

# Lung Cancer

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# Disclosures

- None

# Objectives

- Lung cancer
  - Epidemiology
  - Lung Cancer Screening
  - Diagnostic Workup
  - Staging, treatment, and prognosis
  - Future of lung cancer treatment

# Epidemiology

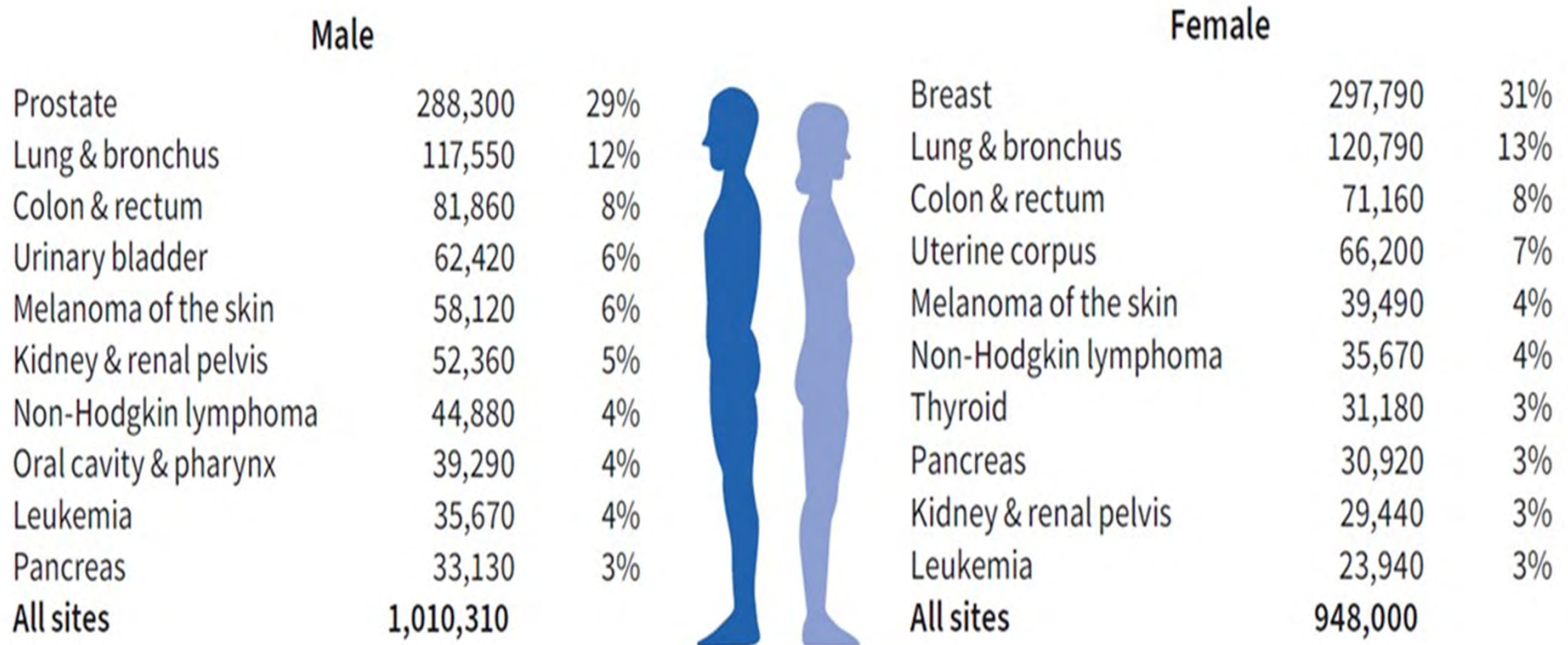
- 3rd most common cancer in US
- 236,740 new cases in 2022 in US
- More people in US will die from lung cancer than any other disease
- Incidence rising globally
- Avg age of diagnosis: 70
- African American Men are highest risk in US
- Most are non-small cell lung cancer (NSCLC) 82%

*Thandra KC et al Epidemiology of lung cancer. Contemp Oncol (Pozn). 2021;25(1):45-52. doi: 10.5114/wo.2021.103829. Epub 2021 Feb 23. PMID: 33911981; PMCID: PMC8063897.*

[U.S. Cancer Statistics: Lung Cancer Stat Bite | CDC](#)

# Epidemiology

## Estimated New Cancer Cases in the US in 2023



<https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2023-cancer-facts-figures.html>

# Epidemiology

## Estimated Cancer Deaths in the US in 2023

Male			Female		
Lung & bronchus	67,160	21%	Lung & bronchus	59,910	21%
Prostate	34,700	11%	Breast	43,170	15%
Colon & rectum	28,470	9%	Colon & rectum	24,080	8%
Pancreas	26,620	8%	Pancreas	23,930	8%
Liver & intrahepatic bile duct	19,000	6%	Ovary	13,270	5%
Leukemia	13,900	4%	Uterine corpus	13,030	5%
Esophagus	12,920	4%	Liver & intrahepatic bile duct	10,380	4%
Urinary bladder	12,160	4%	Leukemia	9,810	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,400	3%
Brain & other nervous system	11,020	3%	Brain & other nervous system	7,970	3%
<b>All sites</b>	<b>322,080</b>		<b>All sites</b>	<b>287,740</b>	



<https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2023-cancer-facts-figures.html>

# Epidemiology

## Trends in Five-year Relative Survival Rates (%), US, 1975–2018

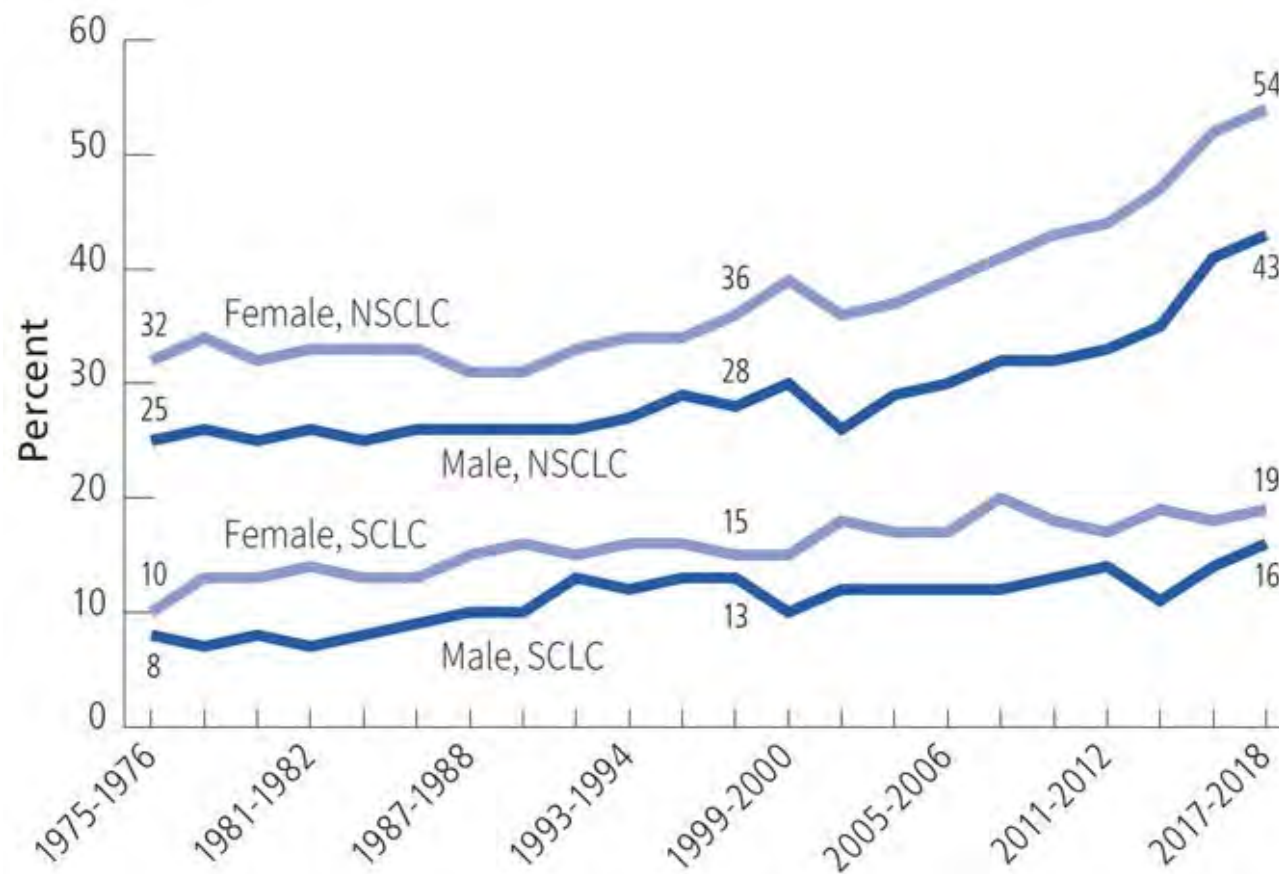
	1975-77	1995-97	2012-18
All sites	49	63	68
Breast (female)	75	87	91
Colon & rectum	50	61	65
Leukemia	34	48	66
Lung & bronchus	12	15	23
Melanoma of the skin	82	91	94
Non-Hodgkin lymphoma	47	56	74
Ovary	36	43	50
Pancreas	3	4	12
Prostate	68	97	97
Urinary bladder	72	80	77
Uterine cervix	69	73	67
Uterine corpus	87	84	81

<https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2023-cancer-facts-figures.html>

# Epidemiology

## Special Section: Lung Cancer

### Trends in 2-year Relative Survival Rates for Lung Cancer by Sex and Subtype, US, 1975-2018



<https://www.cancer.org/research/cancer-facts-statistics/all-cancer-facts-figures/2023-cancer-facts-figures.html>



# Lung Cancer Risk Factors

Smoking

Second Hand  
Exposure

Occupational

Age

Radon

Air pollution

Family  
History

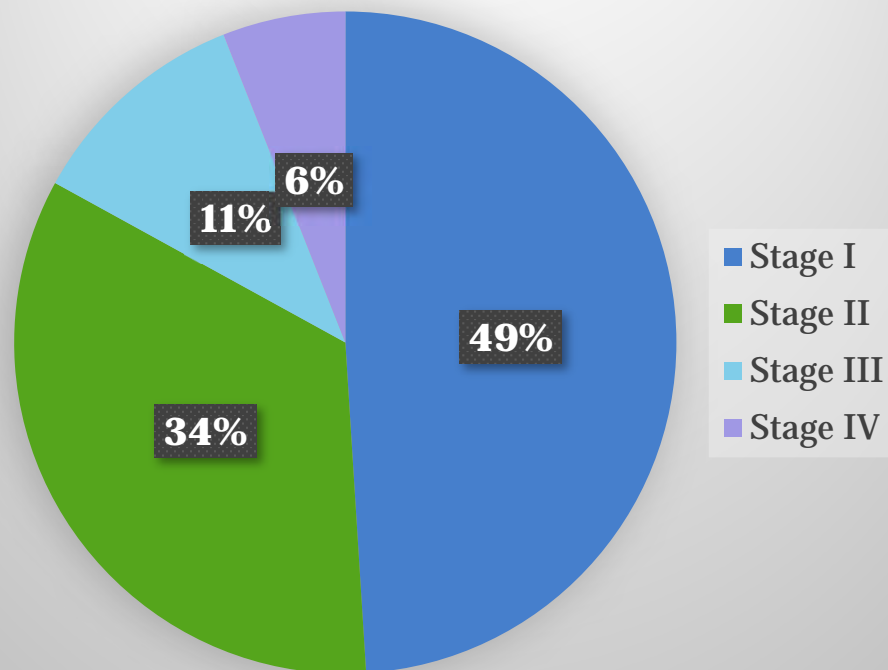
Asbestos

Infection

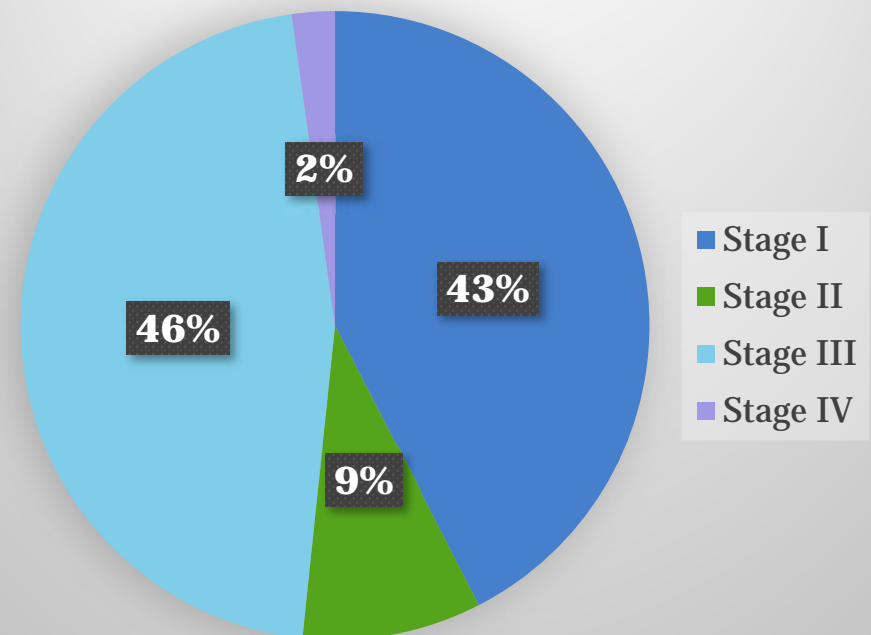
Thandra KC ,Barsouk A ,Saginala K ,Aluru JS ,Barsouk A .Epidemiology of lung cancer. Contemp Oncol (Pozn). 2021 25 (1 ):45-52 .doi: 10.5114/woc.2021.103829 .Epub 2021 Feb 23 .PM ID : 33911981 ;PMCID :PMC8063897 .

# Screening: WHY?

## Breast Cancer



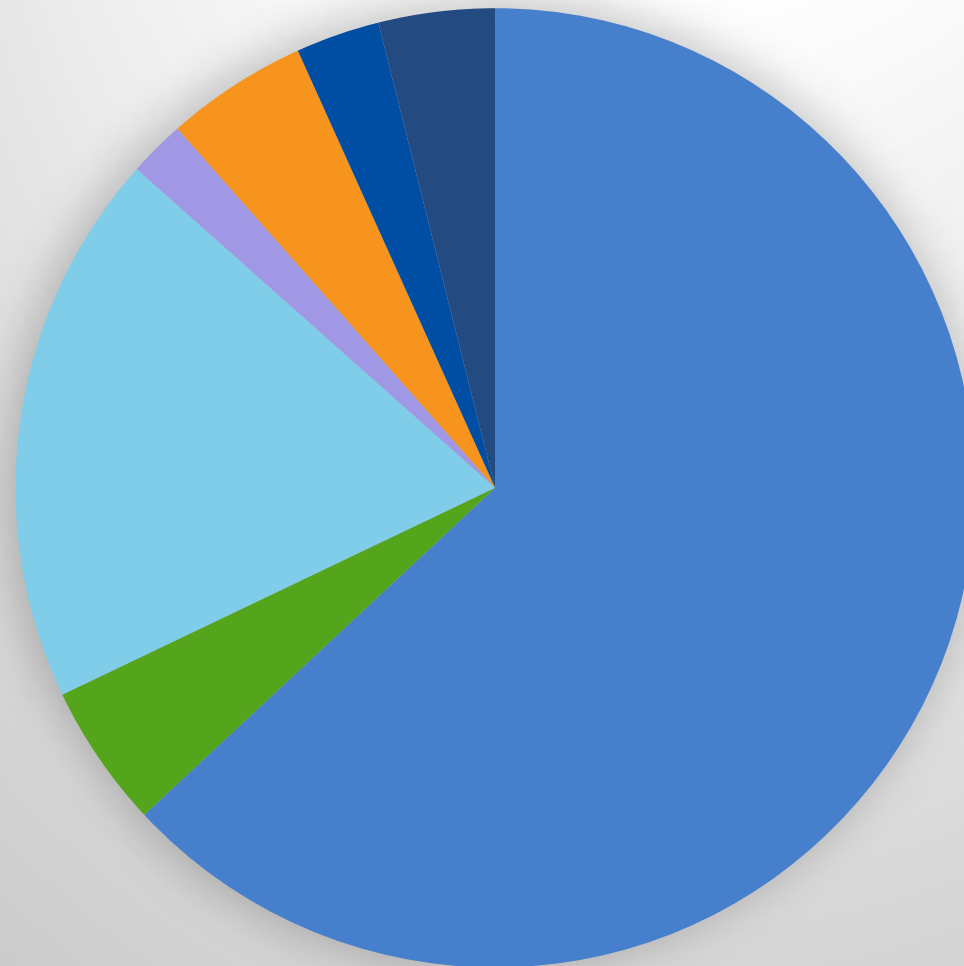
## Lung Cancer



Cronin KA et al Annual Report to the Nation on the Status of Cancer, part I: National cancer statistics. Cancer. 2018 Jul 1;124(13):2785-2800. doi: 10.1002/cncr.31551. Epub 2018 May 22. PMID: 29786848; PMCID: PMC6033186.

# Multiple Randomized Trials

## Trials



- NLST (53454)
- DLCST (4104)
- NELSON (15822)
- ITALUNG (1613)
- LUSI (4052)
- DANTE (2400)
- LSS (3318)

# National Lung Screening Trial

*The* **NEW ENGLAND**  
**JOURNAL** *of* **MEDICINE**

ESTABLISHED IN 1812

AUGUST 4, 2011

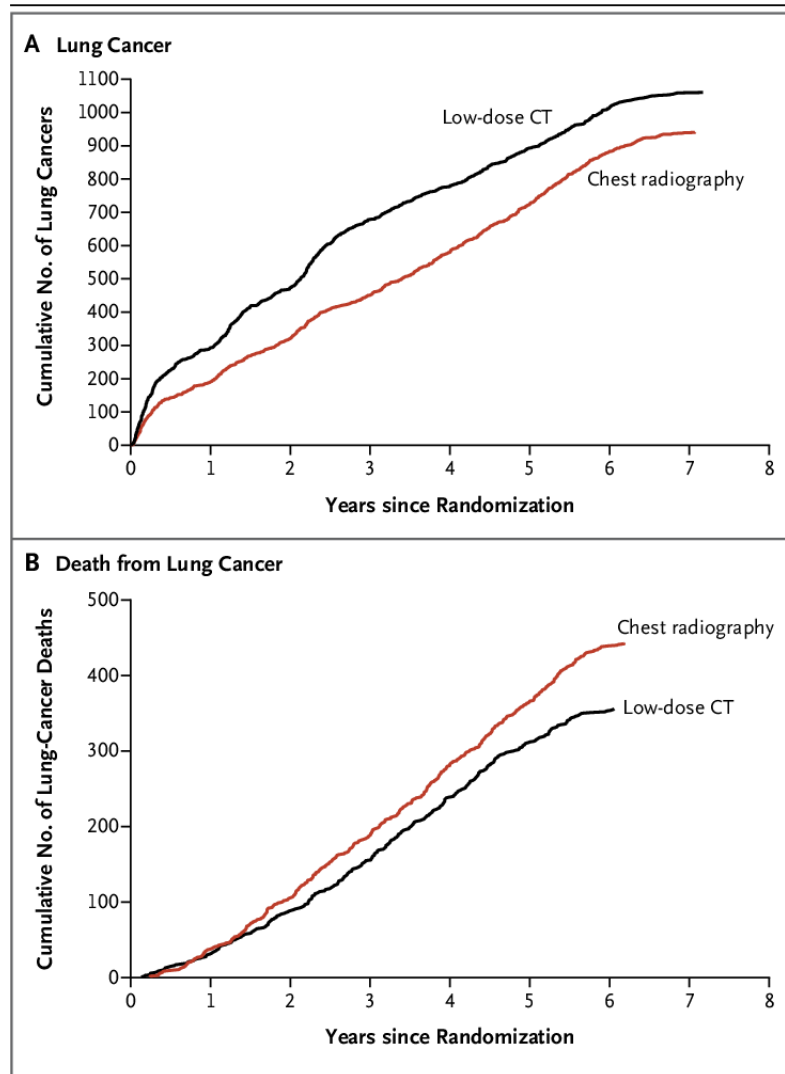
VOL. 365 NO. 5

Reduced Lung-Cancer Mortality with Low-Dose Computed  
Tomographic Screening

The National Lung Screening Trial Research Team\*

- U.S. multicentered (33) RCT 2002-2007 (NLST)
- N=53,454
- Age 55-74
- $\geq 30$  pk-yr, or quit past 15y  
→ CXR or low-dose CT
- Relative reduction in mortality in the CT screening group by 20%

# NLST



# NELSON trial

*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

FEBRUARY 6, 2020

VOL. 382 NO. 6

## Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial

H.J. de Koning, C.M. van der Aalst, P.A. de Jong, E.T. Scholten, K. Nackaerts, M.A. Heuvelmans, J.-W.J. Lammers, C. Weenink, U. Yousaf-Khan, N. Horeweg, S. van 't Westeinde, M. Prokop, W.P. Mali, F.A.A. Mohamed Hoesein, P.M.A. van Ooijen, J.G.J.V. Aerts, M.A. den Bakker, E. Thunnissen, J. Verschakelen, R. Vliegthart, J.E. Walter, K. ten Haaf, H.J.M. Groen, and M. Oudkerk

- Dutch-Belgian RCT 2004-2006 (NELSON trial)
- N=15,792
- Age 50-74
- $\geq 30$  pk-yr, or quit past 10y  
→ CT or no CT
- Relative reduction in mortality in the CT screening group by 26%

# Lung Cancer Screening Guidelines

## Screening for Lung Cancer CHEST Guideline and Expert Panel Report



*Peter J. Mazzone, MD, MPH, FCCP; Gerard A. Silvestri, MD, FCCP; Sheena Patel, MPH;  
Jeffrey P. Kanne, MD, FCCP; Linda S. Kinsinger, MD; Renda Soylemez Wiener, MD, MPH;  
Guy Soo Hoo, MD, FCCP; and Frank C. Detterbeck, MD, FCCP*

### **CT Chest w/o contrast, annual**

- 1. Age 55-77, and**
- 2.  $\geq 30$  pk-yr smoking history**
- 3. If not currently smoking, quit in the past 15yrs**

# Lung Cancer Screening Guidelines



Final Recommendation Statement

## Lung Cancer: Screening

March 09, 2021

*Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.*





# Lung Cancer Screening Guidelines



Trials	
NLST (2011)	55-74, 30pkyr/quit<15y
NELSON trial (2020)	50-74, 30pkyr/quit<10y



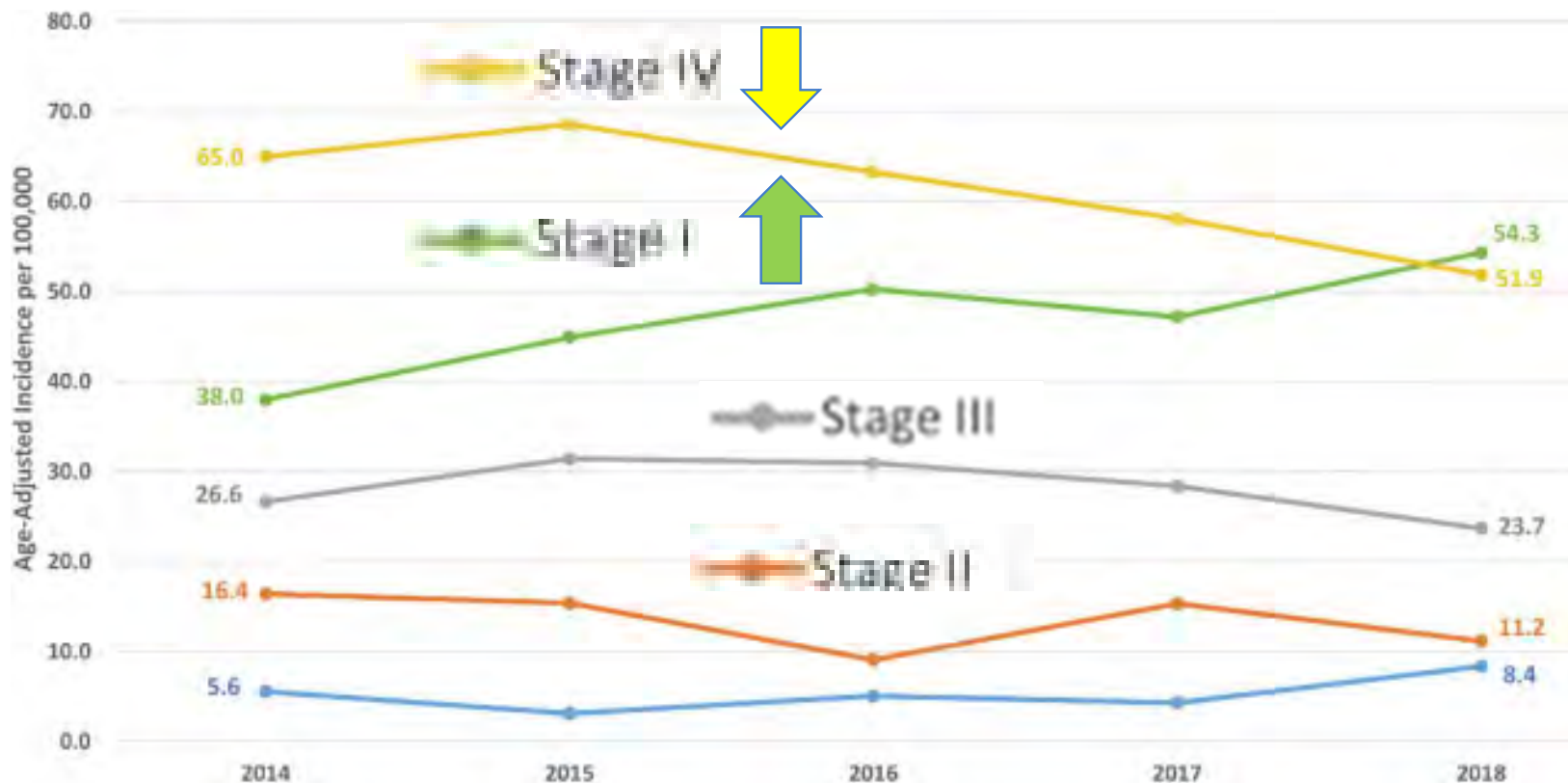
Guidelines	
USPSTF (2014)	55-80, 30pkyr/quit <15y
CHEST (2018)	55-77, 30pkyr/quit<15y
<b>USPSTF (2021)</b>	<b>50-80, 20pkyr/quit&lt;15y</b>



# Stage Migration and Lung Cancer Incidence After Initiation of Low-Dose Computed Tomography Screening

<sup>a</sup>Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania  
<sup>b</sup>Institute for Health Research, Kaiser Permanente Colorado, Aurora, Colorado  
<sup>c</sup>Henry Ford Health System and Henry Ford Cancer Institute, Detroit, Michigan  
<sup>d</sup>Center for Integrated Healthcare Research, Kaiser Permanente Hawaii, Oahu, Hawaii  
<sup>e</sup>Marshfield Clinic Research Institute, Marshfield, Wisconsin

Anil Vachani, MD, MS,<sup>a,\*</sup> Nikki M. Carroll, MS,<sup>b</sup> Michael J. Simoff, MD,<sup>c</sup> Christine Neslund-Dudas, PhD,<sup>c</sup> Stacey Honda, MD, PhD,<sup>d</sup> Robert T. Greenlee, PhD, MPH,<sup>e</sup> Katharine A. Rendle, PhD, MSW, MPH,<sup>a</sup> Andrea Burnett-Hartman, PhD,<sup>b</sup> Debra P. Ritzwoller, PhD<sup>b</sup>



# Who Screens?

## Editorials: *Controversies in Family Medicine*

### Should Family Physicians Routinely Screen for Lung Cancer in High-Risk Populations?

► See related U.S. Preventive Services Task Force Recommendation Statement at <http://www.aafp.org/afp/2014/0715/od1.html>, Putting Prevention into Practice on page 117, and POEM on page 112.

#### No: The USPSTF's Recommendation for Lung Cancer Screening Is Overreaching

DEAN A. SEEHUSEN, MD, MPH, *Fort Belvoir Community Hospital, Fort Belvoir, Virginia*

The U.S. Preventive Services Task Force (USPSTF) was premature in issuing a level B recommendation for annual computed tomography (CT)-based lung cancer screening.<sup>1</sup> This relatively aggressive stance is surprising because the USPSTF typically issues very measured recommendations when questions remain. There is still considerable uncertainty about the true magnitude of benefit, as well as the financial costs; therefore, the scope of recommendation should be limited to



This is one in a series of pro/con editorials discussing controversial issues in family medicine.

► See related editorial at <http://www.aafp.org/afp/2014/0715/od2.html>.

clinically, whereas the USPSTF recommendations extend annual screening beyond the initial three years. Additional annual screening will detect more cancers, but will result in many more false-positive results.

The sum of these key differences is that the results of annual CT-based lung cancer screening will differ from the findings in the NLST. The magnitude of differences in patient characteristics, the sensitivity of

#### Risks of Screening:

1. False Positive – suspicious lesion that is found to be benign
2. Radiation
3. Incidental Findings – Identifying other lesions in area of chest eg: thyroid nodule
4. Downstream results of scan

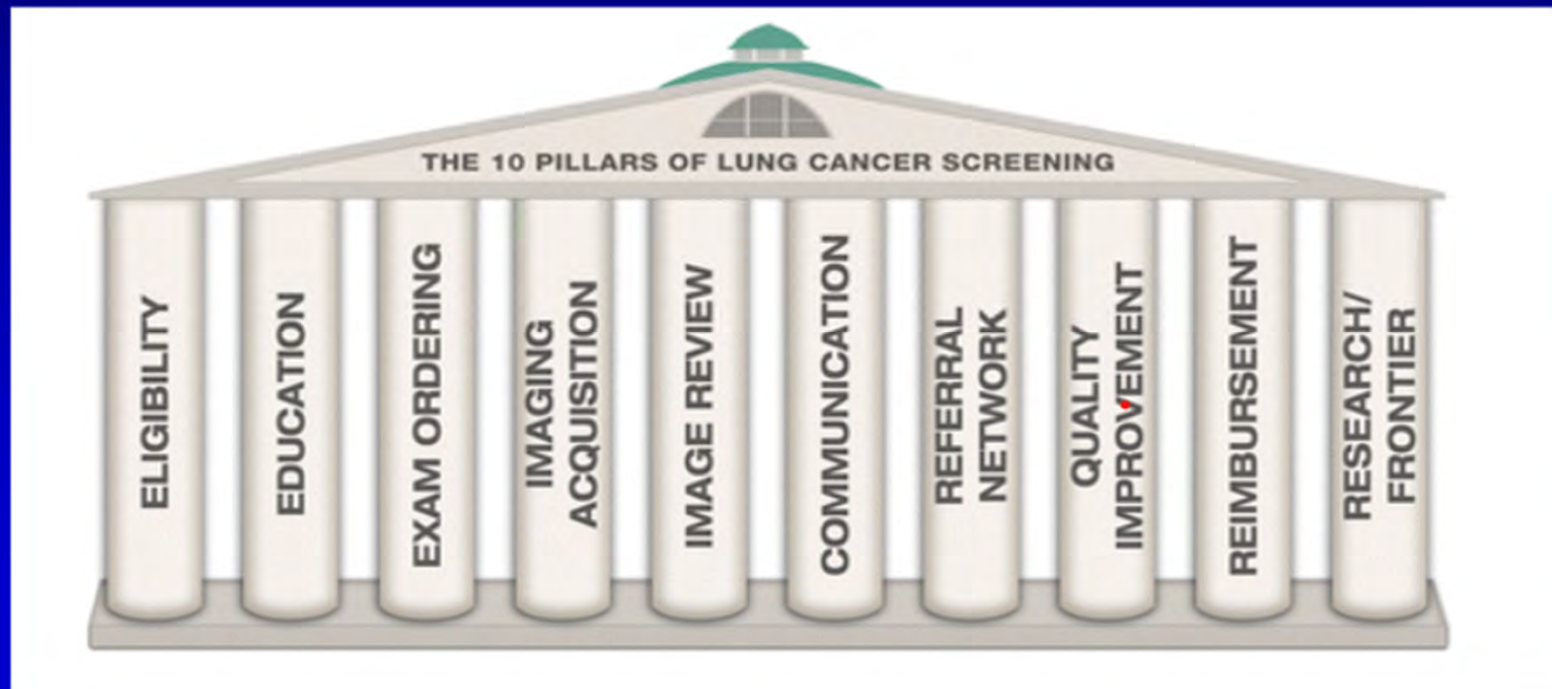


# Lung Cancer Screening Program

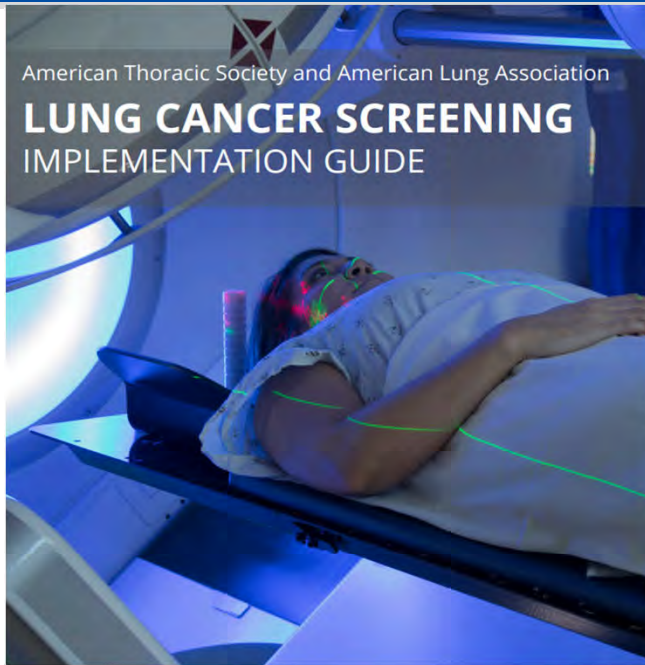
“Lung cancer screening is not solely an imaging test; it is a process that should take place within an organized system.”

*Peter Mazzone, MD, MPH, FCCP; Charles A. Powell, MD; Douglas Arenberg, MD, FCCP; Peter Bach, MD; Frank Detterbeck, MD, FCCP; Michael K. Gould, MD, FCCP; Michael T. Jaklitsch, MD; James Jett, MD, FCCP; David Naidich, MD, FCCP; Anil Vachani, MD; Renda Soylemez Wiener, MD; and Gerard Silvestri, MD, FCCP*

[ 147#2 CHEST FEBRUARY 2015 ]



# Resources



American Thoracic Society and American Lung Association  
**LUNG CANCER SCREENING IMPLEMENTATION GUIDE**

## LUNG CANCER SCREENING PROGRAM RISK ASSESSMENT TOOL

If all three apply to you:

- Between the ages of 55 and 80\*
- Smoking at least a pack a day for at least 30 years or two packs a day for 15 years
- Still smoking or stopped within 15 years

**High Risk**  
 Talk to your doctor about Low Dose screening Chest CT.

Checked two of the above, plus one or more of the following:

- Exposure to radon
- Exposure to asbestos or other cancer causing agents such as arsenic, beryllium, cadmium, chromium, nickel, coal smoke, soot, silica or diesel fumes
- History of other cancers
- Family members who have had lung cancer
- Personal history of lung disease
- Second hand smoke exposure

**Intermediate Risk**  
 Talk to your doctor to see if screening may be appropriate.

If you have checked fewer than three of the above...

**Low Risk**  
 Any questions, talk to your doctor.



16	Asian (0=No; 1=Yes)	0	-0.394478	0.7434744		
17	Native Hawaiian/Pacific Islander (0=No; 1=Yes)	0	-0.466595	0		
18	American Indian/Alaskan Native (0=No; 1=Yes)	0	1.027852			
19	Smoking status: 0 = Former-smoker 1 = Current-smoker	1	0.2597431			
20	Average number of cigarettes smoked per day**	10	0.597845839	-1.822606	-1.089637413	nonlinear
21	Duration smoked (years)	48	0.0317321	0.6663741	1.03	
22	Years ago quit smoking. Enter zero for current smokers	0	-0.0308572	0.308572	0.97	
23	Model constant		-4.532506			
24				-2.81624713		
25				E <sup>xP1+bx</sup>	0.0598	
26						
27						
28						
	<b>Probability of lung cancer in 6 years =</b>	<b>0.05642</b>				

\* U.S. Preventive Services Task Force (USPSTF).  
 Screening for lung cancer: U.S. Preventive Services Task Force recommendation statement. Ann Intern Med. 2014 Mar 4;160(5):330-9

[www.LungCancerInitiativeNC.org](http://www.LungCancerInitiativeNC.org)

## Calculate my lung cancer risk (shouldiscreen.com)

### Lung Cancer Screening: Should I do it?



Given your age and smoking history, you are **eligible** for screening according to the US Preventive Services Task Force criteria.



The chance of you developing lung cancer in the next 6 years is 2.2%. Talk to your doctor about the option to screen or not to screen as they will understand your situation best.

Your lung cancer risk: 2.2 %

< 1% low risk  
 1-2% intermediate risk  
 > 2% high risk



## CODES FOR LUNG CANCER SCREENING



### REIMBURSEMENT CODES

HCPCS CODE	DESCRIPTION
G0296	Provider shared decision-making discussion about lung cancer screening
G0297	Lung cancer screening with low-dose CT (LDCT)

### CODES TO DOCUMENT PATIENT ELIGIBILITY\*

ICD-10 CODE	DESCRIPTION
Z87.891	Former smokers (personal history of nicotine dependence)
F17.210	Nicotine dependence, cigarettes, uncomplicated
F17.211	Nicotine dependence, cigarettes, in remission
F17.213	Nicotine dependence, cigarettes, with withdrawal
F17.218	Nicotine dependence, cigarettes, with other nicotine-induced disorders
F17.219	Nicotine dependence, cigarettes, with unspecified nicotine-induced disorders

\*These are the ICD-10 codes required by CMS for Medicare beneficiaries. Some commercial payer coding requirements to document patient eligibility may differ.

### QUESTIONS?

Contact the GO2 Foundation for Lung Cancer at [screening@go2foundation.org](mailto:screening@go2foundation.org).

Contact Angela Criswell (GO2 Foundation, formerly Lung Cancer Alliance) at 202-774-5389.

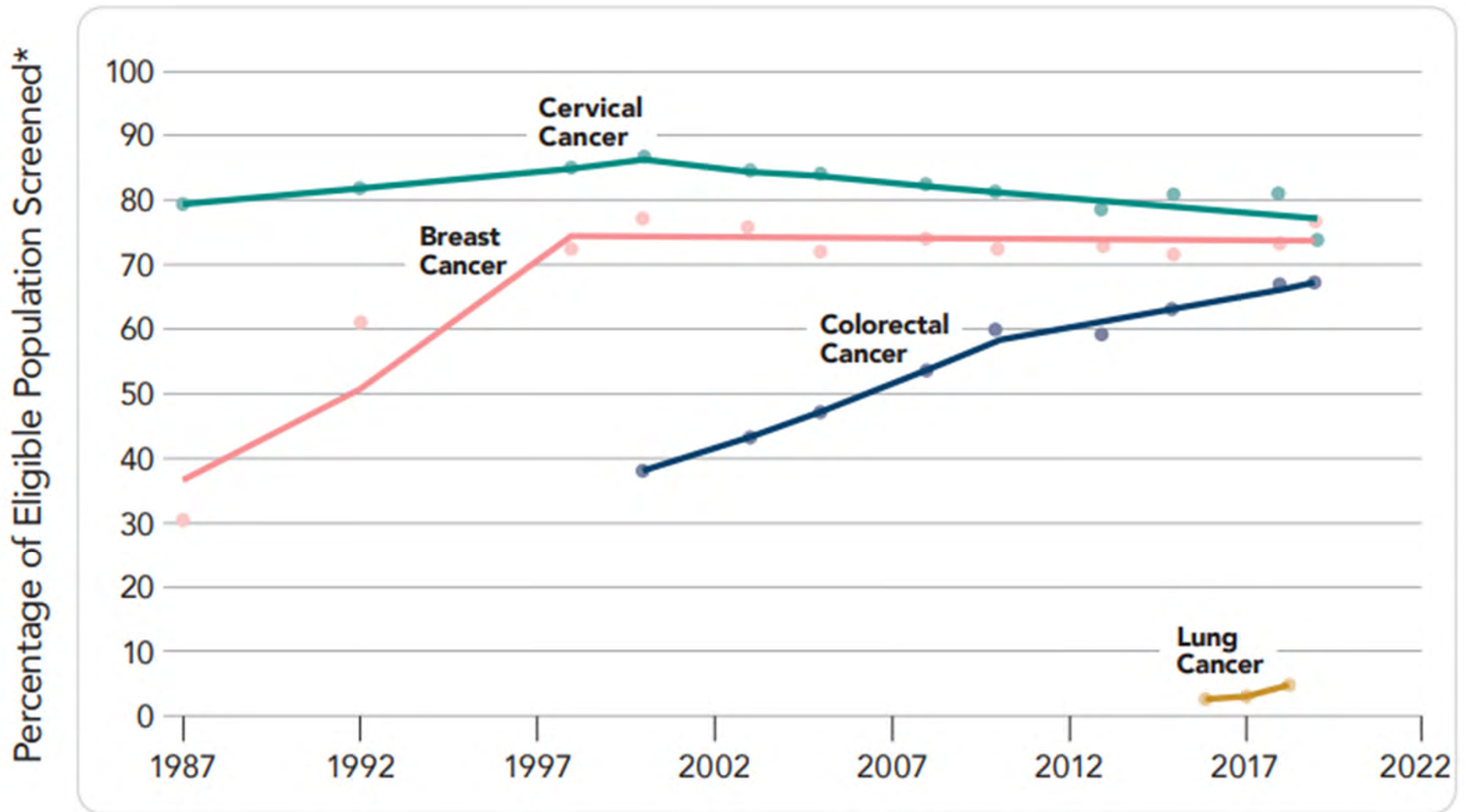
Contact the American College of Radiology at [LCScoverage@acr.org](http://LCScoverage@acr.org).

**SOURCES:**  
 Centers for Medicare and Medicaid Services, accessed October 23, 2019.  
<https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/dm10c18.pdf>  
 American College of Radiology, accessed October 23, 2019.  
<https://www.acr.org/Clinical-Resources/Lung-Cancer-Screening-Resources-FAQ>

Version 2.0 10/23/2019

# How are we doing?

## US Cancer Screening Rates



# Barriers to Screening

## Patient

- Distance traveled<sup>1, 2, 3</sup>
- Cost<sup>4</sup>
- Insurance status<sup>5</sup>
- Fear of results, stigma<sup>3, 7</sup>

## Provider

- Time constraints<sup>3</sup>
- Awareness<sup>3</sup>

## Institutional / Systemic

- Availability of imaging centers<sup>4</sup>
- Insurance expansion<sup>5</sup>

1) Sahar et al. Cancer 2022; 2) Shin et al. J Am Coll Radiol 2022; 3) Brown et al. BMC Public Health 2022; 4) Schutte et al. Public Health Reviews 2018; 5) Lozier et al. JAMA Netw Open 2021; 6) Coughlin et al. JTD 2020; 7) Wang et al. Radiology 2019

# Goals to Optimize Screening



## Improve and align communication

- Conduct large- and small-scale communications campaigns
- Create and expand National Cancer Roundtables



## Facilitate equitable access

- Provide and fund community-oriented outreach and support
- Increase access to self-sampling



## Strengthen workforce collaborations

- Empower healthcare team members
- Expand access to genetic testing and counseling



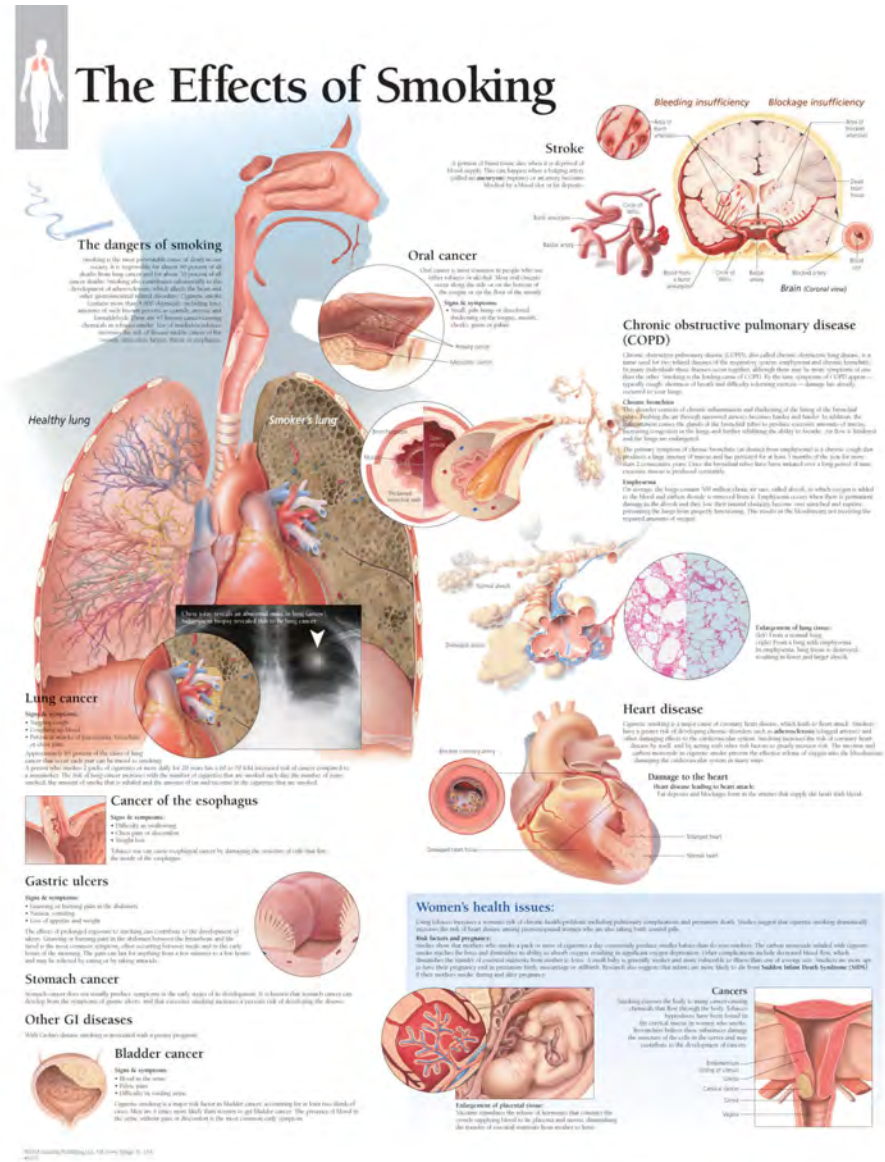
## Create effective health IT

- Create computable guidelines
- Create and deploy clinical decision support tools



# Smoking Cessation

- 1 out of every 3 cancer deaths is related to cigarette smoking
- Each day 1600 youth try their first cigarette
- Smoking increases:
  - risk of death
  - risk of development of additional primary cancers
  - poorer tx response, increase tx related toxicity
- Hallmark of lung cancer = DNA damage which is most apparent with smoking



What does the USPSTF recommend?	<p><b>Nonpregnant adults:</b></p> <ul style="list-style-type: none"> <li>• Ask about tobacco use</li> <li>• Provide behavioral interventions and pharmacotherapy for cessation to those who use tobacco</li> </ul> <p><b>Grade A</b></p>
	<p><b>Pregnant persons:</b></p> <ul style="list-style-type: none"> <li>• Ask about tobacco use</li> <li>• Provide behavioral interventions for cessation to those who use tobacco</li> </ul> <p><b>Grade A</b></p>
	<p><b>Pregnant persons who use tobacco:</b></p> <ul style="list-style-type: none"> <li>• The evidence is insufficient to assess the balance of benefits and harms of pharmacotherapy for tobacco cessation</li> </ul> <p><b>I statement</b></p>
	<p><b>Adults and pregnant persons who use tobacco:</b></p> <ul style="list-style-type: none"> <li>• The evidence is insufficient to assess the balance of benefits and harms of using e-cigarettes for tobacco cessation. Clinicians should direct patients to other cessation interventions with proven effectiveness and established safety</li> </ul> <p><b>I statement</b></p>
To whom does this recommendation apply?	Adults 18 years or older, including pregnant persons.
What's new?	This recommendation is consistent with the 2015 USPSTF recommendation. This recommendation incorporates newer evidence and language in the field of tobacco cessation, including new evidence on the harms of e-cigarettes (ie, vaping).
How to implement this recommendation?	<ol style="list-style-type: none"> <li>1. Ask all adults, including pregnant persons, about tobacco use, using methods such as <ul style="list-style-type: none"> <li>• "5 As": Ask, Advise, Assess, Assist, Arrange follow-up</li> <li>• "Ask, Advise, Refer"</li> <li>• "Vital Sign": Treat smoking status as a vital sign</li> </ul> </li> <li>2. Provide cessation interventions to persons who use tobacco <ul style="list-style-type: none"> <li>• For nonpregnant adults who use tobacco, provide behavioral counseling and pharmacotherapy for cessation <ul style="list-style-type: none"> <li>◦ Effective behavioral counseling interventions include physician advice, nurse advice, individual counseling, group behavioral interventions, telephone counseling, and mobile phone-based interventions</li> <li>◦ FDA-approved pharmacotherapy for cessation includes nicotine replacement therapy, bupropion sustained-release, and varenicline</li> <li>◦ Combined behavioral counseling and pharmacotherapy includes at least 4 or more behavioral counseling sessions with 90 to 300 minutes of total contact time</li> </ul> </li> <li>• For pregnant persons who use tobacco, provide behavioral counseling for cessation <ul style="list-style-type: none"> <li>◦ Effective behavioral counseling includes cognitive behavioral, motivational, and supportive therapies such as counseling, health education, feedback, financial incentives, and social support</li> </ul> </li> </ul> </li> </ol>
What are other relevant USPSTF recommendations?	The USPSTF has made a recommendation on primary care interventions for prevention and cessation of tobacco use in children and adolescents. This recommendation is available at <a href="https://www.uspreventiveservicestaskforce.org">https://www.uspreventiveservicestaskforce.org</a>
Where to read the full recommendation statement?	Visit the USPSTF website to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

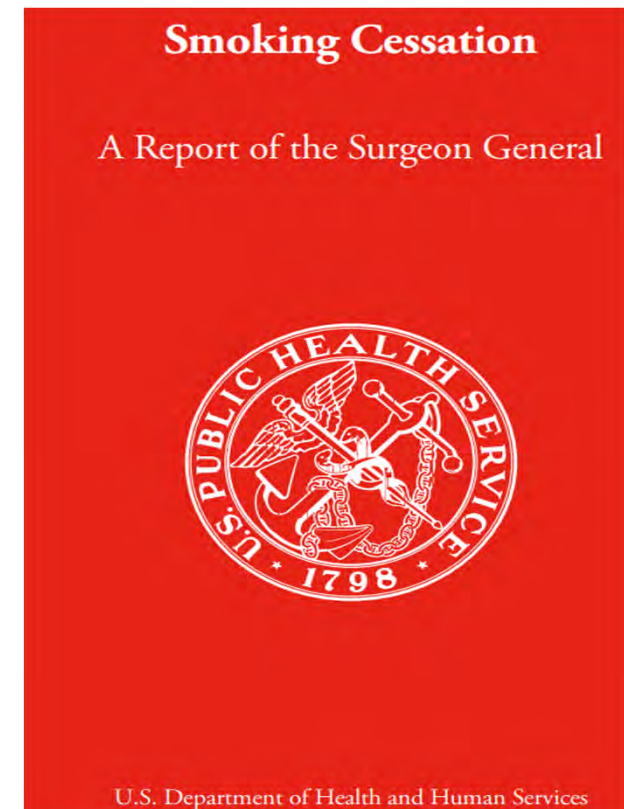


Executive Summary

Diagnosis and Management of Lung Cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

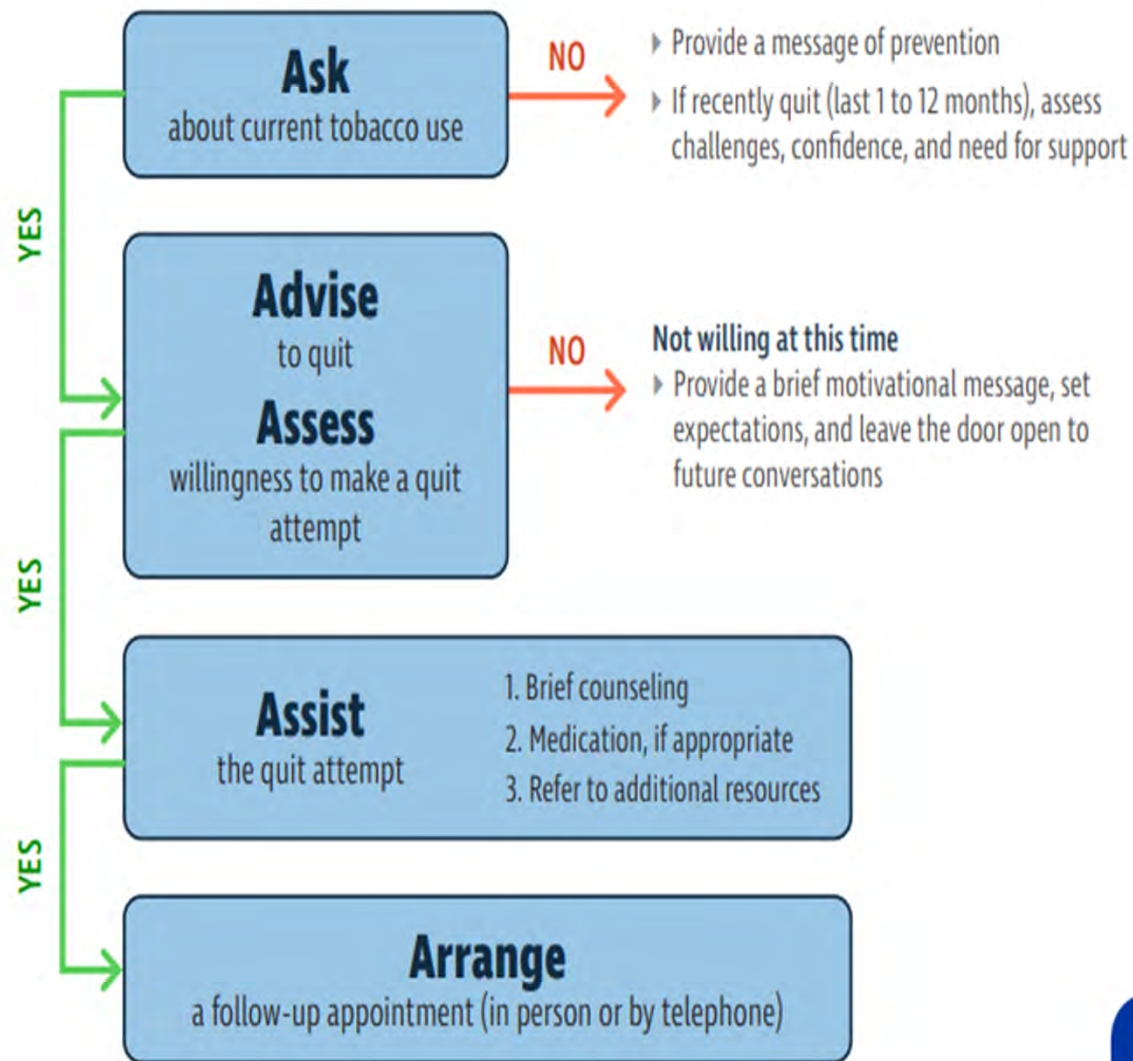
Frank C. Detterbeck, MD, FCCP; Sandra Zelman Letcis, PhD; Rebecca Diekemper, MPH; Doreen J. Adrizzio-Harris, MD, FCCP; and W. Michael Alberts, MD, MBA, FCCP

CHEST 2013; 143(5)(Suppl):7S-37S and it is now a vibrant field with a rapid pace of new information. The evolution of literature makes



US Preventive Services Task Force. Interventions for Tobacco Smoking Cessation in Adults, Including Pregnant Persons: US Preventive Services Task Force Recommendation Statement. JAMA. 2021;325(3):265-279. doi:10.1001/jama.2020.25019

# Overview: Tobacco Cessation Brief Clinical Intervention



# Resources



[Home](#) [Learn more](#) [Join](#) [About us](#)

[Join Now!](#)

Have you been diagnosed with cancer in the past two years? Are you currently receiving or planning to receive cancer treatment? Are you getting ready to quit smoking? Join Quit2Heal, a study comparing two smartphone apps for cancer patients quitting smoking. Begin with just a [click](#).

Quit2Heal is a research study conducted by scientists at Seattle's [Fred Hutchinson Cancer Center](#) in collaboration with the [American Cancer Society](#) and [Memorial Sloan Kettering Cancer Center](#).

Join now to:



## You Can Help Your Patients Quit Tobacco Use



Tobacco use and dependence is a **chronic, relapsing condition** that, like other chronic diseases, may require **repeated intervention** and **long-term support**. Most people who use tobacco want to quit, but most try to quit multiple times before succeeding. As a healthcare professional, you play a critical role in helping people quit using tobacco.

Tobacco use is the **LEADING CAUSE** of **PREVENTABLE DEATH** and disease in the United States.

### Clinical Intervention Works

- Even brief advice from a provider increases the chance a patient will try to quit.
- Counseling and medication can double a patient's chances of quitting.
- Providing tobacco dependence treatment is reimbursable and covered as a preventive service.
- Providing tobacco cessation support increases patient satisfaction with care.

### Advise Quitting and Offer Treatment

- Ask every patient about their tobacco use at every visit.
- Offer patients who use tobacco help quitting at every visit.
- Advise patients who use tobacco that quitting is one of the most important things they can do for their health.
- Offer evidence-based cessation treatment, including counseling and medication.
- Offer referrals to additional cessation resources, including quitlines.
- Follow up with patients to provide support throughout the quitting process.

### Quitting is a Journey

- Every quit attempt is a step closer to quitting.
- Help your patients with every quit attempt. Try new strategies like new medications, medication combinations, or new approaches to handling triggers.
- Encourage patients to learn from what did and did not work and to apply these lessons to their next quit attempt.
- Provide ongoing support to help patients quit for good.
- Don't give up! Quitting is hard, but it is possible – 3 out of 5 American adults who ever smoked have quit.



Every member of the healthcare team can **SUPPORT AND MOTIVATE PATIENTS** in their quit journey.



U.S. Department of Health and Human Services  
Centers for Disease Control and Prevention

CS 306175-A May 16, 2019



## CHEST

Supplement

DIAGNOSIS AND MANAGEMENT OF LUNG CANCER, 3RD ED: ACCP GUIDELINES

### **Evaluation of Individuals With Pulmonary Nodules: When Is It Lung Cancer?**

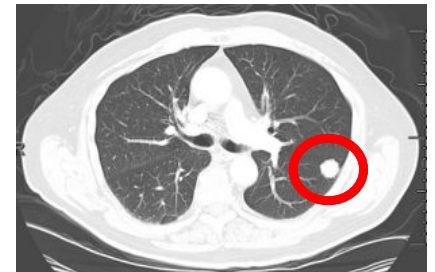
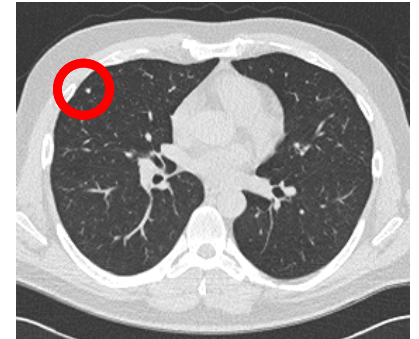
**Diagnosis and Management of Lung Cancer,  
3rd ed: American College of Chest Physicians  
Evidence-Based Clinical Practice Guidelines**

*Michael K. Gould, MD, FCCP; Jessica Donington, MD; William R. Lynch, MD;  
Peter J. Mazzone, MD, MPH, FCCP; David E. Midthun, MD, FCCP;  
David P. Naidich, MD, FCCP; and Renda Soylemez Wiener, MD, MPH*

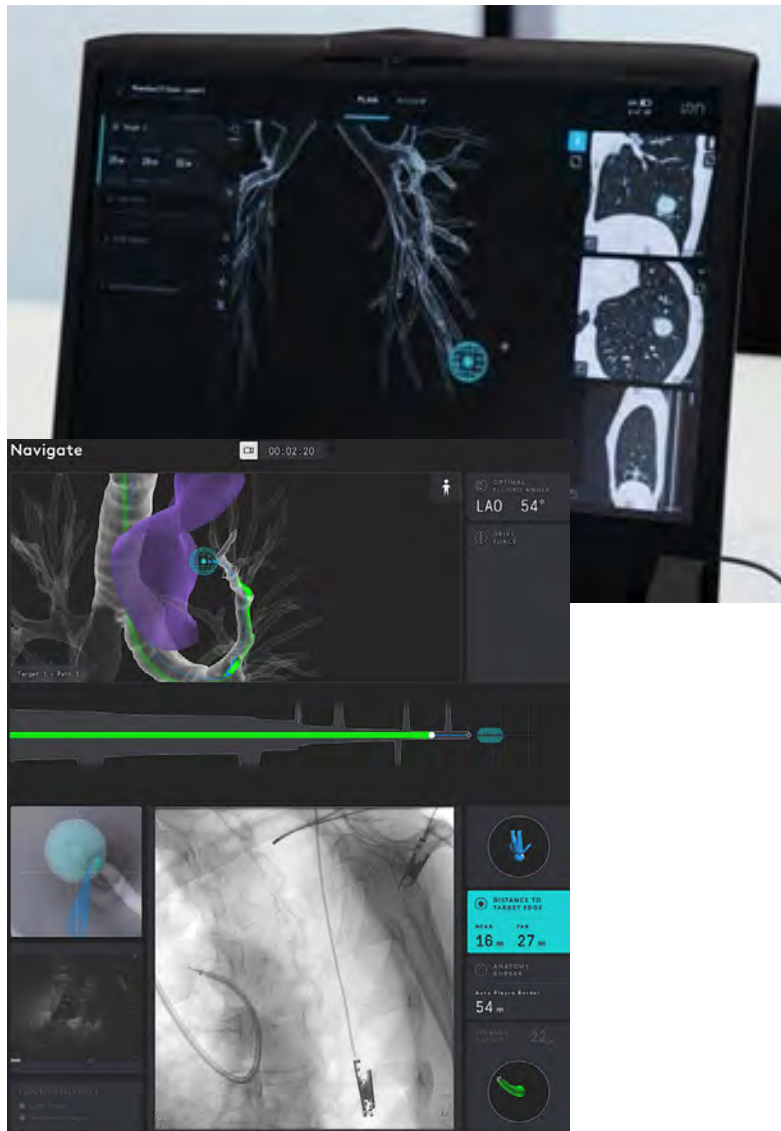
# Diagnostic Workup

## Solid lung nodule on CT → Size?

- Small nodules ( $\leq 8\text{mm}$ )
  - Unlikely malignant
  - f/u CT 6-12mo (Fleischner Society Guidelines)
- Intermediate ( $>8\text{mm}$  and  $\leq 3\text{cm}$ )
  - Could be malignant: Probability calculators, PETCT
  - f/u CT 3-6mo, or Biopsy (perc needle, endobronchial, surgical)
- Large ( $>3\text{cm}$ )
  - Likely malignant
  - Biopsy, Staging, Treatment



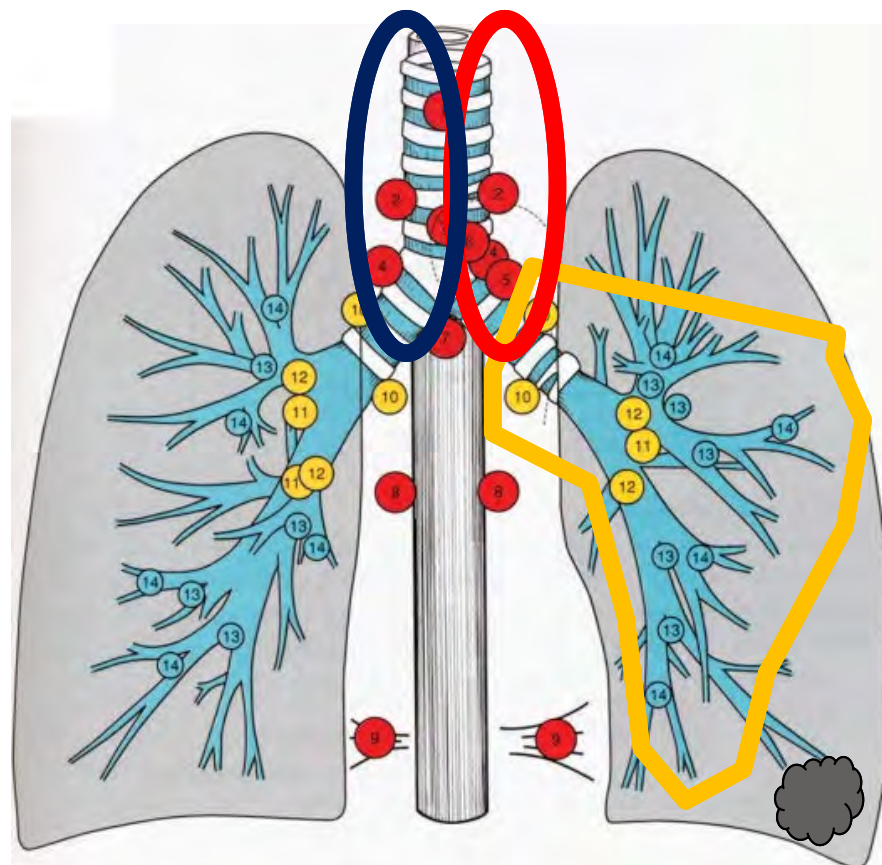
# Diagnostic Workup



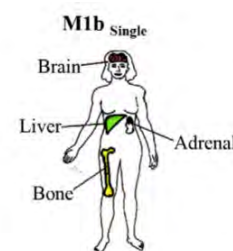
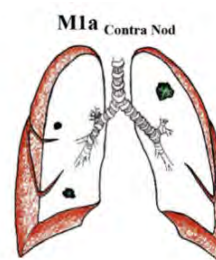
# Staging

## TNM (AJCC 8th)

- Tumor: CT chest
  - T1abc  $\leq$  3cm
  - T2  $>$ 3cm to  $\leq$ 5cm
  - T3  $>$ 5-7cm
  - T4  $>$ 7, or invades local structures
- Nodes: EBUS, mediastinoscopy
  - N1: hilar, lobar
  - N2: ipsilateral mediastinal
  - N3: contralateral mediastinal
- Metastasis: PET, brain MRI
  - Malignant pleural effusion
  - Brain, adrenal, bone, liver



Pleural Nodules  
Malignant  
Pleural  
Effusion





# Treatment Options for lung cancer

## Surgery



## Radiation



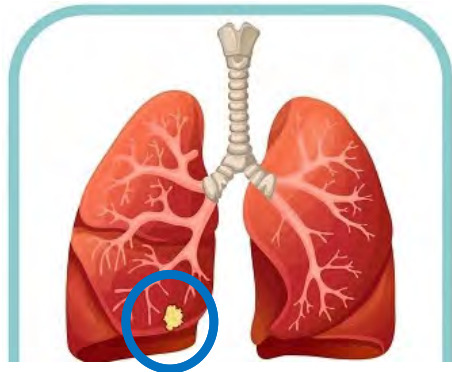
## Chemotherapy Targeted Therapy Immunotherapy



# Staging and Treatment

## Lung Cancer Stage

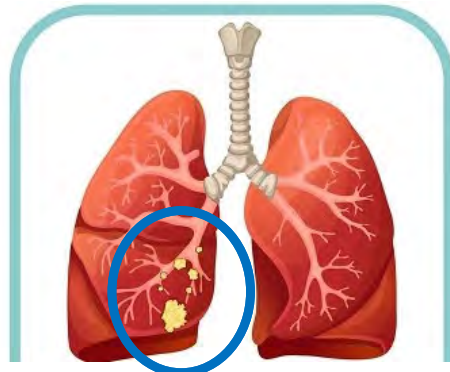
Stage I  
Local



Local

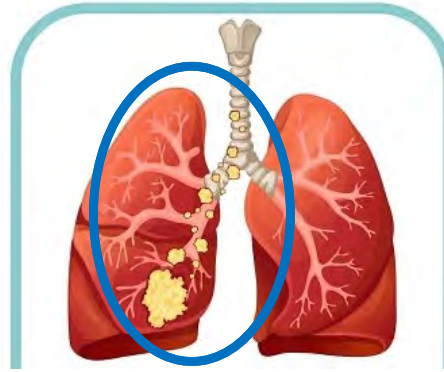
- Surgery
- RT

Stage II  
+ local nodes



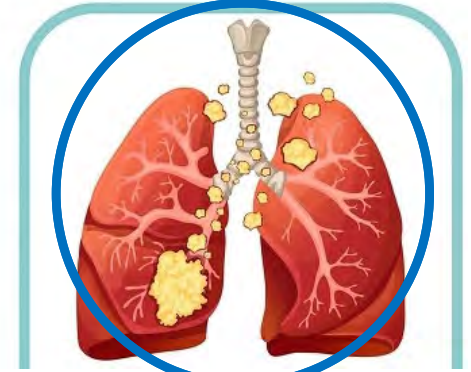
Local + Systemic

Stage III  
+mediastinal



Systemic + Local

Stage IV  
+ distant



Systemic

- Chemotherapy
- Immunotherapy
- Targeted therapy (EGFR, KRAS, ROS1, ALK)

## Lung Cancer Treatment

# Treatment

- Stage I: **N0** (T1,2a)
  - Surgery: Lobectomy, segmentectomy if borderline PFTs
  - Or, SBRT
- Stage II: **N1** (T1,2); T2b,3N0
  - Surgery/SBRT
  - + Chemo
  - + Immunotherapy/EGFR TKI
- Stage IIIA: **N2** (T1,2); T3,4N1; T4N0
  - Chemo + Immunotherapy
  - + Surgery/RT

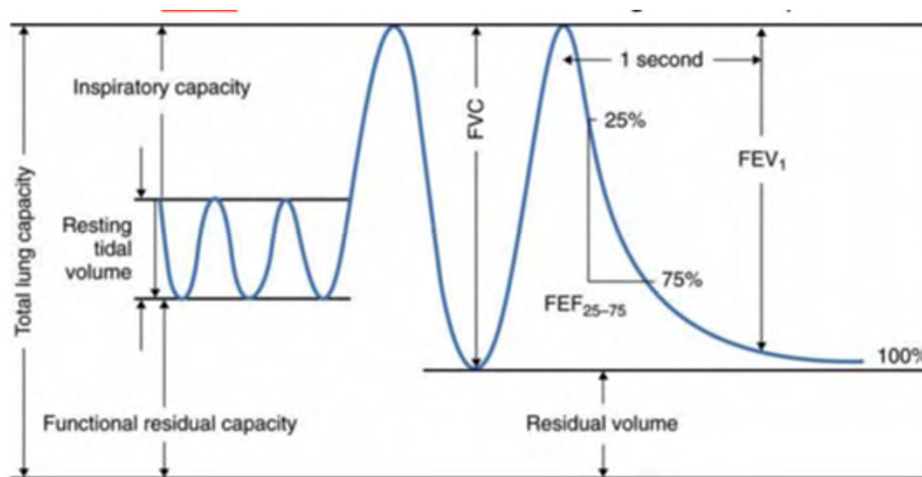
T/M	Label	N0	N1	N2	N3
T1	T1a $\leq 1$	IA1	IIB	IIIA	IIIB
	T1b $>1-2$	IA2	IIB	IIIA	IIIB
	T1c $>2-3$	IA3	IIB	IIIA	IIIB
T2	T2a <i>Cent, Yisc Pl</i>	IB	IIB	IIIA	IIIB
	T2a $>3-4$	IB	IIB	IIIA	IIIB
	T2b $>4-5$	IIA	IIB	IIIA	IIIB
T3	T3 $>5-7$	IIB	IIIA	IIIB	IIIC
	T3 <i>Inv</i>	IIB	IIIA	IIIB	IIIC
	T3 <i>Satell</i>	IIB	IIIA	IIIB	IIIC
T4	T4 $>7$	IIIA	IIIA	IIIB	IIIC
	T4 <i>Inv</i>	IIIA	IIIA	IIIB	IIIC
	T4 <i>Ipsi Nod</i>	IIIA	IIIA	IIIB	IIIC
M1	M1a <i>Contr Nod</i>	IVA	IVA	IVA	IVA
	M1a <i>Pl Dissem</i>	IVA	IVA	IVA	IVA
	M1b <i>Single</i>	IVA	IVA	IVA	IVA
	M1c <i>Multi</i>	IVB	IVB	IVB	IVB

- Stage IIIBC: **N3**; T3,4N2
  - ChemoRT
  - + Immunotherapy
- Stage IV: M1abc
  - Chemo, IO, targeted tx

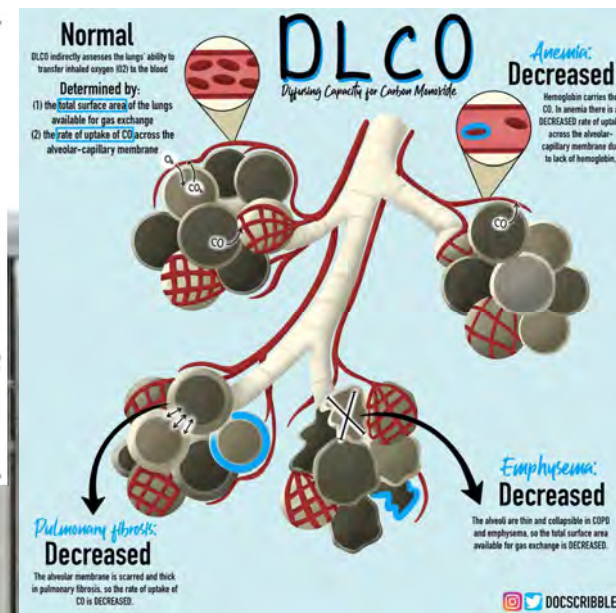
# Surgical Candidacy

## Pulmonary Function Testing FEV1, DLCO

FEV1: Effort dependent



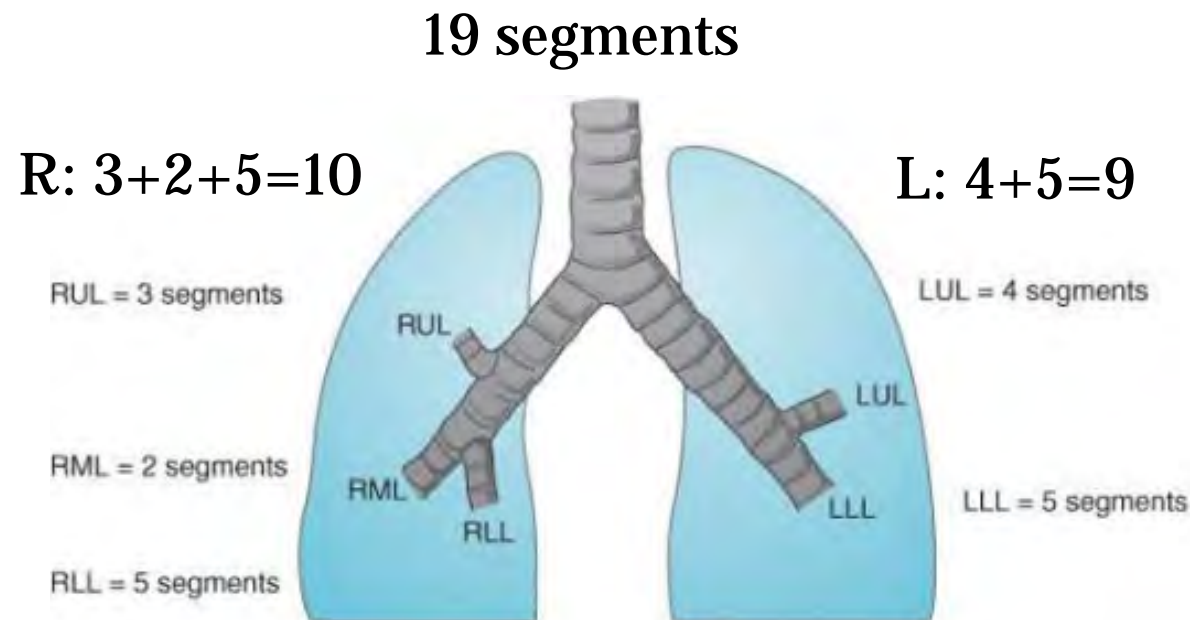
DLCO: Tissue dependent



Brunelli et al. Physiologic Evaluation of the Patient With Lung Cancer Being Considered for Resectional Surgery. CHEST;143(5):e166S-e190S

# Surgical Candidacy

- Pulmonary function testing
  - Postop = Preop – lung to be removed
  - Non-surgical candidate: Postop FEV1 and DLCO <30%



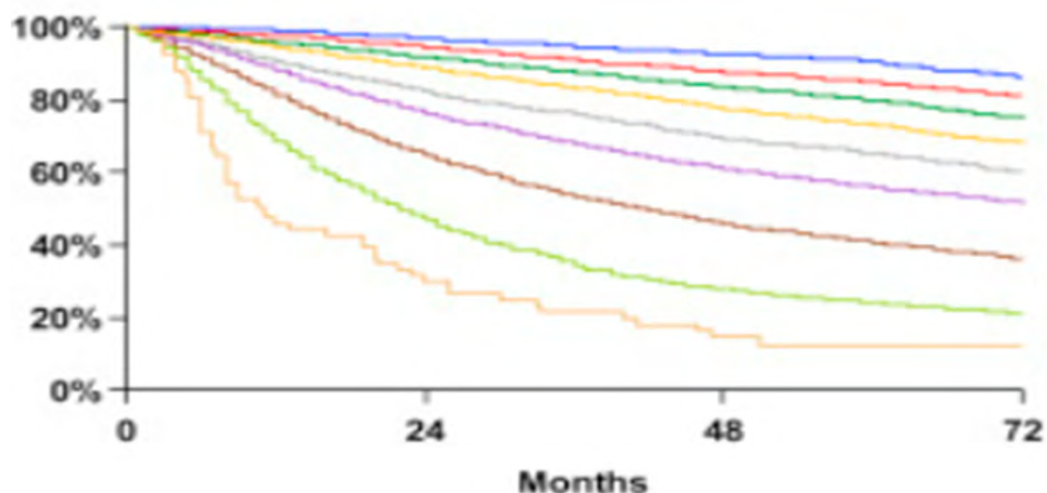
Brunelli et al. Physiologic Evaluation of the Patient With Lung Cancer Being Considered for Resectional Surgery. CHEST;143(5):e166S-e190S

# Surgery

- Frequently minimally invasive (RATS or VATS)
- VIOLET Study
  - superiority of VATS to thoracotomy
  - decreased post-op pain
  - quicker functional recovery
  - shorter length of hospital stay
  - further studies needed on short or long term oncologic outcomes



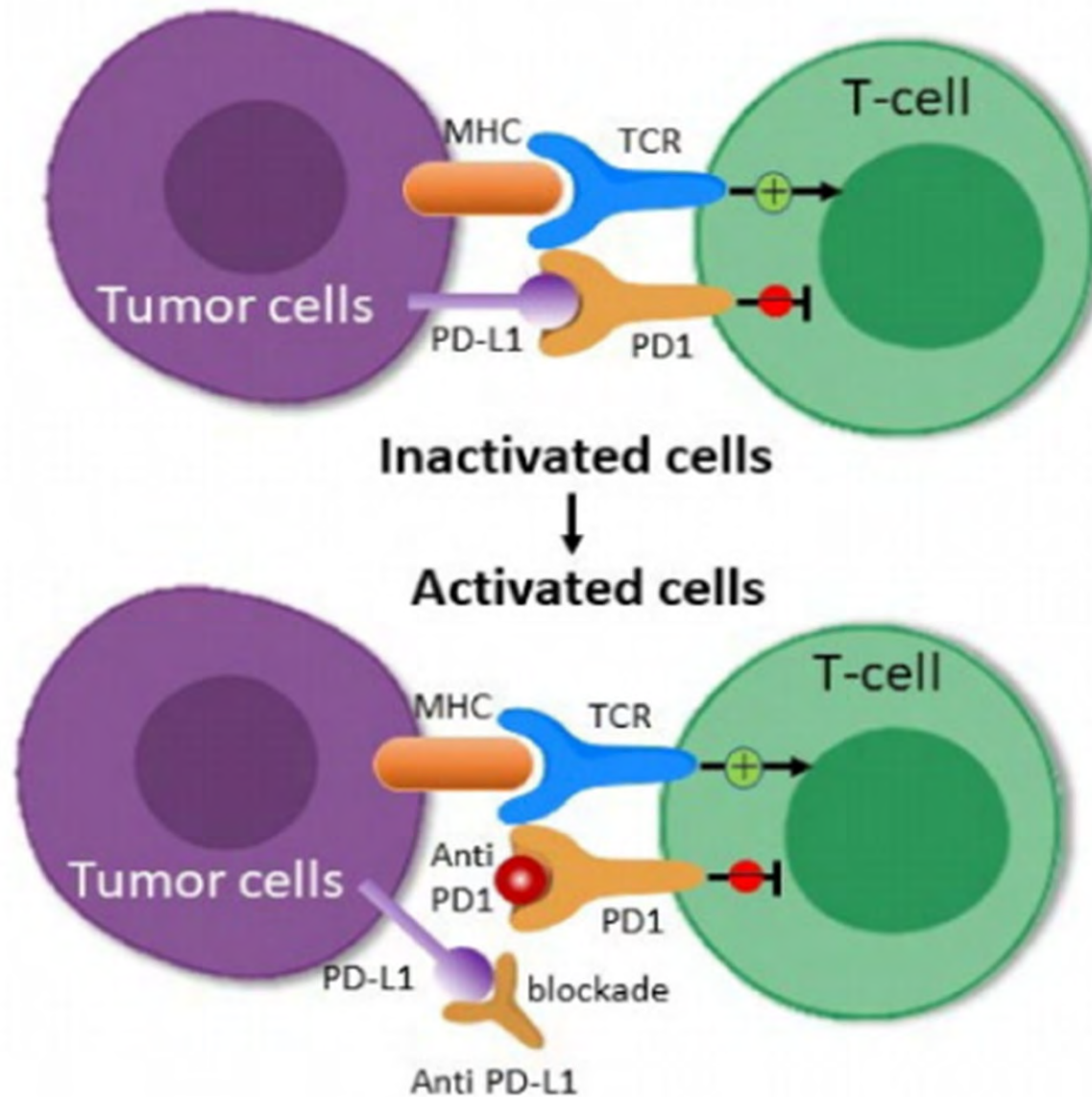
# Prognosis



Proposed	Events / N	MST	24 Month	60 Month
IA1	139 / 1389	NR	97%	90%
IA2	823 / 5633	NR	94%	85%
IA3	875 / 4401	NR	92%	80%
IB	1618 / 6095	NR	89%	73%
IIA	556 / 1638	NR	82%	65%
IIB	2175 / 5226	NR	76%	56%
IIIA	3219 / 5756	41.9	65%	41%
IIIB	1215 / 1729	22.0	47%	24%
IIIC	55 / 69	11.0	30%	12%

Goldstraw, et al. The IASLC Lung Cancer Staging Project: Proposals for Revision of the TNM Stage Groupings in the Forthcoming (Eighth) Edition of the TNM Classification for Lung Cancer. *J Thorac Oncol* 2016; 11:39.

# Immunotherapy





# Immunotherapy

## Immunotherapy for Lung Cancer



### FDA Approved Immunotherapy for Lung Cancer

Nivolumab, Pembrolizumab, Atezolizumab, Durvalumab, Cemiplimab, Ipilimumab + Nivolumab

NSCLC- Non small cell lung cancer  
 SQ- Squamous NSCLC  
 NSQ- Non-squamous NSCLC  
 PDL1- Programmed death ligand 1  
 L- Line of therapy  
 ES SCLC- Extensive stage small cell lung cancer

# PACIFIC trial

## The NEW ENGLAND JOURNAL of MEDICINE

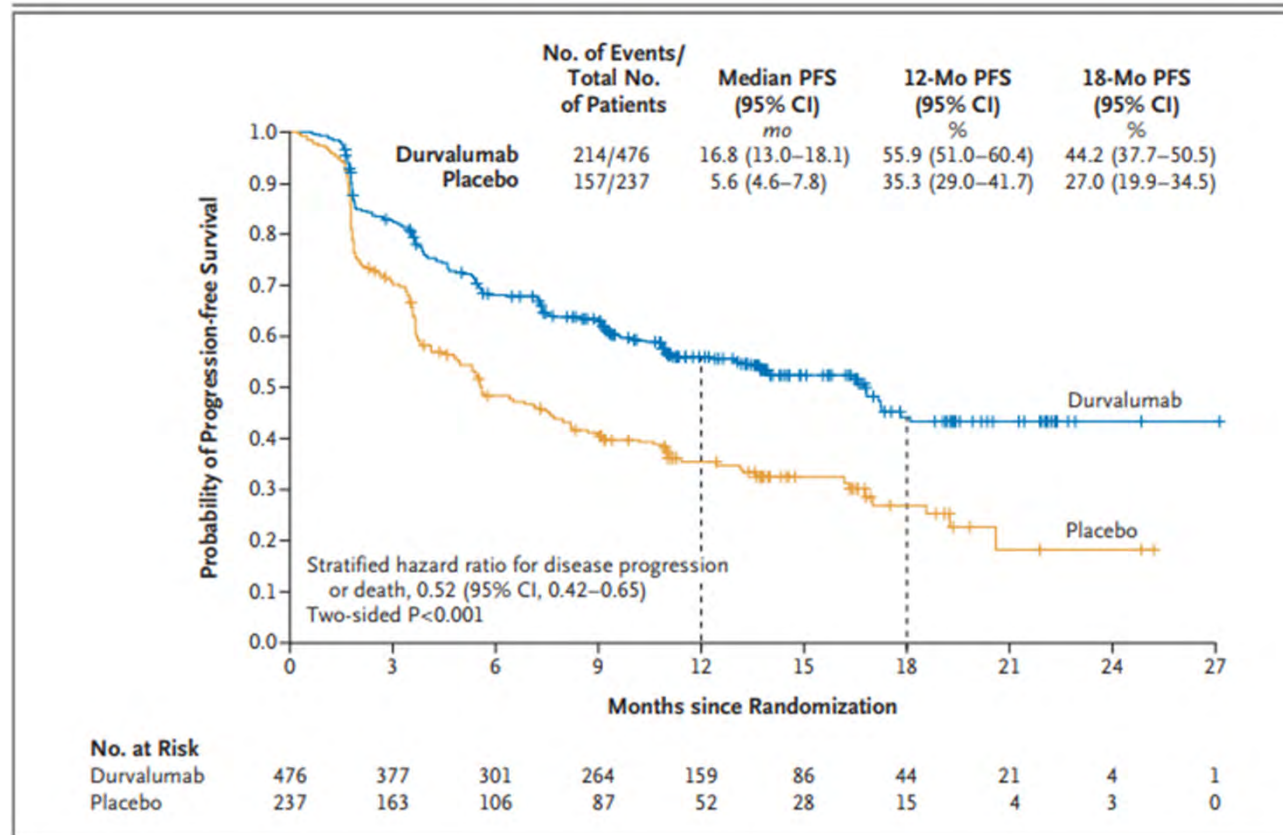
ESTABLISHED IN 1812

NOVEMBER 16, 2017

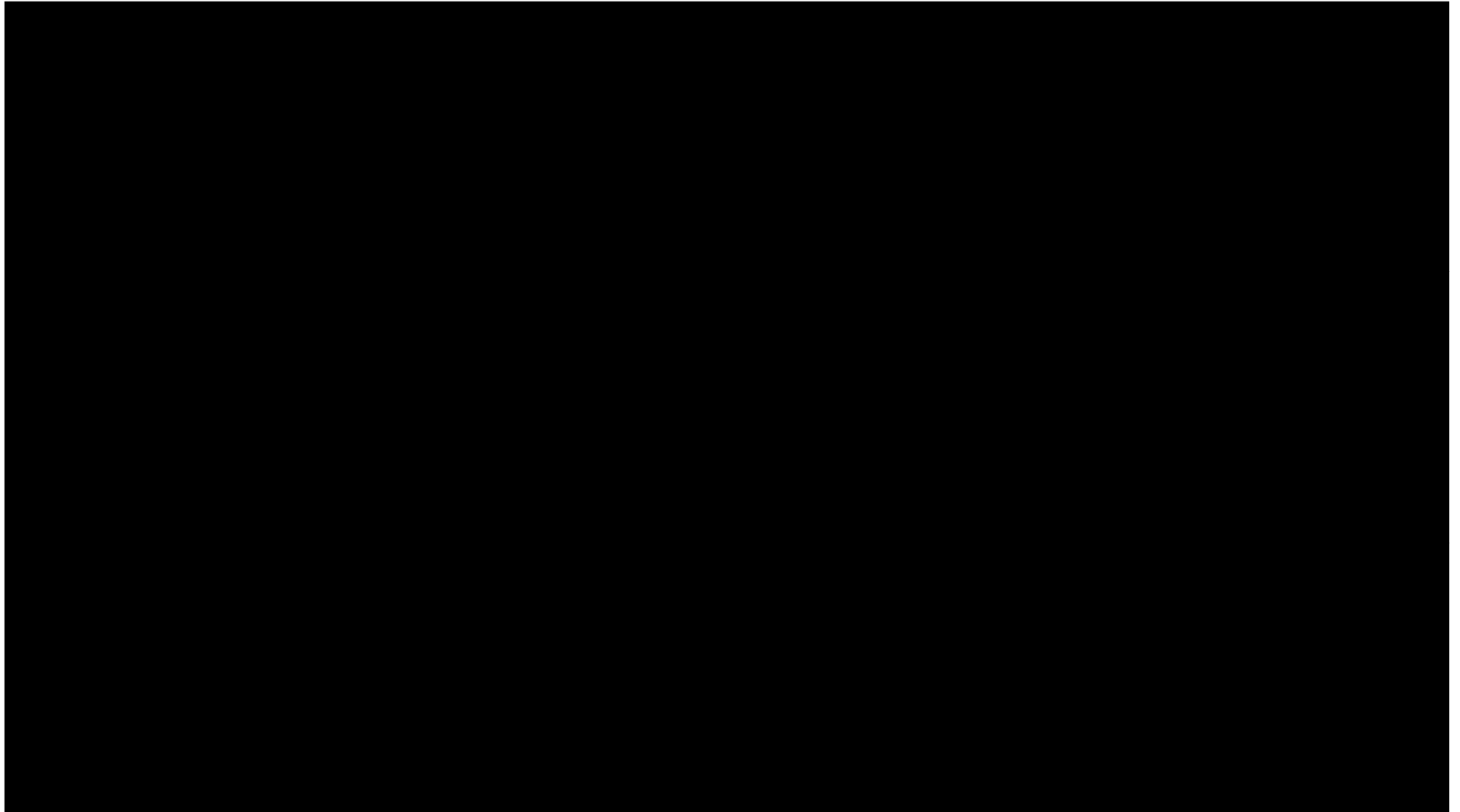
VOL. 377 NO. 20

### Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer

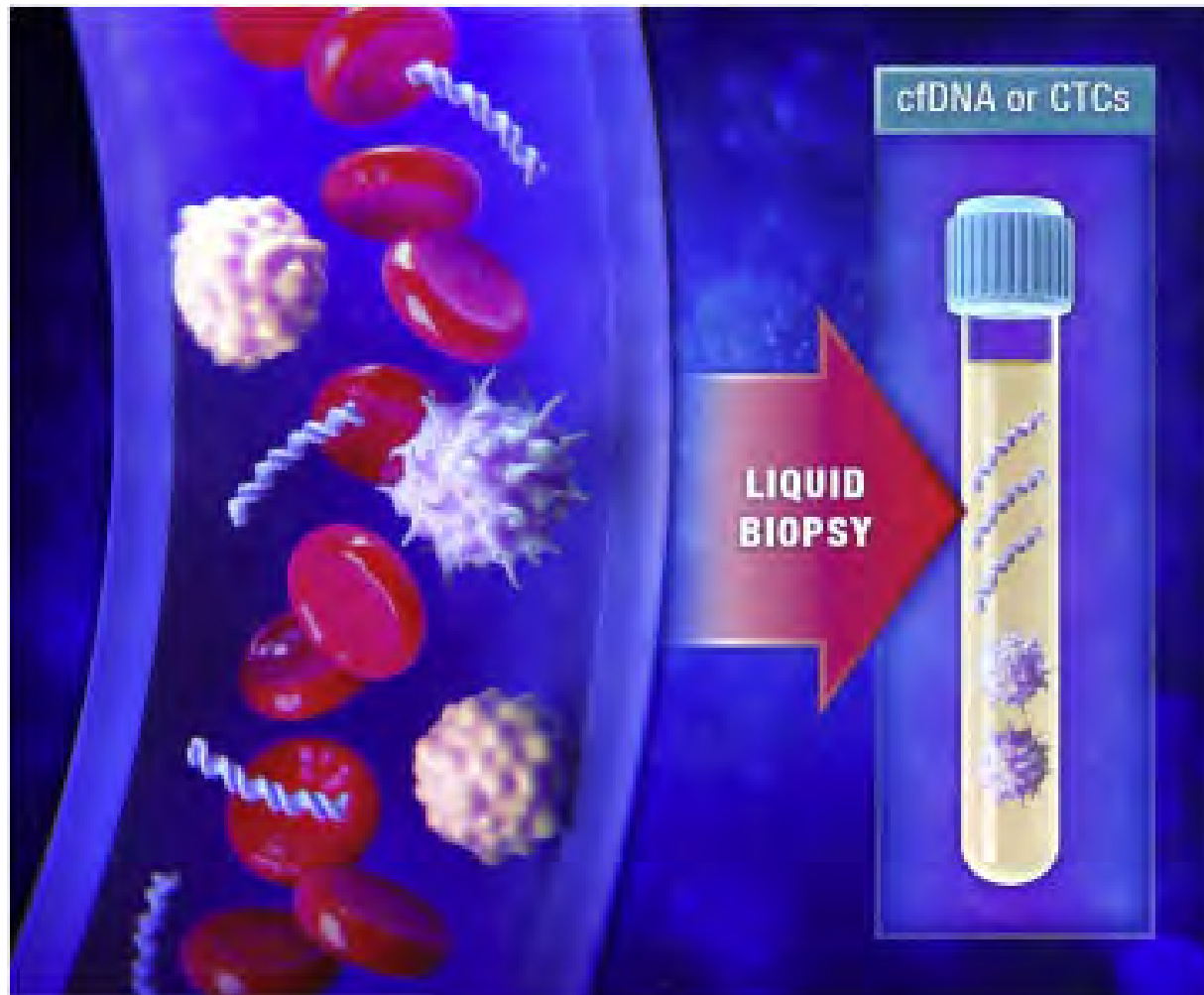
S.J. Antonia, A. Villegas, D. Daniel, D. Vicente, S. Murakami, R. Hui, T. Yokoi, A. Chiappori, K.H. Lee, M. de Wit, B.C. Cho, M. Bourhaba, X. Quantin, T. Tokito, T. Mekhaill, D. Planchard, Y.-C. Kim, C.S. Karapetis, S. Hiret, G. Ostoros, K. Kubota, J.E. Gray, L. Paz-Ares, J. de Castro Carpeño, C. Wadsworth, G. Melillo, H. Jiang, Y. Huang, P.A. Dennis, and M. Özgüroğlu, for the PACIFIC Investigators\*



# Future of Lung Cancer Treatment



# Liquid Biopsy



## DIAGNOSIS:

Genotyping cfDNA in the blood to determine the tumor profile

## RESPONSE AND FOLLOW UP:

Analysis of cfDNA and CTC for real time monitoring of response to treatment

## TUMOR EVOLUTION:

Emergence of molecular alterations associated with resistance to therapy

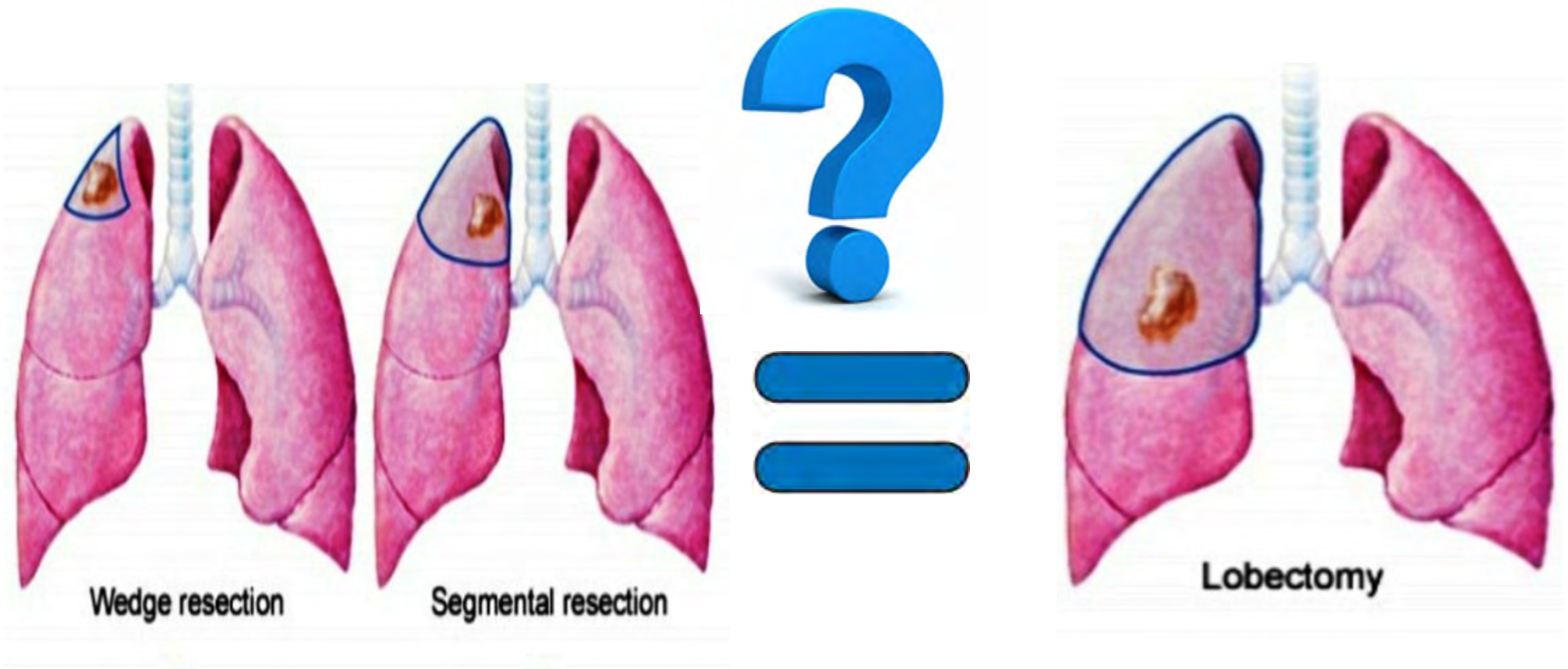
## MINIMAL RESIDUAL DISEASE:

The presence of cfDNA or CTC in the circulation indicates that the disease is still present

*Casagrande, G et al (2023). Liquid Biopsy for Lung Cancer: Up-to-Date and Perspectives for Screening Programs. International Journal of Molecular Sciences. 24. 2505. 10.3390/ijms24032505.*

*Bardelli, A et al (2017) Liquid Biopsies, What We Do Not Know (Yet), Cancer Cell. 31, Issue 2, Pages 172-179, ISSN 1535-6108,*

# Era of “Precision Surgery”



Ginsberg RJ, Rubinstein LV. Randomized trial of lobectomy versus limited resection for T1 N0 non-small cell lung cancer. Lung Cancer Study Group. *Ann Thorac Surg.* 1995 Sep;60(3):615-22; discussion 622-3. doi: 10.1016/0003-4975(95)00537-u. PMID: 7677489.

Altorki N et al. Lobar or Sublobar Resection for Peripheral Stage IA Non-Small-Cell Lung Cancer. *N Engl J Med.* 2023 Feb 9;388(6):489-498. doi: 10.1056/NEJMoa2212083. PMID: 36780674; PMCID: PMC10036605.

# Targeted Therapy



## Osimertinib in Resected *EGFR*-Mutated Non-Small-Cell Lung Cancer

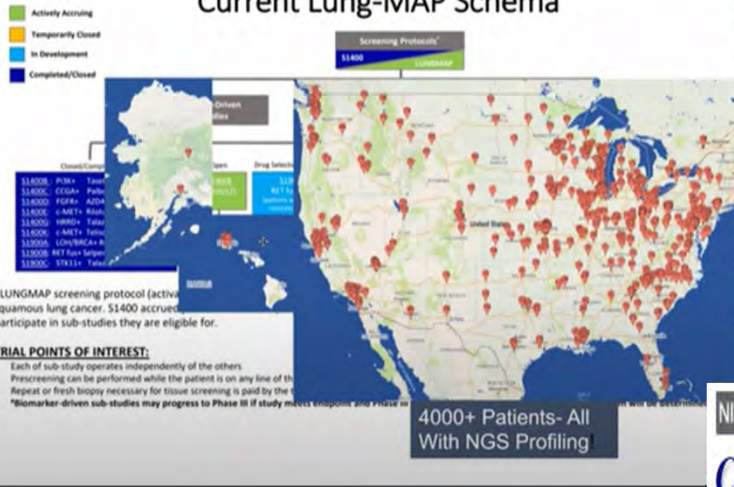
Yi-Long Wu, M.D., Masahiro Tsuboi, M.D., Jie He, M.D., Thomas John, Ph.D., Christian Grohe, M.D., Margarita Majem, M.D., Jonathan W. Goldman, M.D., Konstantin Laktionov, Ph.D., Sang-We Kim, M.D., Ph.D., Tetsufumi Kato, M.D., Huu-Vinh Vu, M.D., Ph.D., Shun Lu, M.D., Kye-Young Lee, M.D., Ph.D., Charuwan Akewanlop, M.D., Chong-Jen Yu, M.D., Ph.D., Filippo de Marinis, M.D., Laura Bonanno, M.D., Manuel Domine, M.D., Ph.D., Frances A. Shepherd, M.D., Lingmin Zeng, Ph.D., Rachel Hodges, M.Sc., Ajlan Ataxoy, M.D., Yuri Rukazenkov, M.D., Ph.D., and Roy S. Herbst, M.D., Ph.D., for the ADAURA investigators<sup>1,2</sup>

The image is a screenshot of the The Lancet Oncology website. At the top left is the logo "THE LANCET Oncology". To the right are links for "Submit Article", "Log in", "Register", and "Su". Below the navigation bar is a red banner with white text. The banner contains the text: "ARTICLES | VOLUME 23, ISSUE 10, P1274-1286, OCTOBER 2021". To the right of this text are three icons: a document, a calendar, and a magnifying glass, with the labels "Purchase", "Subscribe", and "Save" below them. The main headline of the article is "Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB-IIIa non-small-cell lung cancer (PEARLS/KEYNOTE-091): an interim analysis of a randomised, triple-blind, phase 3 trial". Below the headline is a list of authors: "Prof Mary O'Brien, MD", "Prof Luis Paz-Ares, MD", "Sandrine Marraud, MD", "Prof Urania Dafni, ScD", "Kersti Oselin, PhD", "Libor Havel, MD", and "et al.". There are also links for "Show all authors" and "Show footnotes".

# Immunotherapy Work

## Lung Master Protocol

### Current Lung-MAP Schema



#### 11400 Screening Protocol -

Opened 6/16/14. Closed 1/28/19 to expand to all histologies of NSCLC with the new LUNGMAP protocol.

- 1864 patients registered

#### LUNGMAP Screening Protocol -

Opened 1/28/19

760 sites with LUNGMAP CIRB approval

- 2158 patients registered

- 1325 pre-screening
- 833 screening

NIH U.S. National Library of Medicine  
**ClinicalTrials.gov**

-70% of patients with advanced NSCLC not responsive to current ICIs  
-Developing resistance to conventional ICIs

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[Home](#) > [Search Results](#) > [Study Record Detail](#)

Save this study

**A Study of Tiragolumab in Combination With Atezolizumab Compared With Placebo in Combination With Atezolizumab in Patients With Previously Untreated Locally Advanced Unresectable or Metastatic PD-L1-Selected Non-Small Cell Lung Cancer (SKYSCRAPER-01)**

ClinicalTrials.gov Identifier: NCT04294810

# Immunotherapy and Surgery

THORACIC: LUNG CANCER: CLINICAL TRIAL | [VOLUME 165, ISSUE 3, P828-839.E5](#),  
MARCH 2023

Surgical results of the Lung Cancer Mutation Consortium 3 trial: A phase II multicenter single-arm study to investigate the efficacy and safety of atezolizumab as neoadjuvant therapy in patients with stages IB-select IIIB resectable non–small cell lung cancer

20% of patients that received immunotherapy followed by surgery = had a major pathological response without increasing AE during surgery



# Conclusions

- Lung cancer is the leading cause of cancer-related death in the US
- Annual low dose CT: age 50-80, 20pkyr smoker or quit in last 15y
- For solid nodule
  - $\leq 8\text{mm}$   $\rightarrow$  probably not malignant  $\rightarrow$  f/u CT
  - $>8$  to  $\leq 3\text{cm}$   $\rightarrow$  maybe malignant, assess likelihood  $\rightarrow$  f/u CT, PETCT, or bx
  - $>3\text{cm}$   $\rightarrow$  likely malignant  $\rightarrow$  biopsy, staging, and treatment
- If biopsy confirms cancer
  - Staging: T (CT scan), N (EBUS/mediastinoscopy), M (PETCT, bMRI)
  - Treatment: local vs systemic according to stage, assess surgical candidacy w/ PFTs
- Follow up discussion of pathology report to determine additional treatments if needed based on PDL expression, specific mutations

# Conclusions

- Many advances made in field of lung cancer
- Treatment is best achieved with a multimodality team (surgery, medical oncology, radiation oncology, pulmonology, pathology, smoking cessation, lung nodule screening program)

