Lung Cancer Screening

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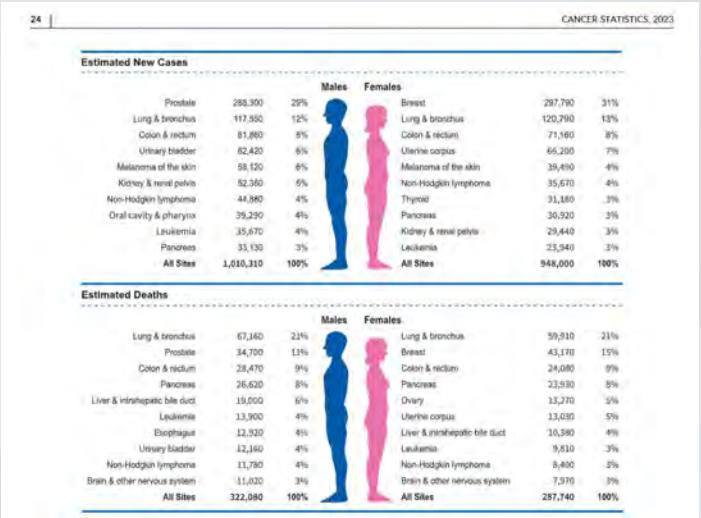
1

Epidemiology



24 | CANCER STATISTICS, 2023

Estimated New Cases

	Males		Females	
Prostate	288,300	29%	Breast	297,790	31%
Lung & bronchus	117,550	12%	Lung & bronchus	120,790	13%
Colon & rectum	81,860	8%	Colon & rectum	71,160	8%
Urinary bladder	62,420	6%	Uterine corpus	66,200	7%
Melanoma of the skin	58,120	6%	Melanoma of the skin	39,490	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	35,670	4%
Non-Hodgkin lymphoma	44,880	4%	Thyroid	31,180	3%
Oral cavity & pharynx	39,290	4%	Pancreas	30,920	3%
Leukemia	35,670	4%	Kidney & renal pelvis	29,440	3%
Pancreas	33,130	3%	Leukemia	23,940	3%
All Sites	**1,010,310**	**100%**	**All Sites**	**948,000**	**100%**

Estimated Deaths

	Males		Females	
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	9,610	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%
All Sites	**322,080**	**100%**	**All Sites**	**287,740**	**100%**

Cancer statistics, 2023. *CA: a cancer journal for clinicians*, *73*(1), 17–48.

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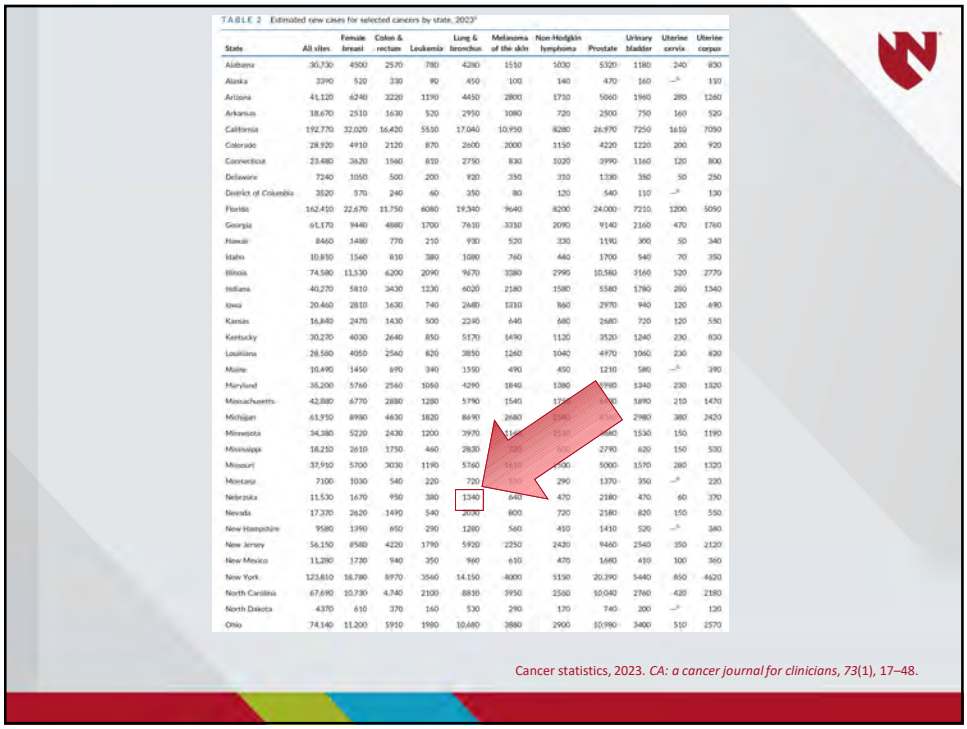

TABLE 2 Estimated new cases for selected cancers by state, 2023[1]

State	All sites	Female breast	Colon & rectum	Leukemia	Lung & bronchus	Melanoma of the skin	Non-Hodgkin lymphoma	Prostate	Urinary bladder	Uterine cervix	Uterine corpus
Alabama	30,730	4500	2570	780	4280	1510	1030	5320	1180	240	830
Alaska	3990	520	330	90	450	100	140	470	160	[2]	110
Arizona	41,120	6240	3220	1190	4450	2800	1710	5060	1960	280	1260
Arkansas	18,670	2510	1630	520	2950	1080	720	2500	750	160	520
California	192,770	32,020	16,420	5510	17,040	10,950	8280	26,970	7250	1610	7050
Colorado	28,920	4910	2120	870	2600	2000	1150	4220	1220	200	920
Connecticut	23,480	3820	1560	810	2750	830	1020	3990	1160	120	800
Delaware	7240	1050	500	200	920	330	310	1330	350	50	250
District of Columbia	3520	570	240	60	350	80	120	540	110	[2]	130
Florida	162,410	22,670	11,750	6080	19,340	9640	8200	24,000	7210	1200	5050
Georgia	61,170	9440	4880	1700	7610	3310	2690	9140	2160	470	1760
Hawaii	8460	1480	770	210	930	520	330	1190	300	50	340
Idaho	10,810	1560	810	380	1080	760	440	1700	540	70	350
Illinois	74,580	11,530	6200	2090	9670	3280	2990	10,580	3160	520	2770
Indiana	40,270	5810	3430	1230	6020	2180	1580	5580	1780	280	1340
Iowa	20,460	2810	1630	740	2680	1310	860	2970	940	120	690
Kansas	16,840	2470	1430	500	2240	640	680	2680	720	120	580
Kentucky	30,270	4030	2640	850	5170	1490	1120	3520	1240	230	830
Louisiana	28,580	4050	2560	820	3850	1260	1040	4970	1060	230	820
Maine	10,490	1450	690	340	1350	490	450	1210	580	[2]	390
Maryland	35,200	5760	2560	1050	4290	1840	1380	7980	1340	230	1320
Massachusetts	42,880	6770	2880	1280	5790	1540	1710	6730	1890	210	1470
Michigan	61,950	8980	4630	1820	8690	2680	2360	8170	2980	380	2420
Minnesota	34,380	5220	2430	1200	3970	2140	1530	5880	1530	150	1190
Mississippi	18,250	2610	1750	460	2830	720	660	2790	620	150	530
Missouri	37,910	5700	3030	1190	5760	1610	1300	5000	1570	280	1320
Montana	7100	1030	540	220	720	550	290	1370	350	[2]	220
Nebraska	11,530	1670	950	380	1340	640	470	2180	470	60	370
Nevada	17,370	2620	1490	540	2030	800	720	2180	820	150	550
New Hampshire	9580	1390	650	290	1280	560	410	1410	520	[2]	340
New Jersey	56,150	8580	4220	1790	5920	2250	2420	9460	2540	350	2120
New Mexico	11,280	1730	940	350	960	610	470	1680	410	100	360
New York	123,610	18,780	8970	3560	14,150	4000	5150	20,390	5440	850	4620
North Carolina	67,690	10,730	4,740	2100	8810	3950	2560	10,040	2760	420	2180
North Dakota	4370	610	370	160	530	290	170	740	200	[2]	120
Ohio	74,140	11,200	5910	1980	10,680	3880	2900	10,980	3400	510	2570

Cancer statistics, 2023. *CA: a cancer journal for clinicians*, *73*(1), 17–48.

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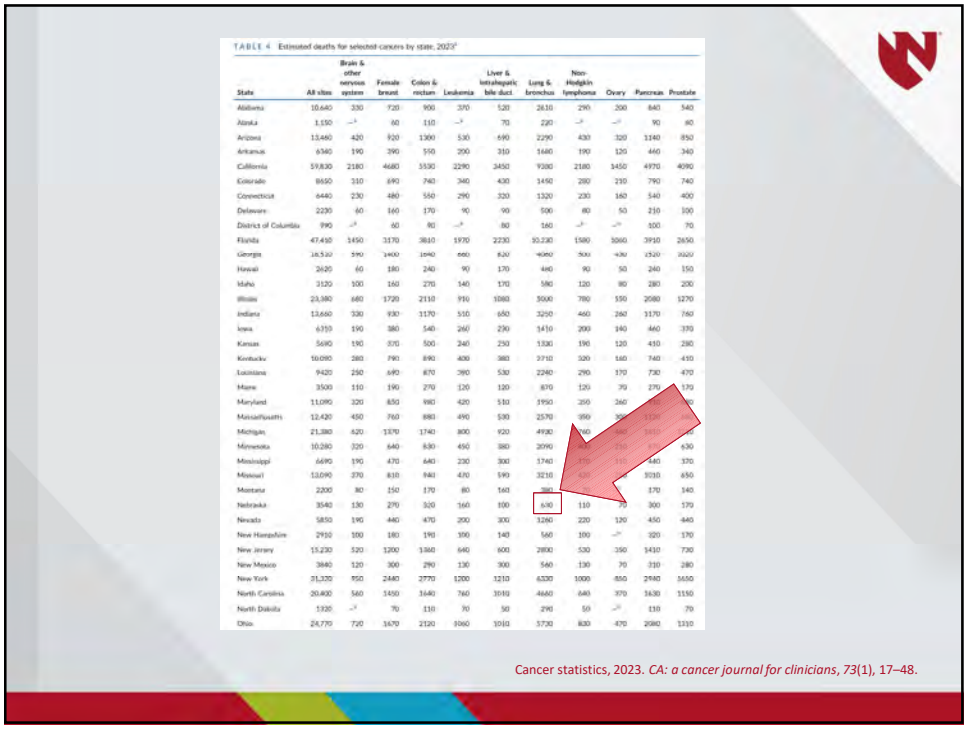

TABLE 4 Estimated deaths for selected cancers by state, 2023[1]

State	All sites	Brain & other nervous system	Female breast	Colon & rectum	Leukemia	Liver & intrahepatic bile duct	Lung & bronchus	Non-Hodgkin lymphoma	Ovary	Pancreas	Prostate
Alabama	10,660	330	720	900	370	520	2610	290	200	840	540
Alaska	1,150	[2]	60	110	[2]	70	220	[2]	[2]	90	80
Arizona	13,460	420	920	1300	530	690	2290	430	320	1140	850
Arkansas	6340	190	390	550	200	310	1440	190	120	440	340
California	59,830	2180	4680	5530	2290	3450	9200	2180	1450	4970	4090
Colorado	8650	310	690	740	340	430	1450	280	210	790	740
Connecticut	6440	230	480	550	290	320	1320	230	160	540	400
Delaware	2230	60	160	170	90	90	500	80	50	210	100
District of Columbia	990	[2]	60	80	[2]	80	160	[2]	[2]	100	70
Florida	47,410	1450	3170	3810	1970	2230	10,230	1580	1060	3910	2650
Georgia	16,530	590	1400	1640	660	820	4080	500	430	1520	1020
Hawaii	2620	60	180	240	90	170	440	90	50	240	150
Idaho	3120	100	160	270	140	170	580	120	80	280	200
Illinois	23,380	680	1720	2110	910	1080	3000	780	550	2080	1270
Indiana	13,660	330	930	1170	510	650	3250	460	280	1170	760
Iowa	6350	190	380	540	260	230	1410	200	140	460	370
Kansas	5690	190	370	500	240	250	1330	190	120	410	280
Kentucky	10,090	280	790	890	400	380	3710	320	160	740	450
Louisiana	9420	250	690	870	380	530	2240	290	170	730	470
Maine	3500	110	190	270	120	120	870	120	70	270	170
Maryland	11,090	320	850	980	420	510	1950	350	260	860	570
Massachusetts	12,420	450	760	880	490	530	2570	390	300	1030	580
Michigan	21,380	620	1370	1740	800	920	4930	700	460	1810	930
Minnesota	10,280	320	640	830	450	380	2090	430	310	740	630
Mississippi	6690	190	470	640	230	300	1740	270	170	640	370
Missouri	13,090	370	810	940	470	590	3210	520	370	1030	650
Montana	2200	80	150	170	80	160	380	[2]	[2]	170	140
Nebraska	3540	130	270	320	160	100	630	110	70	300	170
Nevada	5850	190	440	470	200	300	1260	220	120	450	440
New Hampshire	2910	100	180	190	100	140	560	100	[2]	320	170
New Jersey	15,230	520	1200	1360	640	600	2800	530	350	1410	730
New Mexico	3840	120	300	290	130	300	540	130	70	310	280
New York	31,320	950	2440	2770	1200	1210	6330	1000	850	2940	1650
North Carolina	20,400	560	1450	1640	760	1010	4660	640	370	1630	1150
North Dakota	1320	[2]	70	110	70	50	290	50	[2]	130	70
Ohio	24,770	720	1670	2120	1060	1010	5730	830	470	2080	1310

Cancer statistics, 2023. *CA: a cancer journal for clinicians*, *73*(1), 17–48.

4

Tobacco Epidemic

- In 2020, it was estimated that 47.1 million U.S. adults (19.0%) were using any commercial tobacco product (cigarettes, e-cigarettes, cigars, smokeless tobacco, and pipes)
- In Nebraska:
  - 13.9% of adults smoked.
  - 4.2% of high school students in Nebraska smoked cigarettes on at least one day in the past 30 days. Nationally, the rate was 6.0%.
  - 17.1% of high school students in Nebraska used electronic vapor products on at least one day in the past 30 days. Nationally, the rate was 32.7%

NCCN guidelines . Lung cancer screening V1.2023
MMWR. Morbidity and mortality weekly report, 71(11), 397–405.
Truthinitiative.org

5

Smoking

- A 684 cases of proved lung cancers were studied.
- Data about smoking were collected through special interviews rather than hospital records.
- They interviewed 634 patients, while 33 patients used mail system, and the rest of patients their information were obtained from asking close family members or relatives.

The Journal of the American Medical Association

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Vol. 143, No. 4 — Chicago, Illinois — May 27, 1950

TOBACCO SMOKING AS A POSSIBLE ETIOLOGIC FACTOR IN BRONCHIOGENIC CARCINOMA

A Study of Six Hundred and Eighty-Four Proved Cases

ERNEST L. WYNDER
and
EVARTS A. GRAHAM, M.D.
St. Louis

General Increase.—There is rather general agreement that the incidence of bronchiogenic carcinoma has greatly increased in the last half-century. Statistical studies at the Charity Hospital of New Orleans (Ochsner and DeBakey),[1] the St. Louis City Hospital (Wheeler)[2] and the Veterans Administration Hospital of Hines, Ill. (Avery)[3] have revealed that at these hospitals cancer of the lung is now the most frequent visceral cancer in men.

a few of the workers who thought that there was some evidence that tobacco was an important factor in the increase of cancer of the lungs. Müller[14] in 1939, from a careful but limited clinical statistical study, offered good evidence that heavy smoking is an important etiologic factor. In 1941 Ochsner and DeBakey[15] called attention to the similarity of the curve of increased sales of cigarets in this country to the greater prevalence of primary cancer of the lung. They emphasized the possible etiologic relationship of cigaret smoking to this condition. In a recent paper Schrek[16] concluded that there is strong circumstantial evidence that cigaret smoking is an etiologic factor in cancer of the respiratory tract and finds that his data are in agreement with the results of a preliminary report presented by Wynder and Graham at the National Cancer Conference in February 1949.[17]

Purpose of Study.—The purpose of the present study was to attempt to determine, so far as possible by clini-

J Am Med Assoc 1950;143:329-336

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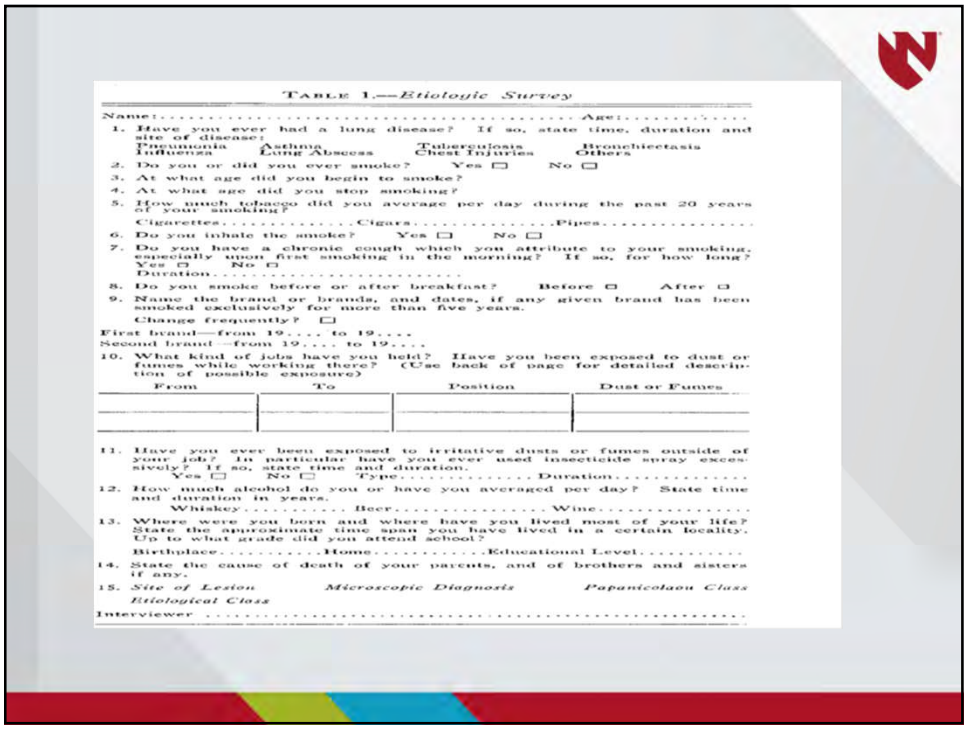

TABLE 1.—*Etiologic Survey*

Name:.....Age:.....

1. Have you ever had a lung disease? If so, state time, duration and site of disease:
   Pneumonia Asthma Tuberculosis Bronchiectasis
   Influenza Lung Abscess Chest Injuries Others
2. Do you or did you ever smoke? Yes ☐ No ☐
3. At what age did you begin to smoke?
4. At what age did you stop smoking?
5. How much tobacco did you average per day during the past 20 years of your smoking?
   Cigarettes.....Cigars.....Pipes.....
6. Do you inhale the smoke? Yes ☐ No ☐
7. Do you have a chronic cough which you attribute to your smoking, especially upon first smoking in the morning? If so, for how long? Yes ☐ No ☐
   Duration.....
8. Do you smoke before or after breakfast? Before ☐ After ☐
9. Name the brand or brands, and dates, if any given brand has been smoked exclusively for more than five years.
   Change frequently? ☐
   First brand—from 19.... to 19....
   Second brand—from 19.... to 19....
10. What kind of jobs have you held? Have you been exposed to dust or fumes while working there? (See back of page for detailed description of possible exposure)

From	To	Position	Dust or Fumes

11. Have you ever been exposed to irritative dusts or fumes outside of your job? In particular have you ever used insecticide spray excessively? If so, state time and duration.
    Yes ☐ No ☐ Type..... Duration.....
12. How much alcohol do you or have you averaged per day? State time and duration in years.
    Whiskey..... Beer..... Wine.....
13. Where were you born and where have you lived most of your life? State the approximate time span you have lived in a certain locality. Up to what grade did you attend school?
    Birthplace.....Home.....Educational Level.....
14. State the cause of death of your parents, and of brothers and sisters if any.
15. *Site of Lesion* *Microscopic Diagnosis* *Papanicolaou Class*
    Etiological Class

Interviewer .....

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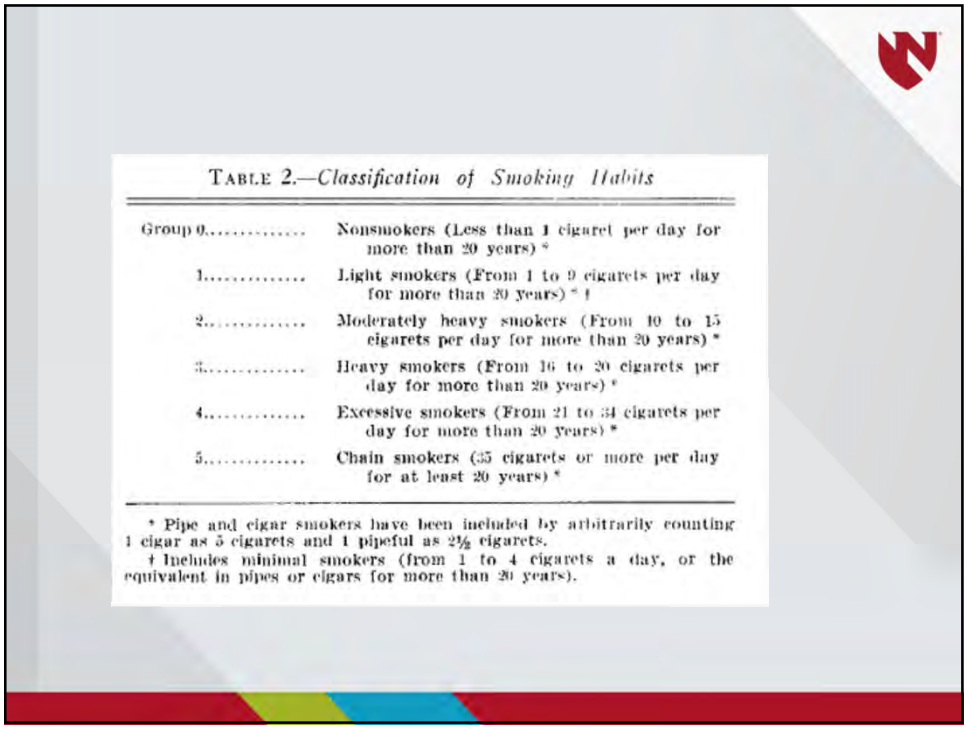

TABLE 2.—*Classification of Smoking Habits*

Group 0.....	Nonsmokers (Less than 1 cigaret per day for more than 20 years) *
1.....	Light smokers (From 1 to 9 cigarets per day for more than 20 years) * †
2.....	Moderately heavy smokers (From 10 to 15 cigarets per day for more than 20 years) *
3.....	Heavy smokers (From 16 to 20 cigarets per day for more than 20 years) *
4.....	Excessive smokers (From 21 to 34 cigarets per day for more than 20 years) *
5.....	Chain smokers (35 cigarets or more per day for at least 20 years) *

* Pipe and cigar smokers have been included by arbitrarily counting 1 cigar as 5 cigarets and 1 pipeful as 2½ cigarets.

† Includes minimal smokers (from 1 to 4 cigarets a day, or the equivalent in pipes or cigars for more than 20 years).

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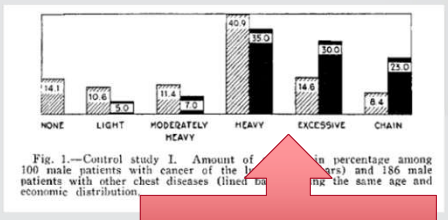


Fig. 1.—Control study I. Amount of ... in percentage among 100 male patients with cancer of the l... ars) and 186 male patients with other chest diseases (lined ... the same age and economic distribution.

95% of cancer cases were at least moderately heavy smokers

9

Smoking is BAD!

- Since that time, it has been clearly established that smoking is associated not only with lung cancer but with other cancers/diseases
- The FDA has defined a list of 93 chemicals that are considered harmful and potentially harmful in tobacco products.
  - Each cigarette has at least 20 carcinogens that are proven to cause lung cancer in laboratory animals or humans. Most importantly is polycyclic aromatic hydrocarbons and the tobacco-specific nitrosamine 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone.
- Cigarette smoking is thought to be causal in 85-90% of all lung cancer.
- The RR for lung cancer is approximately **20-fold higher** for individuals who currently smoke than for those who never smoked

NCCN guidelines 2022
J Natl Cancer Inst 1999;91:1194-1210
Chest. 2003;123(1 Suppl):21S.

10

Smoking is FATAL!!

- In the US, It is estimated that about 480,000 individuals die from smoking-related illnesses annually.
- The WHO estimates that 5 million people globally die from tobacco use every year and estimates that the number will double in the next 15 years.

MMWR Morb Mortal Wkly Rep 2012;61:889-894.
N Engl J Med 2014;370:60-68

11

Passive smoking

- It was first suggested as risk factor in 1980s
- A pooled analysis of 37 published studies found an estimated RR of 1.24 (95% CI, 1.13–1.36) if you live with someone who smokes
- A pooled estimate from 25 studies found an RR of 1.22 (95% CI, 1.13–1.33) if you work with someone who smoke
- Results were not consistent for children who got passive exposure.

The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General (ed 2010/07/30). Atlanta; 2006
The accumulated evidence on lung cancer and environmental tobacco smoke. BMJ 1997;315:980-988

12

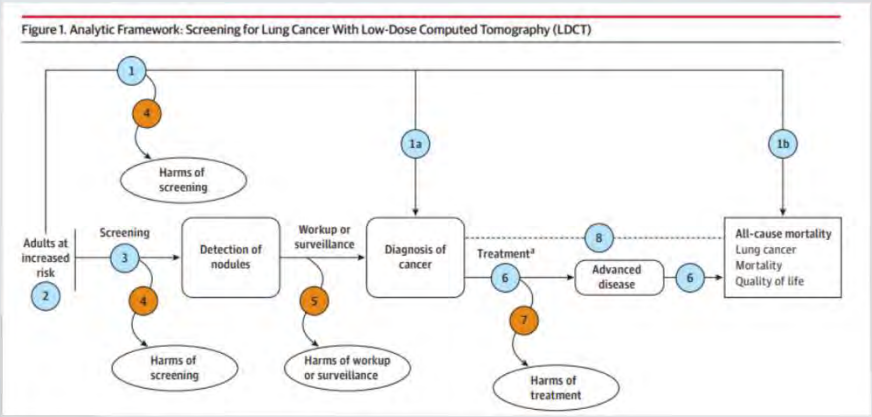
Other risk factors

- Radon exposure→ RR 1.14
- History of other cancers cancer treated with chest irradiation or chemotherapies.
- Family history of lung cancer: RR 1.8
- Non-malignant lung diseases : COPD (even in never smokers) or pulmonary fibrosis

NCCN guidelines . Lung cancer screening V1.2023
J Natl Cancer Inst 1997;89:49-57.
Am J Respir Crit Care Med 2000;161:5-8

13

Who should we screen



JAMA. 2021;325(10):971-987.

14

Who are high risk population

- This definition was based on clinical trials population/guidelines.
- In general: Adults > 50 years with a 20 pack-year or more history of cigarette smoking who currently smoked or had quit within the past 15 years

JACR vol. 12,2 (2015): 192-7.

15

Is this definition enough?

- Studies showed that this definition is not sufficient→ only 27% of patients being diagnosed with lung cancer would be candidates for LDCT screening (based on USPTF)
- So, the old definition is not enough.

JACR vol. 12,2 (2015): 192-7.

16

How to screen

- Sputum cytology + CXR
- Low dose CT scan

17

The Johns Hopkins Lung Project

- A study that was conducted in 1980s
- The study goal/question:
  - Was to determine whether the addition of cytologic screening to the radiographic screening of high-risk volunteers could enhance the early detection of asymptomatic lung cancer.
- The study design:
  - Study involved male volunteers, >=45 year of age, who smoked at least 1 pack of cigarettes per day from the Baltimore metropolitan area.
  - All of the 10,387 acceptable high-risk volunteers received annual chest radiographic screening. By random assignment, one half received cytologic examination of induced sputum in addition to CXR

Am Rev Respir Dis. 1984 Oct;130(4):549-54.

18

Results

- Screening by sputum cytology was found to improve the detection only of squamous cell carcinoma.
- Sputum cytology accounted for 28% of the detected cases,and resulted in 39% additional detection of lung cancer
- Lung cancers detected by cytology alone were found at very early stages.
- Change in survival was felt to be from lead-time bias

19

The Early Lung Cancer Action Project (ELCAP)

- Study conducted in 1990s.
- Study question/goal:
  - Was to evaluate LDCT as a screening technique in people at high risk of lung cancer
  - Comparing chest radiographs and low-dose CT
- Study design:
  - Enrolled 1000 patients, 60 years of age or older, with at least 10 pack-years.
  - CXR and LDCT scan were done for each patient

Oncologist. 2001;6(2):147-52.

20

Results

- Detection of baseline non-calcified nodules were higher in CT scan (23% vs 7%) in CXR.
- Detection of cancer was higher using CT scan compared to CXR (2.7% vs 0.7%)
- Of the 27 CT-detected cancers, 26 were resectable.

21

The National Lung Screening Trial (NLST)

N Engl J Med 2011;365:395-409.

22

Design and Methods

- Conducted between August 2002 through April 2004.
- High risk population defined as
  - Age 55-74 years at the time of randomization.
  - At least 30 packyears smoking history, and, if former smokers, had quit within the previous 15 years.
- It enrolled 53,454 persons at high risk for lung cancer at 33 U.S. medical centers.
- Patients randomized to 2 groups : LDCT vs CXR
- Data were collected on cases of lung cancer and deaths from lung cancer that occurred through December 31, 2009.

23

Table 1. Selected Baseline Characteristics of the Study Participants.*

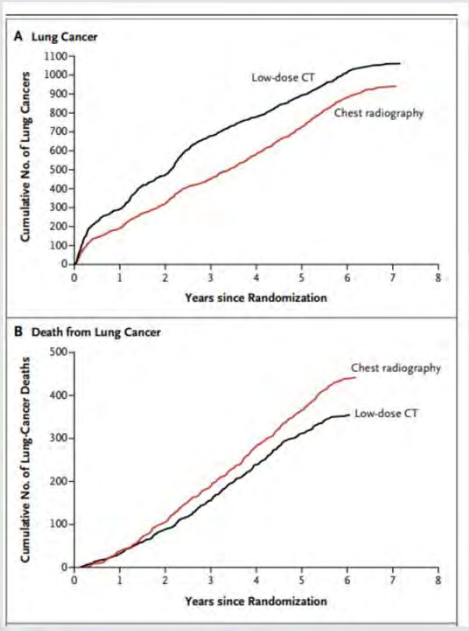
Characteristic	Low-Dose CT Group (N=26,722)	Radiography Group (N=26,732)
	number (percent)	
Age at randomization		
<55 yr†	2 (<0.1)	4 (<0.1)
55–59 yr	11,440 (42.8)	11,420 (42.7)
60–64 yr	8,170 (30.6)	8,198 (30.7)
65–69 yr	4,756 (17.8)	4,762 (17.8)
70–74 yr	2,353 (8.8)	2,345 (8.8)
≥75 yr†	1 (<0.1)	3 (<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)

24

Table 2. Results of Three Rounds of Screening.*

Screening Round	Low-Dose CT				Chest Radiography			
	Total No. Screened	Positive Result	Clinically Significant Abnormality Not Suspicious for Lung Cancer	No or Minor Abnormality	Total No. Screened	Positive Result	Clinically Significant Abnormality Not Suspicious for Lung Cancer	No or Minor Abnormality
			no. (% of screened)				*no. (% of screened)*	
T0	26,309	7191 (27.3)	2695 (10.2)	16,423 (62.4)	26,035	2387 (9.2)	785 (3.0)	22,863 (87.8)
T1	24,715	6901 (27.9)	1519 (6.1)	16,295 (65.9)	24,089	1482 (6.2)	429 (1.8)	22,178 (92.1)
T2	24,102	4054 (16.8)	1408 (5.8)	18,640 (77.3)	23,346	1174 (5.0)	361 (1.5)	21,811 (93.4)

25



26

Results

LDCT

- Rate of positive screen: 24.2%
- Rate of false positive: 96.4%
- Incidence of lung cancer: 645 per 100,000
- Mortality from lung cancer: 247 per 100,000
- NNS to prevent death: 320.

CXR

- Rate of positive screen: 6.9%
- Rate of false positive: 94.5%
- Incidence of lung cancer: 572 per 100,000
- Mortality from lung cancer: 309 per 100,000

- Rate of adherence was >90%
- LDCT resulted in relative reduction in cancer mortality by 20% (95% CI, 6.8 to 26.7; P=0.004)
- Overdiagnosis rate was 18.5%
- Rate of death from any cause was also reduced by LDCT scan by 6.7% (95% CI, 1.2 to 13.6; P=0.02)

27

NLST Extended follow up in 2019

- ❑ The median follow-up times were 11.3 years for incidence and 12.3 years for mortality.
- ❑ NNS to prevent one death was similar (303).
- ❑ There was no difference in incidence (1701 in LDCT vs 1681 in CXR) (RR = 1.01, 95% confidence interval [CI]: 0.95-1.09).
- ❑ Lung cancer mortality RR was 0.89 (95% CI: 0.80–0.997).

Journal of thoracic oncology : official publication of the International Association for the Study of Lung Cancer vol. 14,10 (2019): 1732-1742.

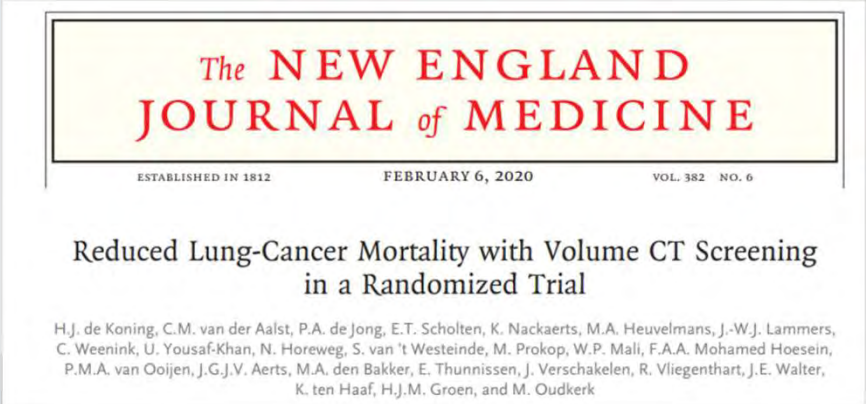
28

NLST impact

- The U.S. Preventive Services Task Force recommended annual screening for persons 55 to 80 years of age with a smoking history of 30 or more pack-years, who currently smoke or quit smoking within the past 15 years.

29

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

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N Engl J Med 2020;382:503-13.

30

Design and Methods

- Conducted between January 2004 - December 2012.
- Aimed to show a 25% reduction in lung-cancer mortality by using LDCT for screening in high risk population
- High risk population defined as
  - Born between 1928-1956
  - Smoked >15 cigarettes/day for >25 years
  - Smoked >10 cigarettes/day for >30 years
  - Current or former smoker who quit smoking =<10 years ago
- Participants were randomly assigned to:
  - Undergo CT screening at T0 (baseline), year 1, year 3, and year 5.5
  - No screening.
- A minimum follow-up of 10 years until December 31, 2015, was completed for all participants.

31

Results

Table 1. Baseline Characteristics of the Male Participants at Randomization.*

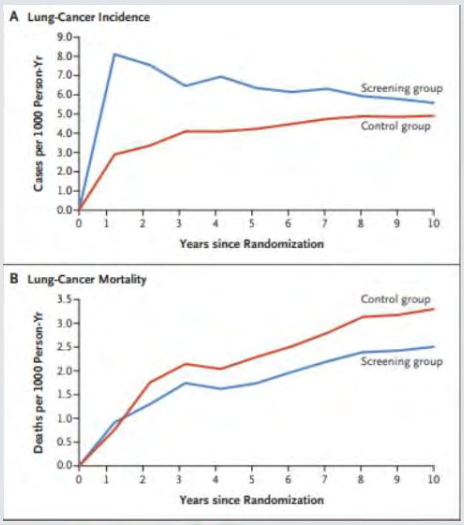
Characteristic	Screening Group (N=6583)	Control Group (N=6612)
Age		
Median (IQR) — yr	58 (55–63)	58 (54–63)
Range — yr	46–76	34–89
Distribution — no./total no. (%)†		
<50 yr	3/6560 (<0.1)	6/6571 (0.1)
50–54 yr	1611/6560 (24.6)	1694/6571 (25.8)
55–59 yr	2226/6560 (33.9)	2231/6571 (34.0)
60–64 yr	1554/6560 (23.7)	1475/6571 (22.4)
65–69 yr	797/6560 (12.1)	781/6571 (11.9)
70–74 yr	329/6560 (5.0)	337/6571 (5.1)
≥75 yr	40/6560 (0.6)	47/6571 (0.7)
Pack-yr of smoking‡		
Median (IQR)	38.0 (29.7–49.5)	38.0 (29.7–49.5)
Range	0.4–159.5	1.3–156.0
Cigarettes smoked per day — no./total no. (%)		
≤10	20/6565 (0.3)	18/6596 (0.3)
11–15	1470/6565 (22.4)	1437/6596 (21.8)
16–20	1859/6565 (28.3)	1859/6596 (28.2)
21–25	1732/6565 (26.4)	1779/6596 (27.0)
26–30	669/6565 (10.2)	723/6596 (11.0)
31–40	454/6565 (6.9)	437/6596 (6.6)
>40	361/6565 (5.5)	343/6596 (5.2)
Duration of smoking — no./total no. (%)		
≤25 yr	25/6563 (0.4)	21/6594 (0.3)
26–30 yr	657/6563 (10.0)	722/6594 (10.9)
31–35 yr	1652/6563 (25.2)	1700/6594 (25.8)
36–40 yr	2030/6563 (30.9)	2105/6594 (31.9)
41–45 yr	1451/6563 (22.1)	1317/6594 (20.0)
≥45 yr	748/6563 (11.4)	729/6594 (11.1)
Age at initiation of smoking — no./total no. (%)		
<15 yr	1153/6560 (17.6)	1141/6588 (17.3)
15–29 yr	5376/6560 (82.0)	5407/6588 (82.1)
≥30 yr	31/6560 (0.5)	40/6588 (0.6)
Smoking status — no./total no. (%)		
Current	3643/6566 (55.5)	3611/6595 (54.8)
Former	2923/6566 (44.5)	2984/6595 (45.2)
Years since cessation of smoking — no./total no. (%)		
<1	489/2908 (16.8)	493/2963 (16.6)
1–5	1316/2908 (45.3)	1334/2963 (45.0)
6–10	1054/2908 (36.2)	1096/2963 (37.0)
>10	49/2908 (1.7)	40/2963 (1.3)

32

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.*

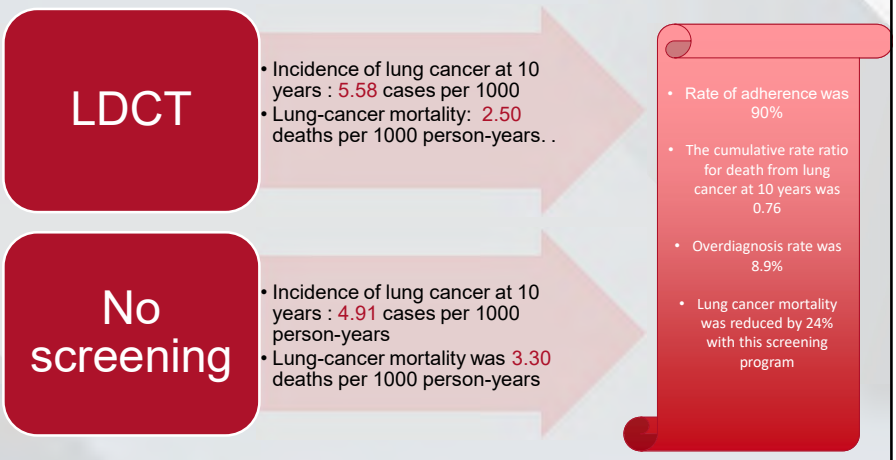
Variable	Screening Group (N=868)	Control Group (N=860)	Total (N=1728)	Rate Ratio (95% CI)
	number (percent)			
Cause of death — no. (%)				
Lung cancer	160 (18.4)	210 (24.4)	370 (21.4)	0.76 (0.62–0.94)
No lung cancer after cause-of-death review, no other specification	6 (0.7)	11 (1.3)	17 (1.0)	0.55 (0.17–1.61)
Other neoplasm	318 (36.6)	289 (33.6)	607 (35.1)	1.10 (0.94–1.30)
Cardiovascular disease	189 (21.8)	181 (21.0)	370 (21.4)	1.05 (0.85–1.29)
Respiratory disease	42 (4.8)	43 (5.0)	85 (4.9)	0.98 (0.62–1.53)
Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified	37 (4.3)	20 (2.3)	57 (3.3)	1.86 (1.05–3.37)
Diseases of the digestive system	30 (3.5)	21 (2.4)	51 (3.0)	1.43 (0.79–2.63)
External causes of illness and death	24 (2.8)	19 (2.2)	43 (2.5)	1.27 (0.67–2.45)
Endocrine, nutritional, and metabolic diseases	21 (2.4)	9 (1.0)	30 (1.7)	2.34 (1.03–5.80)
Diseases of the nervous system	9 (1.0)	19 (2.2)	28 (1.6)	0.48 (0.19–1.10)
Other cause of death	26 (3.0)	28 (3.3)	54 (3.1)	0.93 (0.52–1.65)
Unknown	6 (0.7)	10 (1.2)	16 (0.9)	0.60 (0.18–1.83)
Total person-yr at risk	62,298	62,484	124,782	
All-cause mortality — deaths per 1000 person-yr	13.93	13.76	13.85	1.01 (0.92–1.11)

33



34

Results



35

To summarize

- The NLST:
  - Reduction in lung cancer mortality incidence rate ratio 0.85 [95% CI, 0.75-0.96]
  - NNS to prevent one lung cancer death is 323 over 6.5 years of follow-up with 3 rounds of annual LDCT screening compared with chest radiograph for high-risk current and former smokers aged 55 to 74 years.
- NELSON
  - Reduction in lung cancer mortality incidence rate ratio 0.75 [95% CI, 0.61-0.90]
  - NNS to prevent 1 lung cancer death of 130 over 10 years of follow-up with 4 rounds of LDCT screening with increasing intervals compared with no screening for high-risk current and former smokers aged 50 to 74 years.

36

JAMA | US Preventive Services Task Force | EVIDENCE REPORT

Screening for Lung Cancer With Low-Dose Computed Tomography
Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

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JAMA. 2021;325(10):971-987.

37

Table 1. Characteristics of Included RCTs Evaluating Screening With LDCT Compared With Chest Radiography or With No Screening

Source	Recruitment years	Sample size; country	Mean age (ages eligible), y	% Male	Baseline smoking status, %	Eligibility criteria for pack-years; years since quitting	Screening rounds, No.	Screening intervals, y	Total median follow-up, y	Quality
DANTE[12-14]	2001-2006	2472; Italy	65 (60-74)	100	Current: 57 Former: 43 Mean No. of pack-years: 47	≥20; <10 y	5	0, 1, 2, 3, 4	8.4	Fair
DLCST[15,16]	2004-2006	4104; Denmark	58 (50-70)	56	Current: 76 Former: 24 Mean No. of pack-years: 36	≥20; quit after age 50 and <10 y ago	5	0, 1, 2, 3, 4	9.8	Fair
ITALUNG[17]	2004-2006	3206; Italy	61 (55-69)	65	Current: 65 Former: 35 Median No. of pack-years: 39	≥20 in the last 10 y or quit within the last 10 y	4	0, 1, 2, 3	9.3[a]	Fair
LSS[18-20b]	2000-2001	3318; US	NR (55-74)	59	Current: 58 Former: 42 Median No. of pack-years: 54	≥30; <10 y	2	0, 1	5.2	Fair
LUSI[21-23]	2007-2011	4052; Germany	NR (50-69)	65	Current: 62 Former: 35 Mean No. of pack-years: NR	≥25 y of 15 cigarettes or ≥30 y of 10 cigarettes; ≤10 y	5	0, 1, 2, 3, 4	8.8	Fair
NELSON[24-28]	2003-2006	15 792; the Netherlands and Belgium	Median, 58 (50-74)	84	Current: 55 Former: 45 Median No. of pack-years: 38	>15 cigarettes/d for >25 y or >10 cigarettes/d for >30 y; ≤10 y	4	0, 1, 3, 5.5	10	Fair
NLST[29-37b]	2002-2004	53 542; US	61 (55-74)	59	Current: 48 Former: 52 Mean No. of pack-years: 56	≥30; ≤15 y	3	0, 1, 2	7 (and posttrial follow-up to 12.3 y)	Good[c]

Abbreviations: DANTE, Detection and Screening of Early Lung Cancer by Novel Imaging Technology and Molecular Essays; DLCST, Danish Lung Cancer

[a] The ITALUNG study reported 9.3 years for lung cancer-specific mortality and 8.5 years for lung cancer incidence.

38

Recommendation Summary

Population	Recommendation	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	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in 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. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B

39

Guidelines for lung cancer screening

Organization	Recommendation	Year
American Association of Thoracic Surgery	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 79 years with ≥30 pack-year history of smoking and current smoker or quit within past 15 years; ages 50 to 79 years with ≥20 pack-year history and cumulative risk >5% over next 5 years; or lung cancer survivors with no incidence of disease for ≥4 years).	2012
American Cancer Society	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 74 years with ≥30 pack-year history of smoking and current smoker or quit within past 15 years).	2013
American College of Chest Physicians	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 77 years with ≥30 pack-year history of smoking and current smoker or quit within past 15 years).	2018
American Society of Clinical Oncology	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55 to 74 years with ≥30 pack-year history of smoking and current smoker or quit within past 15 years).	2019
Canadian Task Force on the Periodic Health Examination	Recommends screening asymptomatic adults aged 55 to 74 years with at least a 30 pack-year smoking history who smoke or quit smoking <15 years ago with low-dose CT every year for 3 consecutive years.	2016
National Comprehensive Cancer Network	Recommends annual low-dose CT scan screening for high-risk individuals (age 50 years or greater with ≥20 pack-year history of smoking). Screening is not recommended for individuals with functional status or comorbidity that would prohibit curative-intent therapy.	2022
US Preventive Services Task Force	Recommends annual low-dose CT scan screening for high-risk individuals (ages 50 to 80 years with a 20 pack-year history of smoking and current smoker or quit within past 15 years). Discontinue when person has not smoked for 15 years or if limited life expectancy.	2021
Centers for Medicare and Medicaid Services	Recommends annual low-dose CT scan screening after completion of a shared decision-making visit for high-risk individuals (ages 50 to 77 years with ≥20 pack-year history of smoking and current smoker or quit within the past 15 years).	2022
American Academy of Family Physicians	Supports the United States Preventive Services Task Force recommendation for annual screening for lung cancer with low-dose CT in adults (ages 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years).	2021

This table covers some of the more common societies and governmental agencies. It is not meant to be comprehensive.

Risk of developing cancer can be calculated by the Tammemägi 2012 PLCO(m2012) lung cancer risk prediction model.[1]

CT: computed tomography.

References

1. Tammemägi MC, Church TR, Hocking WG, et al. Evaluation of the lung cancer risks at which to screen ever- and never-smokers: screening rules applied to the PLCO and NLST cohorts. PLoS Med 2014; 11:e1001764.

UpToDate

Uptodate.com

40

Making decision with patients

- Lung cancer has many characteristics that makes screening an effective:
  - High morbidity
  - High mortality
  - Significant prevalence
  - Identified risk factors allowing targeted screening for high-risk individuals

But is it true for everyone?

41

Benefits of screening

1. Detect early cancers:
   - Can increase cure rate.
   - Improves mortality based on clinical trial.
   - Allow more limited surgical resection.
2. Can affect smoking cessation rates.
   - A reviewed data from NELSON trial showed that 17% of participants quit smoking compared to 3% in general population

Thorax vol. 65,7 (2010): 600-5.

42

Harms of screening

1. False positive findings (benign findings)
   - In NLST→ 96% were false-positive , 11% led to invasive procedure
2. Radiation exposure
3. Patient distress
4. Overdiagnosis

43

Dilemma of screening

- ❑ Could be a moral obligation for physician!
  - ❑ Hippocratic oath → promise first to do no harm
- ❑ You need to balance
  - ❑ If not screening… can miss a cancer
  - ❑ But also, can lead to overdiagnosis, invasive testing or procedures, and the anxiety.

44

45