing or Dying of Cancer Software, Version 6.5.0, NCI 2010

Cancer Death Rates Among Men, 1930-2007

Cancer Death Rates Among Women, 1930-2007

Source: US Mortality Data 1960-2007, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention
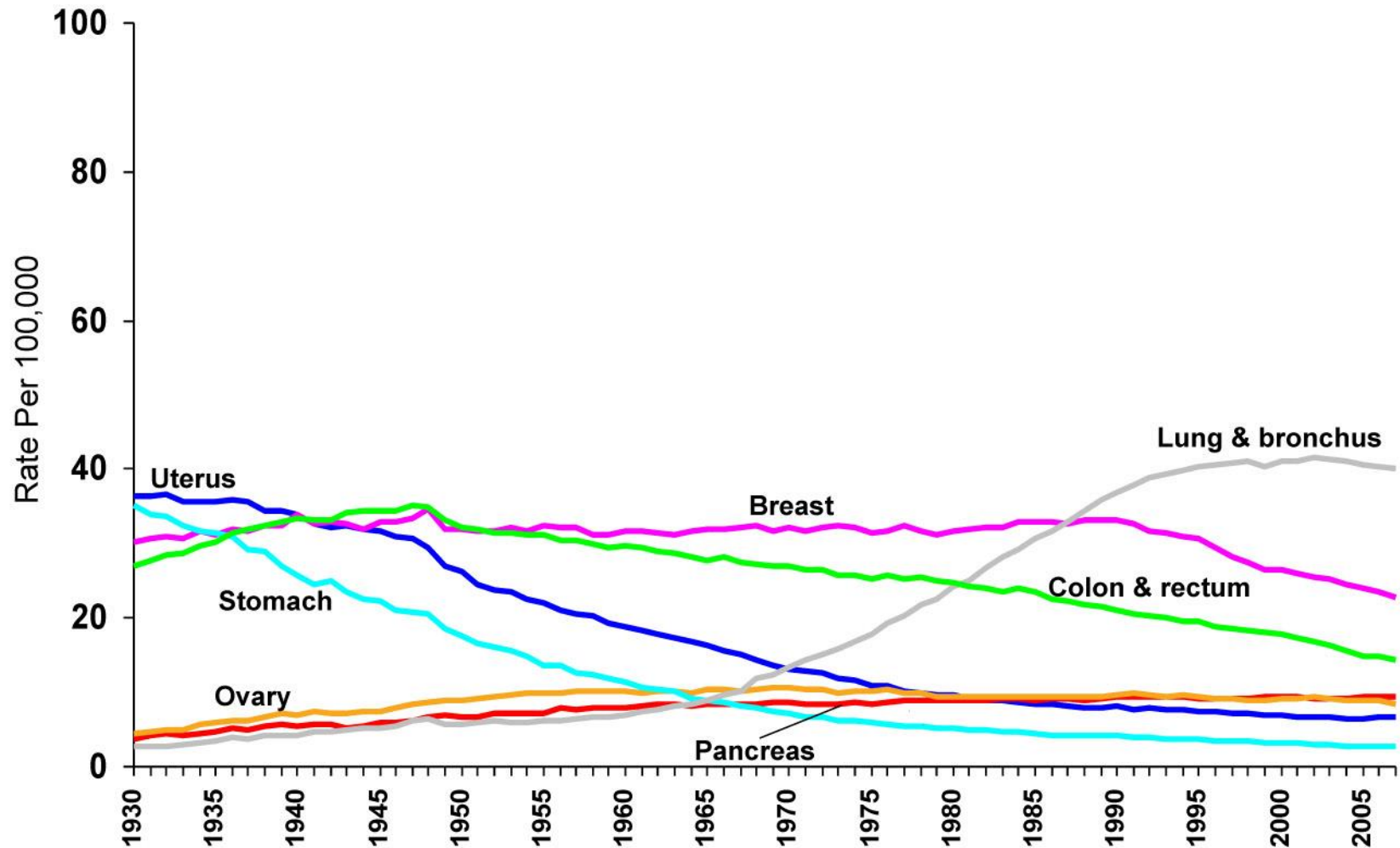
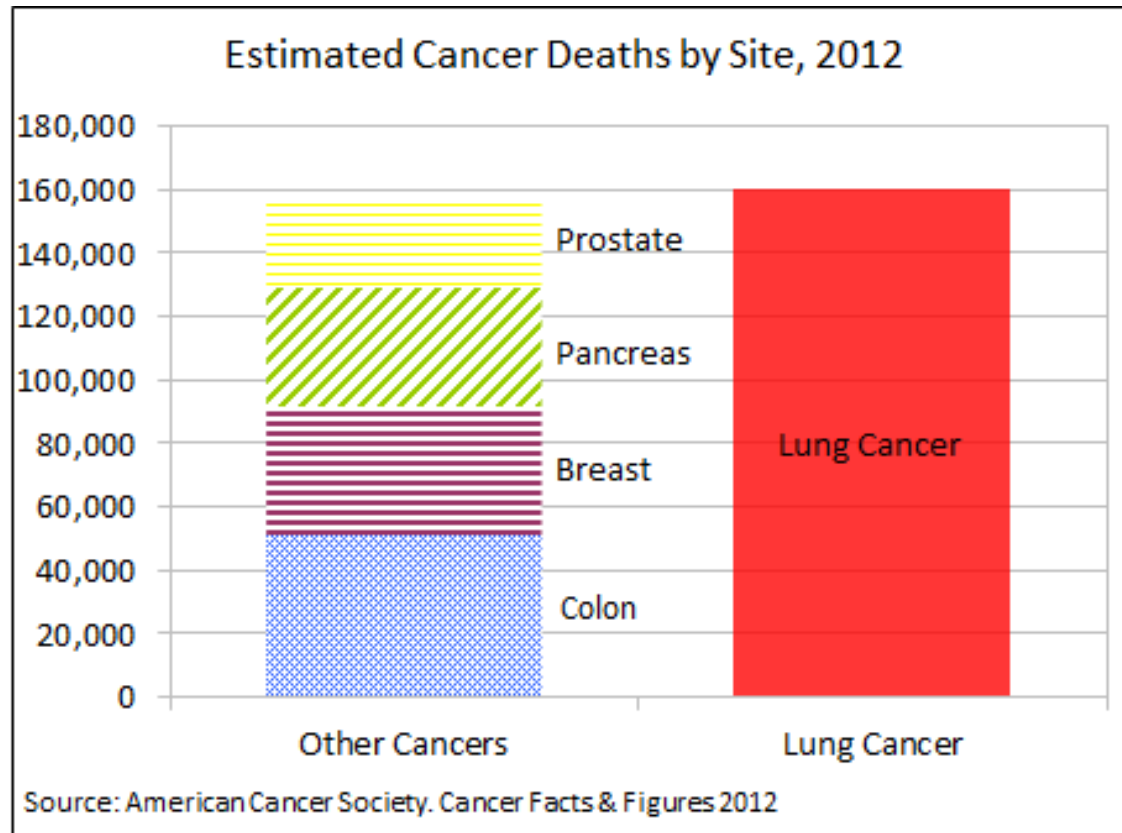# Lung Cancer Survival By Stage

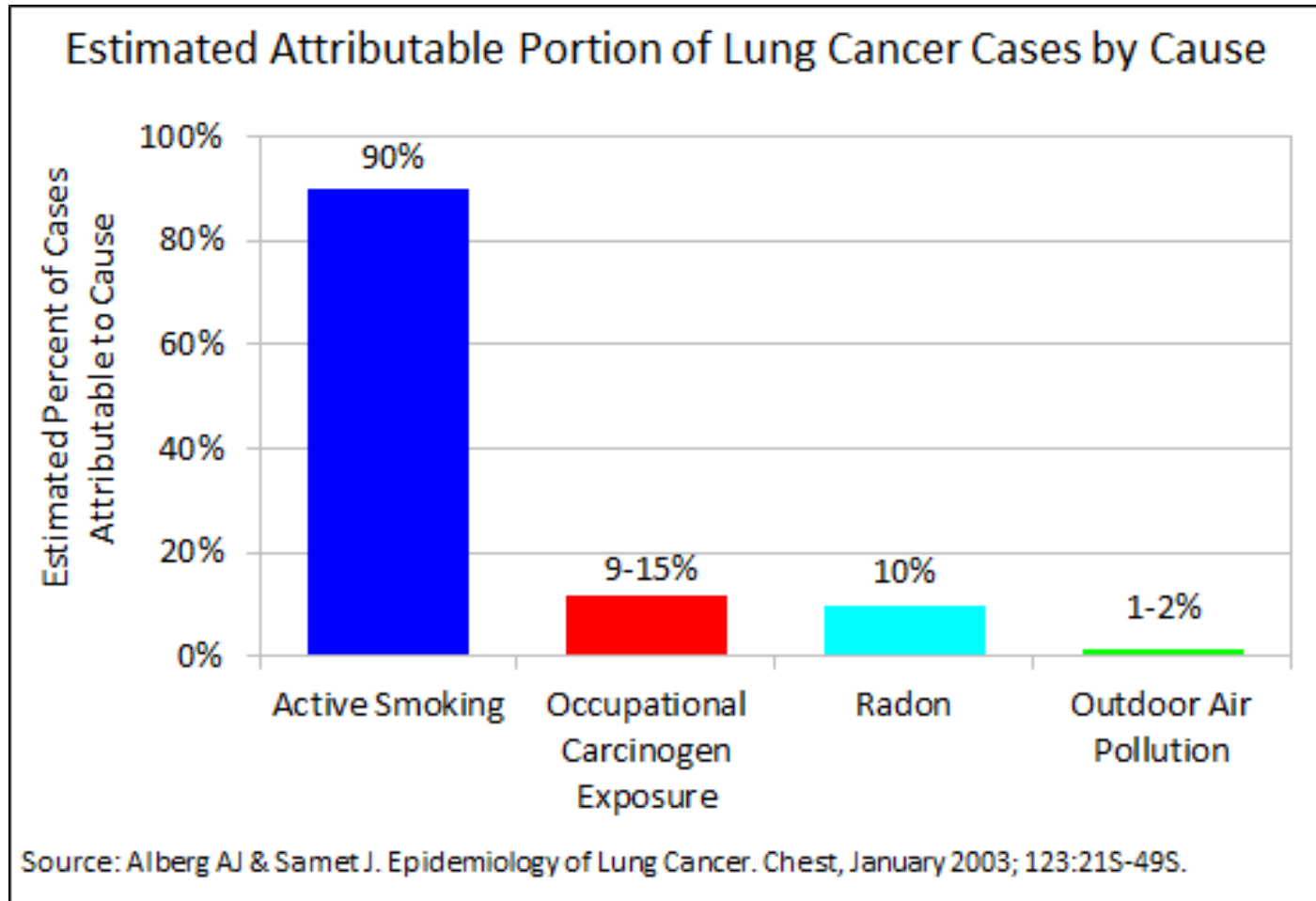Lung Cancer Diagnosis and Survival By Stage, 2001-2007
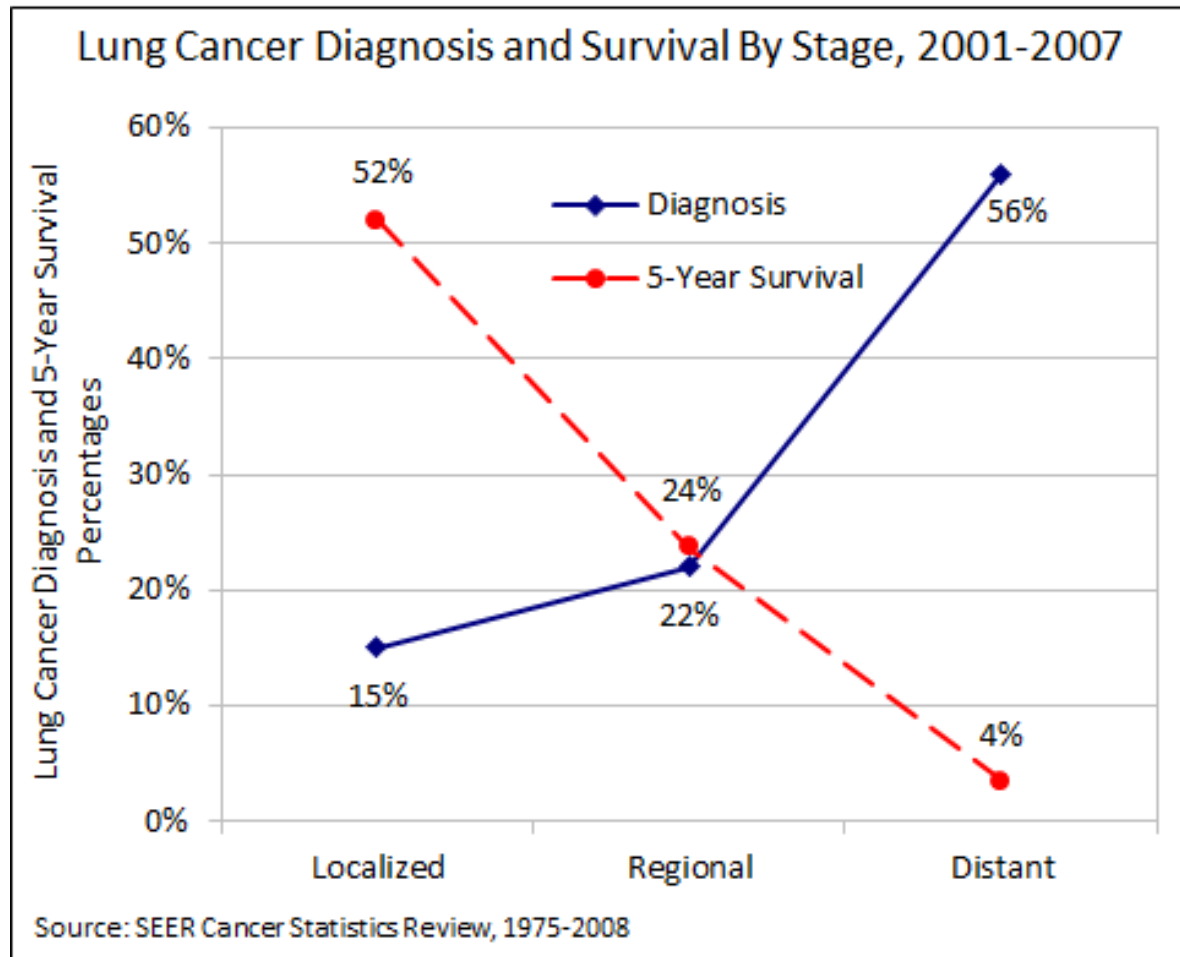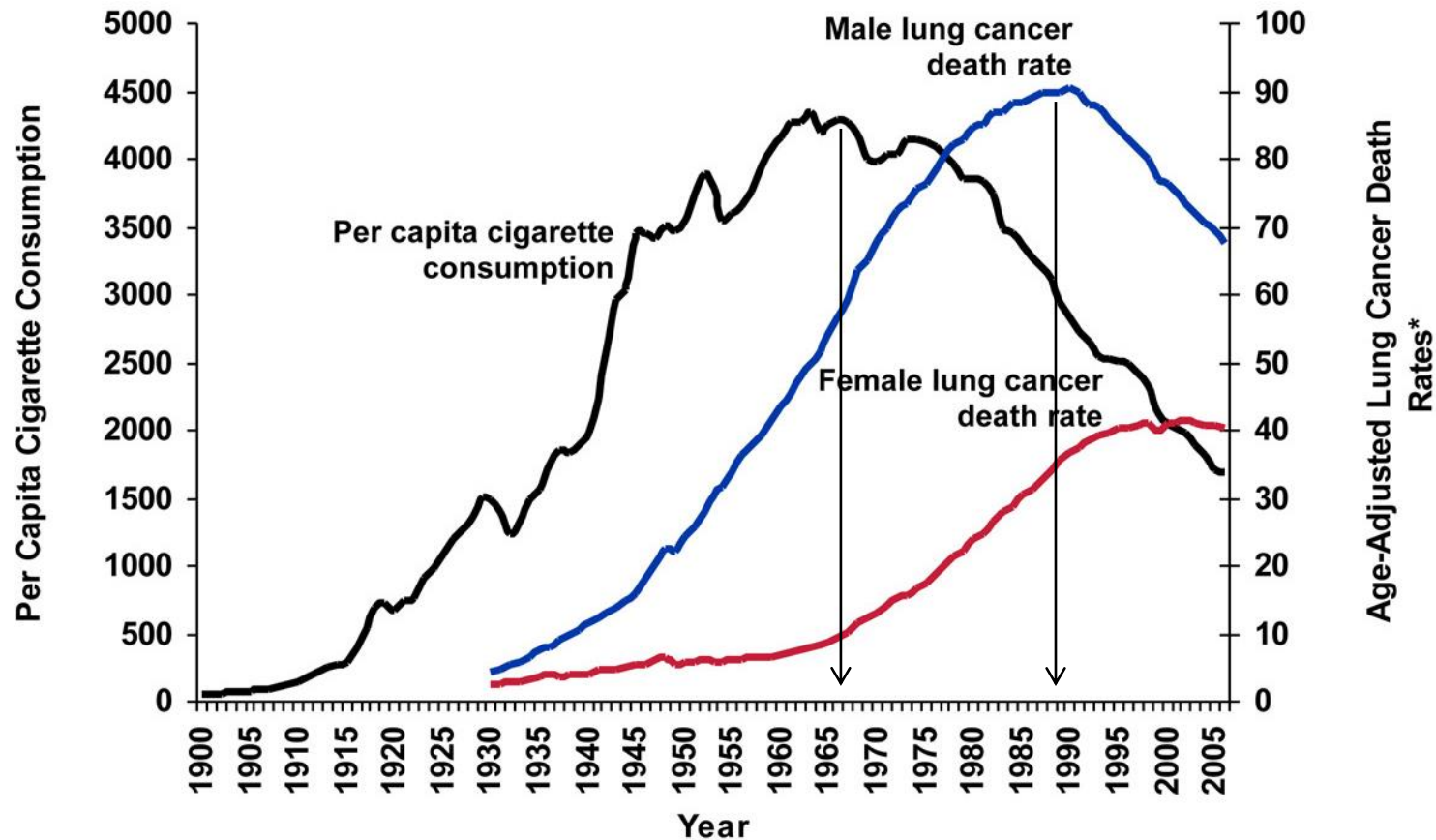
Cancer Mortality

Incidental Lung Cancer

- Autopsy study

- 24708 cases; 56% estimated natural causes

- Incidental lung cancer in 0.34%

- Incidental non-small cell lung cancer in 0.2%

- Prostate cancer

- Men older than 50: 23-46% of autopsies
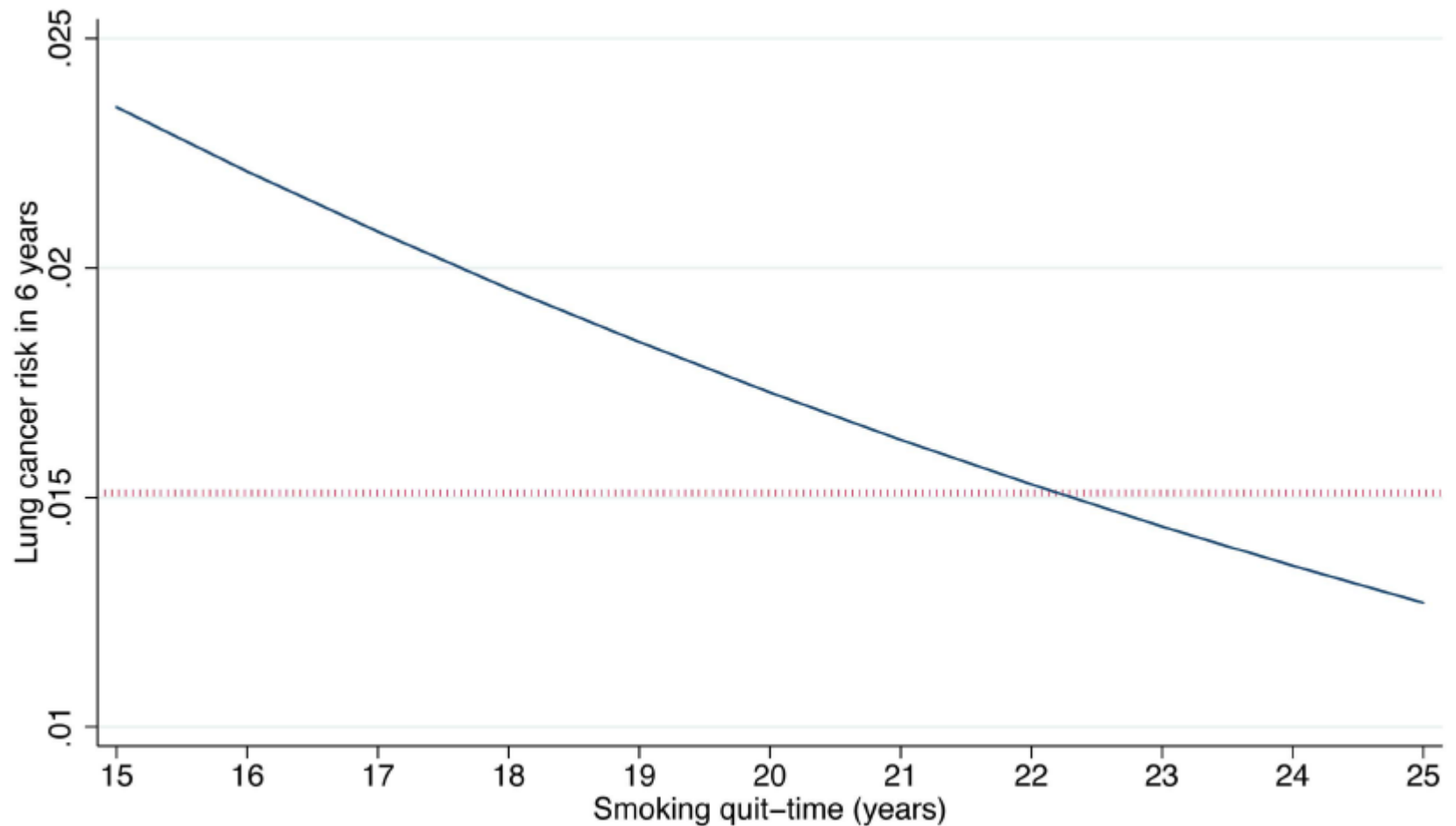
Causes of Lung Cancer

Estimated Attributable Portion of Lung Cancer Cases by Cause

Source: Alberg AJ & Samet J. Epidemiology of Lung Cancer. Chest, January 2003; 123:21S-49S.

Tobacco Use in the US, 1900-2006

Sources: US Mortality Data 1960-2006; US Mortality Volumes 1930-1959; National Center for Health Statistics, Center for Disease and Control Prevention, 2009; US Department of Agriculture, 1900-2007
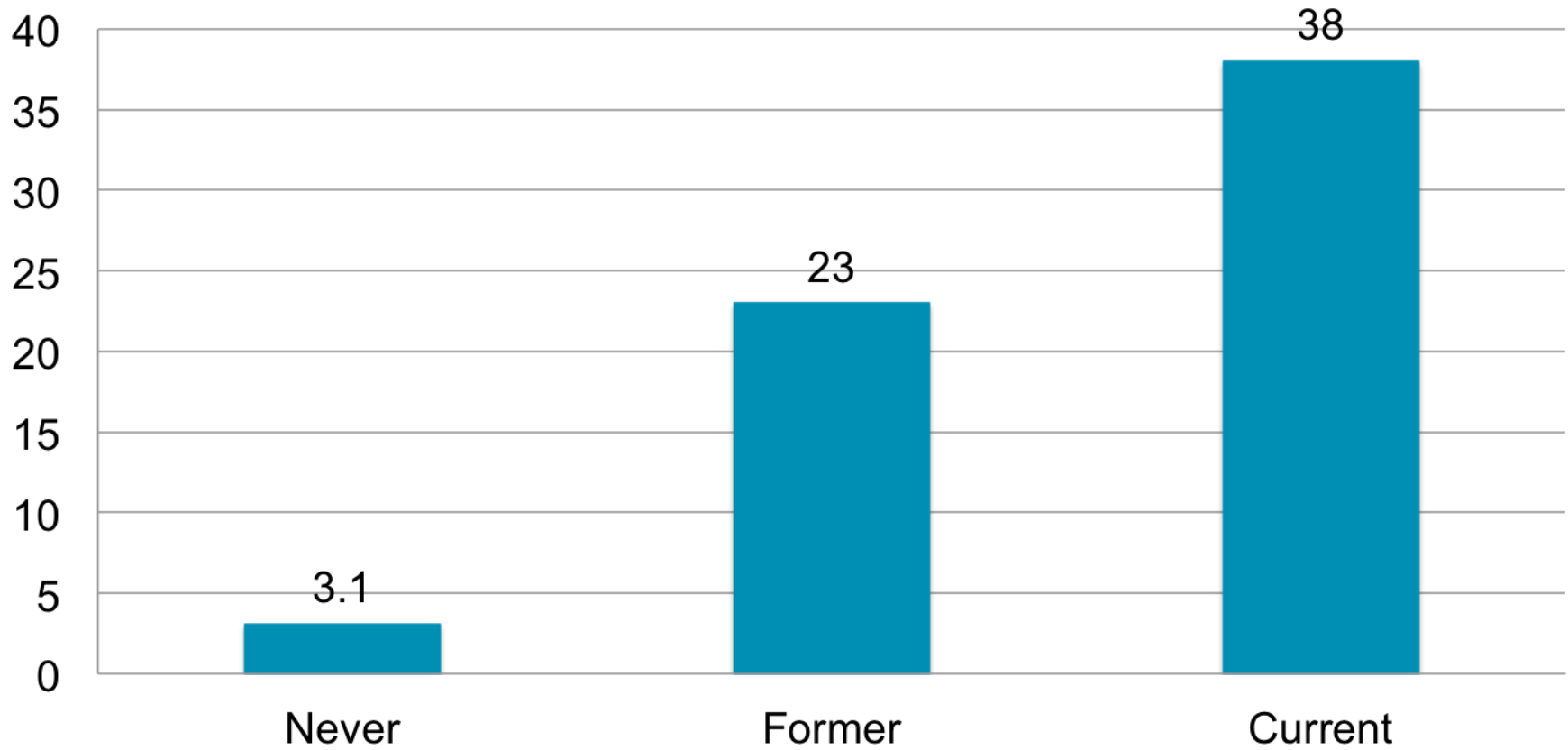
Declining Risk After Quitting Smoking

Risk of Malignancy: Smoking History

per 100,000 person years

Oken et al. JAMA 306: 1865, 2011

Disease Characteristics for Screening: Lung Cancer

- Prevalent **+**

- Serious **+**

- Defined risk factors **+**

- Stage-dependent survival **+**

- Established detection method **+**

- Defined premalignant lesions **–**

Timeline of Screening Studies

Lung Cancer Screening Studies: PLCO
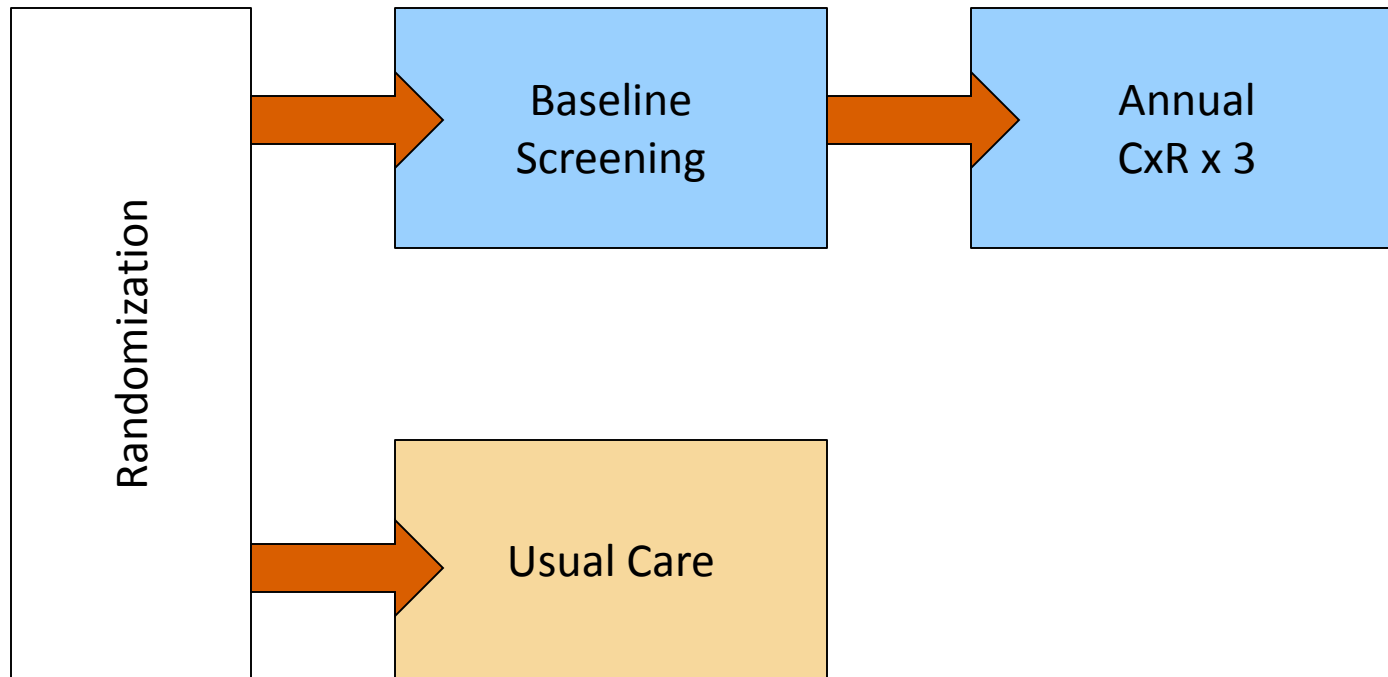
PLCO: Lung Cancer Mortality by Year

Oken et al. JAMA 306: 1865, 2011
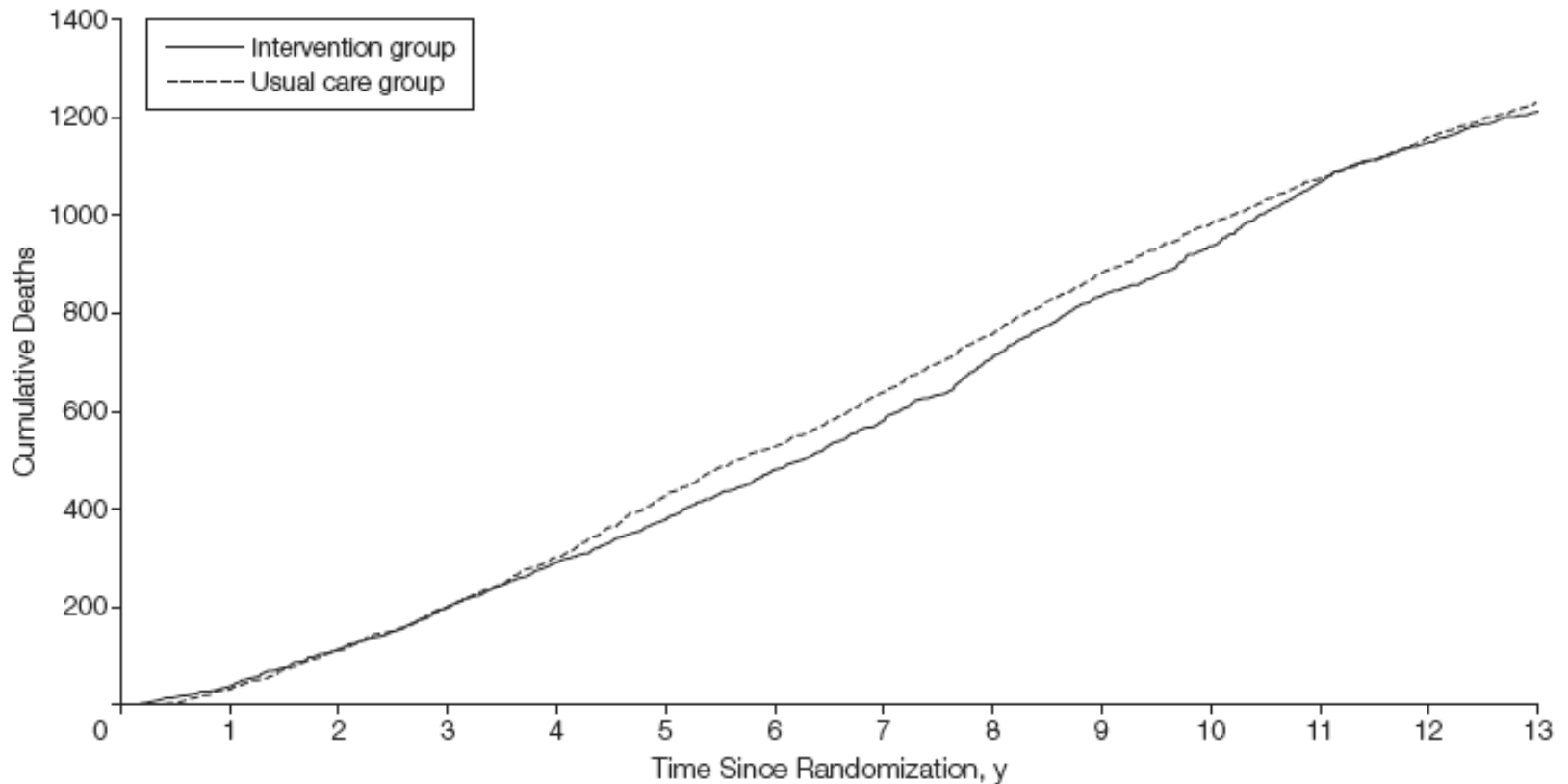
PLCO: Lung Cancer Cases

	Screened	Control
N	77445	77456
Lung Cancer Cases	1696	1620
Small Cell	14%	15%
NSCLC		
Stage I	32%	27%
Stage II	8%	8%
Stage III	25%	26%
Stage IV	35%	38%
Screen Detected	18%	N/a

Low Dose CT scan

- No strict definition of low dose CT
- Non contrast scan
- Generally, 10-30% of standard-dose CT scan
- Compared to high resolution CT scan:
  - As accurate for detecting solid pulmonary nodules
  - Less sensitive for low density lesions (GGOs)
- Thin sections (1 mm) can improve definition of subsolid nodules

Lung Cancer Screening Studies: NLST

Randomization

CT T0	CT T1	CT T2
26,309	24,715	24,102

CxR T0	CxR T1	CxR T2
26,035	24,089	23,346
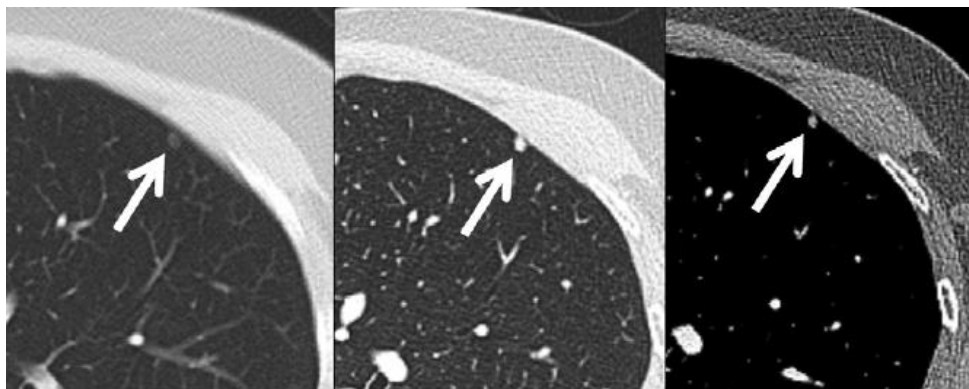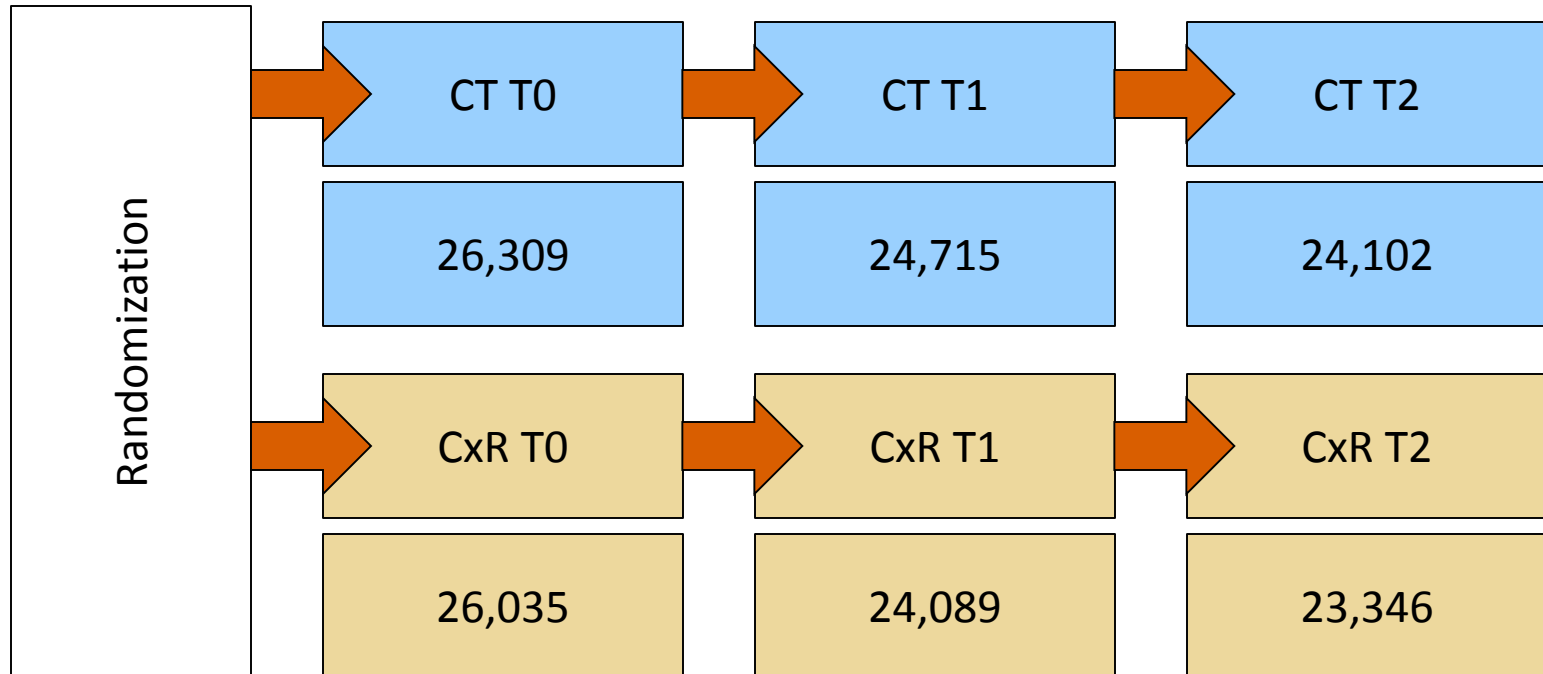
NLST: Cumulative Number of Lung Cancers
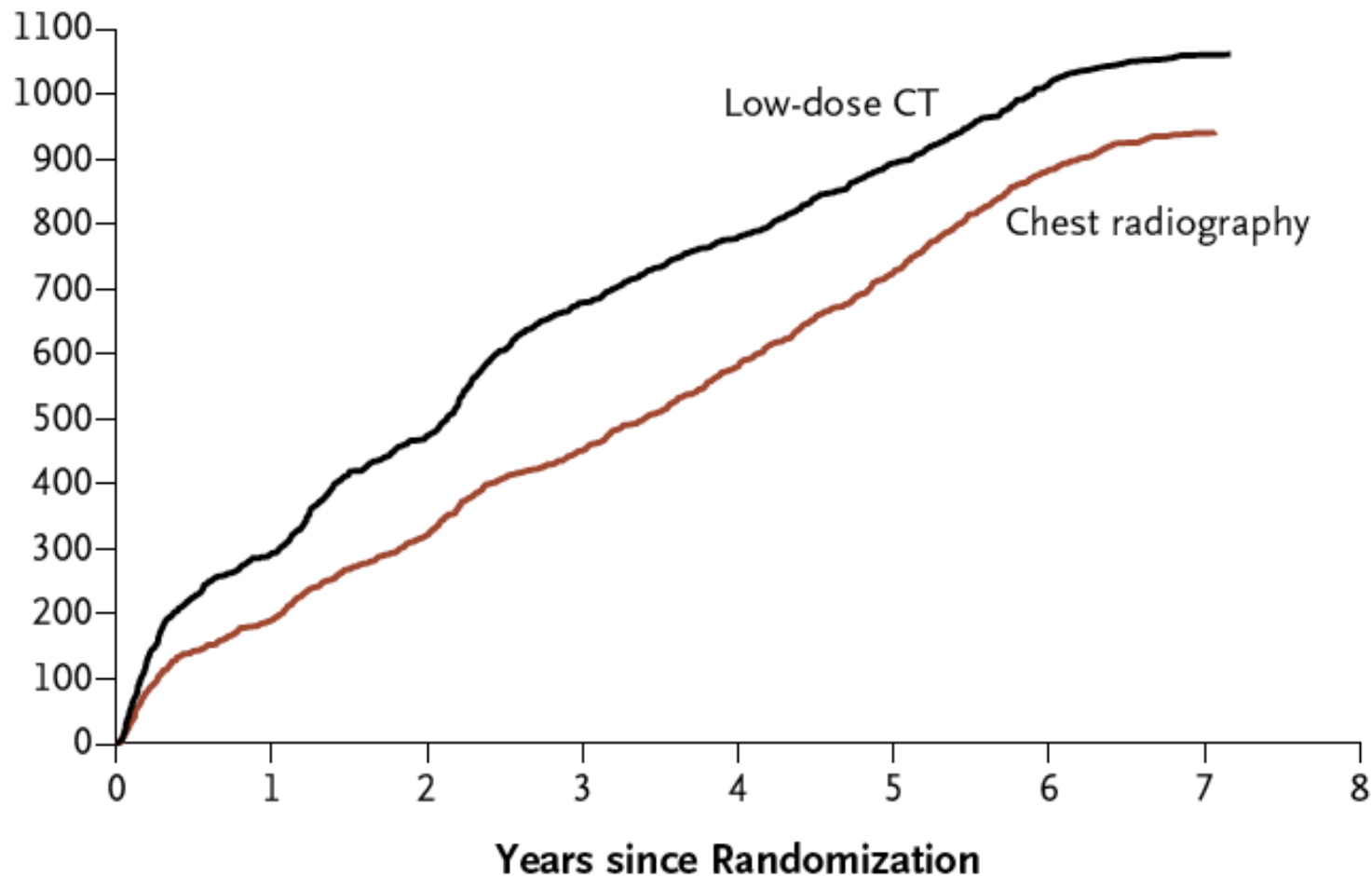
NLST: Deaths from Lung Cancers
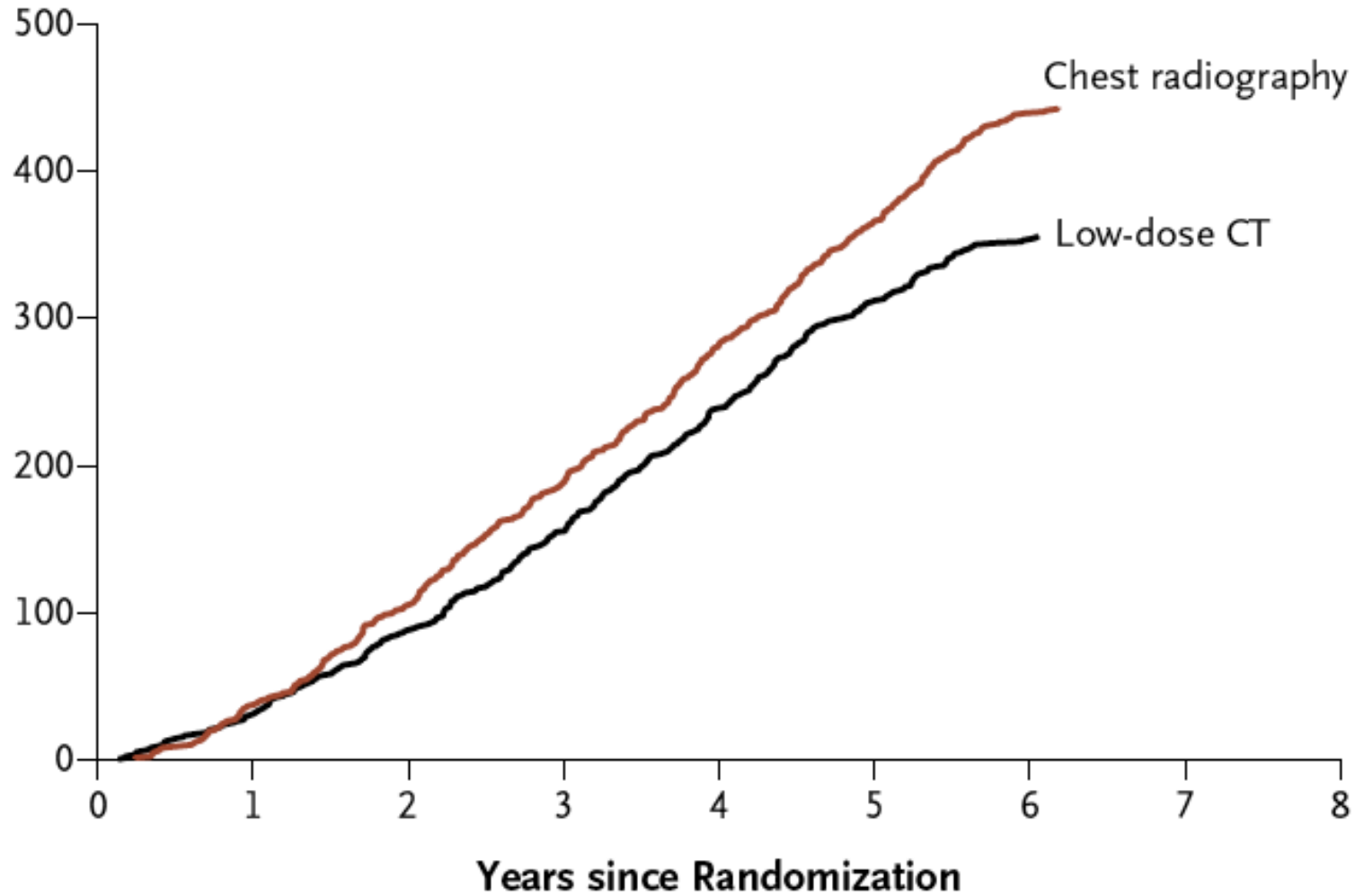
NLST: Lung Cancer Cases

	CT	CxR
N	26,309	26,035
Lung Cancer Cases	1060	941
Small Cell	13.1%	17.1%
NSCLC		
Stage I	50%	31.1%
Stage II	7.1%	7.9%
Stage III	21.2%	24.8%
Stage IV	21.7%	36.1%
Screen Detected	61.2%	29.6%

Who Should Be Screened?

National Lung Screening Trial

- Age 55 – 74

- Cigarette smoking of at least 30 pack years

- Quit smoking within 15 years

- No history of lung cancer, chest CT within 18 months, hemoptysis, unexplained weight loss of 15 lb. in the preceding year

Society Recommendations

The NCCN Lung Cancer Screening Panel recommends lung cancer screening using helical LDCT for individuals with … high risk factors

ASCO suggests that annual screening with LDCT should be offered over both annual screening with chest radiograph or no screening, but only in settings that can deliver the comprehensive care provided to NLST participants.

Practice Guideline of the American College of Chest Physicians and the American Society of Clinical Oncology

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Society Recommendations

American Association for Thoracic Surgery

Guidelines call for annual lung cancer screening with low-dose CT for North Americans from age 55-79 years with a 30 pack-year history of smoking. Lung cancer survivors should have annual low-dose CT until the age of 79 years. Annual low-dose CT should be offered starting at age 50 years with 20 pack-years if there is a risk of developing lung cancer of 5% or greater over the following 5 years

US Preventive Services Task Force

The USPSTF recommends annual screening for lung cancer with low-dose computed tomography in adults ages 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within the past 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

Jaklitsch et al. J Thorac Cardiovasc Surg 144: 33, 2012
http://www.uspreventiveservicestaskforce.org/uspstf/uspslung.htm Release Date: December 2013

Centers for Medicare & Medicaid Services (CAG-00439N)

- Approved February 2015;

- Age 55 – 74 years (proposed);

- Age 55 – 77 years (final);

- Asymptomatic (no signs or symptoms of lung disease);

- Tobacco smoking history of at least 30 pack-years (one pack-year = smoking one pack per day for one year; 1 pack = 20 cigarettes);

- Current smoker or one who has quit smoking within the last 15 years

http://www.cms.gov/medicare-coverage-database/details/nca-proposed-decision-memo.aspx?NCAId=274
http://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=274&NcaName=Screening+for+Lung+Cancer+with+Low+Dose+Computed+Tomography+(LDCT)&TimeFrame=7&DocType=All&bc=AQAAIAAAAgAAAA%3d%3d&

# Lung Cancer Risk Factors

- Increasing age

- Chronic obstructive pulmonary disease

- Pulmonary fibrosis

- Personal history of cancer

- Family history of lung cancer

- Smoking status

Prediction Model-Based Screening Eligibility

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

Online Prediction Calculators

Probability of Lung Cancer Diagnosis by Risk Model
67 y/o male former smoker at 20 cigarettes per day for 40 years (40 pack-years)

http://lungcancerrisk.s3-website-us-east-1.amazonaws.com
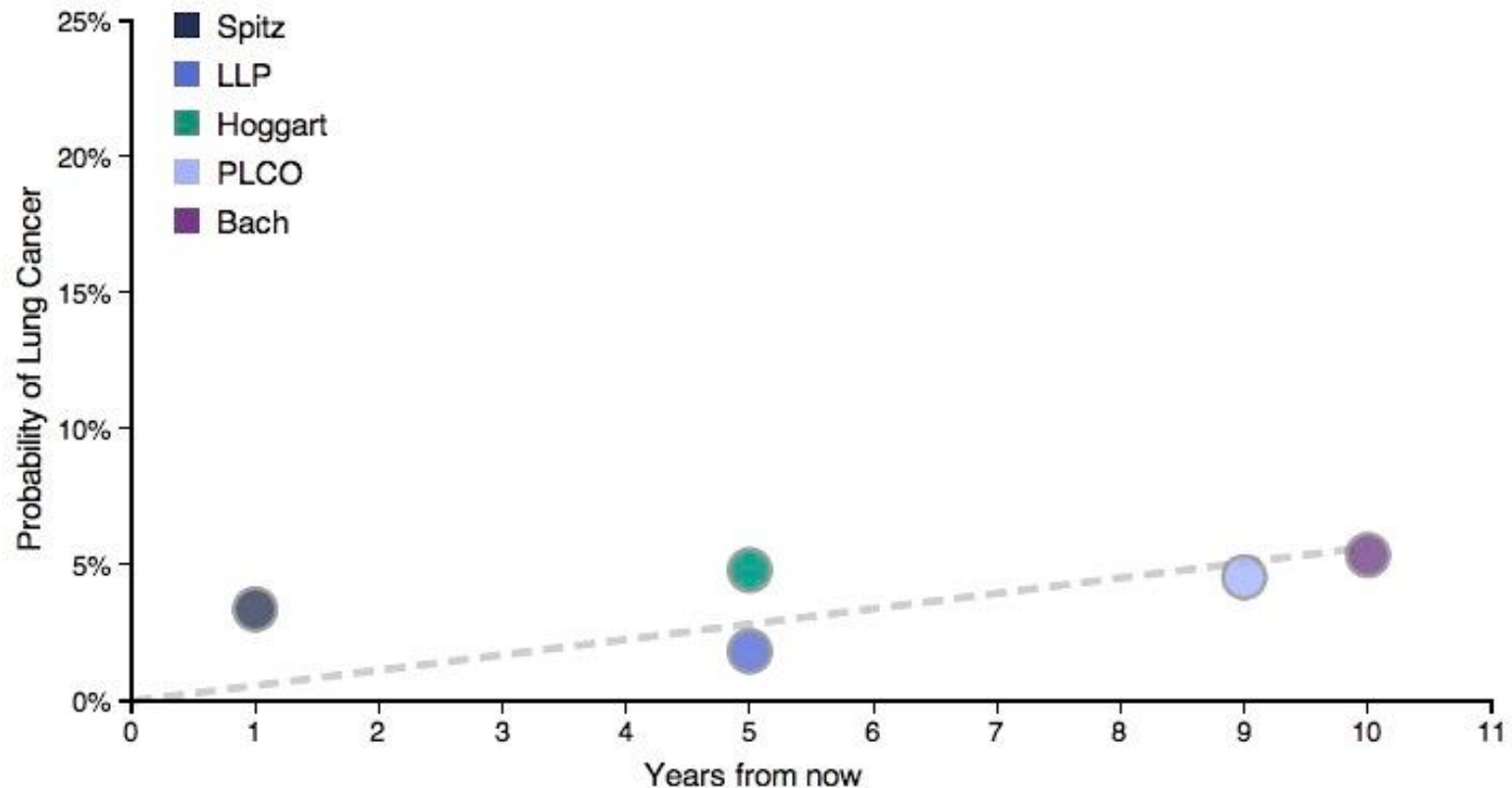
PLCO$_{m2012}$ versus USPSTF

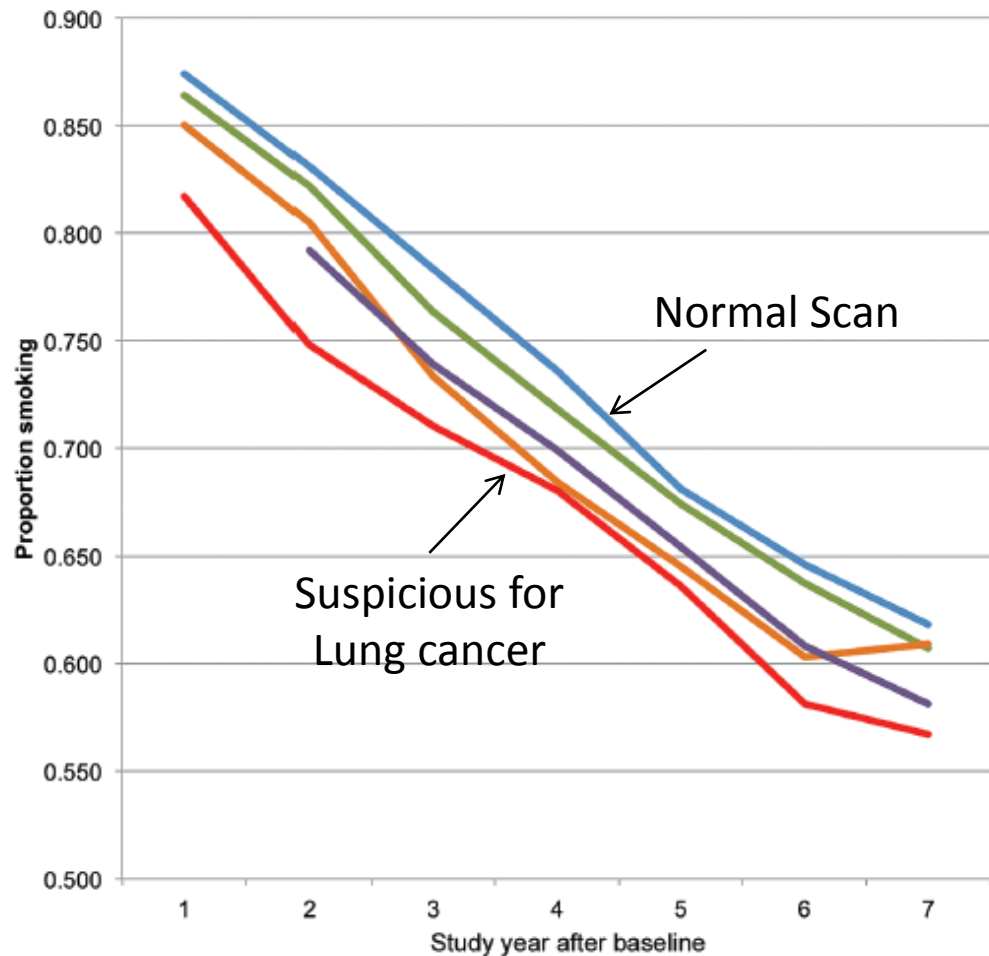| PLCO$_{m2012}$ risk	USPSTF Criteria Negative	USPSTF Criteria Positive	Total
PLCO$_{m2012}$ risk ≥0.0151 negative	$n = 20{,}712$ (cell percent $= 55.5\%$) Lung cancers $= 101$ Lung cancer deaths $= 141$ (a)	$n = 3{,}695$ (cell percent $= 9.9\%$) Lung cancers $= 33$ Lung cancer deaths $= 48$ (b)	$n = 24{,}407$ (column percent $= 65.4\%$) Lung cancers $= 135$ Lung cancer deaths $= 189$
PLCO$_{m2012}$ risk ≥0.0151 positive	$n = 2{,}445$ (cell percent $= 6.6\%$) Lung cancers $= 93$ Lung cancer deaths $= 102$ (c)	$n = 10{,}475$ (cell percent $= 28.1\%$) Lung cancers $= 449$ Lung cancer deaths $= 554$ (d)	$n = 12{,}920$ column percent $= 34.6\%$) Lung cancers $= 542$ Lung cancer deaths $= 656$
Total	$n = 23{,}157$ (row percent $= 62.0\%$) Lung cancers $= 195$ Lung cancer deaths $= 243$	$n = 14{,}170$ (row percent $= 38.0\%$) Lung cancers $= 482$ Lung cancer deaths $= 602$	$N = 37{,}327$ (cell percent $= 100\%$) Lung cancers $= 677$ Lung cancer deaths $= 845$

PLCO$_{m2012}$ versus USPSTF

- PLCO$_{m2012}$

  - Selected 8.8% fewer individuals for screening

  - Identified 12.4% more lung cancers

  - Had higher PPV (4.2% versus 3.4%)

  - 26% of USPSTF positive individuals have risks below PLCO$_{m2012}$ threshold

  - 8.5% of PLCO former smokers who quit > 15 years had PLCO$_{m2012}$ risk above threshold

Smoking Cessation in Screened Populations

- PLCO:

  - 6807 current smokers

    - 65.2% ongoing smoking

    - Younger, black or Hispanic, less educated, unmarried, lower income, lower BMI and no family history of lung cancer

- NLST:

  - 14661 current smokers

    - 76.5% ongoing smoking at 3 years

    - Lower with positive finding suspicious for lung cancer

Chart with y-axis "Proportion smoking" (0.500–0.900) and x-axis "Study year after baseline" (1–7), labeled "Normal Scan" and "Suspicious for Lung cancer"

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Smoking Cessation in Lung Cancer Patients

- 154 early stage non-small cell lung cancer patients

- At 12 months after surgery 36.9% were smoking

- 60% of patients lapsed within the first 2 months

- Predictors

  - Shorter quit duration

  - Intense appetite cravings

  - Lower income

  - Higher level of education