Lung Cancer: What the Primary Care Physician Needs To Know

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Center for Continuing Medical Education

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Case history & physical exam

History:

- 46 year old banker
- 2 month history of non-productive cough
- 15 pound weight loss
- Smoked 1 PPD for 30 years

Physical Exam:

- Decreased breath sounds over right lower lobe
- Dullness to percussion lower right lung

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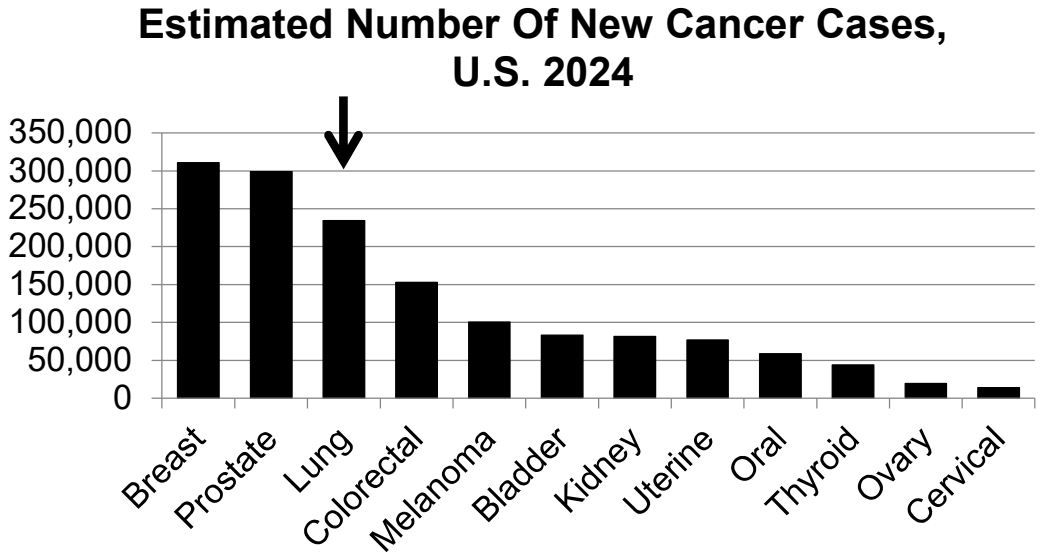
Lung Cancer Epidemiology

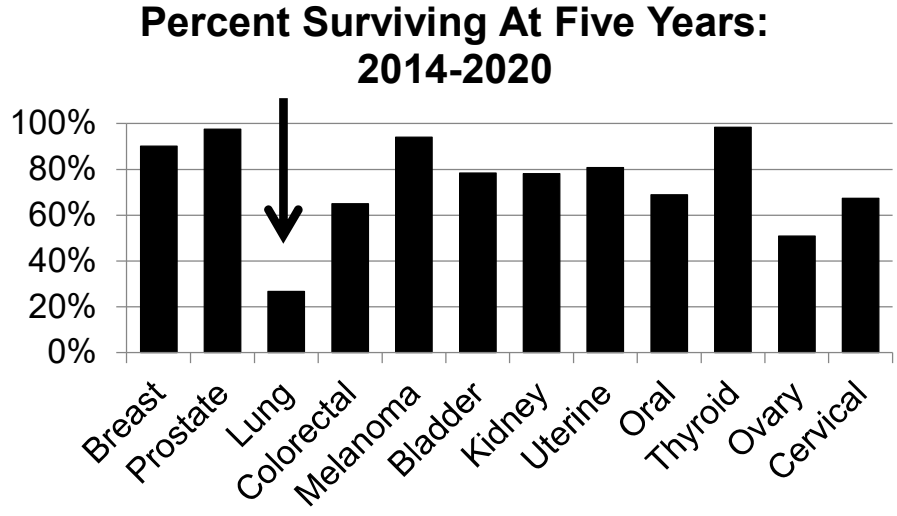
- 238,340 new cases per year
- 127,070 U.S. deaths annually
- Lifetime risk:
  - 1:15 men
  - 1:17 women

Incidence Of Common Cancers



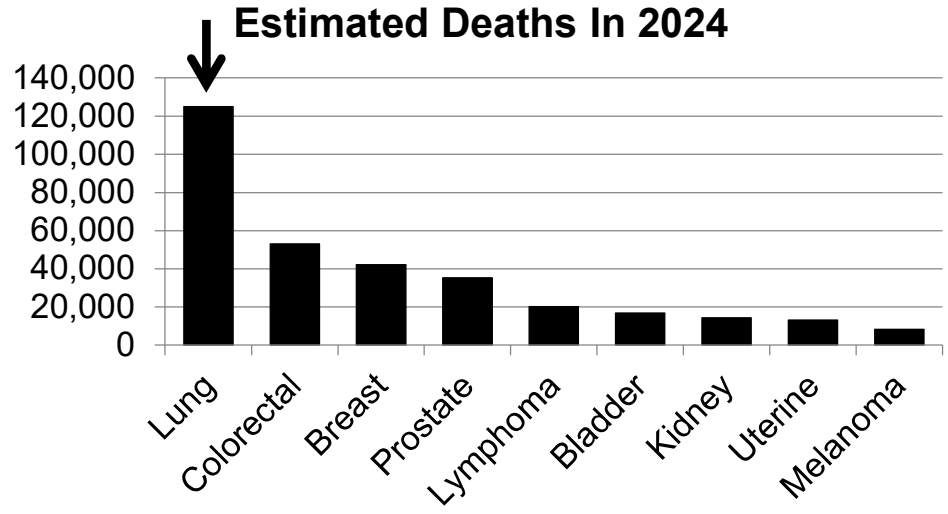
National Cancer Institute SEER Data

Five-Year Survival Rates Of Common Cancers



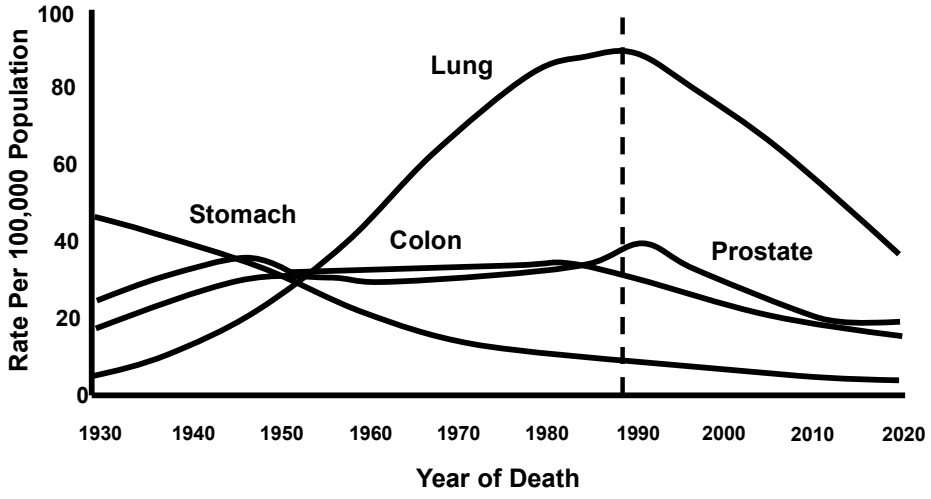
National Cancer Institute SEER Data

Lung Cancer Kills More Americans Than Any Other Type Of Cancer



National Cancer Institute SEER Data

Trends in Age-adjusted Cancer Death Rates by Site, Males, U.S., 1930-2021



Data from CDC

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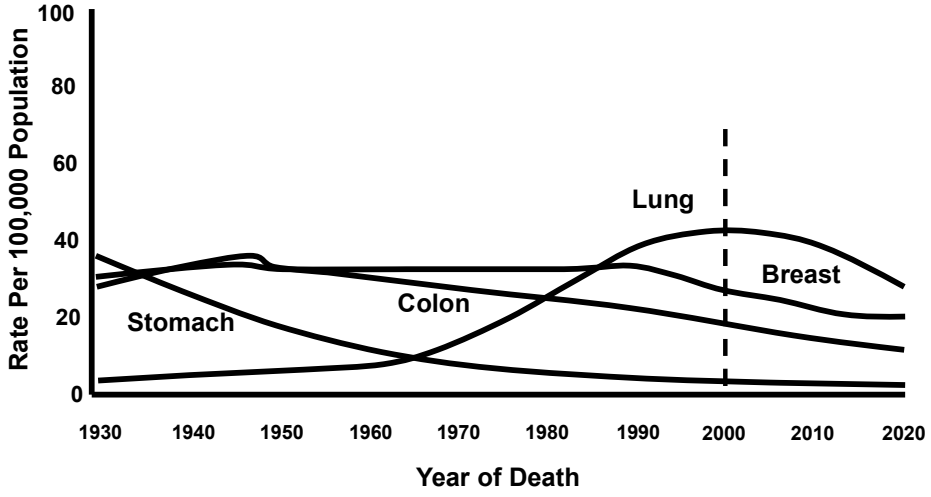
Trends in Age-adjusted Cancer Death Rates by Site, Females, U.S., 1930-2020



Data from CDC

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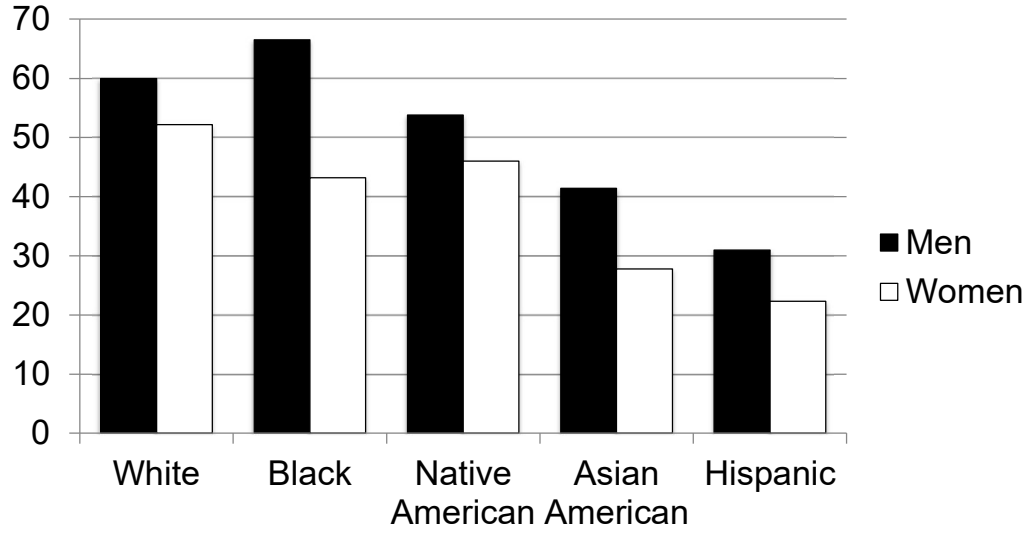
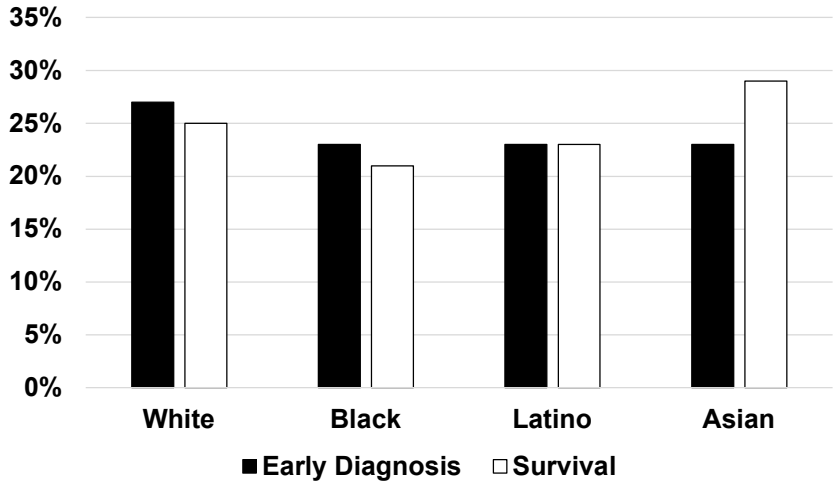
Incidence of lung cancer (per 100,000 population)

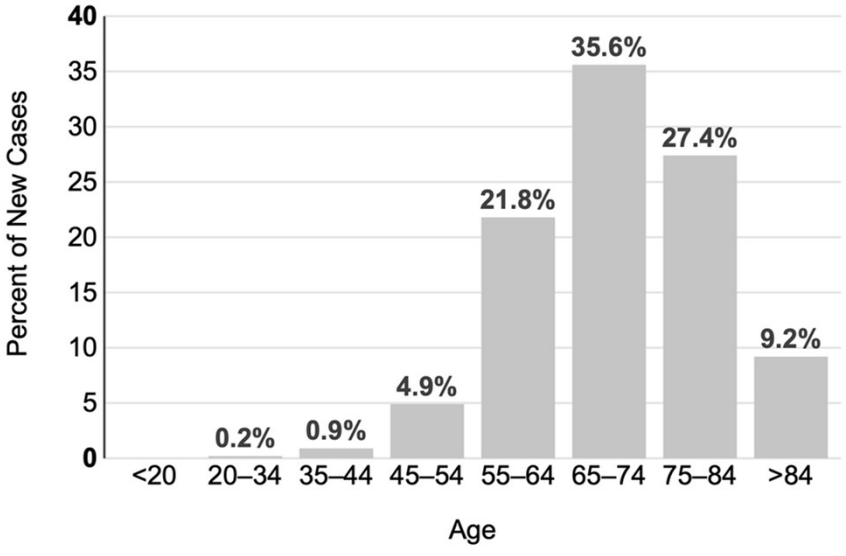


National Cancer Institute SEER Data (2017-2021)

There are racial differences in lung cancer diagnosis and survival



Age of diagnosis of lung cancer:



National Cancer Institute SEER data 2024 (2017-2021)

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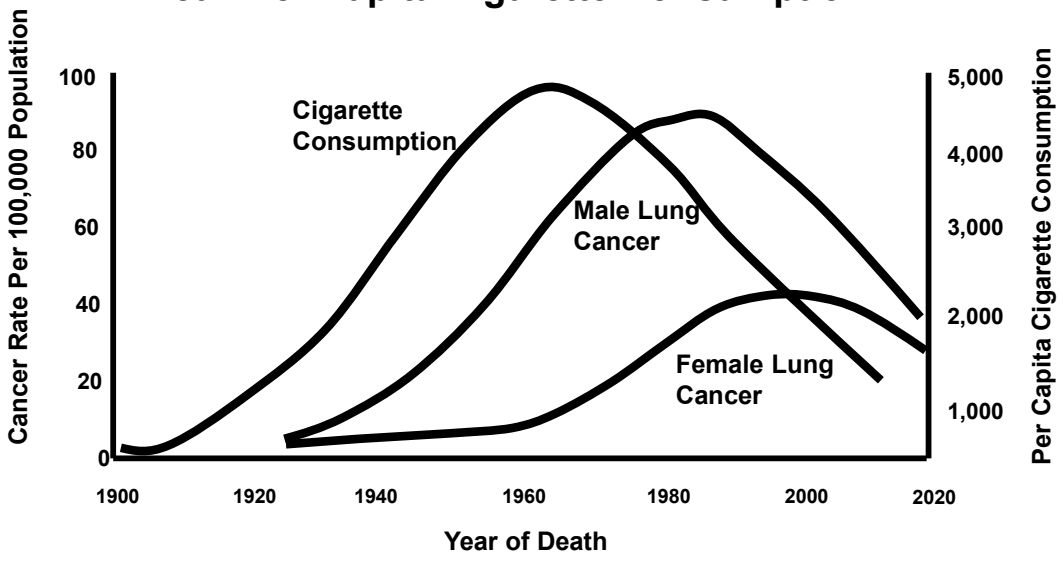
Risk Factors For Lung Cancer

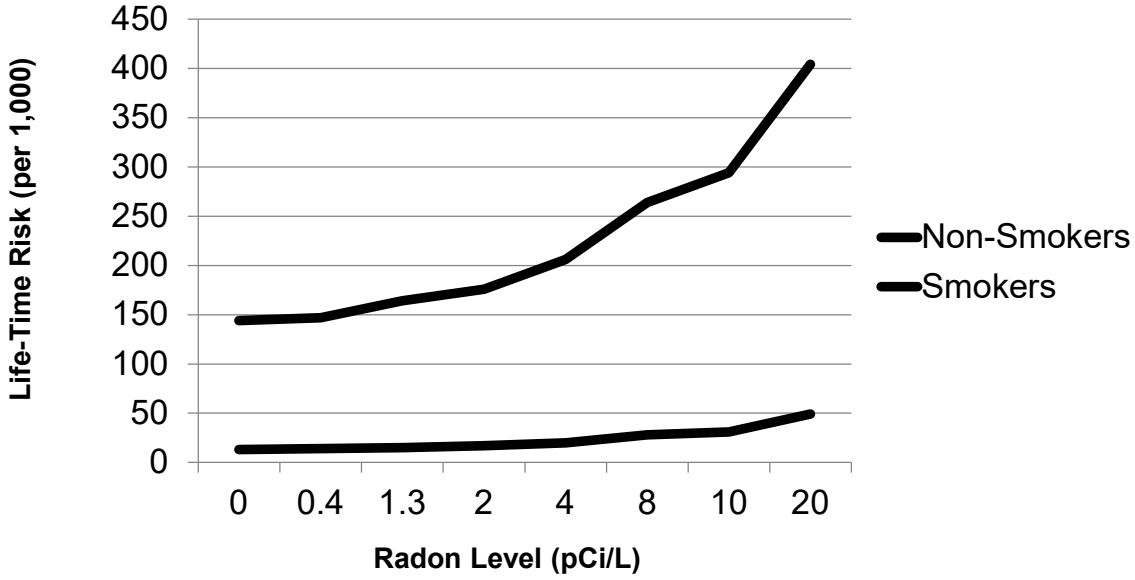
- **Smoking**
- Environmental tobacco smoke
- Genetics
- Radon
- Asbestos
- Radiation therapy
- Emphysema
- Pulmonary fibrosis

Peak Lung Cancer Rate Is 30-40 Years After Peak Per Capita Cigarette Consumption



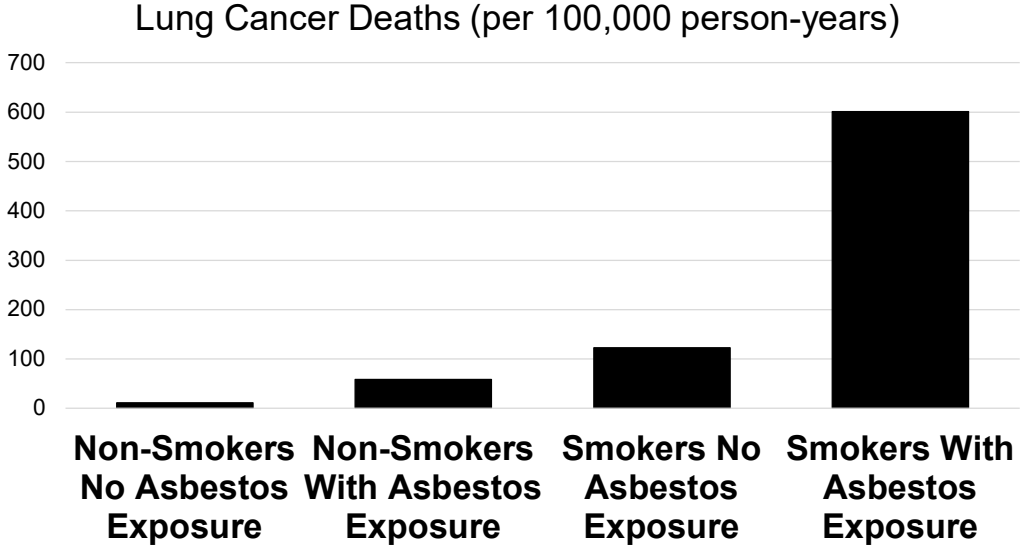
Data from CDC & U.S. Department of Agriculture

Radon And Lung Cancer Risk

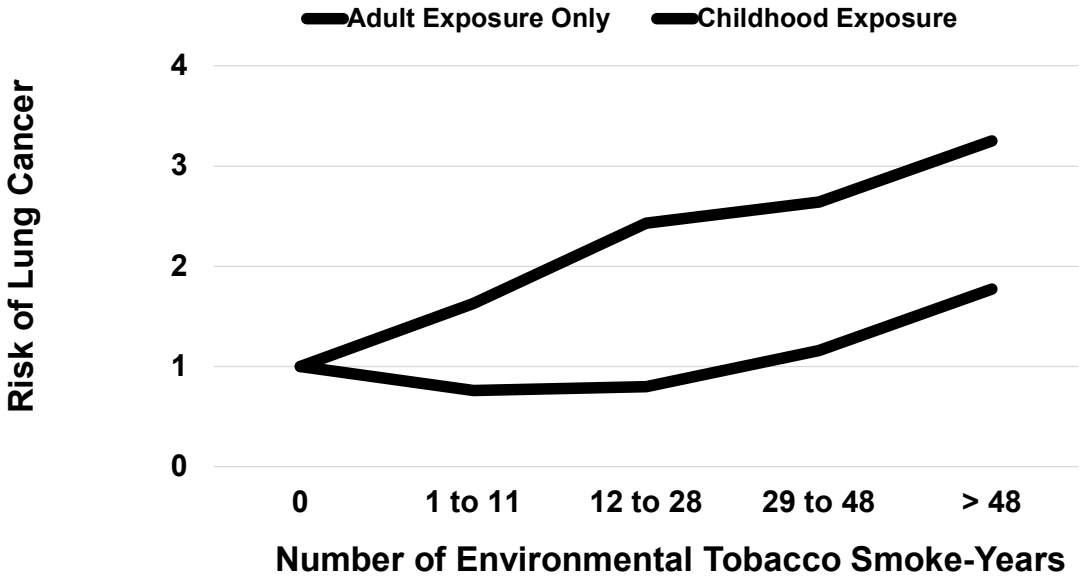


Data: CDC Agency for Toxic Substances & Disease Registry

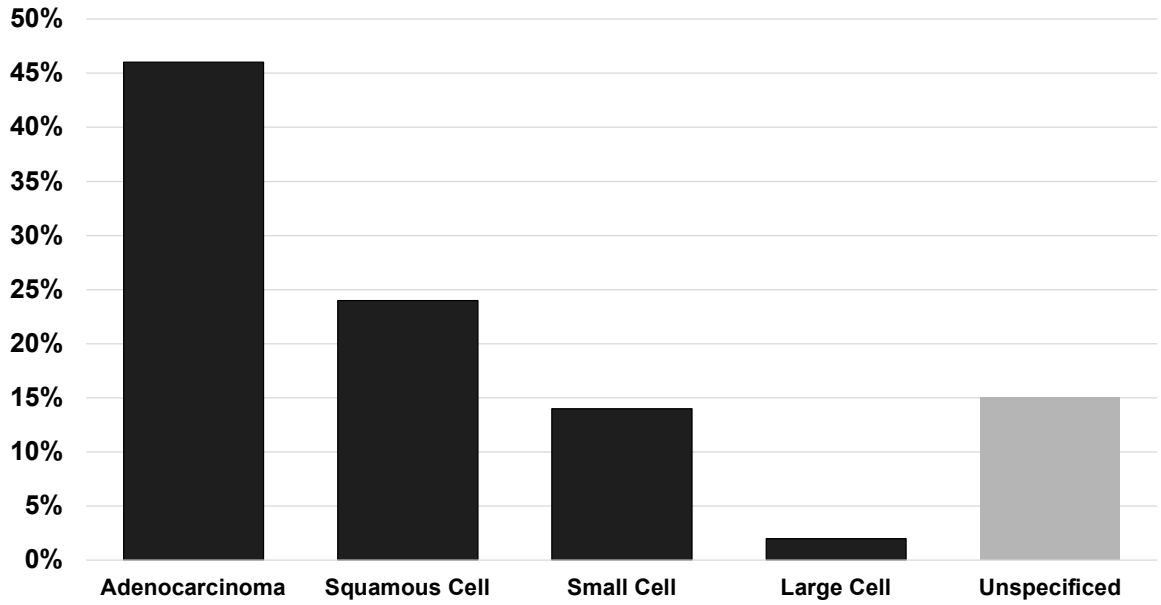
The Relation Between Asbestos and Lung Cancer



Environmental Tobacco Smoke Causes Lung Cancer



Histologic Types of Lung Cancer (U.S.)



Common presenting symptoms of lung cancer:

- Cough
- Hemoptysis
- Chest pain
- Hoarseness
- Dyspnea
- Malaise/anorexia

Clubbing

Making A Tissue Diagnosis:

	When Used	How Used
Sputum cytology	Rarely	Large central lesions
Bronchoscopy	Commonly	Lesions > 2 cm
CT-guided needle biopsy	Occasionally	Peripheral lesions
Thoracentesis	Occasionally	Pleural effusion
Endobronchial ultrasound	Occasionally	Large lymph nodes
Mediastinoscopy	Occasionally	Large lymph nodes
Thoracotomy/VATS	Commonly	Other tests indeterminate

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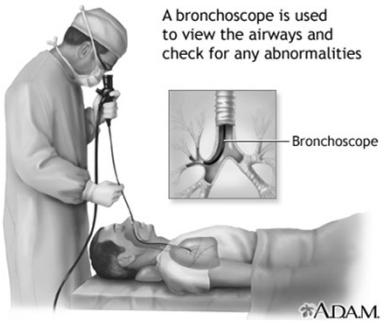
Bronchoscopy



Diagnostic Utility:

If endobronchial lesion visible: 94%

If peripheral nodule > 2 cm: 40-50%

If peripheral nodule < 2 cm: 10%

Image Courtesy of the National Library of Medicine

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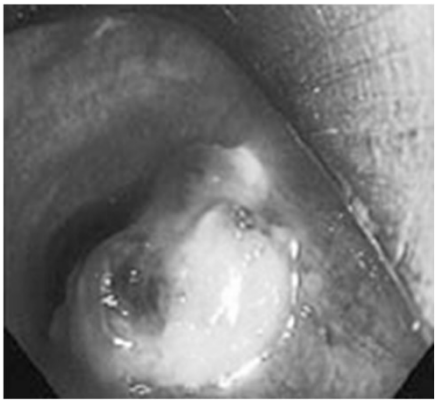
Case Bronchoscopic Findings



- Endobronchial tumor involving RML and RLL
- Biopsy = large cell undifferentiated lung cancer

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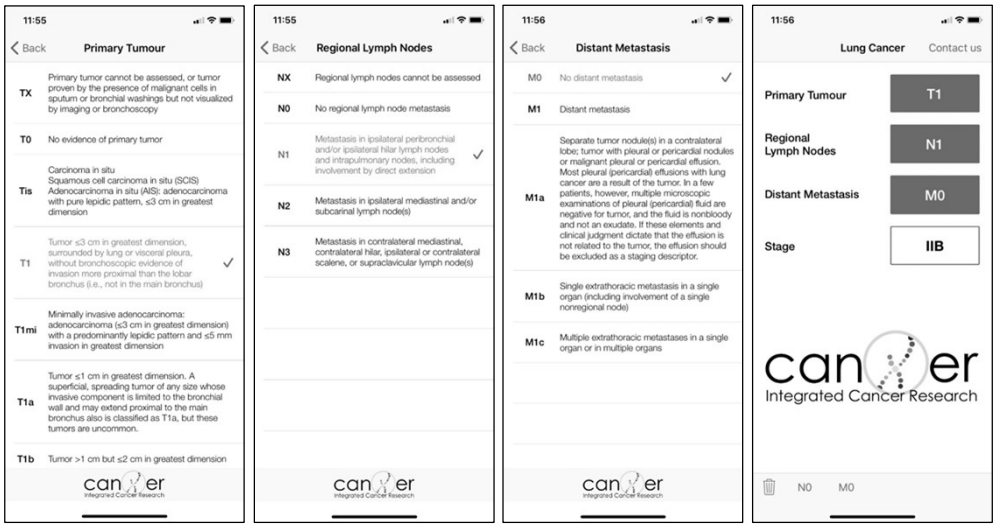
Staging System For Lung Cancer

- T = Tumor
  - 0-4; subcategorized as “a”, “b”, & “c”
  - based on size & location
- N = Nodes
  - 0-3
  - based on location of involved lymph nodes
- M = Metastases
  - 0-1; subcategorized as “a”, “b”, & “c”
  - Based on presence or absence of metastases

TNM Score Determines Stage

T/M	N0	N1	N2	N3
T1a	IA1	IIB	IIIA	IIIB
T1b	IA2	IIB	IIIA	IIIB
T1c	IA3	IIB	IIIA	IIIB
T2a	IB	IIB	IIIA	IIIB
T2b	IIA	IIB	IIIA	IIIB
T3	IIB	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC
M1a/b	IVA	IVA	IVA	IVA
M1c	IVB	IVB	IVB	IVB

But… There's an app for that



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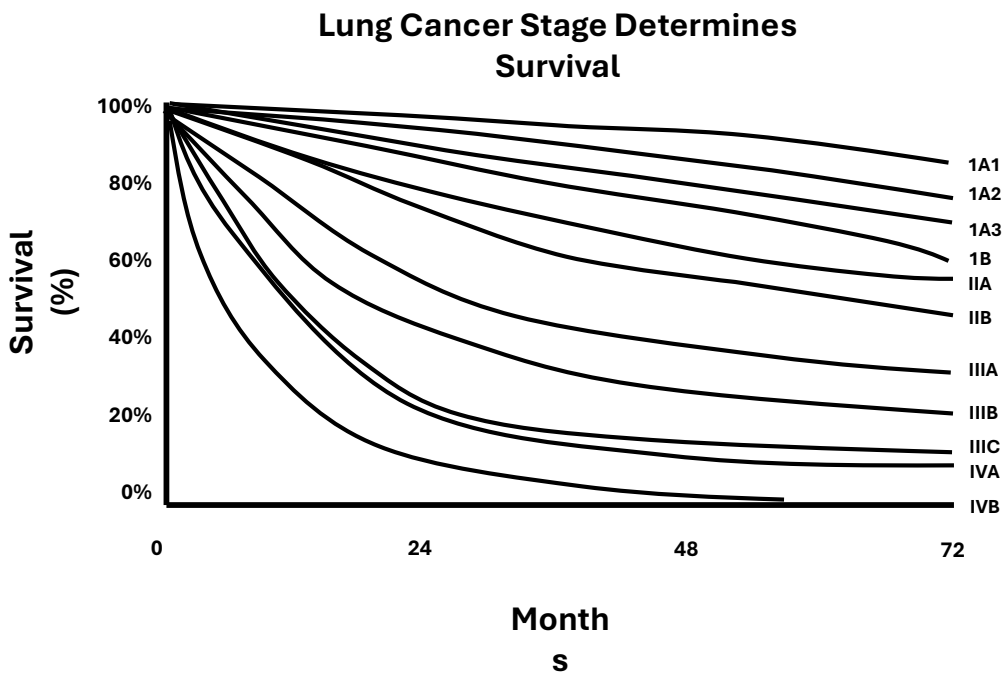

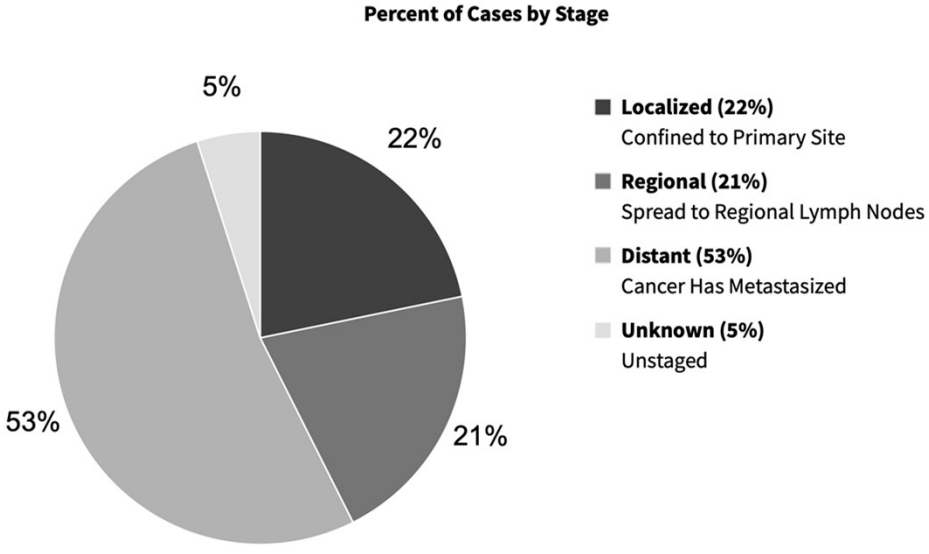

National Cancer Institute SEER data (2014-2020)

Staging approach for non-small cell lung cancer

- History & physical examination
- Labs: CBC, chemistry profile, calcium, liver enzymes
- Chest CT
- PET scan (in clinical stage IB, IIA, and IIB)
- Other imaging studies if metastases suspected
- Bronchoscopy with EBUS or mediastinoscopy if lymph nodes are large
- Biopsy abnormal sites if it will affect management

Chest CT

- Advantages:
  - Excellent determination of calcification patterns
  - Provides guide to bronchoscopy & mediastinoscopy
- Disadvantages:
  - Large number of false positive adrenal masses (approximately 2/3 of adrenal masses will be benign)
  - Large number of false positive lymph nodes

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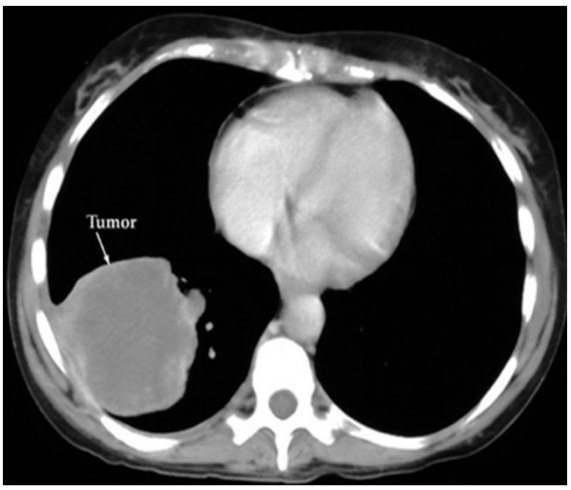
Case CT



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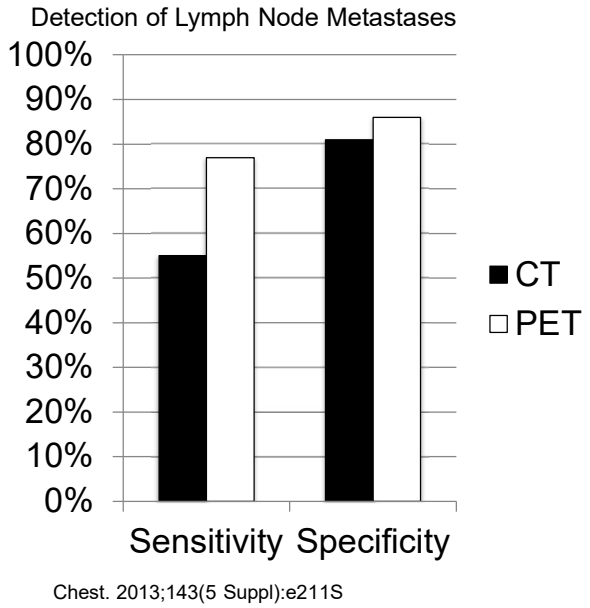
PET-CT Scans In Lung Cancer Staging



Chest. 2013;143(5 Suppl):e211S

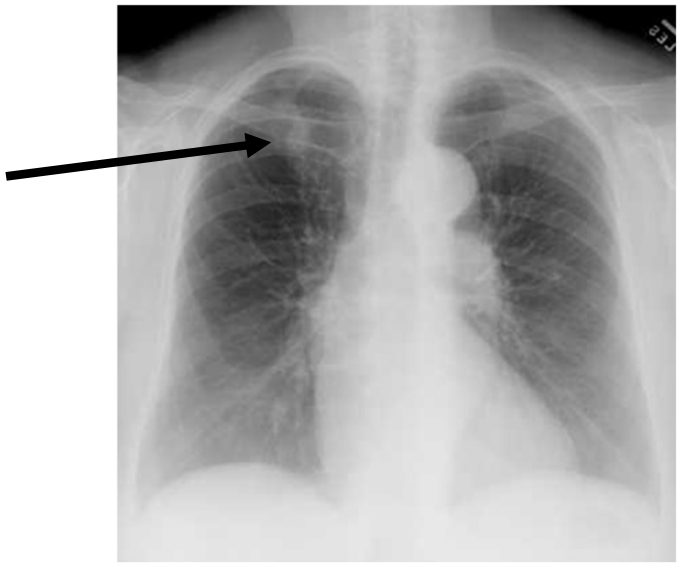
Disadvantages:

- Poor for "T" staging
- Poor for brain metastases
- False positives common

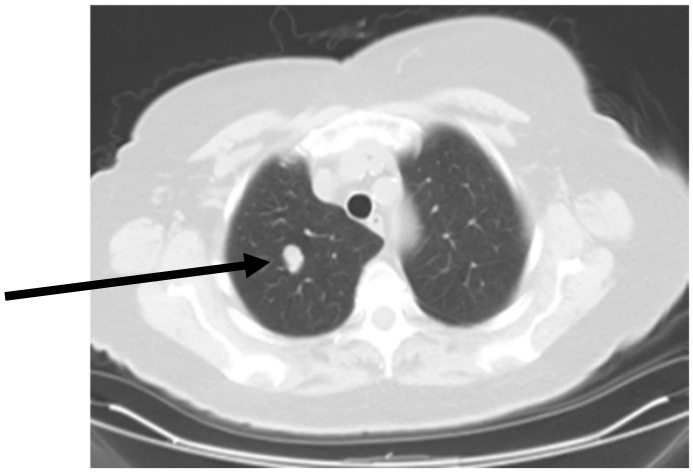
Advantages:

- Improved detection of mediastinal involvement
- Improved detection of distant metastases

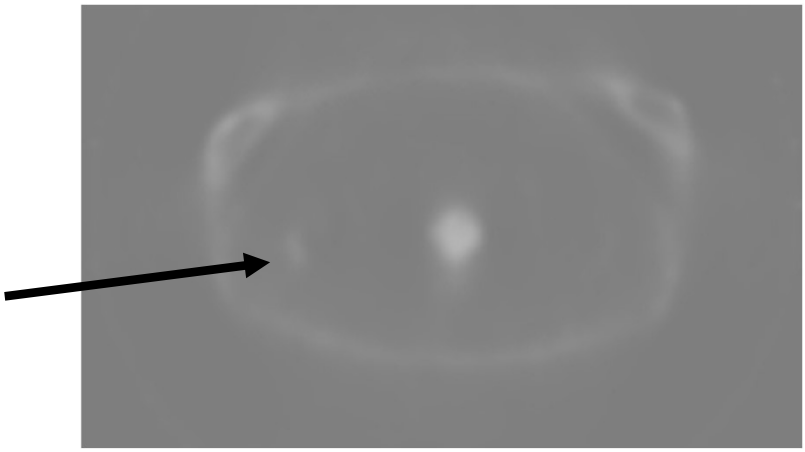
Chest X-Ray



Chest CT



PET Scan



PET CT

Endobronchial Ultrasound (EBUS)

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Mediastinoscopy

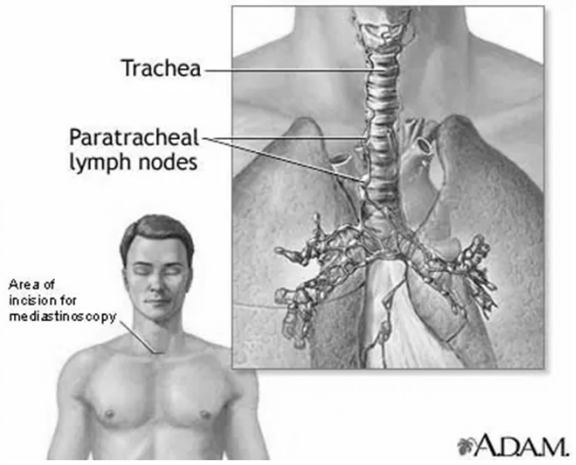

Image Courtesy of the National Library of Medicine

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Non-Small Cell Lung Cancer Treatment

Stage Ia Surgery

Stage Ib Surgery (with *possible* adjuvant chemotherapy, immunotherapy, and/or osimertinib*)

Stage II Surgery + adjuvant chemotherapy, immunotherapy, and/or osimertinib*

Stage III Chemotherapy ± radiation therapy followed by immunotherapy

Possible late surgery

Stage IV Chemotherapy ± Immunotherapy or driver-directed treatment

*Adjuvant chemotherapy = cisplatin + second drug
Immunotherapy if PD-L1 ≥ 1%
Osimertinib if tumor is EGFR positive

Pre-op evaluation*

- PFTs: FEV1 & DLCO > 80% desirable
- If FEV1 and/or DLCO are < 80%
  - The predicted post-operative FEV1 and DLCO should be calculated, typically using quantitative ventilation/perfusions scans
  - A low tech exercise test (ability to walk up 5 flights of stairs) or high tech exercise test (cardiopulmonary exercise test) should be performed.
- ABG: PCO2 < 45 desirable (?)

*Never Miss An Opportunity To Refer A Surgically Curable Patient For Surgery!

Cardiopulmonary Exercise Testing For The Patient With A Marginal FEV1:

- mVO2 > 20 ml/kg/min
  - Surgery
- mVO2 < 10 ml/kg/min:
  - Surgery is too high risk
- mVO2 10-20 ml/kg/min:
  - *Possible* surgery
  - Consider pulmonary rehabilitation first

Case Outcome:

- Stage IIB
- Pre-op FEV1 = 2.74 liters (70% of predicted)
- Predicted post-op FEV1 = 50% of predicted
- Able to easily walk up 5 flights of stairs
- ABG: PCO2 = 40 (normal)
- Underwent right middle and lower lobe resection
- Cancer free 30 years later

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Small Cell Lung Cancer

Limited Stage:

- 30% of patients
- Average survival = 17 months
- Treatment:
  - Stage I: surgery plus chemotherapy
  - Stage II & III: radiation plus chemotherapy
  - Prophylactic cranial radiation recommended
- Cure rate = 20%

Extensive Stage:

- 70% of patients
- Average survival = 12 months
- Treatment: chemotherapy ± immunotherapy
- Cure rate = 1 – 2%

Small cell lung cancer is essentially never curable by surgery alone!!!

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Staging approach to small cell lung cancer*

- Chest CT
- Abdominal CT
- Pelvic CT
- Lab tests
- Brain MRI (or head CT)
- PET scan

*Staging should not delay starting chemotherapy and is mainly to determine whether radiation should be given (limited stage)

Inoperable ≠ Untreatable

Medical Treatment of Advanced Non-Small Cell Lung Cancer in 2025

- Driver mutations can guide treatment:
  - EGFR (+) --- EGFR tyrosine kinase inhibitors such as osimertinib
  - ALK (+) --- ALK tyrosine kinase inhibitors such as alectinib
  - BRAF (+) – BRAF/MEK inhibitors such as dabrafenib and trametinib
  - ROS1 (+) – ROS1 inhibitor crizotinib
  - Others: MET, RET, NTRK, KRAS

Medical Treatment of Advanced Non-Small Cell Lung Cancer in 2025 (continued)

- If PD-L1 (programmed death receptor-ligand 1) high (> 50%), immunotherapy with *possible* chemotherapy*:
  - Pembrolizumab – monoclonal antibody against programmed death receptor-1 (PD-1); aka checkpoint inhibitor
- If PD-L1 low (< 50%) or negative, immunotherapy with chemotherapy:
  - Chemotherapy* + pembrolizumab)

*Chemotherapy is typically a platinum drug plus a second drug

In 10 years, the preferred treatments for advanced non-small cell lung cancer will have changed… a lot

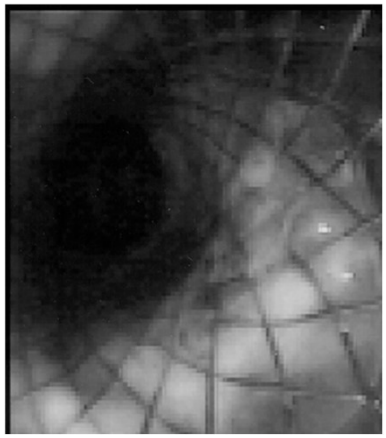
Tomorrow's Patients Will Owe Their Lives To Today's Patients In Clinical Trials

Palliation of Lung Cancer

- External beam radiation
- Brachytherapy
- Cryotherapy
- Argon plasma coagulation
- Stents
- Photodynamic therapy
- Laser
- Pleurodesis

68 Year Old Man With Tracheal Squamous Cell Carcinoma

Trachea Pre-Stent



Trachea Post-Stent

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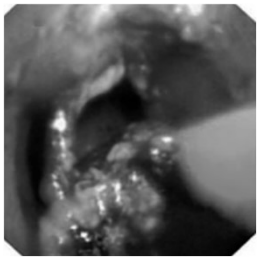
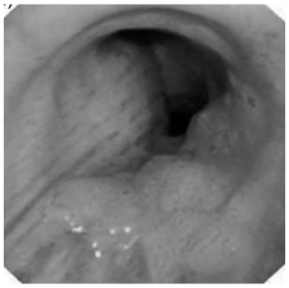
Argon Plasma Coagulation





CC BY-NC 4.0: Wang Y, Li Y, Wang F, et al. J Inter Med Res 2021 49(9):1-9

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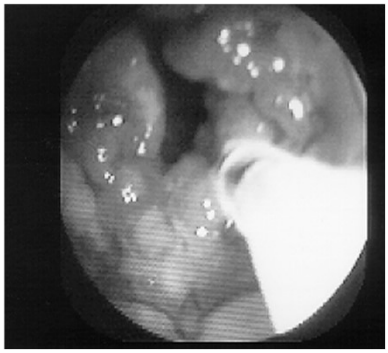
Cryotherapy

- Bronchoscopic probe placement
- Nitrous oxide
- Probe tip = -40° C



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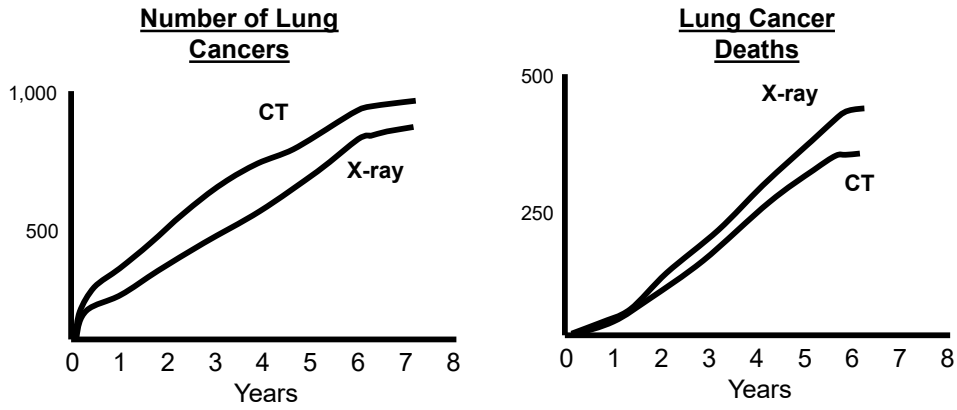
Screening Chest CT Scans For Lung Cancer



N = 53,454

N Engl J Med 2011. 365:395-409

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Results of screening chest CTs:

- Lung cancers found in earlier stages
- Overall, 20% reduction in mortality
- High false positive rate:
  - Overall 30% of CT scans were abnormal
  - A suspicious abnormality was 27 times more likely to be benign than malignant
- Screening CTs plus follow-up CTs are very expensive

Medicare Lung Cancer Screening Requirements:

- Age 50-80
- Asymptomatic
- More than 20 pack-year smoking history
- Current smoker or quit in the past 15 years
- Counseling session that includes risks/benefits of screening and includes smoking cessation counseling

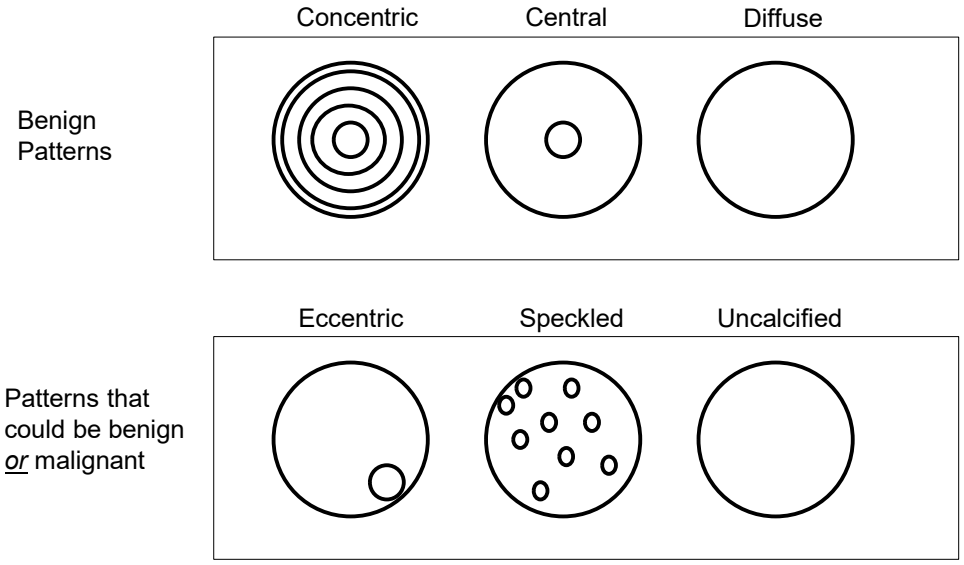
*Continue screening annually until > 15 years since quit smoking

What do you do about the incidentally identified solitary pulmonary nodule?

Indicators of benign pulmonary nodules

- Calcification patterns
- Age
- Smoking history
- Size
- History of cancer
- Radiographically stable over time

Calcification Patterns In Solitary Pulmonary Nodules



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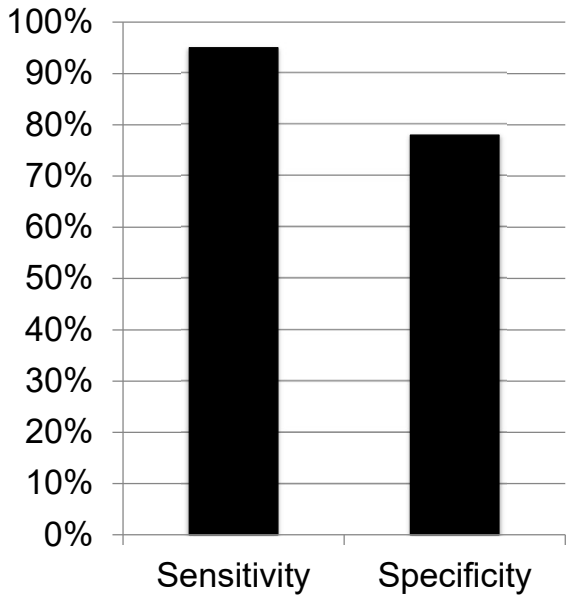
PET Scan And The Solitary Pulmonary Nodule

- False negatives in:
  - Well-differentiated adenocarcinomas
  - Carcinoid tumors
  - Hyperglycemia
  - Tumors < 8 mm
- False positives in:
  - Tuberculosis
  - Fungal infections
  - Sarcoidosis



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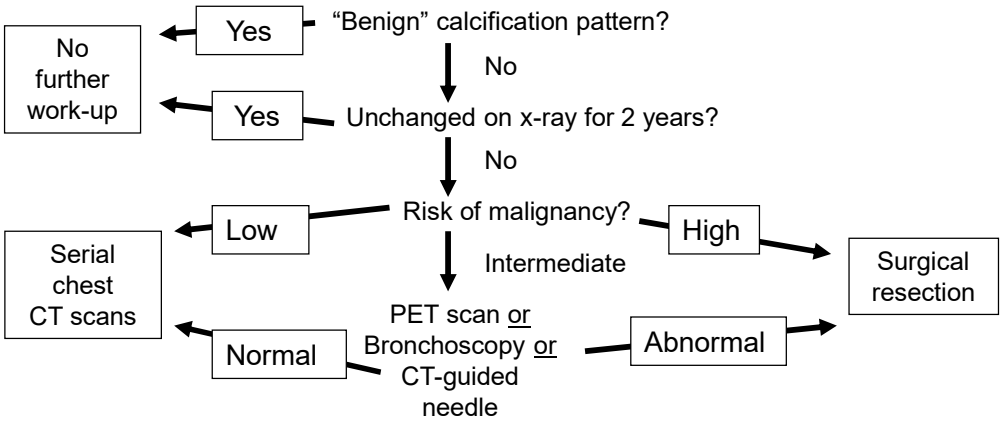
Clinical Approach To The Solitary Pulmonary Nodule



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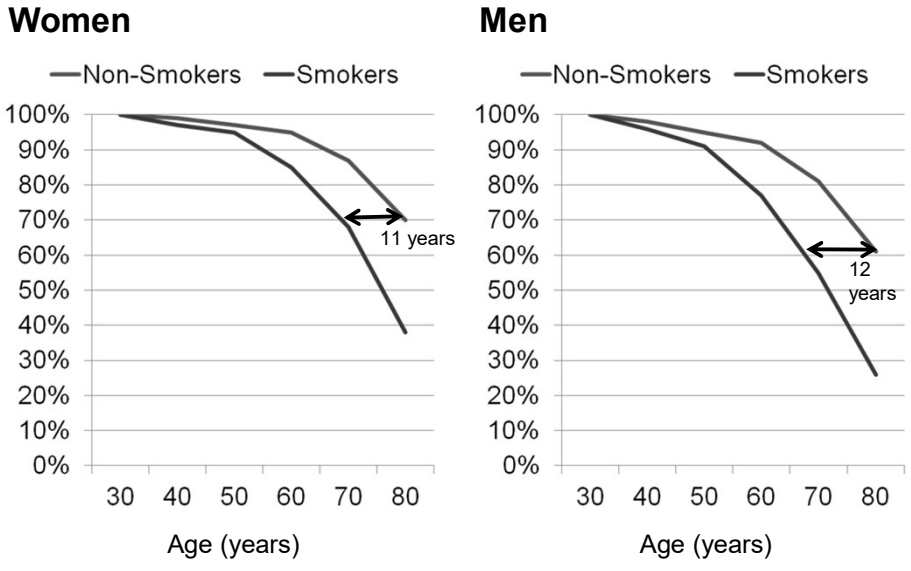
Life expectancy for smokers and non-smokers



N Engl J Med 2013; 368:341-50

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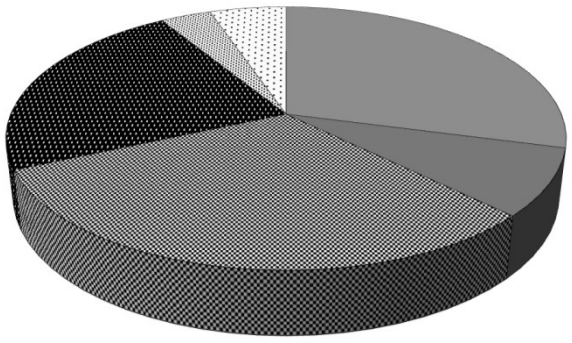
The average smoker loses 14 minutes of life for every cigarette smoked

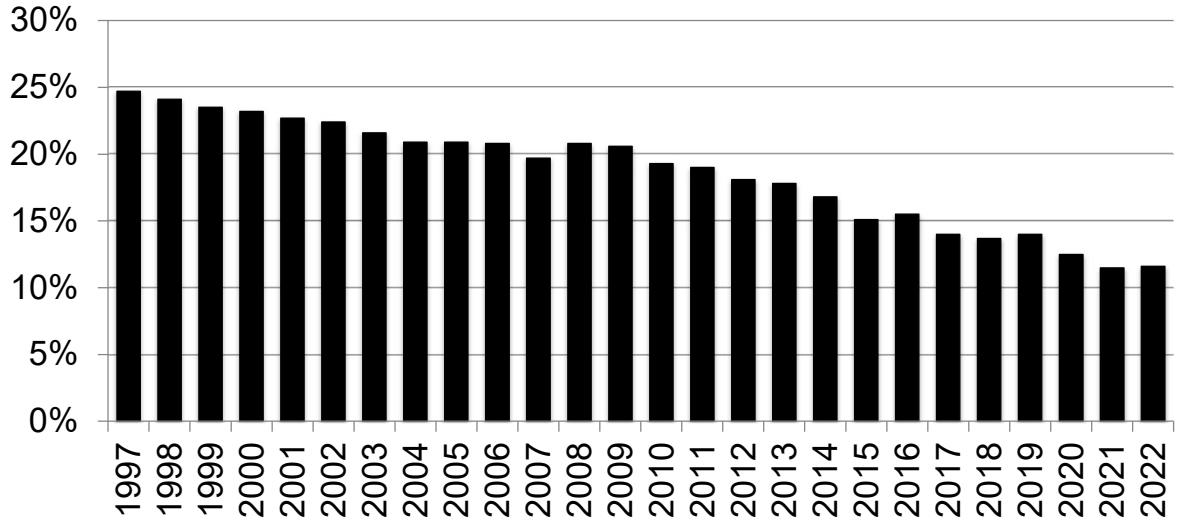
Cigarette smoking causes > 480,000 U.S. deaths per year*



1 out of 5 U.S. deaths are attributable to cigarette smoking

Data source: CDC

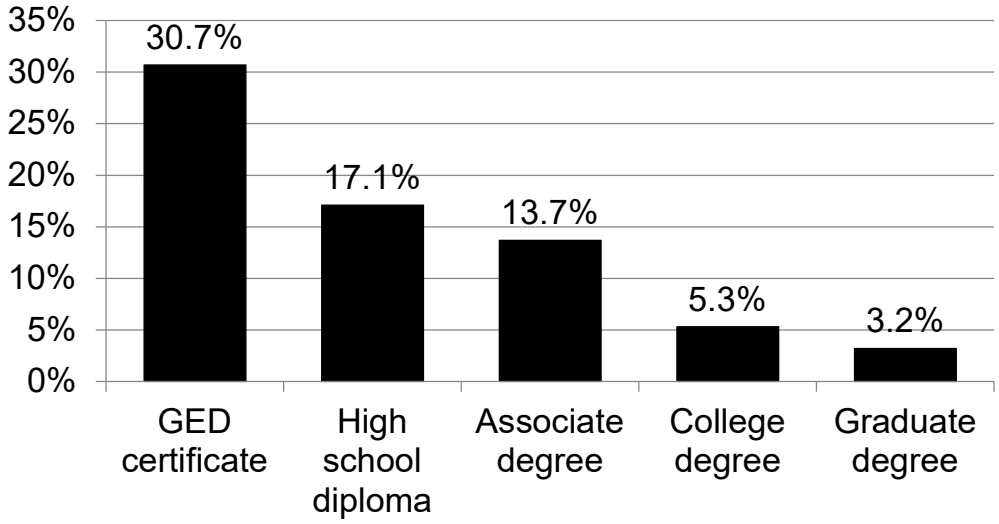
Prevalence of Adult Smokers In The U.S.



In 2022: Male adult smokers = 13.2%; Female adult smokers = 10.0%

Data: Centers for Disease Control 2025

Who Smokes In The United States?



Centers for Disease Control 2024

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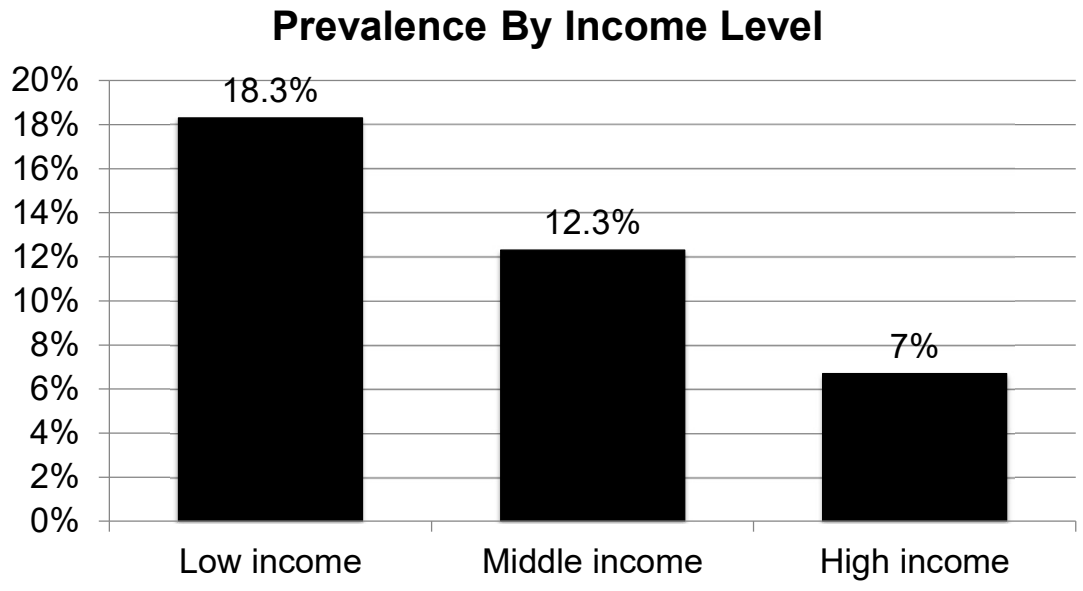

Centers for Disease Control 2024

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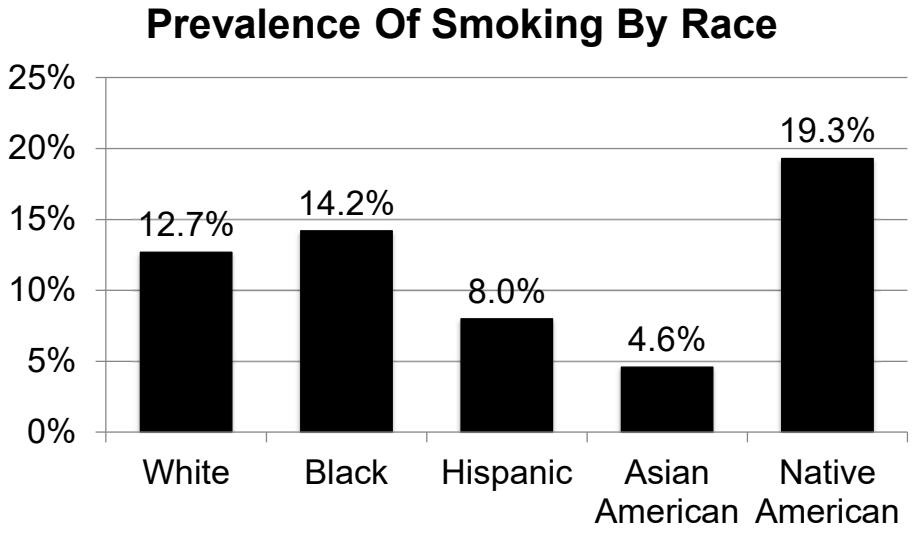

Centers for Disease Control 2025

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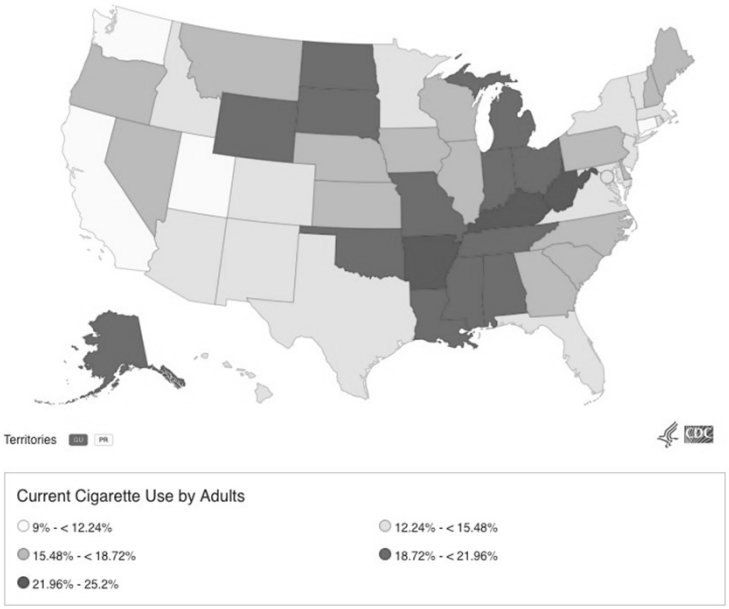
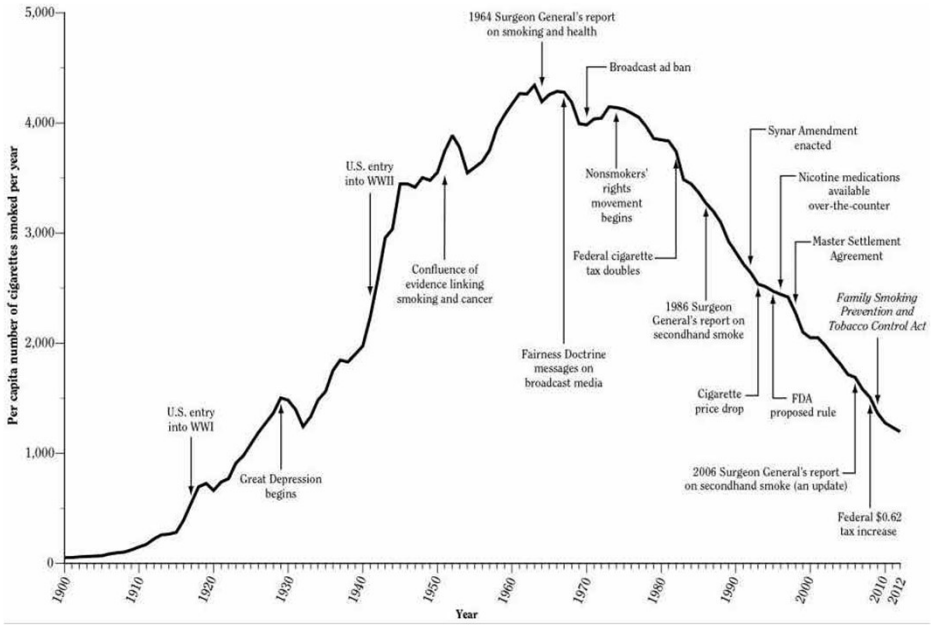


Source: CDC 2024

Who Smokes In The World?

Multiple sources compiled by World Bank (2021) – processed by Our World in Data

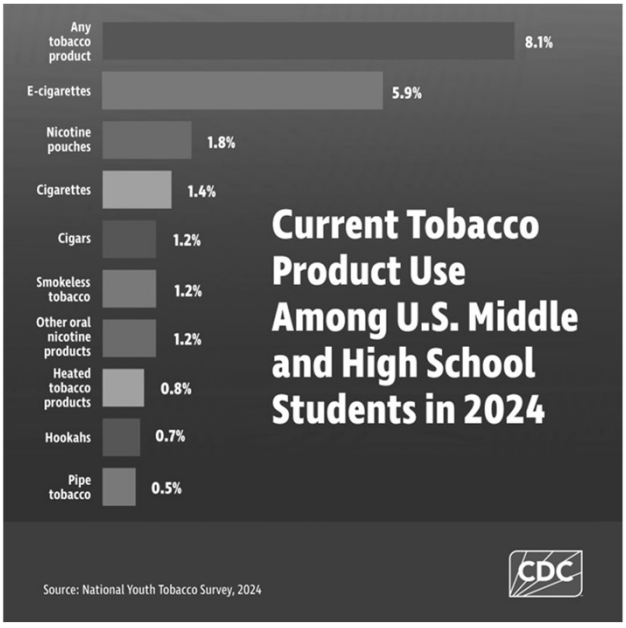


U.S. Surgeon General Report 2014

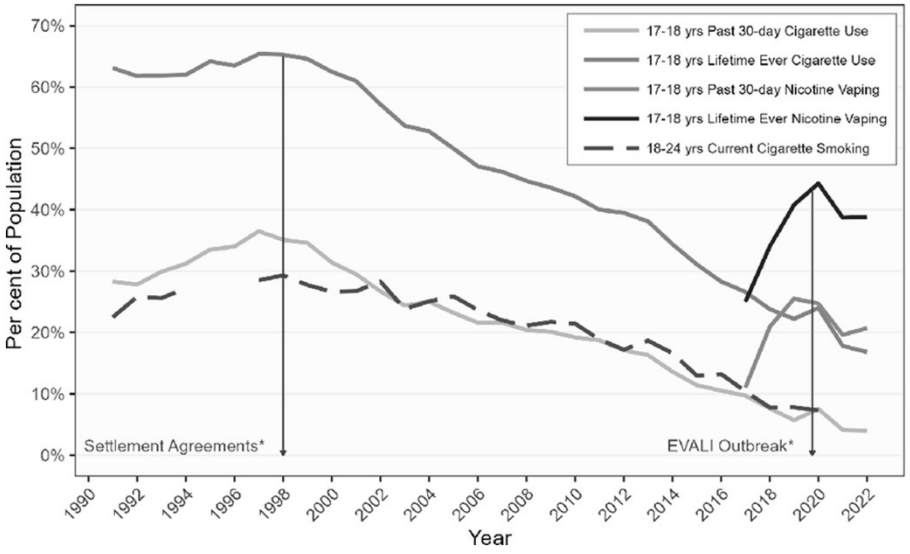
Smoking is a **childhood** epidemic

90% of smokers begin before age 18

10.1% of high school students and 5.4% of middle school students use tobacco products



30-Day Prevalence of Daily Use of Cigarettes and Nicotine Vapes 1990 - 2022



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Key Points About Lung Cancer

- Extremely high mortality rate
- Caused by cigarettes
- Screening chest CTs now recommended
- Stage dictates treatment and prognosis
  - Small cell - extensive/non-extensive
  - Non-small cell - TNM system

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