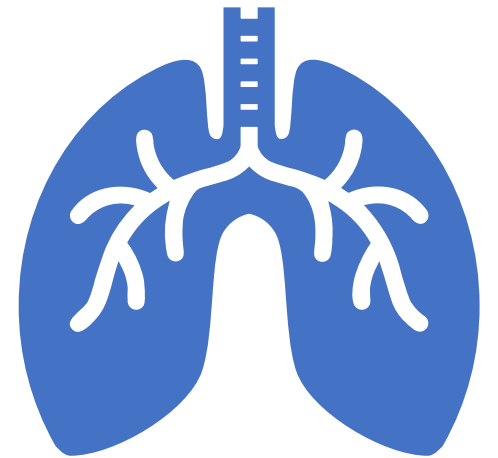


Paul Lederer M.D.

May 3, 2025

# Lung Cancer Screening

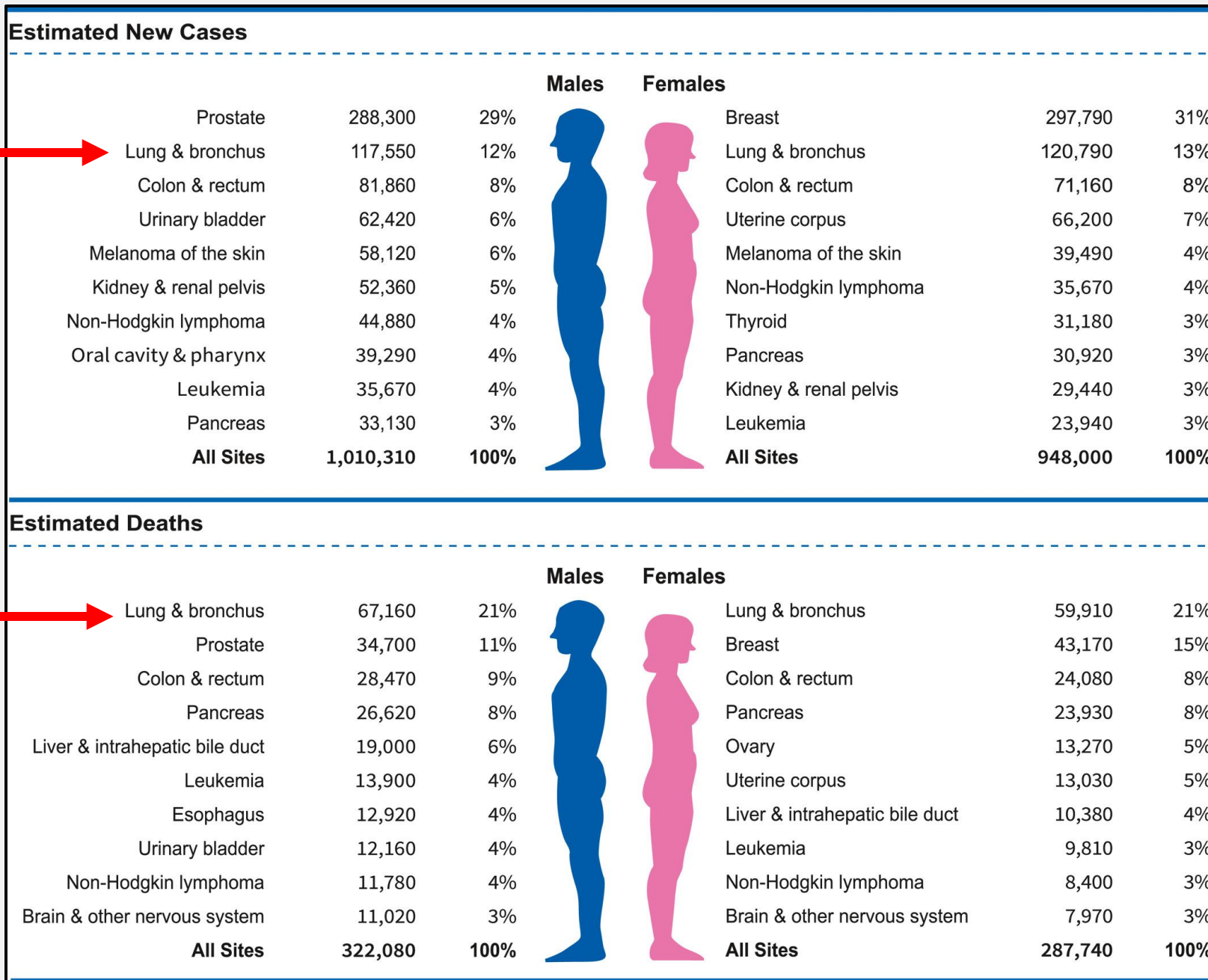


# Disclosures of Conflicts of Interest

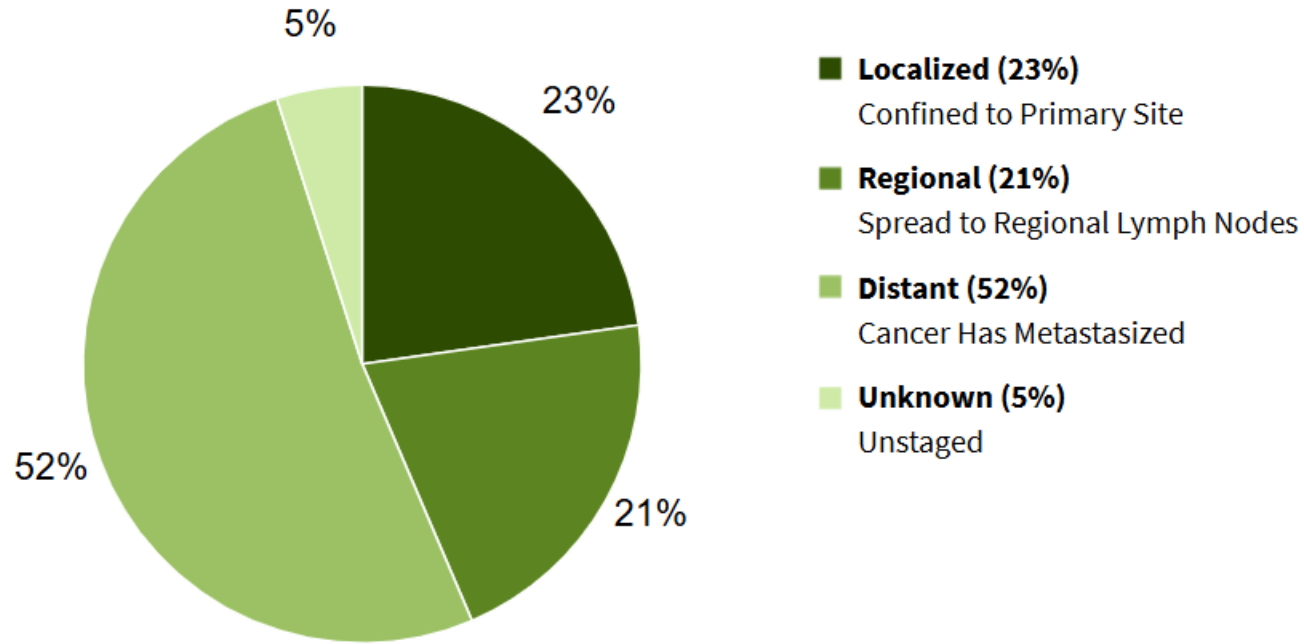
- None

# Objectives

- Demonstrate the epidemiologic burden of lung cancer
- Discuss USPSTF screening criteria with 2021 updates
- Review the evidence basis for screening and when not to screen
- Examine lung cancer as an evolving disease
- Address patient related concerns
- Preview future directions



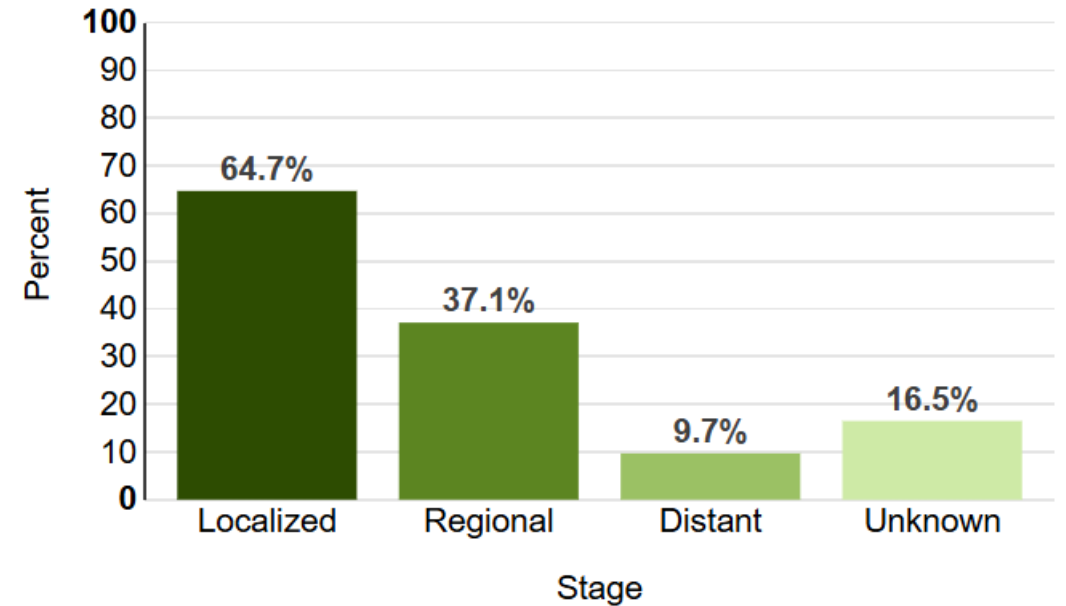
**Percent of Cases by Stage**



**Late-stage diagnosis is common...**

**and predicts poor survival rates.**

**5-Year Relative Survival**



- 1 The Task Force recommends *annual* screening for lung cancer with *low-dose computed tomography* in adults aged 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 the individual has not smoked for 15 years or develops *a health problem that significantly limits life expectancy or the ability or willingness to have curative lung surgery.* **Grade B**

# 2021: USPSTF Updated Recommendations

| Population   | Recommendation  | Grade    |
|--|---|----------|
| Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years | The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 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. | <b>B</b> |



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**ASCO**<sup>®</sup> AMERICAN SOCIETY OF  
CLINICAL ONCOLOGY





# Your patient has questions

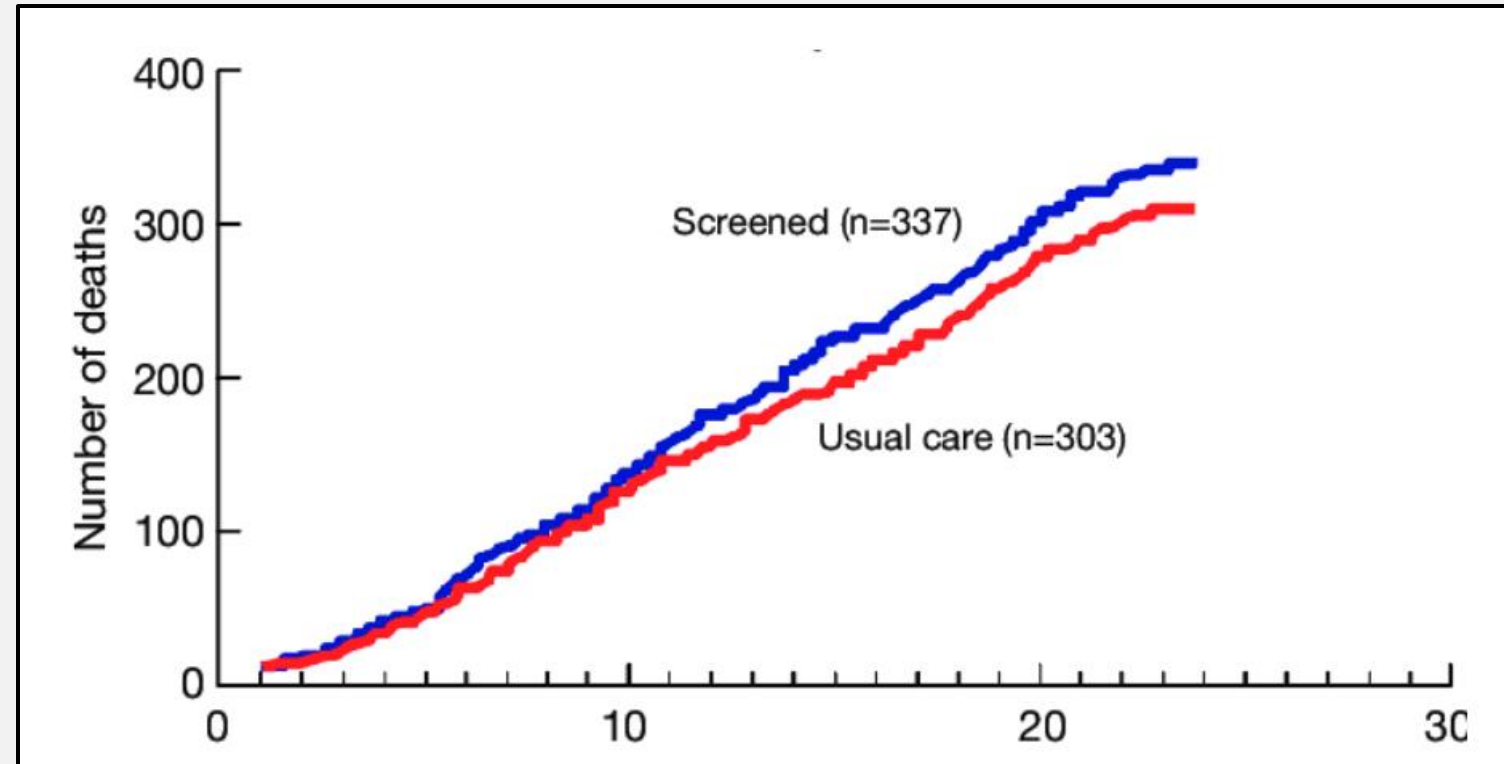
A 75 year old man, new to your clinic, was recommended for lung cancer screening at his initial visit based on age and smoking history of 30 pack years, having quit 10 years ago. After consideration, he has concerns:

- My last doctor ordered me an Xray every year, isn't that good enough?
- Is a CT scan a lot of radiation?
- Is this necessary if I don't have symptoms?

# Early Lung Cancer Screening

## 1970s Mayo Lung Project

- Chest X-ray and sputum cytology
- Every 4 months for 6 years
- Median followup 20.5 years



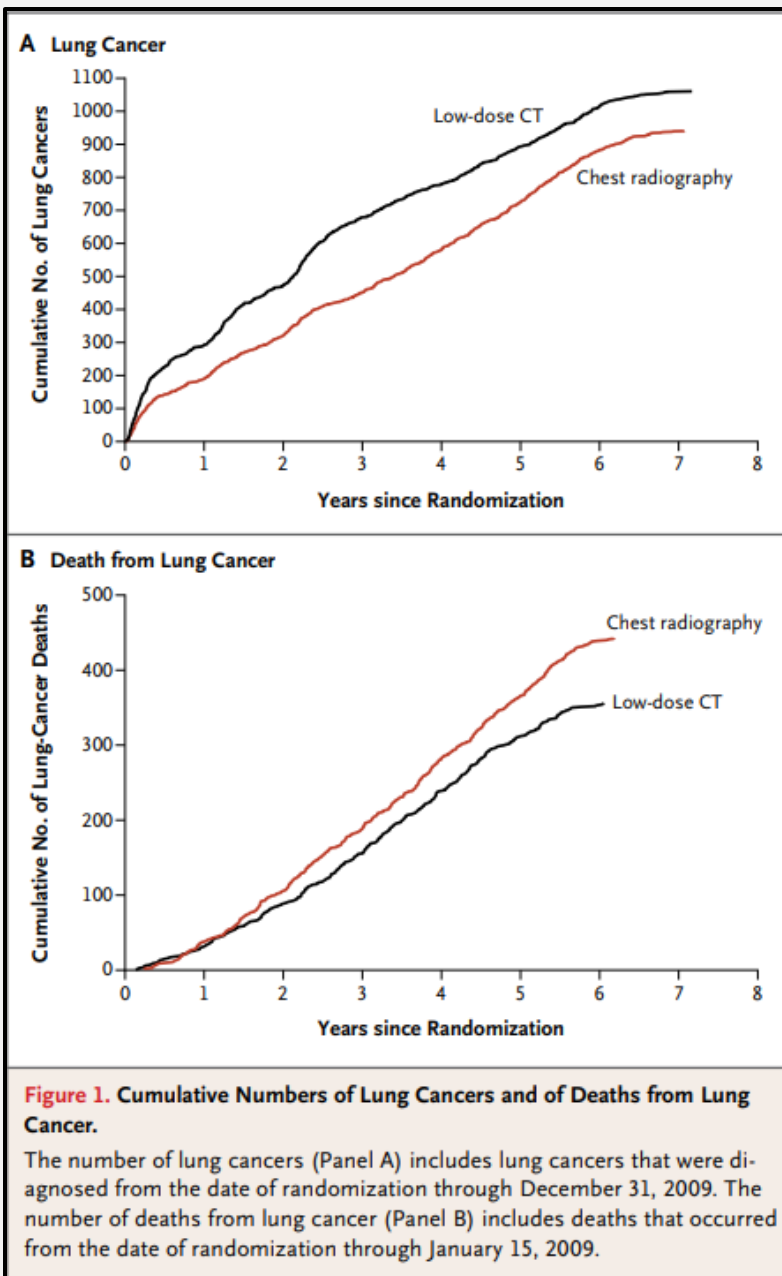
Marcus et. al., J Natl Cancer Inst 2000  
Image from thoracic.org Patient Education Series

# National Lung Screening Trial (NEJM 2011)

## Total lung cancers identified

- **LDCT group (n=1020)**
  - Positive screen: 649
  - Negative screen: 55
  - Missed or after screen: 367
- **Chest X-ray group (n=941)**
  - Positive screen: 279
  - Negative screen: 137
  - Missed or after screen: 525

| Stage | LDCT             | CXR             |
|-------|------------------|-----------------|
| IA    | 416/1040 (40.0%) | 196/929 (21.1%) |
| IB    | 104/1040 (10.0%) | 93/929 (10.0%)  |
| IIA   | 35/1040 (3.4%)   | 32/929 (3.4%)   |
| IIB   | 38/1040 (3.7%)   | 42/929 (4.5%)   |
| IIIA  | 99/1040 (9.5%)   | 109/929 (11.7%) |
| IIIB  | 122/1040 (11.7%) | 122/929 (13.1%) |
| IV    | 226/1040 (21.7%) | 335/929 (36.1%) |



20% reduction in lung cancer mortality  
6.7% reduction all cause mortality

### Concerns:

- Generalizability
- False positive rate
- Overdiagnosis
- Invasive procedure risk
- Radiation risk

*“Although some agencies and organizations are contemplating the establishment of lung-cancer screening recommendations on the basis of the findings of the NLST, the current NLST data alone are, in our opinion, insufficient to fully inform such important decisions.”*

# Nodule Risk Stratification

## NELSON trial (2016)

- Volumetric nodule assessment
- Protocolized evaluation
- Introduced “Indeterminate” nodule and growth as a biomarker
- 24% mortality reduction at 10 years

## Lung-RADS

- Data from NLST, NELSON, IELCAP
- American College of Radiology released criteria in 2014

|                 | NLST | NELSON |
|-----------------|------|--------|
| Positivity Rate | 24%  | 2.1%   |
| PPV             | 3.8% | 43.5%  |

# Imaging Selection

|                          |          |                           |
|--------------------------|----------|---------------------------|
| Chest X-ray              | ~0.1 mSv | 10 days of background USA |
| Chest CT Scan (Standard) | ~7.0 mSv | 2+ years background USA   |
| Chest CT Scan (Low Dose) | ~1.4 mSv | 6 months background USA   |

Per EPA.gov, annual background radiation for the average American is roughly 3 mSV.

Choosing your image:

- Chest Xray: No role in lung cancer screening or evaluation
- Low Dose CT Scan: Validated for lung cancer screening
- Standard Chest CT: Improved imaging of pleural, hilar, vascular structures

# Radiation Safety

- Radiation Exposure
  - Est. 0.26-0.81 cancers per person (10 years annual)
  - ~1 cancer death per 2500 screened



# Your medical student is impressed!

Why did they change the guidelines in 2021?

If the mortality benefit was 20% back then, it must be even higher now...right?

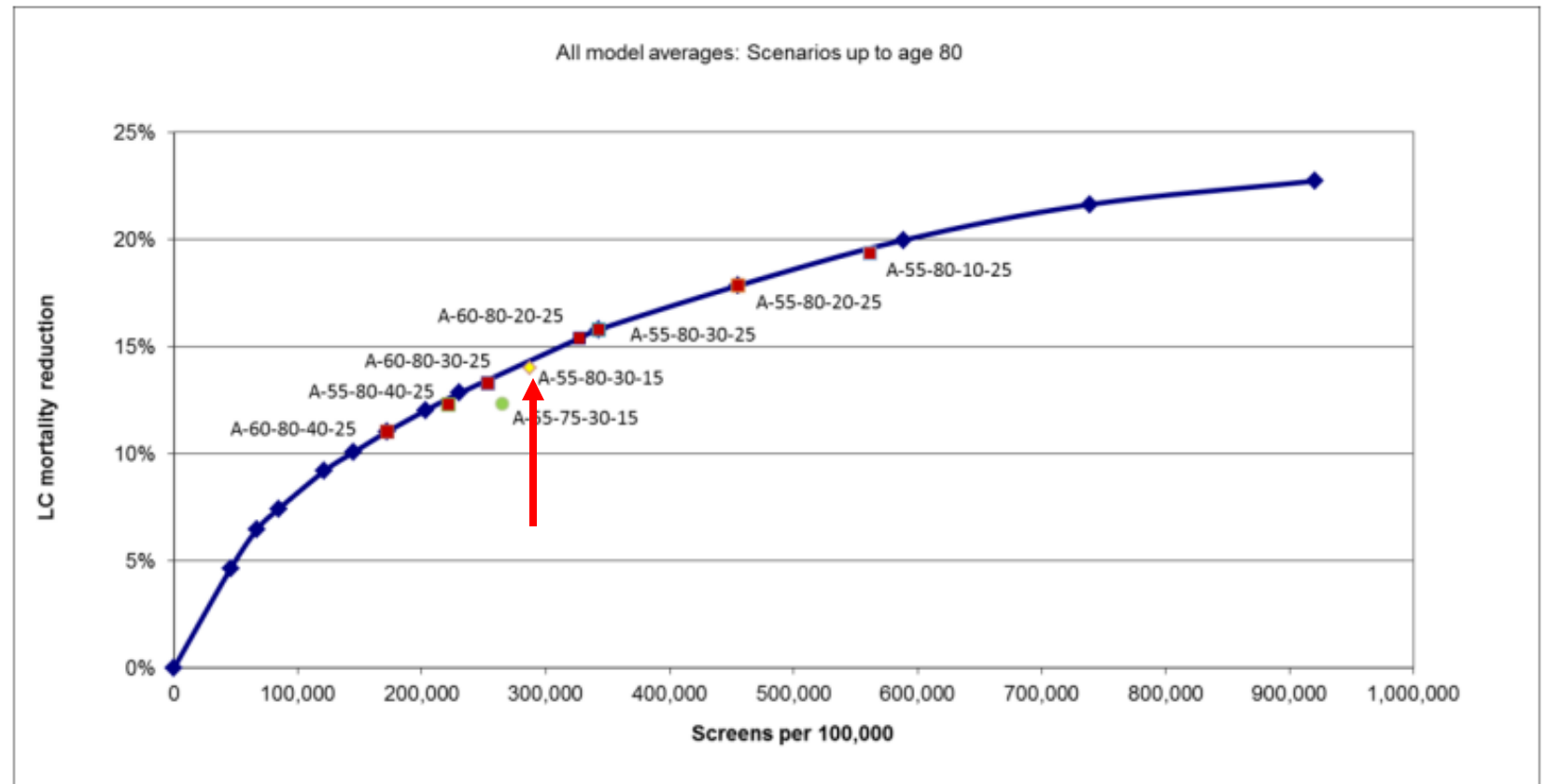


# US Preventive Services Task Force (USPSTF 2013)

| Variable         | Value                  |
|------------------|------------------------|
| Frequency        | <b>1y</b> , 2y, 3y     |
| Starting Age     | 45, 50, <b>55</b> , 60 |
| Ending Age       | 75, <b>80</b> , 85     |
| Min. Pack-years  | 10, 20, <b>30</b> , 40 |
| Years since quit | 10, <b>15</b> , 20, 25 |

- Mortality reduction: 14%
- NNS: 37
- Scans per death prevented: 550
- Scans/year gained: 52

**Figure 3. Estimated Lung Cancer Mortality Reduction (Average of Five Models) From Annual Computed Tomography Screening in the 1950 Birth Cohort for Programs With Eligible Ages of 55 to 80 Years and Different Smoking Eligibility Cutoffs\***

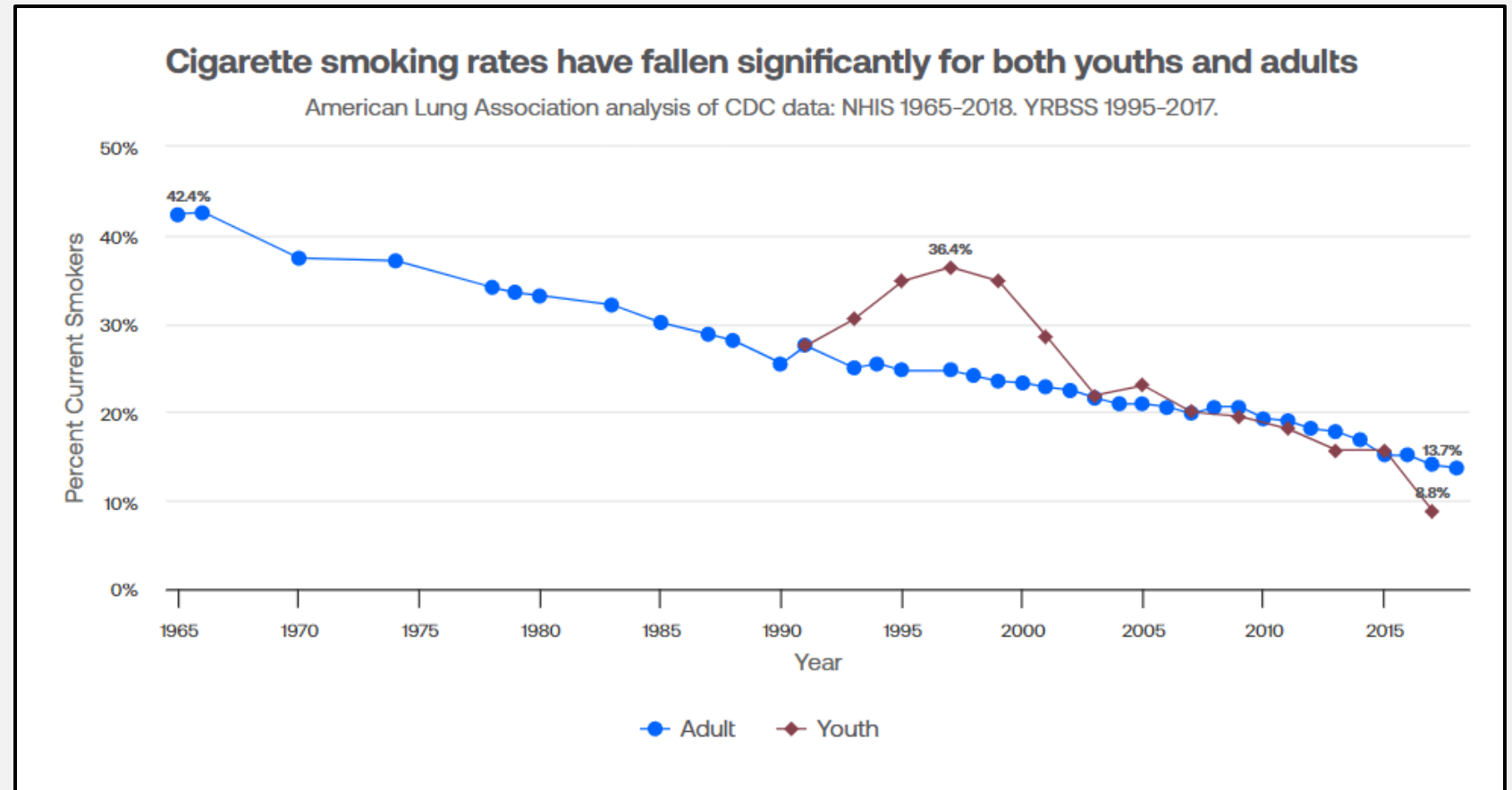


\*Highlighted scenarios in Tables 2 and 3 are labeled.

# Smoking Rates in Steady Decline

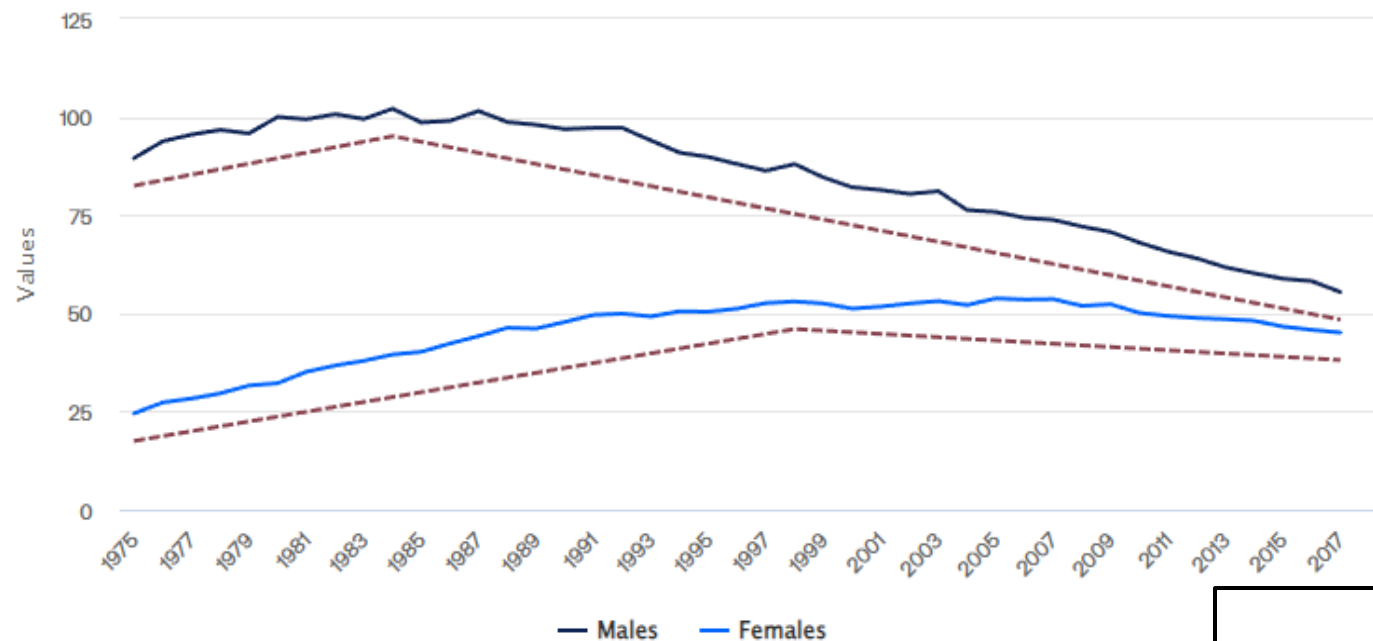
## Declining rates of:

- Packs per day
- Youth tobacco use
- Vape/E-cigarette



### Incidence Rates by Sex and Year, 1975-2017

Source: SEER 1975-2017

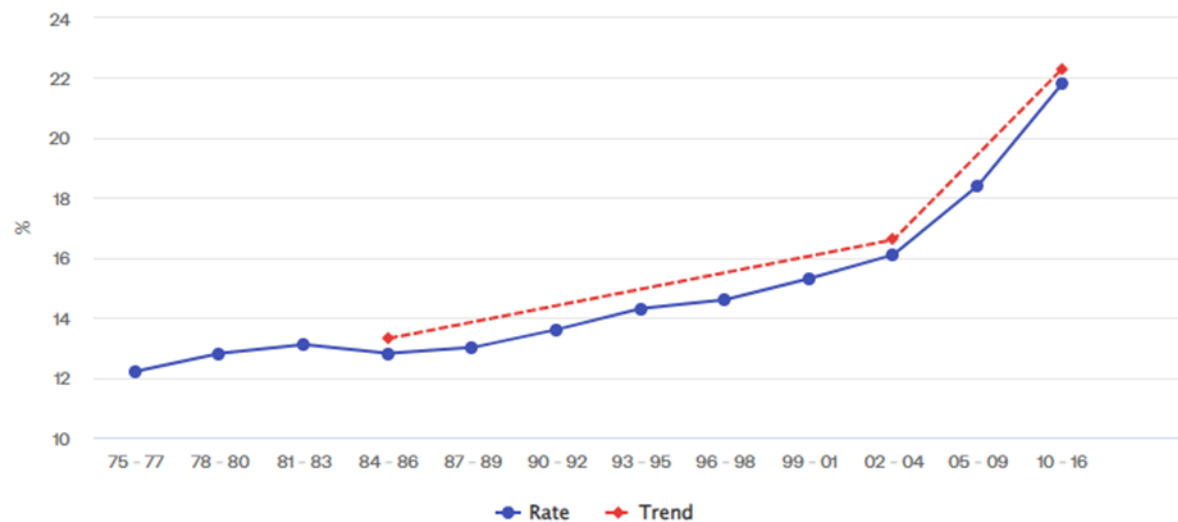


Incidence rate is declining and the gender gap narrowing.

Early recognition and advances in treatment have improved survival.

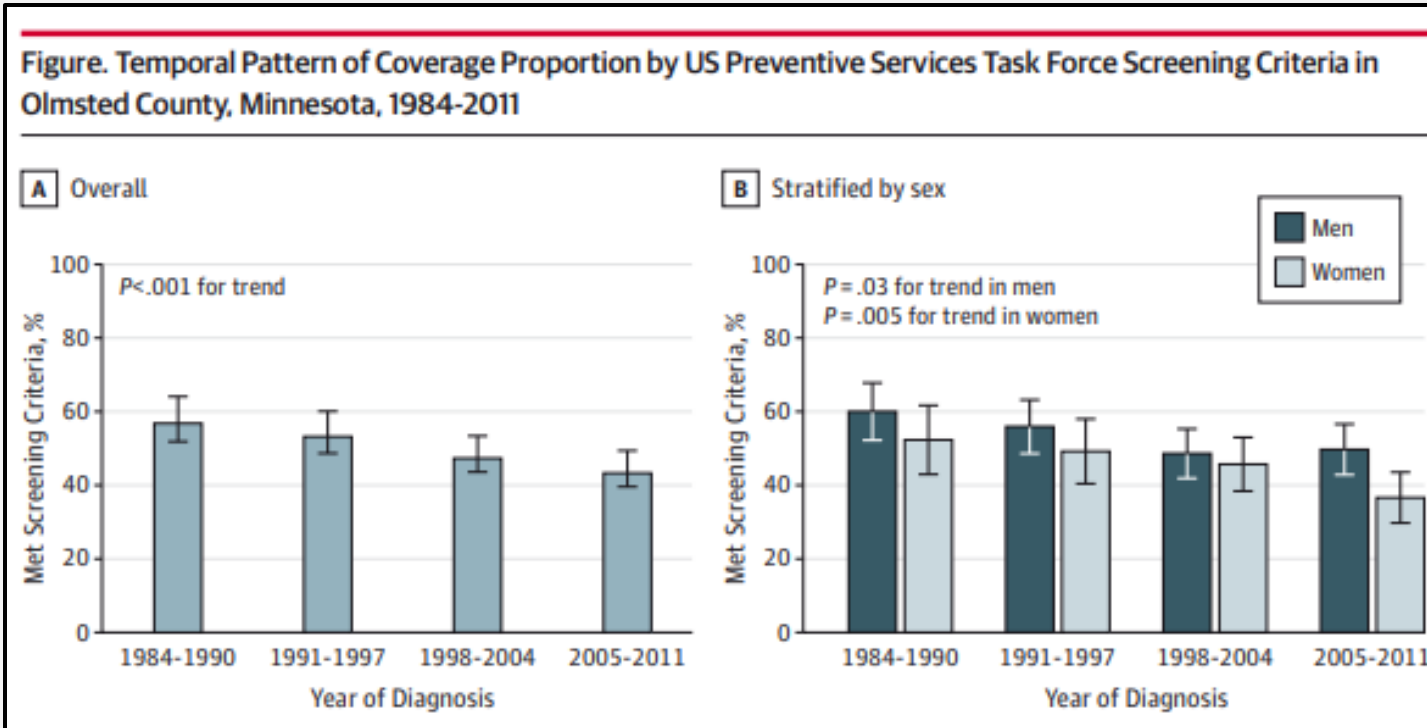
### 5-Year Lung Cancer Survival Rates by Year

Source: SEER Cancer Statistics Review, 1975-2017



SEER data as presented by ALA State of Lung Cancer

# Diminishing Validity of Criteria



**1351 incident lung cancers**

- Declining rate in men
- Constant rate in women
- Fewer 30 pack-year smokers
- More with >15 years abstinence

**2013 USPSTF criteria were losing sensitivity over time**

# Were women adequately represented?

## Women may benefit more than men

NLST: 32% mortality reduction

NELSON: 61% mortality reduction

## CHEST 2019 case series

294 women with lung cancer

237 did not meet criteria

- Age <55: 81
- Pack-Year <30: 118

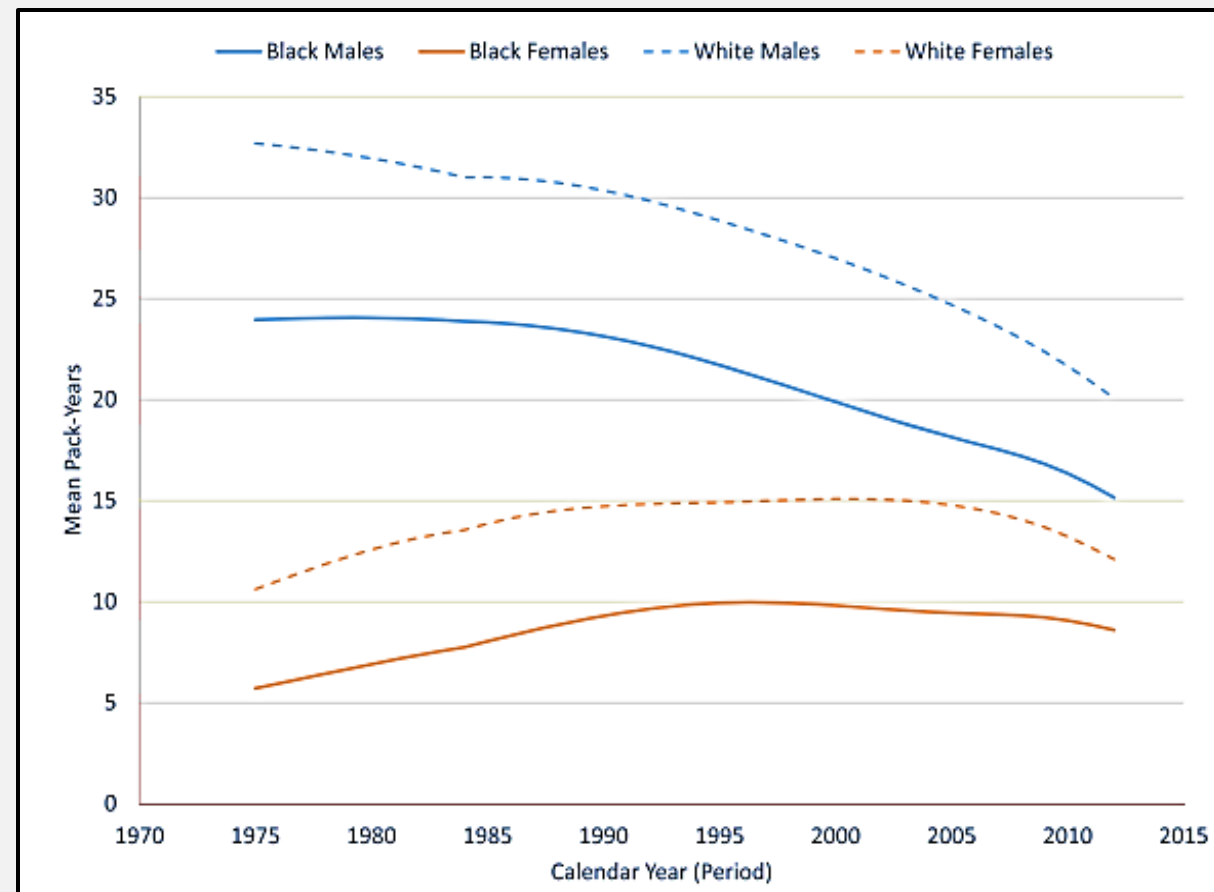
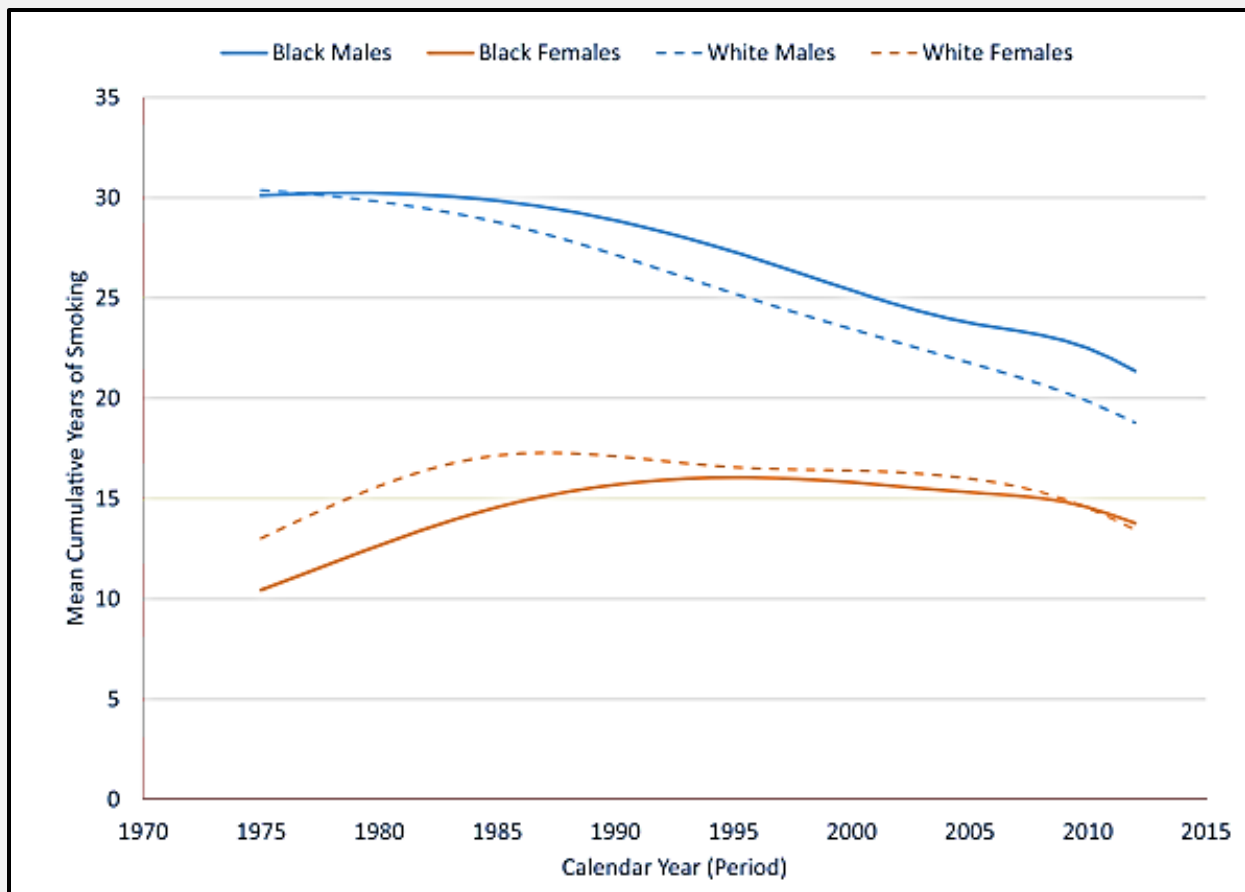
# Do the Same Criteria Apply to Black Americans?

- **Highest incidence rate of lung cancer**
- **More likely to present at a younger age**
- **15% less likely to be diagnosed stage I/II**

|           | White | Black | Native Am. | Asian/PI | Hispanic |
|-----------|-------|-------|------------|----------|----------|
| Total     | 69.7  | 76.1  | 48.4       | 38.4     | 37.3     |
| Age <40   | 0.9   | 0.9   | 0.5        | 0.7      | 0.4      |
| Age 40-49 | 21.1  | 32.9  | 12.1       | 10.9     | 9.2      |
| Age 50-59 | 85.5  | 117.8 | 54.8       | 39.9     | 39.6     |
| Age 60-69 | 261.4 | 286.2 | 174.2      | 117.1    | 121.2    |
| Age 70-79 | 432.9 | 422.7 | 313.1      | 237.1    | 233.8    |
| Age >80   | 356.9 | 340.3 | 260.0      | 276.6    | 247.9    |

**Lung cancer annual incidence rate per 100,000 population**

# Racial Differences in Smoking Patterns



# Effect of a 20 Pack-Year Threshold

Table 3. US population age 55–80 years in various smoking history categories (in millions)\*

| Category   | All                 | Men                | Women               | Non-Hispanic white  | Racial/ethnic minorities† |
|--|---------------------|--------------------|---------------------|---------------------|---------------------------|
| Meets USPSTF smoking eligibility criteria                                    | 10.0                | 5.9                | 4.1                 | 8.5                 | 1.4                       |
| Current smoker 20–29 pack-years  | 1.6                 | 0.72               | 0.91                | 1.2                 | 0.4                       |
| Meets USPSTF smoking eligibility criteria or current smoker 20–29 pack-years | 11.6                | 6.6                | 5.0                 | 9.7                 | 1.8                       |
| % increase (95% CI) ‡  | 16.3 (13.6 to 19.0) | 12.2 (9.3 to 15.3) | 22.2 (17.9 to 26.7) | 14.1 (11.1 to 17.0) | 30.0 (24.2 to 36.0)       |

**Lowering pack-year threshold to 20 would expand lung cancer screening to groups that were not as well captured in the 2013 guidelines**



# Maintaining Impact Required Expansion

|      | % Eligible | LDCT Screens | Detected LC | Mortality Red. | Deaths Averted | Life Years Gained | LYG Per Death Averted | Scans Per LYG | Screens Per Death Averted | NNS |
|------|------------|--------------|-------------|----------------|----------------|-------------------|-----------------------|---------------|---------------------------|-----|
| 2013 | 14.1       | 227,443      | 1,102       | 9.8%           | 381            | 4,882             | 12.8                  | 47            | 597                       | 37  |
| 2021 | 22.6       | 419,030      | 1,401       | 13.0%          | 503            | 6,918             | 13.8                  | 61            | 833                       | 45  |

Projected numbers per 100,000-person cohort followed from age 45 to 90

- **32% more deaths avoided**
- **42% gain in life years**
- **60% increase in eligible patients**
- **84% increase in CT scans**

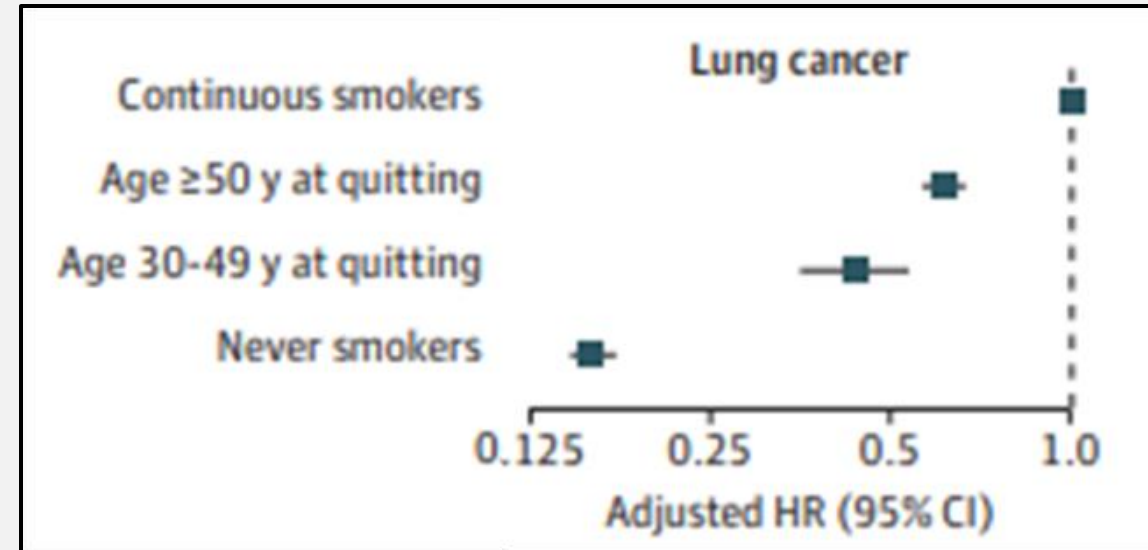
# Stopping Screening for Quitters

A 68 year-old man with a 32 pack-year smoking history comes to your office. He quit smoking when he was 53 and has undergone low dose CT scan annually for 10 years with no significant findings. He feels healthy and well.

- Does he require continued screening?
- Is his risk of lung cancer lower now than it was?

# Reversal of Risk After Quitting

- 2007 International Agency for Research on Cancer (IARC) meta-analysis estimated 50% risk reduction for lung cancer with 10-15 years smoking cessation
- More recent analyses show age of cessation matters.
- Age related risk outweighs quit years at older ages



# Life Expectancy and Surgical Candidacy

A 70-year-old man with congestive heart failure requiring multiple hospitalizations and COPD with oxygen dependent respiratory failure is here for a post-discharge visit. He has heard about lung cancer screening and is interested in discussing options.

- Does he qualify for screening?
- Are there nonsurgical options to cure lung cancer?

# Benefit is Dependent on Intervention

- Detection of resectable stage I and II disease is the primary driver of years of gain in life years and deaths avoided
- Stereotactic Body Radiation Therapy (SBRT) shows promise, but the evidence is “inconsistent” and “imprecise”
- Surgical Resection remains the standard of care

# Overdiagnosis

- Defined as a true positive lung cancer diagnosis that would not have had a significant clinical impact
- NLST and NELSON estimated low rates (<20%) that decreased with longer followup (<10%)
- Tobacco use and advancing age place patients at risk for other illness that may attenuate the benefits of lung cancer screening

# What Else Will We Find?

A 65 year old man, a 40 pack-year active smoker is in your clinic. He understands the process and rationale behind lung cancer screening, but has reservations. Last year his brother spent five days in the hospital after “his lung collapsed when they did a biopsy that turned out to be nothing”. He isn’t sure he wants to go on a “fishing trip”.

- How safe is this?

# False Positives and Incidentals

|                               | Chest 2023 | NLST 2011 | NELSON 2012 |
|-------------------------------|------------|-----------|-------------|
| Pulm Procedure Risk (False +) | 0.40%      | 1.71%     | 2.42%       |
| • Bronch or Needle Asp        | 0.20%      | 1.1%      | 1.77%       |
| • Surgery                     | 0.20%      | 0.61%     | 0.65%       |
| Rate of neg. resection        | 12%        | 24%       | 24%         |

## Procedures without malignancy

- 0.8% insignificant
  - 0.4% pulmonary
  - 0.4% extrapulmonary
- 0.95% clinically relevant diagnosis

**1 in 668 screened patients without lung cancer experienced a complication**



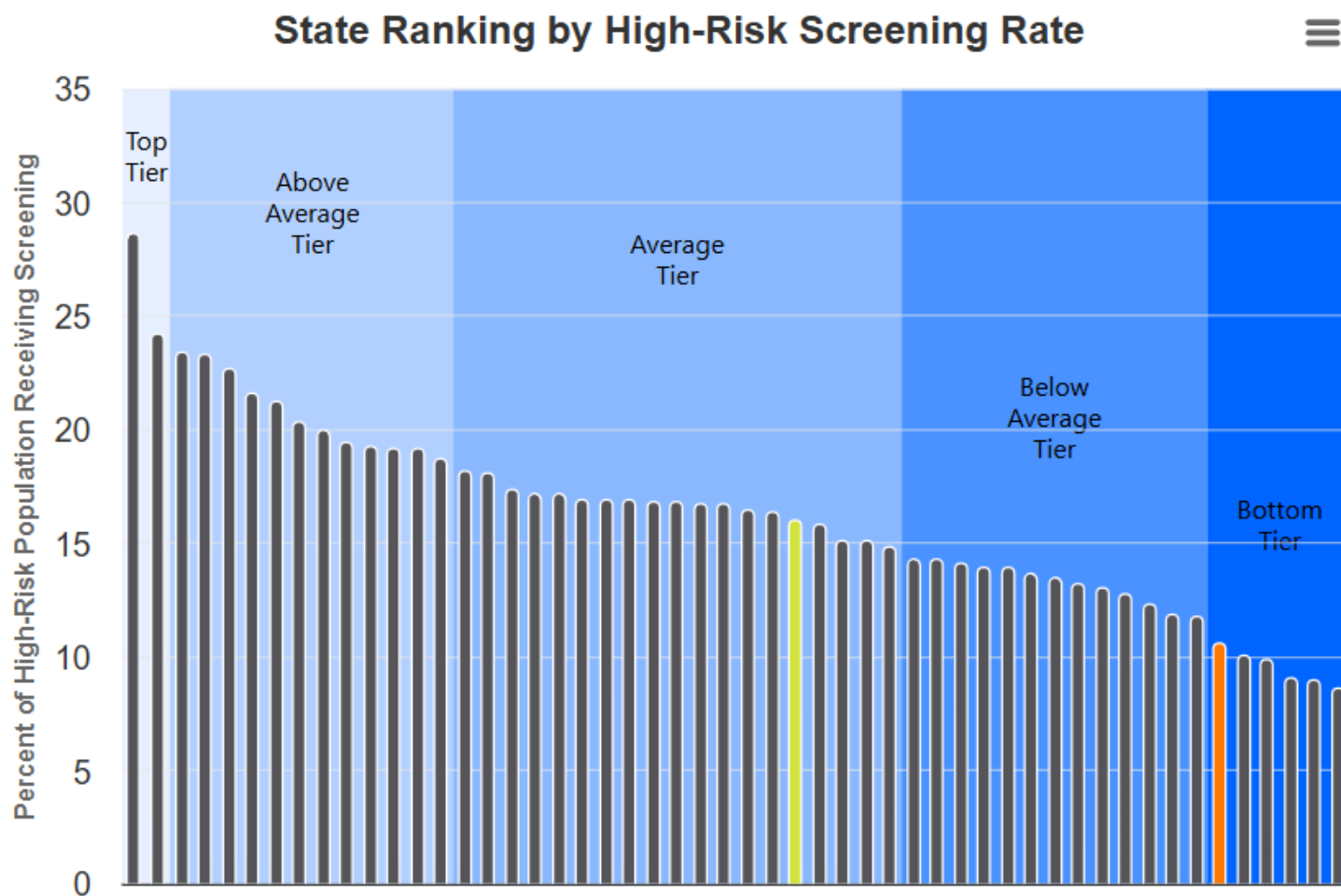
# What about other risk factors?

A 47 year old woman with no smoking history and no known medical conditions is here for an initial visit. Her father died of lung cancer at the age of 58 after smoking for 30 years. Her sister has just been diagnosed with lung cancer at the age of 49 despite being a never-smoker.

- Is she eligible for lung cancer screening?

# Guidelines vs. Clinical Judgment

- There is insufficient evidence to recommend widespread screening for lung cancer based on factors other than smoking history and age.
- Providers can use clinical judgment and engage in shared decision making
- More complex modeling that includes other risk factors (PLCOm2012 model) is currently not recommended



### Screening for High Risk:

- In Texas, **10.6%** of those at high risk were screened, which was **significantly lower** than the national rate of 16.0%.
- It ranks **46th** among all states, placing it in the **bottom tier**.

# Future Direction

- Patient Selection
  - Modeling new cohort
  - Risk assessment models
- Imaging Technology
  - “Ultra” Low Dose CT
  - AI second read and image analysis
- Adjusting to new treatments
  - SBRT or microwave ablation
  - Years gained from non-curative treatment
- Supplemental testing
  - Blood and Sputum biomarkers

# Take Home Message

- Lung cancer screening saves lives
  - All lung cancer screening should be combined with smoking cessation
  - Screening methods and criteria will continue to evolve
  - Widespread implementation is still lacking
- **AGE:**
    - **55-80**
  - **EXPOSURE:**
    - **20 Pack-year**
  - **SMOKING STATUS:**
    - **Active or quit <15 years**

Thank You!

Questions?

*‘Wisdom burned upon a shelf,  
who’ll kill the raging cancer?’*

*“Lungs”* by Townes Van Zandt

