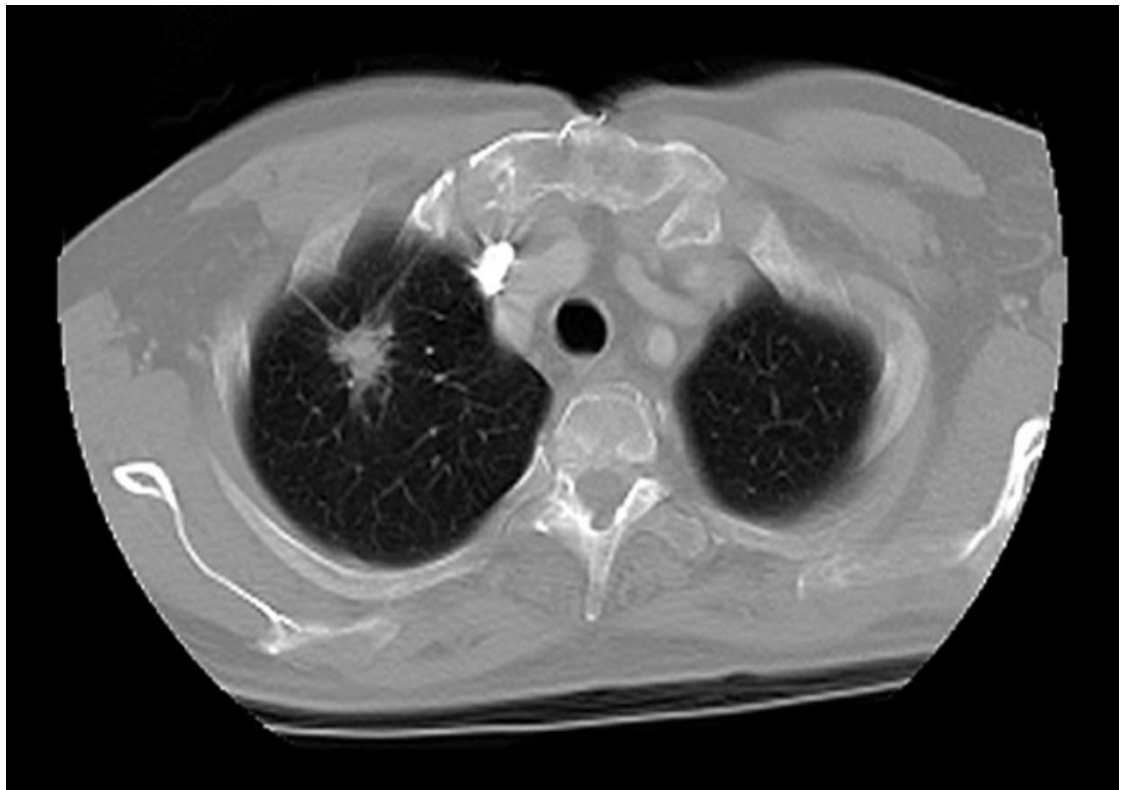


Lung cancer screening, diagnosis, and staging

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BRIGHAM AND
WOMEN'S HOSPITAL

| The Lung Center |

Disclosures/Conflicts of Interest

- None

Outline

- **Epidemiology**
- **Screening**
- **Diagnostic approach to lung nodules**
- **Lung cancer staging**

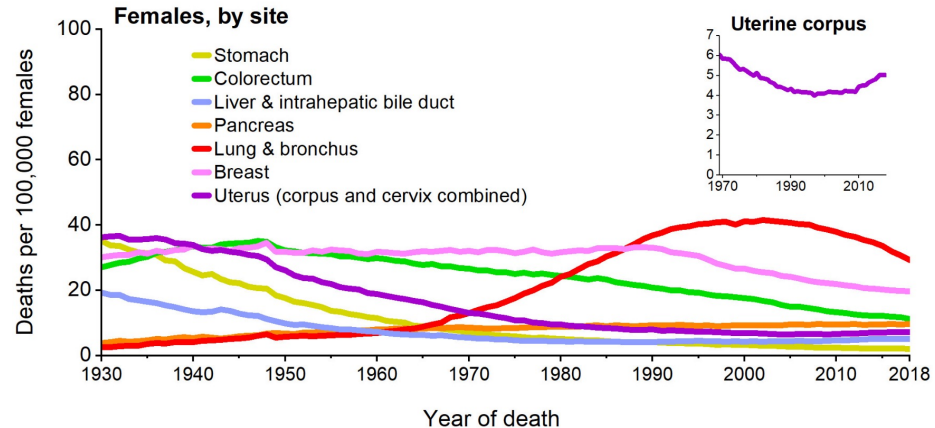
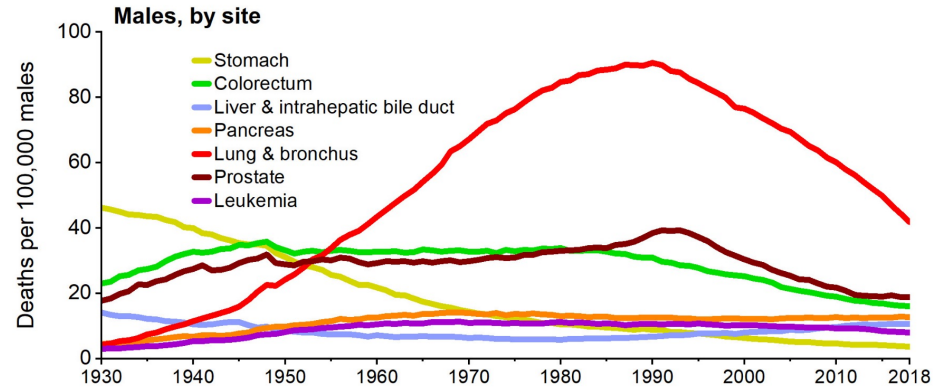
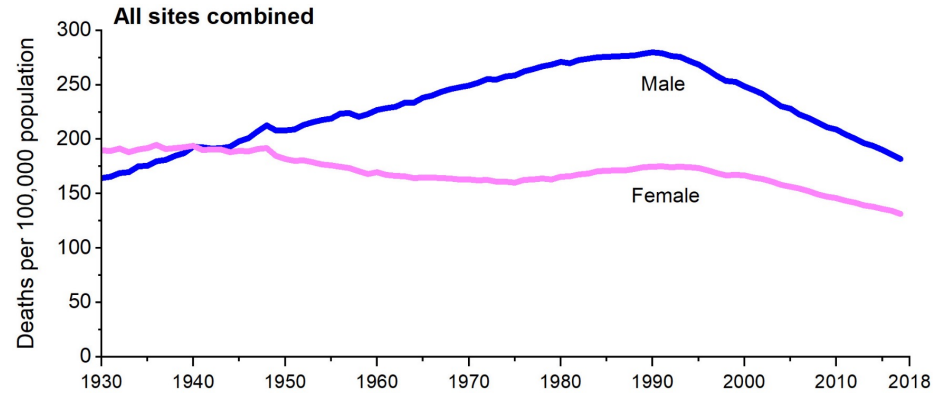
Lung Cancer 2021

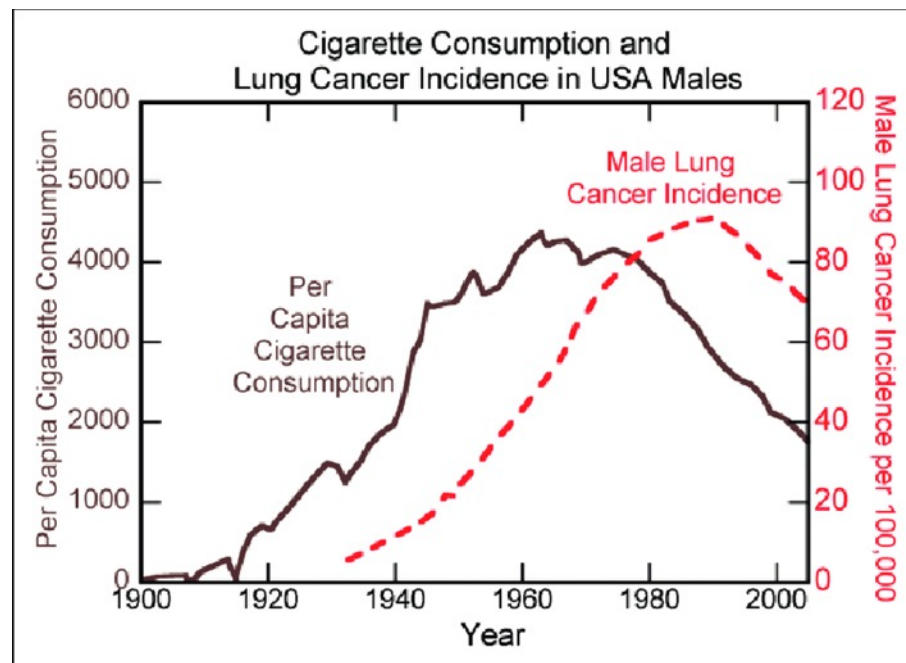
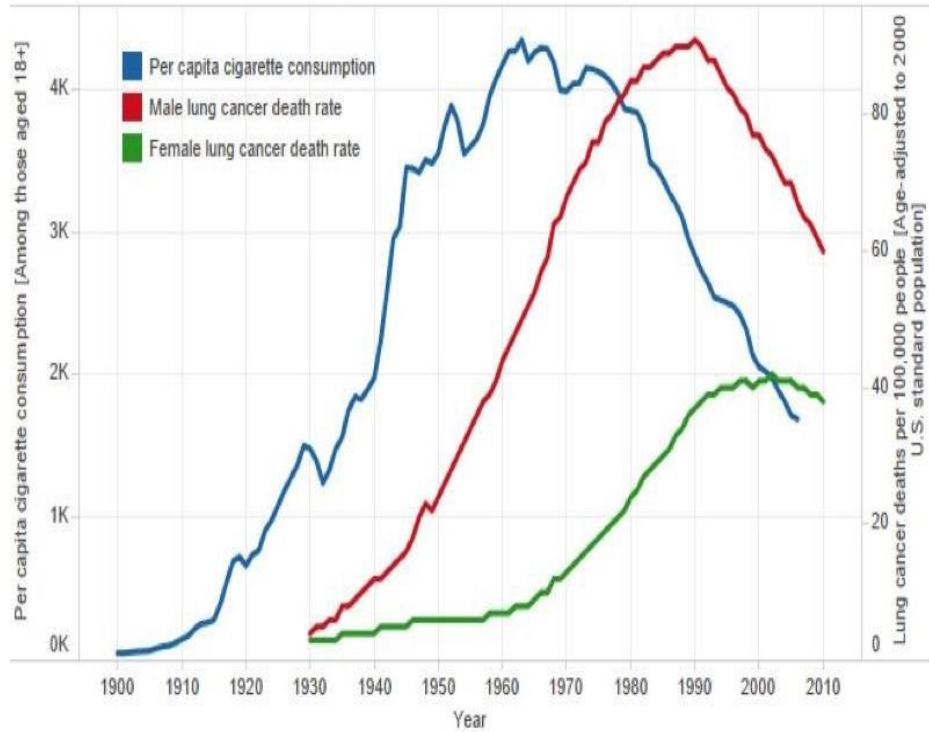
Estimated new cases: 235,760

Estimated deaths: 131,880

Note: In 2016 the estimated # of deaths: 160,340

- Increasing worldwide corresponding with increasing smoking;
- **Decreasing in men in the U.S. corresponding with decreasing smoking.**
- 85-90% believed to be caused by cigarette smoking
- High death rate related to advanced stage at diagnosis in 75% of patients





Smoking cessation works!



ORIGINAL ARTICLE

The Effect of Advances in Lung-Cancer Treatment on Population Mortality

Nadia Howlader, Ph.D., Gonçalo Forjaz, D.V.M., Meghan J. Mooradian, M.D.,
 Rafael Meza, Ph.D., Chung Yin Kong, Ph.D., Kathleen A. Cronin, Ph.D.,
 Angela B. Mariotto, Ph.D., Douglas R. Lowy, M.D., and Eric J. Feuer, Ph.D.

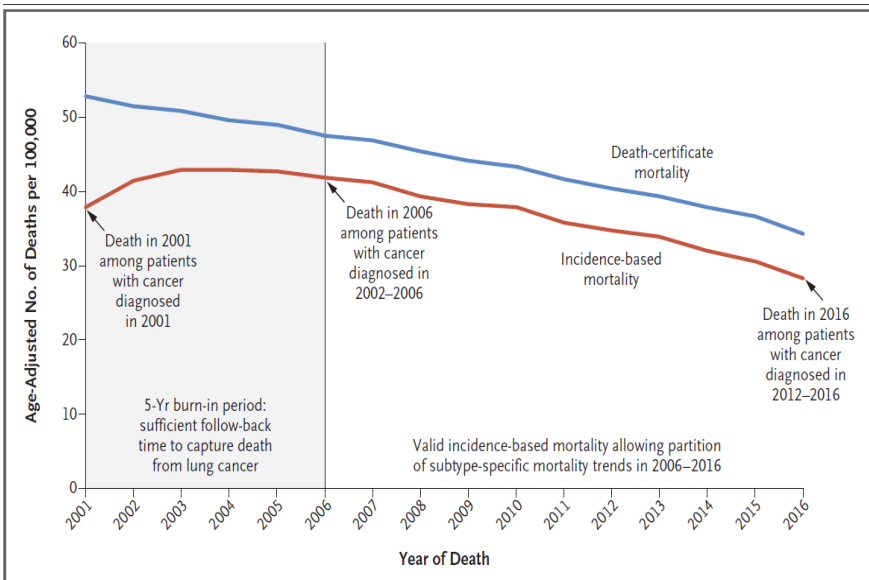


Figure 1. Mortality Estimates Based on Data from Death Certificates and on Incidence among Patients with Lung or Bronchus Cancer.

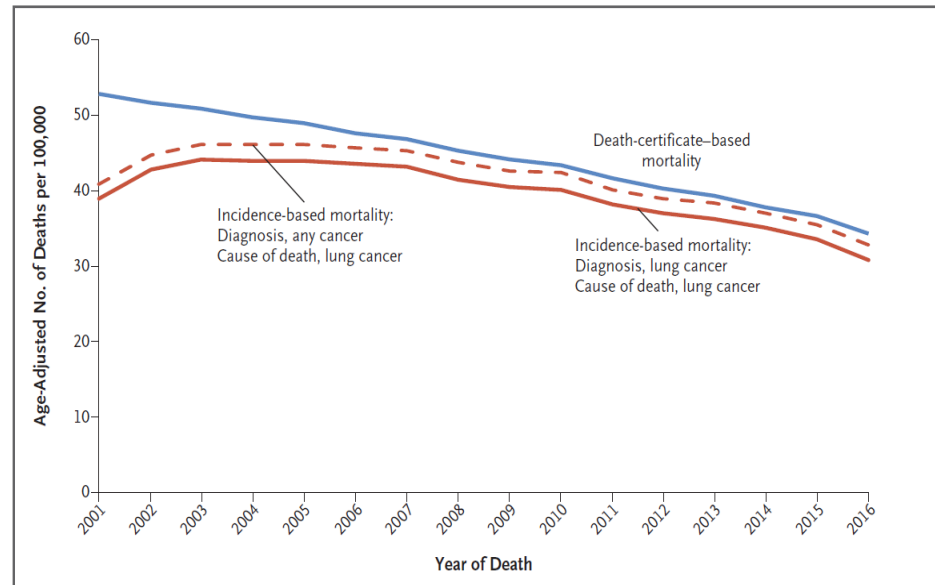
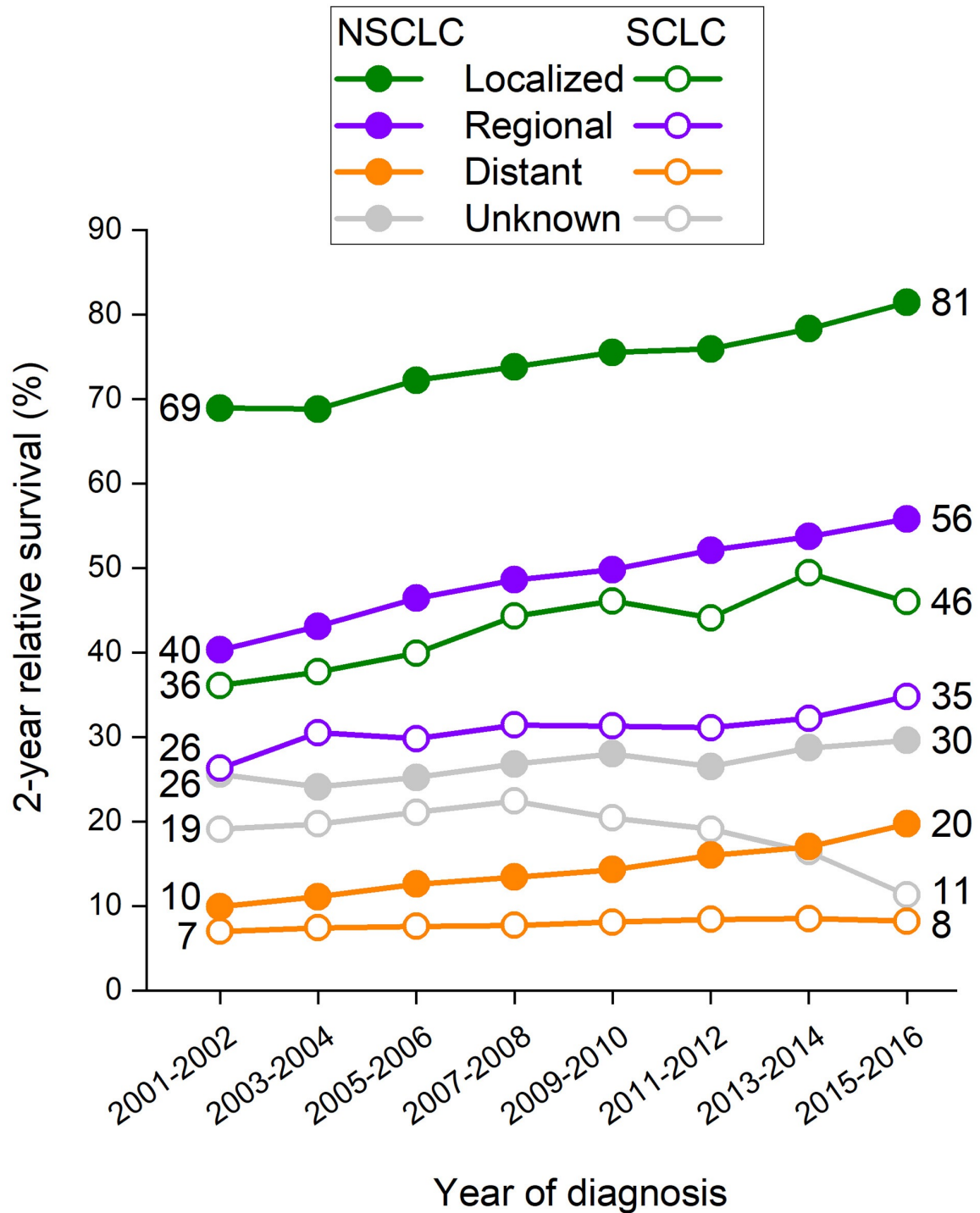
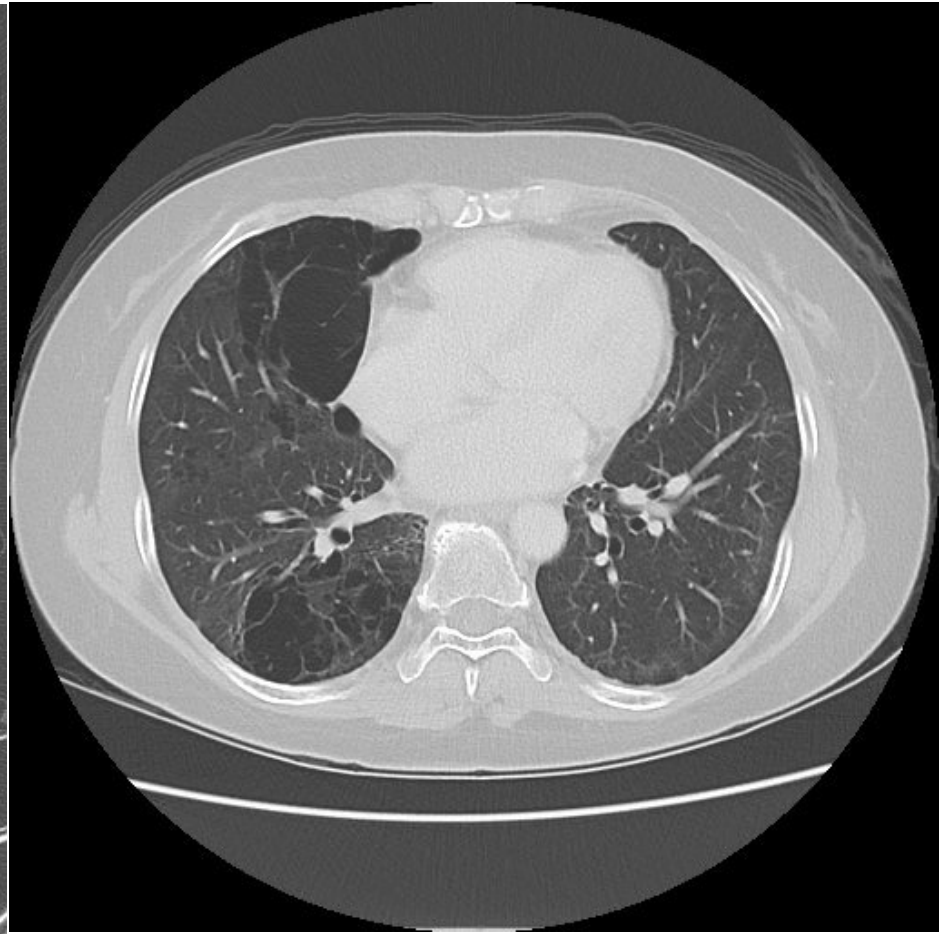


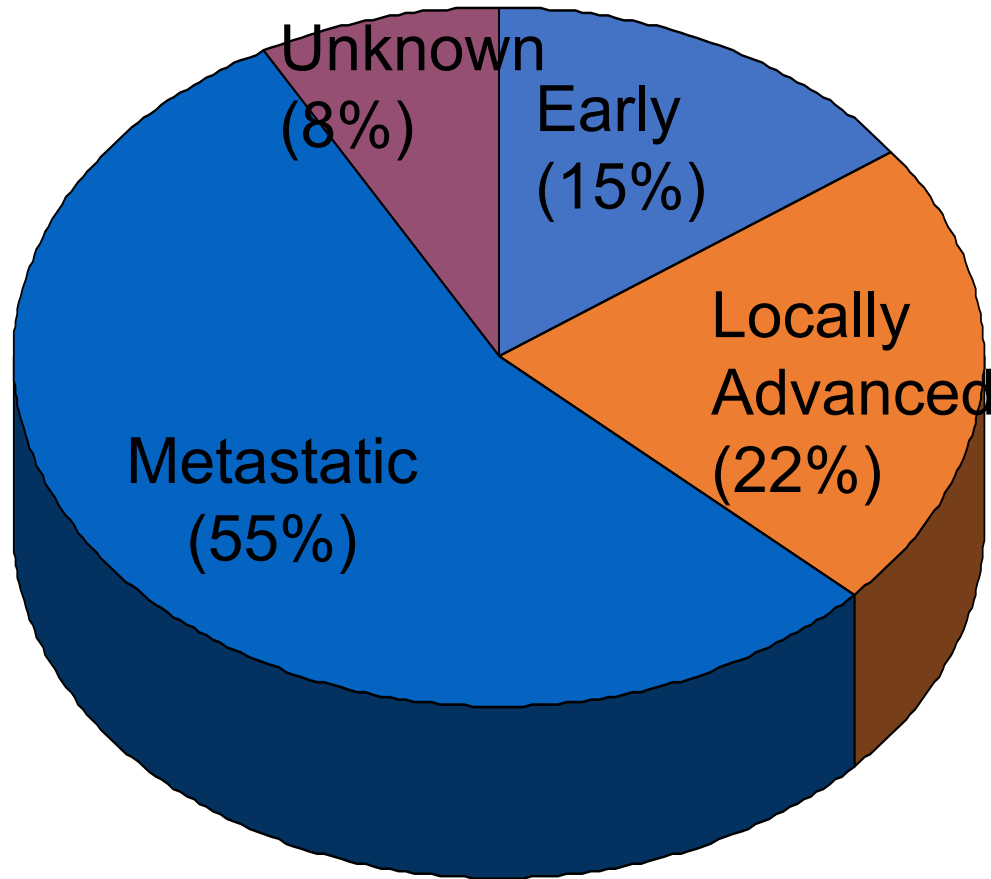
Figure 2. Comparison of Mortality Estimates Based on Data from Death Certificates and on Two Measures of Incidence among Patients with Lung or Bronchus Cancer.



Treatment for lung cancer is getting better



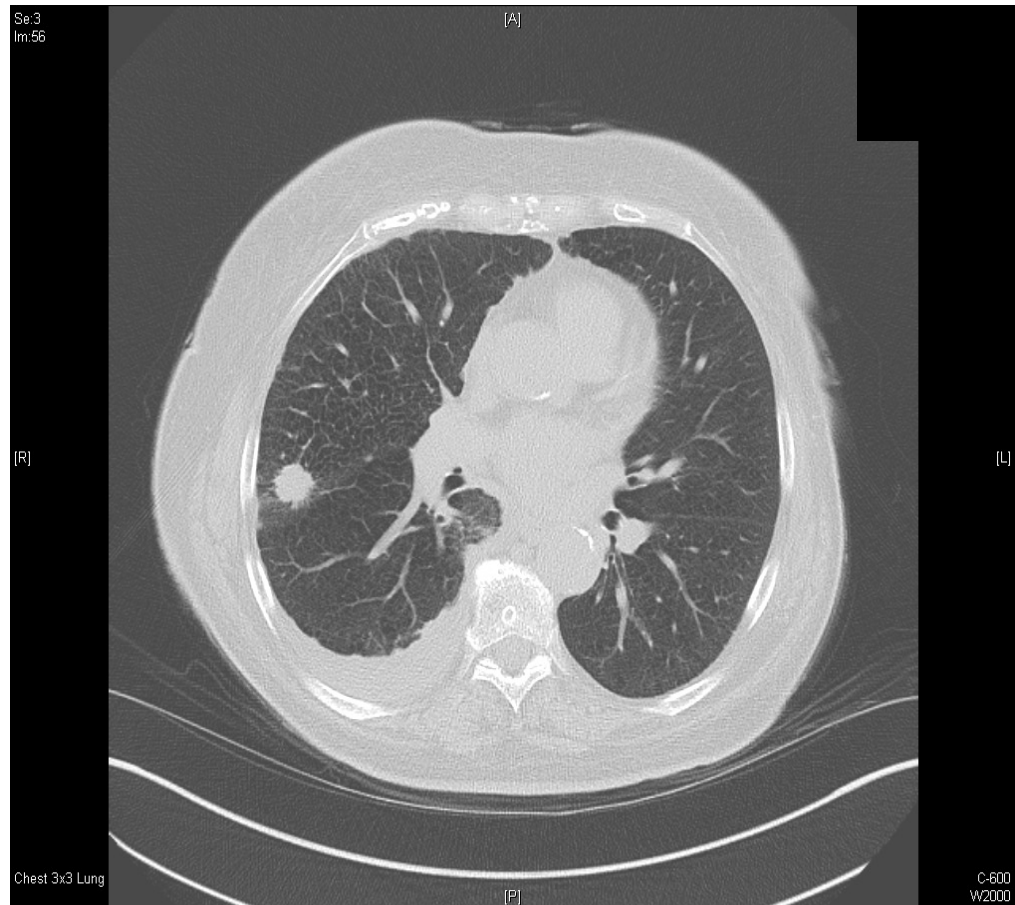
Lung Cancer: Stage at diagnosis in the U.S.



Prognosis

- **Five year survival:**

- Breast cancer 90%
- Colon cancer 65%
- Prostate cancer 98%
- **LUNG CANCER 21%**
- **Stage I NSCCA 58-73%**



How to beat lung cancer

- **1. Smoking cessation:** Fewer smokers, fewer lung cancers
- **2. Better treatment:** Longer, better quality of life
- **3. Earlier detection:** Screening

Lung Cancer Screening

Pro

- Outcome and treatment related to stage at diagnosis
- Identifiable risk factors
- High prevalence
- Lengthy pre-clinical phase

Con

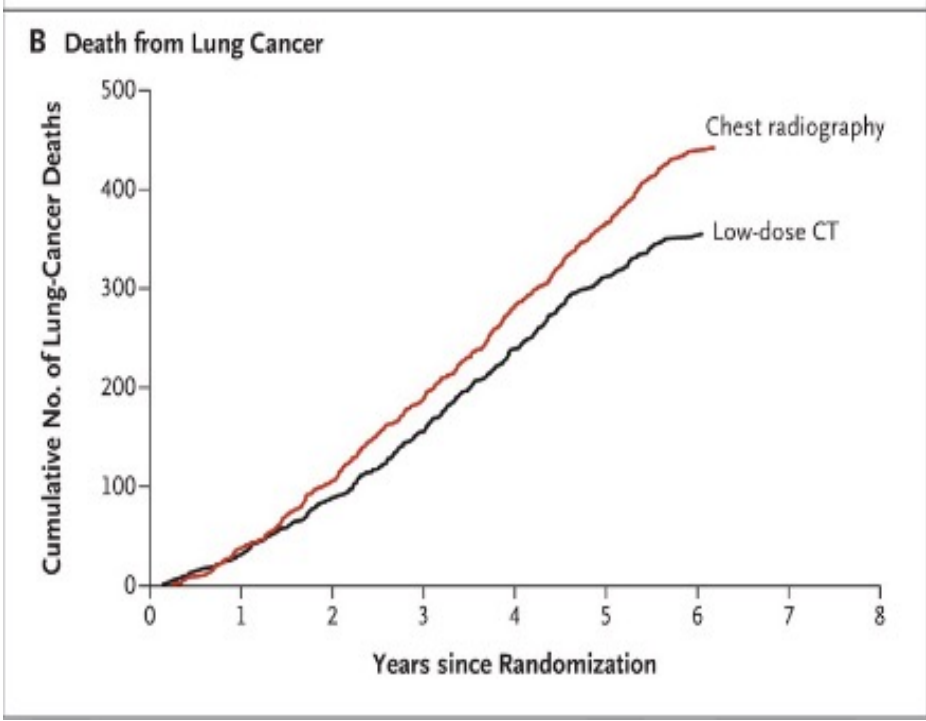
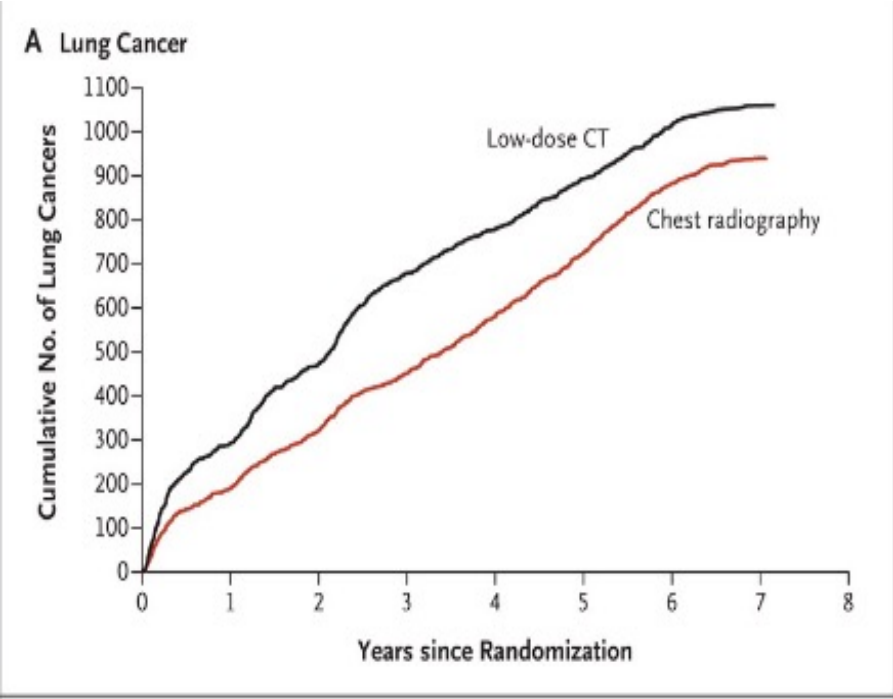
- Radiation exposure
- False positives leading to additional tests, procedures, and anxiety
- Cost
- Disparities in care

National Lung Screening Trial (NLST)

Prospective, randomized trial comparing low-dose helical CT screening to chest x-ray screening with the endpoint of lung cancer specific mortality in high risk participants

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

National Lung Screening Trial (NLST)



NLST Investigators, *NEJM*
epublished 2011

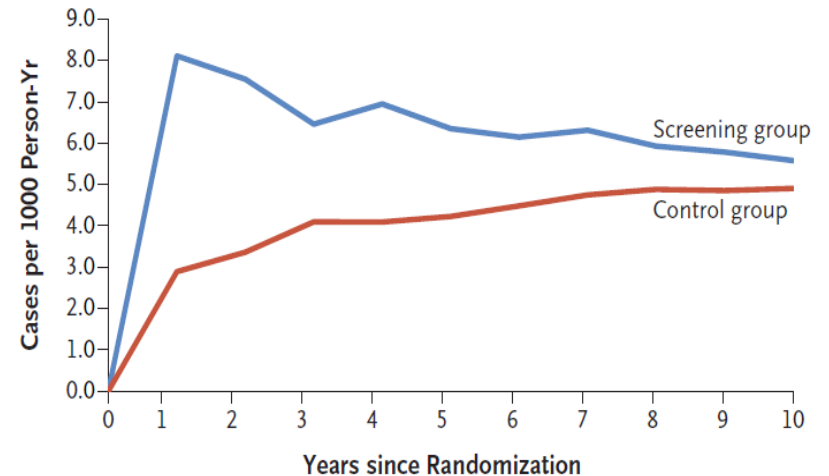
Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial

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. Yousof-Khan, N. Horeweg, S. van 't Westeinde, M. Prokop, W.P. Mali, F.A.A. Mohamed Hoessein, P.M.A. van Ooijen, J.G.J.V. Aerts, M.A. den Bakker, E. Thunnissen, J. Verschakelen, R. Vliegenthart, J.E. Walter, K. ten Haaf, H.J.M. Groen, and M. Oudkerk

The NELSON Trial

- 15 cig/day for > 25 yr, or
- > 10 cig/day for > 30 yr
- If quit, within 10 yr
- 10 year follow-up
- Focused on men participants
- 13,195 men, 2594 women
- CT screening intervals 1, 2, 2.5 yr
- Follow-up at 5,7,and 10-11 years
- Primary outcome lung cancer specific mortality

A Lung-Cancer Incidence



B Lung-Cancer Mortality

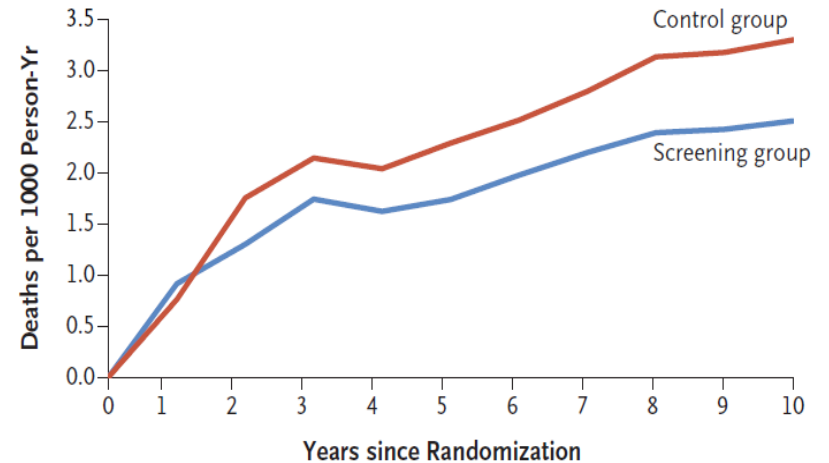


Figure 1. Lung-Cancer Incidence and Lung-Cancer Mortality among Male Participants.

Table 4. Cause of Death of Deceased Male Participants at 10 Years of Follow-up or until the Data-Cutoff Date of December 31, 2015.^a

Variable	Screening Group (N=868)	Control Group (N=860)	Total (N=1728)	Rate Ratio (95% CI)
	<i>number (percent)</i>			
Cause of death — no. (%)				
Lung cancer	160 (18.4)	210 (24.4)	370 (21.4)	0.76 (0.62–0.94)
No lung cancer after cause-of-death review, no other specification	6 (0.7)	11 (1.3)	17 (1.0)	0.55 (0.17–1.61)

Mortality benefit was enjoyed by women as well

Using volume CT screening led to fewer harms, fewer false positives, and fewer unnecessary workups without jeopardizing favorable outcomes.

U.S. Preventive Services Task Force Issues Draft Recommendation Statement on Screening for Lung Cancer

New evidence shows screening can help more people at high risk

WASHINGTON, D.C. – July 7, 2020 – The U.S. Preventive Services Task Force (USPSTF) today posted a draft recommendation statement, draft evidence review, and draft modeling study on screening for lung cancer in people who do not have signs or symptoms.

Based on the evidence, the USPSTF recommends annual screening using a low-dose computed tomography (CT) scan for people aged 50 to 80 years old who are at high risk for lung cancer because of their smoking history. This is a B recommendation.

Grade in this recommendation:

B: Recommended.

[Learn more here](#)

Smoking is the leading cause of lung cancer. Those at high risk are people who have smoked at least 20 pack-years over their lifetime, and still smoke or have quit smoking within the last 15 years. A *pack-year* is a way of calculating how much a person has smoked. One pack-year is the equivalent of smoking an average of 20 cigarettes, or one pack, per day for a year. People between 50 and 80 years old who are current or former smokers should talk to their doctor about whether they are at high risk for lung cancer. If they are, they should discuss the benefits and harms of screening so they can determine whether screening for lung cancer is right for them.

Important consideration when thinking about whether or not to screen for lung cancer!

- Surgical candidacy
- Potentially life-limiting co-morbidities
- If you find an early stage lung cancer but the patient is not a surgical candidate, have you done them any favors?

Addressing Disparities in Lung Cancer Screening Eligibility and Healthcare Access

An Official American Thoracic Society Statement

M. Patricia Rivera, Hormuzd A. Katki, Nichole T. Tanner, Matthew Triplette, Lori C. Sakoda, Renda Soylemez Wiener, Roberto Cardarelli, Lisa Carter-Harris, Kristina Crothers, Joelle T. Fathi, Marvella E. Ford, Robert Smith, Robert A. Winn, Juan P. Wisnivesky, Louise M. Henderson*, and Melinda C. Aldrich*; on behalf of the American Thoracic Society Assembly on Thoracic Oncology

THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY WAS APPROVED SEPTEMBER 2020

Lung Cancer Risk Factors

Intrinsic factors

- Genetic mutations
- Female sex
- Race and ethnicity
- Familial risk

Extrinsic factors

- Exogenous risk factors*
 - Tobacco smoke
 - Occupational and environmental exposures
 - Lifestyle and behavioral factors
 - Socioeconomic status
- Endogenous risk factors*
 - DNA-repair capacity
 - Growth factors
 - Hormones (estrogen and progesterone)
 - Aging
 - Inflammation
 - HIV

Lung cancer risk calculator

“Should I be screened”

1. What is your age? *

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?

YesNo

11. Does your family have a history of lung cancer?

YesNo

12. Have you ever been told by your doctor that you have chronic pulmonary disease also known as COPD (chronic bronchitis or emphysema)?

YesNo

54 yr old

Current smoker

35 years

20/day

Female

College graduate

White, non-Hispanic

5'7"

150 lbs

No prior cancer

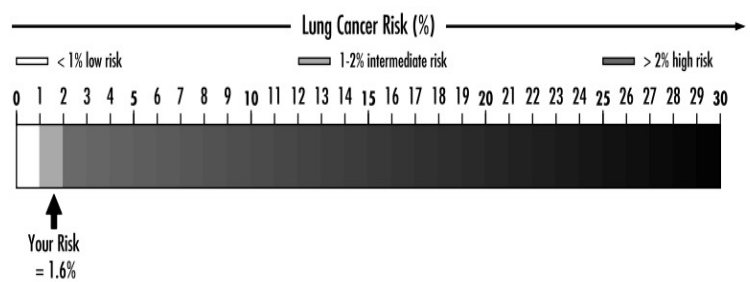
No family history

Emphysema

Lung Cancer Screening - Should I Do It?

According to your age and smoking exposure, the US Preventive Services Task Force **does not recommend*** lung cancer screening for you.

*However, the chance of you developing lung cancer in the next 6 years is 1.6%, which is above the threshold where we believe the benefits of screening are large enough to consider CT screening as an option. You should consider talking to your doctor about whether lung cancer screening might still be a good choice for you.



Compared to other people like you, there will be 3 fewer deaths out of 1000 in the next 6 years if you get screened.

BENEFITS



3 in 1000

fewer people like you will die from lung cancer among those who were screened compared to those who were not screened.

HARMS

- 365 in 1000 people who were screened found a lung nodule that was not cancer.
- 18 in 1000 had an invasive procedure, such as biopsy or surgery, due to a lung nodule that was not cancer.
- 3 in 1000 had a major complication from invasive procedures.
- ◆ Of the lung cancers found by screening, about 1 in 10 would have never harmed you. This may lead to unnecessary treatment and complications.



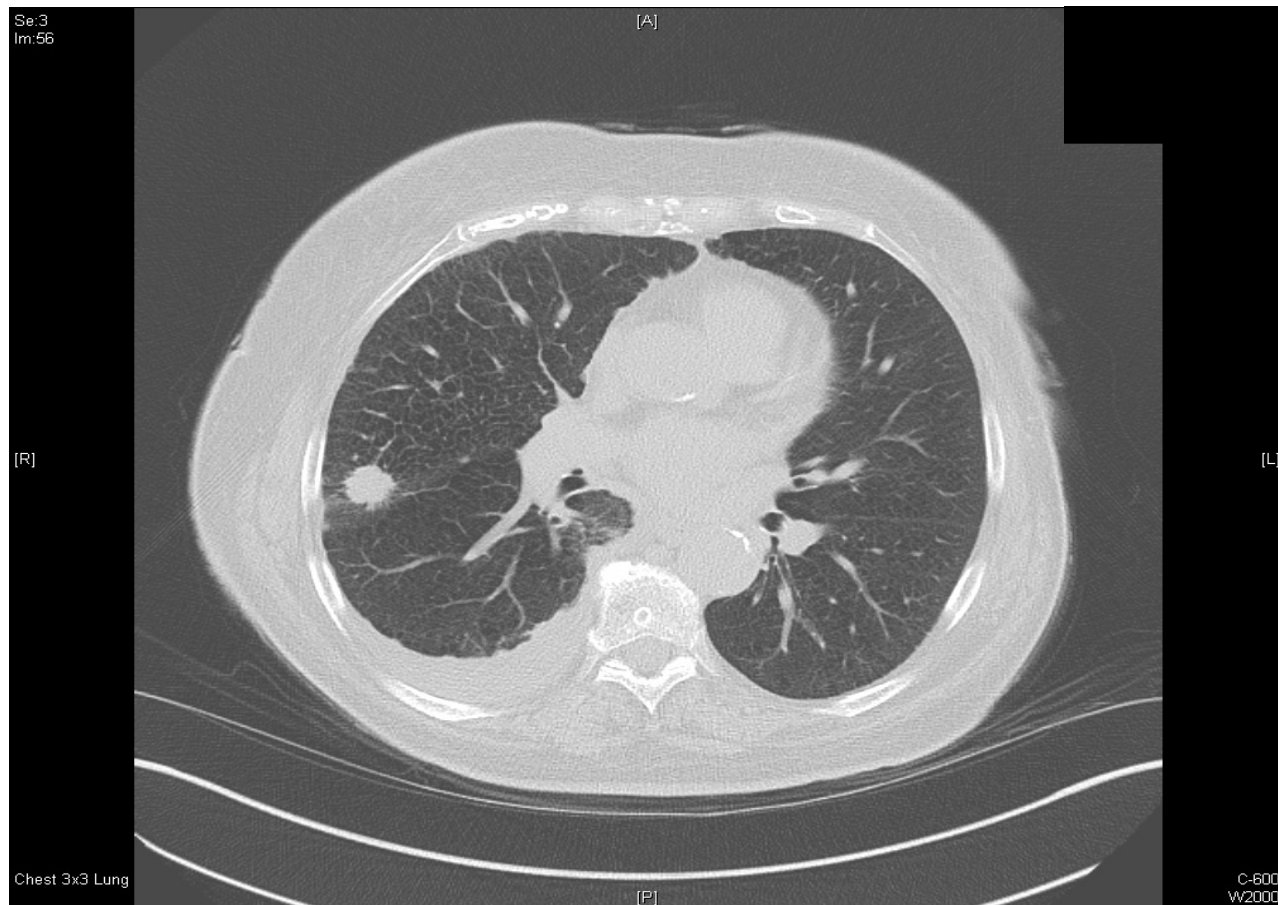
Lung Cancer Screening

- **“Systematic” screening is not recommended**
- **Any program of screening undertaken would have to be prepared for:**
 - long term follow-up
 - counseling on the implications of the results
 - should include smoking cessation as the most established means of prevention
- **We can still do better:**
 - How can we reduce the false positives
 - How can we reduce the radiation risk
 - How does screening affect smoking behavior
 - How can we make it more cost effective
 - How do we address the disparities in care

Solitary Pulmonary Nodule

Spherical opacity measuring up to 3 cm in greatest diameter, surrounded by lung parenchyma.

“Nodule” becomes a “mass” arbitrarily 3-4 cm



Solitary Pulmonary Nodule

<ul style="list-style-type: none"> • Infectious disease <p>Tuberculosis (tuberculoma) Round pneumonia Lung abscess Fungal disease Parasitic disease Atypical mycobacteria Nocardia <i>Pneumocystis jiroveci</i> Measles Septic embolus</p>	<ul style="list-style-type: none"> • Benign tumor <p>Hamartoma Chondroma Fibroma Neurofibroma Schwannoma Lipoma Sclerosing hemangioma Plasma cell granuloma Endometriosis</p>	<ul style="list-style-type: none"> • Malignant tumor <p>Lung cancer Pulmonary carcinoid Solitary metastasis Teratoma Leiomyoma</p>
<ul style="list-style-type: none"> • Inflammatory disease <p>Organizing pneumonia Rheumatoid arthritis Granulomatosis with polyangiitis Microscopic polyangiitis Sarcoidosis</p>	<ul style="list-style-type: none"> • Vascular origin <p>Arteriovenous malformation Pulmonary infarct Pulmonary artery aneurysm Pulmonary venous varix Hematoma</p>	<ul style="list-style-type: none"> • Lymphatic origin <p>Intrapulmonary or subpleural lymph node Lymphoma</p>
<ul style="list-style-type: none"> • Miscellaneous <p>Rounded atelectasis Lipoid pneumonia Amyloidosis Mucoïd impaction Infected bulla Pulmonary scar Pleural thickening, mass or fluid (pseudotumor)</p>	<ul style="list-style-type: none"> • Congenital malformation <p>Bronchogenic cyst Lung sequestration Bronchial atresia with mucoïd impaction</p>	

Risk of malignancy

Historic

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

Risk of malignancy

Radiographic

- Large > small
- Upper lobe > lower lobe
- Irregular “spiculated” border versus smooth
- Pattern of calcification
 - Asymmetric (eccentric) pattern more likely malignant than “popcorn”, diffuse, concentric, central patterns.
- Less dense versus more dense
 - Solid, part-solid, sub-solid (“ground glass”)
- Growth

Risk of malignancy

- **Estimates of the probability of malignancy can be made based on tables of likelihood ratios incorporating clinical and radiographic features.**
- **Management needs to be individualized in partnership with the patient.**
- **An old x-ray or other imaging study may provide crucial information related to the age of the lesion and thus the likelihood it is malignant or benign.**

Management approach

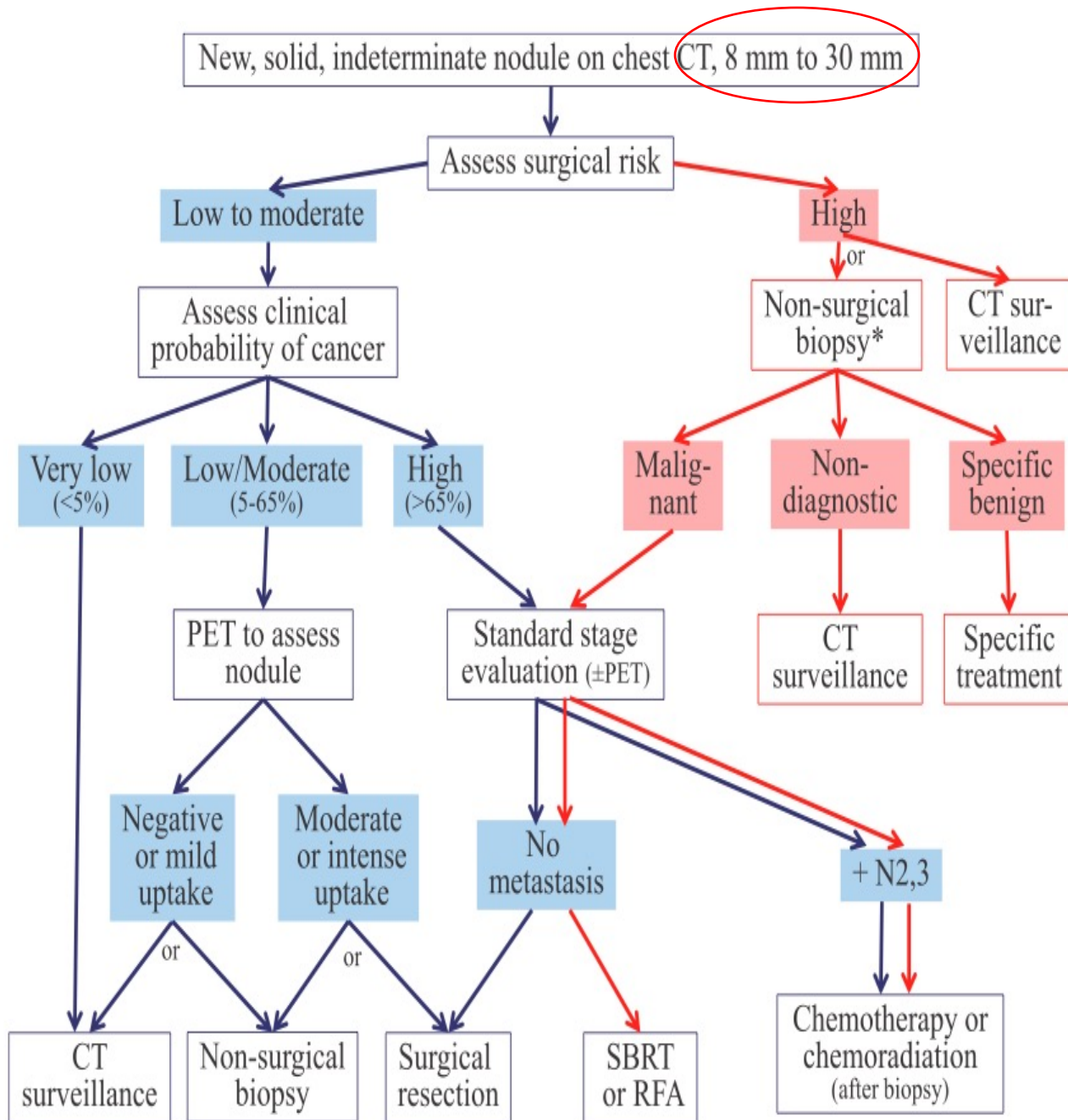
- **Principles:**

- **A nodule observed to grow on serial CT should be excised or biopsied.**
- **A solid nodule that has been stable for > 2 yr may be considered benign.**
- **A nodule larger than 1 cm may be evaluated by PET scan**
- **A nodule smaller than 1 cm may be observed if intermediate or low probability of malignancy**
- **Any nodule that is low probability of malignancy can be observed**
- **Any nodule that is high probability of malignancy should be excised.**

Guidelines for CT Management of Pulmonary Nodules

Statement from the Fleischner Society

Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults				
A: Solid Nodules*				
Nodule Type	Size			Comments
	<6 mm (<100 mm ³)	6–8 mm (100–250 mm ³)	>8 mm (>250 mm ³)	
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).



1. Radiology

2. Surgical Risk

3. Probability of cancer

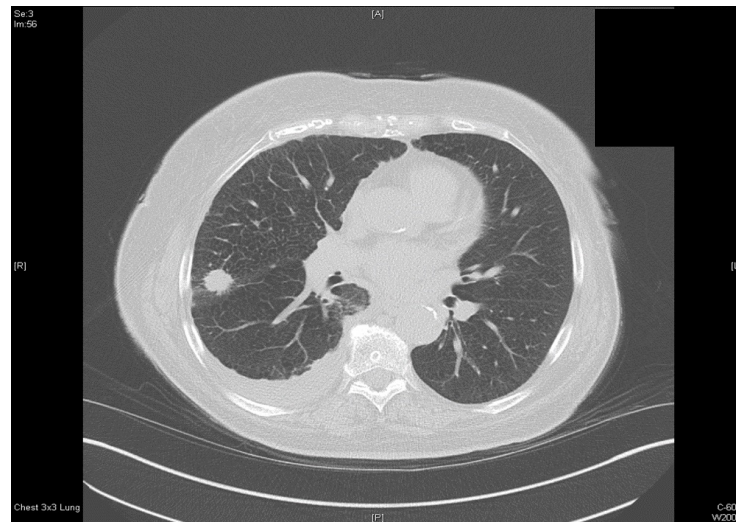
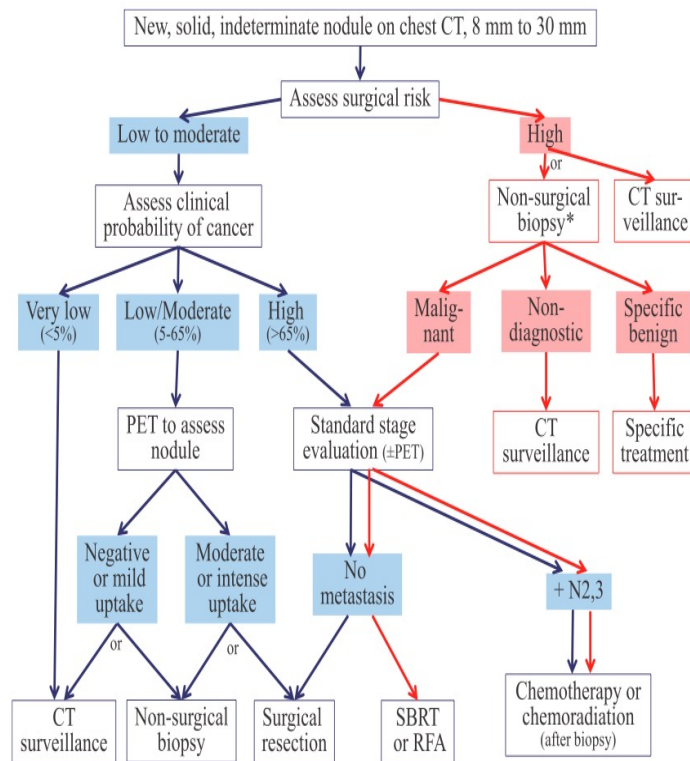
4. Shared Decision-making

Probability of malignancy (Mayo Clinic Risk Calculator)

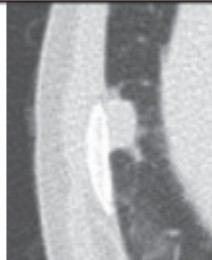
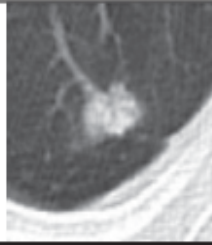
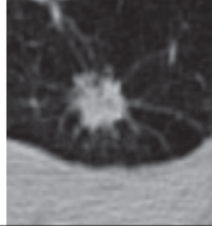
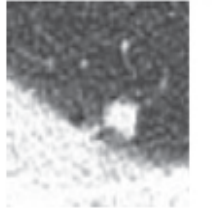
- **Age:** 80
- **History of smoking:** smoker
- **Extrathoracic Cancer** (more than 5 yr prior): no
- **Diameter:** 16 mm
- **Spiculated:** yes
- **Upper lobe:** yes

Surgical risk : moderate

Probability of malignancy:
72.2%



Lung cancer probability (risk) models: be aware of their validation population

Clinical Scenarios		Probability Models							Diagnosis
		Gurney	Mayo	Herder	VA	Brock	TREAT	BIMC	
<p>53-yr-old woman, former smoker, 10 pack-years</p> <p>Quit 15 yr ago</p> <p>No emphysema</p> <p>Smooth RLL 1.2-cm module</p> <p>Hypermetabolic SUVmax 3.3</p>		76%	8%	54.4%	15.2%	6.9%	38%	52%	Necrotizing granuloma
<p>69-yr-old man, former smoker, 38 pack-years</p> <p>Quit 20 yr ago</p> <p>History of emphysema</p> <p>Irregular LUL 1.6-cm nodule</p> <p>Hypermetabolic SUVmax 3.2</p>		98%	63%	90%	42.3%	41.2%	73%	85%	Non-small cell carcinoma
<p>54-yr-old man, active smoker, 58 pack-years</p> <p>History of emphysema</p> <p>Spiculated RUL 1.4-cm nodule</p> <p>Hypermetabolic SUVmax 12</p>		100%	42%	83%	36.1%	25.3%	69%	97%	Adenocarcinoma
<p>72-yr-old woman, active smoker, 75 pack-years</p> <p>History of emphysema</p> <p>RUL 6-mm nodule found on low-dose CT scan for lung cancer screening</p> <p>No FDG-PET</p>		62%	16%	16%	48%	4.2%	68%	12%	Likely benign Stable for >2 yr

Management of subsolid pulmonary nodules

B: Subsolid Nodules*

Nodule Type	Size		Comments
	<6 mm (<100 mm ³)	≥6 mm (>100 mm ³)	
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).

Non-Small Cell Lung Cancer staging: TNM system

8th Edition

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 , main bronchus (not carina), atelectasis to hilum ^b	T2 _{Visc Pl} 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 or invading chest wall, pericardium, phrenic nerve or separate tumor nodule(s) in the same lobe	T3 _{>5-7} T3 _{Inv} T3 _{Satell}
T4	Tumor >7 cm or tumor invading: mediastinum, diaphragm, heart, great vessels, recurrent laryngeal nerve, carina, trachea, esophagus, spine; or tumor nodule(s) in a different ipsilateral lobe	T4 _{>7} T4 _{Inv} 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 or separate tumor nodule(s) in a contralateral lobe;	M1a _{Pl Dissem} 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; 151(1):193-203

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

- **Beating lung cancer involves:**
 - **smoking cessation to reduce the incidence**
 - **better treatments for improved prognosis after diagnosis**
 - **early detection by lung cancer screening**
- **Screening is recommended for select patients who meet criteria and who can be seen at a center with an infrastructure that supports a screening program.**
- **Evaluation of a solitary pulmonary nodule is based on the risk of malignancy and patients' candidacy for surgery**

Question #1

- **A 66 year old asymptomatic smoker of 1 pack per day for the past 45 years with a history of 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 x-ray 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**

References

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Thanks

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