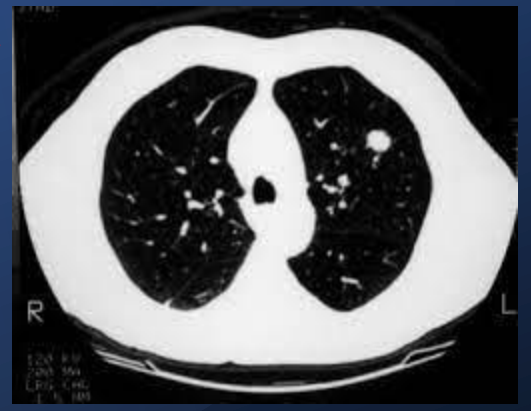
Lung Cancer Screening and Approach to the Lung Nodule



Nov 8th, 2024

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DISCLOSURES/CONFLICTS OF INTEREST

NONE

OBJECTIVES

- Epidemiology of lung cancer
- Screening
- Outcomes of Screening
- Diagnostic Approach to Lung Nodules
- Lung cancer Staging

LUNG CANCER EPIDEMIOLOGY - 2024

Remains the leading cause of cancer death worldwide

Worldwide (2020) : New cases : ~ 2.2 million, Deaths : 1.8 million

US (2024):

- Estimated new cases : 234,580
- Estimated deaths : 127, 070 (in the US)

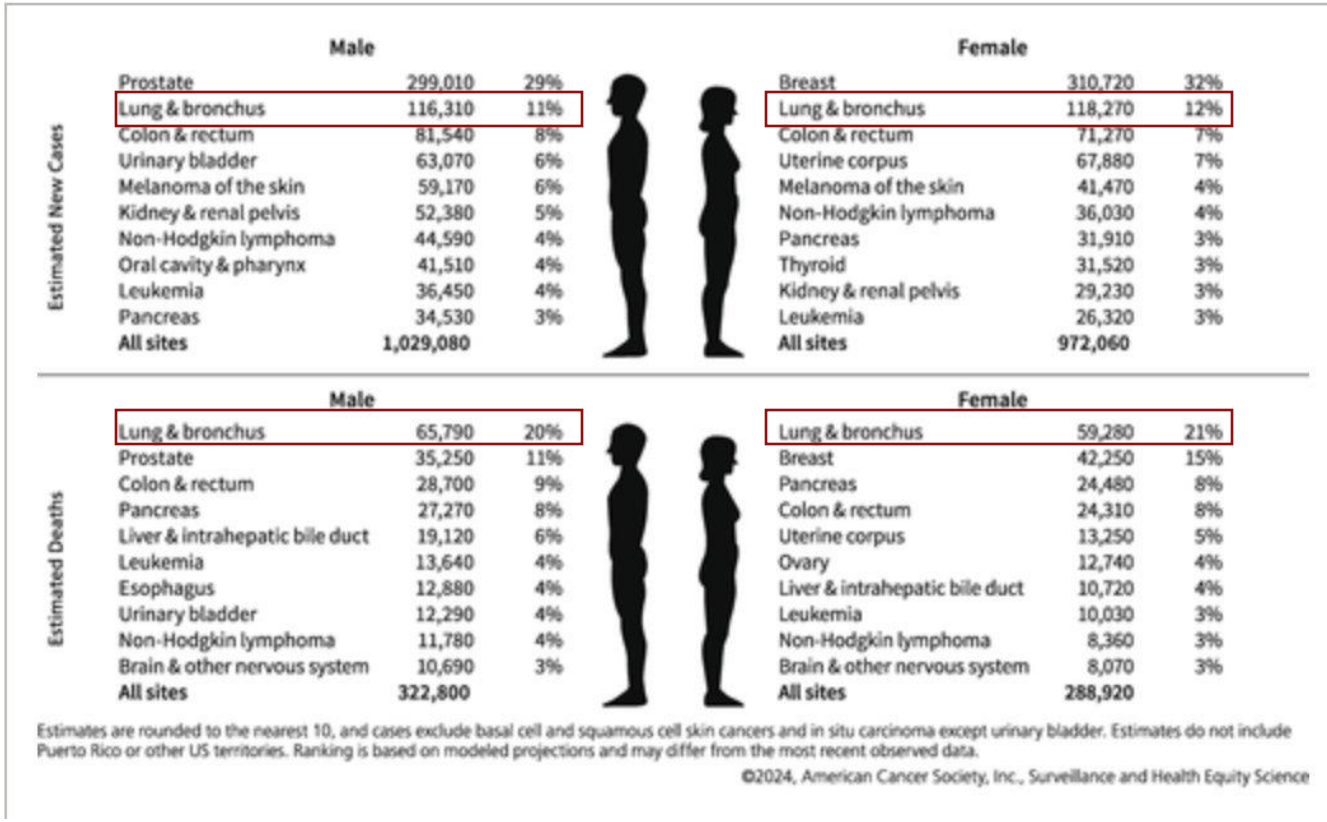
- 1 in 16 men and 1 in 17 women will be diagnosed with lung cancer in their lifetime

- **~80% of the deaths are related to smoking**

  Other risk factors : radon gas exposure, secondhand smoke, asbestos, radiation, air pollution, etc

- **~20% deaths are never smokers**

- Estimated deaths in never smokers : 47,660



Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	

Estimated Deaths

Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	

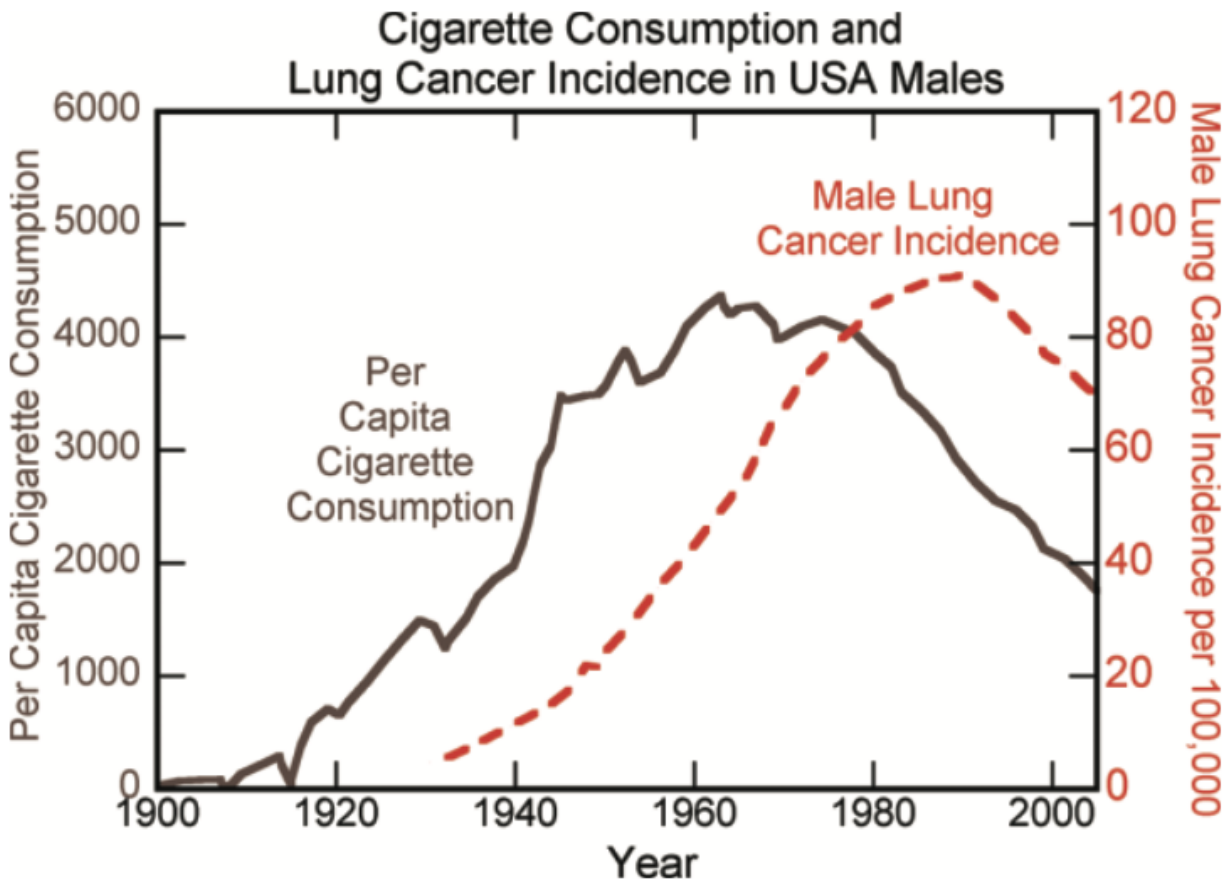
Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

Lung Cancer Research Foundation
Siegel, R et al. Cancer Statistics 2024

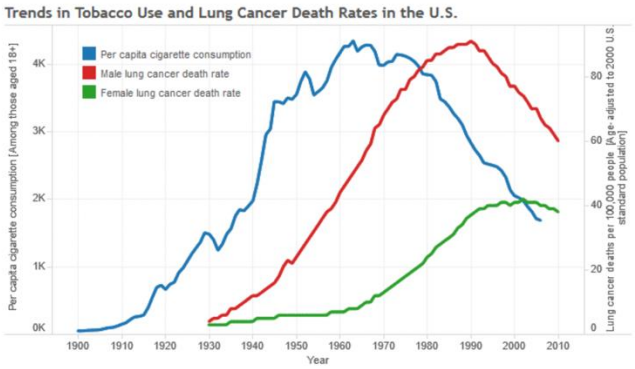
HISTORICAL PERSPECTIVE

Lung cancer is strongly linked to tobacco smoke

Rise in lung cancer parallels increase in tobacco smoking in late 1800s and 1900s



Doss M, Dose-Response 2016



Cigarette sales and lung cancer mortality in the US

Our World in Data

Cigarettes sold per adult per day

Rate of lung cancer deaths per 100,000 men

1970: the US bans cigarette ads on radio and television

1964: Surgeon General's report links smoking to deaths from cancer and heart disease

In the late 1940s and early 50s epidemiologists establish that smoking is harmful to people's health

1945: The Second World War ends

1983: federal tax on cigarettes doubles

1986: Surgeon General's report on secondhand-smoke

Increasing bans on inflight smoking

1929: The Great Depression

Nicotine replacement medications become widely available over the counter

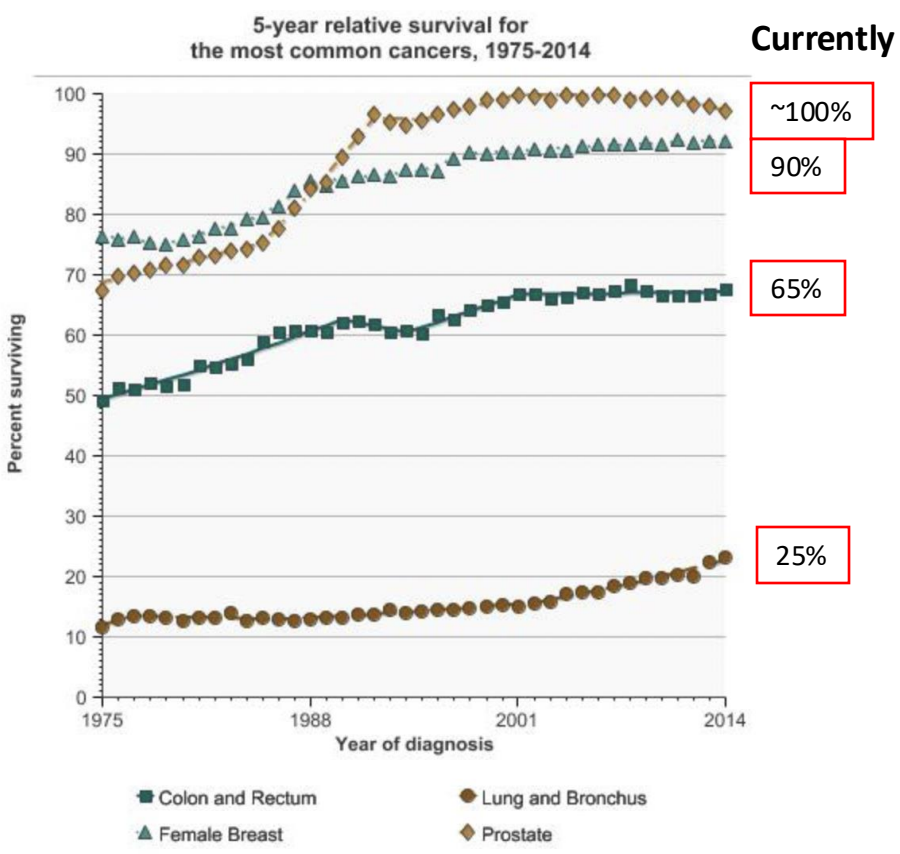
1998: California bans smoking in restaurants

2009: federal tax increased again from $0.39 to $1.01 per pack

Data sources: International Smoking Statistics (2017); WHO Cancer Mortality Database (IARC). The death rate from lung-cancer is age-standardized.

Data from CDC, WHO

LUNG CANCER STATISTICS



Currently

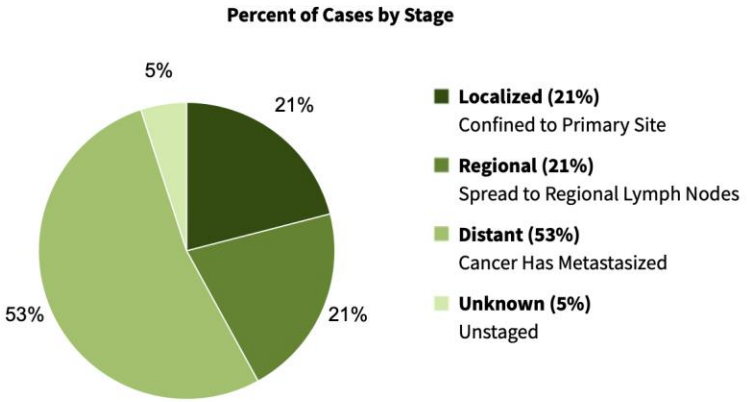
~100%

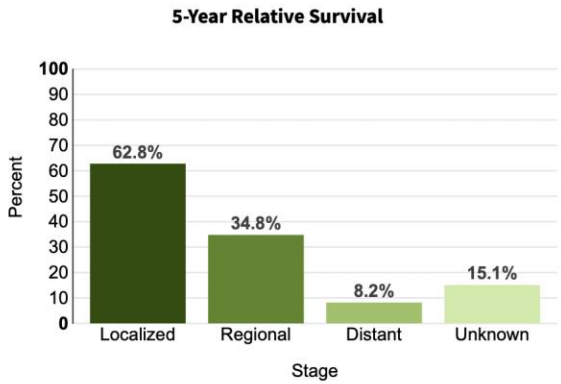
90%

65%

25%

SEER (Survey, Epidemiology and End Results) Program, National Cancer Institute





SEER 22, 2013-2019, National Cancer Institute
All races, both sexes

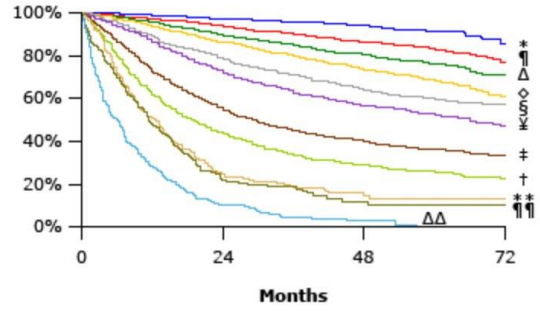
Only ~ 21% diagnosed at an early stage (increased in last 5 years)

53% already with distant metastasis !!!

Overall 5-year survival rate ~ 25 %

(even lower in African Americans)

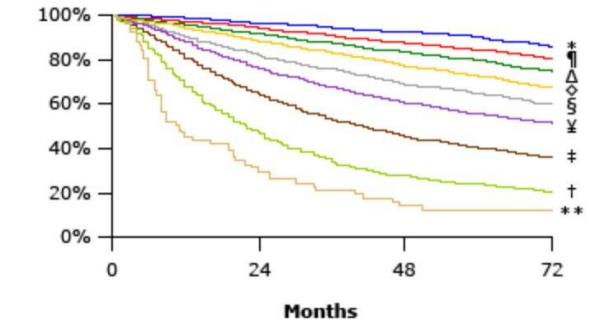
OVERALL SURVIVAL BASED ON 8TH ED STAGING



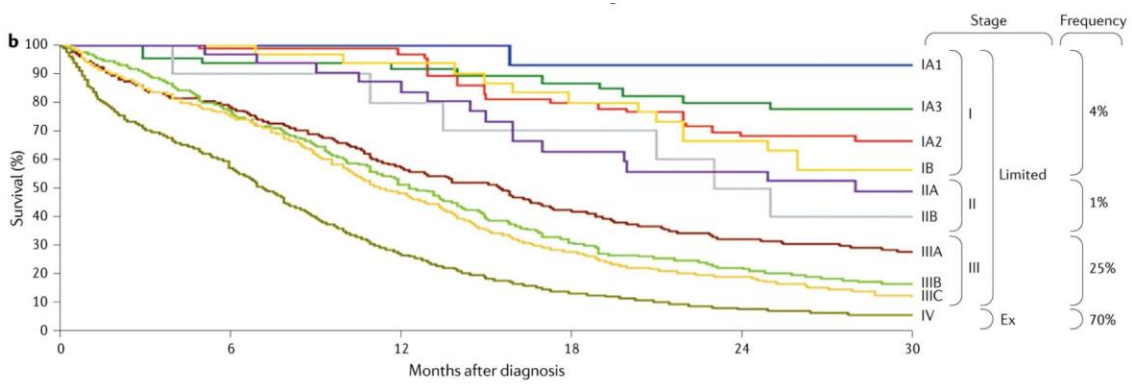
8th edition	Events / N	MST	24 month	60 month
* IA1	68 / 781	NR	97%	92%
¶ IA2	505 / 3105	NR	94%	83%
Δ IA3	546 / 2417	NR	90%	77%
◇ IB	560 / 1928	NR	87%	68%
§ IIA	215 / 585	NR	79%	60%
¥ IIB	605 / 1453	66.0	72%	53%
‡ IIIA	2052 / 3200	29.3	55%	36%
† IIIB	1551 / 2140	19.0	44%	26%
** IIIC	831 / 986	12.6	24%	13%
¶¶ IVA	336 / 484	11.5	23%	10%
ΔΔ IVB	328 / 398	6.0	10%	0%

NON-SMALL CELL LUNG CANCER

Stage 1 = 68-92%



8th edition	Events / N	MST	24 month	60 month
* IA1	139 / 1389	NR	97%	90%
¶ IA2	823 / 5633	NR	94%	85%
Δ 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%



SMALL CELL LUNG CANCER (pathological stage)

Limited Stage – Median survival – 15-30 mths
5yr survival 10-13%

Extensive Stage - Median survival 8-13 mths
5yr survival – 1-2%

STAGE AT DIAGNOSIS MATTERS !
EARLY STAGE = SIGNIFICANTLY IMPROVED SURVIVAL

SCREENING IS CRITICAL

IASCLC Staging Project, JTO 2017
Rudin et al Nat Rev Dis Prim 2021

SCREENING

- Definition - Testing of people at risk of Lung Cancer (LC), but without symptoms or signs of disease

- Goal – Detection of cancer at a stage when cure is possible, and reduce mortality

- Ideal Test –

  Little risk to patients
  Sensitive for detecting disease early
  Few false positive results
  Acceptable to patient
  Relatively inexpensive to patient and health system

BEFORE 2000

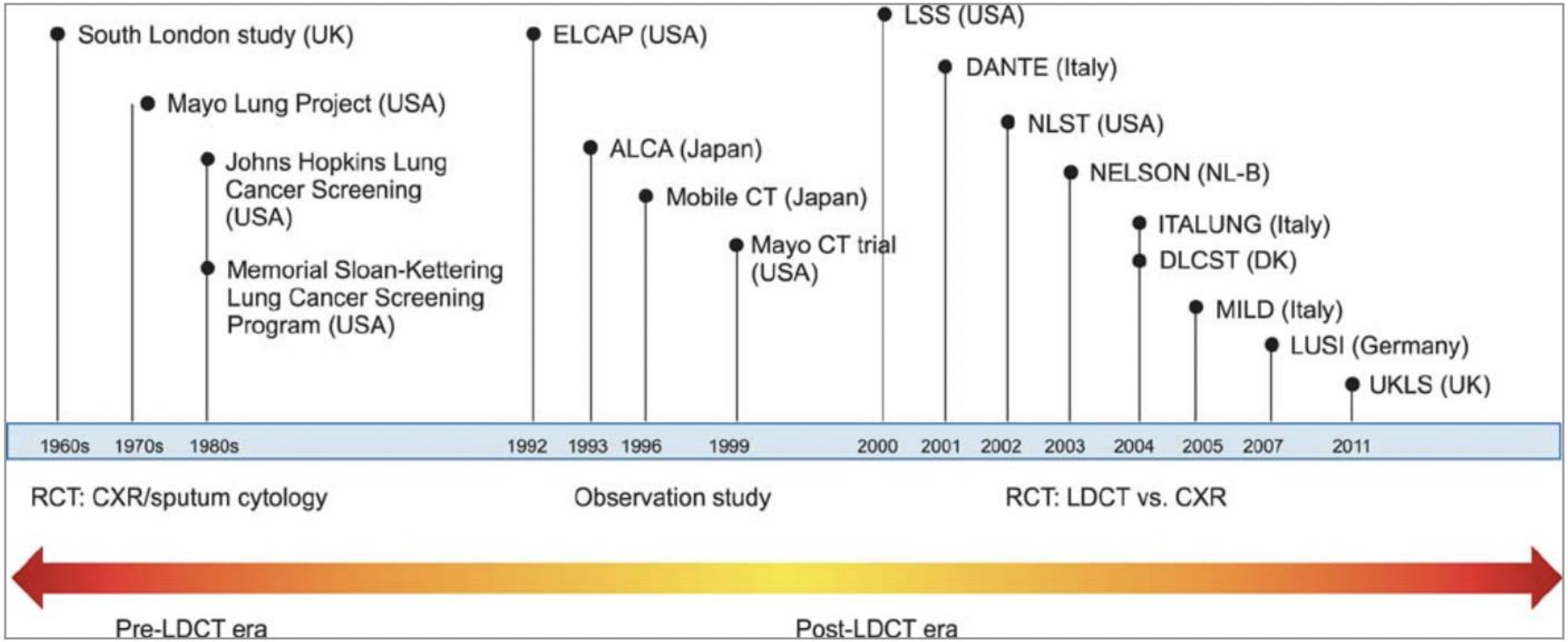
Chest x-ray

Sputum cytology

≠

No significant mortality difference

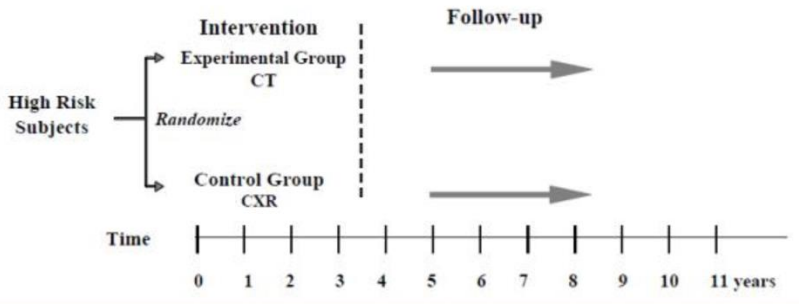
HISTORY OF LC SCREENING



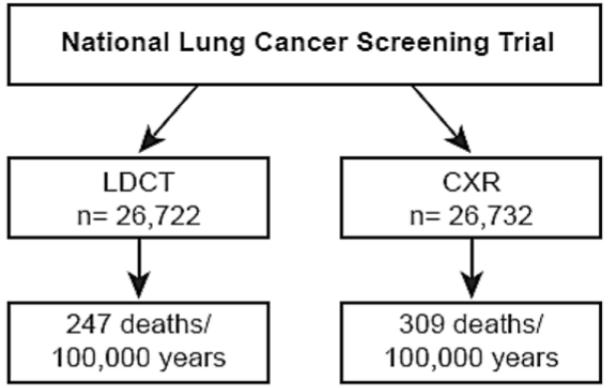
Park YS Tuberc Resp Dis 2014

NATIONAL LUNG SCREENING TRIAL (NLST)

- Prospective, randomized trial
- N = 53,454
- Annual screening with Low dose computed tomography (LDCT) was compared to CXR x 3 years
- End-point – LC specific mortality



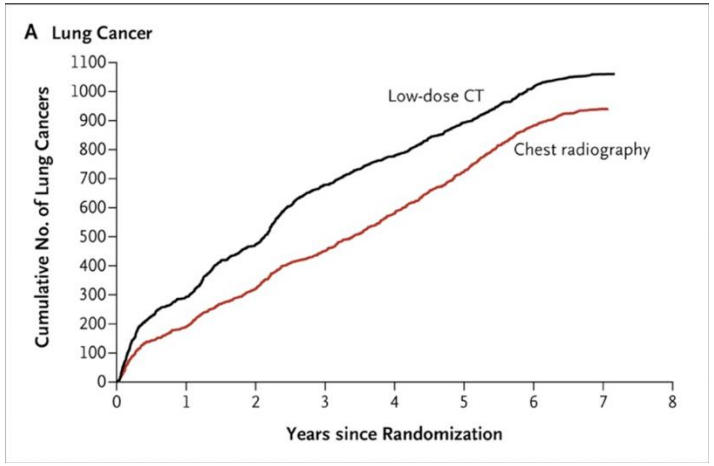
- **Ages 55 – 74**
- **30 pack year smoking history**
- **If former smoker, must have quit within 15 years**

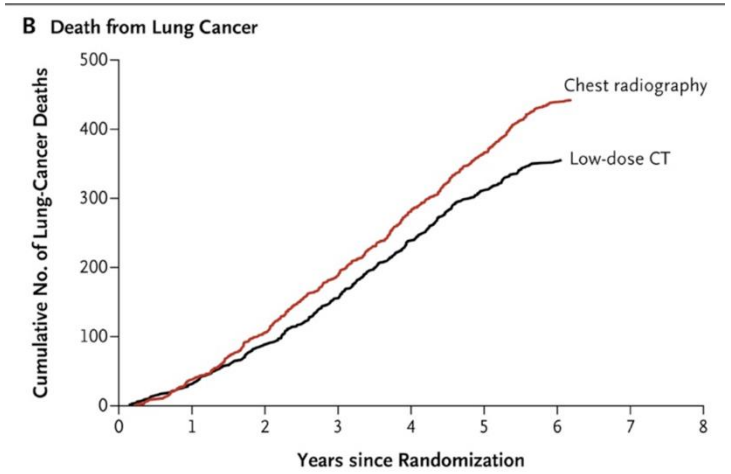


NLST Study Group NEJM 2011
Sudarshan M, Gen Thor Cardiovasc Surg 2020

NLST RESULTS

	LD-CT	CXR	Stats
Lung Cancer cases per 100,000 person-years	645	572	RR 1.13, 95% CI 1.03-1.23
Lung cancer deaths per 100,000 person years	247	309	Relative reduction of 20% (95% CI 6.8 - 26.7, p = 0.004)
Deaths from any cause, N	1877	2000	Relative reduction of 6.7% (95% CI 1.2-13.6, p = 0.02)



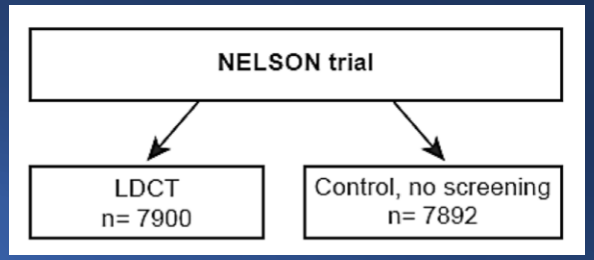


Number needed to screen to prevent one death from :

- Lung cancer : 320
- Breast cancer : 1,904
- Colon cancer : 1,250

NEJM Study Group 2011
Goulart BH et al. J Natl Compr Canc Netw 2012
Warner E. N Engl J Med 2011
Richardson A. J Med Screen 2001

NELSON TRIAL



- Prospective, randomized trial (2nd largest)
- N= 15,492 - 13,195 men, 2594 women (male focused)
- Smoking history : 15 cig/day for > 25 yr
  > 10 cig/day for > 30 yr
  Or quit < 10 years ago

- Volume CT screening at 0, 1, 2 and 2.5yrs vs NO screening
- Follow-up at 5, 7 and 10-11 years (min 10 years)

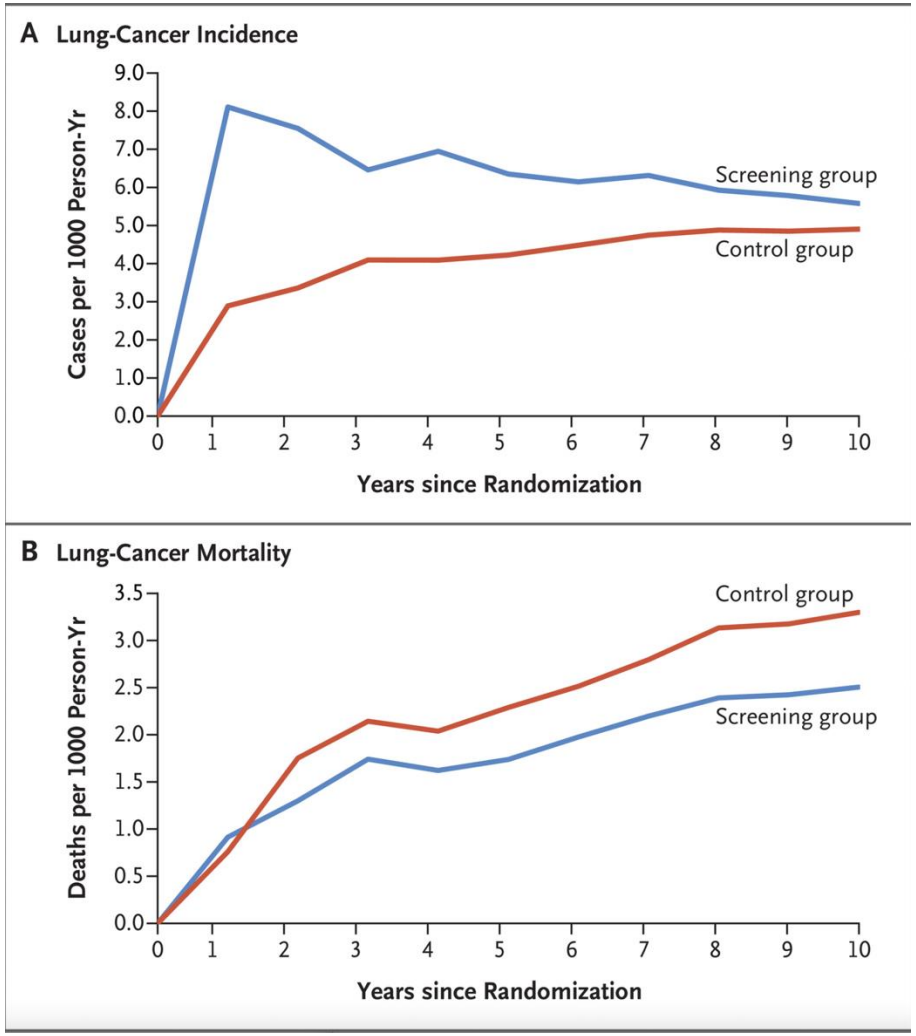
Primary outcome : Lung cancer specific mortality

RESULTS : Improvement in mortality in both high risk men and women

Cancers detected at an early stage (50% early stage, 65-70% were Stage IA-II, 70% Stage III/IV)

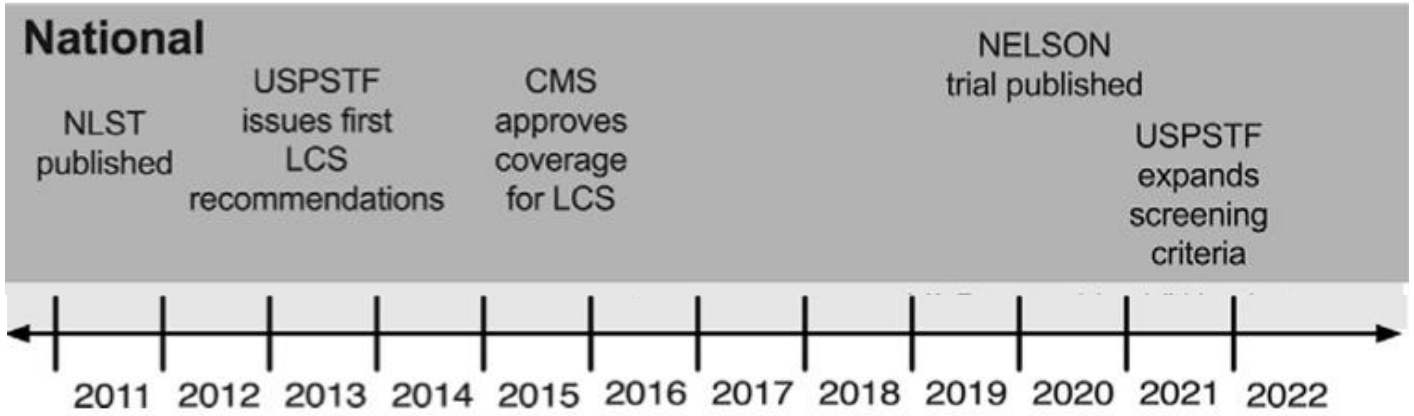
At 10 years, 26% decrease in mortality rate ratio in men (p=.0003)
39% reduction in women (p=0.0054)

Volume CT screening led to fewer harms (false positives, unnecessary workups) without jeopardizing favorable outcomes



De Koning et al, NEJM 2020

SCREENING GUIDELINES



Clinician Summary of USPSTF Recommendation

Screening for Lung Cancer

March 2021

What does the USPSTF recommend?

B 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:

- **Screen** for lung cancer with low-dose computed tomography (CT) every year.
- Stop screening once a person has not smoked for 15 years or has a health problem that limits life expectancy or the ability to have lung surgery.

What's new?

The USPSTF has revised the recommended ages and pack-years for lung cancer screening. It expanded the age range to 50 to 80 years (previously 55 to 80 years), and reduced the pack-year history to 20 pack-years of smoking (previously 30 pack-years).

Maurice N, Tanner NT. Semin Oncol 2022
www.uspreventiveservicestaskforce.org

DOES QUIT DATE MATTER ?

Modeling study by Landy et al , augmented USPSTF LC screening criteria from 2021 – with persons who gain the most life-years from screening from Life Years from Screening CT predictive model

- Increase in absolute cancer risk by 8.7% per year for persons with > 15 quit-years of smoking (after counteracting effects of aging and quit-years)
- Estimated that 4.9 million more people would be eligible for screening if quit years were eliminated
- Screening all eligible individuals would increase proportion of preventable lung cancer deaths from 63.7% to 74.2%

Landy et al J Natl Can Inst 2021
Nierengarten Cancer 2024

Screening for lung cancer: 2023 guideline update from the American Cancer Society

November 2023 :

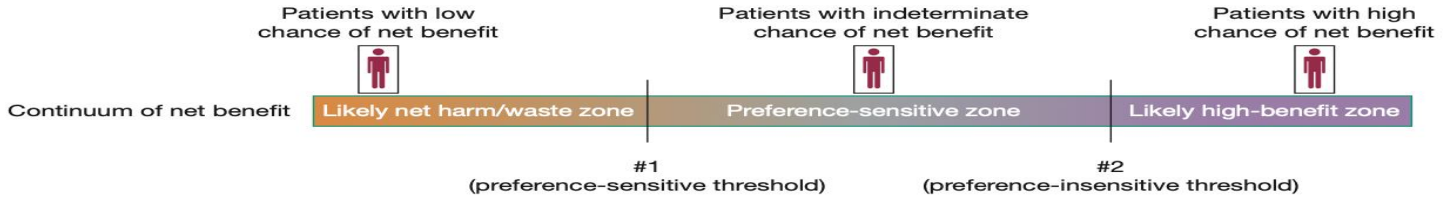
American Cancer Society completely eliminates quit date requirements in new guidelines

Eligibility Criteria	Previous Recommendations	New Recommendations
Age for eligibility	55-74 years	50-80 years
Pack-year (PY) history	30+ PY	20+ PY
Years since quitting (YSQ)	≤ 15 YSQ	No Longer Required

Wolf et al CA: A Canc J Clin 2023

SHARED DECISION MAKING (SDM)

Continuum of net benefit of LC screening for different patients



PROS	CONS
Diagnosis at early stage	False positives
Decreased all cause and LC specific mortality	False negatives (Missed diagnoses)
	Overdiagnosis
	Invasive Procedures/Complications
	Radiation Exposure
	Psychosocial Impact
	Incidental Findings

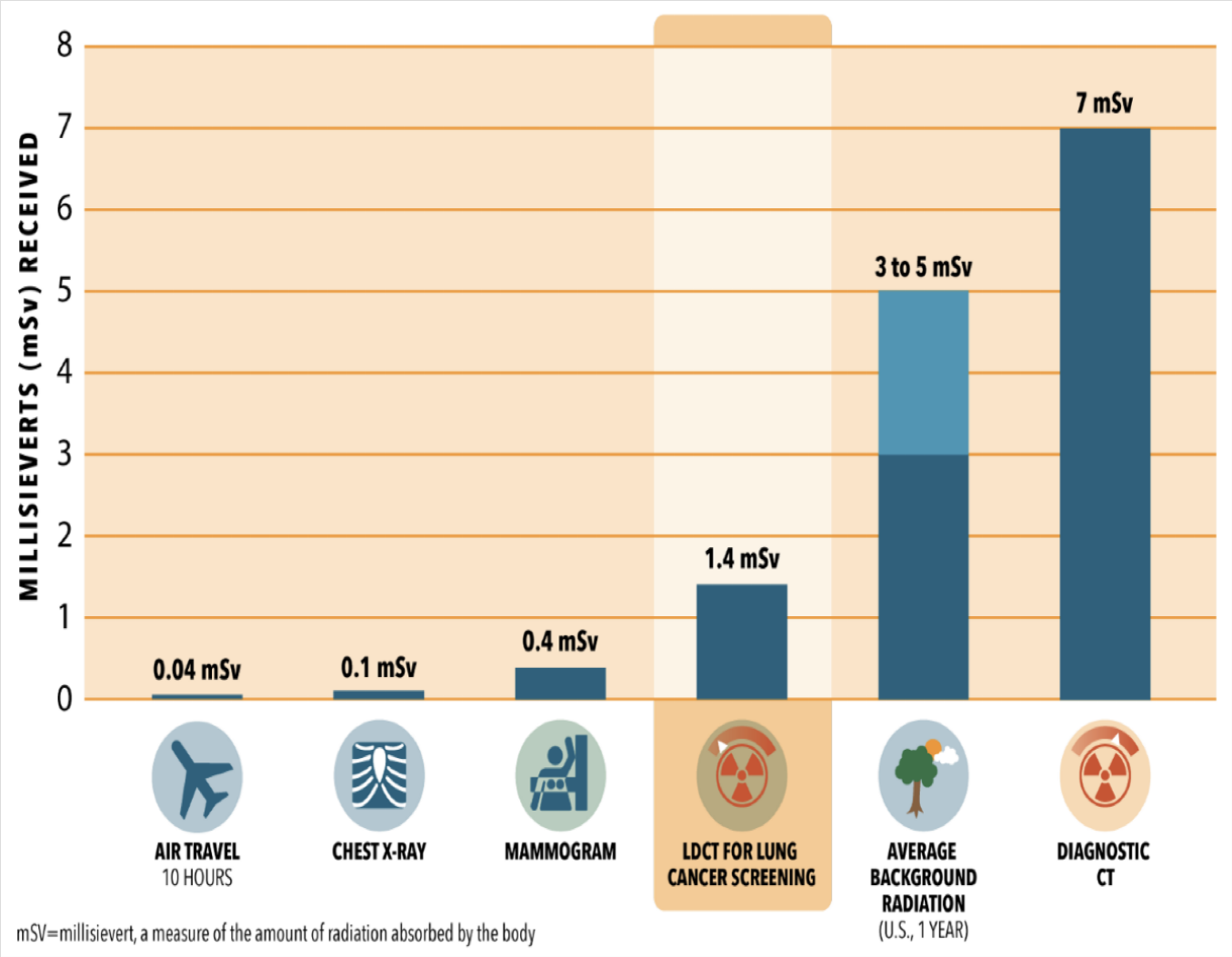
Evidence-based risk-benefit discussion with the patient re: LDCT screening, with decisions made taking into account patient's values and preferences

Goal – Promote patient-centered care

Informed decision-making process is important, not the actual outcome/decision

Ramaswamy, A. Curr Pulm Reports 2022
Mazzone et al. CHEST 2021
Tanner et al. CHEST 2019

RADIATION RISK



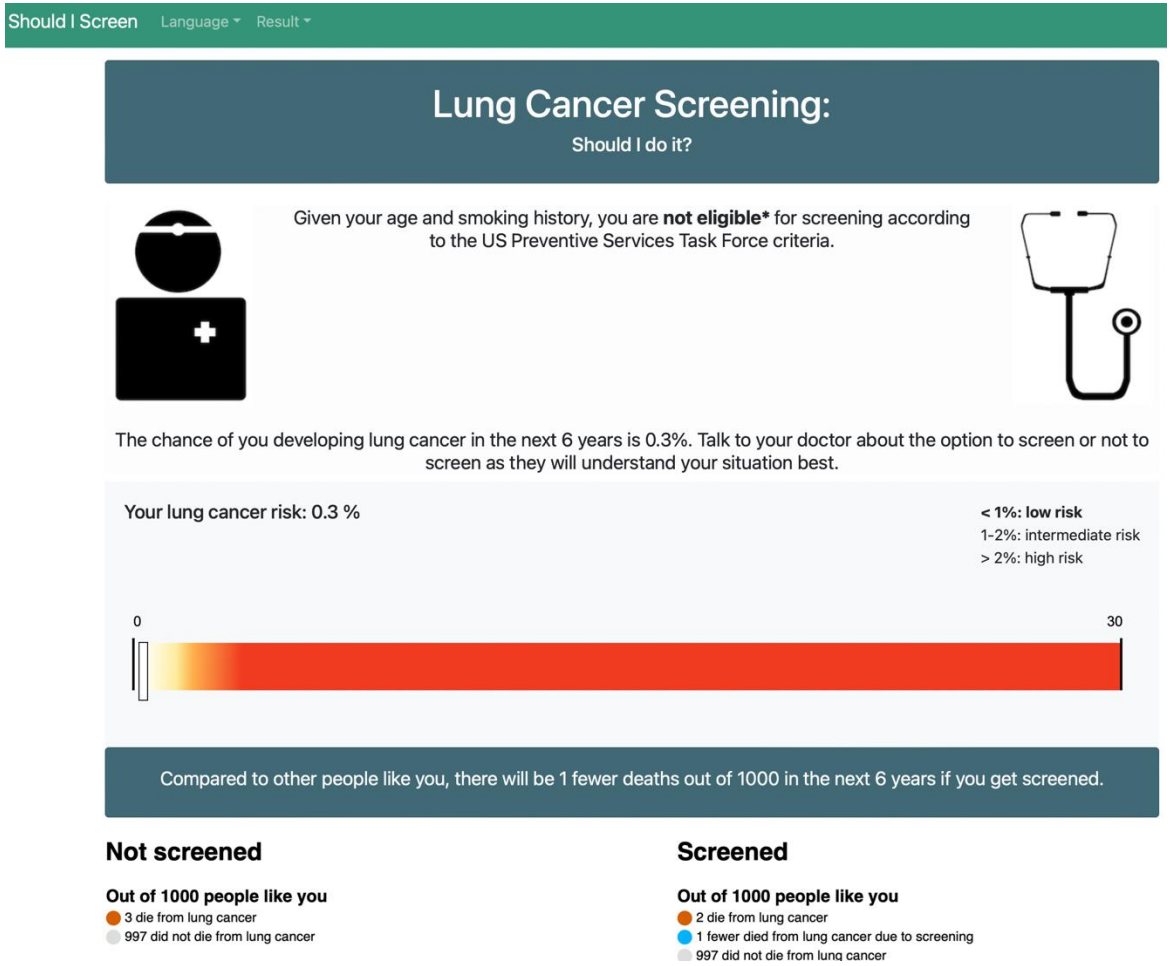
Based on average dose of 4.3mGy from LDCT, lifetime attributable risk of LC mortality is 0.07% in men and 0.14% in women

Frank et al Semin Respir Crit Care 2013

RISK CALCULATORS AND DECISION AIDS

1. How old are you?*
2. What is your current smoking status?*
Smoker
Former Smoker
Never Smoker
2.1. At what age did you quit smoking for the last time?*
3. For how many years total have you smoked cigarettes?*
4. On average, how many cigarettes do/did you smoke per day?*
5. What is your gender?
6. What is the highest grade or year of school you completed?
7. How would you describe your race/ ethnicity?
8. How tall are you? ft. in.
9. How much do you weigh? (lbs.)
10. Have you ever been told by a doctor that you have cancer?
Yes No
11. Does your family have a history of lung cancer?
Yes No
12. Have you ever been told by your doctor that you have chronic pulmonary disease also known as COPD (chronic bronchitis or emphysema)?
Yes No

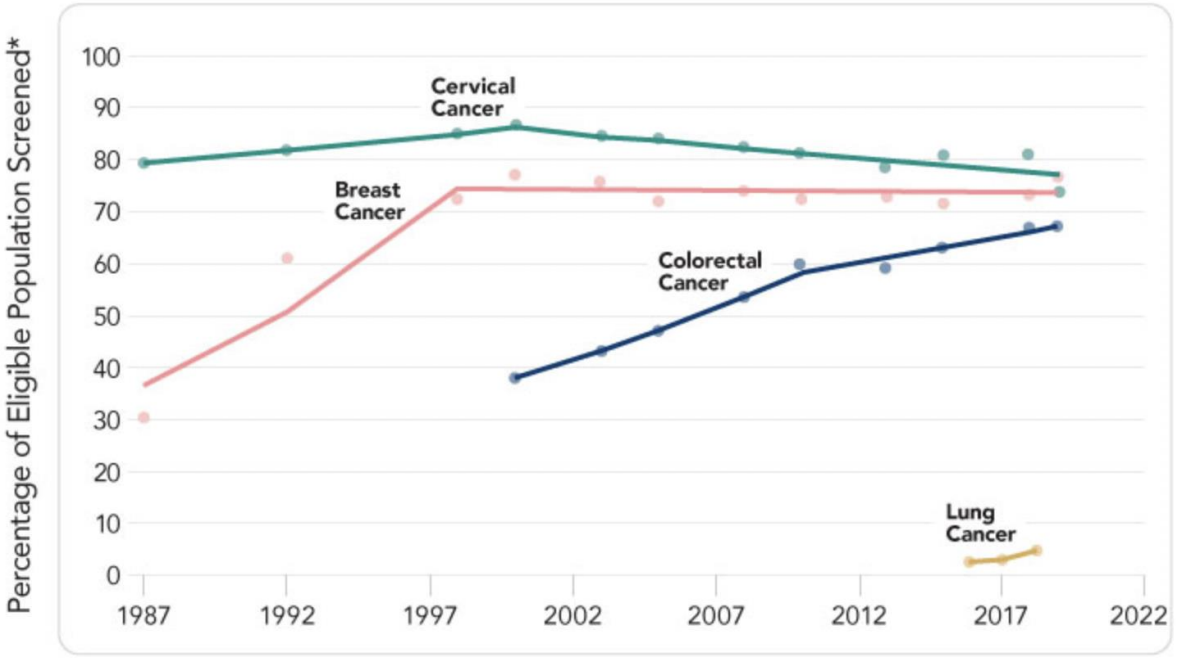
49 years old
Current smoker
35 years
20/day
Female
College graduate
White, non-Hispanic
5'7"
150 lbs
No prior cancer
No family history
Emphysema

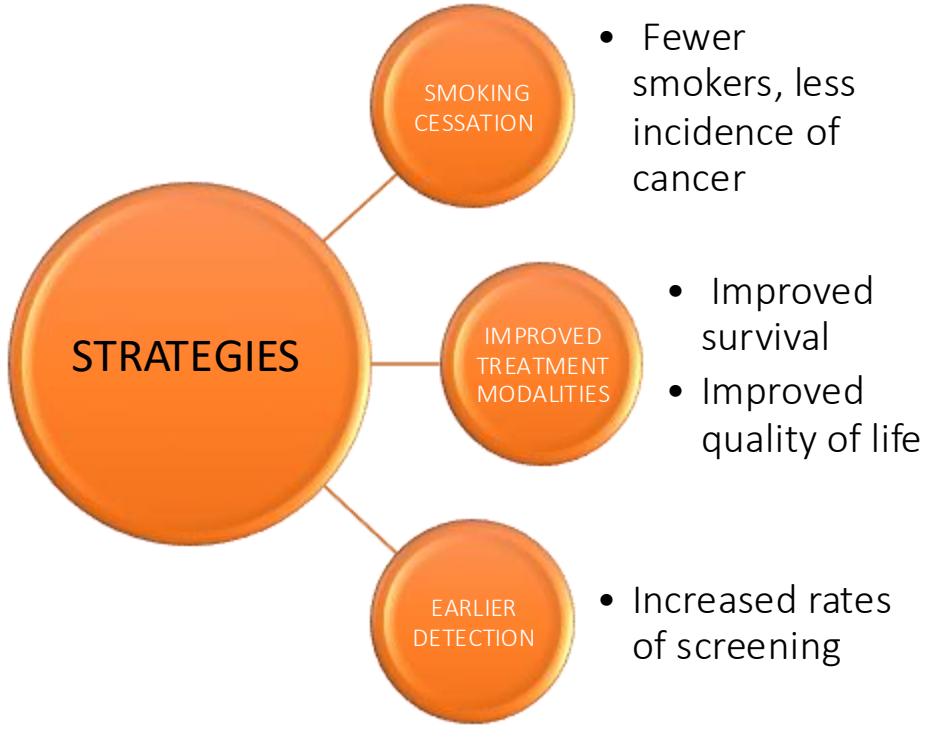


Shouldiscreen.com
Created by UMich

FIGHT AGAINST LUNG CANCER

U.S. Cancer Screening Rates





National Health Interview survey : 4% in 2015
and only ~ 6% now

President's Cancer Panel Feb 2022
Jemal et al. JAMA Oncology 2017
American Lung Association

SMOKING CESSATION

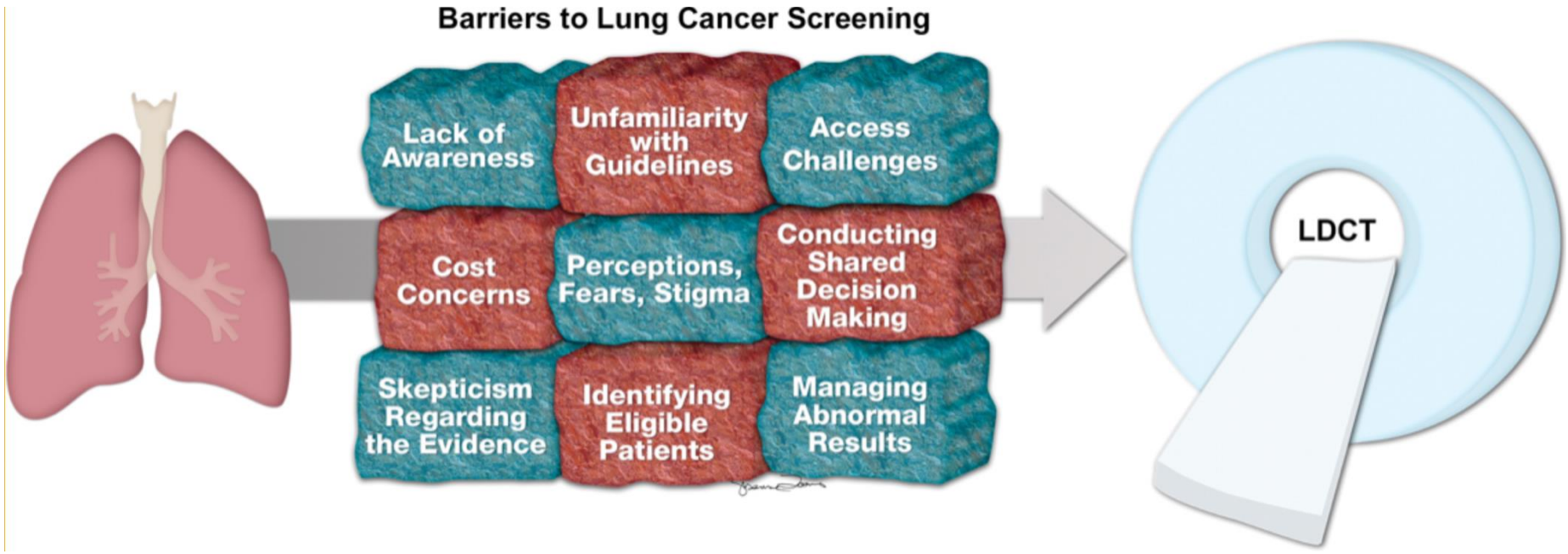
- LC screening is a **teachable moment** for smoking cessation
- Approx. 50% of patients enrolled in screening are smokers
- **20% mortality benefit after 7 years of smoking cessation – SIMILAR to that seen with LDCT screening in NLST trial !**
- Greater benefit when smoking cessation is combined with screening
- Only 12-20% of smokers are willing to quit within a month at any time
- All smokers should be offered intervention - > this improves quit rates
- Clinician training required in motivational interviewing and counseling (5As)
- SCALE (Smoking Cessation at Lung Examination) Collaboration – Multi-Institutional collaboration of 8 clinical trials – results awaited

"The question is not *whether*. The question is *how* to provide cessation services in the setting of lung cancer screening."

– **Stephanie Land**, Ph.D., Behavioral Research Program

National Cancer Institute
Ramaswamy A. Curr Pulm Reports 2022
Tanner NT et al. AJRCCM 2016

BARRIERS - for Patients and Providers



Wang et al. Radiology 2019

DISPARITIES IN SCREENING

	Disparity
Race	AA patients have a higher LC risk (15% more) - at an earlier age and with lower pack-year smoking history Lower screening rates, 18% less likely to be diagnosed early Delayed follow-up, 9% more likely to receive no treatment
Ethnicity	Hispanic and Asian Americans have lower smoking-adjusted LC risk Lower LC incidence in Alaska Native and American Indian
Gender	Women are at higher risk despite variation in smoking practices LC gets diagnosed at a younger age in women
HIV	Higher independent risk for LC (1.4- 1.7 fold)
Literacy	May not benefit equally from SDM tools, individuals who smoke tend to be less educated with less access to PCP/screening
Geography	Medicaid is state-based, few states do not cover it, and few states have no information 15-28% adults in any state have no access to a center within 30 min Some states are better (MA-16%) than others (NV 1%) in LC screening
Smoking behavior	Differences in behavior changes the risk - Lighter smokers (lower intensity) vs former heavy smokers (higher lifetime risk of LC)

Existing screening guidelines DO NOT consider disparities such as gender, race, ethnicity, socioeconomic status

Rivera MP et al. AJRCCM 2020
Aldrich MC. JAMA Oncol 2019
American Lung Association

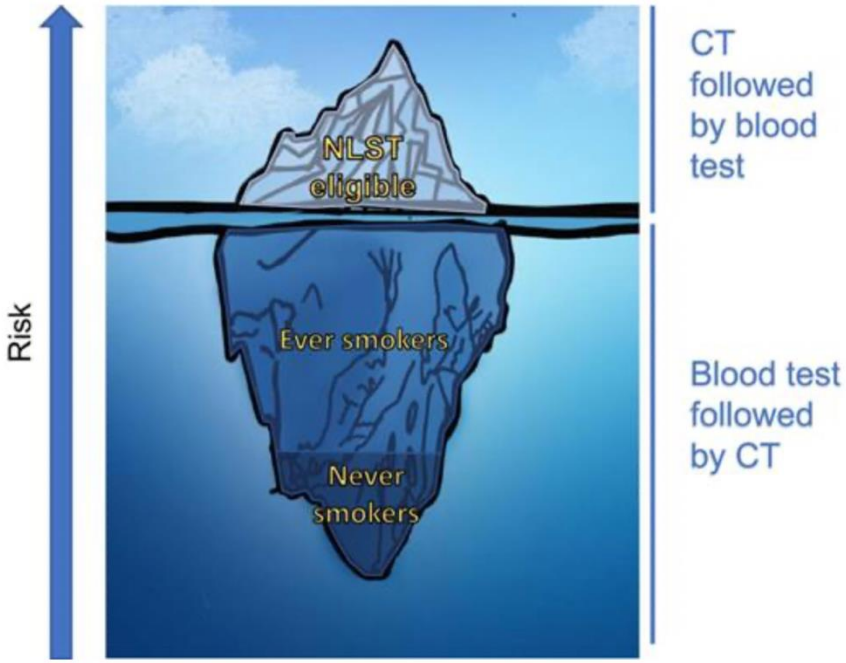
> Chest. 2023 Jul;164(1):241-251. doi: 10.1016/j.chest.2023.02.003. Epub 2023 Feb 10.

Outcomes From More Than 1 Million People Screened for Lung Cancer With Low-Dose CT Imaging

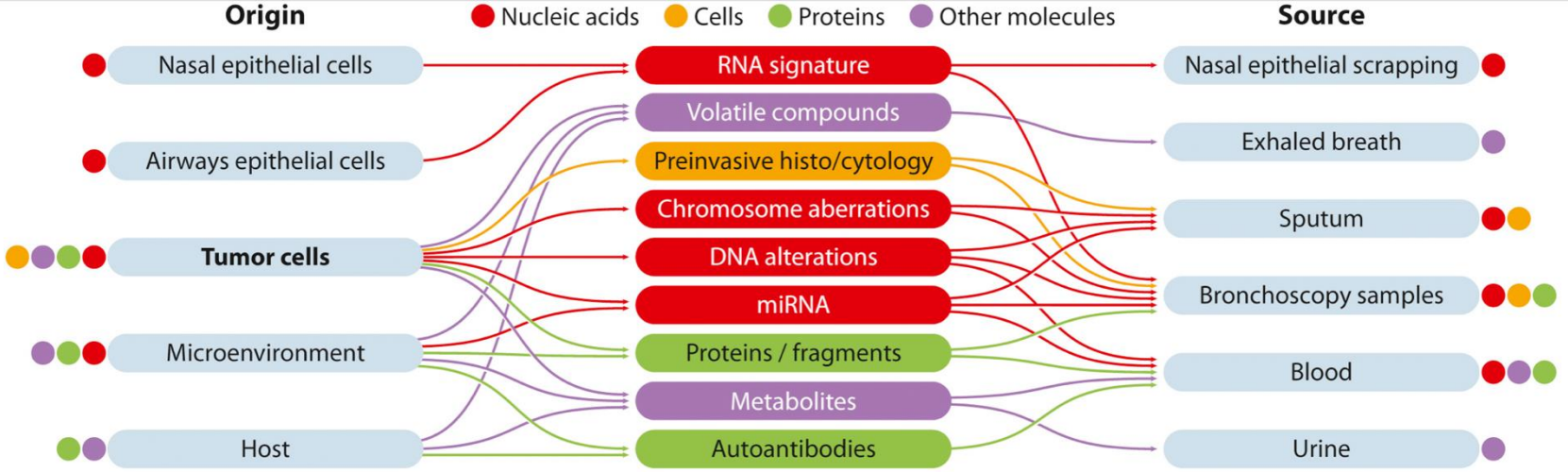
- Cohort study evaluating first 1 million people after screening
- 82.6% - > negative results, 17.3% --> positive results
- Overall cancer detection was 0.56%
- **Significant stage shift towards early lung cancers was noted -->** 53.5% were diagnosed with Stage 1, 14.3% diagnosed as Stage 4
- **Low adherence of 22.3% to annual screening**
- Predictors of poor adherence :
  - -Current smoking status
  - -Hispanic or Black race
  - -Lower education
  - -Lack of insurance

Silvestri et al. CHEST 2023

BIOMARKERS



EarlyCDT-Lung (7 AutoAb panel)
Nodify XL2 (blood protein panel)
Percepta (genomic classifier)



Only 27% LCs would be detected if ALL eligible people undergo screening

73% of LCs occur in patients ineligible for screening

Biomarkers in high risk people DECREASE false positives and in lower risk people, can identify patients at higher risk who may benefit from screening

Seijo et al. JTO 2019
Ostrin et al. CEBP 2020

SUMMARY - 1

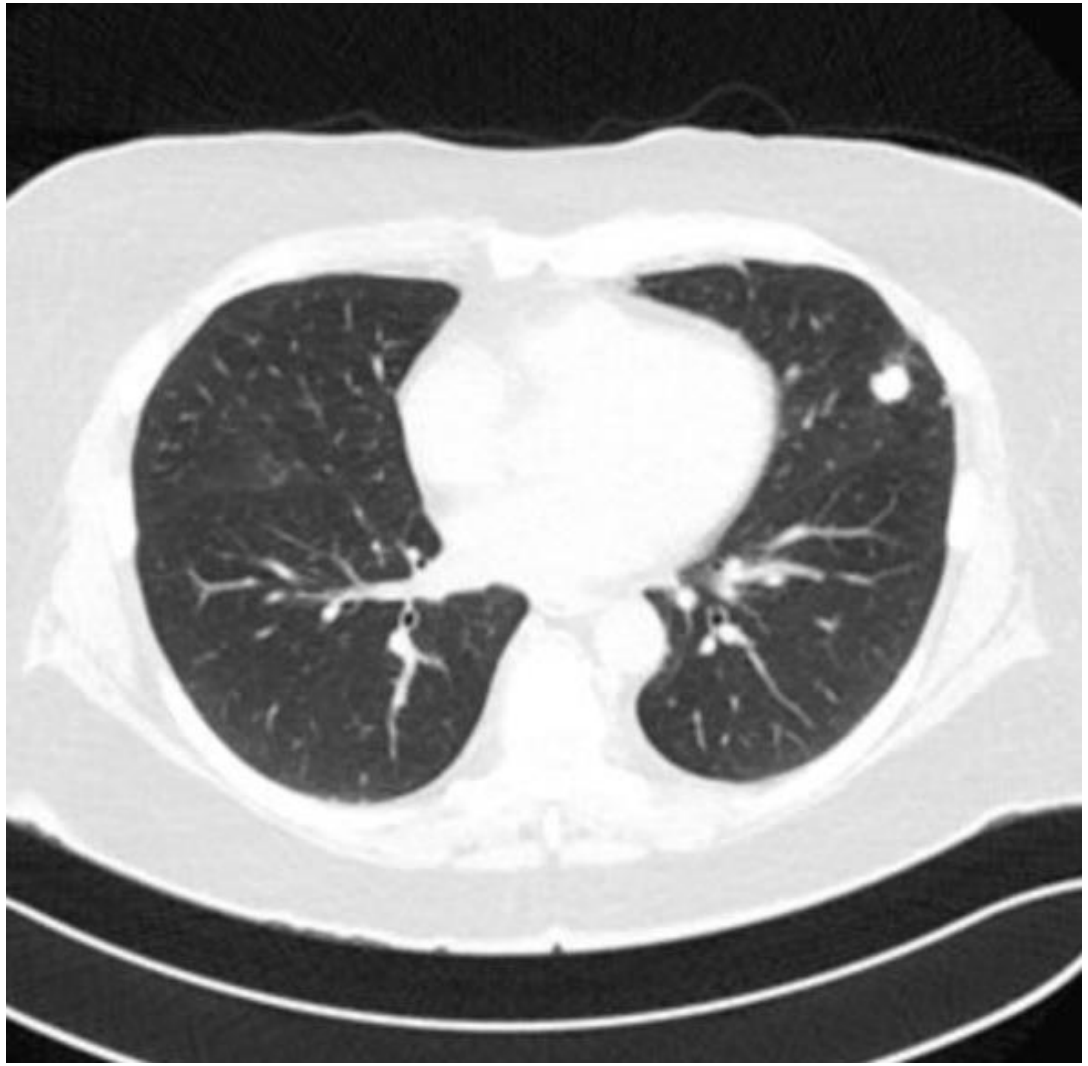
- Lung cancer screening with LDCT improves mortality
- Screening is recommended for select patients meeting criteria and at a center with an infrastructure supporting a screening program
- Smoking cessation counseling is a key component of a lung cancer screening program
- We need better strategies for overcoming several barriers and disparities in LC screening, and improving poor adherence rates

QUESTION #1

A 66 year old asymptomatic smoker of 1 pack per day for the past 45 years with a history of severe congestive heart failure should be counseled on the importance of smoking cessation and :

A. Should not be considered for lung cancer screening
B. Undergo a yearly CT Scan of the chest
C. Undergo an initial chest-xray and sputum cytology
D. Screening could be considered, but may not be advisable based on potential, severe, life-limiting comorbidities
E. Undergo an initial regular, diagnostic CT scan of the chest

APPROACH TO THE LUNG NODULE : DIAGNOSIS AND STAGING



QUESTIONS :

1. What are the nodule characteristics that indicate a malignant risk ?
2. What are the imaging guidelines for follow-up ?
3. When would you choose to biopsy a nodule and what are the different techniques ?
4. When should you consider staging the mediastinum if there is a peripheral lesion ?
5. What are the different staging modalities available ?

DIFFERENTIALS OF A SOLITARY PULMONARY NODULE

• Infectious disease Tuberculosis (tuberculoma) Round pneumonia Lung abscess Fungal disease Parasitic disease Atypical mycobacteria Nocardia *Pneumocystis jiroveci* Measles Septic embolus	• Benign tumor Hamartoma Chondroma Fibroma Neurofibroma Schwannoma Lipoma Sclerosing hemangioma Plasma cell granuloma Endometriosis	• Malignant tumor Lung cancer Pulmonary carcinoid Solitary metastasis Teratoma Leiomyoma
• Inflammatory disease Organizing pneumonia Rheumatoid arthritis Granulomatosis with polyangiitis Microscopic polyangiitis Sarcoidosis	• Vascular origin Arteriovenous malformation Pulmonary infarct Pulmonary artery aneurysm Pulmonary venous varix Hematoma	• Lymphatic origin Intrapulmonary or subpleural lymph node Lymphoma
• Miscellaneous Rounded atelectasis Lipoid pneumonia Amyloidosis Mucoid impaction Infected bulla Pulmonary scar Pleural thickening, mass or fluid (pseudotumor)	• Congenital malformation Bronchogenic cyst Lung sequestration Bronchial atresia with mucoid impaction	

PATIENT CHARACTERISTICS (HISTORIC)

- Age/demographics
- Smoking
- Other exposure, i.e. asbestos, radon, passive smoke, pollution (coal)
- Family history
- History of other malignancy

NODULE CHARACTERISTICS - KEY CONSIDERATIONS

- Nodule vs Mass
- Solid vs semisolid vs ground glass
- Single vs Multiple
- Central vs Peripheral
- Presence of intrathoracic lymphadenopathy or extrathoracic lesions

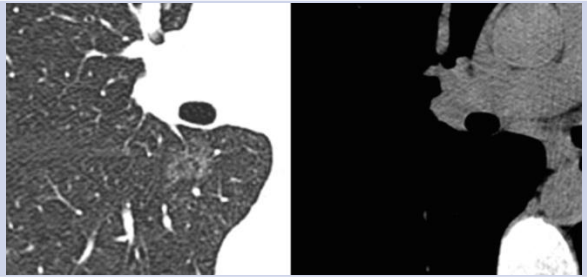
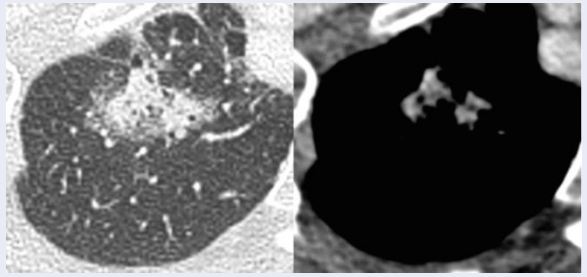
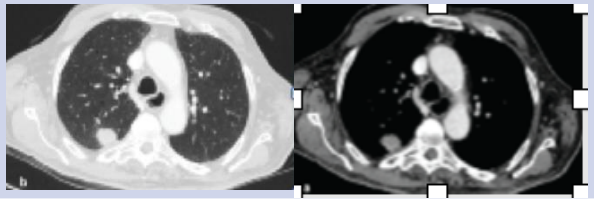
SIZE

- NODULE < 3cm
- MASS > 3cm in largest diameter
- “Conventional” Bronchoscopy
  - Brush/EBBx/TBBx without EBUS/EMN

Size	Prevalence of Malignancy	Yield of Conventional Bronchoscopy
< 0.5cm	0-1%	~ 34%
0.5-1.0 cm	6-28%	
1-2 cm	33-64%	
> 2 cm	64% - 82%	Up to 63%
> 3 cm	93-97%	

Rivera Chest 2013
Ha et al Cleveland MedEd 2014
Ost Fishman’s Pulm Diseases 5 e

NODULE CHARACTERISTICS

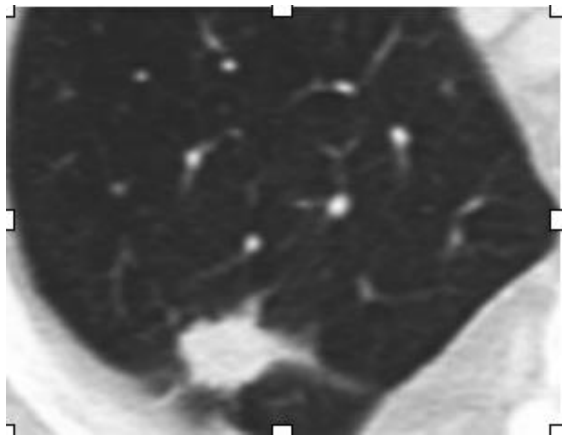
Attenuation	Imaging	Risk of malignancy
GGO		< 0.5 cm : AAH 0.5cm – 3cm : AIS
PART-SOLID		Specificity for invasiveness : 86-96%
SOLID		Risk based on size

AAH –Atypical Adenomatous Hyperplasia

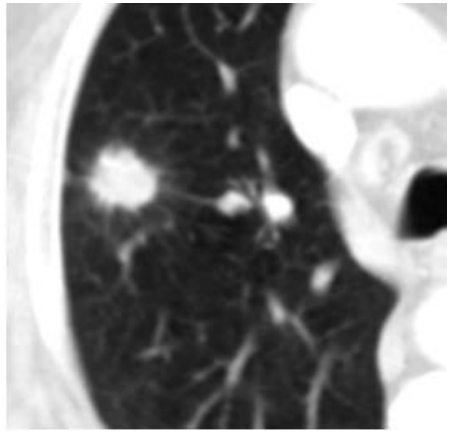
AIS – Adenoca In situ

Revel Radiology 2018
Cardinale IJCCR 2016

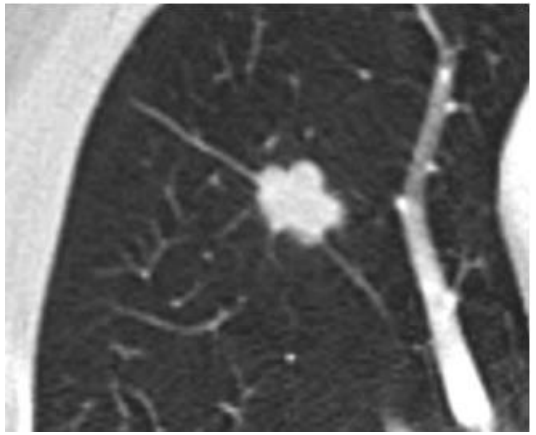
BORDERS



Irregular

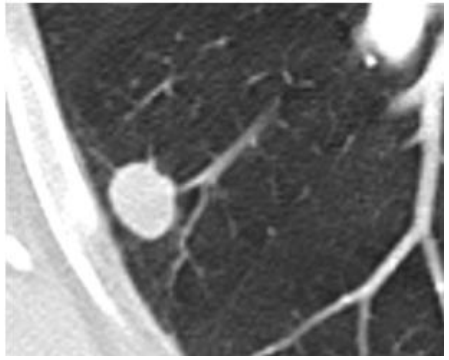


Spiculated



Lobulated

MALIGNANT

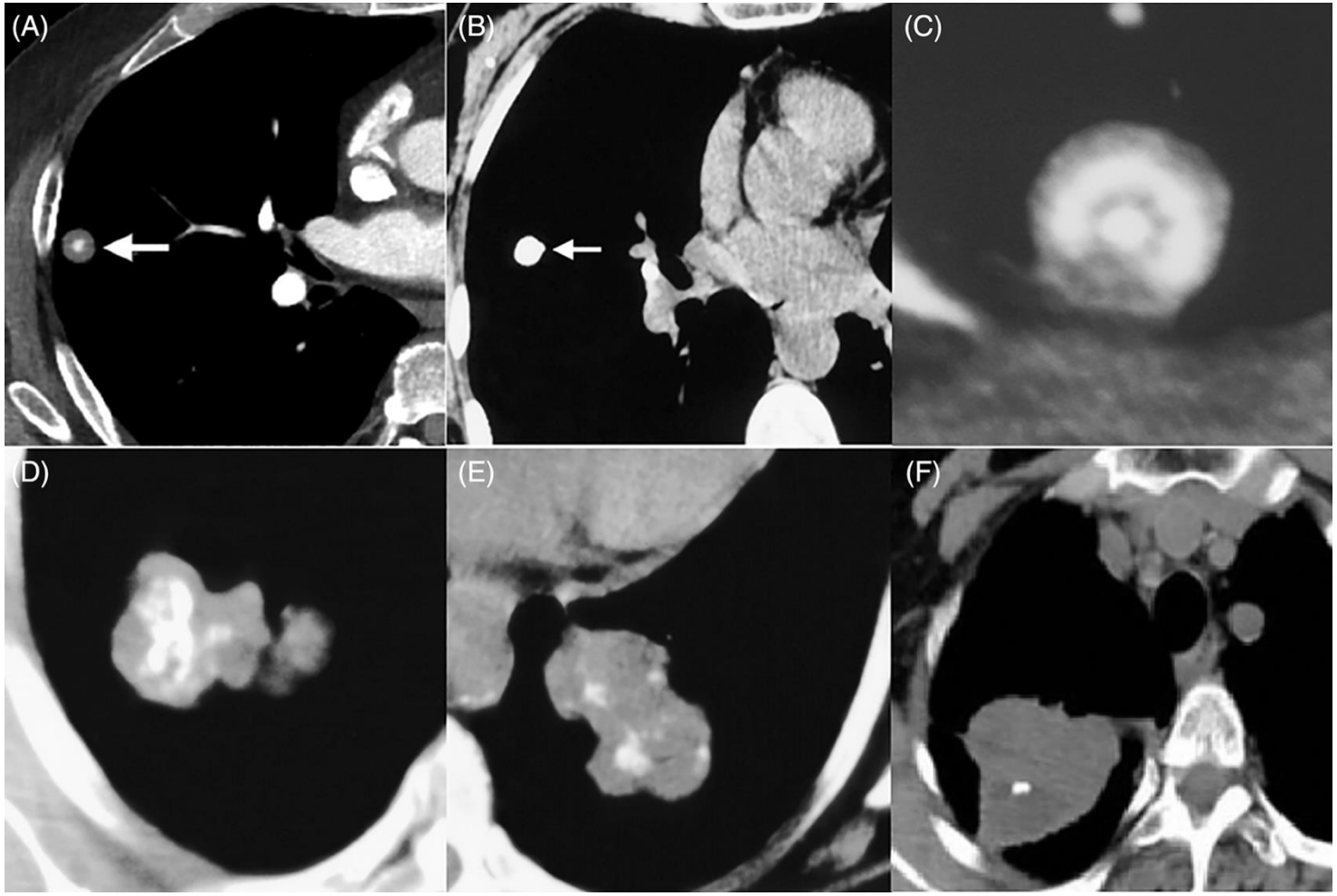


Smooth, well-defined

BENIGN

Choromanska Pol J Rad 2012
Ost AJRCCM 2012

CALCIFICATION

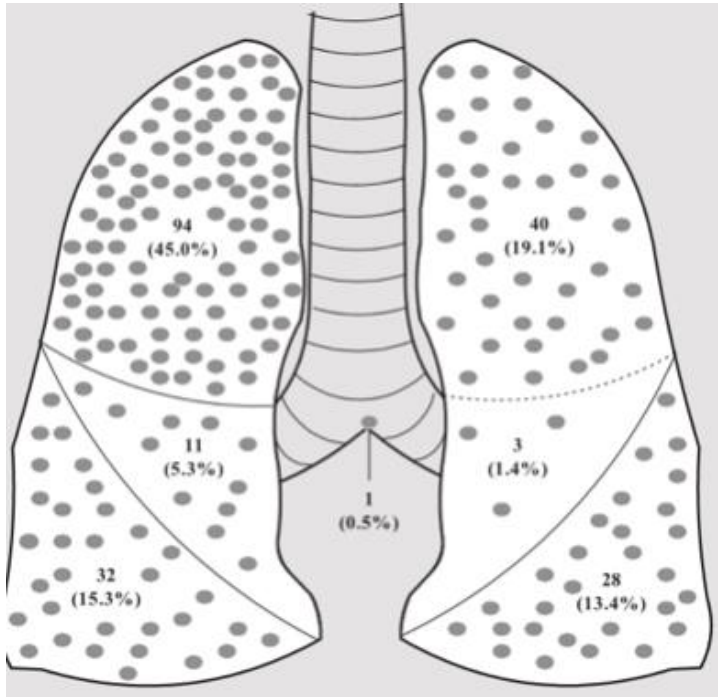


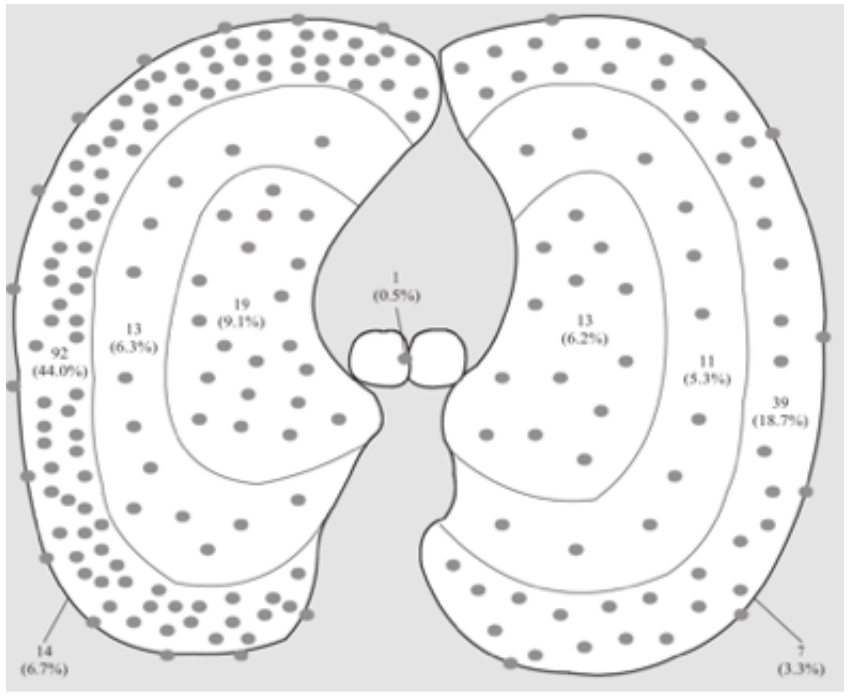
A) Central or "bull's eye" - benign granuloma
B) Diffuse pattern – benign granuloma
C) Laminated pattern – benign granuloma
D) Popcorn – pulmonary hamartoma
E) Scattered punctate – malignant carcinoid
F) Eccentric – primary lung adenocarcinoma

Cruickshank et al. Int Med J 2019

LOCATION: What is peripheral vs central?

NELSON trial : 15,822 participants
- 62% in the periphery (outer 1/3rd)
- RUL predominance (45%)





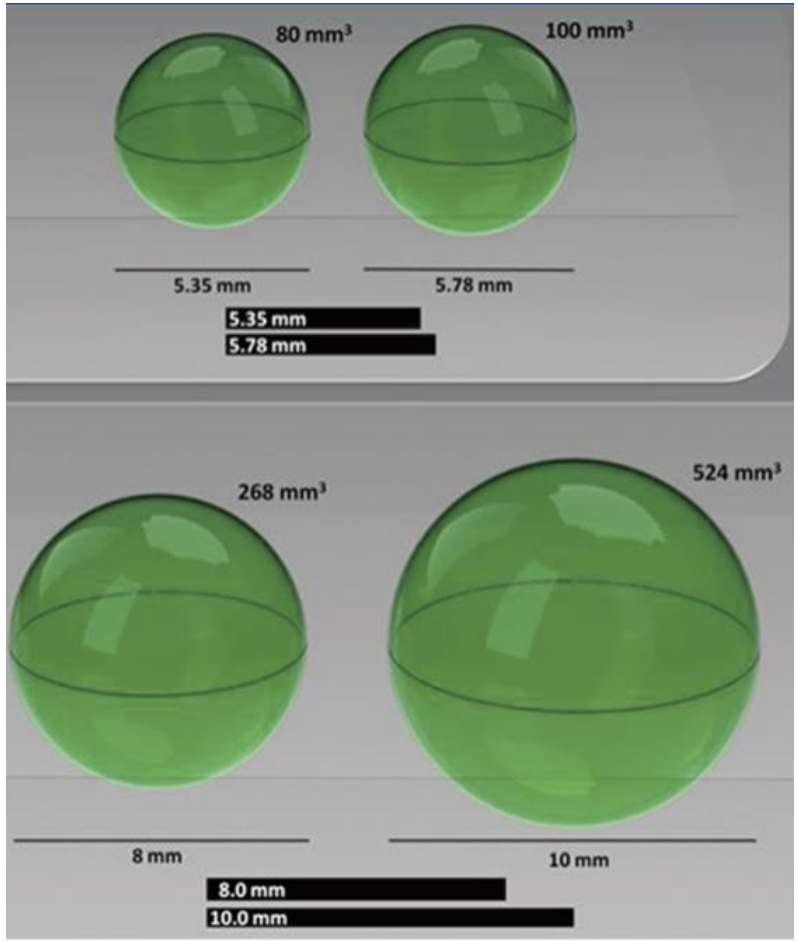
Horeweg AJRCCM 2013

GROWTH

Volume Doubling Time – 25% increase in diameter

DT < 20 days or > 400 days are less likely to be malignant

$$V = \tfrac{4}{3}\pi r^3$$



Field , Trans Lung Canc Res 2017

PROBABILITY OF MALIGNANCY

Low (<5%)	Intermediate (5-65%)	High (>65%)
Young		Older
Less smoking		Heavy smoking
No prior cancer	Mixture of low and high	Prior cancer
Smaller nodule size	probability features	Larger size
Regular margins		Irregular/spiculated margins
Non-upper lobe location		Upper lobe location

An old chest imaging study may provide crucial information related to the age of the lesion and the likelihood of benignity or malignancy

Gould Chest 2013

RISK PREDICTION MODELS

Brock University Cancer Prediction Equation

$$Logodds = (0.0287 * (Age - 62)) + Sex + FamilyHistoryLungCa + Emphysema - (5.3854 * ((Nodulesize/10)^{-0.5} - 1.58113883)) + Noduletype + NoduleUpperLung - (0.0824 * (Nodulecount - 4)) + Spiculation - 6.7892$$

$$Cancerprobability = 100 * (e^{(Logodds)} / (1 + e^{(Logodds)}))$$

Input:

Age		years
Sex	○ Female (0.6011)	
	○ Male (0)	
Family history of lung cancer	☐ (0.2961)	
Emphysema	☐ (0.2953)	
Nodule size		mm
Nodule type	○ Nonsolid or ground-glass (-0.1276)	
	○ Partially solid (0.377)	
	○ Solid (0)	
Nodule in upper lung	☐ (0.6581)	
Nodule count		#
Spiculation	☐ (0.7729)	

Brock and Mayo clinic models were compared

Approximately 10% of nodules > 8mm are lung cancers, with greater size and current smoking being important predictors.

Existing prediction models have acceptable accuracy, but seem to overestimate the probability of cancer

McWilliams NEJM 2013
Vachani CHEST 2022

LUNG-RADS v2022

(Screen Associated Nodules)

Lung-RADS	Category Descriptor	Findings	Management
0	**Incomplete** Estimated Population Prevalence: ~ 1%	Prior chest CT examination being located for comparison (see note 9)	Comparison to prior chest CT;
		Part or all oflungs cannot be evaluated	Additional lung cancer screening CT imaging needed;
		Findings suggestive of an inflammatory or infectious process (see note 10)	1-3 month LDCT
1	**Negative** Estimated Population Prevalence: 39%	**No lung nodules OR**	12-month screening LDCT
		Nodule with benign features: • Complete, central, popcorn, or concentric ring calcifications **OR** • Fat-containing	
2	**Benign** - Based on imaging features or indolent behavior Estimated Population Prevalence: 45%	**Juxtapleural nodule:** • < 10 mm (524 mm^3) mean diameter at baseline or new **AND** • Solid; smooth margins; and oval, lentiform, or triangular shape	
		Solid nodule: • < 6 mm (< 113 mm^3) at baseline **OR** • New < 4 mm (< 34 mm^3)	
		Part solid nodule: • < 6 mm total mean diameter (< 113 mm^3) at baseline	
		Non solid nodule (GGN): • < 30 mm (< 14,137 mm^3) at baseline, new, or growing **OR** • ≥ 30 mm (≥ 14,137 mm^3) stable or slowly growing (see note 7)	
		Airway nodule, subsegmental - at baseline, new, or stable (see note 11)	
		Category 3 lesion that is stable or decreased in size at 6-month follow-up CT **OR** Category 4B lesion proven to be benign in etiology following appropriate diagnostic workup	
3	**Probably Benign** - Based on imaging features or behavior Estimated Population Prevalence: 9%	**Solid nodule:** • ≥ 6 to < 8 mm (≥ 113 to < 268 mm^3) at baseline **OR** • New 4 mm to < 6 mm (34 to < 113 mm^3)	6-month LDCT
		Part solid nodule: • ≥ 6 mm total mean diameter (≥ 113 mm^3) with solid component < 6 mm (< 113 mm^3) at baseline **OR** • New < 6 mm total mean diameter (< 113 mm^3)	
		Non solid nodule (GGN): • ≥ 30 mm (≥ 14,137 mm^3) at baseline or new	
		Atypical pulmonary cyst: (see note 12) • Growing cystic component (mean diameter) of a thick-walled cyst	
		Category 4A lesion that is stable or decreased in size at 3-month follow-up CT (excluding airway nodules)	
4A	**Suspicious** Estimated Population Prevalence: 4%	**Solid nodule:** • ≥ 8 to < 15 mm (≥ 268 to < 1,767 mm^3) at baseline **OR** • Growing < 8 mm (< 268 mm^3) **OR** • New 6 to < 8 mm (113 to < 268 mm^3)	3-month LDCT; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm^3) solid nodule or solid component
		Part solid nodule: • ≥ 6 mm total mean diameter (≥ 113 mm^3) with solid component ≥ 6 mm to < 8 mm (≥ 113 to < 268 mm^3) at baseline **OR** • New or growing < 4 mm (< 34 mm^3) solid component	
		Airway nodule, segmental or more proximal - at baseline (see note 11)	
		Atypical pulmonary cyst: (see note 12) • Thick-walled cyst **OR** • Multilocular cyst at baseline **OR** • Thin- or thick-walled cyst that becomes multilocular	
4B	**Very Suspicious** Estimated Population Prevalence: 2%	**Airway nodule**, segmental or more proximal - stable or growing (see note 11)	Referral for further clinical evaluation
		Solid nodule: • ≥ 15 mm (≥ 1767 mm^3) at baseline **OR** • New or growing ≥ 8 mm (≥ 268 mm^3)	Diagnostic chest CT with or without contrast; PET/CT may be considered if there is a ≥ 8 mm (≥ 268 mm^3) solid nodule or solid component; tissue sampling; and/or referral for further clinical evaluation Management depends on clinical evaluation, patient preference, and the probability of malignancy (see note 13)
		Part solid nodule: • Solid component ≥ 8 mm (≥ 268 mm^3) at baseline **OR** • New or growing ≥ 4 mm (≥ 34 mm^3) solid component	
		Atypical pulmonary cyst: (see note 12) • Thick-walled cyst with growing wall thickness/nodularity **OR** • Growing multilocular cyst (mean diameter) **OR** • Multilocular cyst with increased loculation or new/increased opacity (nodular, ground glass, or consolidation)	
		Slow growing solid or part solid nodule that demonstrates growth over multiple screening exams (see note 8)	
4X	Estimated Population Prevalence: < 1%	Category 3 or 4 nodules with additional features or imaging findings that increase suspicion for lung cancer (see note 14)	
S	**Significant or Potentially Significant** Estimated Population Prevalence: 10%	**Modifier:** May add to category 0-4 for clinically significant or potentially clinically significant findings unrelated to lung cancer (see note 15)	As appropriate to the specific finding

Developed by American College of Radiology

Positive screen >/= 6mm

American College of Radiology Nov 2022

FLEISCHNER SOCIETY GUIDELINES 2017
SOLID nodule(s)

A: Solid Nodules*

Nodule Type	Size: <6 mm (<100 mm³)	Size: 6–8 mm (100–250 mm³)	Size: >8 mm (>250 mm³)	Comments
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).
Multiple				
Low risk†	No routine follow-up	CT at 3–6 months, then consider CT at 18–24 months	CT at 3–6 months, then consider CT at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).
High risk†	Optional CT at 12 months	CT at 3–6 months, then at 18–24 months	CT at 3–6 months, then at 18–24 months	Use most suspicious nodule as guide to management. Follow-up intervals may vary according to size and risk (recommendation 2A).

McMahon et al. Radiology 2017

FLEISCHNER SOCIETY GUIDELINES 2017
SUBSOLID (Semisolid) nodule(s)

B: Subsolid Nodules*

Table 1

Nodule Type	Size		Comments
	<6 mm (<100 mm³)	≥6 mm (>100 mm³)	
Single			
Ground glass	No routine follow-up	CT at 6–12 months to confirm persistence, then CT every 2 years until 5 years	In certain suspicious nodules < 6 mm, consider follow-up at 2 and 4 years. If solid component(s) or growth develops, consider resection. (Recommendations 3A and 4A).
Part solid	No routine follow-up	CT at 3–6 months to confirm persistence. If unchanged and solid component remains <6 mm, annual CT should be performed for 5 years.	In practice, part-solid nodules cannot be defined as such until ≥6 mm, and nodules <6 mm do not usually require follow-up. Persistent part-solid nodules with solid components ≥6 mm should be considered highly suspicious (recommendations 4A-4C)
Multiple	CT at 3–6 months. If stable, consider CT at 2 and 4 years.	CT at 3–6 months. Subsequent management based on the most suspicious nodule(s).	Multiple <6 mm pure ground-glass nodules are usually benign, but consider follow-up in selected patients at high risk at 2 and 4 years (recommendation 5A).

McMahon et al. Radiology 2017

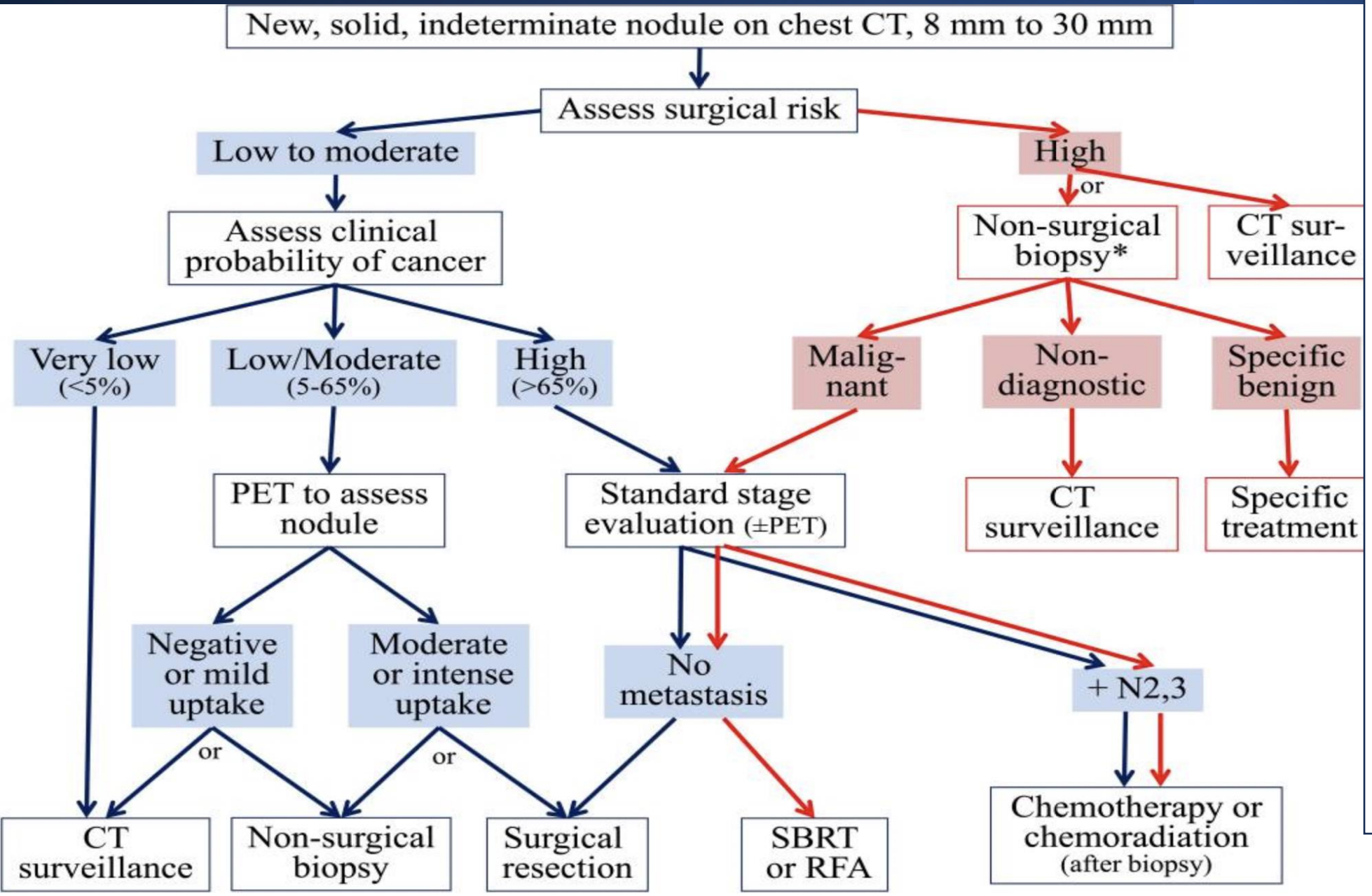
SUMMARY - 2

- Risk of malignancy increases with size of nodule, >6mm solid component, upper lobe location, spiculated borders and number up to 4 nodules

- Part-solid GGOs have a higher risk of malignancy than pure GGOs

- Evaluation of a pulmonary nodule is based on risk of malignancy and patient's characteristics and preferences for diagnosis/intervention

MANAGEMENT ALGORITHM



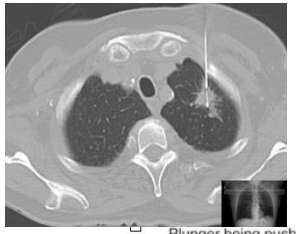
1. Radiology
2. Surgical risk
3. Probability of cancer, consider biopsy
4. Additional imaging
5. Intervention

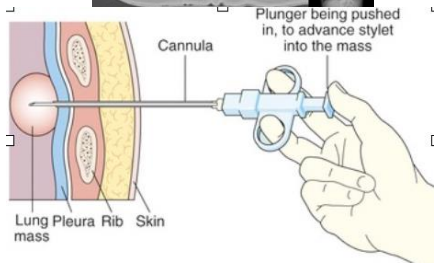
CHEST guidelines 2013

BIOPSY OF A PERIPHERAL NODULE

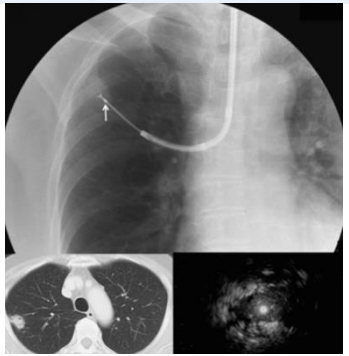
WHEN ?

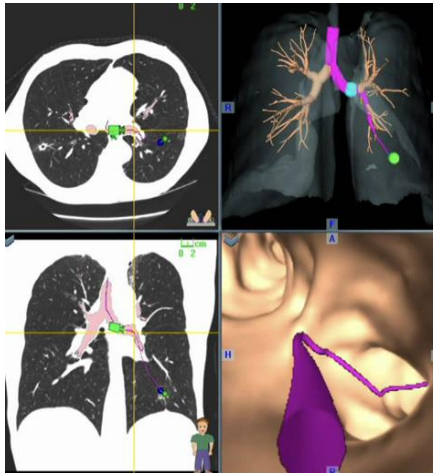
- Discordant pretest probability and imaging
- Probability of malignancy is low to moderate (~ 10% to 60%)
- High surgical risk
- Suspected benign diagnosis requiring specific treatment
- Patient preference





TECHNIQUES





ROBOTIC BRONCHOSCOPY

PRECISION-1 TRIAL – 60 procedures with mean nodule size 16.5 +/- 1.5mm - yield was greatest for robotic bronchoscopy compared to other technique (radial endobronchial ultrasound and electromagnetic navigation)

Localization, Puncture, and Successful Navigation Study Outcomes

Study Arm	No.	Study Outcomes		
		Localization and Puncture (Primary End Point)[a]	Localization and Puncture (Secondary End Point)[b]	Successful Navigation
		% (No.)	% (No.)	% (No.)
UTB-rEBUS	20	25 (5)	35 (7)	65 (13)
EMN	20	45 (9)	65 (13)	85 (17)
RB	20	80 (16)	90 (18)	100 (20)

Yarmus et al CHEST 2020

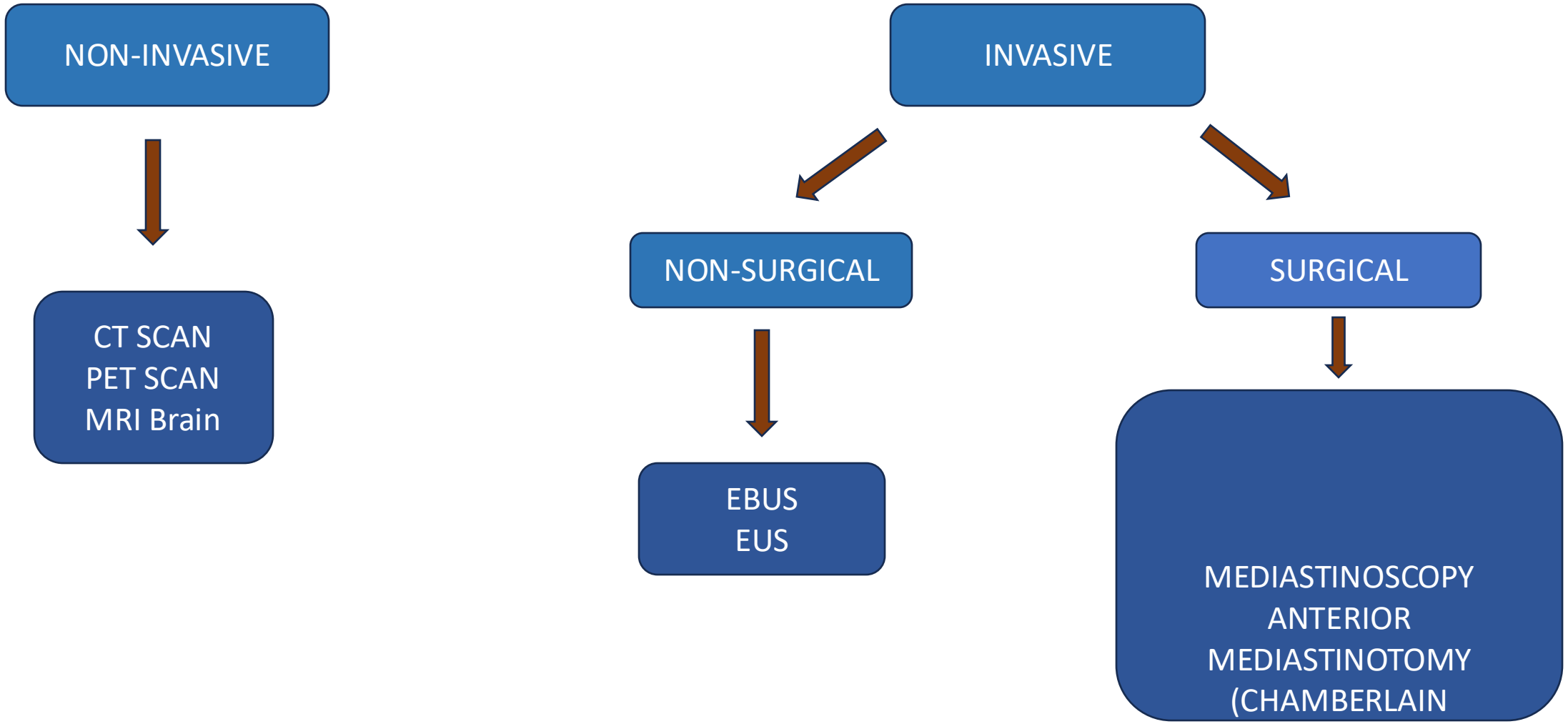
ROBOTIC BRONCHOSCOPY

Review/summary :

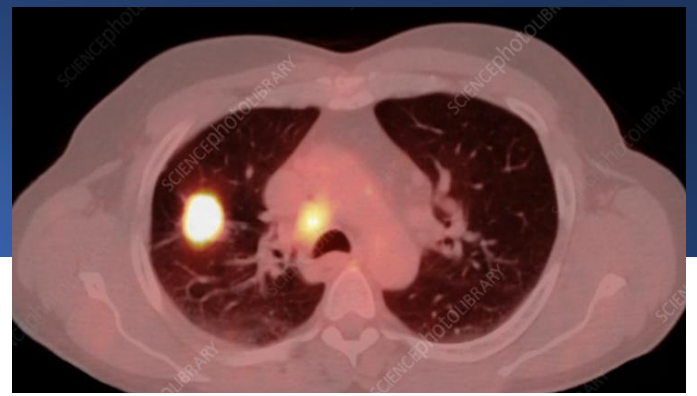
- Size of the lesion predicts diagnostic accuracy, several studies had mean diameter of < 2cm
- Nodule localization rates 85-96.6%
- Diagnostic yield ranges from 69-79%, this has increased to 86-94% with use of advanced fluoroscopy systems or cone beam CT imaging
- Overall pneumothorax rate 0-5.8%, ½ requiring chest tube placement
- Bleeding complications 2.4-3.2%

Yarmus et al CHEST 2020
Diddams Life 2023

STAGING


NON-INVASIVE
CT SCAN
PET SCAN
MRI Brain
INVASIVE
NON-SURGICAL
EBUS
EUS
SURGICAL
MEDIASTINOSCOPY
ANTERIOR
MEDIASTINOTOMY
(CHAMBERLAIN

IMAGING



PET SCAN :

- Recommended for non-invasive staging of the mediastinum
- Sensitivity 80-90%, specificity 88-90%, PPV 50%, NPV 87-98%
- Greater accuracy than CT
- High rate of false positives (inflammatory process, infectious disease)
- Low sensitivity for lesions < 1cm (lower metabolic activity in small nodules, lower grade cancers)
- Strongly recommended in clinical stage 1B to 3B, with intention of curative treatment
- In clinical stage 1A, PET is considered adequate for staging, when the intent is curative treatment

MRI Brain, CT Abdomen – looking for distant M disease

Stamatis G ERJ 2015

INVASIVE STAGING RECOMMENDATIONS

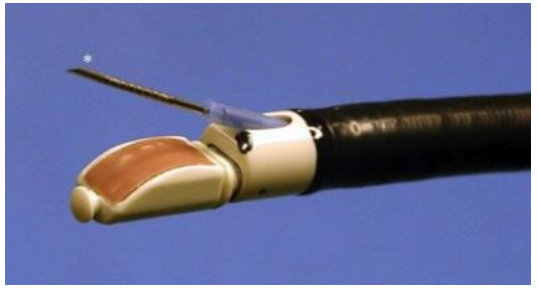
ACCP Guidelines 2013 -

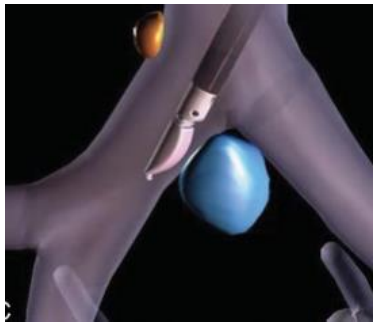
- Suspected N1 nodes --> In 30% of patients with N1 disease, involved N2 or N3 nodes were found (Grade 1C)

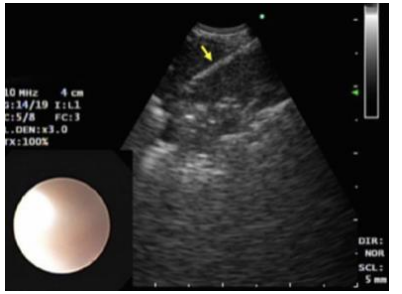
- Tumors > 3cm

- Centrally located tumors --> in these tumors without suspected nodes on CT or PET , pathologic N2 disease was noted to be as high as 22% (Grade 1C)

- If high suspicion of N2 or N3 involvement (LN enlargement or PET uptake) and no distant mets, a needle technique is recommended over surgical staging as a best first test (Grade 2B)







Staging EBUS samples nodes from N3 --> N2 --> N1
Generally > 5mm

CHEST Guidelines 2013
Bhatti JOBIP 2013

NON-SMALL CELL LUNG CANCER (NSCLC) - TNM STAGING 8TH ED

T (Primary Tumor)		Label
T0	No primary tumor	
Tis	Carcinoma in situ (Squamous or Adenocarcinoma)	Tis
T1	Tumor ≤3 cm,	
T1a(mi)	Minimally Invasive Adenocarcinoma	T1a*(mi)*
T1a	Superficial spreading tumor in central airways[a]	T1a *SS*
T1a	Tumor ≤1 cm	T1a *≤1*
T1b	Tumor >1 but ≤2 cm	T1b *>1-2*
T1c	Tumor >2 but ≤3 cm	T1c *>2-3*
T2	Tumor >3 but ≤5 cm or tumor involving:	
	visceral pleura[b],	T2 *Visc Pl*
	main bronchus (not carina), atelectasis to hilum[b]	T2 *Centr*
T2a	Tumor >3 but ≤4 cm	T2a *>3-4*
T2b	Tumor >4 but ≤5 cm	T2b *>4-5*
T3	Tumor >5 but ≤7 cm	T3 *>5--7*
	or invading chest wall, pericardium, phrenic nerve	T3 *Inv*
	or separate tumor nodule(s) in the same lobe	T3 *Satell*
T4	Tumor >7 cm	T4 *>7*
	or tumor invading: mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, esophagus, spine;	T4 *Inv*
	or tumor nodule(s) in a different ipsilateral lobe	T4 *Ipsi Nod*
N (Regional Lymph Nodes)		
N0	No regional node metastasis	
N1	Metastasis in ipsilateral pulmonary or hilar nodes	
N2	Metastasis in ipsilateral mediastinal/subcarinal nodes	
N3	Metastasis in contralateral mediastinal/hilar, or supraclavicular nodes	
M (Distant Metastasis)		
M0	No distant metastasis	
M1a	Malignant pleural/pericardial effusion[c] or pleural /pericardial nodules	M1a *Pl Dissem*
	or separate tumor nodule(s) in a contralateral lobe;	M1a *Contr Nod*
M1b	Single extrathoracic metastasis	M1b *Single*
M1c	Multiple extrathoracic metastases (1 or >1 organ)	M1c *Multi*

T/M	Label	N0	N1	N2	N3
T1	T1a *≤1*	IA1	IIB	IIIA	IIIB
	T1b *>1-2*	IA2	IIB	IIIA	IIIB
	T1c *>2-3*	IA3	IIB	IIIA	IIIB
T2	T2a *Cent, Visc Pl*	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 *Inv*	IIB	IIIA	IIIB	IIIC
	T3 *Satell*	IIB	IIIA	IIIB	IIIC
T4	T4 *>7*	IIIA	IIIA	IIIB	IIIC
	T4 *Inv*	IIIA	IIIA	IIIB	IIIC
	T4 *Ipsi Nod*	IIIA	IIIA	IIIB	IIIC
M1	M1a *Contr Nod*	IVA	IVA	IVA	IVA
	M1a *Pl Dissem*	IVA	IVA	IVA	IVA
	M1b *Single*	IVA	IVA	IVA	IVA
	M1c *Multi*	IVB	IVB	IVB	IVB

CHEST 2017

SMALL CELL LUNG CANCER STAGING

• **Limited disease**: Confined to the ipsilateral hemithorax, which can be safely encompassed within a tolerable radiation field (T any, N any, M0; except T3-T4 due to multiple lung nodules that do not fit in a tolerable radiation field).
Supraclavicular lymph nodes might still be considered limited stage as long as ipsilateral and within a reasonable radiation field

• **Extensive disease**: Beyond ipsilateral hemithorax, which may include malignant pleural or pericardial effusion or hematogenous metastases
(T any, N any, M1a/b/c; T3-T4 due to multiple lung nodules that do not fit in a tolerable radiation field)

SUMMARY 3

- Lung cancer staging is critical for prognosis, treatment and even eligibility into clinical trials

- Mediastinal staging is still recommended in certain cases of a "negative" mediastinum by CT or PET

- Invasive mediastinal staging with endoscopic needle techniques (such as EBUS) is used as first line

THANK YOU !

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