

Screening for lung cancer

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- Lung cancer is the leading cause of cancer mortality worldwide.
- ▶ In 2019, it is estimated that about 24% of all the US deaths from cancer were occure from lung cancer.
- ► Five year survival rates for lung cancer are only 19% partly because most patients have advanced stage lung cancer at intial of diagnosis.

- Lung cancer symptoms occur late in the disease, so the majority of patients with lung cancer present with advanced disease, the disease will not be curable with currently available therapies.
- early detection might be a valuable approach to detect the disease at an earlier, asymptomatic and potentially curable stage.

Screening Tests

A screening test is done to detect potential health disorders or diseases in people who do not have any symptoms of disease. The goal is early detection and lifestyle changes or surveillance, to reduce the risk of disease, or to detect it early enough to treat it most effectively.

Screening tests are not considered diagnostic, but are used to identify a subset of the population who should have additional testing to determine the presence or absence of disease.

- ► Early detection is a process that involves screening tests, surveillance, diagnosis, and early treatment.
- Screening refers to the use of tests across a healthy population in order to identify individuals who harbor asymptomatic disease.
- For a screening program to be successful, there must be a high burden of disease within the target population; the test must be sensitive, specific, accessible, and cost effective; and there must be effective treatment that can reduce mortality.

With any screening procedure, it is important to consider the possible influence of:

- ▶ lead-time bias (detecting the cancer earlier without an effect on survival)
- length-time bias (indolent cancers are detected on screening and may not affect survival, whereas aggressive cancers are likely to cause symptoms earlier in patients and are less likely to be detected)

overdiagnosis (diagnosing cancers so slow growing that they are unlikely to cause the death of the patient). ▶ Because a majority of lung cancer patients present with advanced disease beyond the scope of surgical resection, there is understandable skepticism about the value of screening in this condition. Randomized controlled trials conducted in the 1960s to 1980s using screening chest x-rays (CXR), with or without sputum cytology, reported no impact on lung cancer-specific mortality in patients characterized as high risk (males age ≥45 years with a smoking history)



Controlled Clinical Trials

-272S

Controlled Clinical Trials

(23)

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The Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial of the National Cancer Institute: History, organization, and status

PLCO Project Team, John K. Gohagan PhD FACE ^a, Philip C. Prorok PhD ^a, Richard B. Hayes PhD ^b, Barnett-S. Kramer MD MPH ^{a, 1}

- A total of 154,901 individuals between 55 and 74 years of age were enrolled (77,445 assigned to annual CXR screenings; 77,456 assigned to usual care).
- ► Through 13 years of follow-up, cumulative lung cancer incidence rates (20.1 vs 19.2 per 10,000 person-years; rate ratio [RR], 1.05; 95% confidence interval [CI], 0.98-1.12) and lung cancer mortality (n = 1213 vs n = 1230) were identical between the two groups.

Screening evaluated in relatively small trials failed to show benefit if periodical chest X-ray and/or sputum cytology were used; screening by these techniques is therefore not recommended.

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

The National Lung Screening Trial Research Team*

- ▶ Eligible participants were between 55 and 74 years of age at the time of randomization, had a history of cigarette smoking of at least 30 packyears, and, if former smokers, had quit within the previous 15 years.
- ▶ Persons who had previously received a diagnosis of lung cancer, had undergone chest CT within 18 months before enrollment, had hemoptysis, or had an unexplained weight loss of more than 6.8 kg in the preceding year were excluded.

Table 1. Selected Baseline Characteristics of the Study Participants.*				
Characteristic	Low-Dose CT Group (N = 26,722)	Radiography Group (N = 26,732)		
	number (percent)			
Age at randomization				
<55 yr†	2 (<0.1)	4 (<0.1)		
55–59 yr	11,440 (42.8)	11,420 (42.7)		
60–64 yr	8,170 (30.6)	8,198 (30.7)		
65–69 yr	4,756 (17.8)	4,762 (17.8)		
70-74 yr	2,353 (8.8)	2,345 (8.8)		
≥75 yr†	1 (<0.1)	3 (<0.1)		
Sex				
Male	15,770 (59.0)	15,762 (59.0)		
Female	10,952 (41.0)	10,970 (41.0)		
Race or ethnic group:				
White	24,289 (90.9)	24,260 (90.8)		
Black	1,195 (4.5)	1,181 (4.4)		
Asian	559 (2.1)	536 (2.0)		
American Indian or Alaska Native	92 (0.3)	98 (0.4)		
Native Hawaiian or other Pacific Islander	91 (0.3)	102 (0.4)		
More than one race or ethnic group	333 (1.2)	346 (1.3)		
Data missing	163 (0.6)	209 (0.8)		
Hispanic ethnic group:				
Hispanic or Latino	479 (1.8)	456 (1.7)		
Neither Hispanic nor Latino	26,079 (97.6)	26,039 (97.4)		
Data missing	164 (0.6)	237 (0.9)		
Smoking status				
Current	12,862 (48.1)	12,900 (48.3)		
Former	13,860 (51.9)	13,832 (51.7)		

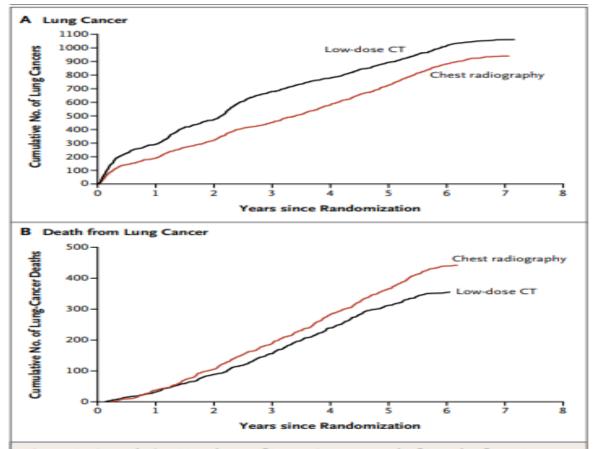


Figure 1. Cumulative Numbers of Lung Cancers and of Deaths from Lung Cancer.

The number of lung cancers (Panel A) includes lung cancers that were diagnosed from the date of randomization through December 31, 2009. The number of deaths from lung cancer (Panel B) includes deaths that occurred from the date of randomization through January 15, 2009.

The much larger National Lung Cancer Screening Trial (NLST) comparing low-dose computed tomography (LDCT) to chest X-ray in over 53 000 current or former heavy smokers (30 pack-years or15 years since smoking cessation), aged between 55 and 74 years, showed a 20% reduction in lung cancer-related death and an overall all-cause mortality reduction of 6.7%.

this positive outcome generates new questions on the rate of overdiagnosis of indolent cancers, such as lepidic adenocarcinomas (previously named bronchioloalveolar carcinoma) Published in final edited form as: JAMA Intern Med. 2014 February 1; 174(2): 269–274. doi:10.1001/jamainternmed.2013.12738.

Overdiagnosis in Low-Dose Computed Tomography Screening for Lung Cancer

Lung Cancer Counts Used to Derive Overdiagnosis Rates

	LDCT			CXR		
Lung Cancer Type	Not Screen Detected	Screen Detected	Total	Not Screen Detected	Screen Detected	Total
All lung cancers	440	649	1089	690	279	969
All NSCLC, including BAC and NOS	335	591	926	546	247	793
All NSCLC, excluding BAC and including NOS	319	496	815	523	234	757
BAC only	16	95	111	23	13	36

AMERICAN THORACIC SOCIETY DOCUMENTS

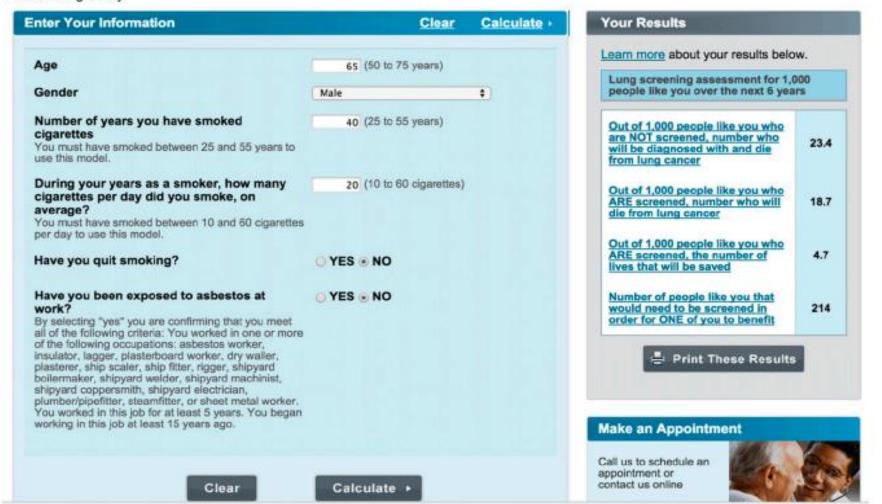
An Official American Thoracic Society/American College of Chest Physicians Policy Statement: Implementation of Low-Dose Computed Tomography Lung Cancer Screening Programs in Clinical Practice

AMERICAN THORACIC SOCIETY DOCUMENTS

Lung Cancer Screening Decision Tool

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Our lung cancer screening decision tool helps clinicians and patients determine the chance that screening will be beneficial based on a patient's age and smoking history.



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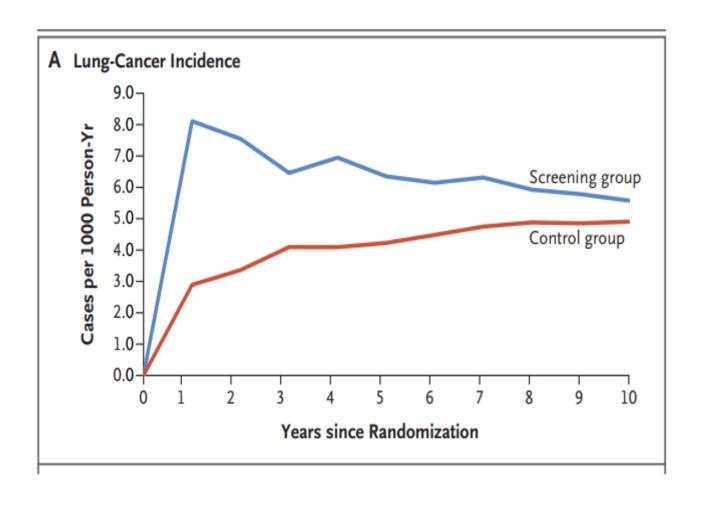
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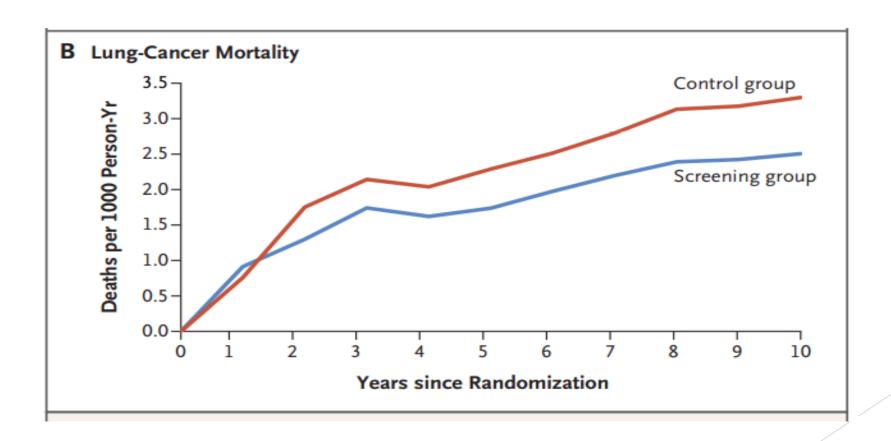
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Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial

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,





Randomized Controlled Trial

> Lancet Oncol. 2016 Jul;17(7):907-916.

doi: 10.1016/S1470-2045(16)30069-9. Epub 2016 Jun 6.

Occurrence and lung cancer probability of new solid nodules at incidence screening with low-dose CT: analysis of data from the randomised, controlled NELSON trial

study shows that new solid nodules are detected at each screening round in 5-7% of individuals who undergo screening for lung cancer with low-dose CT. These new nodules have a high probability of malignancy even at a small size. These findings should be considered in future screening guidelines, and new solid nodules should be followed up more aggressively than nodules detected at baseline screening



screening with LDCT reduces lung cancer-related mortality [I, A]. It is not yet ready for large-scale implementation, mainly because the lung cancer mortality reduction rate lacks definite proof of a second study result, and partly because of remaining questions regarding definition of the at-risk population, timing, interval and method of computed tomography (CT, especially 2D versus 3D evaluation), how to handle (false-) positive findings and especially cost-effectiveness, notably in relation to smoking cessation [1, A].



▶ LDCT screening can be carried out outside a clinical trial provided it is offered within a dedicated programme with quality control, in a centre with experience in CT screening, a large volume of thoracic oncology activity and multidisciplinary management of suspicious findings [I, B].



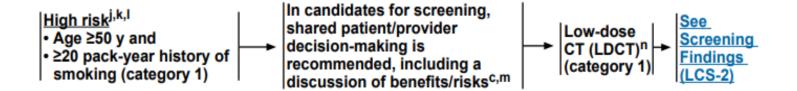
➤ Candidates are current or former heavy smokers (30 pack-years or,15 years since smoking cessation) aged 55-74 years, who are well informed about potential benefits and risks. Individuals offered LDCT screening should be referred to a smoking cessation programme



- ▶ Other screening methods, such as chest X-ray, sputum analysis or biomarkers are not recommended for clinical use [I, C].
- LDCT screening should not be offered on an ad hoc individual basis, but patients requesting screening should be referred to a dedicated programme, as recommended above [V, B].



NCCN Guidelines Version 1.2022 Lung Cancer Screening





*Fleischner society guidelines; modified from: H. MacMahon, et al: Radiology 2005; 237;395-400

Nodule size (a):	Low-risk patient (b):	High-risk patient (c):
≤4 mm	No follow-up needed (d)	Follow-up at 12 months; if unchanged, no further follow-up
>4-≤6 mm	Follow-up CT at 12 months; if unchanged, no further follow-up	Follow-up CT at 6–12 months; then 18–24 months if no change
>6-≤8 mm	Follow-up CT at 6–12 months; then 18–24 months if no change	Follow-up CT at 3–6 months; then 9–12 and 24 months if no change
>8 mm	Follow-up CT at 3, 9, and 24 months; dynamic contrast- enhanced CT, PET, and/or biopsy	Same as low-risk patient

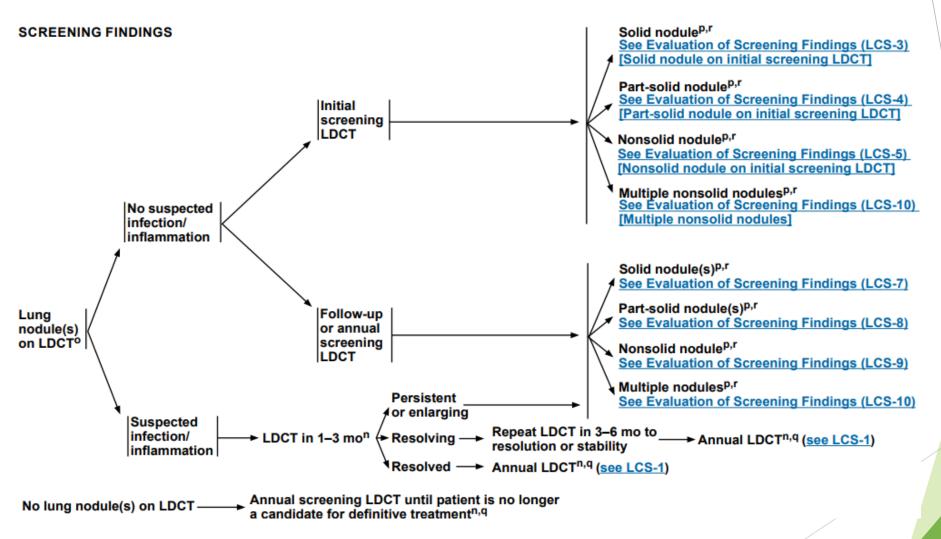
- (a) Average of largest and smallest axial diameters of the nodule
- (b) No smoking history and absence of other risk factors
- (c) Previous or current smoking history or other risk factors
- (d) Risk of malignancy (<0.1%) is substantially lower than for an asymptomatic smoker

Assessment of Risk of Cancer in Patients with Solitary Pulmonary Nodules

	RISK				
VARIABLE	LOW	INTERMEDIATE	HIGH		
Diameter (cm)	<1.5	1.5-2.2	≥2.3		
Age (years)	<45	45–60	>60		
Smoking status	Never smoker	Current smoker (<20 cigarettes/d)	Current smoker (>20 cigarettes/d)		
Smoking cessation status	Quit ≥7 years ago or quit	Quit <7 years ago	Never quit		
Characteristics of nodule margins	Smooth	Scalloped	Corona radiata or spiculated		



NCCN Guidelines Version 1.2022 Lung Cancer Screening



Potential Benefits

Potential Harms

Mortality benefits 20% relative decrease in lung cancer death (from 1.66 to 1.33%, or 3 fewer deaths per 1,000 screened) 7% relative reduction in all-cause mortality

Harms related to test characteristics Radiation exposure from screening CT False reassurance (aggressive cancers may develop in intervals between screening examinations) Overdiagnosis of clinically insignificant cancers (15-20% of tumors detected)

Psychosocial benefits and behavioral changes Harms related to findings of test Reassurance if normal CT Teachable moment for smoking cessation

False positives and other incidental findings Potential harms from downstream evaluation of findings

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