

# Dépistage Cancer Pulmonaire: Recommandations?

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Service de Pneumologie



# Lung Cancer: Global Leading Cause of Mortality

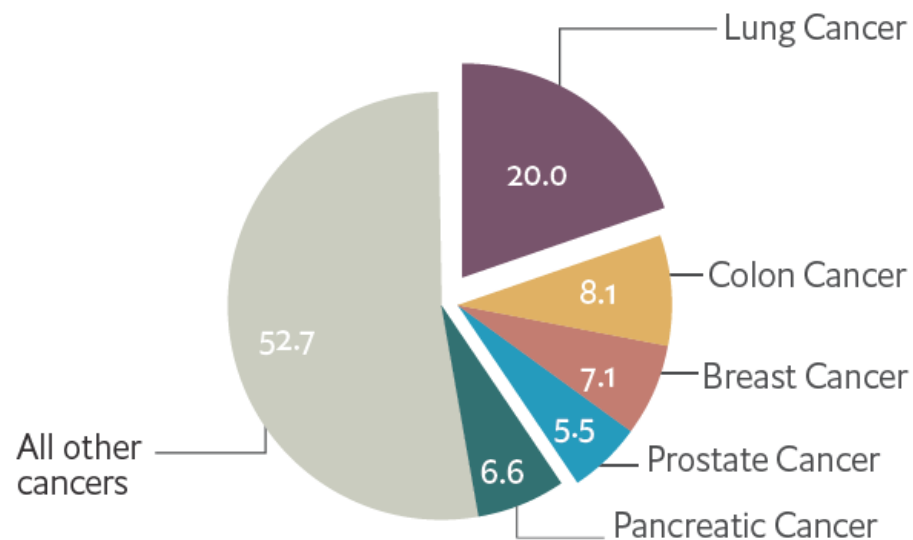
1990	2007	Mean percentage change in number of YLLs, 1990-2007	Mean percentage change in all-age YLL rate, 1990-2007	Mean percentage change in age-standardised YLL rate, 1990-2007	2017	Mean percentage change number of YLLs, 2007-17	Mean percentage change in all-age YLL rate, 2007-17	Mean percentage change in age-standardised YLL rate, 2007-17
1 Neonatal disorders	1 Neonatal disorders	-21.2	-37.2	-20.7	1 Ischaemic heart disease	17.3	3.9	-9.8
2 Lower respiratory infections	2 Lower respiratory infections	-38.6	-51.0	-41.1	2 Neonatal disorders	-24.1	-32.8	-26.2
3 Diarrhoeal diseases	3 Ischaemic heart disease	20.9	-3.6	-20.2	3 Stroke	12.1	-0.7	-13.8
4 Ischaemic heart disease	4 Diarrhoeal diseases	-39.5	-51.8	-42.6	4 Lower respiratory infections	-25.9	-34.4	-32.6
5 Stroke	5 HIV/AIDS	419.0	313.7	316.4	5 Diarrhoeal diseases	-32.0	-39.8	-38.1
6 Congenital anomalies	6 Stroke	12.9	-10.0	-24.0	6 Road injuries	-9.7	-20.0	-19.6
7 Tuberculosis	7 Malaria	30.1	3.7	24.2	7 COPD	13.2	0.3	-14.3
8 Road injuries	8 Road injuries	1.3	-19.3	-18.4	8 HIV/AIDS	-51.2	-56.8	-56.6
9 Measles	9 Congenital anomalies	-18.3	-34.9	-19.1	9 Congenital anomalies	-15.3	-25.0	-18.8
10 Malaria	10 Tuberculosis	-19.1	-35.6	-38.2	10 Malaria	-34.5	-42.0	-39.2
11 COPD	11 COPD	-6.9	-25.8	-37.4	11 Tuberculosis	-21.2	-30.2	-33.3
12 Protein-energy malnutrition	12 Cirrhosis	22.7	-2.2	-13.6	12 Lung cancer	24.8	10.6	-4.1
13 Drowning	13 Self-harm	-3.4	-23.0	-26.6	13 Cirrhosis	8.9	-3.5	-11.3
14 Self-harm	14 Lung cancer	28.8	2.6	-11.9	14 Self-harm	-3.4	-14.4	-15.1
15 Meningitis	15 Meningitis	-25.6	-40.7	-29.4	15 Diabetes	29.9	15.0	0.7
16 Cirrhosis	16 Chronic kidney disease	26.2	0.6	-7.2	16 Chronic kidney disease	21.0	7.2	-2.5
17 Lung cancer	17 Diabetes	56.0	24.4	7.1	17 Alzheimer's disease	38.6	22.8	-0.3
18 Tetanus	18 Drowning	-40.9	-52.9	-46.3	18 Interpersonal violence	-1.6	-12.9	-10.9
19 HIV/AIDS	19 Protein-energy malnutrition	-43.4	-54.9	-44.7	19 Liver cancer	21.2	7.4	-4.6
20 Interpersonal violence	20 Interpersonal violence	9.5	-12.7	-13.1	20 Meningitis	-25.2	-33.7	-30.2
24 Chronic kidney disease	21 Measles				24 Drowning			
28 Diabetes	23 Alzheimer's disease				27 Protein-energy malnutrition			
30 Liver cancer	24 Liver cancer				39 Measles			
33 Alzheimer's disease	51 Tetanus				79 Tetanus			

NICOTINE

# Lung Cancer: Europe

## Global incidence of lung cancer increasing 2012: 1.2 million → 2018: 2 million new cases

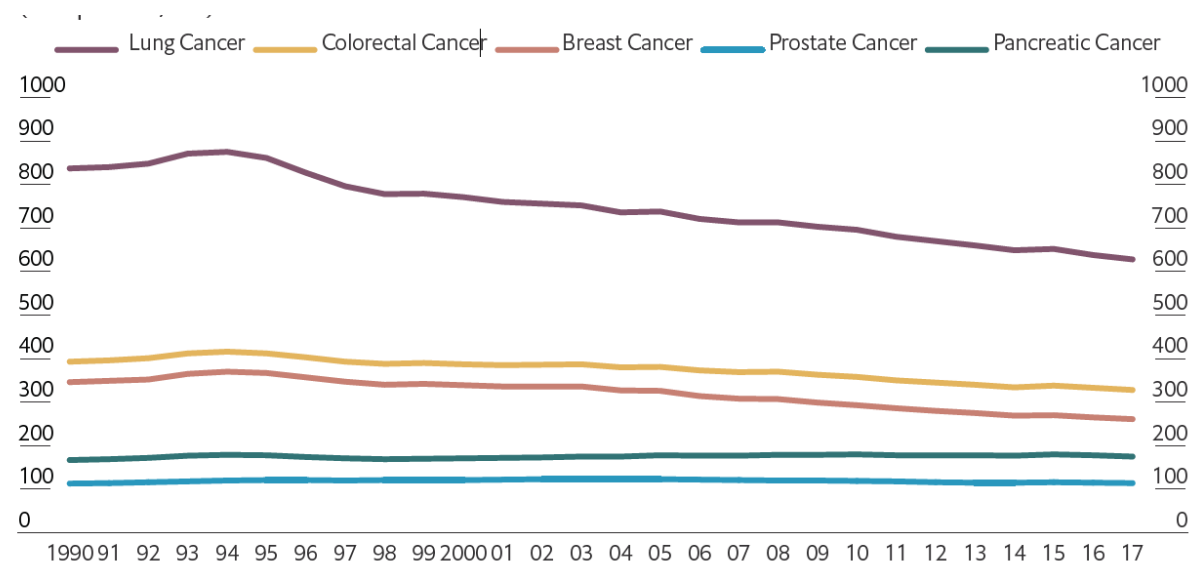
### Top 5 causes cancer mortality Europe



Source Globocan, 2018.

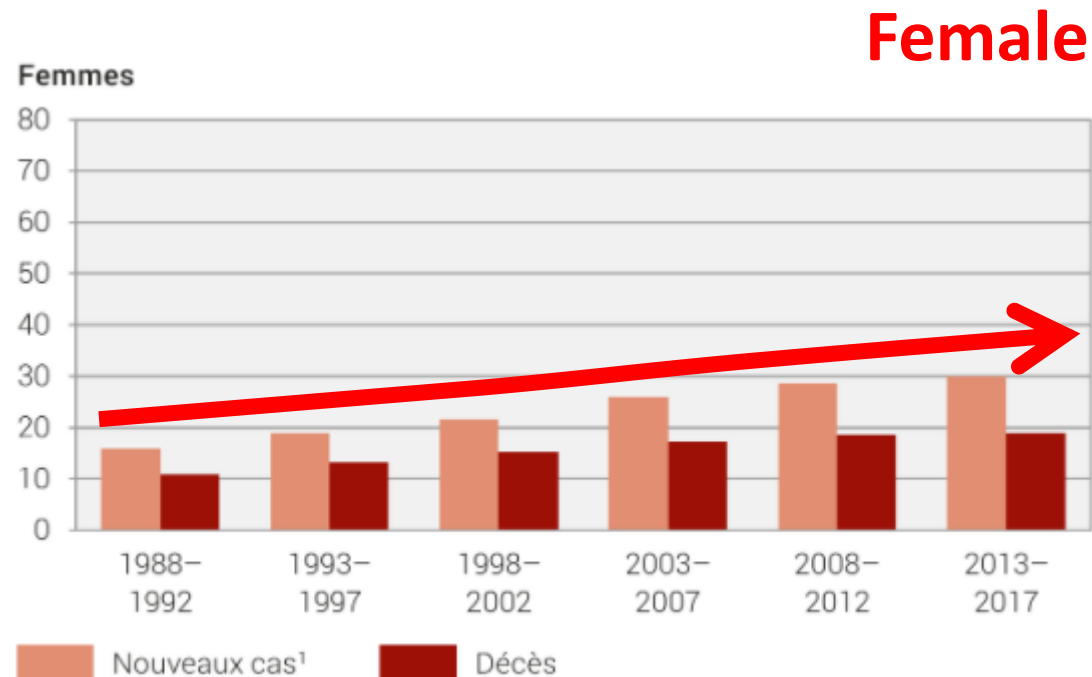
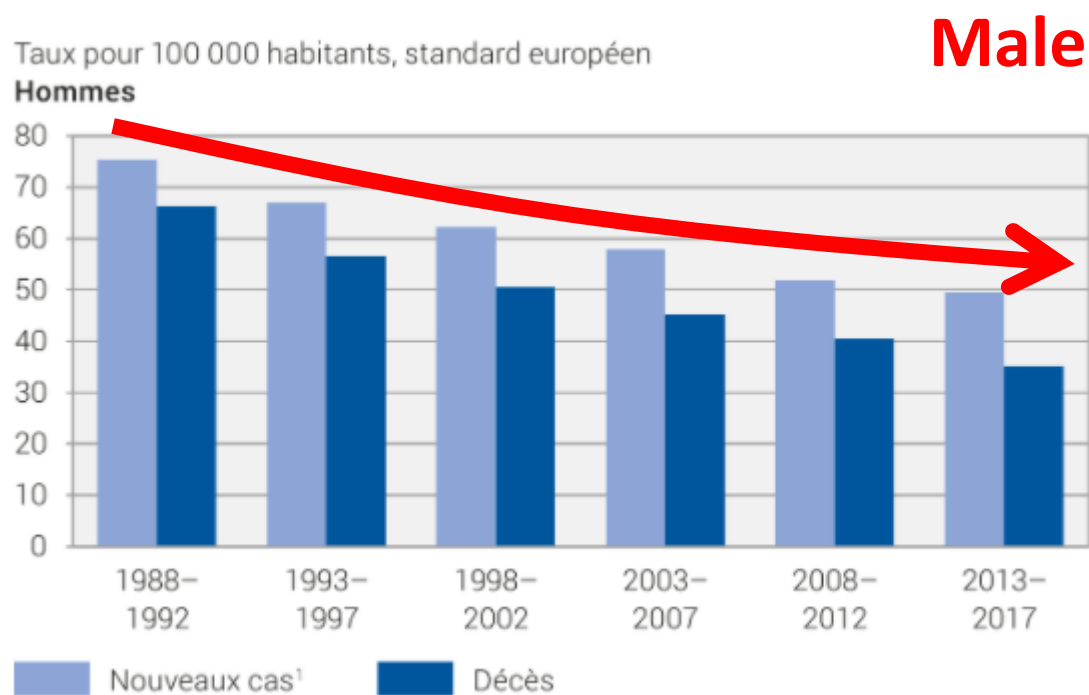
### DALYs among top 5 cancers Europe

Rate per 100 000



Source: Global Burden of Disease, 2017.

# Epidemiology Switzerland



**CH: ~ 5'600 nouveaux cas/an (H:F 1:1) , ~ 3'200 décès par an (HF 2:1)**

**VD: ~ 500 nouveaux cas/an, ~ 300 décès par an**

# Lung Cancer (EU): Economic Burden

## Direct cost per patient

- + 50% 2006 – 2016
- cost of novel targeted therapies and immunotherapies not included

## Large variations cost/QALY depending on stage / treatment modalities

- |                    |                         |                 |
|--------------------|-------------------------|-----------------|
| - Early stage      | → Lobectomy             | ≈10'000 €/QALY  |
| - Locally advanced | → Chemoradiotherapy     | ≈16'000 €/QALY  |
| - Advanced         | → 1st line chemotherapy | ≈20'000 €/QALY  |
|                    | → Targeted agents       | ≈25'000 €/QALY  |
|                    | → Immunotherapy         | ≈100'000 €/QALY |

# Lung Cancer: Priority in Switzerland?

## Lung Cancer is a strategic priority

Low	Moderately Low	Moderate	Moderately High	High
	Belgium Bulgaria Croatia Czech Republic Hungary	Austria Finland France Germany Greece Israel Italy Netherlands Romania Serbia Spain	Ireland Norway Portugal Russia Slovakia Slovenia <b>Switzerland</b> United Kingdom	Denmark Poland Sweden

## Lung Cancer is a public health issue

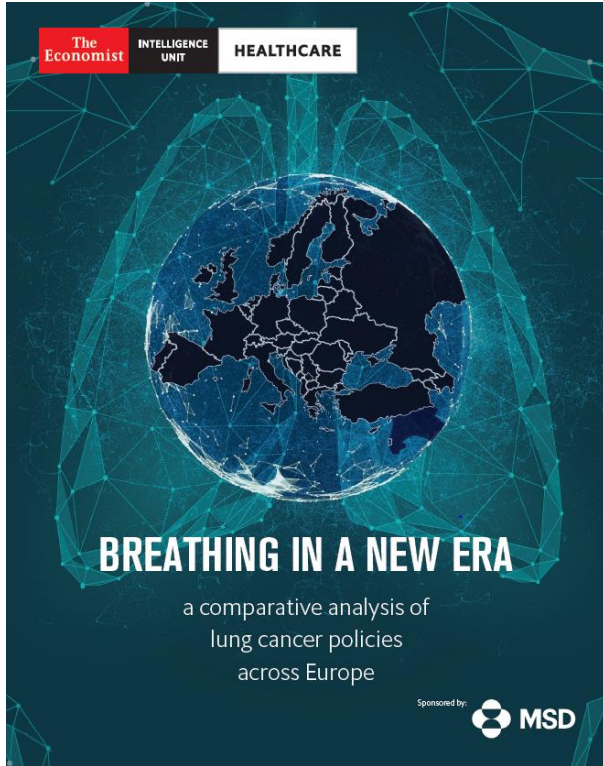
Low	Moderately Low	Moderate	Moderately High	High
		Serbia Slovakia Slovenia <b>Switzerland</b>	Austria Belgium Bulgaria Croatia Czech Republic Finland Germany Greece	Denmark France Poland United Kingdom

## Lung Cancer is a race against time

Low	Moderately Low	Moderate	Moderately High	High
Finland Greece Hungary Spain	Croatia Czech Republic France Germany Italy Poland Romania Russia Serbia <b>Switzerland</b>	Austria Belgium	Israel Slovakia	Bulgaria Denmark Ireland Netherlands Norway Portugal Slovenia Sweden United Kingdom

## Lung Cancer is a focus for research

Low	Moderately Low	Moderate	Moderately High	High
	Greece	France Germany Hungary Italy Poland Portugal Romania Russia Serbia Spain	Belgium Bulgaria Croatia Czech Republic Denmark Israel Netherlands Norway <b>Switzerland</b>	Austria Finland Ireland Slovakia Slovenia United Kingdom



# Conditions for Lung Cancer Screening

**High morbidity + mortality**



**Significant prevalence (0.5-2.2%; CH  $\approx$ 1.5%)**



**Identifiable risk factors (targeted screening)**



**Long pre-clinical phase**



**Efficacious therapy early stage**



# 20yrs Milestones Lung Cancer Screening

1999

**Early Lung Cancer Action Project: overall design and findings from baseline screening**  
Claudia I Henschke, Dorothy I McCauley, David F Yankelevitz, David P Naidich, George Geann, McGuinness, Olli S Miettinen, Daniel M Libby, Mark W Pasmantier, June Kozami, Nasser K Altorki, James P Smith  
*Lancet* 1999; **354**: 99-105

2009

**ORIGINAL ARTICLE**  
**Management of Lung Nodules Detected by Volume CT Scanning**  
Rob J. van Klaveren, M.D., Ph.D., Matthijs Oudkerk, M.D., Ph.D.,  
Matthias Prokop, M.D., Ph.D., Ernst T. Scholten, M.D., Ph.D.,  
N Engl J Med 2009;361:2221-9.

2011

**The NEW ENGLAND JOURNAL of MEDICINE**  
ESTABLISHED 1812  
AUGUST 4, 2011  
vol. 365 no. 5

**Reduced Lung-Cancer Mortality with Low-Dose Computed Tomographic Screening**  
The National Lung Screening Trial Research Team\*  
N Engl J Med 2011;365:395-409.

2013

**Original Article**  
**The National Lung Screening Trial: Results Stratified by Demographics, Smoking History, and Lung Cancer Histology**  
Paul F. Pinsky, PhD<sup>1</sup>; Timothy R. Church, PhD<sup>2</sup>; Grant Izmirlian, PhD<sup>3</sup>; and Barnett S. Kramer, MD, MPH<sup>1</sup>  
*Cancer* 2013;119:3976-83

**European position statement on lung cancer screening**  
Matthijs Oudkerk, Anand Devaraj, Rozemarijn Vliegenhart, Thomas Henzler, Helmut Prosch, Claus P Heussel, Gorka Bastarika, Nicola Sverzellati, Mario Mascialchi, Stefan Debarne, David R Baldwin, Matthew E Callister, Nikolaus Becker, Marjolain A Heuvelmans, Witold Petyman, Maurizio V Infante, Ugo Pastorino, Jesper H Pedersen, Eugenio Paci, Stephen W Duffy, Harry de Koning, John K Field  
*Lancet Oncol* 2017;18:e754-66

2017

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

H.J. de Koning, C.M. van der Aalst, P.A. de Jong, E.T. Scholten, K. Nackaerts, M.A. Heuvelmans, J.-W.J. Lammers, C. Weenink, U. Yousof, Khan, N. Horeweg, P.M.A. van Ooijen, M. Prokop, W.P. Mali, F.A.A. Mohamed Hoesein, J. Verschakelen, R. Vliegenhart, J.-E. Aerts, M.A. den Bakker, E. Thunnissen, and M. Oudkerk  
**JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT**  
**Screening for Lung Cancer**  
**US Preventive Services Task Force Recommendation Statement**

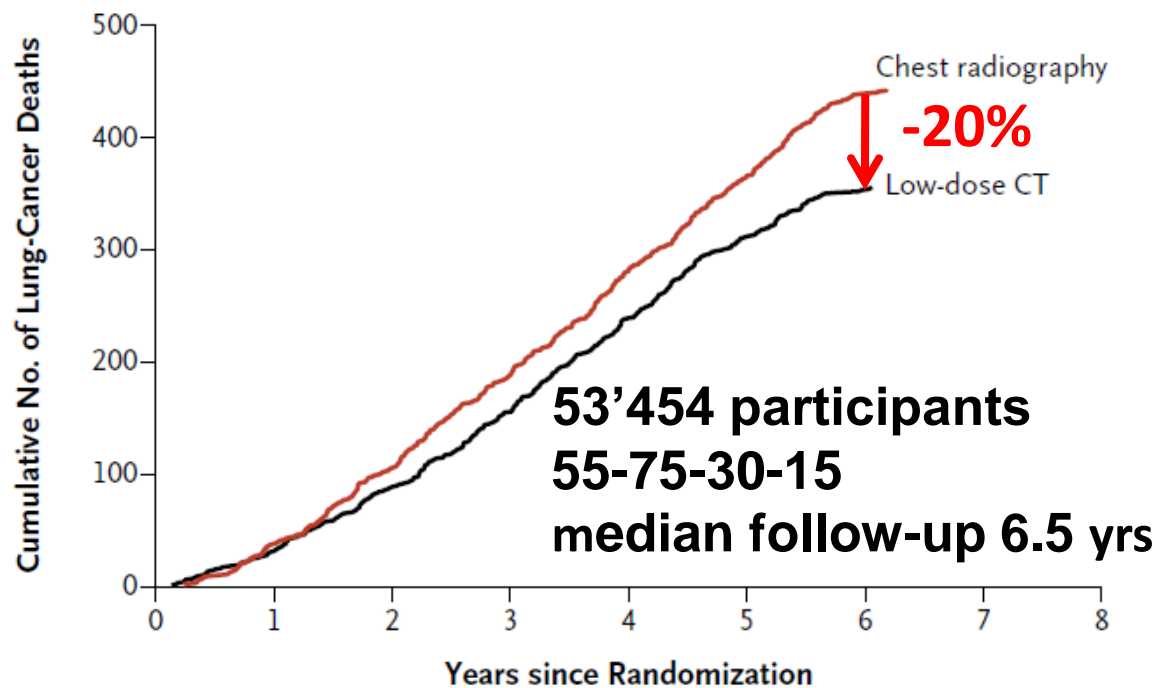
2020

**JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT**  
**Screening for Lung Cancer**  
**US Preventive Services Task Force Recommendation Statement**

2021

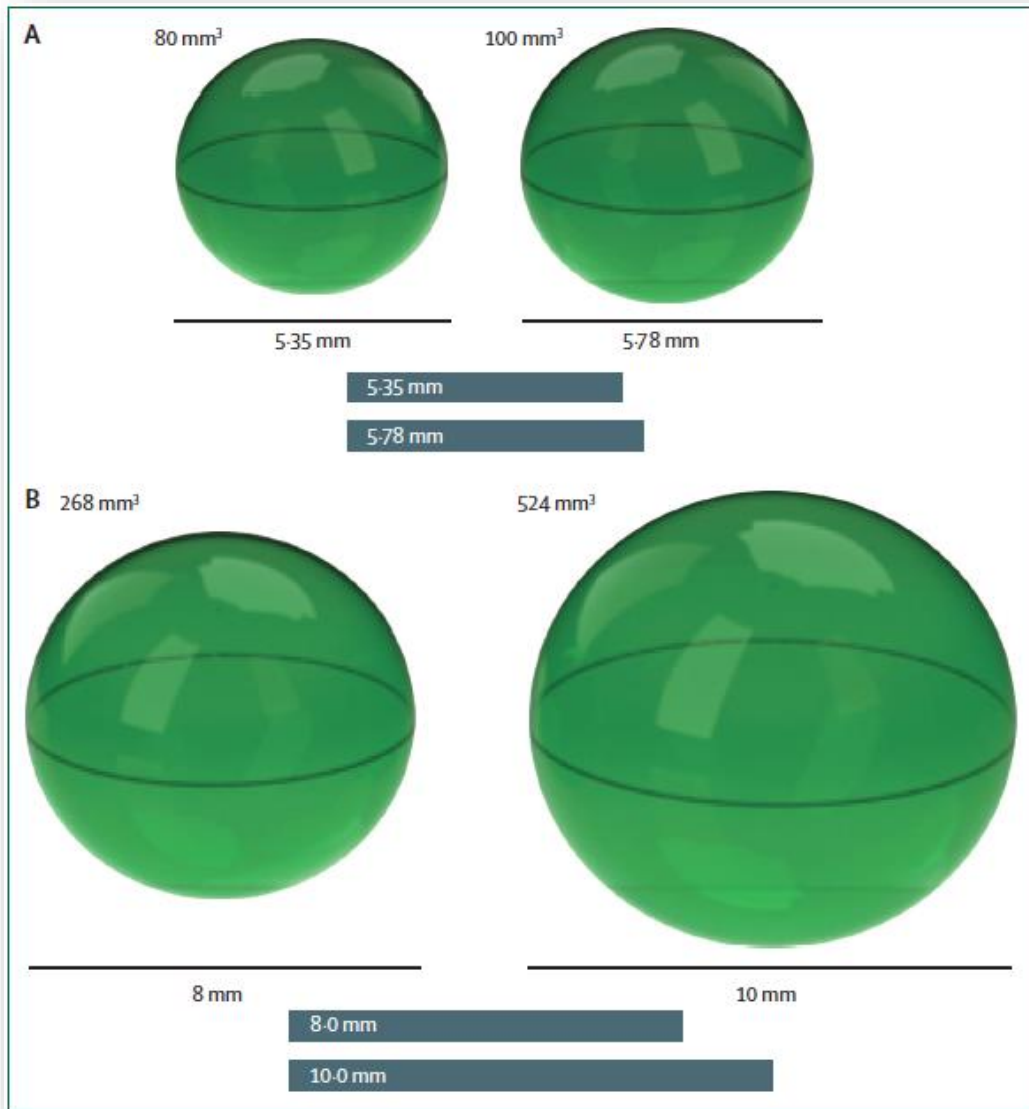


# NSLT Mortality Lung Cancer



Positive Tests (%)	24.2%*
False Positives (%)	23.3%*
True Positives	1.1%*
Stage I (%)	63%
NNS	320

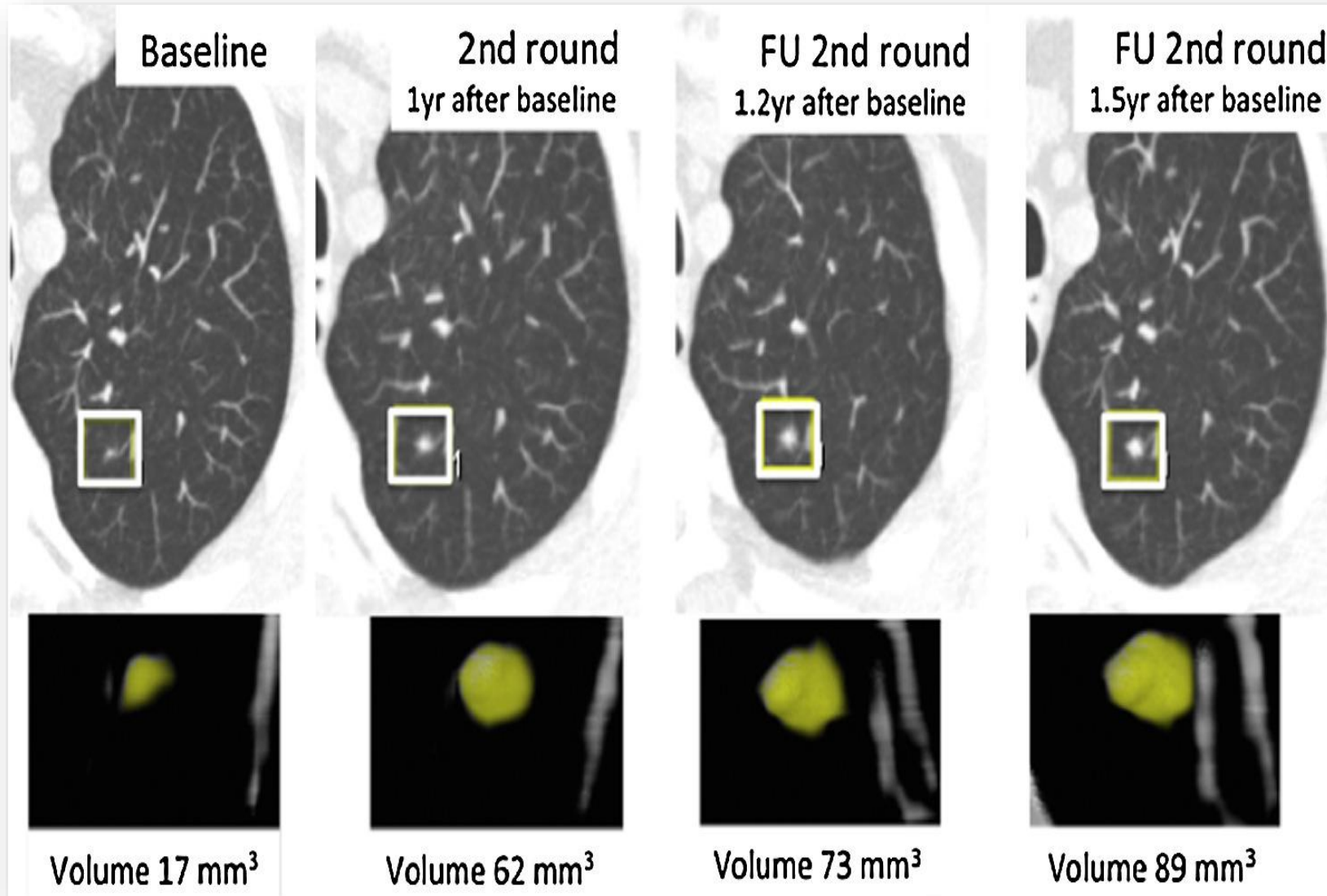
# Volume versus Diameter



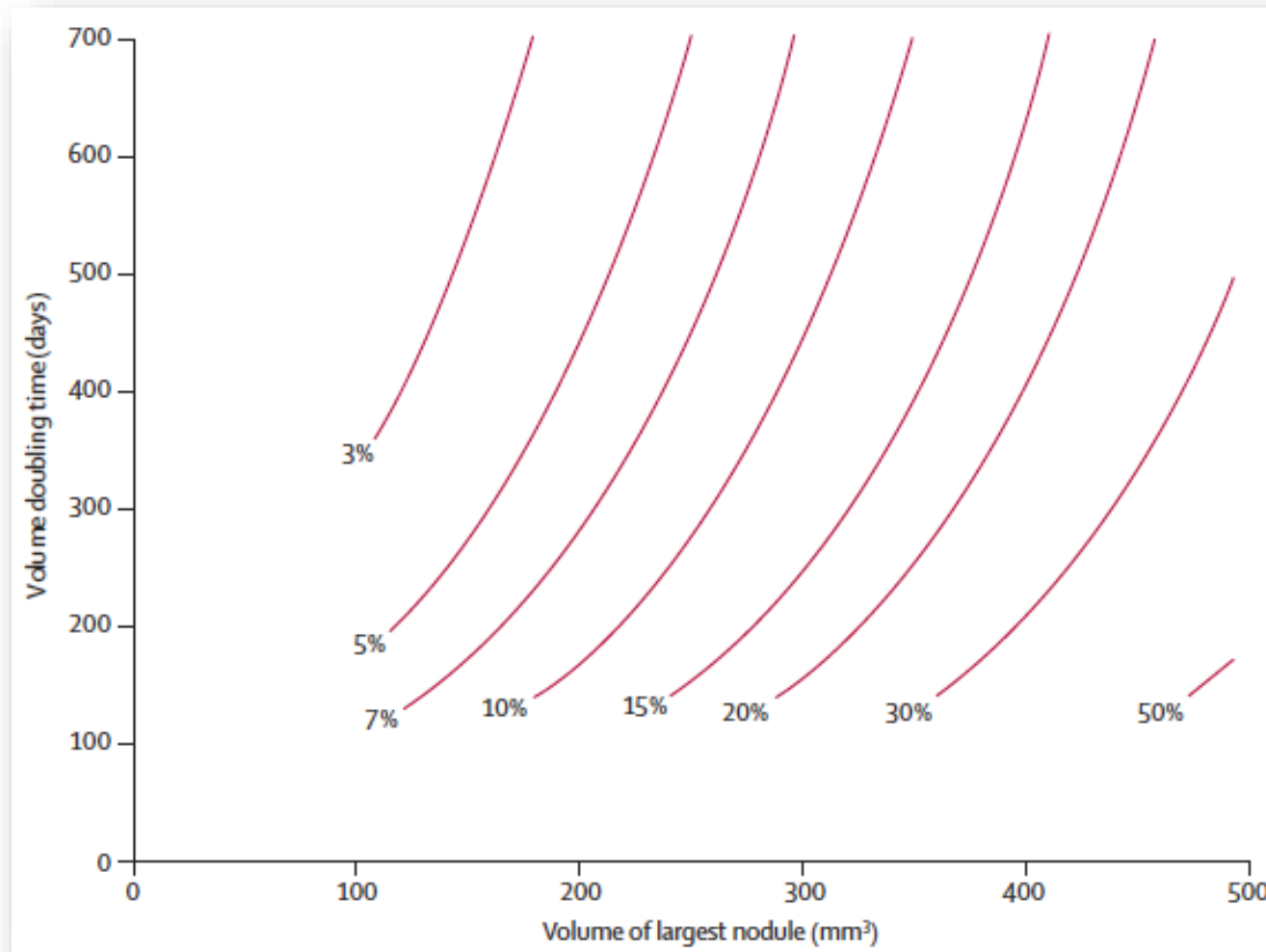
**+ 25% Volume → + 7% Diameter**

**+ 25% Diameter → + 95% Volume**

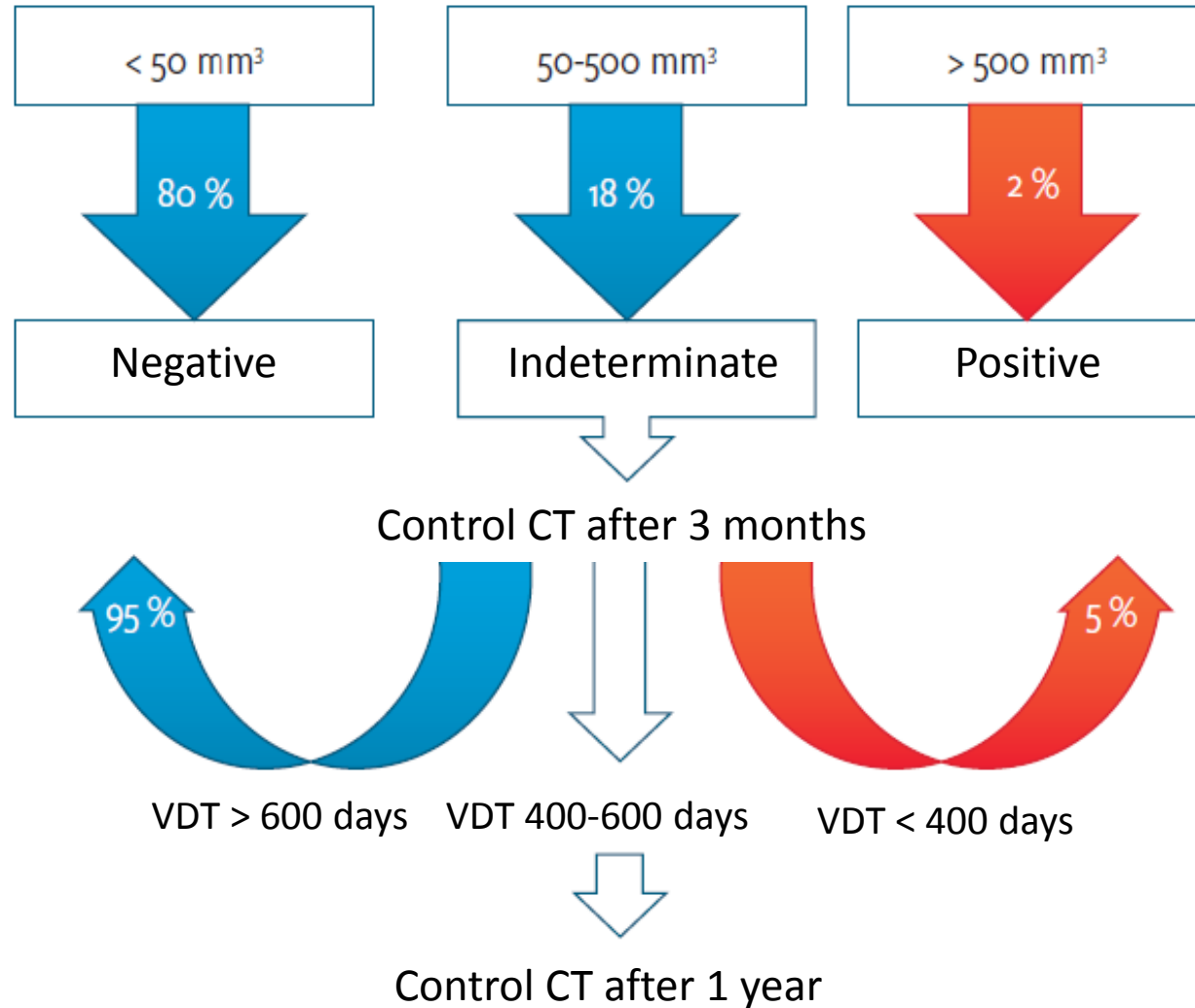
# Volume versus Diameter



# Effects Nodal Volume and Doubling Times on 2-Year Probability of Lung Cancer



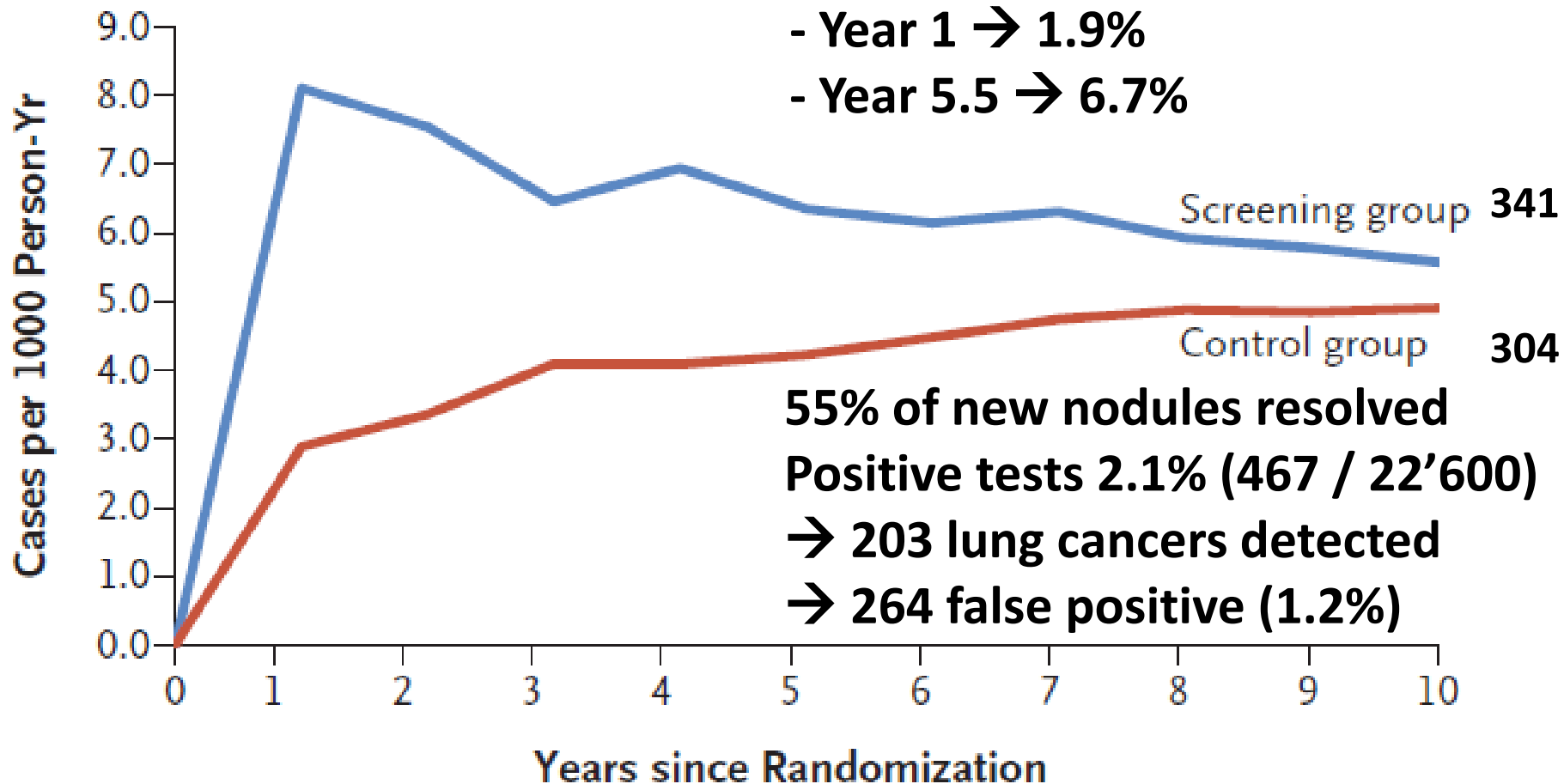
# NELSON Trial Design



# NELSON Trial: Lung Cancer Incidence

**MEN ONLY**

Lung-Cancer Incidence



Uptake 90%

Indeterminate 9.2% (2069 / 22'600)

- Baseline → 19.7%

- Year 1 → 1.9%

- Year 5.5 → 6.7%

55% of new nodules resolved

Positive tests 2.1% (467 / 22'600)

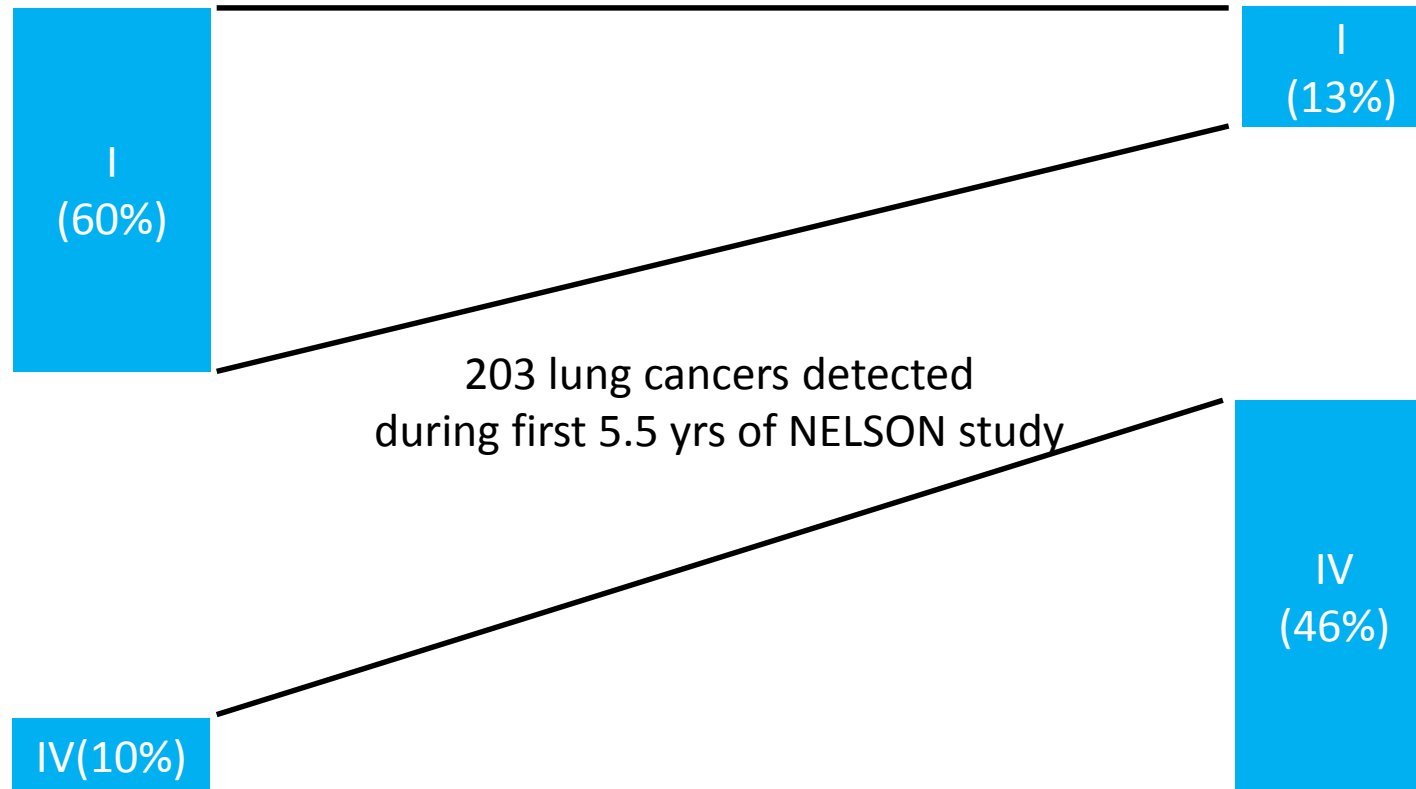
→ 203 lung cancers detected

→ 264 false positive (1.2%)

# NELSON Trial: Lung Cancer Stage Shift

**Screening group**  
341 lung cancers diagnosed

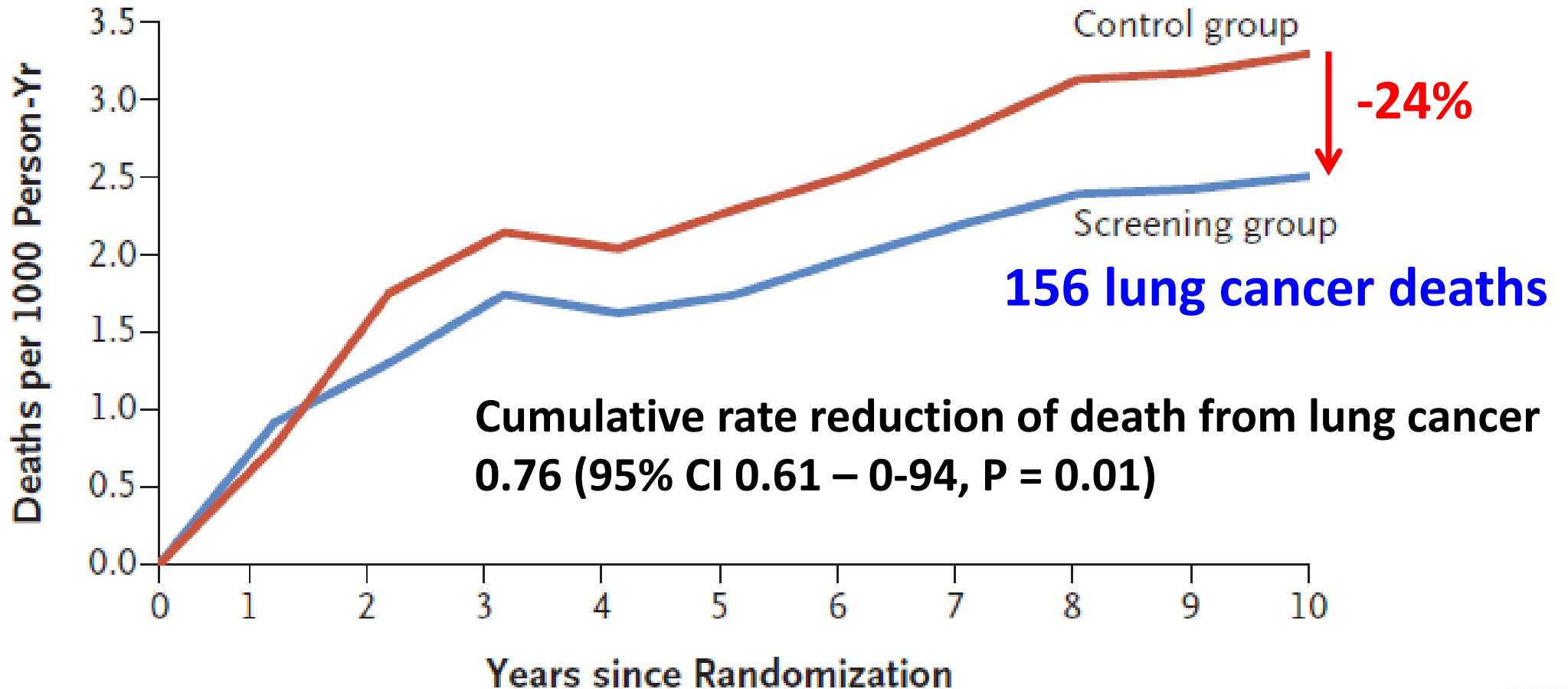
**Control group**  
304 lung cancers diagnosed



# NELSON Trial: Lung Cancer Mortality

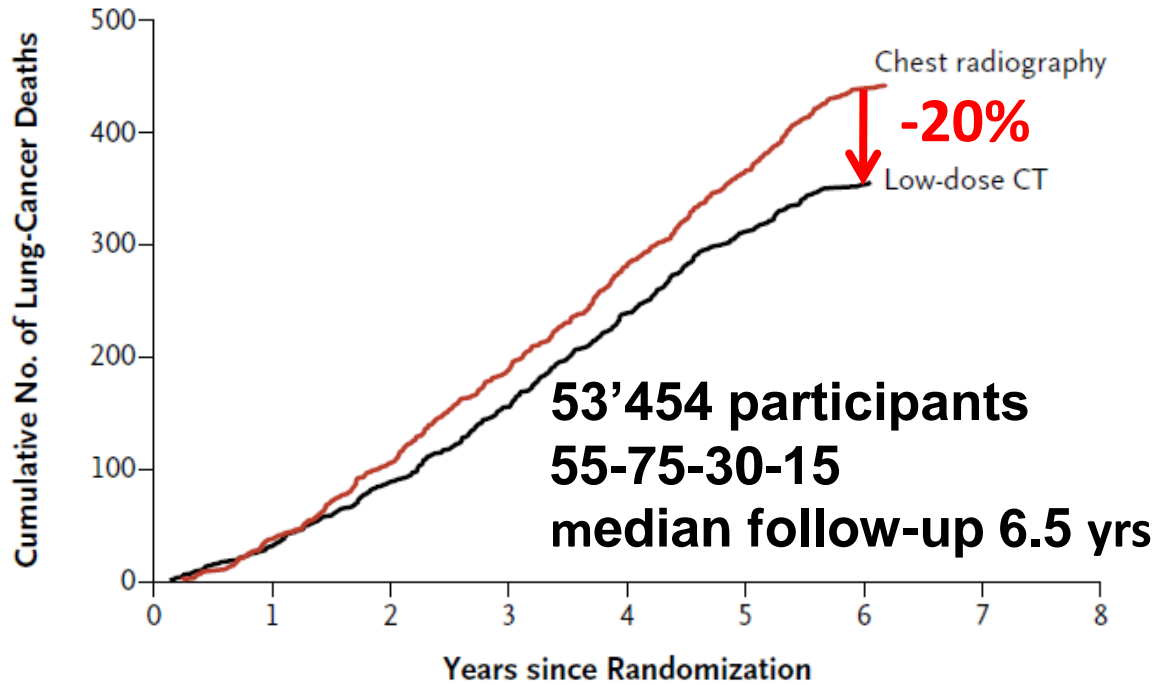
## MEN ONLY

### Lung-Cancer Mortality

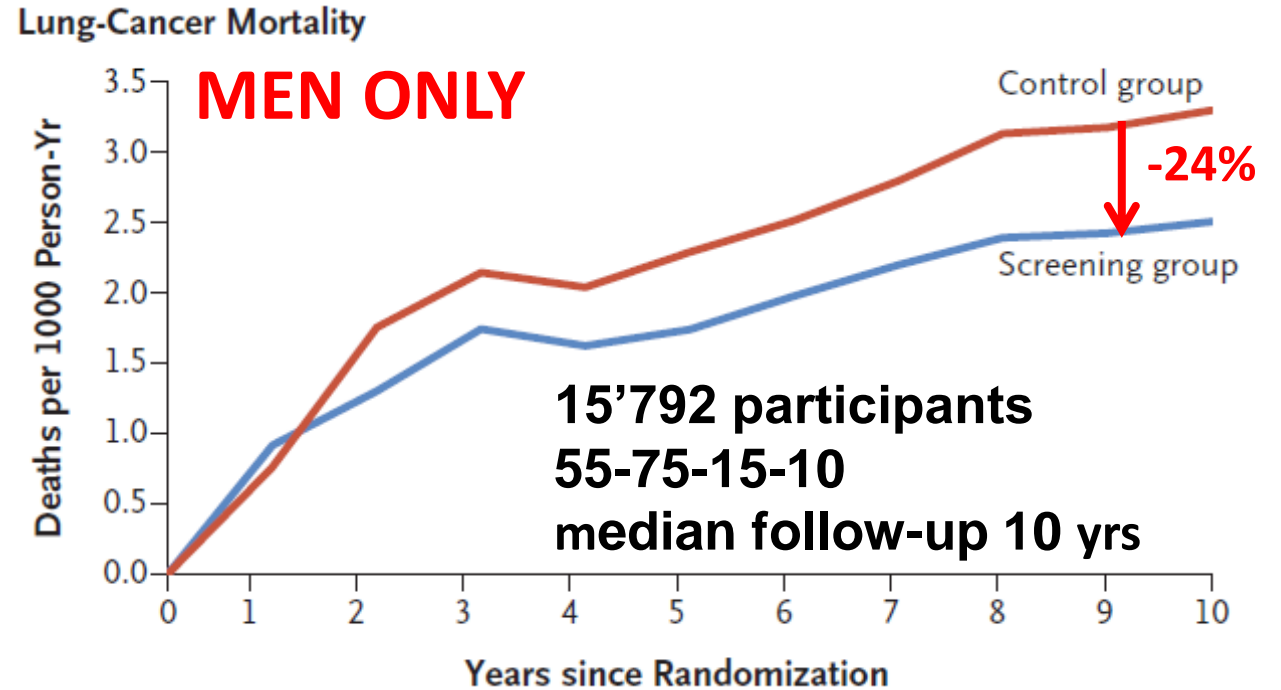




# NSLT / NELSON Mortalité Cancer Pulmonaire



Positive Tests (%)	24.2%*
False Positives (%)	23.3%*
True Positives	1.1%*
Stage I (%)	63%
NNS	320



Positive Tests (%)	2.1%*
False Positives (%)	1.2%*
True Positives	0.9%*
Stage I (%)	59%
NNS	130

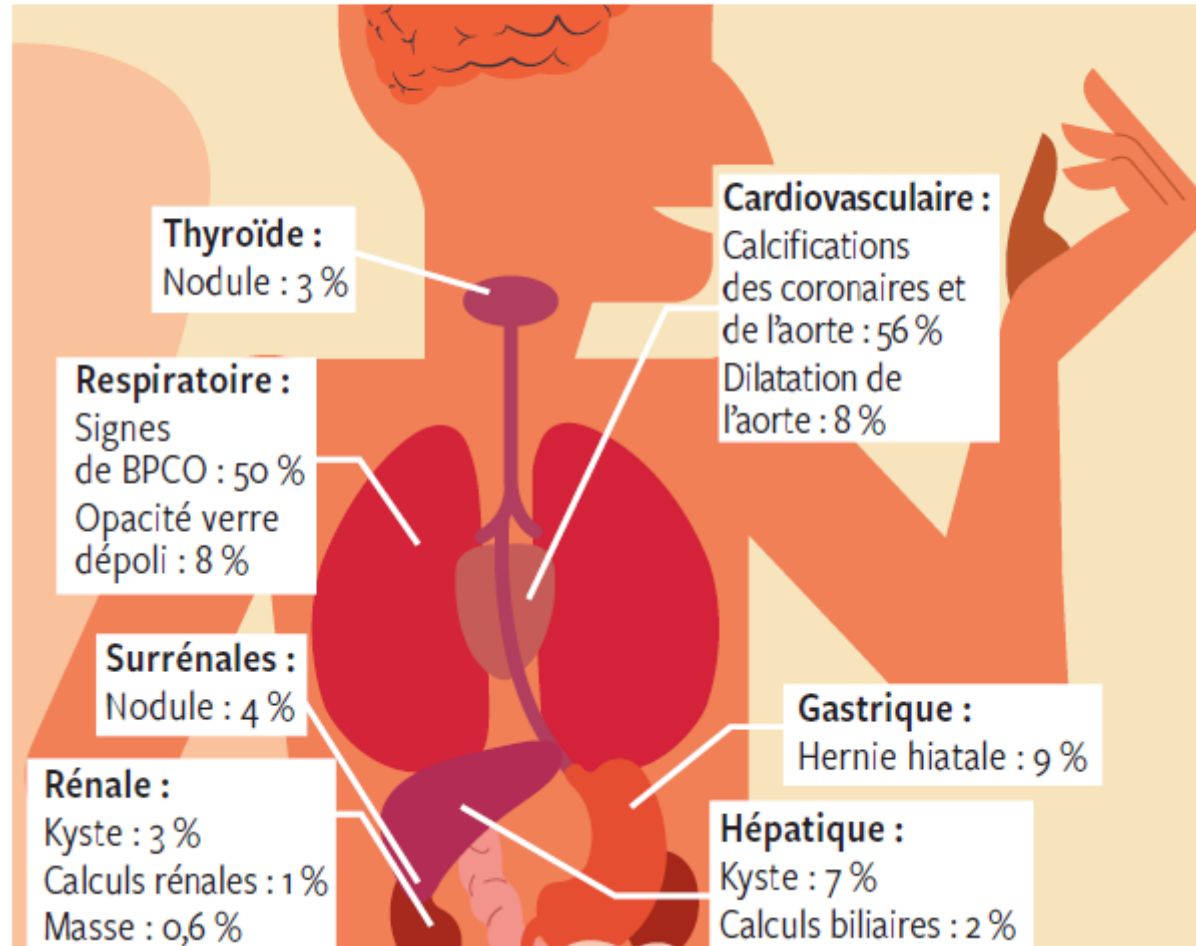
\* % screening population

# NELSON Trial: Overall Lung Cancer Mortality

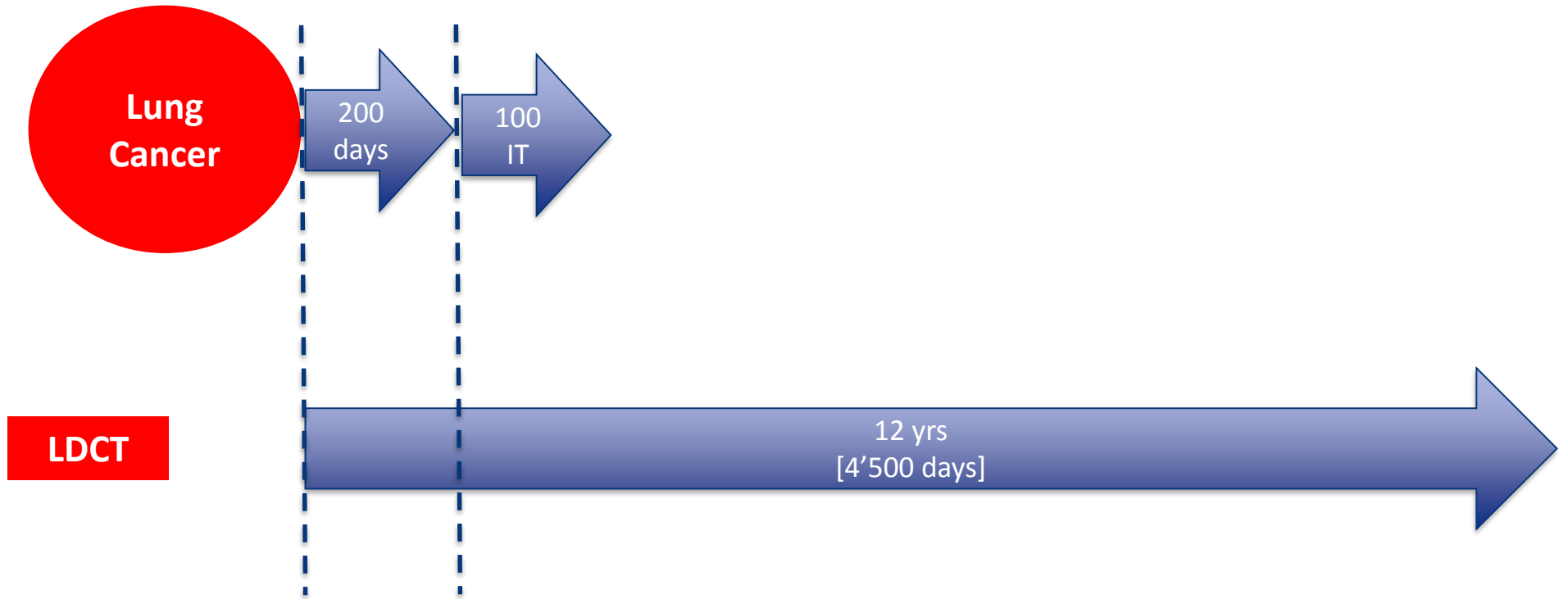
Lung cancer mortality rate ratio (95% CI)	Year 8	Year 9	Year 10	Year 11
Males	<b>0.76</b> (0.67 – 0.95)	<b>0.76</b> (0.61 – 0.96)	<b>0.76</b> (0.61 – 0.94)	<b>0.78</b> (0.63 – 0.95)
Females	<b>0.41</b> (0.19 – 0.84)	<b>0.52</b> (0.29 – 0.84)	<b>0.67</b> (0.38 – 1.14)	<b>0.78</b> (0.47 – 1.29)

# NELSON Trial: Incident Co-Morbidities











Dans les suites de la prise en charge, 15% des patients ont eu des consultations supplémentaires, 9% des imageries, 3% une procédure médicale et 1% une chirurgie.



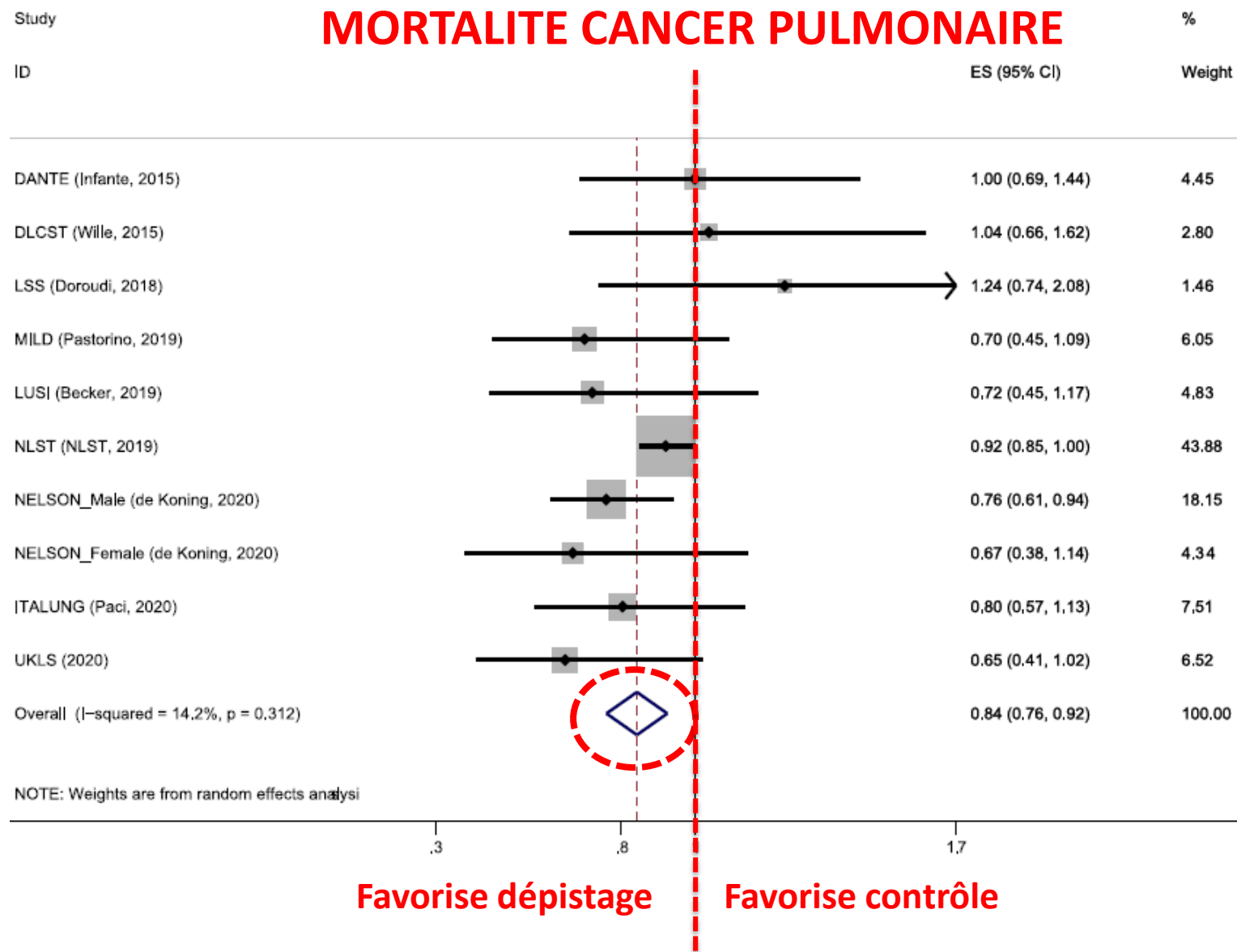
# LDCT survival benefit



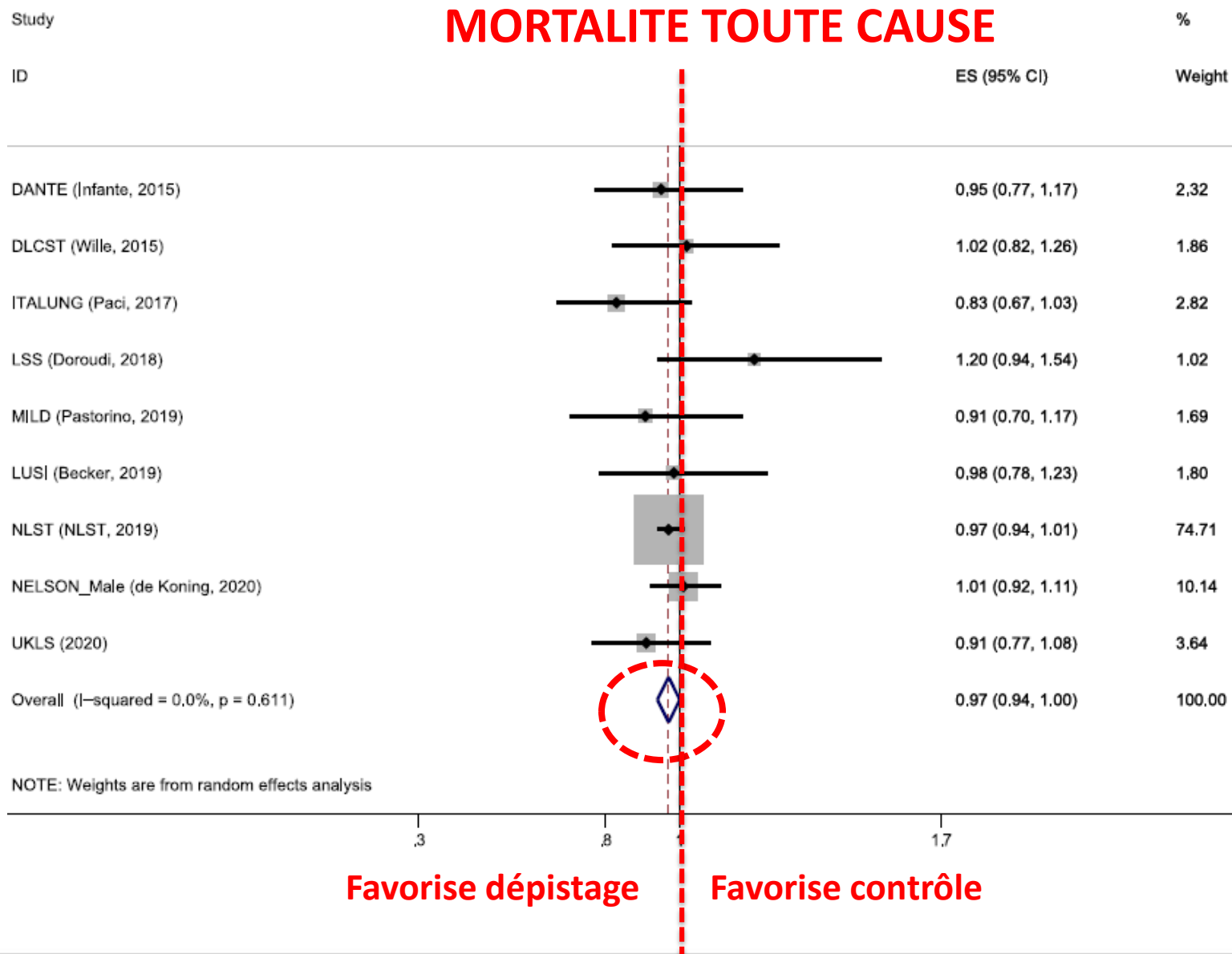
# Dépistage Cancer Pulmonaire: Evidence

Trial (country)	Control arm	CT schedule (years)								N exp. N cont.	Age		Tobacco	Other	Nodule interpretation model	Follow-up	Result Lung cancer mortality (Overall mortality)	Ref.
		0	1	2	3	4	5	6	7		8	On.						
DEPISCAN 	CXR									385 380	50	75	>15cig/d > 20y Form. <15y		NELSON like	<2y	<i>Not reported</i>	Blanchon T et al. Lung Cancer. 2007;58(1):50-8.
LSS 	CXR									1660 1658	55	74	>30 PY Form. <10y		NLST	5.2y	1.24 [0.74-2.08] (1.20 [0.94-1.54])	Doroudi M et al. JNCI Cancer Spectr. 2018; 2(3): pky042.
NLST 	CXR									26722 26732	55	74	>30 PY Form. <15y		NLST >4mm	6.5y	0.8 [0.73-0.93] (0.93 [0.86-0.99])	National Lung Screening Trial Research Team, N Engl J Med. 2011;365(5):395-409.
DANTE 	CXR baseline then observ.									1264 1186	60	75		Male only	NLST (≥10mm)	8y	<u>Pooled with MILD</u> 0.83 [0.61-1.12] (0.89 [0.74-1.06])	Infante M et al. Eur J Cancer Prev. 2017;26(4):324-329.
MILD 	Observ.									2376 1723	50	75	> 20PY Form. <10y			10y	0.61 [0.39-0.95] (0.8 [0.62-1.03])	Pastorino U et al. Ann Oncol. 2019;30(7):1162-1169
DLCST* 	Observ.									2052 2052	50	70		FEV1 > 30%		5y	1.03 [0.66-1.6] (1.02 [0.82-1.27])	Saghir Z et al. Thorax. 2012;67(4):296-301.
ITALUNG* 	Observ.									1613 1593	55	70			NELSON like	10y	0.70 [0.47-1.03] (0.83 [0.67-1.03])	Paci E et al. Thorax. 2017;72(9):825-831
LUSI* 	Observ.									2029 2023	50	70	>15cig/d > 25y OR >10cig/d > 30y Form. <10y			8.8y	M: 0.94 [0.54-1.61] F: 0.31 [0.10-0.96]	Becker N et al. Int J Cancer. 2020;146(6):1503-1513
NELSON* 	Observ.							OPTION		7907 7915	50	75				11y	M: 0.76 [0.61-0.94] F: 0.67 [0.38-1.14] (M: 1.01 [0.92-1.11])	De Koning HJ et al. N Engl J Med. 2020;382(6):503-513
UKLS 	Observ.									1987 1981	50	75	-	LLPv2 > 4.5%		7.3	0.65 [0.41-1.02]	Field JK et al. Lancet Reg Health Eur. 2021

# Dépistage Cancer Pulmonaire: Evidence



# Dépistage Cancer Pulmonaire: Evidence



# Screening for Lung Cancer

## US Preventive Services Task Force Recommendation Statement

### **Annual screening for lung cancer with LDCT for:**

- adults aged 50 - 80 years
- smokers  $\geq 20$  pack-years and currently smoke or quit  $\leq 15$  years

### **Discontinued screening if:**

- >15 years smoking cessation
- appearance of health problem that substantially limits life expectancy or the ability to undergo curative lung surgery



# Lung Cancer Screening: Switzerland?

## Swiss Lung Cancer Screening Implementation Group (CH-LSIG)

### Pulmonologists

D. Adler  
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C. Eich  
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P. Gasche-Soccal  
M. Kohler  
A. Lovis  
S. Stöhr  
A. Turk  
C. von Garnier

### Epidemiologists

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Y. Tomonaga

### Oncologists

O. Gautschi

### Radiologists

C. Beigelman-Aubry  
J. Bremerich  
U. Bürgi  
A. Christe  
L. Ebner  
T. Frauenfelder  
J. Heverhagen  
N. Horwarth  
R. Meuli  
X. Montet  
T. Niemann

### Steering Committee

P. Gasche-Soccal  
C. von Garnier  
C. Beigelman-Aubry  
T. Frauenfelder  
I. Schmitt-Opitz  
S. Neuner-Jehle  
M. Puhan  
O. Gautschi

### BAG/OFSP

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M. Menig  
Ph. Giroud

### Thoracic Surgeons

I. Schmitt-Opitz  
D. Schneiter  
W. Weder

### General Practitioners

O. Senn  
S. Neuner-Jehle  
K. Selby

### Leagues

Ph. Giroud  
A. Flatz

National  
Cancer  
Screening  
Committee



# Feasibility for Introducing LDCT Screening

- Assess the feasibility of introducing a national lung cancer screening program in Switzerland
- Describe the characteristics of such a LDCT lung cancer screening

Bottom-up approach:

- Literature review
- Interviews with international experts and site visit in Manchester
- 22 Interviews and workshops with national stakeholders

# Lung Cancer Screening: Conclusion

- ✓ **Nelson and NLST trials provide evidence that LDCT screening:**
  - ✓ **increases the probability to detect lung cancer**
  - ✓ **increases the likelihood to detect lung cancer stages I - II**
  - ✓ **is associated with a decrease in lung cancer mortality**
- ✓ **The cost per quality-adjusted life year (QALY) gained likely < 50'000Euro**
- ✓ **Several questions still open: interval, duration, costs**
- ✓ **CH-LSIG prepares implementation, need for pilot programs in CH**
- ✓ **Routine screening not admissible / recommended**