

# Lung Cancer Screening & Prevention: The New Lung Cancer Toolkit

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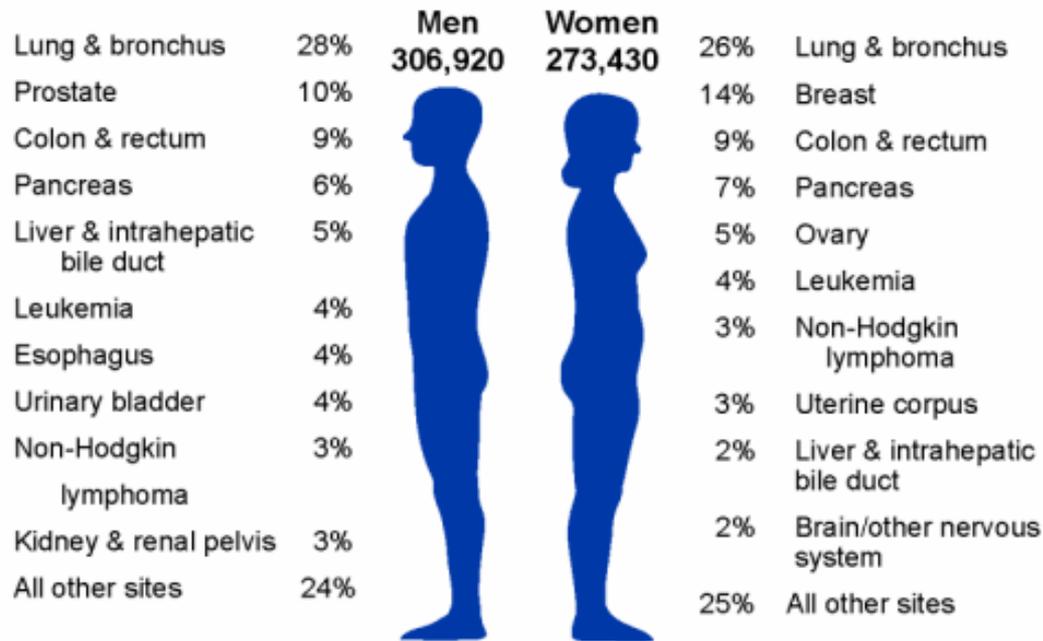


# Outline

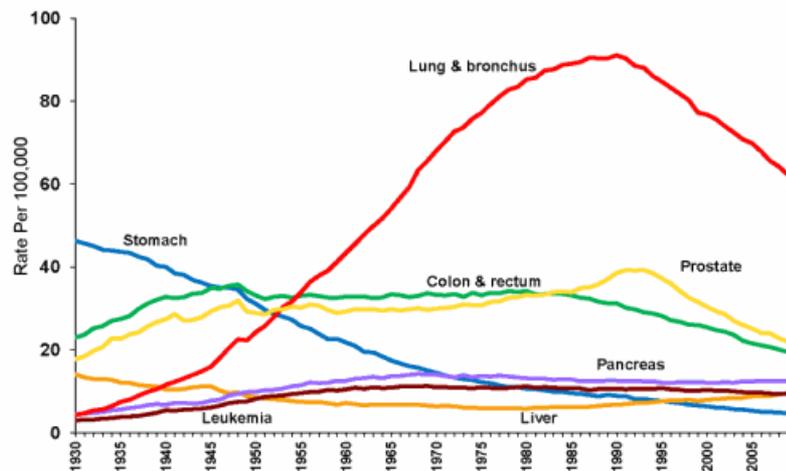
- Lung Cancer Statistics
- Prior Studies for Lung Cancer Screening
- NLST
- Studies Following NLST
- Future Directions

# Lung Cancer

Estimated Cancer Deaths in the US in 2013

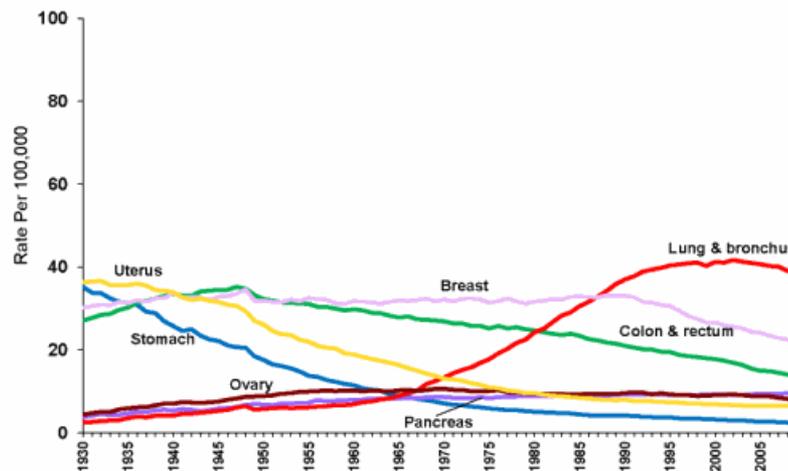


Cancer Death Rates\* Among Men, US, 1930-2009



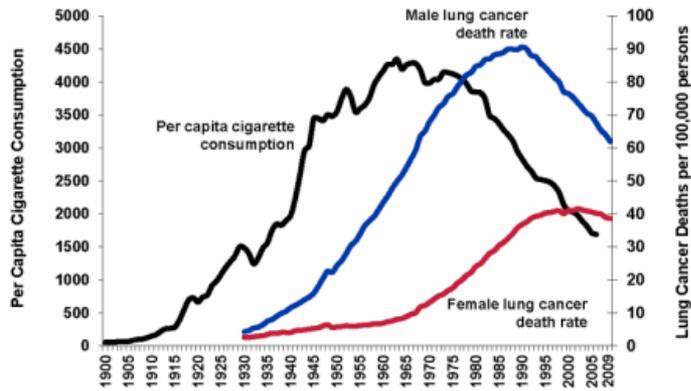
\*Age-adjusted to the 2000 US standard population.  
 Source: US Mortality Data 1960-2009, US Mortality Volumes 1930-1959,  
 National Center for Health Statistics, Centers for Disease Control and Prevention.

Cancer Death Rates\* Among Women, US, 1930-2009



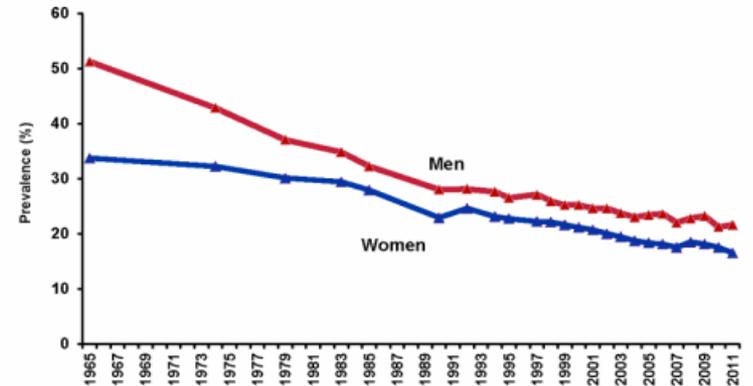
\*Age-adjusted to the 2000 US standard population.  
 Source: US Mortality Data 1960-2009, US Mortality Volumes 1930-1959,  
 National Center for Health Statistics, Centers for Disease Control and Prevention.

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



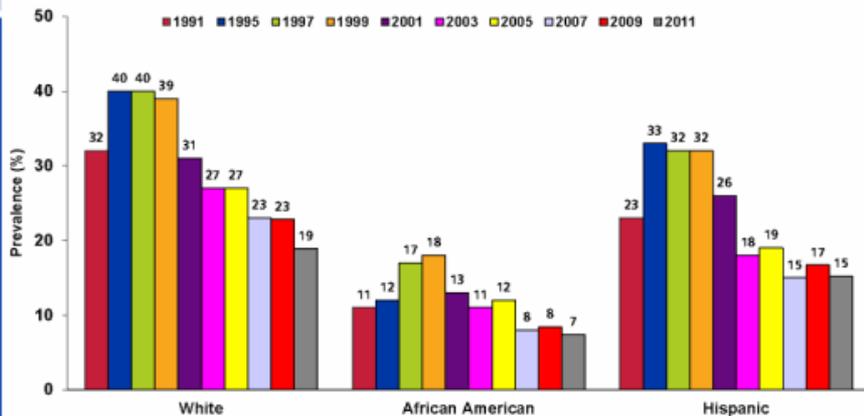
\*Age-adjusted to 2000 US standard population.  
 Source: Death rates: US Mortality Data, 1960-2009, US Mortality Volumes, 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention. Cigarette consumption: US Department of Agriculture, 1900-2007.

### Trends in Cigarette Smoking, Adults 18 and Older, US, 1965-2011



Redesign of survey in 1997 may affect trends. Estimates are age adjusted to the 2000 US standard population.  
 Source: National Health Interview Survey, National Center for Health Statistics, Centers for Disease Control and Prevention, 2012.

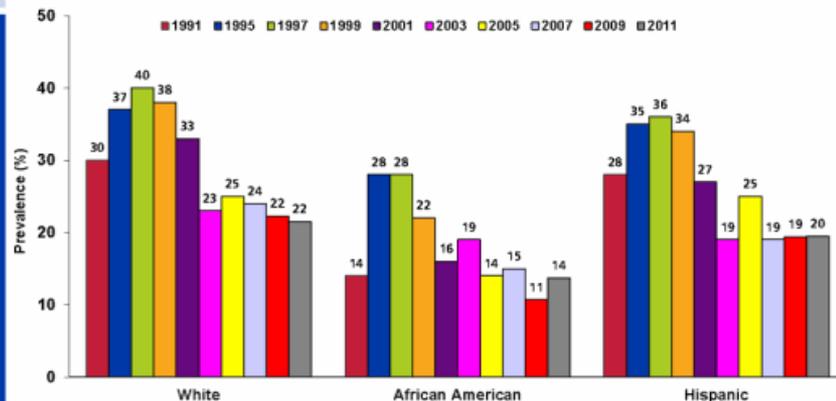
### Trends in Cigarette Smoking\* among Female High School Students, US, 1991-2011



\*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.

### Trends in Cigarette Smoking\* among Male High School Students, US, 1991-2011



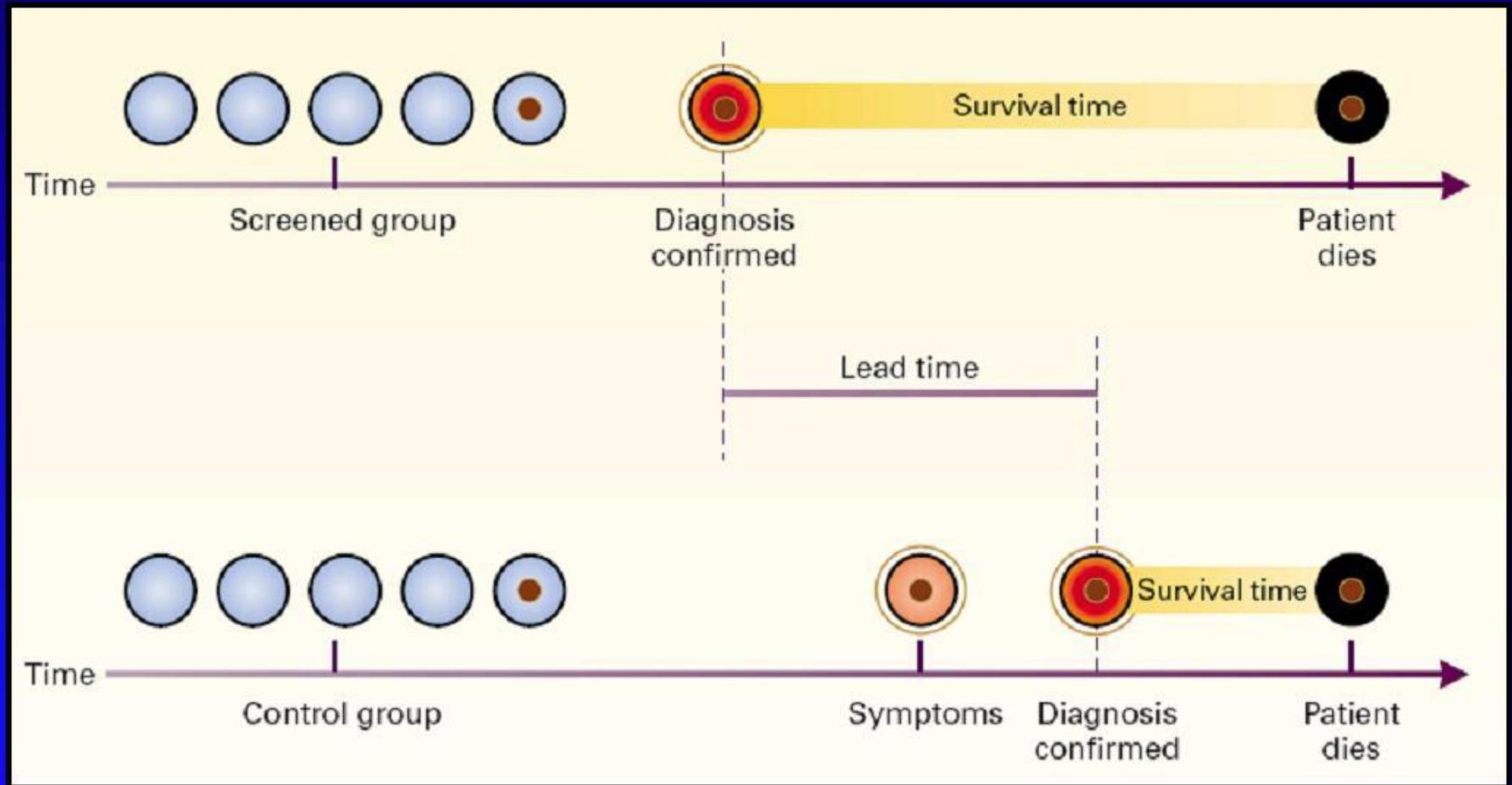
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Source: Youth Risk Behavior Surveillance System, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, 2012.

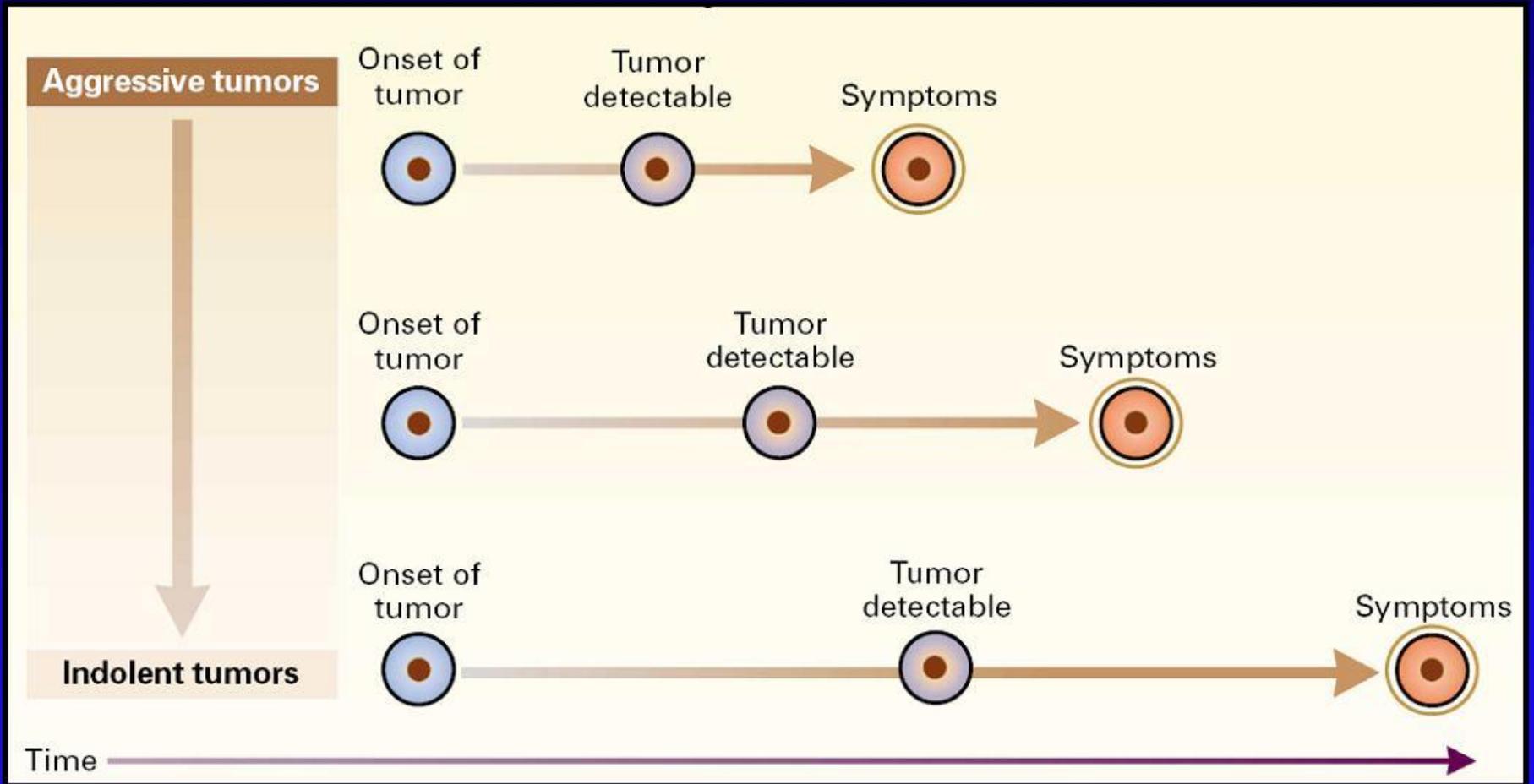
# Cancer Screening Success Stories

- Breast Ca (88%)
- Colon Ca (65%)
- Prostate Ca (100%)
- Cervical Ca (93%)

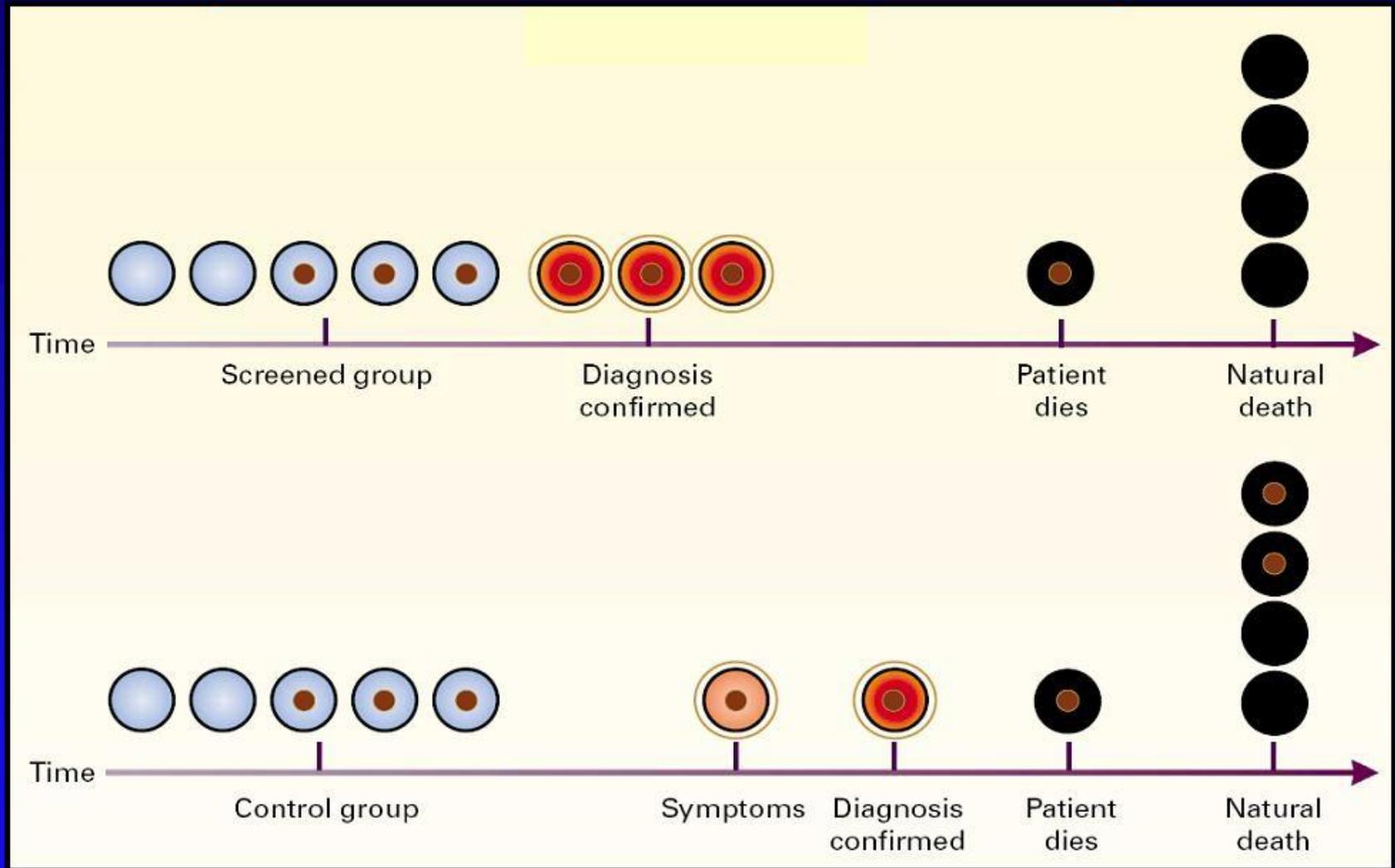
# Lead Time Bias



# Length-Time Bias



# Overdiagnosis Bias



# Ideal Screening Test

- Sensitive
- Non-invasive
- Low-risk
- Cost-effective
- Detect disease early enough to allow for improved treatment
- Results quantifiable and reproducible

# Screening

- Mortality reduction NOT Survival improvement
- Is a PROCESS rather than a TEST



# Lung Cancer Screening

1970-1980s:

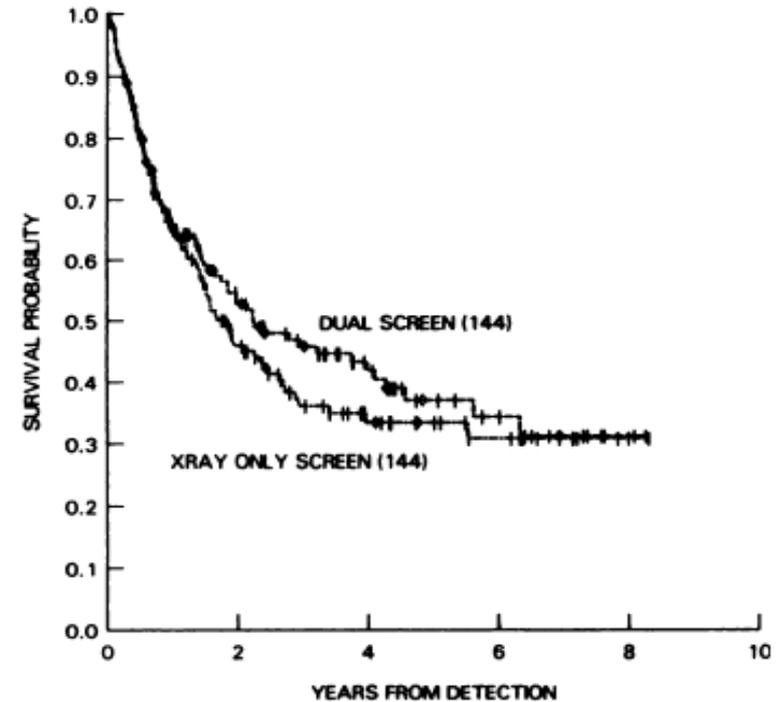
- NCI supported lung cancer screening trials
- MSK, Johns Hopkins and Mayo Clinic
- Prospective, randomized
  - Enrolled >30,000 men current or former smokers, age >45
  - Only exclusion was prior cancer
  - CXR +/- Cytology every 4 months
  - Survival at 5 yrs 35% compared to 13%
  - Mortality remained at 3.2/1000 person-years vs. 3/1000 person-years

Frost et al. *Am Rev Respir Dis* 1984; 130: 549-554  
Fontana et al. . *Am Rev Respir Dis* 1984; 130: 561-565

# Screening for Cancer-MSK

**Table 5—Lung Cancers Classified by Study Group, Stage and Resectability**

Stage	Dual Screen		X-Ray Only Screen	
	Total	Complete Resection	Total	Complete Resection
I	59	54 (92%)	58	55 (95%)
II	7	6 (86%)	11	9 (82%)
III	78	13 (17%)	75	13 (17%)
<b>Total</b>	<b>144</b>	<b>73 (51%)</b>	<b>144</b>	<b>77 (53%)</b>



**FIGURE 7.** Survival from lung cancer by study group.

# PLCO

- CXR vs. Usual Care
- 154,901 participants
  - Baseline CXR + annual CXR x 3 yrs vs. No screening
  - Follow-up 13 years
- Sub-group analysis for patients who met NLST criteria

# PLCO

**Table 2.** Histology and Stage of Lung Cancers by Group and Mode of Detection<sup>a</sup>

	No. (%) of Participants					
	Intervention Group				Total	Usual Care Group
	Screen Detected	Interval	Never Screened	After Screening		
All	307	198	193	998	1696	1620
Type						
Small cell	22 (7)	42 (21)	27 (14)	138 (14)	229 (14)	235 (15)
Squamous	63 (21)	37 (19)	51 (27)	195 (20)	346 (20)	329 (20)
Adenocarcinoma <sup>b</sup>	172 (56)	71 (36)	70 (36)	383 (38)	696 (41)	658 (41)
Large cell	21 (7)	12 (6)	5 (3)	39 (4)	77 (5)	53 (3)
Other Non-small cell lung cancer <sup>c</sup>	27 (9)	31 (16)	38 (20)	239 (24)	335 (20)	338 (21)
Unknown	2 (0.7)	5 (3)	2 (1)	4 (0.4)	13 (0.8)	7 (0.4)
Non-small cell lung cancer						
Total	283 (92)	151 (76)	164 (85)	856 (86)	1454 (86)	1378 (85)
Stage						
I	141 (50)	40 (26)	38 (23)	243 (28)	462 (32)	374 (27)
II	26 (9)	10 (7)	12 (7)	64 (8)	112 (8)	105 (8)
III	67 (24)	44 (29)	32 (20)	216 (25)	359 (25)	365 (26)
IV	49 (17)	54 (36)	82 (50)	329 (38)	514 (35)	530 (38)
Unknown	0	3 (2)	0	4 (0.5)	7 (0.5)	4 (0.3)
Stage of small cell						
Limited	12 (55)	11 (26)	11 (41)	44 (32)	78 (34)	74 (32)
Extensive	8 (36)	29 (69)	16 (59)	89 (65)	142 (62)	145 (62)
Unknown	2 (9)	2 (5)		5 (4)	9 (4)	16 (7)

<sup>a</sup>Percentages may not sum to 100 due to rounding.

<sup>b</sup>Includes bronchioalveolar adenocarcinoma.

<sup>c</sup>Includes spindle cell carcinoma, intermediate cell carcinoma, giant cell carcinoma, clear cell carcinoma, adenosquamous carcinoma, adenoid cystic carcinoma, nonsmall cell (not otherwise specified [NOS]), carcinoma (NOS), mixed small and nonsmall cell, neuroendocrine nonsmall cell (NOS).

# PLCO

**Table 5.** Results for National Lung Screening Trial Subset

	Intervention Group (n = 15 183)	Usual Care Group (n = 15 138)	Rate Ratio (95% CI)
Men, No. (%)	9252 (60.9)	9110 (60.2)	
Current smoker, No. (%)	6146 (40.5)	6069 (40.3)	
Median pack-years	52.0	52.5	
Adherence with baseline screen, No. (%) <sup>a</sup>	13 035 (85.9)		
Overall adherence, No. (%) <sup>a</sup>	48 330 (81.4)		
Results through 6 y of follow-up			
Diagnosed cases, No.	518	520	1.00 (0.89-1.13)
Person-years for incidence	85 428	85 474	
Lung cancer deaths, No.	316	334	0.94 (0.81-1.10)
Person-years for death	87 473	87 198	

<sup>a</sup>Percentage of expected screens.

# Why was CT screening avoided for so long?

- Cost
- Time
- Radiation exposure
  
- New LDCT:
  - 15 seconds, 1 breath hold
  - 2 mSev
  - Comparable to conventional CT in sensitivity and specificity for pulmonary nodules

# Non-Randomized CT screening

- 1999: Kaneko et al.
  - 1369 high risk patients screened with LDCT and CXR
  - 15 vs 4 cases of peripheral lung cancer detected
    - Of the NSCLC 93% stage 1
- 1998: Sone et al.
  - 3958 patients screened with LDCT and CXR
  - 19 vs 4 cases of lung cancer
    - 84% stage 1

Kaneko et al. *Radiology* 1999; 201: 798-802  
Sone et al. *Lancet* 1998; 351: 1242-1245

# Non-Randomized CT screening

- ELCAP
  - 1000 high risk patients
    - Age  $\geq$  60 years
    - $\geq$  10 pack year current or former smokers
  - Screened with both LDCT and CXR
  - 27 prevalence nodules found with LDCT
    - Only 7 of them found with CXR
  - 4 x more lung cancers found
  - 6 x more stage I lesions
  - 11% of patients with a non-calcified pulmonary nodule had cancer

# NLST

- Largest RCT; 33 sites
- 53,454 patients enrolled from 08/2002- 04/2004
  - Current or former heavy smokers ( $\geq 30$  pack years)
  - Ages 55-74 years
  - No CT scan within last 18 months
- LDCT vs. CXR
  - Baseline, year 1, year 2
  - Followed for mean of 6.5 years
- Primary End-Point: Mortality from Lung Cancer
- 90% power to detect 21% decrease in mortality

# NLST

- Positive Screen:
  - $\geq 4$ mm non-calcified nodule
  - 27% vs 9% of patients in LDCT vs. CXR arm had positive baseline scan
    - 96% vs. 95% false positive
  - Only 2.7% of patients who underwent invasive testing had benign lesions
    - 1.4% with complications

# Benefits of NLST

- Academic Centers
- Minimum equipment standard
- Standard screening protocol
  - Everyone was assured LDCT screening
- Specially-trained radiologists and technicians

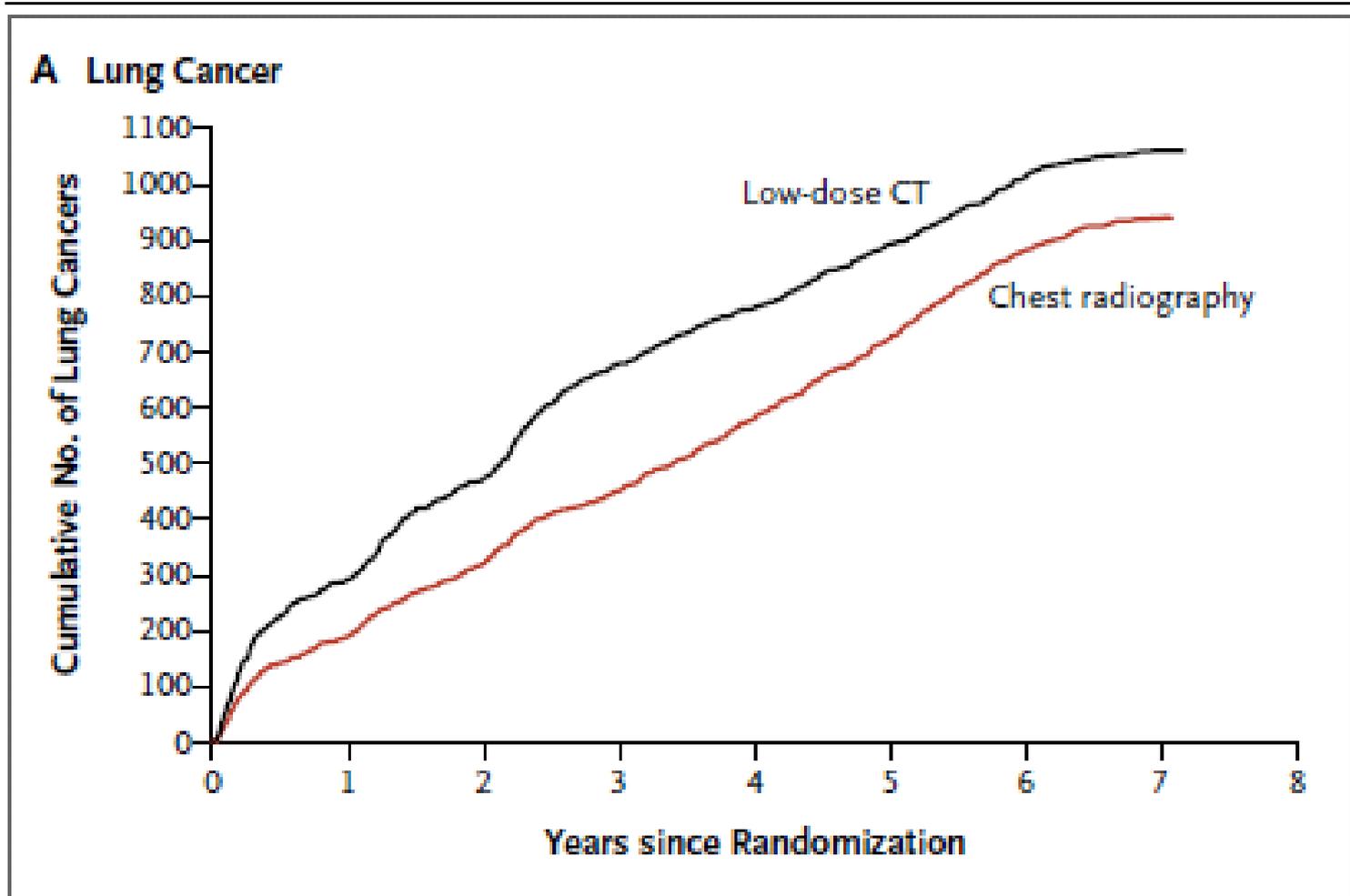
# NLST

Screening method	# Cancers Detected				
	Screening	Interval	Follow-Up	Stage I	Stages III/IV
CXR	279	137	525	47.6	43.2
LDCT	649	44	367	63	29.8

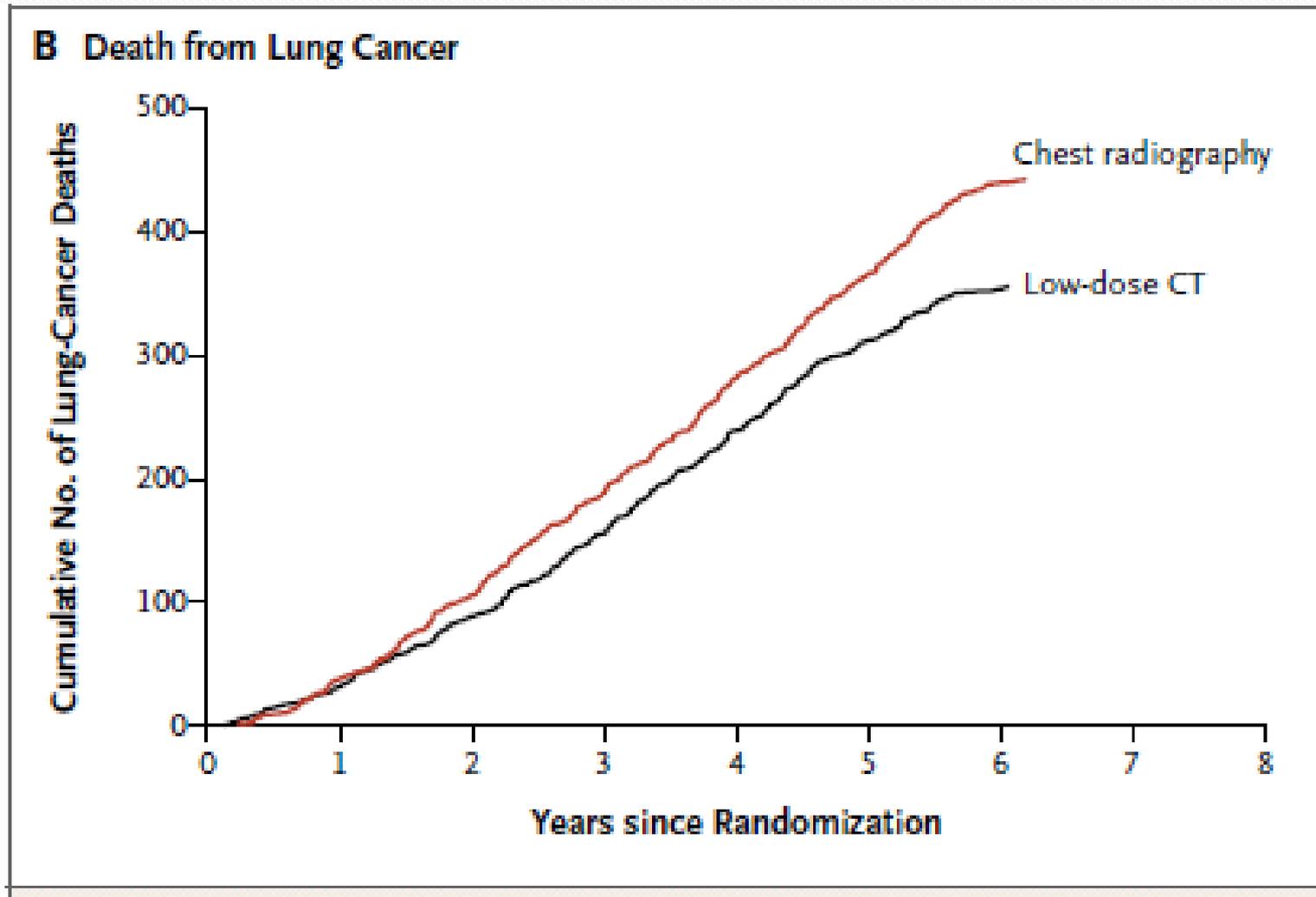
# NLST

- October 2010:
  - 356 vs 443 deaths in the LDCT vs CXR
  - 247 vs 309 lung Ca mortality rates /100,000 person years in LDCT vs CXR
  - 20.3% reduction in mortality
  - Saw a shift in stage at diagnosis from late to early
  - NNS= 320
    - FOBT=1250
    - Mammogram=781
  - All cause mortality 6.7% lower in LDCT

# NLST



# NLST



# NLST Take Home Points

- Decreased mortality
  - Lung cancer
  - All cause
- Decreased # interval cancers
- Shift to earlier cancer stage
- Decreased PPV but increased NPV

# Smaller RCT for LDCT Screening

- NELSON: 7557 patients; LDCT screening vs. no screening; Health-related QoL
- ITALUNG: 3206; LDCT vs. no screening
- DLCST: 4104; LDCT vs no screening
- DANTE: 2472; LDCT vs no CT

# Pitfalls to Screening

- False + scans
  - Thickness of collimation
- Benign nodule resection
- Radiation effects
- Strain on healthcare system
- Anxiety
- Patients being reassured
  - Using screening rather than smoking cessation
- Cost

# Who should be Screened?

- NLST criteria only?
- COPD?
- Family history with 1<sup>st</sup> degree relative with lung cancer?
- Any other predictors?

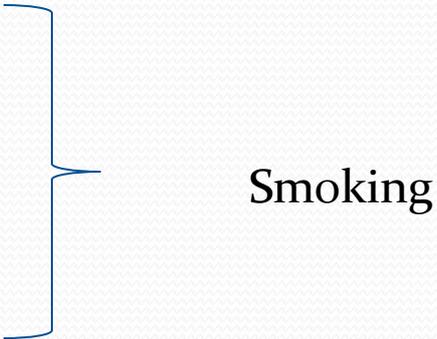
# Guidelines

Organization	Screening		Other Recommendations
	Yes	No	
American Cancer Society	NLST Criteria	Not NLST Criteria	<p>Discussion about benefits and risks of screening</p> <p>Multi-disciplinary team</p> <p>Experienced Center</p> <p>Smoking Cessation</p> <p>CXR should not be used</p>
American Association of Thoracic Surgery	<p>NLST Criteria</p> <p>Long-term cancer survivors (stop at age 79)</p> <p>Age &gt;50 + smoking &gt;20 pack/yrs + 5% risk of cancer in next 5 yrs</p>	If treatment is impractical (comorbidities or age)	<p>Experienced Center</p> <p>Smoking Cessation</p> <p>Data Collection</p>
American Lung Association	NLST Criteria	Not NLST Criteria	<p>Discussion about benefits and risks of screening</p> <p>Multi-disciplinary team</p> <p>Smoking Cessation</p>

# Guidelines

Organization	Screening		Other Recommendations
	Yes	No	
National Comprehensive Cancer Network	NLST Criteria OR Age >50 + Smoking >20 pack yrs + >1 other risk factor	Not NLST Criteria Not high risk	Discussion about benefits and risks of screening Multi-disciplinary team Follow-up for testing and nodules
American Society of Clinical Oncology and American College of Chest Physicians	NLST Criteria	Not NLST Criteria If treatment is impractical (co- morbidities)	Discussion about benefits and risks of screening Multi-disciplinary team Experienced Center Smoking Cessation Registry for follow-up Quality metrics
U.S. Preventive Services Task Force	Evidence is insufficient to recommend for or against screening asymptomatic persons for lung cancer with either LDCT, CXR , sputum cytology, or a combination of these tests.		

# Questions that Remain Unanswered

- Age to begin and end screening
  - How much effect does:
    - Age at initiation
    - Duration
    - Intensity
    - Age of cessation
    - Current age
  - Screening interval and when to stop
  - Screening tools
- 
- Smoking

# Future Directions for Screening

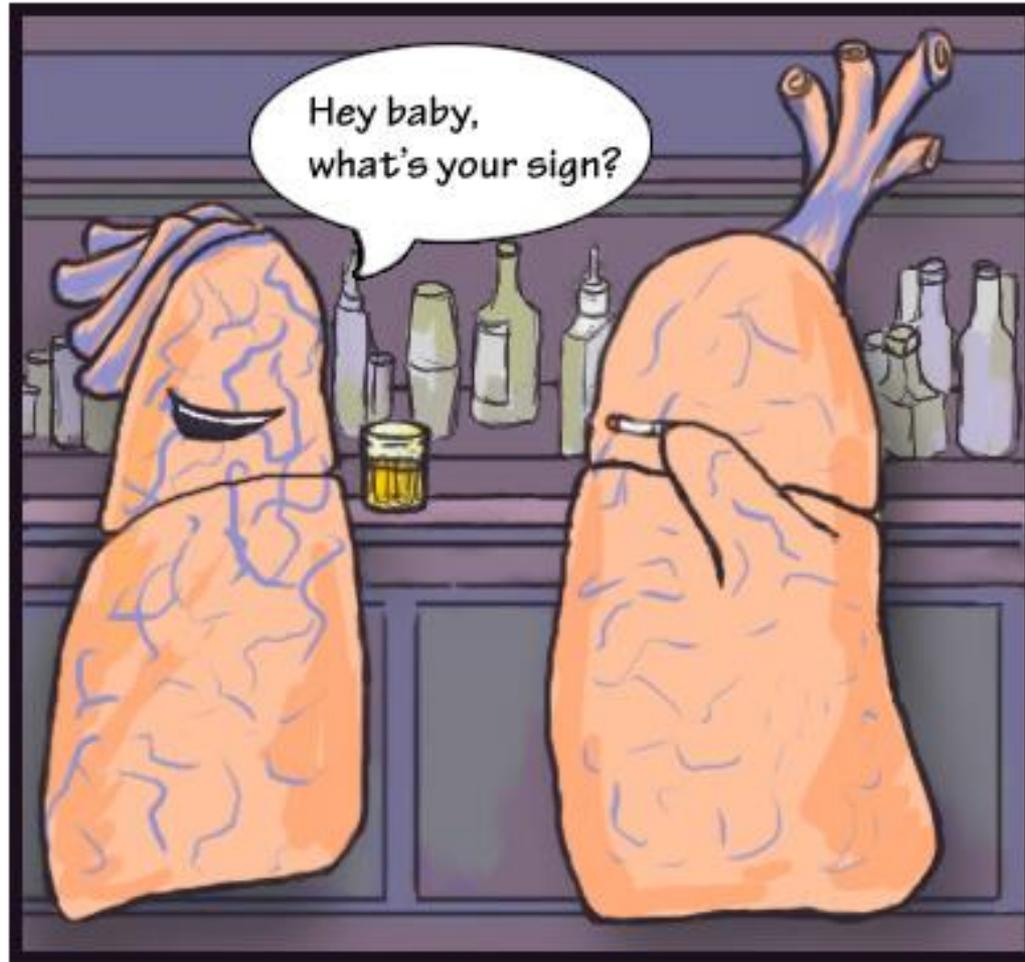
- Molecular and Genetic biomarkers
  - Airway epithelium
  - Sputum
  - Blood
  - Breath condensate

# The Future of Screening

- Large centers
- Multi-disciplinary teams; focused
- Counseling
- Research/Registry



# Thanks! questions?



Cancer.

# PLCO: Lung Cancer Mortality

