Sistema Socio Sanitario
Ospedale di Bergamo
Regione Lombardia
ASST Papa Giovanni XXIII

UNIVERSITÀ DEGLI STUDI DI MILANO

Inquadramento clinico e diagnostico al paziente a rischio di neoplasia polmonare

Fabiano Di Marco

Università degli Studi di Milano
ASST – Ospedale Papa Giovanni XXIII, Bergamo
fabiano.dimarco@unimi.it

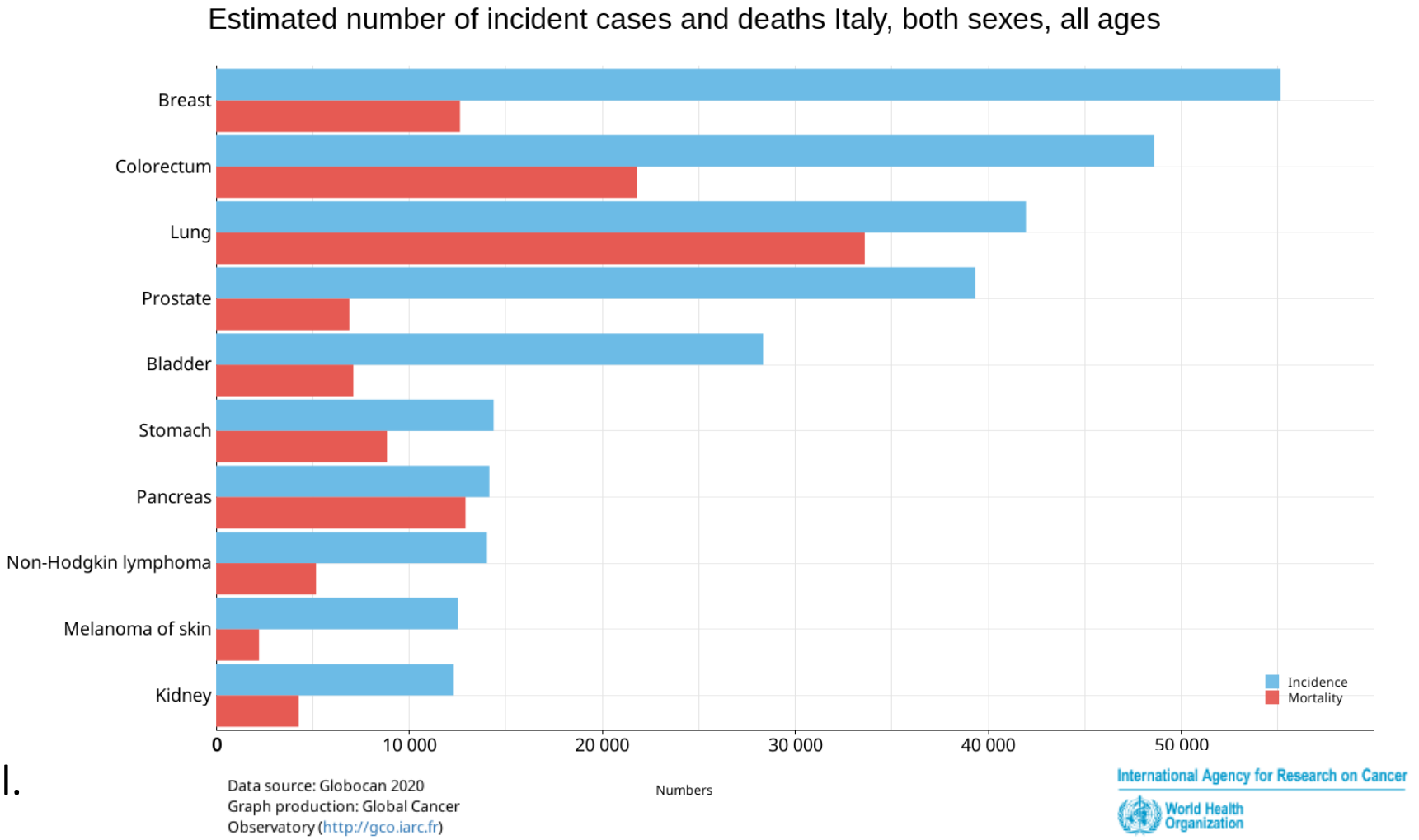
LUNG CANCER SCREENING: WHY?

Estimated 2.20 million new cases and 1.79 million deaths per year: lung cancer **is one of the most frequently diagnosed cancers** and **the leading cause of cancer-related deaths** worldwide.

- The 5-year relative survival for
  - stage I: 50%–90%
  - stage IV : 3%–6%

- improvements in understanding of disease biology, application of predictive biomarkers and refinements in treatment

AIM --> to diagnose at an earlier stage to decrease lung cancer-related deaths and improve survival.

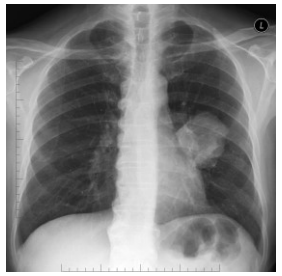


- Thai AA, Solomon BJ, Sequist L V., Gainor JF, Heist RS. Lung cancer. Lancet. 2021;398(10299):535–54
- Gierada DS, Black WC, Chiles C, Pinsky PF, Yankelevitz DF. Low-Dose CT Screening for Lung Cancer: Evidence from 2 Decades of Study. Radiol Imaging Cancer. 2020 Mar 1;2(2):e190058

LUNG CANCER SCREENING: HOW?

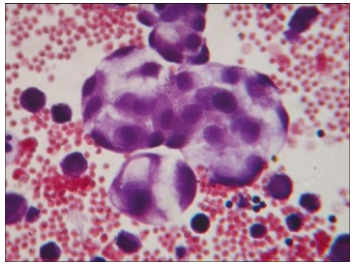
Historically:
(1970s - 1980s)

Chest RX



+/-

sputum cytology



=

no improvement of outcomes.

From the 2000s:

CT Scan

+

=

significantly reduced lung cancer mortality

2 RCTs

NSLT

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

The National Lung Screening Trial Research Team*

NELSON

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, P.M.A. van Ooijen, J.G.J.V. Aerts, M.A. den Bakker, E. Thunnissen, J. Verschakelen, R. Vliegenthart, J.E. Walter, K. ten Haaf, H.J.M. Groen, and M. Oudkerk

- Thai AA, Solomon BJ, Sequist L V., Gainor JF, Heist RS. Lung cancer. Lancet. 2021;398(10299):535–54
- Gierada DS, Black WC, Chiles C, Pinsky PF, Yankelevitz DF. Low-Dose CT Screening for Lung Cancer: Evidence from 2 Decades of Study. Radiol Imaging Cancer. 2020 Mar 1;2(2):e190058

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

The National Lung Screening Trial Research Team*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 4, 2011 VOL. 365 NO. 5

- U.S.A : 2002-2009
- N= 53 454 high-risk volunteer participants at 33 U.S. locations,
  - age 55–74 years,
  - Smoking history : minimum of 30 pack-years , currently smoking or quit within the last 15 years
  - Exclusion: previous diagnosis of lung cancer, chest CT within 18 months before enrollment, hemoptysis or unexplained weight loss (> 6.8 kg) in the last year.

The primary endpoint of the NLST was **lung cancer mortality**.

Secondary endpoints include all-cause mortality, incidence of lung cancer, lung cancer case survival (as measured from age of diagnosis), and lung cancer stage distribution.

-National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011 Aug 4;365(5):395–409.
-Gatsonis CA, Aberle DR, Berg CD, Black WC, Church TR, Fagerstrom RM, et al. The national lung screening trial: Overview and study design. Radiology. 2011;258(1):243–53.

N= 53 454 RANDOMIZED:

Low-dose CT screening [LDCT] (n. 26,722) or **Chest radiography** (26,732)

CT	
Negative or minor abnormality: not suspicious for lung cancer	No findings or minor findings not suspicious for lung cancer, such as morphologically benign nodules or noncalcified nodules < 4 mm
Clinically important abnormality: not suspicious for lung cancer	Important findings not suspicious for lung cancer but requiring some form of clinical follow-up
Positive: suspicious for lung cancer	Findings suspicious for lung cancer, such as noncalcified nodule ≥ 4 mm, lung consolidation or obstructive atelectasis, nodule enlargement, and nodules with suspicious changes in attenuation

Chest radiography	
Negative or minor abnormality, not suspicious for lung cancer	No findings or minor findings not suspicious for lung cancer, such as nodules containing benign patterns of calcification
Clinically important abnormality, not suspicious for lung cancer	Important findings not suspicious for lung cancer, but requiring some form of clinical follow-up
Positive, suspicious for lung cancer	Findings suspicious for lung cancer, such as noncalcified nodule or pulmonary opacity

3 screenings (T0, T1, and T2) at 1-year intervals,
T0= performed soon after the time of randomization.

The **median duration of follow-up was 6.5 years**, with a maximum duration of 7.4 years in each group.
Participants in whom lung cancer was diagnosed were not offered subsequent screening tests.

-National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011 Aug 4;365(5):395–409.
-Gatsonis CA, Aberle DR, Berg CD, Black WC, Church TR, Fagerstrom RM, et al. The national lung screening trial: Overview and study design. Radiology. 2011;258(1):243–53.

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 rate of adherence : 90%
- The rate of positive screening tests:
  - **LDCT 24.2%**
  - **RX 6.9%**
- False positive results:
  - **LDCT 96.4%**
  - **RX 94.5%**

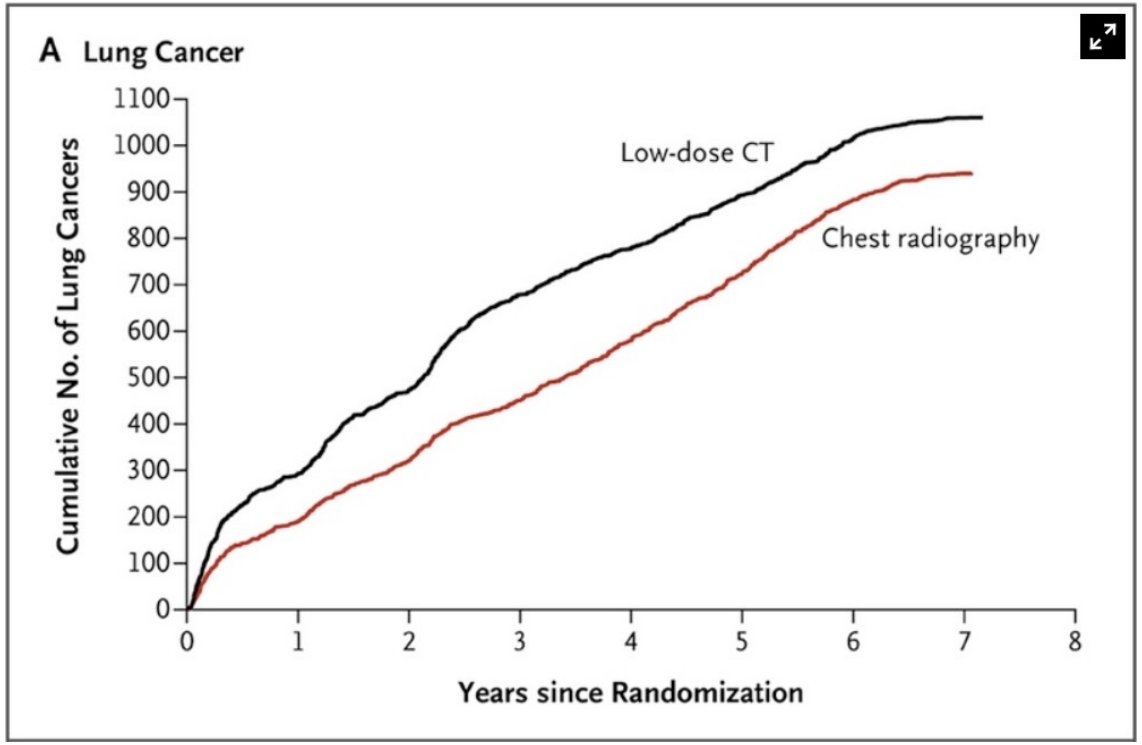
LDCT group: **1060 lung cancers** (645 per 100,000 person-years)

- 649 after a positive screening test,
- 44 after a negative screening test
- 367 among participants who missed the screening or after trial screening phase was over

XR group: **941 lung cancers** (572 per 100,000 person-years)

- 279 after a positive screening test,
- 137 after a negative screening test,
- 525 among participants who missed the screening or after trial screening phase was over

(rate ratio, 1.13; 95% [CI], 1.03 to 1.23).



-National Lung Screening Trial Research Team, Aberle DR, Adams AM, Berg CD, Black WC, Clapp JD, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. N Engl J Med. 2011 Aug 4;365(5):395–409.

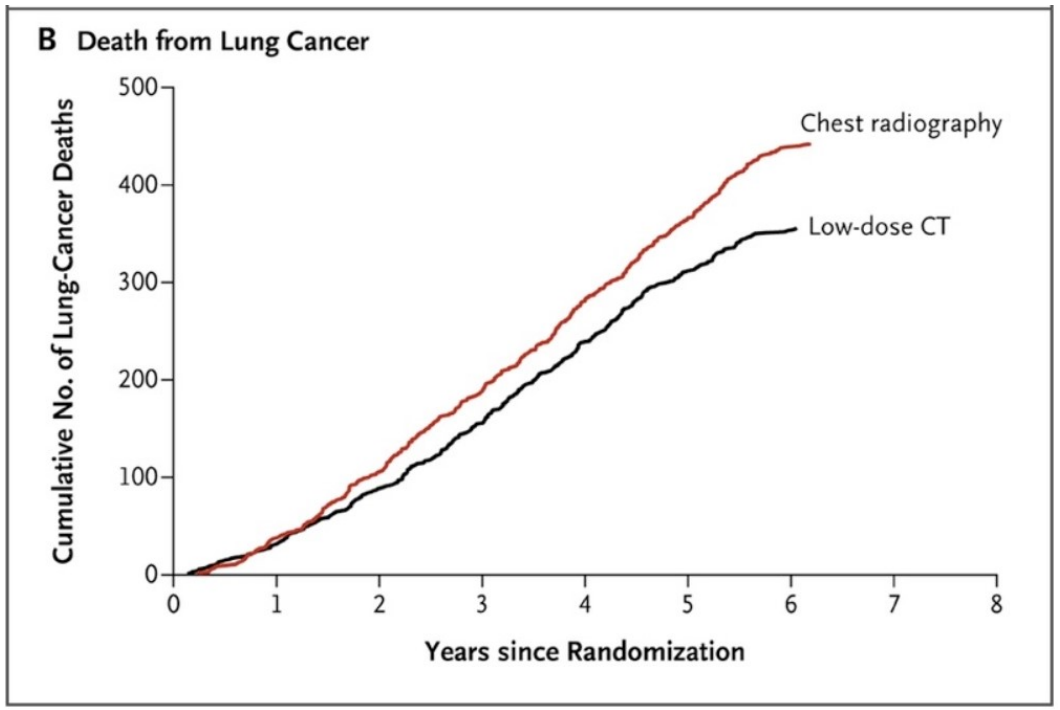
Table 5. Stage and Histologic Type of Lung Cancers in the Two Screening Groups, According to the Result of Screening.*

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)

Stage IA and stage IB highest among cancers diagnosed after a positive screening test in each group
Fewer stage IV cancers in the low-dose CT group than in the RX group at the 2nd and 3rd rounds

→ the stage distribution was more favorable in the low-dose CT group than in the radiography group

The primary endpoint of the NLST was lung cancer mortality.



LDCT : 356 deaths from LC -> rates of death 247/100,000 pers-years
XR: 443 deaths from LC -> rates of death 309/100,000 pers-years

→ **relative reduction in the rate of death from LC with LDCT of 20%**
(95% CI, 6.8 to 26.7; P = 0.004).

1 : 320

one death prevented	number of patients needed to screen (LDCT)

There were 1877 deaths in the low-dose CT group, as compared with 2000 deaths in the radiography group, representing a significant with low-dose CT screening of 6.7% (95% CI, 1.2 to 13.6) in the rate of death from any cause (P = 0.02).

Lung cancer accounted for 24.1% of all the deaths in the trial.

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, P.M.A. van Ooijen, J.G.J.V. Aerts, M.A. den Bakker, E. Thunnissen, J. Verschakelen, R. Vliegenthart, J.E. Walter, K. ten Haaf, H.J.M. Groen, and M. Oudkerk

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 6, 2020 VOL. 382 NO. 6

- Dutch–Belgian (**NE**derlands–**L**euvens Longkanker **S**creenings **ON**derzoek [NELSON]): population based RCT 2004-2012
- N= 13195 high-risk male participants
    - age 50-74 years
    - Current or former smokers > 15 cig/day x >25 yrs or >10 cig/day x >30 yrs or formers who quit ≤10 yrs ago
    - Exclusion: inability to climb two flights of stairs; weight >140 kg; current or past renal cancer, melanoma, or breast cancer; lung cancer or treatment related to lung cancer within the past 5 years; or a chest CT scan within the past year.

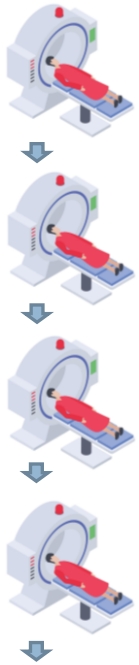
- AIM: reduction in lung-cancer mortality of 25% or more with volume-based, low-dose CT lung- cancer screening in high-risk male participants at 10 years of follow-up.

→ The primary outcome of the NELSON trial was **lung cancer–specific mortality**.

De Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med. 2020 Feb 6;382(6):503–13.

N= 13195 RANDOMIZED:

Screening group(n. 6583) or **control** group(6612)



Baseline scan

Year 1 scan

Year 3 scan

Year 5,5 scan

LC mortality 10 yrs FU

LC mortality 10 yrs FU

- 4 rounds of **low-dose CT** screening
- Analysis of semiautomated segmentation of nodules and determination of **volume**.

Screen round 1: baseline		Screen round 1: follow-up scan		Screen round 2-3		Screen round 4	
Screening result	Protocol	Screening result	Protocol	Screening result	Protocol	Screening result	Protocol
NEGATIVE - NODCAT I - NODCAT II	Screening next round	NEGATIVE - GROWCAT A - GROWCAT B	Screening next round	NEGATIVE - new and NODCAT I - GROWCAT A	Screening next round	NEGATIVE - NODCAT I - NODCAT II - GROWCAT A	End of screening
INDETERMINATE - NODCAT III	Follow-up scan after 3 months	POSITIVE - GROWCAT C	Referral pulmonologist	INDETERMINATE - GROWCAT B - new and NODCAT II	Follow-up scan after 12 months	INDETERMINATE - GROWCAT B	Follow-up scan after 12 months
POSITIVE - NODCAT IV	Referral pulmonologist			INDETERMINATE - new and NODCAT III	Follow-up scan after 6-8 weeks	INDETERMINATE - new and NODCAT III	Follow-up scan after 6-8 weeks
				POSITIVE - GROWCAT C - new and NODCAT IV	Referral pulmonologist	POSITIVE - NODCAT IV - GROWCAT C	Referral pulmonologist

NODULE CATEGORy based on volume

NODCAT I	nodule with benign characteristics, as fat/benign calcifications
NODCAT II	solid nodules with a volume of <50 mm³ pleural-based solid nodules with a minimal diameter of <5 mm non-solid component partial solid nodule with a mean diameter of <8 mm non-solid nodules with a mean diameter of <8 mm
NODCAT III	solid nodules with a volume of 50-500 mm³ pleural-based solid nodules with a minimal diameter of 5-10 mm solid nodule with a non-solid component with a mean diameter of ≥8mm
NODCAT IV	solid nodules with a volume of >500 mm³ pleural-based solide nodule with a minimal diameter of >10 mm solid component in a partial solid nodule with a volume of >500 mm³

NODULE CATEGORY based on volumedoublingtime (growth)

GROWCAT A	volumedoublingtime >600 dagen
GROWCAT B	volumedoublingtime 400-600 dagen
GROWCAT C	volumedoublingtime <400 dagen new solid component in previously exisiting non-solid nodule

Depending on the volume & volume-doubling time, a screening could be negative, indeterminate, or positive

De Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med. 2020 Feb 6;382(6):503–13.

Table 2. Screening-Test Results in Each Screening Round for Male Participants in the Screening Group.

Screening	Screening Uptake		Indeterminate Test	Positive Test	Detection of Lung Cancer	Positive Predictive Value
	Men Eligible for Screening	Men Undergoing Randomization	*number/total number (percent)*			*percent*
Round 1	6309/6583 (95.8)	6309/6583 (95.8)	1241/6309 (19.7)	147/6309 (2.3)	56/6309 (0.9)	38.1
Round 2	6086/6459 (94.2)	6086/6583 (92.5)	357/6086 (5.9)	95/6086 (1.6)	45/6086 (0.7)	47.4
Round 3	5768/6285 (91.8)	5768/6583 (87.6)	385/5768 (6.7)	136/5768 (2.4)	65/5758 (1.1)	47.8
Round 4	4437/5771 (76.9)	4437/6583 (67.4)	86/4437 (1.9)	89/4437 (2.0)	37/4437 (0.8)	41.6
Total	22,600/25,098 (90.0)	22,600/26,332 (85.8)	2069/22,600 (9.2)	467/22,600 (2.1)	203/22,600 (0.9)	43.5

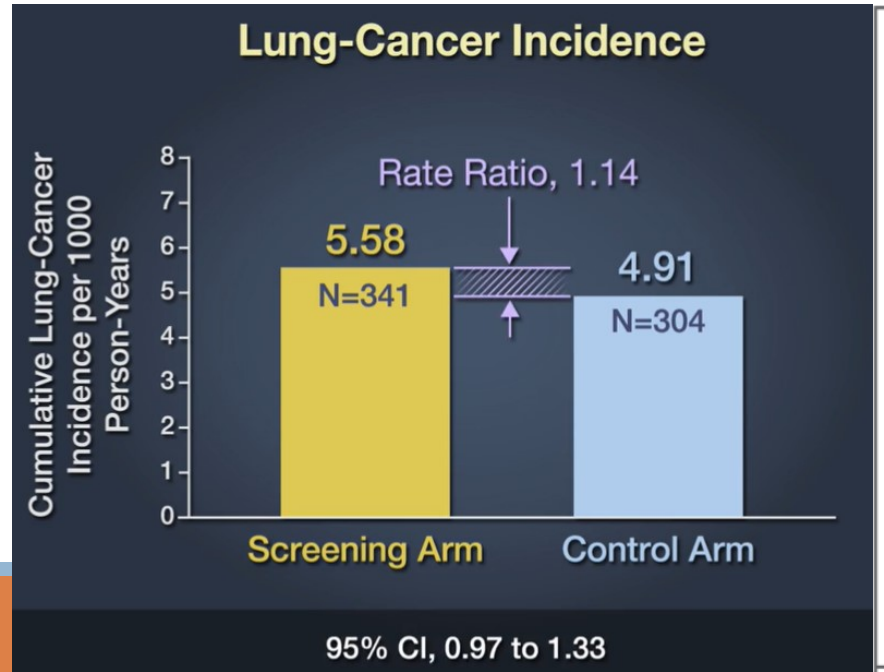
In follow-up rounds, 55% of new nodules resolved.

indeterminate screening test: repeat CT scan to calculate volume-doubling time before the final screening-test outcome.

Required further workup by the pulmonologist, leading to 203 screening-detected lung cancers

The **overall positive predictive value** of a positive screening test was **43.5%** - over all rounds 1.2% had a false positive test

At 10-year follow-up, the cumulative incidence of LC :



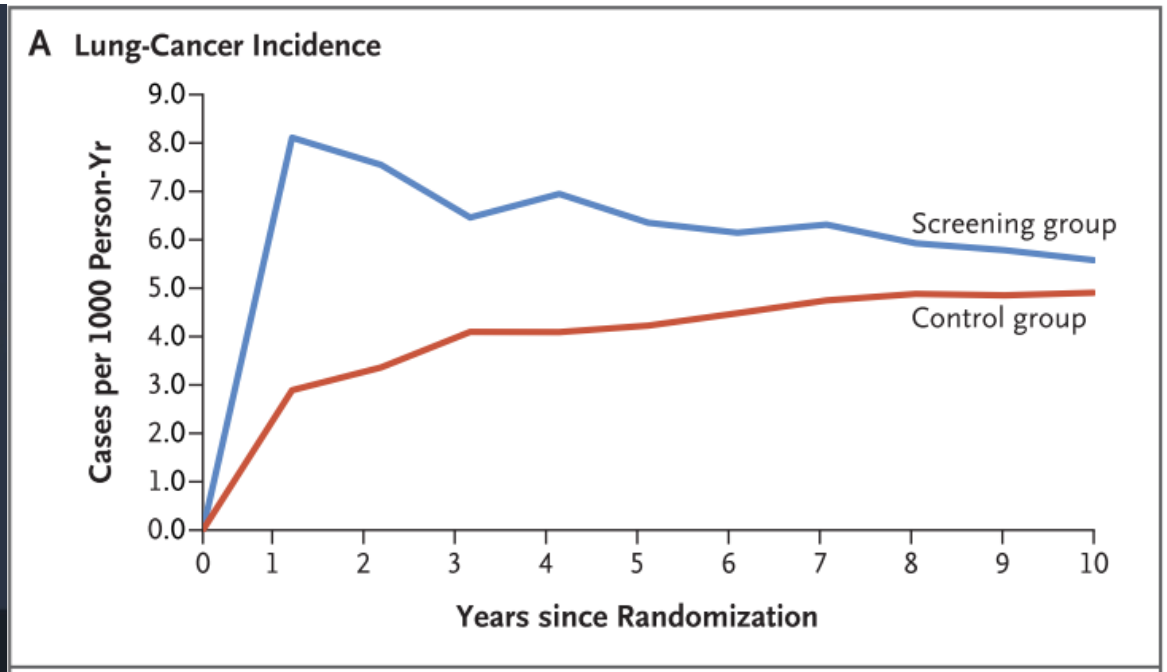


Table 3. Lung-Cancer Stage and Histologic Type of All First-Detected Lung Cancers in Male Participants at 10 Years of Follow-up or on December 31, 2015.*

Variable	Screening Group			Control Group
	Screening-Detected Lung Cancer (N=203)†	Non–Screening-Detected Lung Cancer (N=141)	Any Lung Cancer (N=344)	Any Lung Cancer (N=304)
	number of participants (percent)			
Stage				
IA	95 (46.8)	10 (7.1)	105 (30.5)	21 (6.9)
IB	24 (11.8)	10 (7.1)	34 (9.9)	20 (6.6)
IIA	8 (3.9)	4 (2.8)	12 (3.5)	13 (4.3)
IIB	11 (5.4)	6 (4.3)	17 (4.9)	17 (5.6)
IIIA	20 (9.9)	14 (9.9)	34 (9.9)	43 (14.1)
IIIB	13 (6.4)	14 (9.9)	27 (7.8)	34 (11.2)
IV	19 (9.4)	73 (51.8)	92 (26.7)	139 (45.7)
Unknown	13 (6.4)	10 (7.1)	23 (6.7)	17 (5.6)
Histologic type‡				
Adenocarcinoma	123 (60.6)	56 (39.7)	179 (52.0)	133 (43.8)
Squamous-cell carcinoma	39 (19.2)	38 (27.0)	77 (22.4)	94 (30.9)
Small-cell carcinoma	13 (6.4)	27 (19.1)	40 (11.6)	46 (15.1)
NSCLC	8 (3.9)	8 (5.7)	16 (4.7)	13 (4.3)
Other	20 (9.9)	12 (8.5)	32 (9.3)	18 (5.9)

59% (Screening-Detected Lung Cancer)

58,6% (Stage IA or IB, screening-detected)

14,2% (Stage IA or IB, non–screening-detected)

13,5% (Stage IA or IB, control group)

59.0% of all lung cancers in the screening group were detected on screening;
12.8% (44 of 344) were interval cancers

stage IA or IB :
58.6% screening group
vs.14.2% in non-screening detected
and 13.5% in control group

Stage IV
51.8% in non–screening- detected
45.7% in control group
9.4% of the screening-detected

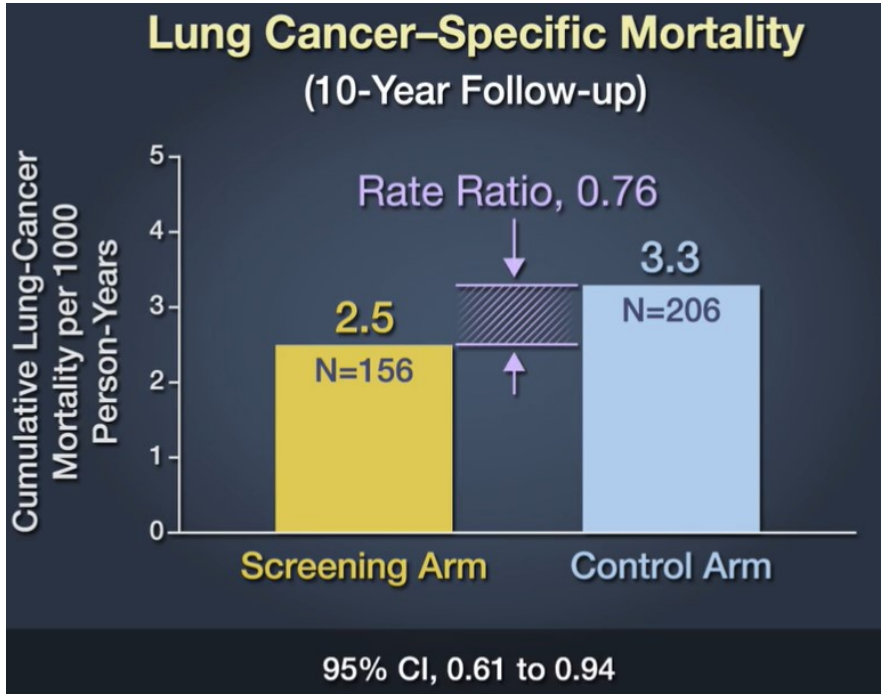
Most (screening- detected) lung cancers were adenocarcinomas

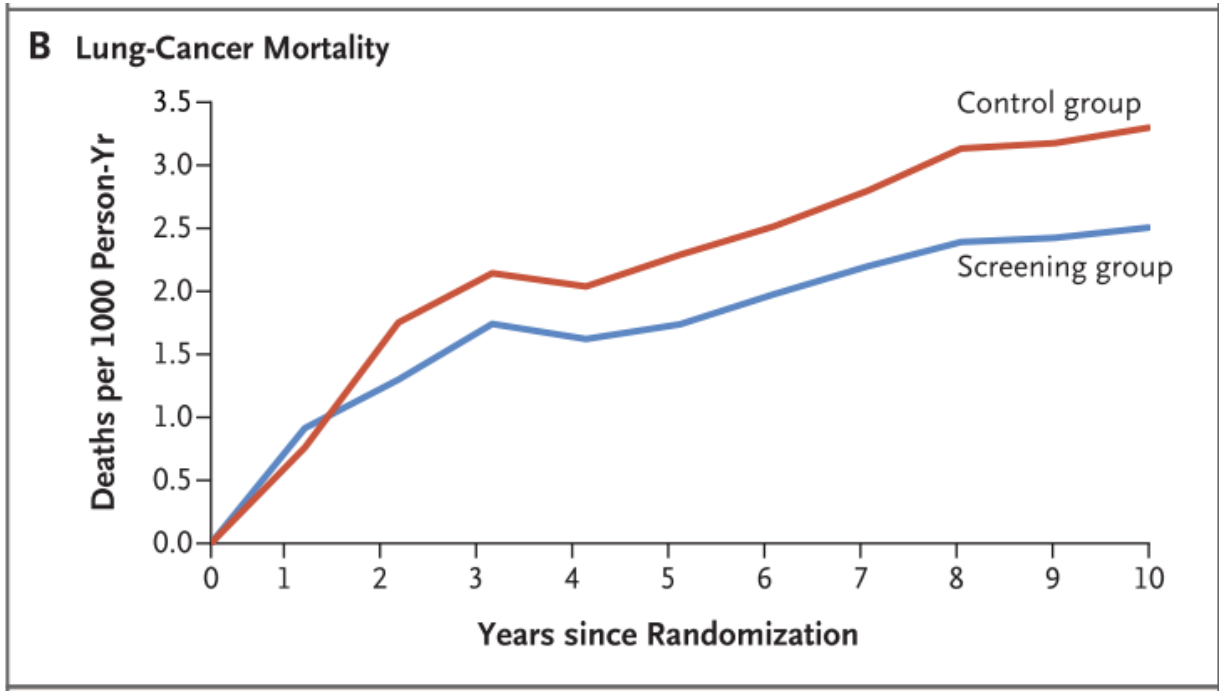
substantial shift to lower-stage cancers at the time of diagnosis = more frequent eligibility for curative treatment (mainly surgical)

2.5-year interval reduced the effect of screening and resulted in more interval cancers and more advanced tumors than a one-year or a two-year interval

De Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med. 2020 Feb 6;382(6):503–13.

Death from LC at 10 years of follow-up:





Lung Cancer specific mortality → Reduced by 24% in screening arm!

De Koning HJ, van der Aalst CM, de Jong PA, Scholten ET, Nackaerts K, Heuvelmans MA, et al. Reduced Lung-Cancer Mortality with Volume CT Screening in a Randomized Trial. N Engl J Med. 2020 Feb 6;382(6):503–13.

The observation that low-dose CT screening can reduce the rate of death from lung cancer has generated many questions:

Will populations with risk profiles that are different from those of the NLST/NELSON participants benefit?
Are less frequent screening regimens equally effective?
For how long should screening continue?

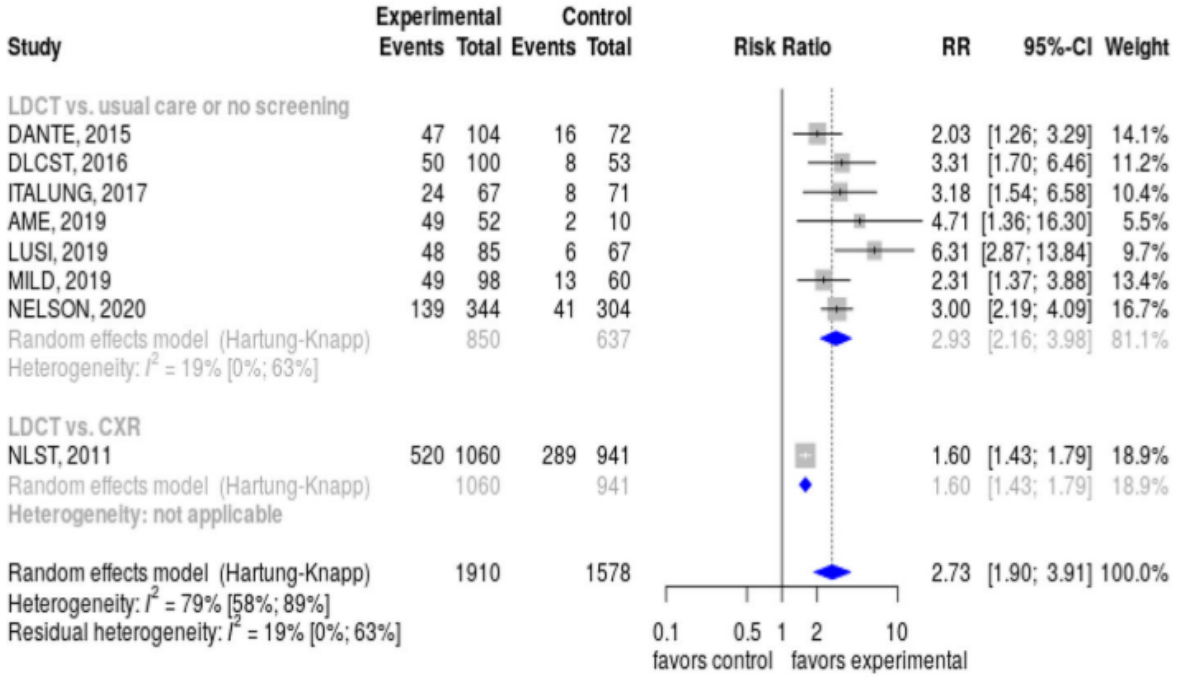
META-ANALYSIS! (1,2)

- **LDCT** → significantly increased **likelihood** of detecting a **stage I** lung cancer [RR = 2.73]

  → significantly **reduced** the risk of **lung cancer mortality** by **20%** (RR= 0,80) [2]
- Gender specific effects: **non-significantly lower** risk of lung cancer mortality for **women** than for men
- **N =265 to screen to prevent 1 LC death**, based on 3 to 5 rounds of screening with up to 10 years of follow-up in high-risk smokers → compares favorably with other cancer screening programs.
- LC screening does not significantly reduce the risk of overall mortality

1. Hunger T, Wanka-Pail E, Brix G, Griebel J. Lung cancer screening with low-dose ct in smokers: A systematic review and meta-analysis. Diagnostics. 2021;11(6):NA.
2. Hoffman RM, Atallah RP, Struble RD, Badgett RG. Lung Cancer Screening with Low-Dose CT: a Meta-Analysis. Vol. 35, Journal of General Internal Medicine. Springer; 2020. p. 3015–25.

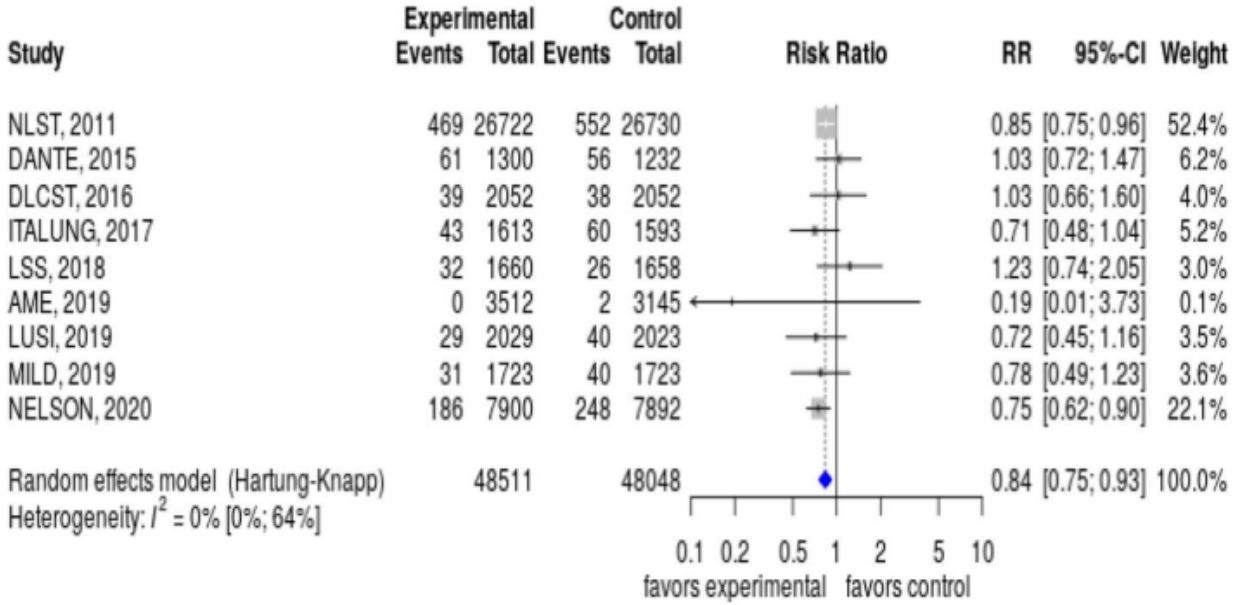
Diagnosis of stage I lung cancer



Test for differences among subgroups: p = 0.000

Test for funnel plot asymmetry: too few studies to test

Lung cancer mortality



Test for funnel plot asymmetry: too few studies to test

2. Hoffman RM, Atallah RP, Struble RD, Badgett RG. Lung Cancer Screening with Low-Dose CT: a Meta-Analysis. Vol. 35, Journal of General Internal Medicine. Springer; 2020. p. 3015–25.

META-ANALYSIS! (1,2)

- **False positive rate = 8%**

  N.B. NLST, which primarily defined positive studies using a nodule diameter ≥ 4 mm, had a false positive rate of 23.3%; NELSON trial, which had a false positive rate of only 1.2%, used volumetric criteria.

- **Complications** (Only NLST) **:** Overall, 17/1000 with a false positive LDCT had an invasive diagnostic procedure and 0.4 /1000 suffered a major complication.

- **Overdiagnosis rate of 33%** = overdiagnosing and overtreating indolent cancers; BUT Overdiagnosis in trials is strongly dependent on the duration of follow-up, the individual remaining life expectancy, and competing risks of death -> lack of sufficient follow-up time.

  E.g. NELSON: initially estimated an overdiagnosis rate of 19.7% through 10 years of follow- up; however, extending follow-up to 11 years reduced the rate to only 8.9%.

1. Hunger T, Wanka-Pail E, Brix G, Griebel J. Lung cancer screening with low-dose ct in smokers: A systematic review and meta-analysis. Diagnostics. 2021;11(6):NA.
2. Hoffman RM, Atallah RP, Struble RD, Badgett RG. Lung Cancer Screening with Low-Dose CT: a Meta-Analysis. Vol. 35, Journal of General Internal Medicine. Springer; 2020. p. 3015–25.

META-ANALYSIS! (1,2)

- 7.5% **incidental findings** (>> emphysema and coronary artery calcification)

- The optimal **number and frequency** of LDCT screening rounds are **uncertain** -> *Less frequent* screening intervals, particularly following a negative baseline scan, could make screening *more cost effective and reduce radiation exposure*

- **No statistical association** between patient characteristics (age, pack-years or smoking status) and LC mortality benefits seen with screening

  → using **comprehensive risk models** (e.g. additional socio-demographic characteristics, clinical features, and family history) to select patients for screening may be more cost effective.

1. Hunger T, Wanka-Pail E, Brix G, Griebel J. Lung cancer screening with low-dose ct in smokers: A systematic review and meta-analysis. Diagnostics. 2021;11(6):NA.
2. Hoffman RM, Atallah RP, Struble RD, Badgett RG. Lung Cancer Screening with Low-Dose CT: a Meta-Analysis. Vol. 35, Journal of General Internal Medicine. Springer; 2020. p. 3015–25.

«**To translate the benefit** of screening as shown by the considered RCTs to a **population-based** screening activity**, high-quality standards and stringent requirements**, as in the RCTs, have to be implemented. To meet these standards, the screening activities should be embedded in a **structured screening process and involve interdisciplinary medical teams** with expertise in radiology, pulmonology, and thoracic surgery.»

1. Hunger T, Wanka-Pail E, Brix G, Griebel J. Lung cancer screening with low-dose ct in smokers: A systematic review and meta-analysis. Diagnostics. 2021;11(6):NA

… In practice

US Preventive Services Task Force
RECOMMENDATION STATEMENT
Screening for Lung Cancer

What does the USPSTF recommend?	**Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years:** • Screen for lung cancer with low-dose computed tomography (CT) every year. • Stop screening once a person has not smoked for 15 years or has a health problem that limits life expectancy or the ability to have lung surgery. **Grade: B**
To whom does this recommendation apply?	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. (See below for definition of pack-year.)
What's new?	The USPSTF has revised the recommended ages and pack-years for lung cancer screening. It expanded the age range to 50 to 80 years (previously 55 to 80 years) and reduced the pack-year history to 20 pack-years of smoking (previously 30 pack-years).
How to implement this recommendation?	1. **Assess risk based on age and pack-year smoking history:** Is the person aged 50 to 80 years and have they accumulated 20 pack-years or more of smoking? a. A pack-year is a way of calculating how much a person has smoked in their lifetime. One pack-year is the equivalent of smoking an average of 20 cigarettes—1 pack—per day for a year. 2. **Screen:** If the person is aged 50 to 80 years and has a 20 pack-year or more smoking history, engage in shared decision-making about screening. a. The decision to undertake screening should involve a discussion of its potential benefits, limitations, and harms. b. If a person decides to be screened, refer them for lung cancer screening with low-dose CT, ideally to a center with experience and expertise in lung cancer screening. c. If the person currently smokes, they should receive smoking cessation interventions.
How often?	• Screen every year with low-dose CT. • Stop screening once a person has not smoked for 15 years or has a health problem that limits life expectancy or the ability to have lung surgery.
What are other relevant USPSTF recommendations?	The USPSTF has made recommendations on interventions to prevent the initiation of tobacco use in children and adolescents, and on behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women. These recommendations are available at https://www.uspreventiveservicestaskforce.org
Where to read the full recommendation statement?	Visit the USPSTF website (https://www.uspreventiveservicestaskforce.org) to read the full recommendation statement. This includes more details on the rationale of the recommendation, including benefits and harms; supporting evidence; and recommendations of others.

The USPSTF recognizes that clinical decisions involve more considerations than evidence alone. Clinicians should understand the evidence but individualize decision-making to the specific patient or situation.

USPSTF indicates US Preventive Services Task Force.

Krist AH, Davidson KW, Mangione CM, Barry MJ, Cabana M, Caughey AB, et al. Screening for Lung Cancer: US Preventive Services Task Force Recommendation Statement. JAMA - J Am Med Assoc. 2021 Mar 9;325(10):962–70.

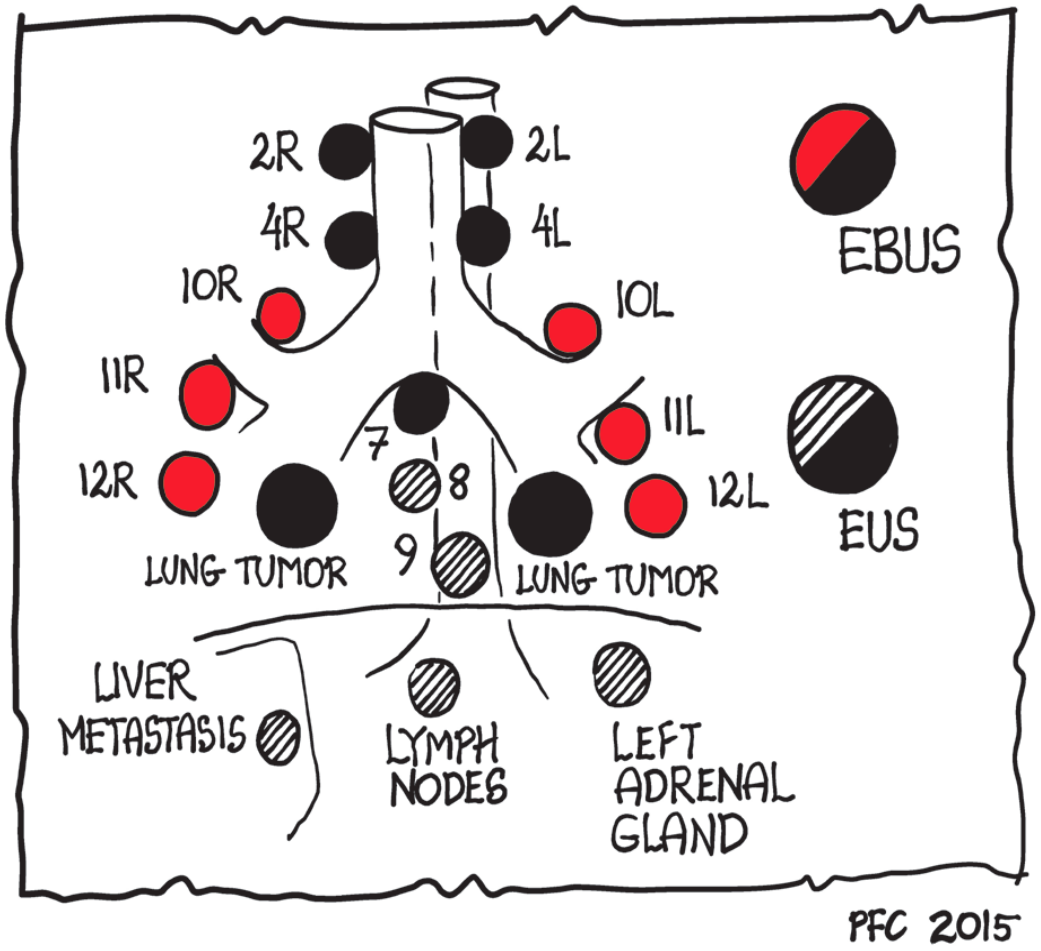
Minimally Invasive Endoscopic Staging of Suspected Lung Cancer

Michael B. Wallace, MD, MPH
Jorge M. S. Pascual, MD
Massimo Raimondo, MD
Timothy A. Woodward, MD
Barbara L. McComb, MD
Julia E. Crook, PhD
Margaret M. Johnson, MD
Mohammad A. Al-Haddad, MD
Seth A. Gross, MD
Surakit Pungpapong, MD
Joy N. Hardee, CCRA
John A. Odell, MD

Procedure	Fraction (%) [95% CI][a]	
	Sensitivity	NPV
TBNA	15/42 (36) [22-52]	96/123 (78) [70-85]
EUS-FNA	29/42 (69) [53-82]	96/109 (88) [80-93]
EBUS-FNA	29/42 (69) [53-82]	96/109 (88) [80-93]
EUS-FNA + TBNA	33/42 (79) [63-90]	96/105 (91) [84-96]
EBUS-FNA + TBNA	32/42 (76) [61-88]	96/106 (91) [83-95]
EUS-FNA + EBUS-FNA	39/42 (93) [81-99]	96/99 (97) [91-99]

JAMA. 2008;299(5):540-546

EBUS + EUS(-B)


2R
2L
4R
4L
10R
10L
11R
11L
12R
12L
7
8
9
LUNG TUMOR
LUNG TUMOR
EBUS
EUS
LIVER METASTASIS
LYMPH NODES
LEFT ADRENAL GLAND
PFC 2015

Mediastinoscopy vs Endosonography for Mediastinal Nodal Staging of Lung Cancer

A Randomized Trial

Jouke T. Annema, MD, PhD
Jan P. van Meerbeeck, MD, PhD
Robert C. Rintoul, FRCP, PhD
Christophe Dooms, MD, PhD
Ellen Deschepper, PhD
Olaf M. Dekkers, MA, MD, PhD
Paul De Leyn, MD, PhD
Jerry Braun, MD
Nicholas R. Carroll, FRCP, FRCR
Marleen Praet, MD, PhD
Frederick de Ryck, MD
Johan Vansteenkiste, MD, PhD
Frank Vermassen, MD, PhD
Michel I. Versteegh, MD
Maud Veselic, MD
Andrew G. Nicholson, FRCPath, DM
Klaus F. Rabe, MD, PhD
Kurt G. Tournoy, MD, PhD

Table 2. Diagnostic Performance[a]

	No./Total No. (%) [95% Confidence Interval]		
Nodal Invasion, N2/N3	Surgical Staging (n = 118)	Endosonography and Surgical Staging (n = 123)	*P* Value
Sensitivity	41/52 (79) [66-88]	62/66 (94) [85-98]	.02
Negative predictive value	66/77 (86) [76-92]	57/61 (93) [84-97]	.18

Table 3. Secondary Outcomes

	Surgical Staging, No. (n = 118)	Endosonography and Surgical Staging, No. (n = 123)	*P* Value
Unnecessary thoracotomies, all	21	9	.02
Complications, all	7	6	.78

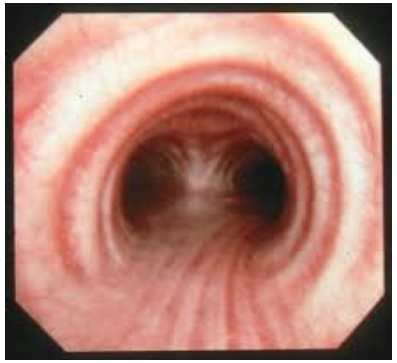
JAMA. 2010;304(20):2245-2252

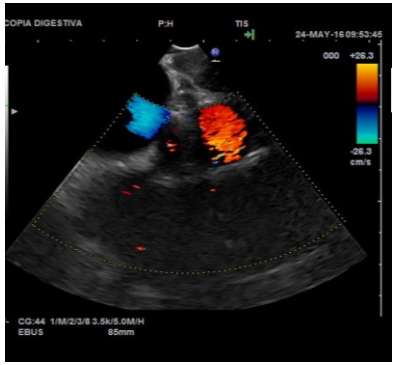
Endoscopic ultrasound (with bronchoscope) fine needle aspiration (*EUS-B-FNA*)

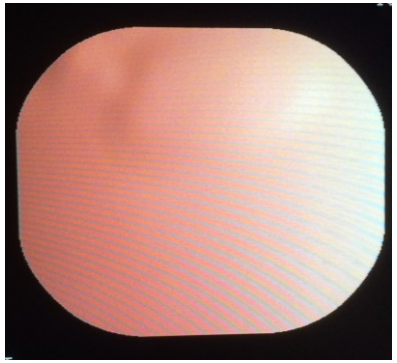
Transoesophageal needle aspiration using a convex probe ultrasonic bronchoscope

BIN HWANGBO,[1]* HEE SEOK LEE,[1]* GEON-KOOK LEE,[1] KUN-YOUNG LIM,[1] SOO-HYUN LEE,[2] HYAE-YOUNG KIM,[1] JONG-YEUL LEE[3] AND JAE ILL ZO[1]

Although combining EBUS-TBNA and EUS-FNA may be beneficial, EUS-FNA is not provided as a procedure that complements bronchoscopy at many institutions because of its limited availability, cost and time requirements. In this study, we used transoesophageal needle aspiration with a convex probe ultrasonic puncture bronchoscope, which may be an alternative to EUS-FNA. We refer to this method as endoscopic ultrasound (with bronchoscope)-guided fine needle aspiration (EUS-B-FNA).







Medical Thoracoscopy

Sameer K. Avasarala, MD[a], Robert J. Lentz, MD[b,c], Fabien Maldonado, MD, FCCP[b,c,*]

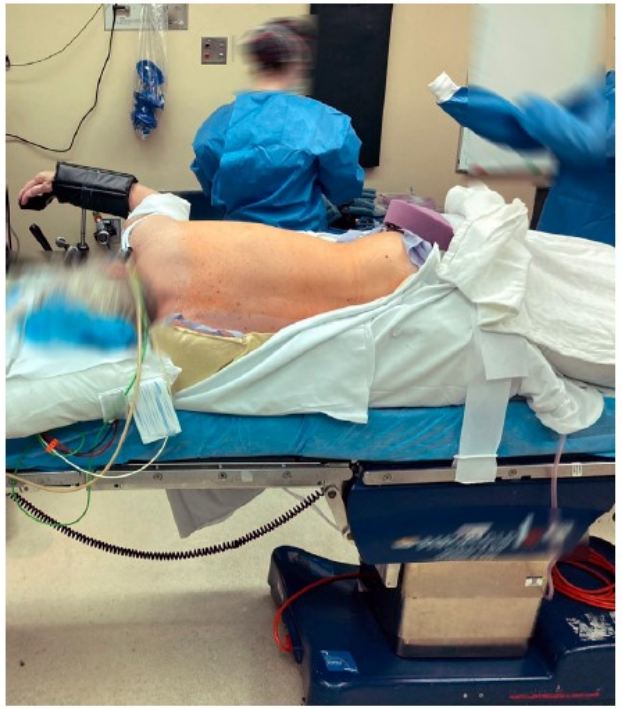


Fig. 2. The patient should be positioned with the affected side facing up. Their pressure points should be supported appropriately. The affected side's arm should be positioned in a manner that places it out of the surgical field. In this image, an arm supported is used to position the patient's right arm.

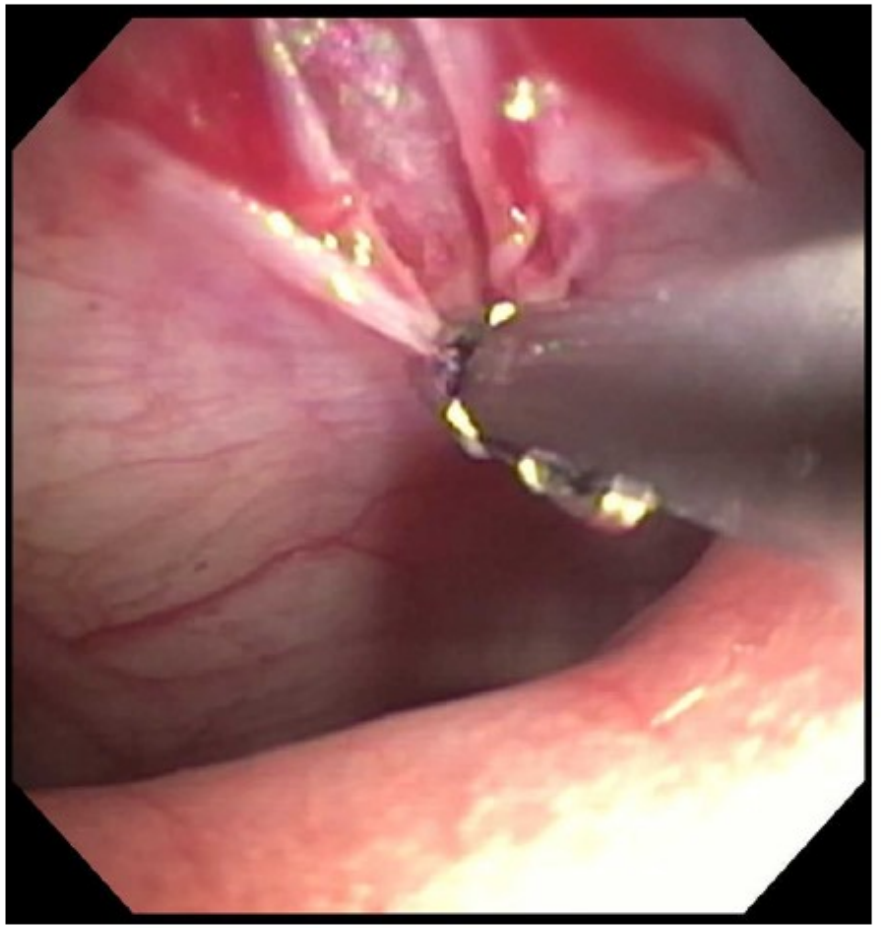
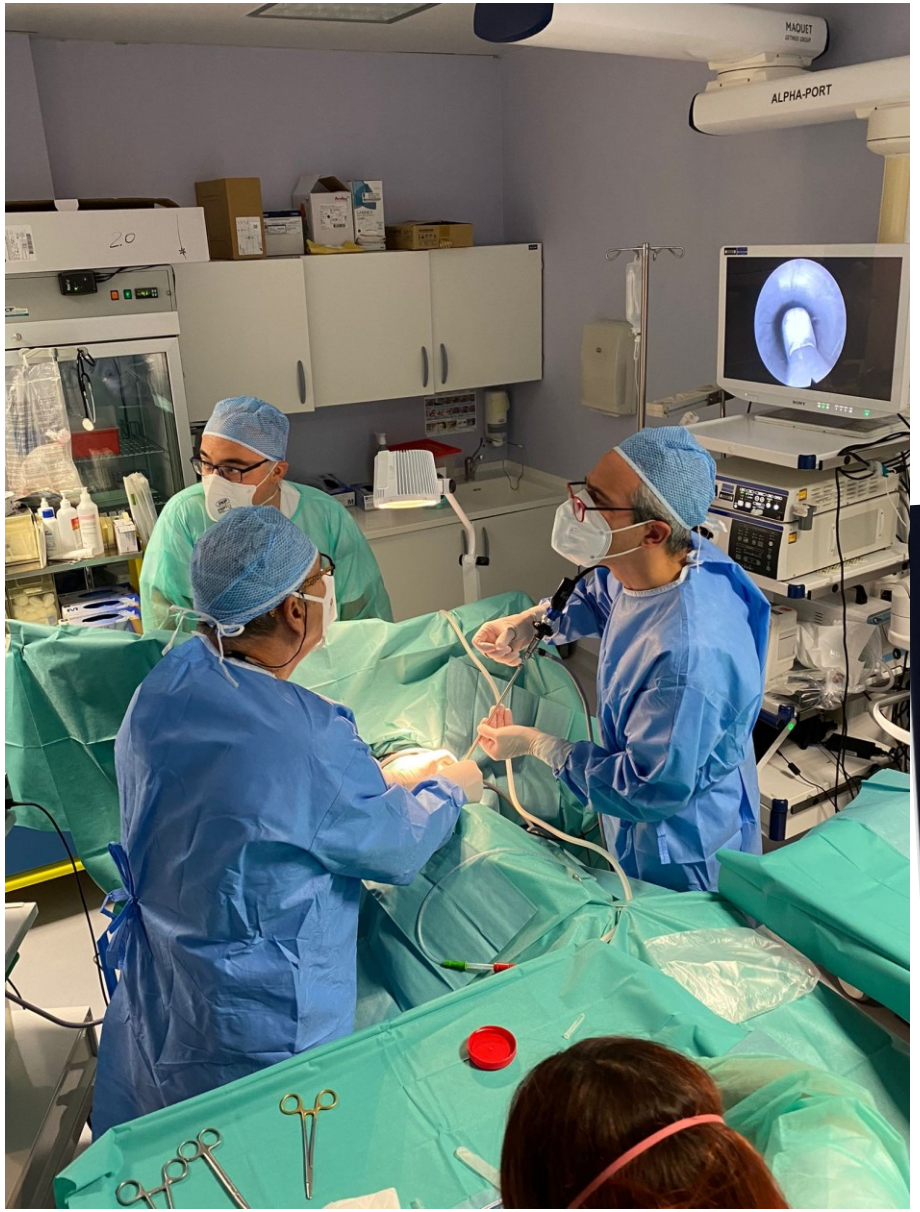
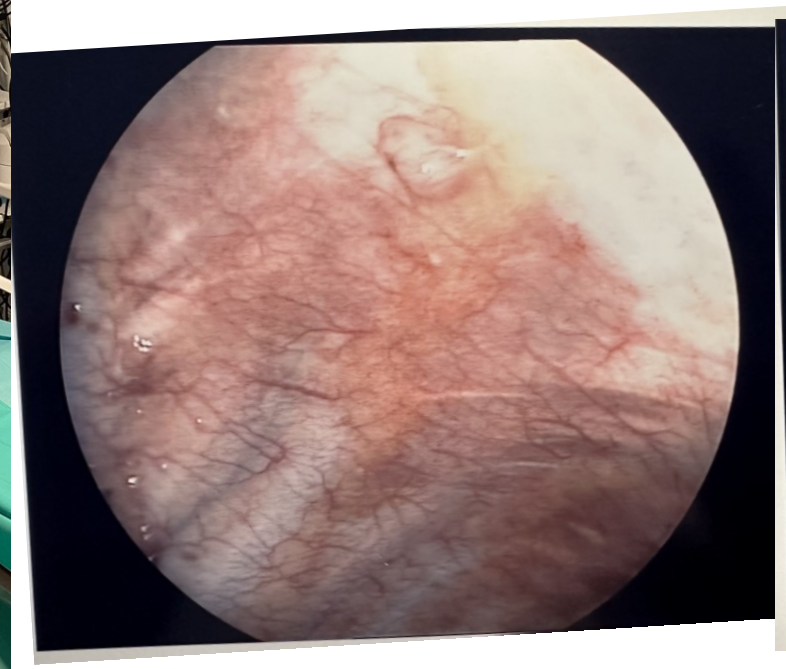


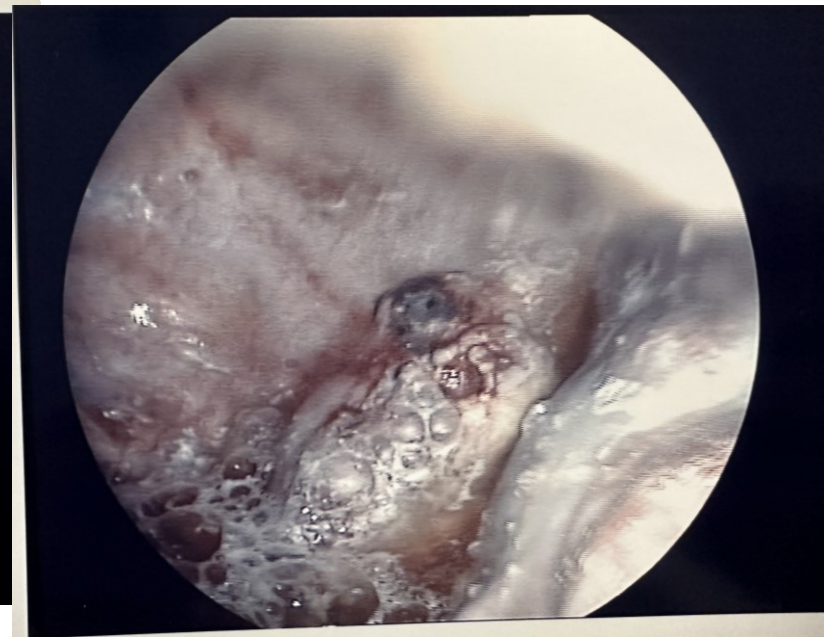
Fig. 11. Forceps can be used to "peel" the parietal pleural biopsies. It is thought that this method is safer than "punching" and allows for more immediate recognition of any bleeding that may occur.

Clin Chest Med 42 (2021) 751–766



La prima toracoscopia medica al PG23 (26 ottobre 2022)





Sistema Socio Sanitario
Ospedale di Bergamo
Regione Lombardia
ASST Papa Giovanni XXIII

UNIVERSITÀ DEGLI STUDI DI MILANO

Inquadramento clinico e diagnostico al paziente a rischio di neoplasia polmonare

Fabiano Di Marco

Università degli Studi di Milano
ASST – Ospedale Papa Giovanni XXIII, Bergamo
fabiano.dimarco@unimi.it