



# Lung Cancer Screening

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# Objectives

- Understand lung cancer
- Understand who high-risk patients are
- Understand risks from cigarette smoking
- Understand lung cancer screening
  - What harm is there in screening?
  - Why screening might be important

# What is Lung Cancer?

- Lung cancer occurs due to an abnormality in the cells of the lung
- Normally, the body has a system of checks and balances on cell growth so that cells divide to produce new cells only when needed
- In cancer, this system is disrupted & there is uncontrolled division and proliferation of cells that eventually form a tumor

# What is Lung Cancer?

- **Cancer = malignant tumor**
- **Malignant tumors can grow aggressively & invade other tissues of the body**
  - Includes lymphatic system (lymph nodes)
  - Metastases – areas of tumor growth at distant sites

# What is Lung Cancer?

- Lung cancer may spread to any organ however most common:
  - Adrenal Glands
  - Liver
  - Brain
  - Bones
- Lung is also a common site for metastases from other types of cancer

# What is Lung Cancer?

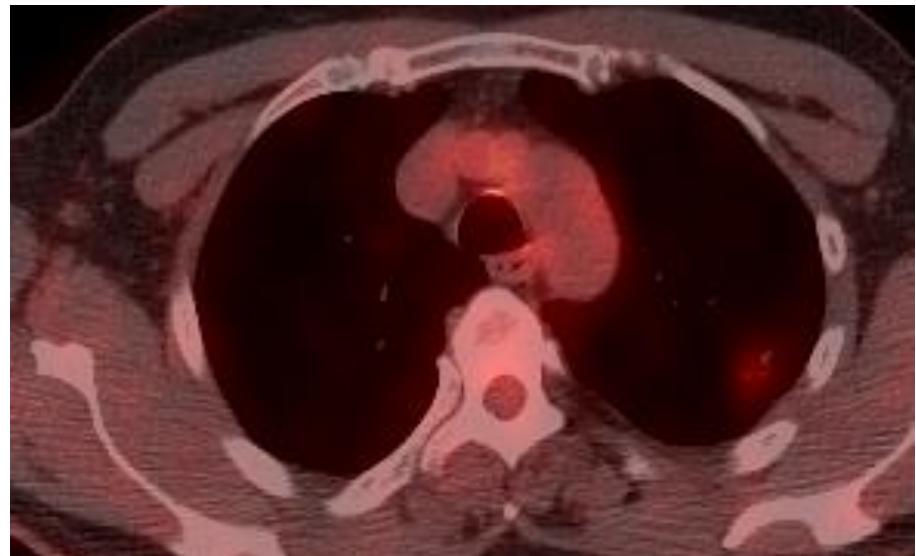
- Lung cancers can arise from any part of the lung but 90 – 95% arise from the cells lining the airways
  - Sometimes referred to as bronchogenic carcinoma
- Lung cancers can also arise from the pleura (lining around the lung)
  - Mesothelioma
  - Related to asbestos exposure

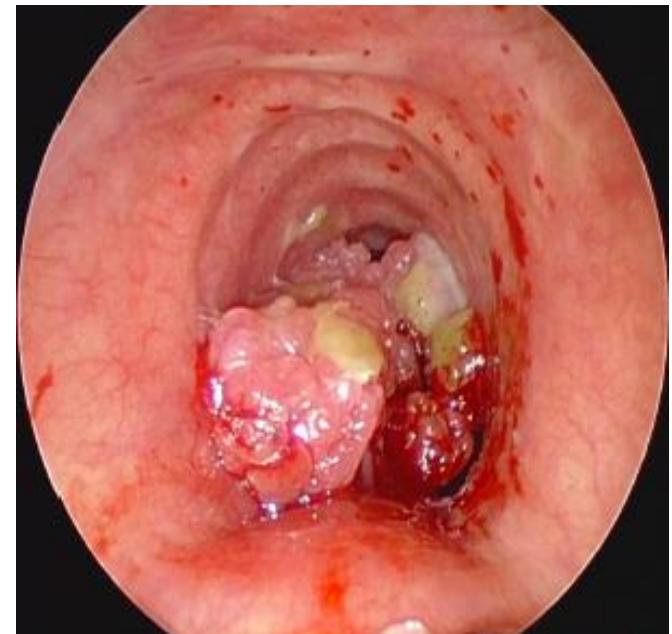
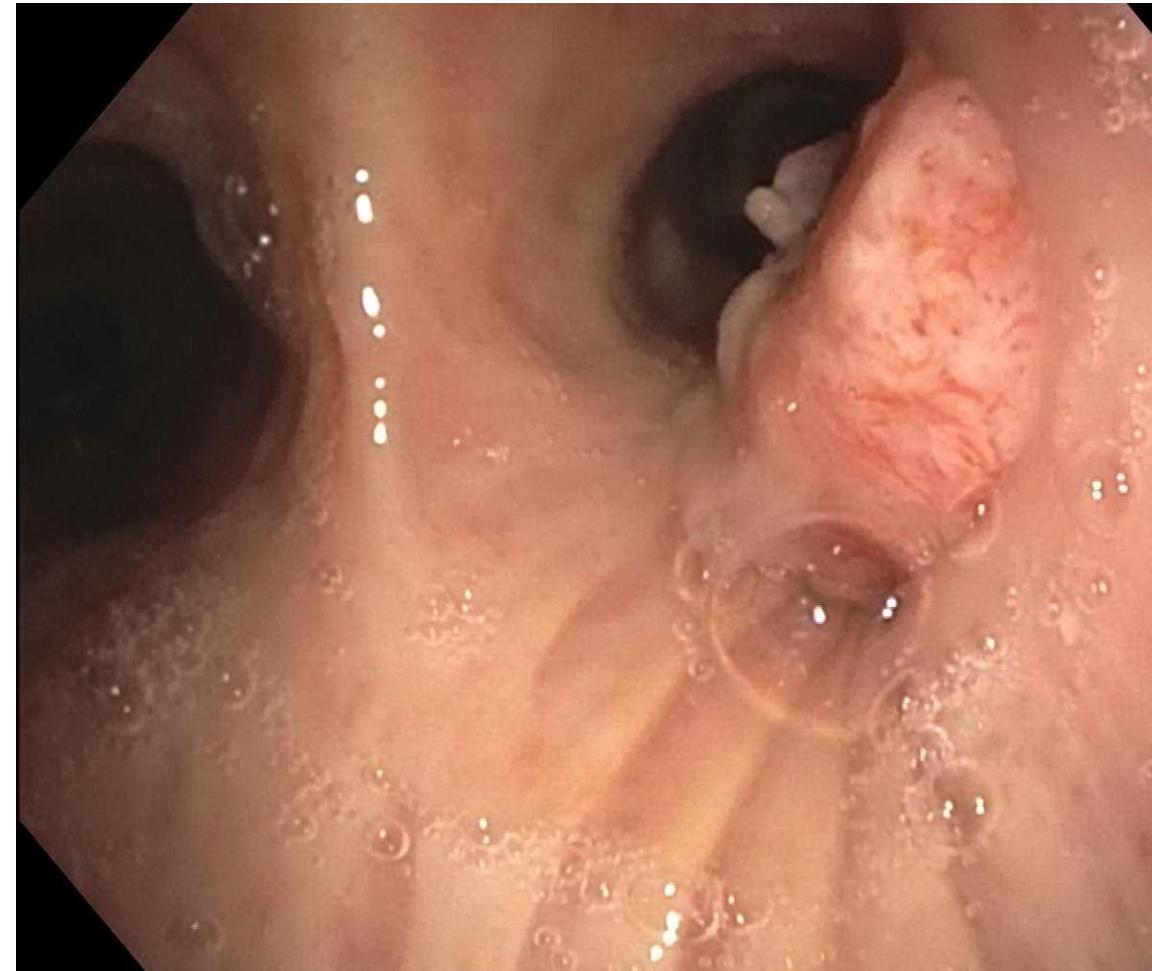
# What is Lung Cancer?

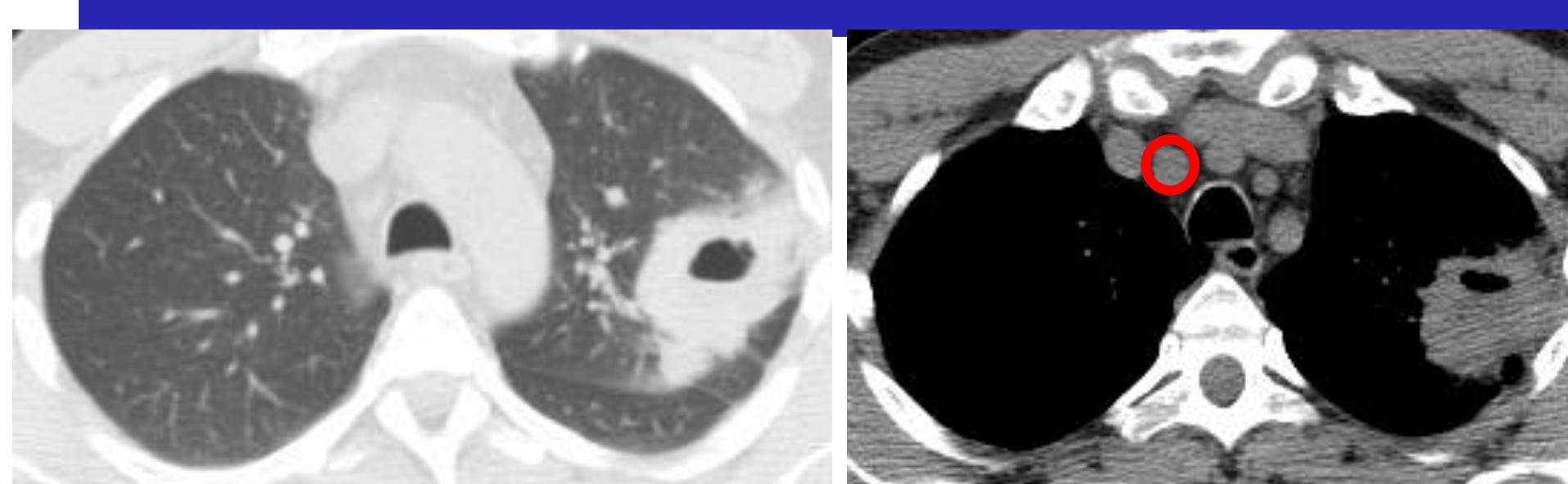
- Lung cancers broadly classified into two types based on microscopic appearance of the tumor cells
  - Small cell lung cancer
    - 20% of lung cancers
    - Most aggressive, rapidly growing
  - Non-small cell lung cancer
    - 80% of lung cancers

# What is Lung Cancer?

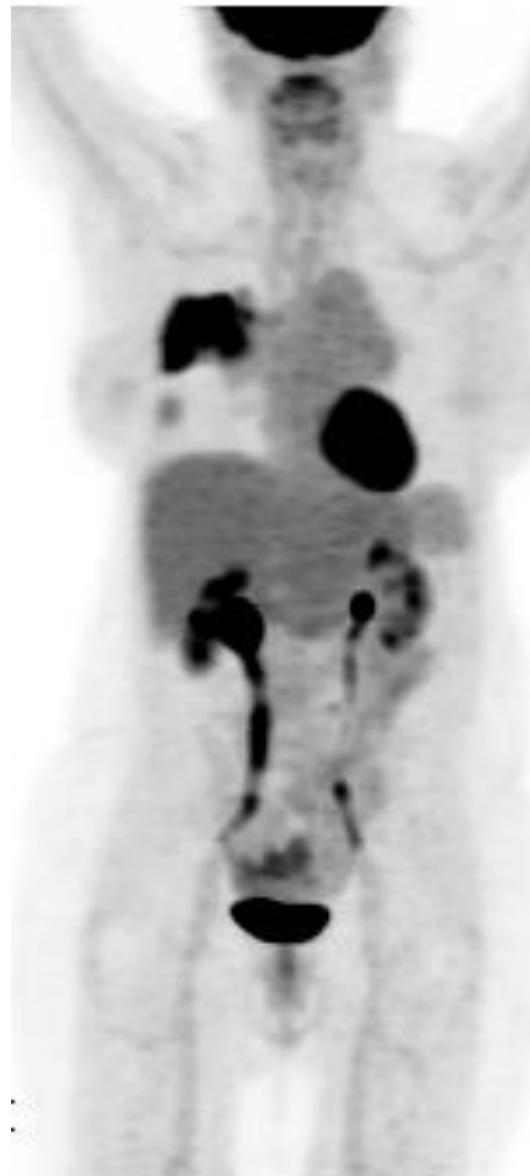
- Non-small cell lung cancers
  - Adenocarcinoma
    - Most common
    - Bronchioloalveolar carcinoma
  - Squamous Cell Carcinoma
  - Large Cell Carcinoma
  - Mixtures of different types







**Squamous cell cancer**



# Background

- Lung cancer = Number 1 cause of cancer death in the US & Worldwide
  - 28% of all cancer deaths in men; 26% in women
- Third most common type of cancer
- **Cigarette smoking** is the primary risk factor for getting lung cancer
  - Second-hand smoke exposure is also a risk factor

# Background

- 94 million current & former smokers in US
  - 85% lung cancer due to smoking
  - Risk of getting lung cancer continues even after smoking cessation
- Cigarettes & cigarette smoke contain more than 4,000 chemicals (carcinogens)
  - Damages the cilia on airway cells which normally sweep out the toxins

# Background

- For most lung cancers, prevention is best by never smoking and avoiding second-hand smoke
- For smokers who quit, within 10 years, the risk of getting lung cancer drops to that of a non-smoker



# Quitting Smoking

- Realize why it is important to stop smoking
- You don't have to go “cold turkey”
  - Nicotine = addiction
  - Replacement products
    - Gum
    - Lozenges
    - Inhalers
    - Patches



# Quitting Smoking

- Nicotine withdrawal
  - Restlessness
  - Depression
  - Anxiety
- Important not to smoke while using nicotine replacement products
- Cravings can be overwhelming
  - Prescription medications can help

# Lung Cancer Myths and Facts

MedicineNet.com

- If you've smoked for years, the damage is done
  - NEVER too late to stop smoking
- Low-Tar or 'Light' cigarettes are safer
  - Light, ultra-light, low-tar are just as dangerous as regular
  - Menthol cigarettes may be more dangerous & harder to quit

# Lung Cancer Myths and Facts

MedicineNet.com

- Smoking marijuana does not increase lung cancer risk
  - Marijuana use may INCREASE lung cancer risk
- Antioxidant supplements protect you from cancer
  - Antioxidant supplements are not protective

# Lung Cancer Myths and Facts

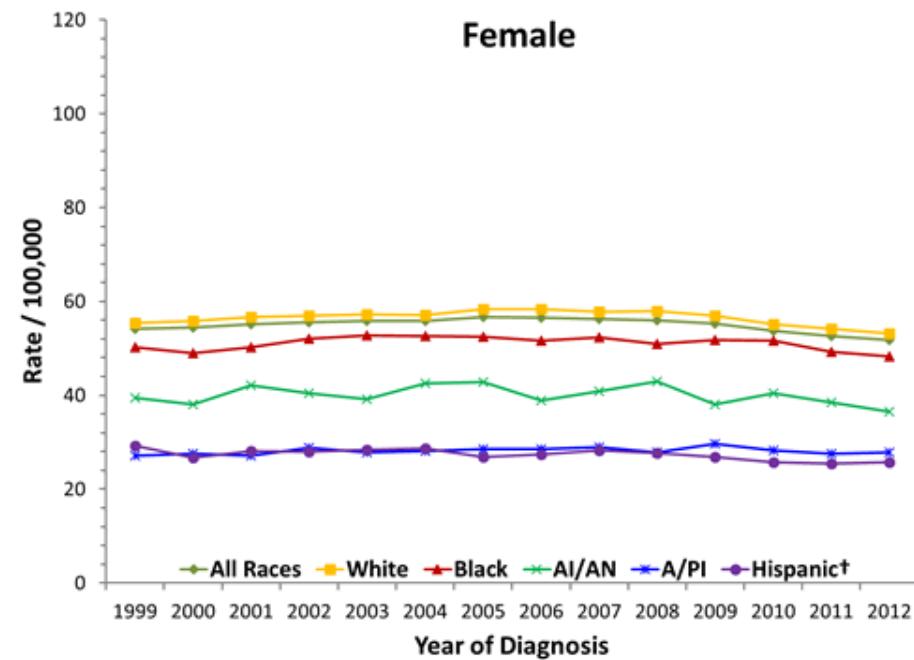
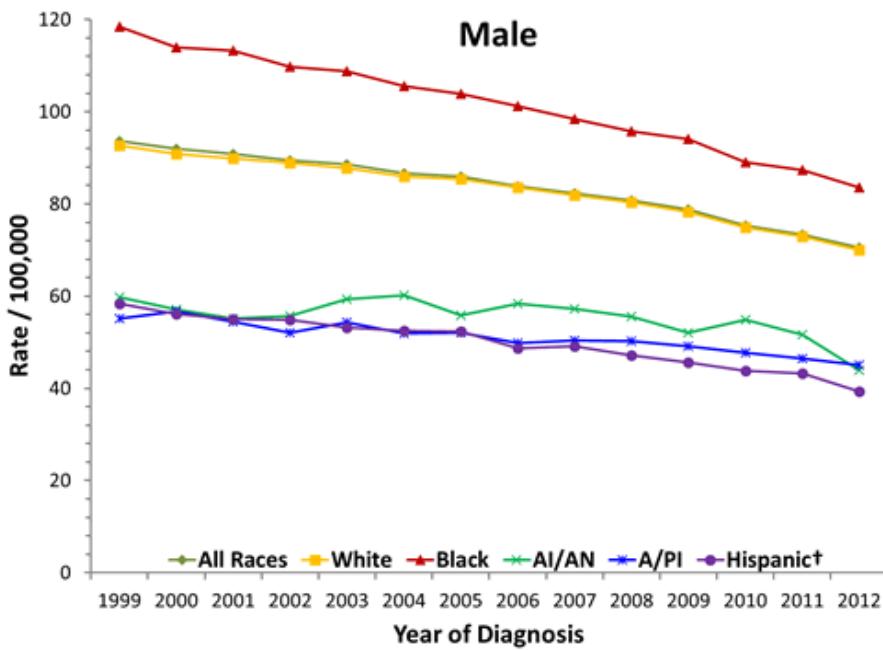
MedicineNet.com

- Pipes and cigars don't cause lung cancer
  - Smoking pipes & cigars increases not only lung cancer risk but also risk for cancers of the mouth, throat, and esophagus
- If diagnosed with lung cancer, quitting is pointless
  - Continued smoking decreases the effectiveness of cancer treatment

# Background

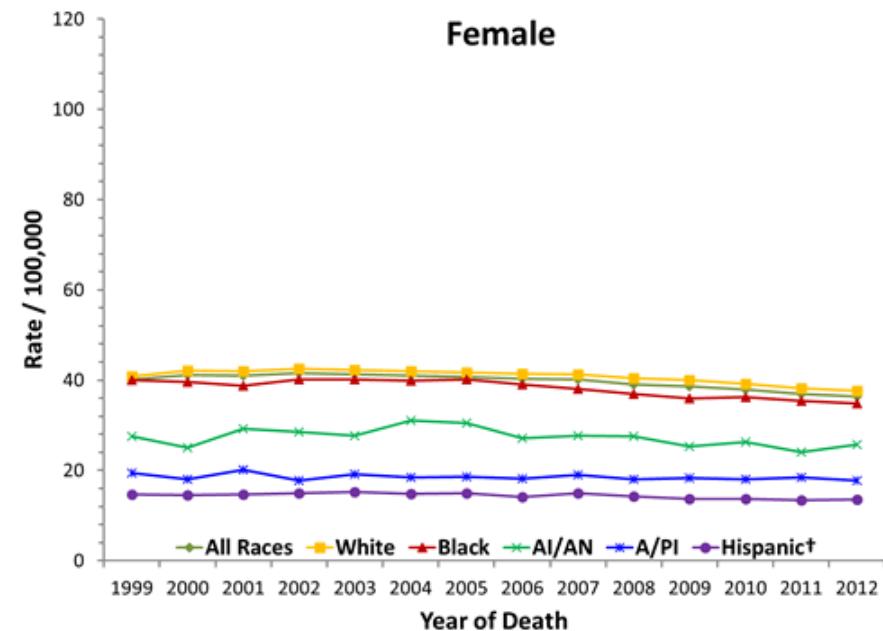
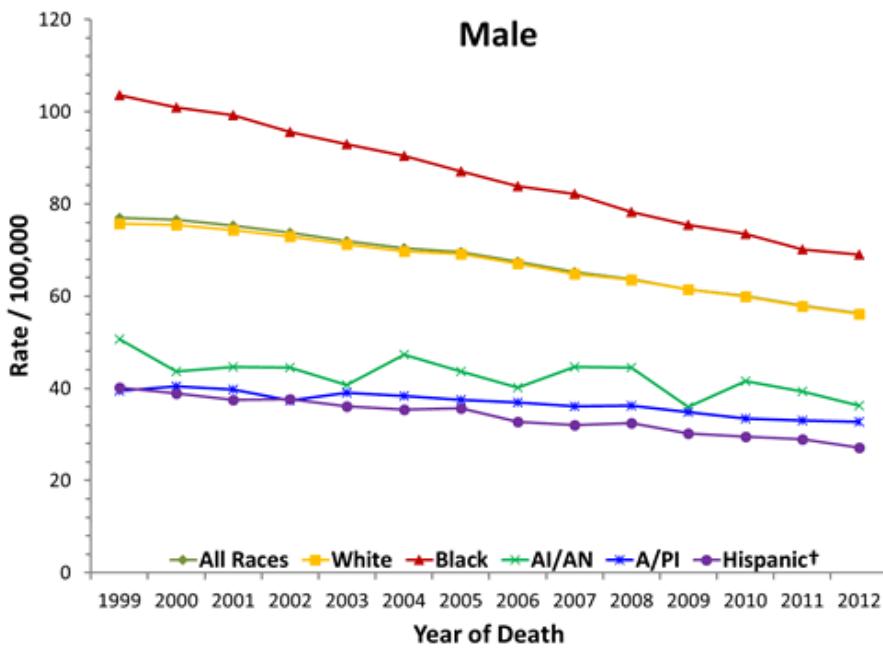
- Radon gas is felt to be the 2<sup>nd</sup> leading cause of lung cancer
  - Odorless and colorless
  - Occurs naturally and can seep into homes, basements, crawl spaces
  - Can be detected with relatively simple & inexpensive test kits

# Incidence Rates by Race & Ethnicity



In 2012, among men, **black** men had the highest rate of getting lung cancer followed by **white**, **Asian/Pacific Islander**, **American Indian/Alaska Native** & **Hispanic** men. Among women, **white** women had the highest rate followed by **black**, **American Indian/Alaska Native**, **Asian/Pacific Islander**, & **Hispanic** women.

# Death Rates by Race & Ethnicity



In 2012, among men, **black** men were more likely to die of lung cancer followed by **white**, **American Indian/Alaska Native**, **Asian/Pacific Islander**, & **Hispanic** men. Among women, **white** women were more likely to die of lung cancer followed by **black**, **American Indian/Alaska Native**, **Asian/Pacific Islander**, & **Hispanic** women.

# Lung Cancer Symptoms

- Symptoms depend on where and how widespread the tumor is
- Usually do not cause pain
- About 25% of patients have no symptoms at all
  - Cancer is found on testing done for other reasons

# Lung Cancer Symptoms

- Chest pain
- Chronic cough
- Fatigue
- Weight loss
- Shortness of breath
- Wheezing

# Lung Cancer Staging

- The stage of lung cancer refers to the extent the cancer has spread in the body
- Early stage lung cancer has 5-year survival of 40 – 50%
- Late stage lung cancer has 5-year survival of 1 – 5%

# Lung Cancer Screening

- Screening means testing for a disease when there are no symptoms or history of that specific disease
- Doctors recommend a screening test to find disease early when treatment might work better
- The only recommended screening test for lung cancer is low-dose computed tomography

# Computed Tomography (CT) Scan



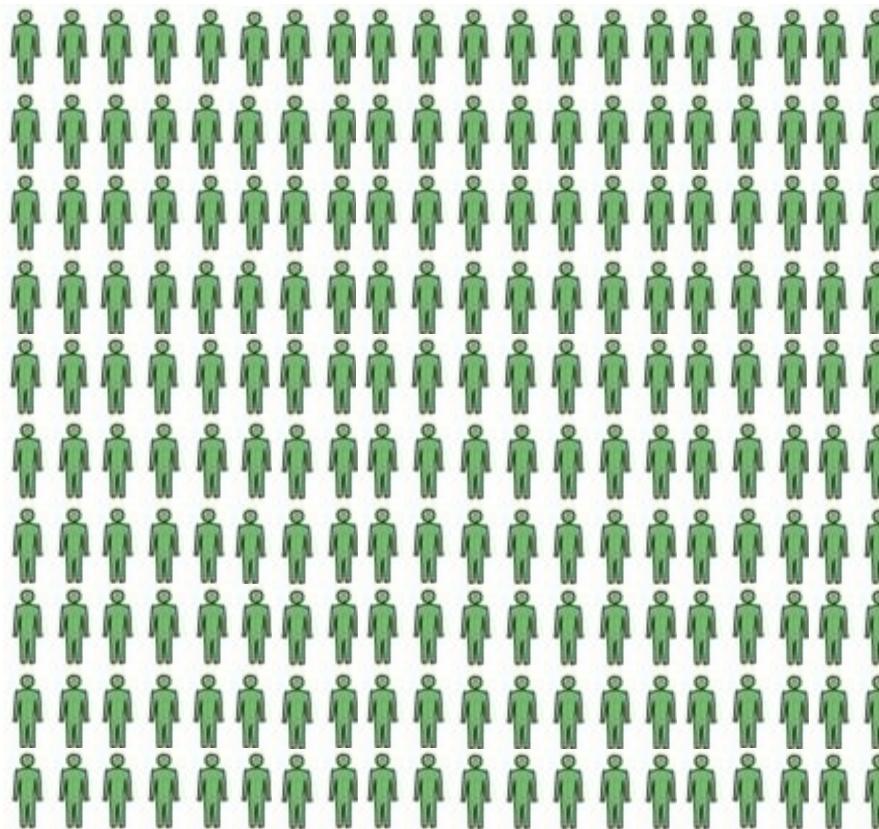
An X-ray machine scans the body and uses low doses of radiation to make detailed pictures of the lungs

# Lung Cancer Screening

- National Lung Screening Trial
  - Studied *asymptomatic* people aged 55 – 74 years
  - Smoking history of at least 1 ppd for at least 30 years
    - Smoked within past 15 years
  - 3 years of LDCT screening reduced the risk of lung cancer death by 20%
    - Increase chance of finding smaller cancers

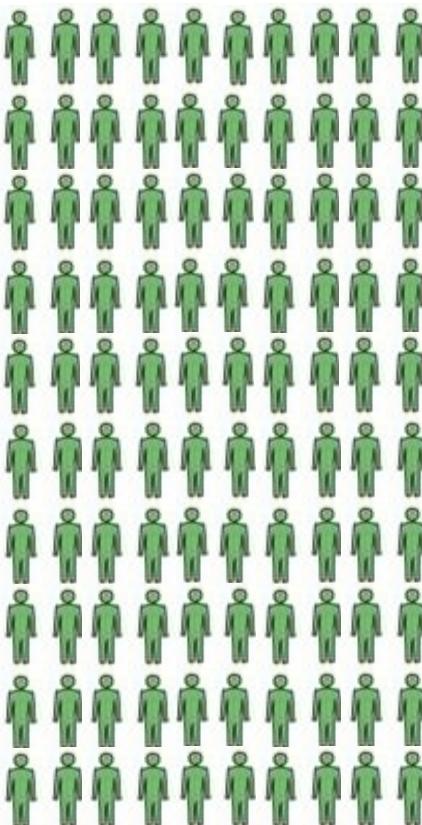
# Eligible participants were randomized

Person at high risk for lung cancer

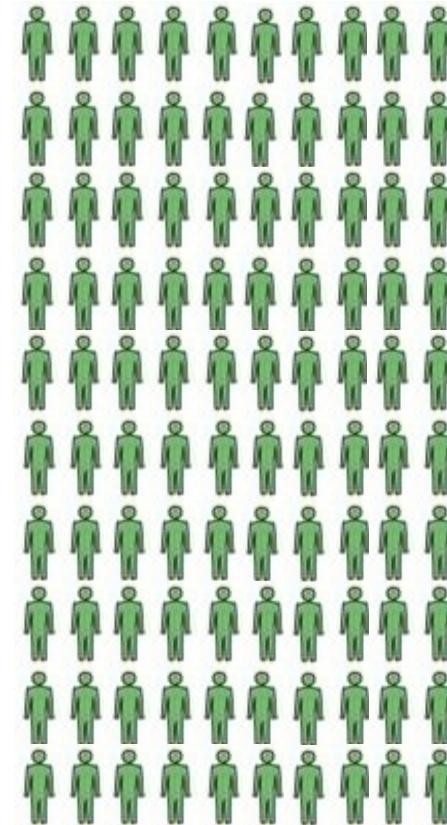


# Randomize (flip of a coin)

CT Screen group



No CT group

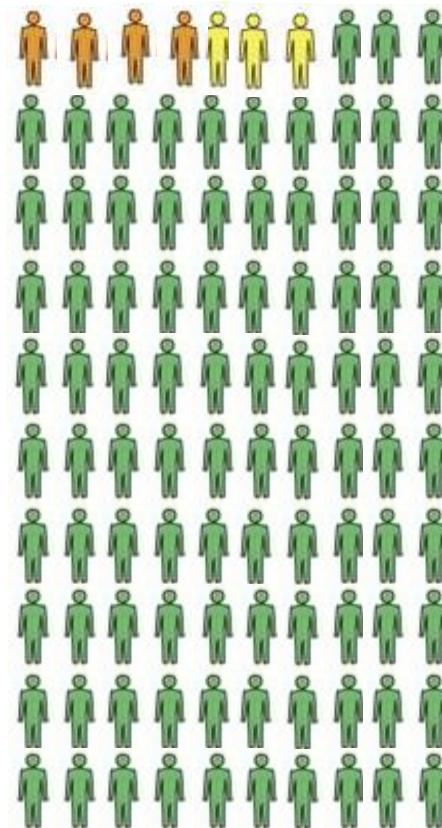
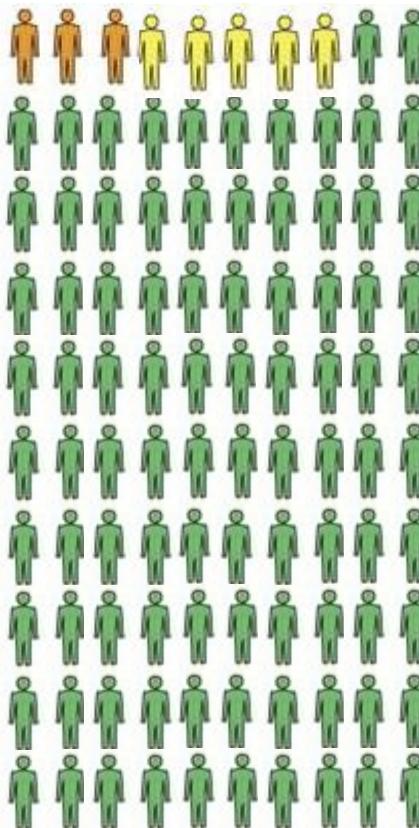


# After 3 scans and a total of 6 years of follow-up

**CT group**

 lung cancer diagnosis  
 death from lung cancer

**No CT group**



# The NLST: things to note

- More cancers were found in the CT group
  - most participants did not develop lung cancer
- Fewer people died from lung cancer in the CT group compared to the no CT group
- Some who got screened with CT still died of lung cancer
- Some of the cancers were likely ‘overdiagnosis’ cancers
  - Cancers that would not have caused symptoms or shortened life even if they had not been found

# LDCT Screening: Potential Benefit

- LDCT screening may find you have a lung cancer at a time when treatment may be more effective or curable.
- Knowing that you have no sign of cancer may be helpful.
- By both not smoking and getting screened you are taking steps to improve your health.

# LDCT Screening: Potential Harm

- It may find lung a cancer that would not have caused any problems and result in unnecessary treatment (over diagnosis)
- Finding of a lung nodule may lead to anxiety
- Finding of a nodule may lead to more testing, biopsy or surgery and results may not be cancer
- Radiation from the CT scan is low but not zero
  - Radiation from repeated scans can cause cancer in otherwise healthy people

# LDCT Screening

- High-risk persons = potential benefits of screening outweigh potential harms
- Some debate about which populations to screen
  - History of COPD/emphysema
  - Family history of lung cancer

## Question 1

- 62 yo woman quit smoking in 1995 after smoking  $\frac{1}{2}$  ppd for 20 years. She complains of a cough with daily sputum production & dyspnea after climbing a flight of stairs. On exam, she wheezes with forced expiration and has 1+ edema. Chest xray is normal.
- Which of the following tests is **not** indicated?

## Question 1

- a. Sputum culture**
- b. Low dose screening CT scan for lung cancer**
- c. Pulmonary function testing**
- d. Echocardiogram**

## Question 1

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# NLST Prevalence Results

- More positive screenings, dx procedures, biopsies, invasive procedures, lung cancers in low-dose CT group at baseline screen
- Prevalence of lung cancer (1.1%) at low end of reported range in prior large studies of pts with similar smoking histories
- High compliance rate

# Results of the 2 Incidence Screens in NLST

- Evaluate rate of adherence to screening protocol
- Results of screening & diagnostic tests
- Features of the lung cancer cases & first-line treatments
- Estimated performance characteristics of both screening methods

# Results of Incidence Screenings in NLST at T1 & T2

- Among lung cancers of known stage:
  - Low-dose CT
    - 87 (47.5%) stage IA
    - 57 (31.1%) stage III or IV at T1
  - Chest X-ray group
    - 31 (23.5%) stage IA
    - 78 (59.1%) stage III or IV at T1

# Harms of Incidence Screenings in NLST at T1 & T2

- Thoracotomy as a result of positive screen with no lung cancer diagnosed:
  - Low-dose CT = 18.9% T1; 15.9% T2
  - Chest X-ray = 11.4% vs. 13.6%
- Performance characteristics influenced by risk of cancer (pretest probability)

# Conclusions of Incidence Study

- Low dose CT more sensitive in detecting early-stage lung cancers
  - BUT PPV lower than with chest X-ray
- 2 annual incidence screenings with CT resulted in decrease in advanced-stage cancers diagnosed & increase in early-stage lung cancers diagnosed

# Prediction Model Results

- # need to screen to prevent 1 lung cancer death decreased from 5,276 among the 20% at lowest risk to 161 among 20% at highest risk
- Also # false positive results decreased from 1648 among 20% at lowest risk to 65 among 20% at highest risk

# Prediction Model Conclusions

- Screening with low-dose CT prevented greatest number of deaths from lung cancer among those at highest risk & prevented very few deaths among those at lowest risk
- Provides empirical support for risk-based targeting of smokers for such screening

# Low-Dose CT for Lung Screening

- Systematic review to update US Preventive Services Task Force Recommendation
  - Four trials – 1 large good-quality trial; 3 small European trials (no benefit, underpowered)
  - Strong evidence shows that LDCT screening can reduce lung cancer & all-cause mortality
  - Harms must be balanced with risks

*Annals of IM 2013; July 30*

# Low-Dose CT for Lung Screening

- Harms
  - Over-diagnosis (false positive)
  - Radiation exposure
    - 1 LDCT ranges from 0.61 – 1.50 mSv
    - Similar to mammography
    - 1 study reported cumulative radiation exposure – 6 – 7 mSv for baseline LDCT & 3 subsequent annual LDCT      *AJR 2006; 187:421-429*
  - Psychosocial consequences

# Comparative Modeling Study

- To identify efficient CT screening scenarios where relatively more lung cancer deaths are averted for fewer CT screening exams
  - 5 independent models
  - Most advantageous strategy was annual LDCT from ages 55 – 80 years for ever-smokers with at least 30 pack years & ex-smokers with less than 15 years since quitting

## Question 2 – Does Nodule Size Matter?

- The chance that a lung nodule is cancer increases dramatically over what size?
  - a. 5mm
  - b. 7mm
  - c. 8mm
  - d. 9mm
  - e. 10mm

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# Nodule Size – Does it Matter?

- Estimate effects of increasing nodule size threshold on lung cancer detection & false-positive rates, test sensitivity/specificity, diagnostic follow-up testing, & lung cancer stage & mortality
- NLST data on nodules > 4mm
- Outcomes assessed = diagnostic tests, histology, stage, mortality

# Nodule Size – Does it Matter?

- 64% positive screens (11,598/18,141) the largest nodule was  $\leq 7\text{mm}$
- Cancer rates increased rapidly at a size of 10mm with aggregate rates of 0.8% for all nodules  $< 10\text{mm}$  & 12% for all nodules  $> 10\text{mm}$

# Nodule Size – Does it Matter?

- For each millimeter increase in nodule size threshold for screen positivity there was a small but steadily increasing proportion of lung cancer diagnoses being delayed or missed & a marked decrease in false-positive rates
  - % of screen detected cancers that would have been missed over all 3 screening years was 1% at 5mm, 3% at 6mm, 5.9% at 7mm, & 10.5% at 8mm

# What are Potential Harms?

- Invasive procedures for lesions that turn out to be benign
  - 25% of invasive procedures would be avoided with a threshold of 8mm
- Cumulative radiation dose
- Patient anxiety about lung cancer & potentially false-positive screens
- ? Cost

# What Have We Learned so Far?

- Increasing the minimum size threshold for positive screening tests may reduce frequency of diagnostic workup
  - NLST – nodules 4 – 6mm in size accounted for about half positive screen results but associated with lung cancer in < 1%
- Diagnostic prediction models may have much to offer

# Take Home Pearls

- Lung cancer is the most common cause of cancer death in men and women
- 2014 – 224,000 cases of lung cancer in the US; 159,000 deaths from lung cancer
  - *American Cancer Society*
- Lung cancer was not common before the 1930's
  - Increased dramatically over following decades as tobacco smoking increased

# Take Home Pearls

- Remember lung cancer screening with low dose CT scan for high risk patients
  - Asymptomatic
  - $\geq 30$  pack year smoking history
  - Quit  $\leq 15$  years
  - Age 55 – 74 in NLST (55 – 80 USPSTF)
- Tobacco cessation more important than screening

# Take Home Pearls

- Lung cancer screening is NOT a substitute for quitting smoking!

# Lung Cancer Screening Guidelines and Recommendations

Organization	Groups eligible for screening	Year
<a href="#">American Academy of Family Practice<sup>1</sup></a>	Evidence is insufficient to recommend for or against screening.	2013
<a href="#">American Association for Thoracic Surgery<sup>2</sup></a>	<ol style="list-style-type: none"> <li>1. Age 55 to 79 years with <math>\geq</math> 30 pack year smoking history.</li> <li>2. Long-term lung cancer survivors who have completed 4 years of surveillance without recurrence and who can tolerate lung cancer treatment following screening to detect second primary lung cancer until the age of 79.</li> <li>3. Age 50 to 79 years with a 20 pack year smoking history and additional comorbidity that produces a cumulative risk of developing lung cancer <math>\geq</math> 5% in 5 years.</li> </ol>	2012
<a href="#">American Cancer Society<sup>3</sup></a>	Age 55 to 74 years with $\geq$ 30 pack year smoking history, who either currently smoke or have quit within the past 15 years, and who are in relatively good health.	2015
<a href="#">American College of Chest Physicians<sup>4</sup></a>	Age 55 to 74 years with $\geq$ 30 pack year smoking history, who either currently smoke or have quit within the past 15 years.	2013
<a href="#">American College of Chest Physicians and American Society of Clinical Oncology<sup>5</sup></a>	Age 55 to 74 years with $\geq$ 30 pack year smoking history, who either currently smoke or have quit within the past 15 years.	2012
<a href="#">American Lung Association<sup>6</sup></a>	Age 55 to 74 years with $\geq$ 30 pack year smoking history and no history of lung cancer.	2012
<a href="#">Centers for Medicare and Medicaid Services<sup>7</sup></a>	Age 55 to 77 years with $\geq$ 30 pack year smoking history and smoking cessation < 15 years.	2015
<a href="#">National Comprehensive Cancer Network<sup>8</sup></a>	<ol style="list-style-type: none"> <li>1. Age 55 to 74 years with <math>\geq</math> 30 pack year smoking history and smoking cessation &lt; 15 years.</li> <li>2. Age <math>\geq</math> 50 years and <math>\geq</math> 20 pack year smoking history and 1 additional risk factor (other than secondhand smoke exposure).<sup>b</sup></li> </ol>	2015
<a href="#">U.S. Preventive Services Task Force<sup>9</sup></a>	Age 55 to 80 years with $\geq$ 30 pack year smoking history and smoking cessation < 15 years.	2013

<sup>a</sup>A pack year is smoking an average of one pack of cigarettes per day for one year. For example, a person could have a 30 pack year history by smoking one pack a day for 30 years or two packs a day for 15 years.

<sup>b</sup>Additional risk factors include cancer history, lung disease history, family history of lung cancer, radon exposure, occupational exposure, and history of chronic obstructive pulmonary disease or pulmonary fibrosis. Cancers with increased risk of developing new primary lung cancer include survivors of lung cancer, lymphomas, cancer of the head and neck, and smoking-related cancers. Occupational exposures identified as carcinogens targeting the lungs include silica, cadmium, asbestos, arsenic, beryllium, chromium (VI), diesel fumes, and nickel.

# Thank You!

