Lung Cancer Screening in 2019

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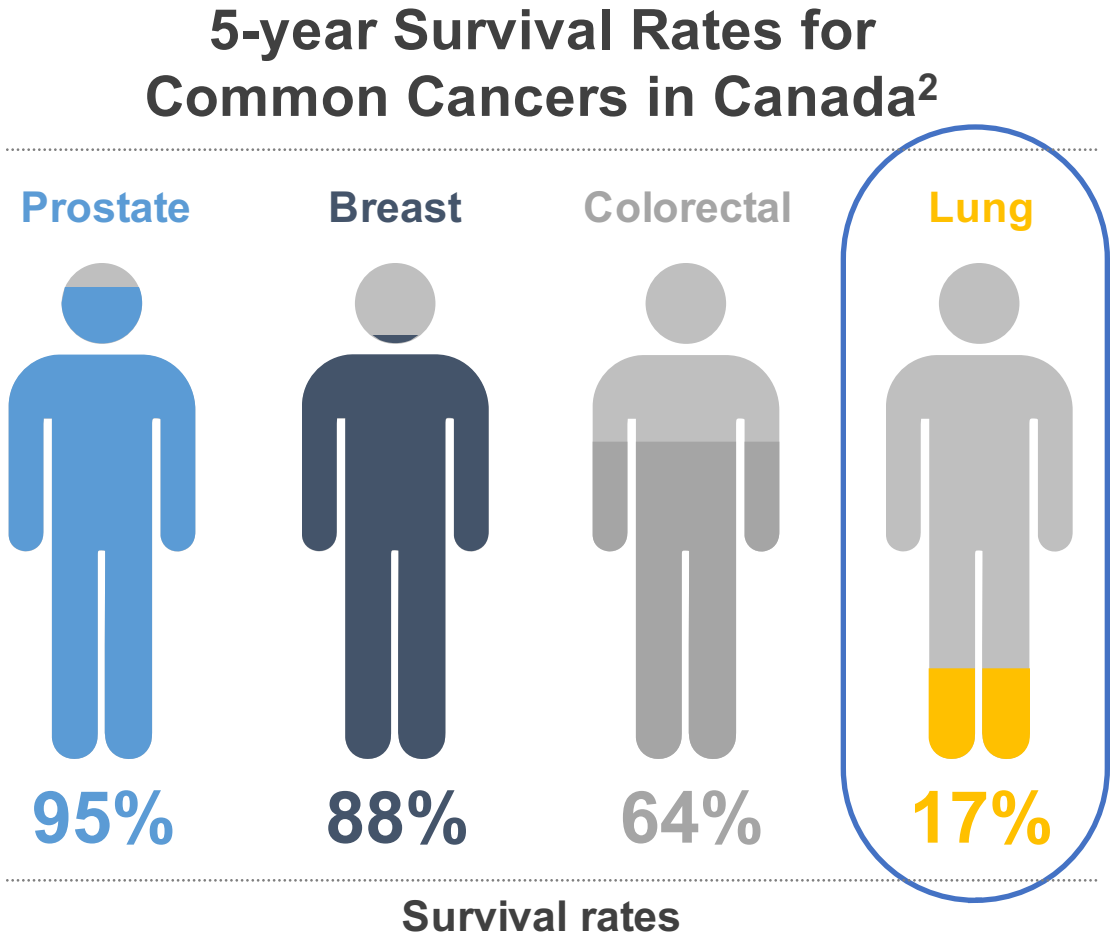
Objectives

- As a result of attending this session, participants should be able to:
- Comprehend Canadian Statistics of lung cancer
- Discuss risk factors for lung cancer
- To interpret lung cancer screening studies
- To review guidelines for lung cancer screening

NSCLC=non-small cell lung cancer

Lung Cancer Continues to Be a Major Health Problem in Canada

- One of the most common cancers in Canada[1]
  - ~28,600 new cases diagnosed in 2017
- Most common cause of cancer-related death in Canada (26% of cancer mortality)[1]
  - Low 5-year survival rates
  - More deaths than breast and colon cancer combined[2]



1. Canadian Cancer Society. *Canadian Cancer Statistics 2018.*
2. Lung Cancer Canada. *2015 Faces of Lung Cancer Report*

Canadian Cancer Statistics 2019 snapshot of incidence, mortality and survival estimates by cancer type

Both sexes combined	Incidence			Mortality			Survival
	Rank	Cases	Trend	Rank	Deaths	Trend	5-year (%)
All cancers	—	**220,400**	↓	—	**82,100**	↓	**63**
Lung and bronchus	1	29,300	↓	1	21,000	↓	19
Breast	2	27,200	↓	4	5,100	↓	88
Colorectal	3	26,300	↓	2	9,500	↓	65
Prostate	4	22,900	↓	5	4,100	—	93
Bladder	5	11,800	→	8	2,500	↓	75
Non-Hodgkin lymphoma	6	10,000	↑	7	2,800	↓	68
Thyroid	7	8,200	→	21	230	→	98
Melanoma	8	7,800	↑	17	1,300	↑	88
Kidney and renal pelvis	9, 10	7,200	→	12	1,900	↓	71
Uterus (body, NOS)	9, 10	7,200	→	18	1,250	—	83
Leukemia	11	6,700	→	6	3,000	↓	59
Pancreas	12	5,800	↑	3	5,200	→	8
Oral	13	5,300	↑	15	1,450	→	64
Stomach	14	4,100	↓	11	1,950	↓	28
Multiple myeloma	15	3,300	↑	14	1,550	↓	44
Brain/CNS	16, 17, 18	3,000	↓	9	2,400	↑	23
Ovary	16, 17, 18	3,000	↓	13	1,900	—	45
Liver	16, 17, 18	3,000	→	16	1,400	↑	19
Esophagus	19	2,300	↓	10	2,200	→	15
Cervix	20	1,350	↓	19	410	—	72
Larynx	21, 22	1,150	↓	20	400	↓	62
Testis	21, 22	1,150	↑	23	35	—	97
Hodgkin lymphoma	23	1,000	↓	22	100	↓	86
All other cancers	—	21,300	→	—	10,300	—	—
Source*	Table 1.2		Table 1.7	Table 2.2		Table 2.7	Table 3.1

Canadian Cancer Statistics 2019 snapshot of incidence, mortality and survival estimates by cancer type, males

Males	Incidence			Mortality			Survival
	Rank	Cases	Trend	Rank	Deaths	Trend	5-year (%)
All cancers	—	**113,000**	↓	—	**43,300**	↓	**61**
Prostate	1	22,900	↓	3	4,100	↓	93
Lung and bronchus	2	14,900	↓	1	10,900	↓	15
Colorectal	3	14,600	↓	2	5,200	↓	65
Bladder	4	9,100	→	5	1,800	↓	75
Non-Hodgkin lymphoma	5	5,600	↑	8	1,600	→	67
Kidney and renal pelvis	6	4,700	→	10	1,250	↓	70
Melanoma	7	4,300	↑	15	840	↑	84
Leukemia	8	4,000	↑	6	1,750	↓	59
Oral	9	3,700	→	13	1,050	→	64
Pancreas	10	3,000	↑	4	2,700	→	8
Stomach	11	2,600	↓	11	1,200	↓	27
Liver	12	2,200	→	12	1,100	↑	18
Thyroid	13	2,100	↑	17	100	→	94
Multiple myeloma	14	1,950	↑	14	860	↓	44
Esophagus	15	1,800	↓	7	1,700	↓	15
Brain/CNS	16	1,650	↓	9	1,400	↓	22
Testis	17	1,150	↑	20	35	↓	97
Larynx	18	980	↓	16	330	↓	63
Hodgkin lymphoma	19	560	↓	18	60	↓	85
Breast	20	230	↑	19	55	↓	80
Other cancers	—	11,000	↑	—	5,300	↓	—
Source*	Table 1.2		Table 1.7	Table 2.2		Table 2.7	Table 3.1

Canadian Cancer Society / Société canadienne du cancer
Government of Canada / Gouvernement du Canada
Cancer-specific stats 2019

Canadian Cancer Statistics 2019 snapshot of incidence, mortality and survival estimates by cancer type, females

Females	Incidence			Mortality			Survival
	Rank	Cases	Trend	Rank	Deaths	Trend	5-year (%)
All cancers	—	**107,400**	↓	—	**38,700**	↓	**65**
Breast	1	26,900	↓	2	5,000	↓	88
Lung and bronchus	2	14,500	↓	1	10,100	↓	22
Colorectal	3	11,700	↓	3	4,400	↓	65
Uterus (body, NOS)	4	7,200	→	6,7,8	1,250	↑	83
Thyroid	5	6,100	→	19	130	↓	99
Non-Hodgkin lymphoma	6	4,400	↑	6,7,8	1,250	↓	70
Melanoma	7	3,500	↑	15	450	↑	91
Ovary	8	3,000	↓	5	1,900	↓	45
Pancreas	9	2,800	→	4	2,500	↓	8
Bladder	10,11	2,700	→	11	700	↓	73
Leukemia	10,11	2,700	→	6,7,8	1,250	↓	59
Kidney and renal pelvis	12	2,500	↑	13	670	↓	72
Oral	13	1,600	↑	16	430	↓	66
Stomach	14	1,450	↓	10	760	↓	29
Multiple myeloma	15	1,400	↑	12	690	↓	45
Cervix	16	1,350	↓	17	410	→	72
Brain/CNS	17	1,300	→	9	1,050	↑	24
Liver	18	780	↑	18	280	↑	21
Esophagus	19	540	↓	14	500	↓	17
Hodgkin lymphoma	20	440	→	21	40	↓	87
Larynx	21	190	↓	20	75	↓	57
Other cancers	—	10,300	↑	—	4,900	↓	—
Source*	Table 1.2		Table 1.7	Table 2.2		Table 2.7	Table 3.1

Statistics - Canada

Canadian Cancer Society

Incidence and mortality

Incidence is the total number of new cases of cancer. Mortality is the number of deaths due to cancer.

It is estimated that in 2019:

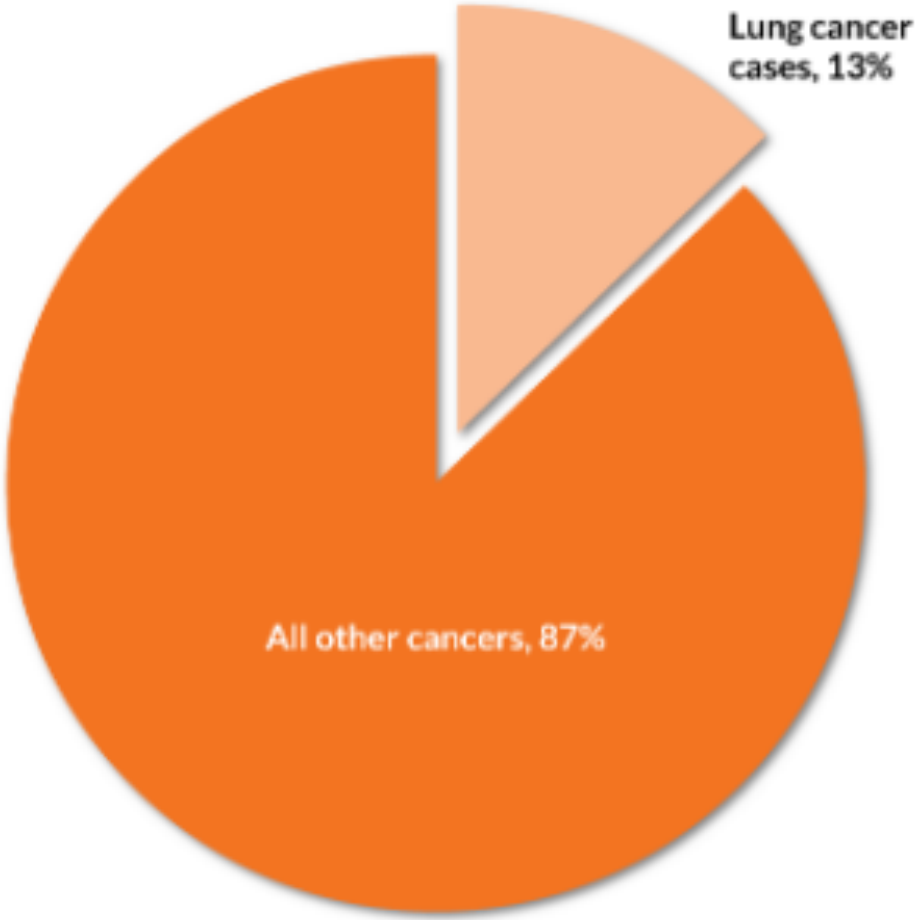
- 29,300 Canadians will be diagnosed with lung cancer. This represents 13% of all new cancer cases in 2019.
- 21,000 Canadians will die from lung cancer. This represents 26% of all cancer deaths in 2019.
- 14,900 men will be diagnosed with lung cancer and 10,900 will die from it.
- 14,500 women will be diagnosed with lung cancer and 10,100 will die from it.
- On average, 80 Canadians will be diagnosed with lung cancer every day.
- On average, 58 Canadians will die from lung cancer every day.

Estimated Canadian lung cancer statistics (2019)

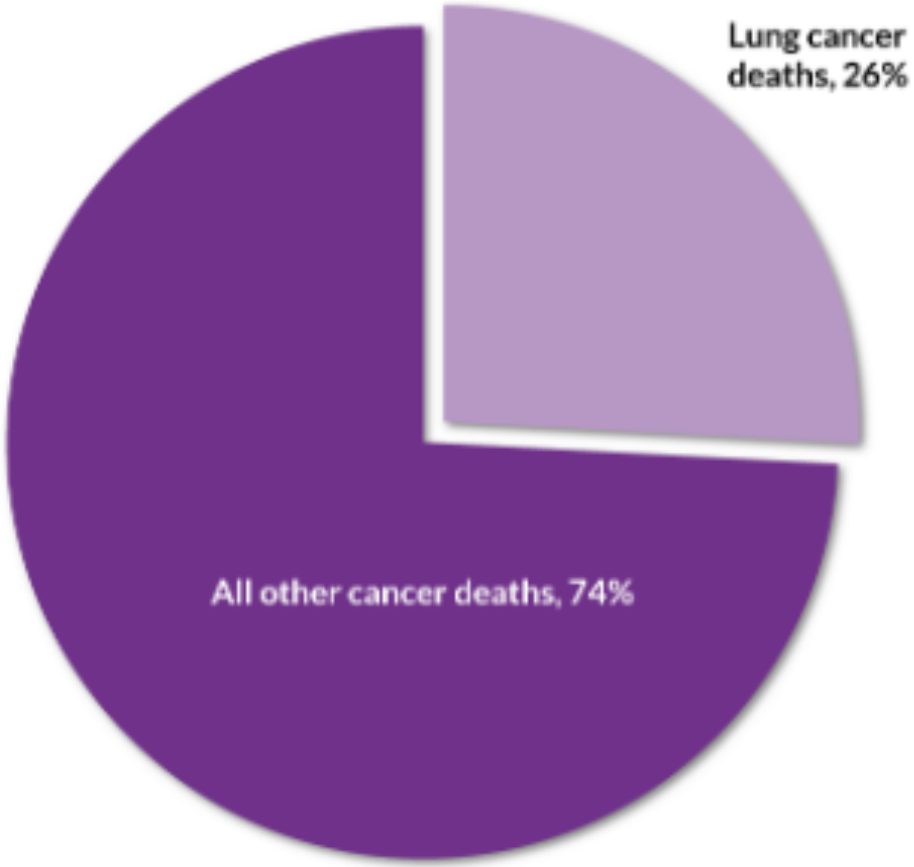
Category	Males	Females
New cases	14,900	14,500
Deaths	10,900	10,100
5-year net survival (estimates for 2012 to 2014)	15%	22%

Canadian Cancer Society

Percentage of All Estimated New Cancer Cases in Both Sexes Combined in 2019



Percentage of All Estimated Cancer Deaths in Both Sexes Combined in 2019



Trends in lung cancer

In Canada, the incidence rate of lung cancer is higher in men than in women. In males, the rate of lung cancer began decreasing in 1990. In females, the lung cancer incidence rate began decreasing in 2011.

The difference in incidence rates and trends between the sexes is likely because of differences in tobacco use. More men smoked than females, and men's smoking rates began to decline earlier than women's smoking rates.

In males, the death rate from lung cancer began to level off in the late 1980s and has been declining ever since. The death rate for females was increasing until 2006 but is now decreasing. Men continue to have a higher rate of lung cancer death than women.

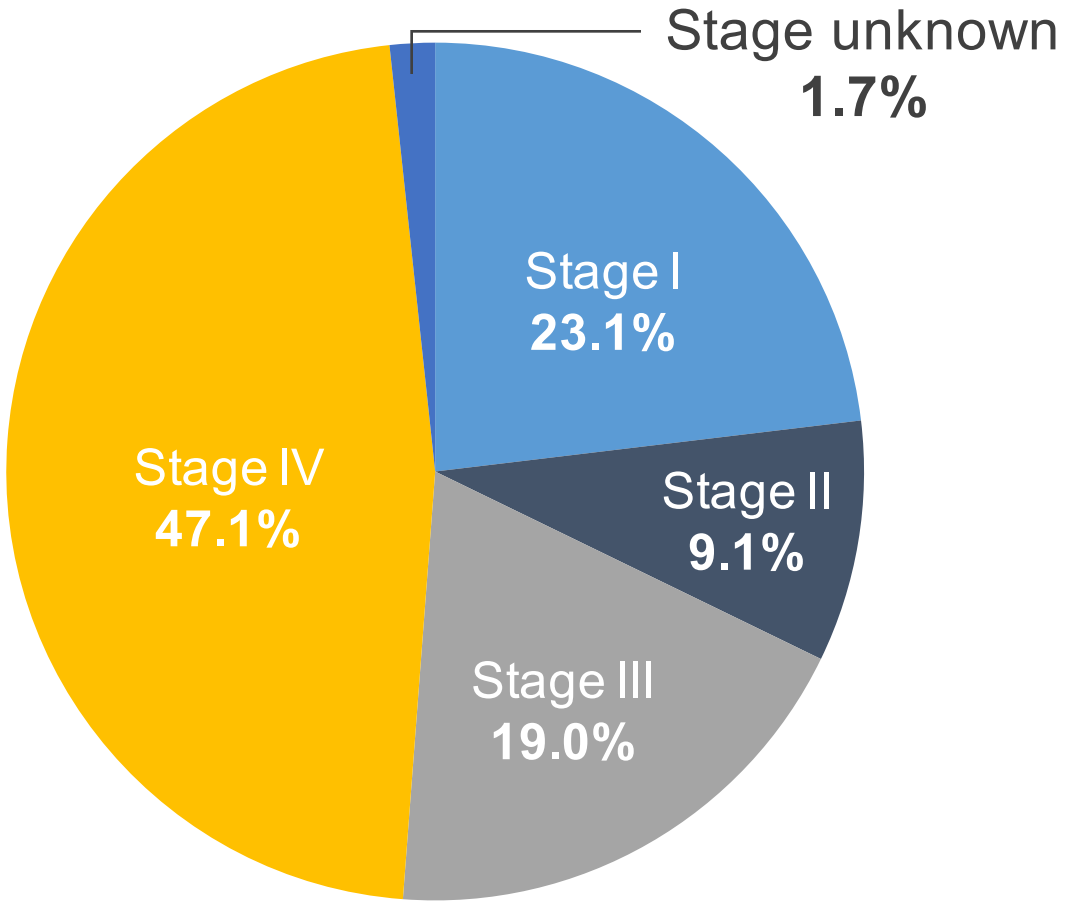
Chances (probability) of developing or dying from lung cancer

It is estimated that about 1 in 14 Canadian men will develop lung cancer during their lifetime and one in 16 will die from it.

It is estimated that about 1 in 15 Canadian women will develop lung cancer during their lifetime and one in 19 will die from it.

Why Is Lung Cancer Mortality so High? Most Are at Advanced Stage at Diagnosis

NSCLC: Percent distribution by stage at diagnosis in Canada, 2011-2015



Canadian Cancer Society. *Canadian Cancer Statistics 2018.*

Cancer in Quebec – 2019 estimates

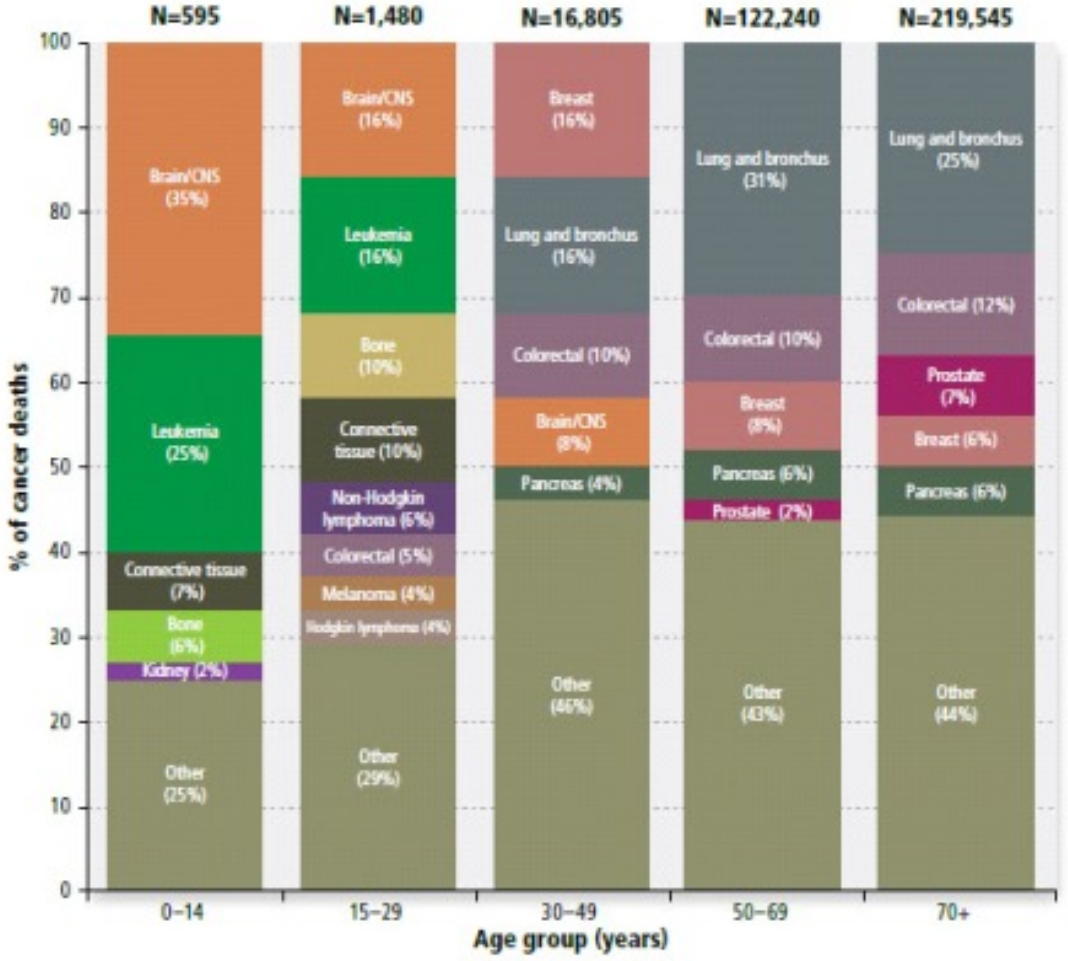
- 4,800 men will be diagnosed with prostate cancer
- 4,300 men will be diagnosed with lung cancer
- 3,800 men will be diagnosed with colorectal cancer

- 3,500 men will die of lung cancer
- 1,450 men will die of colorectal cancer
- 880 men will die of prostate cancer

- 6,500 women will be diagnosed with breast cancer
- 4,100 women will be diagnosed with lung cancer
- 3,000 women will be diagnosed with colorectal cancer

- 3,100 women will die of lung cancer
- 1,300 women will die of breast cancer
- 1,200 women will die of colorectal cancer

FIGURE 4.2 Distribution of cancer deaths for selected cancers by age group, Canada, 2008–2012



N is the total number of cases over 5 years (2008–2012) for each age group; CNS=Central nervous system.

Note: The complete definition of the specific cancers listed here can be found in Table A8.

Analysis by: Surveillance and Epidemiology Division, CCDP, Public Health Agency of Canada
Data source: Canadian Vital Statistics Death database at Statistics Canada

Risk Factors

Known risk factors	Possible risk factors
Smoking tobacco	Occupational exposure to certain chemicals
Second-hand smoke	Genetic mutations
Radon	Smoking marijuana
Asbestos	Physical inactivity
Occupational exposure to certain chemicals	A diet low in vegetables and fruit
Outdoor air pollution	
Personal or family history of lung cancer	
Personal history of lung disease	
Exposure to radiation	
Arsenic in drinking water	
Pollutants from cooking and heating	
Weakened immune system	
Lupus	
Beta carotene supplements in smokers	

Canadian Cancer Society / Société canadienne du cancer

Prevention

- Smoking Cessation
  - Most effective intervention to reduce the risk of lung cancer
- More than 85% of lung cancer cases in Canada are related to smoking tobacco.
- The risk of developing lung cancer increases with how long you have smoked, how old you were when you started smoking and the number of cigarettes you smoke each day.
- The risk is also higher if you smoke tobacco and have other risk factors.
- Pipes, cigars, herbal cigarettes, hookahs, chewing tobacco, low-tar cigarettes and low-nicotine cigarettes also cause cancer and are not considered safe.

CANCER PREVENTION CENTRE
Staff Members
Research and Publications
Past and Future Events
Clinical Services
Be Smoke Free
+ General Information
Prospective Patients
Current Patients
Follow-Up

Smoking Cessation Program

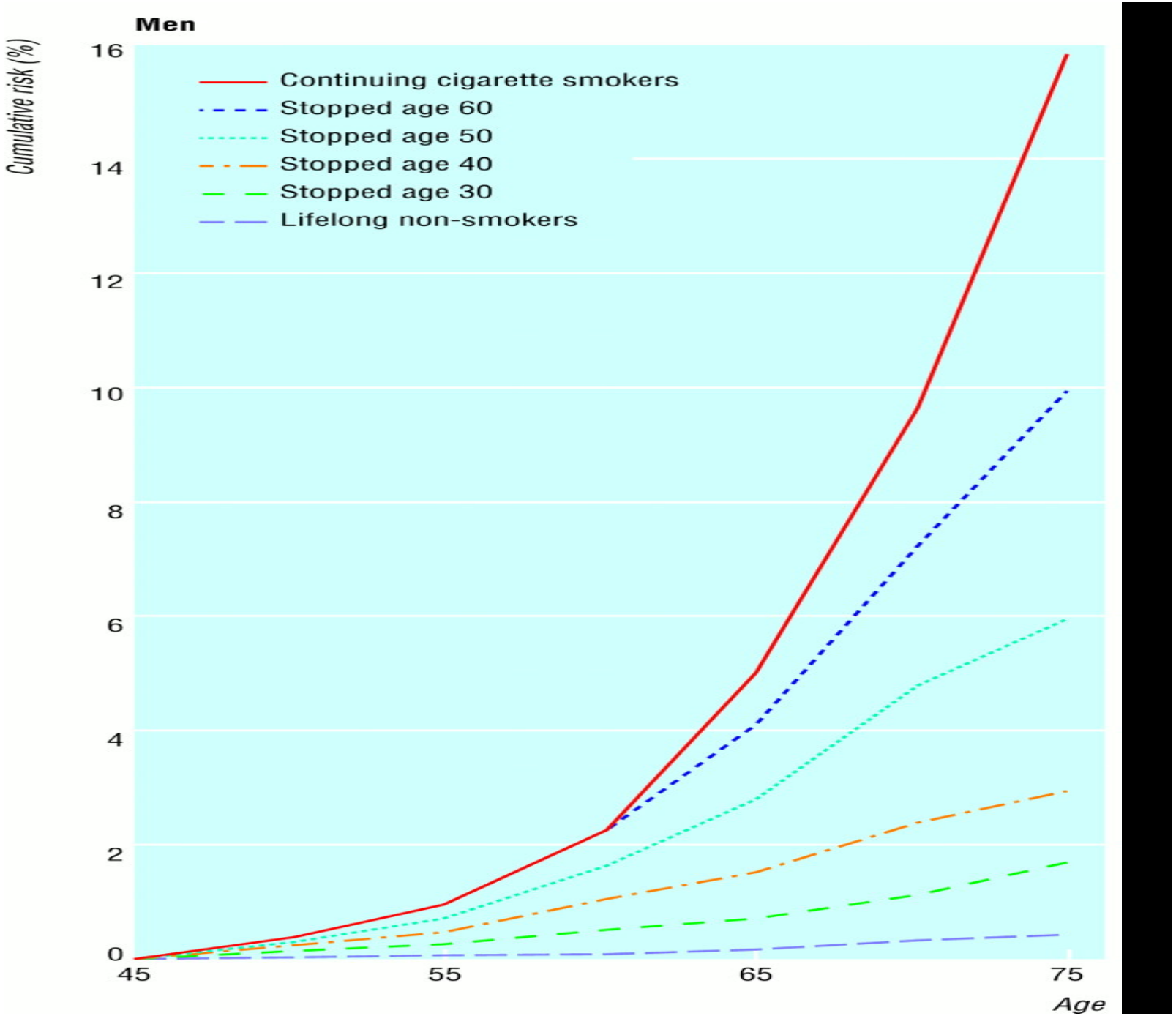
General Information about the Smoking Cessation Program

Introduction to the Smoking Cessation Program:

Nothing is more important for the prevention of several cancers and over 50 other diseases than eliminating the use of tobacco products. The Smoking Cessation Program provides knowledge and support for smokers who want to quit. It consists of a series of 8 group sessions and monthly follow-up support sessions offered at the Cancer Prevention Centre (CPC) at the Jewish General Hospital. The sessions are **FREE** and available to the general public and are given in French and English.

http://jarrete.qc.ca/

http://iquitnow.qc.ca/



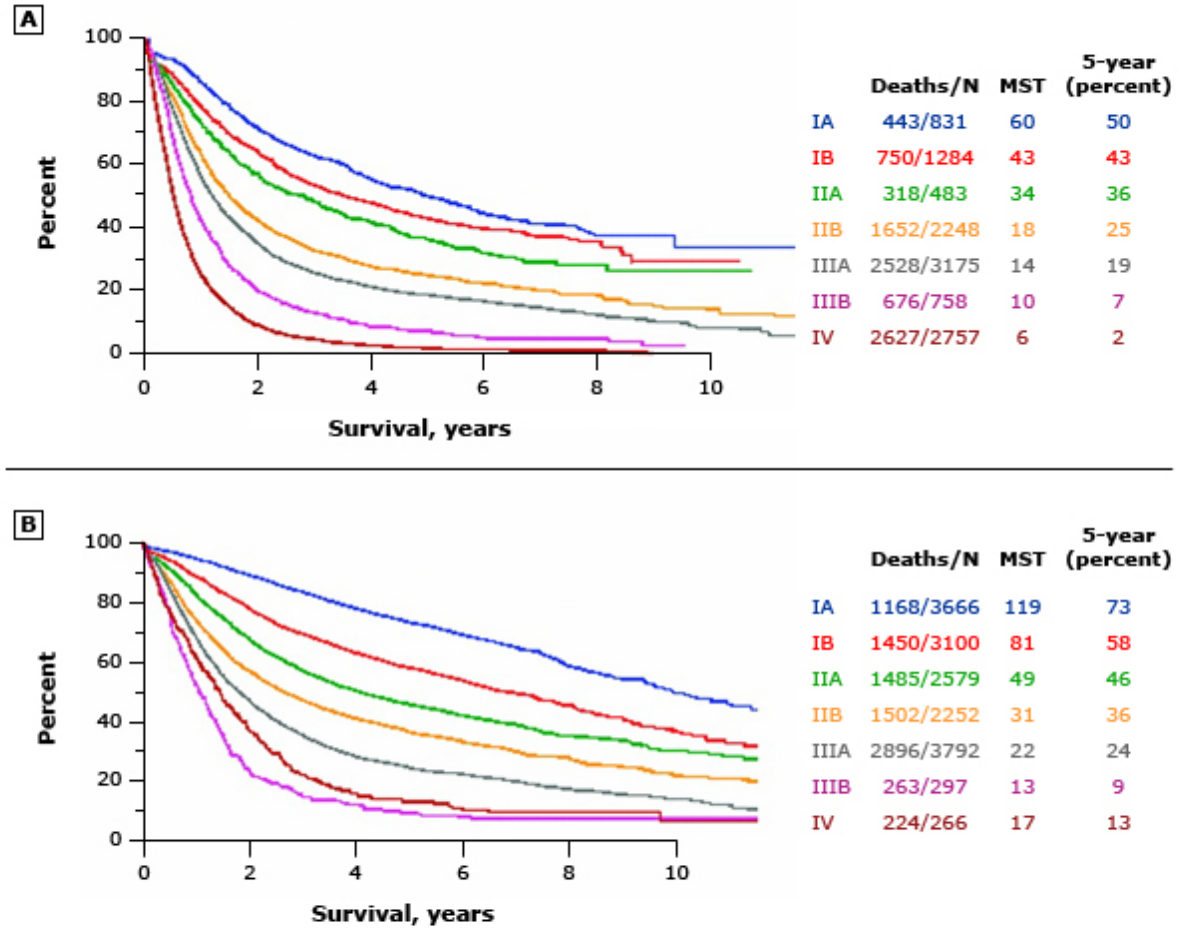
Effects of stopping smoking at various ages on the cumulative risk (%) of death from lung cancer up to age 75, at death rates for men in UK in 1990. Nonsmoker rates were taken from US prospective study of mortality

Peto R, BMJ, 2000

Lung Cancer Screening

Past:	CXR
	Sputum
Present:	Low Dose CT scan
Future:	PET
	Biomarkers (airway epithelium, sputum, exhaled breath, blood)
	Molecular analysis of sputum
	Fluorescence bronchoscopy
	Genomic and proteonomic analysis of bronchoscopic samples
	Serum protein microarrays for detecting molecular markers

Overall survival by TNM grouping, non-small cell lung cancer



Overall survival, expressed as median survival time (MST) and five-year survival, using the seventh edition of TNM staging system by (A) clinical stage and (B) pathologic stage.

Chest radiograph/sputum cytology

- Screening for lung cancer by chest radiograph and/or sputum cytology is not recommended.
- There have been at least seven large scale controlled clinical (six randomized, one non-randomized) trials of chest radiograph screening for lung cancer.
- These studies began as early as 1960, and a 20-year follow-up analysis has been published for one randomized trial. None of the randomized trials have demonstrated a mortality benefit for chest radiograph screening.

- Mayo Lung Project
  - 10,933 high risk outpt males.
  - chest radiographs and sputum cytologic screening examinations every 4 months vs. Mayo Clinic advice to undergo annual examination.
  - No mortality benefit attributable to screening was observed after 6 years of observation and at least 1 year of follow-up.

- Johns Hopkins study
  - 10,387 high-risk volunteers received annual chest radiographic screening.
  - Half also received cytologic examination of induced sputum.
- Czech Study on Lung Cancer Screening (1970s)
  - Cigarette-smoking males (6,364), aged 40-64,
  - randomized into an intervention group which received 6-monthly screening by chest X-ray and sputum cytology,
  - control group which received no asymptomatic investigation.
  - After 3 years, both groups received annual chest X-rays.
  - There was no significant difference in mortality between the 2 groups.

Screening for lung cancer: a systematic review and meta-analysis of controlled trials.

Manser et al. Thorax 2003;58:784–789

Table 1 Design of screening studies comparing different frequencies of chest radiographic screening

Study and year commenced	Subjects	Intervention	Control	Screening duration	Total follow up*
Erfurt County (1972)[3]	Men aged 40–65 years. Smokers and non-smokers	6 monthly chest radiographs	Chest radiographs every 1–2 years.	6 years	6 years
North London study (1960)[14]	Men aged 40+ years. Smokers and non-smokers from 119 work sites (mainly factories)	6 monthly chest radiographs	Chest radiograph at baseline and at the end of 3 years	3 years	3 years
Czech study (1976)[16]	Men aged 40– 64 years. Current heavy smokers.	6 monthly chest radiography and sputum cytology for the first 3 years followed by annual chest radiograph for 3 years	Chest radiograph at baseline and chest radiograph and sputum cytology after 3 years followed by annual chest radiographs for 3 years	6 years	Initially 6 years, later extended to 15 years
Mayo Lung Project (1971)[4]	Men attending the Mayo Clinic aged more than 45 years. Heavy smokers	4 monthly chest radiography and sputum cytology	Advised at the start of the study to have an annual chest radiograph and sputum cytology test	6 years	Initially 11 years, later extended to 24 years.
Kaiser Permanente study (1964)[18]	Men and women aged 35–54 years. Smokers and non-smokers. Members of Kaiser Permanente medical care programme	Encouraged to undergo an annual multiphasic health check up including an annual chest radiograph	Subjects not urged to undergo screening but could do so as part of their usual care if requested	16 years	16 years

*Follow up period includes period of active screening and post screening follow up. The maximum follow up is described; for some studies this varied as subjects were enrolled at different stages.

Table 2 Relative risk of death from lung cancer: studies comparing frequent chest radiographic screening with less frequent screening.

Study	No randomised		No of lung cancer deaths		Relative risk (95% CI)
	Intervention	Control	Intervention	Control	
North London[14]	29723	25311	82	68	1.03 (0.74 to 1.42)
Czech study[16]	3171	3174	247	216	1.14 (0.96 to 1.36)
Mayo Lung Project[4]	4618	4593	337	303	1.11 (0.95 to 1.28)
Kaiser Permanente[18]	5156	5557	44	42	1.13 (0.74 to 1.72)
Total	42668	38635	710	629	1.11 (1.00 to 1.23)*

*Results were identical with random effects and fixed effects models.

Table 3 Relative risk of death from lung cancer: studies comparing annual chest radiography with annual chest radiography plus 4 monthly sputum cytological examination

Study	No randomised		No of lung cancer deaths		Relative risk (95% CI)
	Intervention	Control	Intervention	Control	
Memorial Sloan[15]	4968	5072	115	120	0.98 (0.76 to 1.26)
Johns Hopkins[17]	5226	5161	141	173	0.80 (0.65 to 1.00)
Total	10194	10233	256	293	0.88 (0.74 to 1.03)*

*With the random effects model the pooled results were 0.88 (95% CI 0.73 to 1.06)

Table 4 Relative risk of death (all causes): studies comparing more frequent chest radiographic screening with less frequent screening

Study	No in each group		No of deaths		Relative risk (95% CI)
	Intervention	Control	Intervention	Control	
Erfurt County[3]	41532	102348	3143	8038	0.96 (0.93 to 1.00)
Czech study [16]	3171	3174	341	293	1.16 (1.00 to 1.35)
Mayo Lung Project[4]	4618	4593	688	665	1.03 (0.93 to 1.14)
Kaiser Permanente[18]	5156	5557	585	643	0.98 (0.88 to 1.09)
Total	54477	115672	4757	9639	1.01 (0.94 to 1.08)*

*With the fixed effects model the pooled results were 0.98 (95% CI 0.95 to 1.02).

Prostate, Lung, Colorectal, and Ovarian (PLCO) cancer screening trial

- compared screening with no screening.
- large randomized trial (n = 154,942)
- screening individuals aged 55 - 74 for several cancers, including lung cancer.
- Screening for lung cancer consisted of a single PA CXR at baseline and annually for three years, while the control group received usual care.
- initial screening: 5991 (8.9 %) of all CXR were abnormal
  - 11 % in current smokers
  - 8 % in never smokers.
- Lung cancer incidence was higher in those with prior or current smoking exposure than in nonsmokers
- no difference in incidence or mortality between smokers who were in the screening or control groups (RR 0.94, 95% CI 0.18-1.10 after six years and RR 0.99, 95% CI 0.87-1.22 after 13 years of follow-up).

Original Article

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

The National Lung Screening Trial Research Team

N Engl J Med
Volume 365(5):395-409
August 4, 2011

The NEW ENGLAND JOURNAL of MEDICINE

Low Dose CT

- noncontrast study obtained with a multidetector CT scanner during a single maximal inspiratory breath-hold with a scanning time under 25 seconds.
- High-resolution (1.0 to 2.5 mm interval) images are reconstructed using a soft tissue or thin-section algorithm.
- The overall average effective dose of LDCT used in the National Lung Screening Trial was 2 millisievert (mSv), compared with 7 mSv for a standard-dose diagnostic chest CT examination

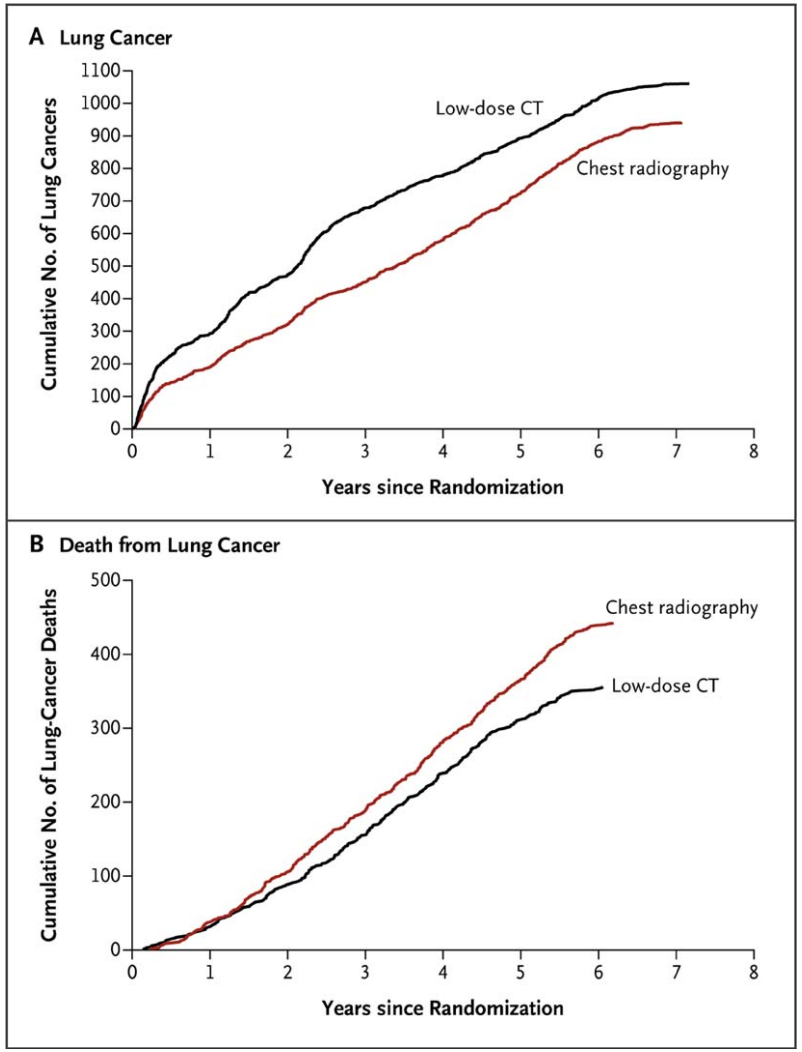
Adult thoracic effective doses

Procedure	Modality	Average effective dose (mSv)	Number of chest x-rays (PA/lateral) with equivalent radiation dose
Chest radiograph (posteroanterior)	Conventional radiography	0.02	0.2
PA and lateral chest radiographs	Conventional radiography	0.1	1
Thyroid scan (iodine 123)	Nuclear medicine	1.9	19
Lung ventilation-perfusion scan	Nuclear medicine	2.2	22
Thoracic angiogram	Conventional fluoroscopy or interventional radiology	5	50
Parathyroid scan	Nuclear medicine	6.7	67
Conventional coronary angiogram	Conventional fluoroscopy or interventional radiology	7	70
CT chest	Computed tomography	8	80
Nuclear cardiac stress test	Nuclear medicine	9.4-12.8	94-128
Cardiac PET	Nuclear medicine	14.1	141
CT pulmonary embolism protocol	Computed tomography	15	150
Coronary angioplasty or stent	Conventional fluoroscopy or interventional radiology	15	150
CT coronary angiogram	Computed tomography	16	160

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

The National Lung Screening Trial investigators report that persons undergoing three annual screening examinations with low-dose computed tomography had a 20% reduction in lung-cancer mortality as compared with those screened with annual chest radiography.

Conclusion: Screening with the use of low-dose CT reduces mortality from lung cancer.



The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

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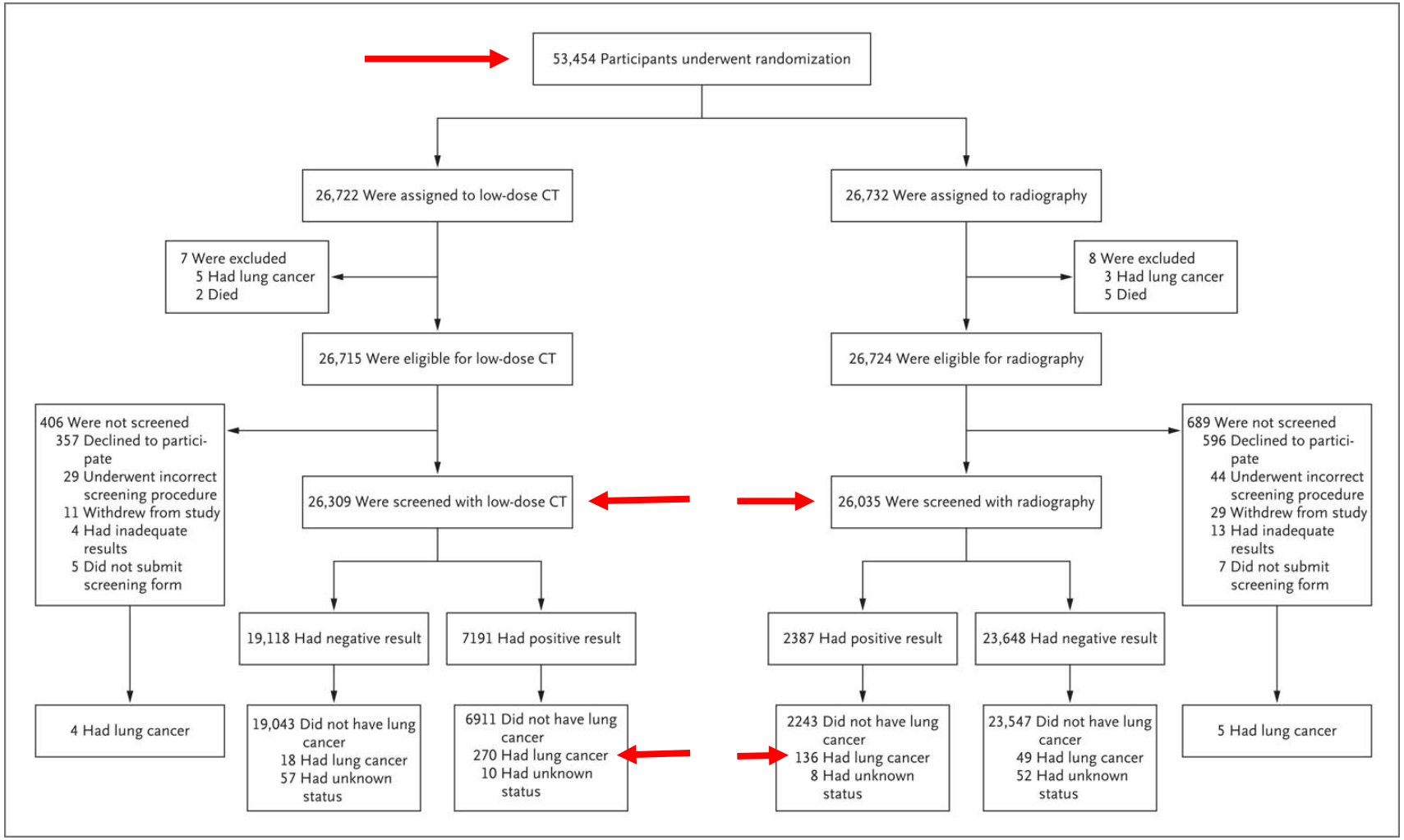
Enrollment and Follow-up of the Study Participants after the Initial Screening.



The National Lung Screening Trial Research Team. N Engl J Med 2013;368:1980-1991

The NEW ENGLAND JOURNAL of MEDICINE

Results of Three Rounds of Screening.

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)

* The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. Results of screening tests that were technically inadequate (7 in the low-dose CT group and 26 in the radiography group, across the three screening rounds) are not included in this table. A screening test with low-dose CT was considered to be positive if it revealed a nodule at least 4 mm in any diameter or other abnormalities that were suspicious for lung cancer. A screening test with chest radiography was considered to be positive if it revealed a nodule or mass of any size or other abnormalities suspicious for lung cancer.

The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

The NEW ENGLAND JOURNAL of MEDICINE

Diagnostic Follow-up of Positive Screening Results in the Three Screening Rounds.

Table 3. Diagnostic Follow-up of Positive Screening Results in the Three Screening Rounds.*

Variable	Low-Dose CT				Chest Radiography			
	T0	T1	T2	Total	T0	T1	T2	Total
	number (percent)							
Total positive tests	7191 (100.0)	6901 (100.0)	4054 (100.0)	18,146 (100.0)	2387 (100.0)	1482 (100.0)	1174 (100.0)	5043 (100.0)
Lung cancer confirmed	270 (3.8)	168 (2.4)	211 (5.2)	649 (3.6)	136 (5.7)	65 (4.4)	78 (6.6)	279 (5.5)
Lung cancer not confirmed†	6921 (96.2)	6733 (97.6)	3843 (94.8)	17,497 (96.4)	2251 (94.3)	1417 (95.6)	1096 (93.4)	4764 (94.5)
Positive screening results with complete diagnostic follow-up information	7049 (100.0)	6740 (100.0)	3913 (100.0)	17,702 (100.0)	2348 (100.0)	1456 (100.0)	1149 (100.0)	4953 (100.0)
Any diagnostic follow-up	6369 (90.4)	3866 (57.4)	2522 (64.5)	12,757 (72.1)	2176 (92.7)	1078 (74.0)	957 (83.3)	4211 (85.0)
Clinical procedure	5089 (72.2)	3190 (47.3)	2151 (55.0)	10,430 (58.9)	1414 (60.2)	723 (49.7)	658 (57.3)	2795 (56.4)
Imaging examination	5717 (81.1)	2520 (37.4)	2009 (51.3)	10,246 (57.9)	2010 (85.6)	968 (66.5)	906 (78.9)	3884 (78.4)
Chest radiography	1284 (18.2)	613 (9.1)	650 (16.6)	2,547 (14.4)	867 (36.9)	381 (26.2)	365 (31.8)	1613 (32.6)
Chest CT	5153 (73.1)	2046 (30.4)	1608 (41.1)	8,807 (49.8)	1546 (65.8)	745 (51.2)	712 (62.0)	3003 (60.6)
FDG PET or FDG PET–CT	728 (10.3)	350 (5.2)	393 (10.0)	1,471 (8.3)	179 (7.6)	105 (7.2)	113 (9.8)	397 (8.0)
Percutaneous cytologic examination or biopsy	155 (2.2)	74 (1.1)	93 (2.4)	322 (1.8)	83 (3.5)	37 (2.5)	52 (4.5)	172 (3.5)
Transthoracic	120 (1.7)	60 (0.9)	74 (1.9)	254 (1.4)	67 (2.9)	31 (2.1)	43 (3.7)	141 (2.8)
Extrathoracic	39 (0.6)	17 (0.3)	24 (0.6)	80 (0.5)	20 (0.9)	6 (0.4)	13 (1.1)	39 (0.8)
Bronchoscopy	306 (4.3)	178 (2.6)	187 (4.8)	671 (3.8)	107 (4.6)	56 (3.8)	62 (5.4)	225 (4.5)
With neither biopsy nor cytologic testing	126 (1.8)	95 (1.4)	99 (2.5)	320 (1.8)	45 (1.9)	19 (1.3)	32 (2.8)	96 (1.9)
With biopsy or cytologic testing	194 (2.8)	95 (1.4)	102 (2.6)	391 (2.2)	74 (3.2)	40 (2.7)	36 (3.1)	150 (3.0)
Surgical procedure	297 (4.2)	197 (2.9)	219 (5.6)	713 (4.0)	121 (5.2)	51 (3.5)	67 (5.8)	239 (4.8)
Mediastinoscopy or mediastinotomy	60 (0.9)	32 (0.5)	25 (0.6)	117 (0.7)	22 (0.9)	12 (0.8)	21 (1.8)	55 (1.1)
Thoracoscopy	82 (1.2)	56 (0.8)	96 (2.5)	234 (1.3)	22 (0.9)	11 (0.8)	20 (1.7)	53 (1.1)
Thoracotomy	197 (2.8)	148 (2.2)	164 (4.2)	509 (2.9)	96 (4.1)	44 (3.0)	44 (3.8)	184 (3.7)
Other procedures	168 (2.4)	96 (1.4)	63 (1.6)	327 (1.8)	55 (2.3)	33 (2.3)	34 (3.0)	122 (2.5)

* The screenings were performed at 1-year intervals, with the first screening (T0) performed soon after the time of randomization. FDG PET denotes ^{18}F-fluorodeoxyglucose positron-emission tomography.

† Positive tests with incomplete information on diagnostic follow-up are included in this category (142 at T0, 161 at T1, and 141 at T2 in the low-dose CT group and 39 at T0, 26 at T1, and 25 at T2 in the radiography group).

The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

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Complications after the Most Invasive Screening-Related Diagnostic Evaluation Procedure, According to Lung-Cancer Status.

Table 4. Complications after the Most Invasive Screening-Related Diagnostic Evaluation Procedure, According to Lung-Cancer Status.*

Complication	Lung Cancer Confirmed					Lung Cancer Not Confirmed				
	Thoracotomy, Thoracoscopy, or Mediastinoscopy	Bron-choscopy	Needle Biopsy	No Invasive Procedure	Total	Thoracotomy, Thoracoscopy, or Mediastinoscopy	Bronchoscopy	Needle Biopsy	No Invasive Procedure	Total
	number (percent)					*number (percent)*				
Low-dose CT group										
Positive screening results for which diagnostic information was complete	509 (100.0)	76 (100.0)	33 (100.0)	31 (100.0)	649 (100.0	164 (100.0)	227 (100.0)	66 (100.0)	16,596 (100.0)	17,053 (100.0)
No complication	344 (67.6)	69 (90.8)	26 (78.8)	26 (83.9)	465 (71.6)	138 (84.1)	216 (95.2)	59 (89.4)	16,579 (99.9)	16,992 (99.6)
At least one complication	165 (32.4)	7 (9.2)	7 (21.2)	5 (16.1)	184 (28.4)	26 (15.9)	11 (4.8)	7 (10.6)	17 (0.1)	61 (0.4)
Most severe complication classified as major	71 (13.9)	2 (2.6)	0	2 (6.5)	75 (11.6)	9 (5.5)	2 (0.9)	0	1 (<0.1)	12 (0.1)
Most severe complication classified as intermediate	81 (15.9)	5 (6.6)	7 (21.2)	2 (6.5)	95 (14.6)	13 (7.9)	9 (4.0)	6 (9.1)	16 (0.1)	44 (0.3)
Most severe complication classified as minor	13 (2.6)	0	0	1 (3.2)	14 (2.2)	4 (2.4)	0	1 (1.5)	0	5 (<0.1)
Death within 60 days after most invasive diagnostic procedure†	5 (1.0)	4 (5.3)	1 (3.0)	0	10 (1.5)	2 (1.2)	4 (1.8)	0	5 (<0.1)	11 (0.1)
Radiography group										
Positive screening results for which diagnostic information was complete	189 (100.0)	46 (100.0)	29 (100.0)	15 (100.0)	279 (100.0	45 (100.0)	46 (100.0)	24 (100.0)	4,559 (100.0)	4,674 (100.0)
No complication	130 (68.8)	42 (91.3)	28 (96.6)	14 (93.3)	214 (76.7)	38 (84.4)	46 (100.0)	23 (95.8)	4,551 (99.8)	4,658 (99.7)
At least one complication	59 (31.2)	4 (8.7)	1 (3.4)	1 (6.7)	65 (23.3)	7 (15.6)	0	1 (4.2)	8 (0.2)	16 (0.3)
Most severe complication classified as major	22 (11.6)	1 (2.2)	0	1 (6.7)	24 (8.6)	1 (2.2)	0	0	3 (0.1)	4 (0.1)
Most severe complication classified as intermediate	32 (16.9)	2 (4.3)	1 (3.4)	0	35 (12.5)	6 (13.3)	0	1 (4.2)	2 (<0.1)	9 (0.2)
Most severe complication classified as minor	5 (2.6)	1 (2.2)	0	0	6 (2.2)	0	0	0	3 (0.1)	3 (0.1)
Death within 60 days after most invasive diagnostic procedure†	4 (2.1)	5 (10.9)	1 (3.4)	1 (6.7)	11 (3.9)	0	0	0	3 (0.1)	3 (0.1)

* In the case of multiple evaluation procedures of the same type, the earliest is included. Complications that occurred before the most invasive procedure are not included. Participants could have up to three positive screening tests and therefore may be included up to three times in any row. Columns of procedures are arranged in decreasing order of invasiveness. In the case of the first procedure column, thoracotomy was considered to be more invasive than thoracoscopy, which was considered to be more invasive than mediastinoscopy.

† For patients who did not undergo an invasive procedure, deaths were included if they occurred within 60 days after the positive screening result.

The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

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Stage and Histologic Type of Lung Cancers in the Two Screening Groups, According to the Result of Screening.

Table 5. Stage and Histologic Type of Lung Cancers in the Two Screening Groups, According to the Result of Screening.*

Stage and Histologic Type	Low-Dose CT				Chest Radiography			
	Positive Screening Test (N=649)	Negative Screening Test (N=44)†	No Screening Test (N=367)‡	Total (N=1060)	Positive Screening Test (N=279)	Negative Screening Test (N=137)†	No Screening Test (N=525)‡	Total (N=941)
	number/total number (percent)							
Stage								
IA	329/635 (51.8)	5/44 (11.4)	82/361 (22.7)	416/1040 (40.0)	90/275 (32.7)	16/135 (11.9)	90/519 (17.3)	196/929 (21.1)
IB	71/635 (11.2)	2/44 (4.5)	31/361 (8.6)	104/1040 (10.0)	41/275 (14.9)	6/135 (4.4)	46/519 (8.9)	93/929 (10.0)
IIA	26/635 (4.1)	2/44 (4.5)	7/361 (1.9)	35/1040 (3.4)	14/275 (5.1)	2/135 (1.5)	16/519 (3.1)	32/929 (3.4)
IIB	20/635 (3.1)	3/44 (6.8)	15/361 (4.2)	38/1040 (3.7)	11/275 (4.0)	6/135 (4.4)	25/519 (4.8)	42/929 (4.5)
IIIA	59/635 (9.3)	3/44 (6.8)	37/361 (10.2)	99/1040 (9.5)	35/275 (12.7)	21/135 (15.6)	53/519 (10.2)	109/929 (11.7)
IIIB	49/635 (7.7)	15/44 (34.1)	58/361 (16.1)	122/1040 (11.7)	27/275 (9.8)	24/135 (17.8)	71/519 (13.7)	122/929 (13.1)
IV	81/635 (12.8)	14/44 (31.8)	131/361 (36.3)	226/1040 (21.7)	57/275 (20.7)	60/135 (44.4)	218/519 (42.0)	335/929 (36.1)
Histologic type								
Bronchioloalveolar carcinoma	95/646 (14.7)	1/44 (2.3)	14/358 (3.9)	110/1048 (10.5)	13/276 (4.7)	1/135 (0.7)	21/520 (4.0)	35/931 (3.8)
Adenocarcinoma	258/646 (39.9)	8/44 (18.2)	114/358 (31.8)	380/1048 (36.3)	112/276 (40.6)	37/135 (27.4)	179/520 (34.4)	328/931 (35.2)
Squamous-cell carcinoma	136/646 (21.1)	13/44 (29.5)	94/358 (26.3)	243/1048 (23.2)	70/276 (25.4)	24/135 (17.8)	112/520 (21.5)	206/931 (22.1)
Large-cell carcinoma	28/646 (4.3)	3/44 (6.8)	10/358 (2.8)	41/1048 (3.9)	12/276 (4.3)	10/135 (7.4)	21/520 (4.0)	43/931 (4.6)
Non–small-cell carcinoma or other§	75/646 (11.6)	4/44 (9.1)	52/358 (14.5)	131/1048 (12.5)	40/276 (14.5)	30/135 (22.2)	88/520 (16.9)	158/931 (17.0)
Small-cell carcinoma	49/646 (7.6)	15/44 (34.1)	73/358 (20.4)	137/1048 (13.1)	28/276 (10.1)	32/135 (23.7)	99/520 (19.0)	159/931 (17.1)
Carcinoid	5/646 (0.8)	0	1/358 (0.3)	6/1048 (0.6)	1/276 (0.4)	1/135 (0.7)	0	2/931 (0.2)

The National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409

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Other LDCT studies

- NELSON trial (Netherlands and Belgium)
  - Randomized LDCT vs. no screening in >15,000 current/former smokers.
- DANTE trial (Italy) - negative
  - <2500 male smokers 60-74 yrs
  - 5 yrs of LDCT vs. annual clinic F/U (baseline CXR and sputum)
- DLCST (Danish study) - negative
  - >4000 smokers 50-70 yrs
- MILD (Italy) – negative
  - >4000 smokers, age 49 yrs or older
- LUSI (German)
  - > 4000 with hx of heavy smoking 50-69 yrs
  - LDCT for 4 yrs vs. no intervention

Potential Benefits and Harms of Three Rounds of Annual Screening with Low-Dose CT, as Compared with Chest Radiography or No Screening.

Table 1. Potential Benefits and Harms of Three Rounds of Annual Screening with Low-Dose CT, as Compared with Chest Radiography or No Screening.*

Outcome	Difference *no. of events/1000 persons screened*
CT vs. chest radiography	
Death from lung cancer	3 to 4 fewer
Death from cause other than lung cancer	0 to 1 fewer
CT vs. no screening	
False positive result on low-dose CT	375 more
Invasive biopsy for benign nodule	41 more
Surgical procedure for benign nodule	10 more
Complication from invasive procedure for benign nodule	3 more
Radiation-induced cancer	Uncertain
Cessation of smoking	Uncertain

* Estimates are based on data from the National Lung Screening Trial.[1]

Gould MK. N Engl J Med 2014;371:1813-1820

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POTENTIAL HARMS OF SCREENING

- **Consequences of evaluating abnormal findings –** Evaluation may involve needle biopsy and/or surgery, with associated morbidity and mortality
- **Radiation exposure** –may add independently to the risk of developing cancers.
- **Patient distress –**
  - Prolonged follow-up of nodules, often lasting several years, may cause anxiety related to fear of having lung cancer.
  - 2014 systematic review of 5 randomized trials and one cohort study found that LDCT screening may be associated with short-term psychologic discomfort but did not affect distress, worry, or health-related quality of life. False-positive results were associated with short-term increases in distress.
- **Overdiagnosis –**
  - Some cancers identified at screening, if never found, would not have affected morbidity or mortality during the patient's lifetime.
  - Observational studies of screening for lung cancer with LDCT have estimated the extent of overdiagnosis to range between 13 and 27%.

Key Elements to Include in a Conversation about Screening for Lung Cancer with the Use of Low-Dose CT.

Table 3. Key Elements to Include in a Conversation about Screening for Lung Cancer with the Use of Low-Dose CT.

Annual lung-cancer screening of high-risk smokers and former smokers with the use of low-dose CT is at least as effective in preventing death from cancer as annual mammographic screening for breast cancer in women 50 to 59 years of age.
Among high-risk smokers and former smokers, screening with low-dose CT (along with subsequent evaluation and treatment) prevents one of five deaths from lung cancer.
Lung-cancer screening with low-dose CT is not a single test. It is a process that involves annual testing and follow-up of screening-detected abnormalities.
False positive test results occur in approximately one of five low-dose CT screening examinations. Each examination is approximately 20 times as likely to yield a false positive result as it is to reveal lung cancer.
Most false positive results will require follow-up with one or more subsequent CT scans, but a minority (5%) will require evaluation with invasive biopsy or surgery.
Screening for lung cancer with low-dose CT is not a substitute for smoking cessation. Stopping smoking is the most effective way to reduce the risk of death from lung cancer and has other important immediate and long-term cardiovascular and respiratory health benefits.

Gould MK. N Engl J Med 2014;371:1813-1820

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- The NELSON trial, a randomized LDCT-based lung cancer trial including 15,822 current or former smokers in the Netherlands and Belgium compared LDCT screening at increasing screening intervals (1, 2, and 2.5 years) with no screening [89-91]. The study was powered to detect a 25 percent decrease in lung cancer mortality after 10 years, as well as the effects of screening on quality of life, smoking cessation, and estimated cost effectiveness. Unlike other screening studies, five-year lung cancer survivors, a group at very high risk of developing a new lung cancer, were eligible for enrollment. This was the first large-scale randomized trial to compare LDCT screening with no screening. Information is available at the Nederlands Trial Register.

In a prespecified analysis, after a median of 8.16 years of follow-up, there were 196 screen-detected cancers in 187 (3 percent) of the 7155 screened participants [90]. The proportion of stage I cancers detected by LDCT was 66 percent. Among patients who were screened with LDCT, 34 patients were diagnosed with 35 interval lung cancers. Interval cancers were more likely to be more advanced stage, more likely to be small cell carcinoma, and less likely to be adenocarcinoma. Extending the interval between screening exams reduced the potential benefit of screening, with a higher proportion of new lung cancers detected at an advanced stage (IIIB/IV) when screening was conducted at 2.5 versus 1.0 years (17.3 versus 6.8 percent) [91].

New solid nodules were detected at each LDCT screening round in 5 to 7 percent of participants, with 6 percent of these nodules being diagnosed as lung cancer [92]. Nodule volume had a high discriminatory power, with a cancer frequency of 0.5 percent among nodules smaller than 27 mm^3, 3.1 percent among those with a volume of 27 mm^3 to 206 mm^3, and 17 percent among those larger than 206 mm^3. A volume cutoff of 27 mm^3 or greater had a sensitivity exceeding 95 percent for the detection of lung cancer.

Referral Centre

- Experienced team
- Multidisciplinary team
  - Pulmonologist
  - Chest and Interventional radiologists
  - Thoracic surgeon
  - Nuclear medicine
  - Tumour board

Organization	Recommendation
Canadian Task Force on Preventive Health Care (current)	Screen asymptomatic adults aged 55 to 74 years with at least a 30 pack-year smoking history who smoke or quit smoking less than 15 years ago for lung cancer with low-dose CT every year for 3 consecutive years
Canadian Task Force on Preventive Health Care (2003)[5]	Do not screen asymptomatic adults for lung cancer with chest radiography; insufficient evidence for using low-dose CT as a screening test for asymptomatic adults
US Preventive Services Task Force (2013)[4]	Screen asymptomatic adults aged 55 to 80 years with a minimum 30 pack-year smoking history who smoke or quit smoking within the last 15 years for lung cancer with low-dose CT annually
Cancer Care Ontario (2013)[26]	Screen high-risk populations (i.e., adults 55–74 yr of age with a minimum smoking history of 30 pack-years or more who currently smoke or quit smoking within the past 15 yr and are free of disease at the time of screening) for lung cancer with low-dose CT for 3 years followed by biennial screening
American Cancer Society (2013)[27]	Screen adults aged 55 to 74 years with a 30 pack-year or more smoking history who smoke or quit smoking within the previous 15 years and are in relatively good health for lung cancer with low-dose CT annually
American College of Chest Physicians (2013)[28]	Screen adults aged 55 to 74 years with a 30 pack-year or more smoking history who smoke or quit smoking within the previous 15 years for lung cancer with low-dose CT annually
American Lung Association (2012, updated 2015)[29]	Screen adults aged 55 to 74 years with a smoking history of at least 30 pack-years and no history of lung cancer who smoke or quit smoking with the last 15 years for lung cancer using low-dose CT annually
American Association for Thoracic Surgery (2012)[30]	Screen adults aged 55 to 79 years with a 30 pack-year or more smoking history; adults with a previous diagnosis of lung cancer who have completed 4 years of surveillance without recurrence, and who can tolerate lung cancer treatment following screening to detect second primary lung cancer until the age of 79 years; and adults aged 50 to 79 years with a 20 pack-year smoking history and an additional comorbidity that produces a cumulative risk of lung cancer of 5% or more in 5 years for lung cancer with low-dose CT annually
National Comprehensive Cancer Network (2015)[31]	Screen adults aged 55 to 74 years with a 30 pack-year or more smoking history who quit smoking less than 15 years ago, and adults aged 50 years or older with a 20 pack-year or more smoking history and 1 additional risk factor (other than exposure to second-hand smoke) for lung cancer with low-dose CT annually
American Academy of Family Physicians (2013)[32]	Insufficient evidence to recommend for or against screening for lung cancer with low-dose CT

- Guidelines
- Recommendations on screening for lung cancer
- Canadian Task Force on Preventive Health Care*⇑

- CMAJ April 5, 2016 vol. 188 no. 6
- First published March 7, 2016, doi: 10.1503/cmaj.151421

Summary of recommendations for clinicians and policy-makers

- These recommendations apply to adults 18 years of age and older who are not suspected of having lung cancer. These recommendations do not apply to adults with previous lung cancer, or signs or symptoms of lung cancer.

- We recommend screening for lung cancer among adults aged 55 to 74 years with at least a 30 pack-year smoking history, who smoke or quit smoking less than 15 years ago, with low-dose computed tomography (CT) every year up to three consecutive years. Screening should only be done in health care settings with access to expertise in early diagnosis and treatment of lung cancer. (Weak recommendation, low-quality evidence.)

- We recommend not screening all other adults, regardless of age, smoking history or other risk factors, for lung cancer with low-dose CT. (Strong recommendation, very low-quality evidence.)

- We recommend that chest radiography, with or without sputum cytology, not be used to screen for lung cancer. (Strong recommendation, low-quality evidence.)

National Comprehensive Cancer Network®

NCCN Guidelines Version 1.2017
Lung Cancer Screening

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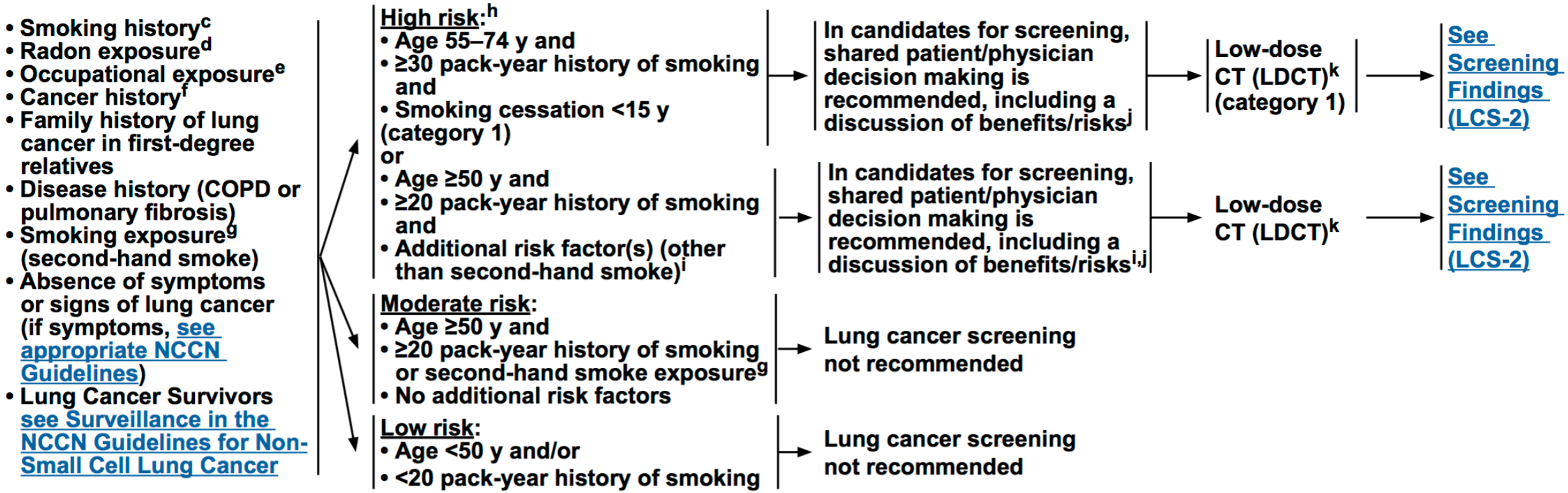
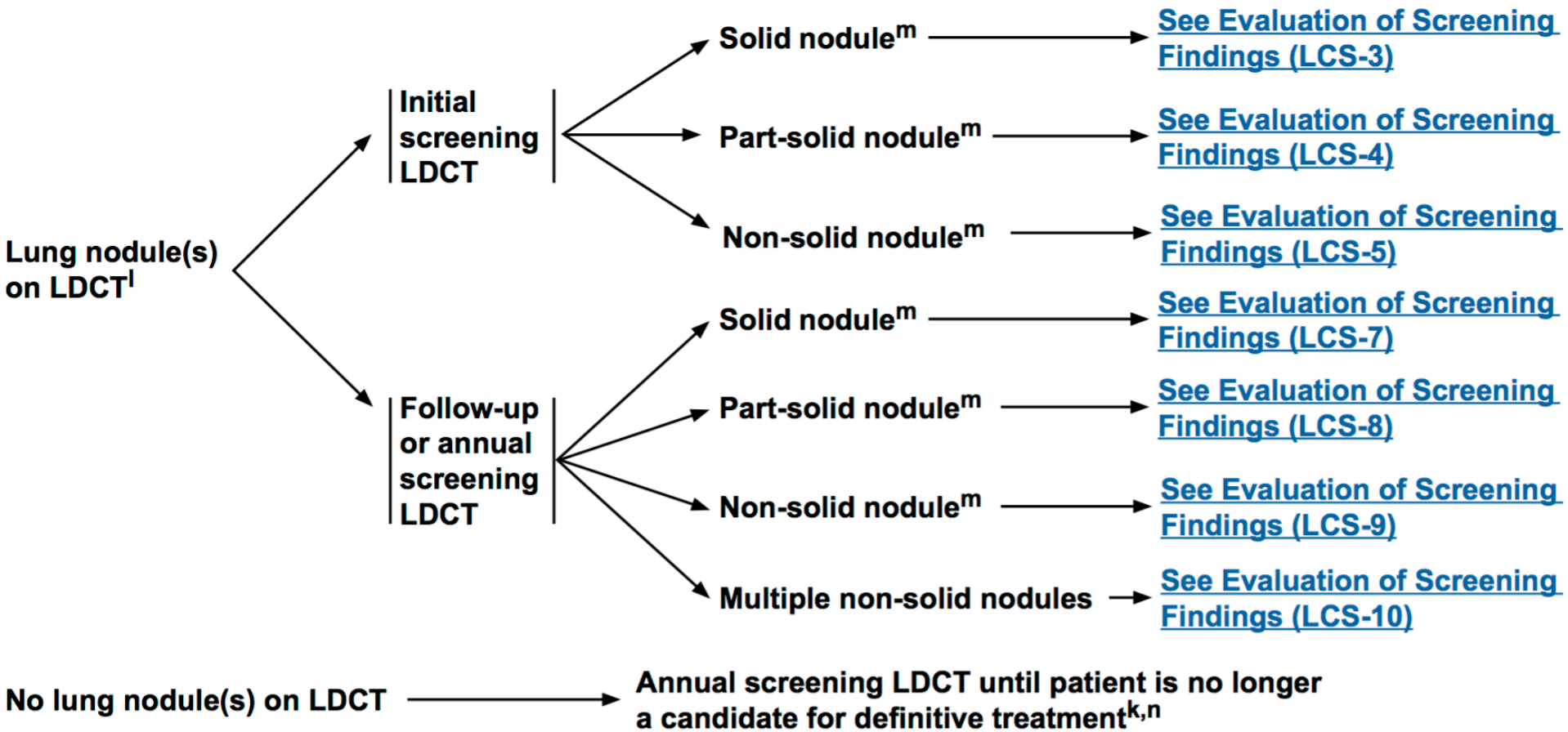


SCREENING FINDINGS



No lung nodule(s) on LDCT → Annual screening LDCT until patient is no longer a candidate for definitive treatment[k,n]

Findings requiring follow-up for diseases other than lung cancer (eg, suspicious for other cancers, COPD, moderate to severe coronary artery calcification, aortic aneurysm)

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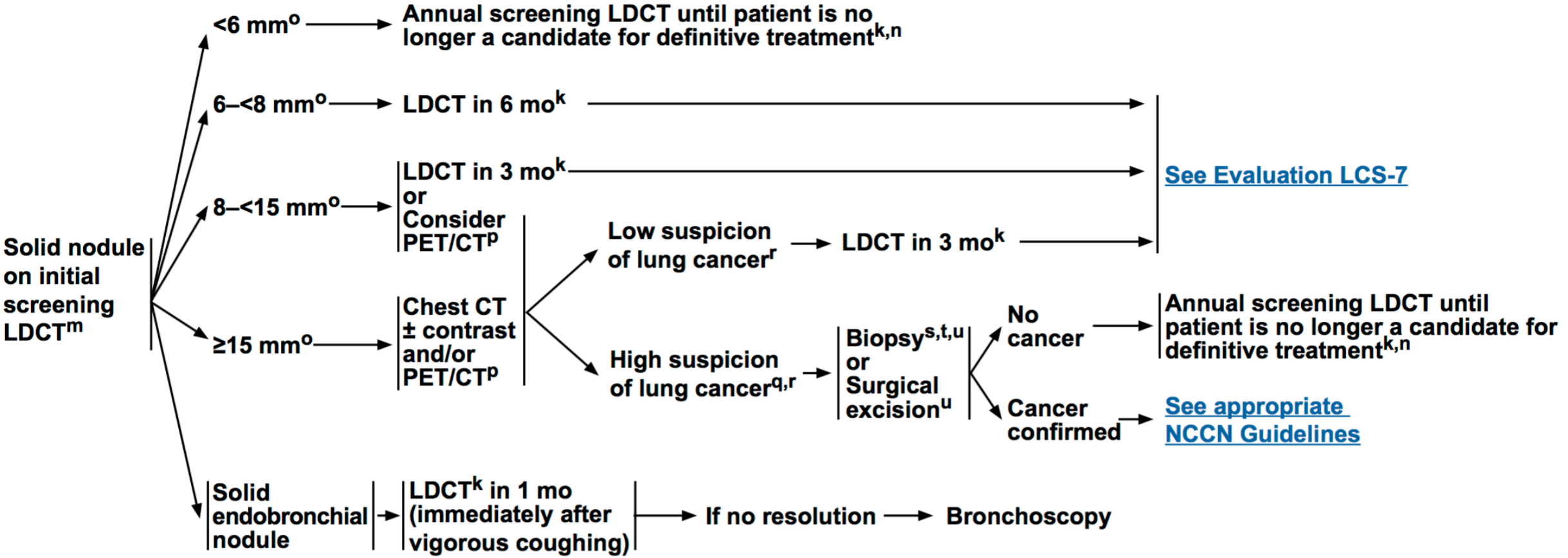
EVALUATION OF SCREENING FINDINGS

FOLLOW-UP OF SCREENING FINDINGS



ORIGINAL ARTICLE

The Cost-Effectiveness of High-Risk Lung Cancer Screening and Drivers of Program Efficiency

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Journal of Thoracic Oncology Vol. 12 No. 8: 1210-1222

In conclusion, high-risk lung cancer screening with LDCT is likely to be considered cost-effective and the use of refined risk prediction tools before LDCT-based screening selection can reduce the budget impact. Improvements to the quality and quantity of life for screened individuals can improve the overall costeffectiveness of LDCT-based lung screening, and effective interventions such as smoking cessation and reduction of coronary risk should be investigated for their potential to further improve program efficiency.

Original Investigation

Cost-effectiveness of Lung Cancer Screening in Canada

John R. Goffin, MD, FRCPC; William M. Flanagan, BM; Anthony B. Miller, MD, FRCPC; Natalie R. Fitzgerald, MA; Saima Memon, MBBS, MPH; Michael C. Wolfson, PhD; William K. Evans, MD, FRCPC

CONCLUSIONS AND RELEVANCE Lung cancer screening with LDCT appears cost-effective in the publicly funded Canadian health care system. An adjunct smoking cessation program has the potential to improve outcomes.

JAMA Oncol. 2015;1(6):807-813. doi:10.1001/jamaoncol.2015.2472
Published online July 30, 2015.

Conclusion

- Lung cancer is the #1 cause of cancer death in men and women
- Prevention – smoking cessation
- Screening with LDCT
  - Risks and benefits
  - Discussion with pt
  - Multidisciplinary team
- Guidelines
  - Ages 55-74
  - 30 p-y (current or quit <15 yrs)


ANY
QUESTIONS
?