XXXIV DIADA PNEUMOLÒGICA.
REUS 15 – 16 D'ABRIL 2016

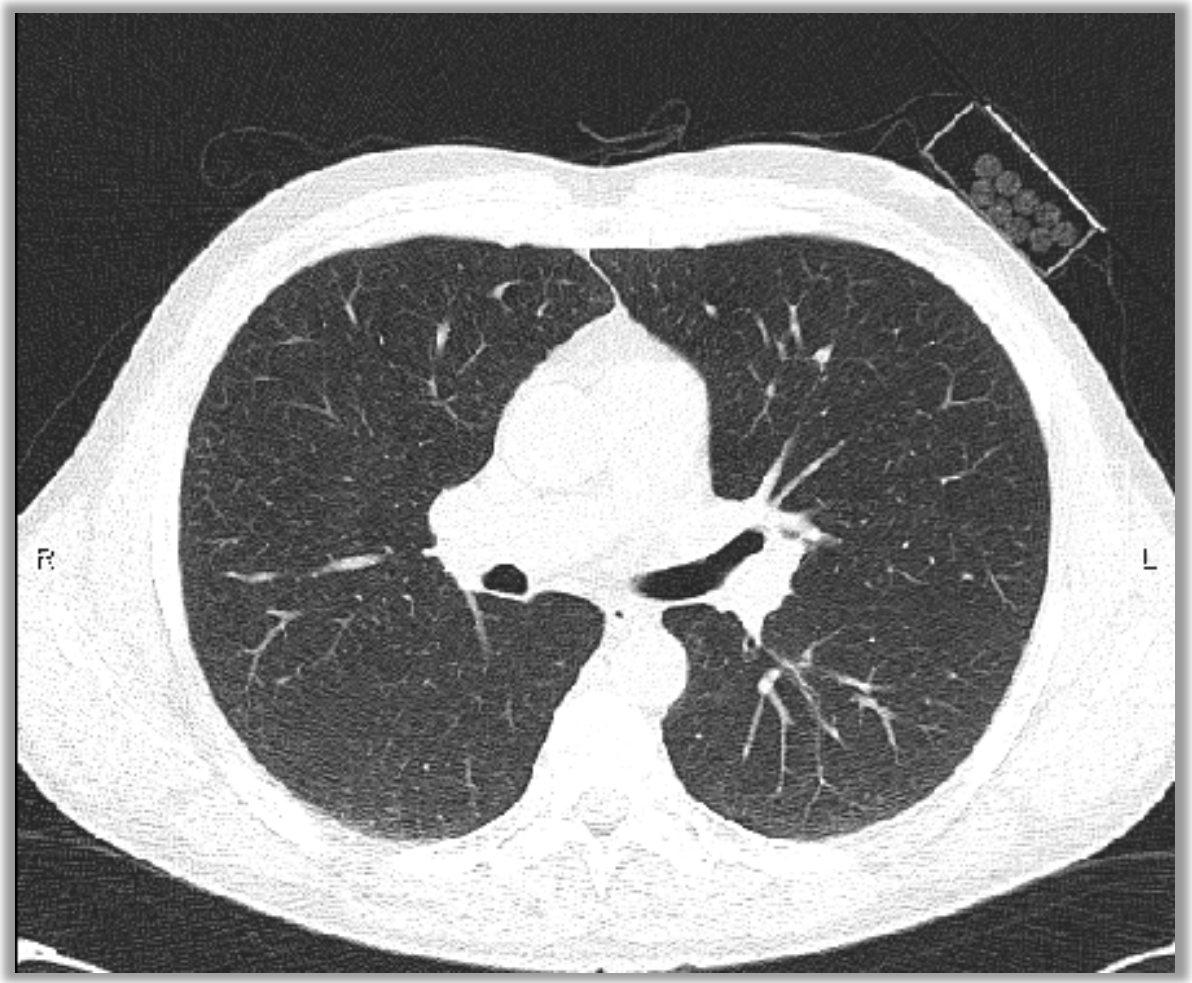
Diagnóstico de Cáncer de Pulmón
TAC de Baja Dosis

Dr. Javier J. Zulueta
Clinica Universidad de Navarra
Universidad de Navarra
Pamplona

Conflictos de interés

- Miembro del Medical Advisory Board y accionista de VisionGate, Inc. (EE.UU).

- Evidencia
- Controversia
- Enfisema y EPOC en el cribado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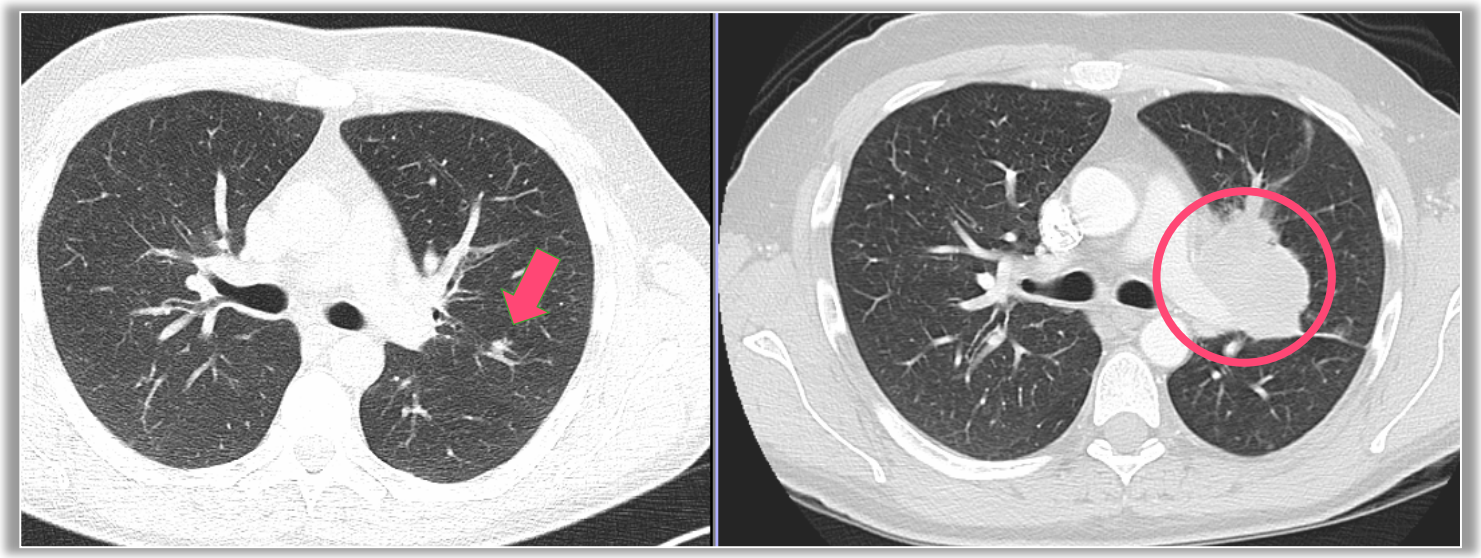
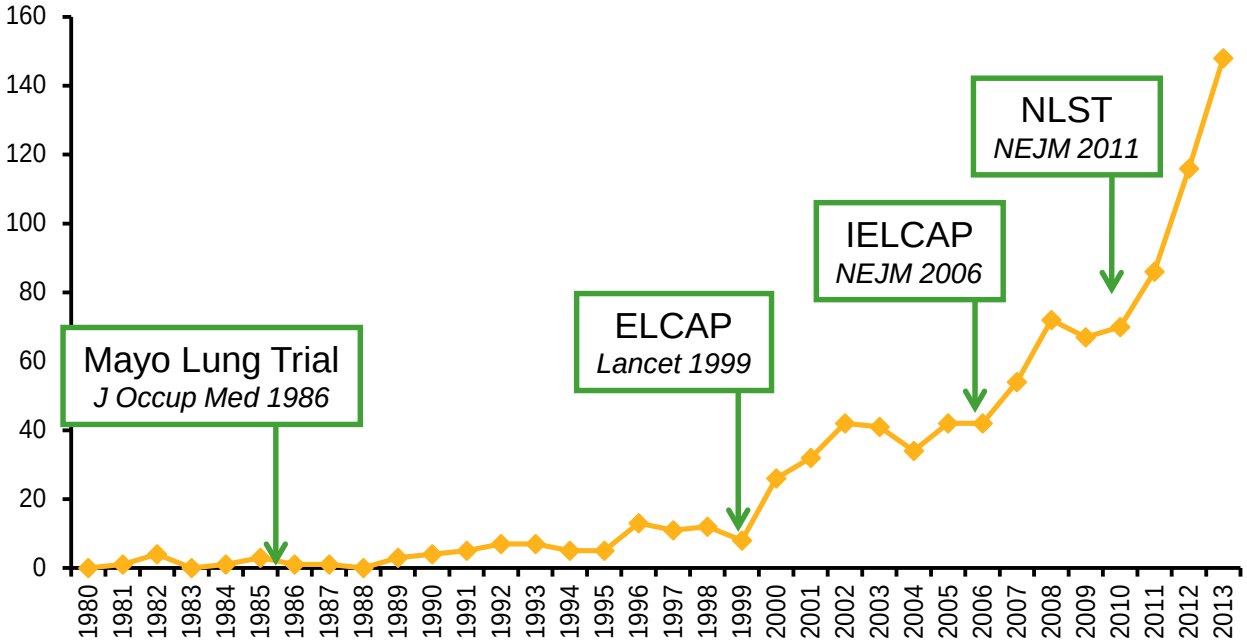


2010

2014

Número de publicaciones sobre cribado de cáncer de pulmón



Fontana et al. J Occup Med.1986;28(8):746-50; Henschke et al. Lancet. 1999;354(9173):99-105;
IELCAP Investigators. N Engl J Med 2006;355:1763-71; NLST Research Team. N Engl J Med 2011;365:395-409

Mayo Clinic Lung Project

	Cribado	Control
n	4618	4593
Incidencia	206 (4.5%)	160 (3.5%)*
Resecabilidad	46%	32%
Supervivencia a 5-y	33%	15%
Tasa de fatalidad	59%	72%*
Mortalidad	122	115

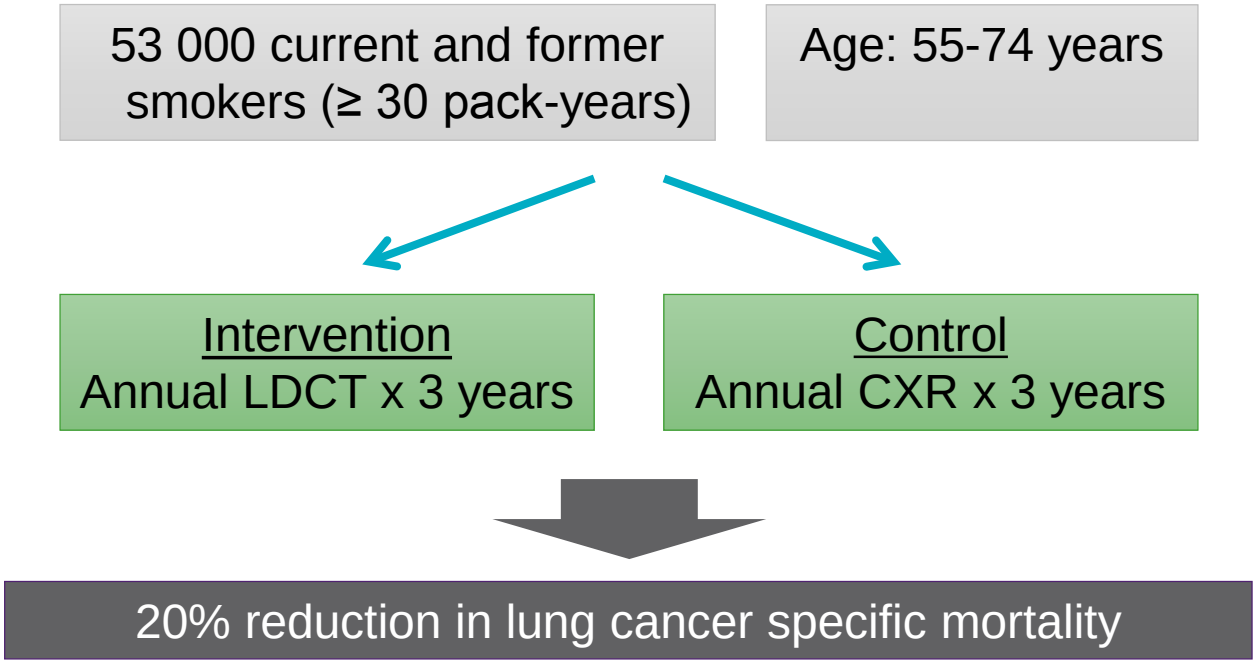
Fontana et al. J Occup Med.1986;28(8):746-50

Sobrediagnóstico

El cribado detecta tumores ‘indolentes’ de crecimiento lento que no causan la muerte del individuo

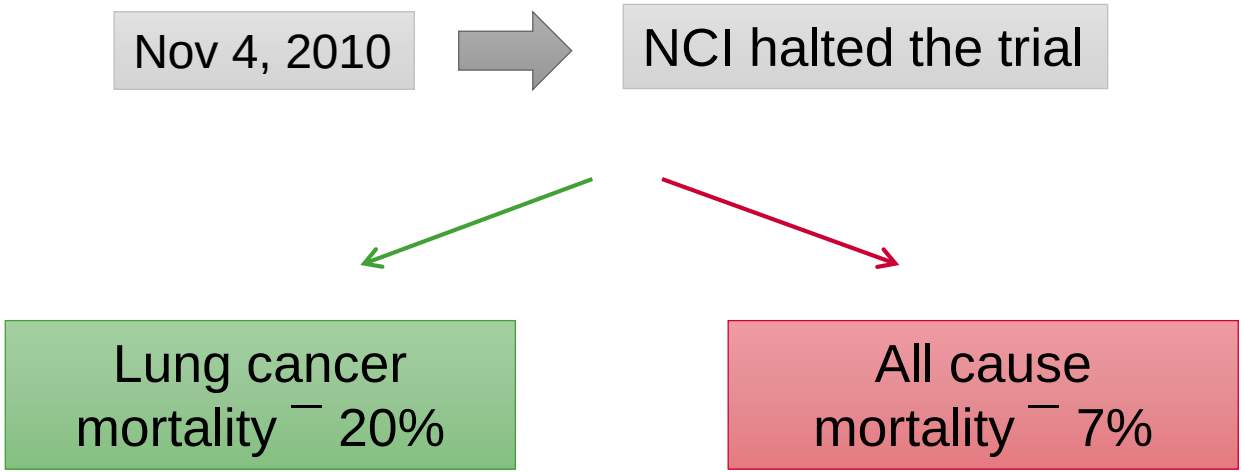
Eddy. Ann Intern Med. 1989;111:232-7

NLST – National Lung Cancer Screening Trial (2002-2010)



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

NLST – National Lung Cancer Screening Trial (2002-2010)

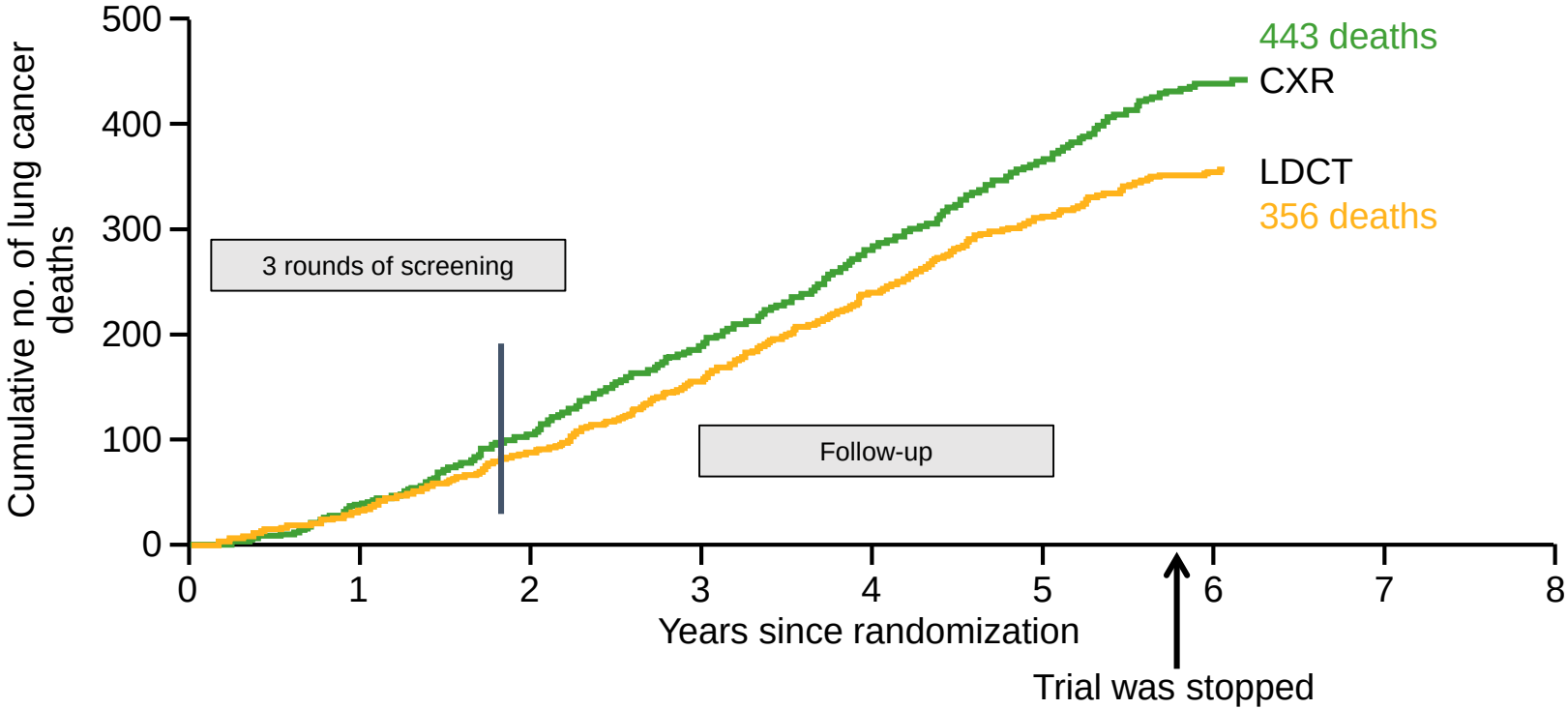


NCI, National Cancer Institute; NLST, National Lung Cancer Screening Trial

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

NLST showed a 20% reduction in the 6-year cumulative mortality rates for CT vs CXR

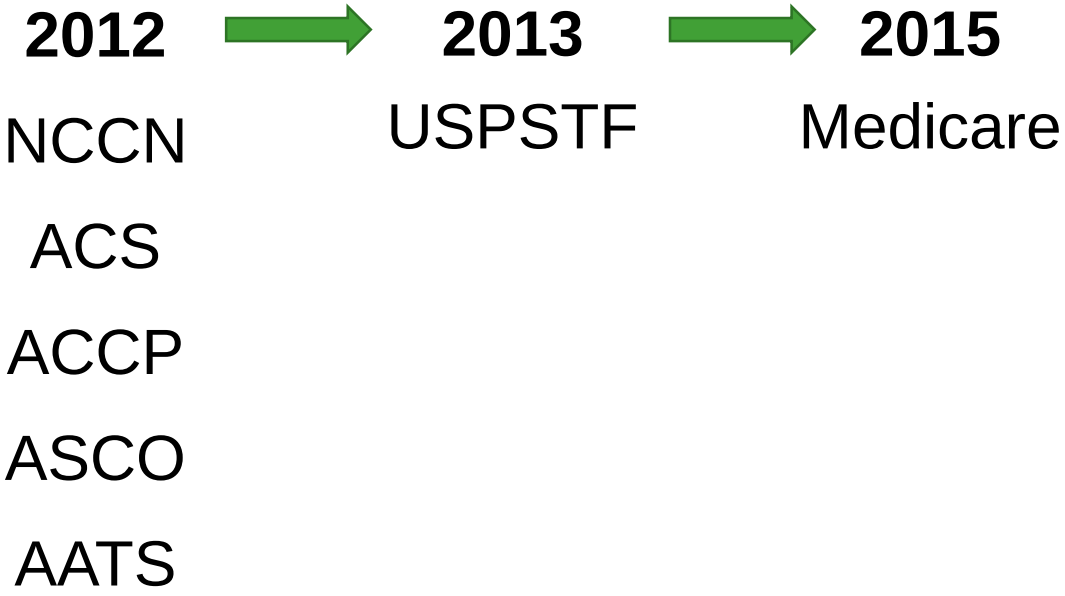
(356 vs 443 deaths)



CT, computed tomography; CXR, chest radiography

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

Recomendaciones de cribado (EEUU)



AATS, American Association for Thoracic Surgery; ACCP, American College of Clinical Pharmacology; ACS, American Cancer Society; ASCO, American Society of Clinical Oncology; NCCN, National Comprehensive Cancer Network; USPSTF, United States Preventative Services Task Force

Recomendaciones del cribado en Europa

Eur Radiol (2015) 25:2519–2531
DOI 10.1007/s00330-015-3697-0

SPECIAL REPORT

ESR/ERS white paper on lung cancer screening

Hans-Ulrich Kauczor[1,9] · Lorenzo Bonomo[2] · Mina Gaga[3] · Kristiaan Nackaerts[4] · Nir Peled[5] · Mathias Prokop[6] · Martine Remy-Jardin[7] · Oyunbileg von Stackelberg[1,9] · Jean-Paul Sculier[8] · on behalf of the European Society of Radiology (ESR) and the European Respiratory Society (ERS)

Journal of Surgical Oncology 2013;108:280–286

European Randomized Lung Cancer Screening Trials: Post NLST

JOHN K. FIELD, PhD, FRCPath,[1]* ROB VAN KLAVEREN, MD, PhD,[2] JESPER H. PEDERSEN, MD, DrSci,[3]
UGO PASTORINO, MD, PhD,[4] EUGINO PACI, MD, PhD,[5] NIKOLAUSS BECKER, MD,[6]
MAURIZO INFANTE, MD, PhD,[7] MATTHIJS OUDKERK, MD, PhD, FACA,[8] HARRY J. DE KONING, MD, PhD,[9]
AND ON BEHALF OF THE EUROPEAN RANDOMIZED SCREENING TRIAL GROUP

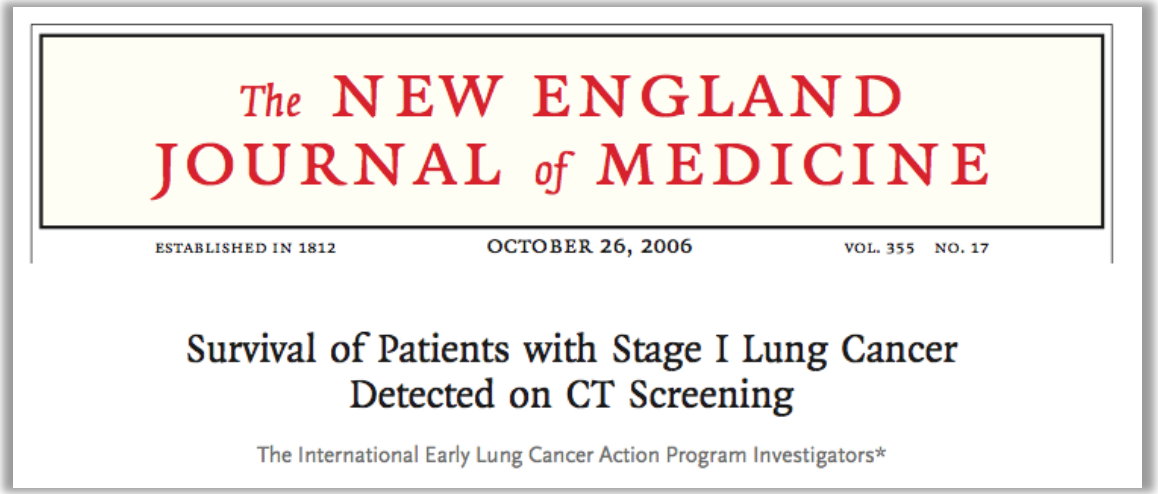
[1]*The University of Liverpool Cancer Research Centre, Liverpool, UK*
[2]*Department of Pulmonary Medicine Lievensberg Hospital, Belgium*
[3]*Department of Thoracic Surgery, University of Copenhagen, Copenhagen, Denmark*
[4]*Department of Thoracic Surgery, European Institute of Oncology, Milan, Italy*
[5]*Unit of Clinical and Descriptive Epidemiology, ISPO, Florence, Italy*
[6]*Division of Cancer Epidemiology, German Cancer Research Center, Heidelberg, Germany*
[7]*Department of Thoracic Surgery, Instituto Clinico Humanitas, Milan, Italy*
[8]*Center for Medical Imaging, University Medical Center Groningen, Netherlands*
[9]*Department of Public Health, Erasmus MC, Rotterdam, The Netherlands*

Antes de que la implementación del cribado de cáncer de pulmón pueda ser considerado, en los próximos 5 años es preciso contestar importantes preguntas de investigación.

Field et al. J Surg Oncology 2013;108:280-6

- Verdadero efecto del cribado
- Sobrediagnóstico
- Falsos positivos
- Radiación
- Coste – perfiles de riesgo

Verdadero efecto del cribado



The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 26, 2006 VOL. 355 NO. 17

Survival of Patients with Stage I Lung Cancer Detected on CT Screening

The International Early Lung Cancer Action Program Investigators*

> 59 000 cribados → 484 cánceres → 85% Estadio I

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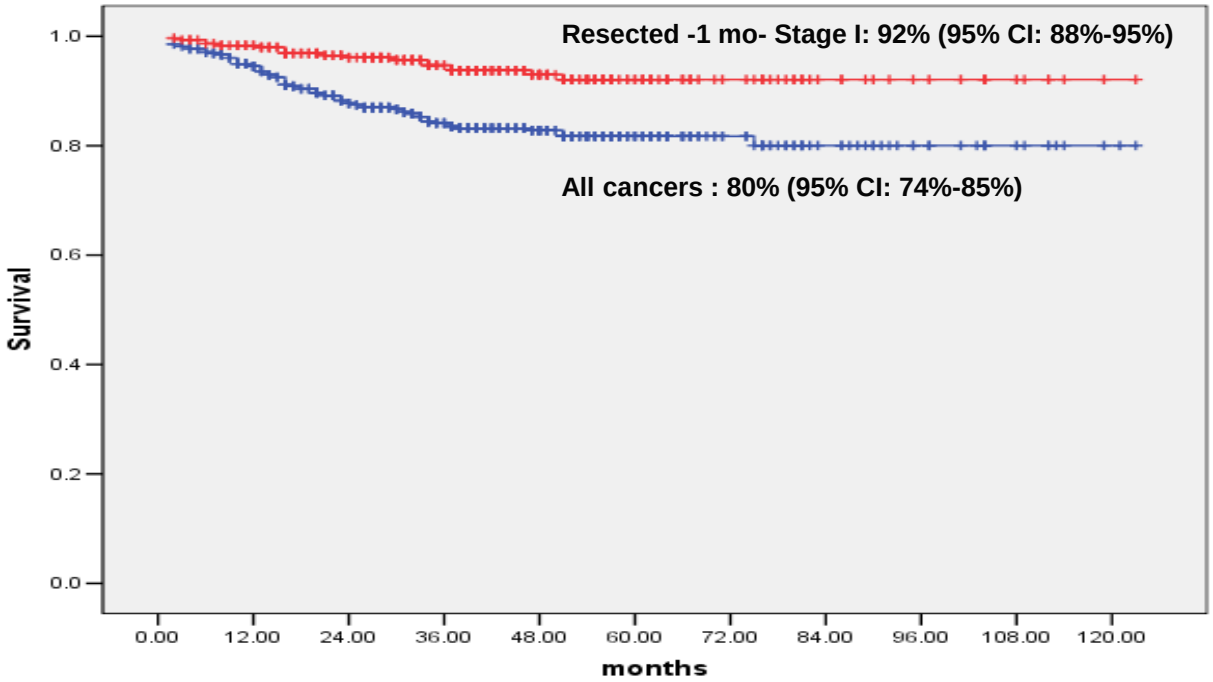
10-year survival



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International Early Lung Cancer Action Program Investigators. N Engl J Med 2006;355:1763-71

Sobrediagnóstico

Sobrediagnóstico

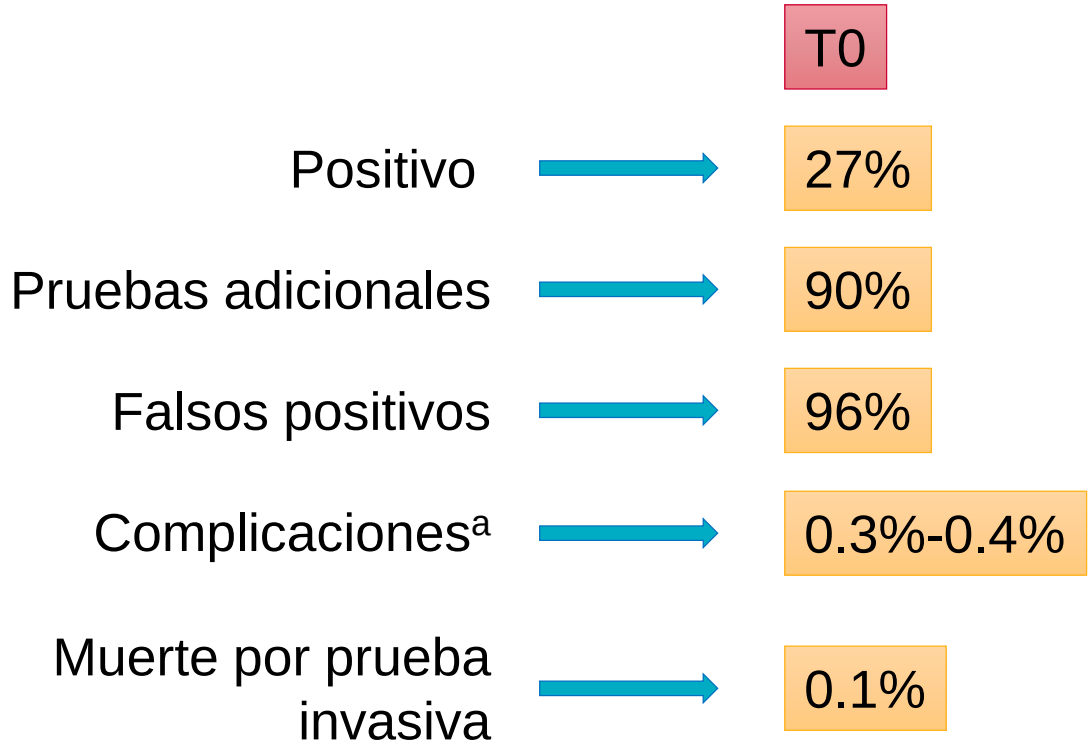
- I-ELCAP: Panel de patólogos (revisión de 375 tumores)
  - 356 (95%) tenían signos de invasión
    - Pleural
    - Membrana basal
    - Vascular
    - Bronquial

I-ELCAP, International Early Lung and Cardiac Action Program

International Early Lung Cancer Action Program Investigators.
N Engl J Med 2006;355:1763-71

Falsos positivos
Biopsias/cirugías innecesarias

NLST – Resultados del TCBD



[a]Individuals without cancer

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

TCBD +	Definición de un positivo	% de cribados basales
NLST	Nódulo sólido ≥ 4 mm	27%
I-ELCAP	Nódulo sólido ≥ 5 mm	13%
NELSON	Nódulo sólido > 9.8 mm o 4.6-9.8 mm con TD (3 m) < 400 d	2.6%

International Early Lung Cancer Action Program Investigators. N Engl J Med 2006;355:1763-71;
National Lung Screening Trial Research Team. N Engl J Med 2011;365:395-409;
Xu et al. Lung Cancer. 2006;54(2):177-84

Nódulos indeterminados – Falsos positivos

I-ELCAP
535 biopsies

→

92% malignant disease

International Early Lung Cancer Action Program Investigators. N Engl J Med 2006;355:1763-71

Radiación

CHEST

Special Features

Scan for podcast

Radiation Risks in Lung Cancer Screening Programs

A Comparison With Nuclear Industry Workers and Atomic Bomb Survivors

Robert J. McCunney, MD, MPH; and Jessica Li, BS

McCunney & Li. Chest 2014;145(3):618-24

Estimaciones según datos del NLST y la Fleischner Society

- ≅20% de participantes en cribado tienen un TCBD positivo en cribado basal
- TCBD + resulta en 3 controles con LDCT durante 2 años

Dosis de radiación por CT:
TCBD: < 1 mSv
mSv
CT convencional: 8 mSv

Dosis total acumulada:
20 años de cribado: < 20 mSv
30 años de cribado: < 30 mSv

McCunney & Li. Chest 2014;145(3):618-24

Coste:efectividad

Coste-efectividad

	Cost of QALY
Screening LDCT (NLST entry criteria)	$81 000 $52 000-$186 000

(20% mortality reduction)

QALY, quality-adjusted life year

Black et al. N Engl J Med 2014;371:1793-1802

Cost-effectiveness

	Cost of QALY
I-ELCAP	$28 000
NLST	$47 000

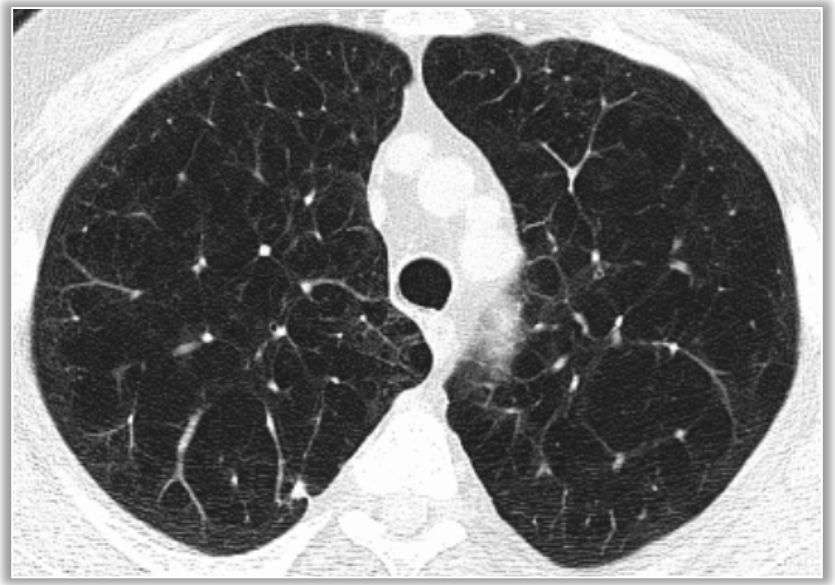
Pyenson. PLoS One. 2013 Aug 7;8(8):e71379

	Cost QALY
UKLS RCT Pilot study	£8 466*

Field JK, et al. Thorax 2015;0:1–10. doi:10.1136/thoraxjnl-2015-207140

* Coste incremental de un TCBD con respecto a presentación sintomática.

Perfiles de riesgo



Assessing the Relationship Between Lung Cancer Risk and Emphysema Detected on Low-Dose CT of the Chest*

Juan P. de Torres, MD; Gorka Bastarrika, MD; Juan P. Wisnivesky, MD, MPH; Ana B. Alcaide, MD; Arantza Campo, MD; Luis M. Seijo, MD; Jesús C. Pueyo, MD; Alberto Villanueva, MD; María D. Lozano, MD; Usua Montes, RN; Luis Montuenga, PhD; and Javier J. Zulueta, MD, FCCP

Chest 2007;132:1932-8

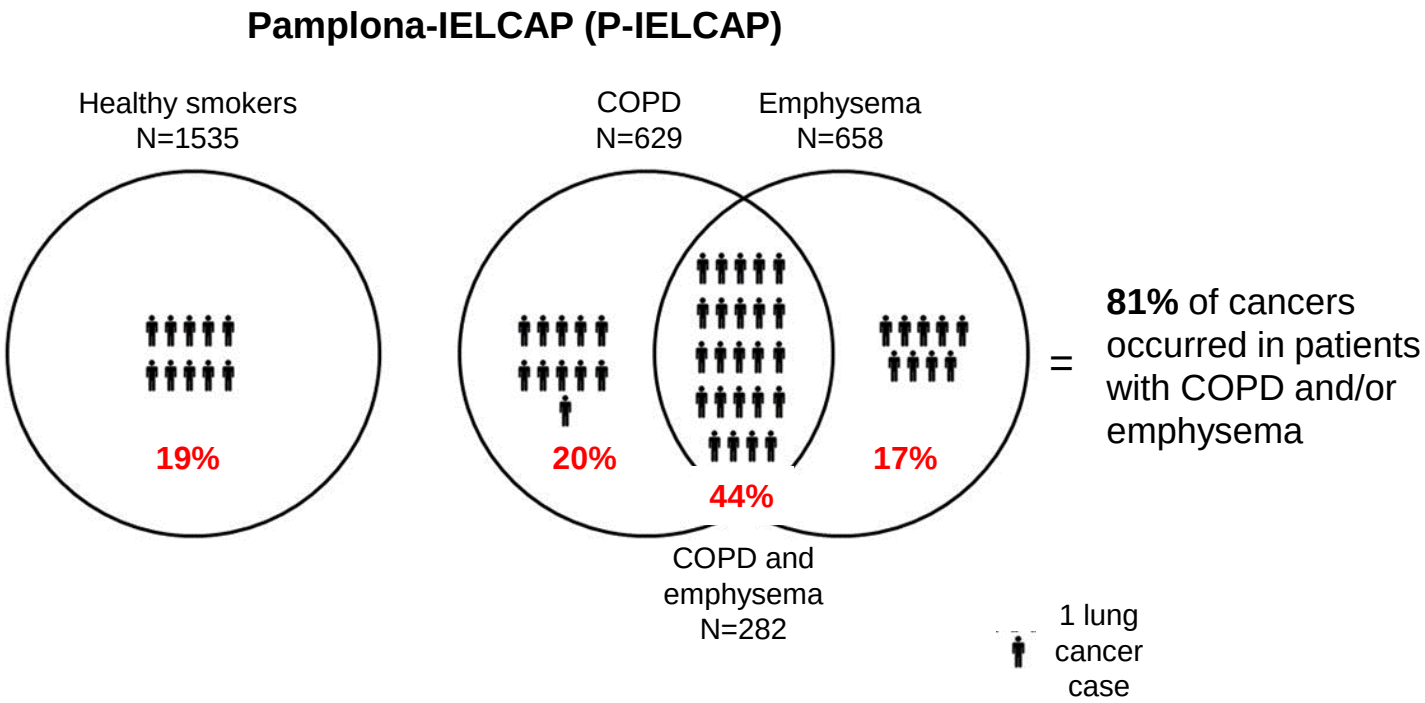
Association of Radiographic Emphysema and Airflow Obstruction with Lung Cancer

David O. Wilson[1], Joel L. Weissfeld[2], Arzu Balkan[1,3], Jeffrey G. Schragin[2], Carl R. Fuhrman[4], Stephen N. Fisher[4], Jonathan Wilson[5], Joseph K. Leader[4], Jill M. Siegfried[6], Steven D. Shapiro[1], and Frank C. Sciurba[1]

[1]Division of Pulmonary Allergy and Critical Care Medicine, Department of Medicine, and [2]Department of Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania; [3]Gulhane Military Medical Academy, Department of Pulmonary Medicine, Ankara, Turkey; [4]Department of Radiology, [5]Heart, Lung, Esophageal Surgery Institute, and [6]Department of Pharmacology, University of Pittsburgh, Pittsburgh, Pennsylvania

Am J Respir Crit Care Med 2008;178:738-44

Lung cancer in different subgroups of a lung cancer screening cohort



Individuals with available lung function tests and LDCT: N=2540 Updated 2015

de Torres et al. Chest 2007;132:1932-8

IELCAP – U. de Navarra

Risk of lung cancer

	RR	95% CI
Emphysema	2.51	1.01, 6.23
COPD	2.10	0.79, 5.58

N=1166; adjusted for age, sex and pack-years

IELCAP, International Early Lung Cancer Action Programme;
CI, confidence interval; RR, relative risk

de Torres et al. Chest 2007;132:1932-8

Pittsburgh Lung Screening Study – PLuSS

Risk of lung cancer

n= 3638

	OR	95% CI
Emphysema	3.14	1.91, 5.15
COPD	1.41	0.87, 2.29

Adjusted for age, sex and pack-years

Wilson et al. Am J Respir Crit Care Med 2008;178:738

COPD – Emphysema in screening cohorts

Trial	n	% COPD	% Emphysema
de Torres, IELCAP UN Chest 2007	1166	25%	29%
Wilson, PLuSS AJRCCM 2008	3638	43%	43%
Zulueta, NY-ELCAP Chest 2012	9047	-	29%
Maisonneuve, COSMOS Cancer Prev Res 2011	4596	15%	40%
IELCAP 2014 ERJ 2014	62 124	-	29%

de Torres et al. Chest. 2007;132(6):1932-8. Wilson et al. Am J Respir Crit Care Med. 2008;178(9):956-61. Zulueta et al. Chest. 2012 May;141(5):1216-23. Maisonneuve et al. Cancer Prev Res (Phila). 2011;4(11):1778-89.

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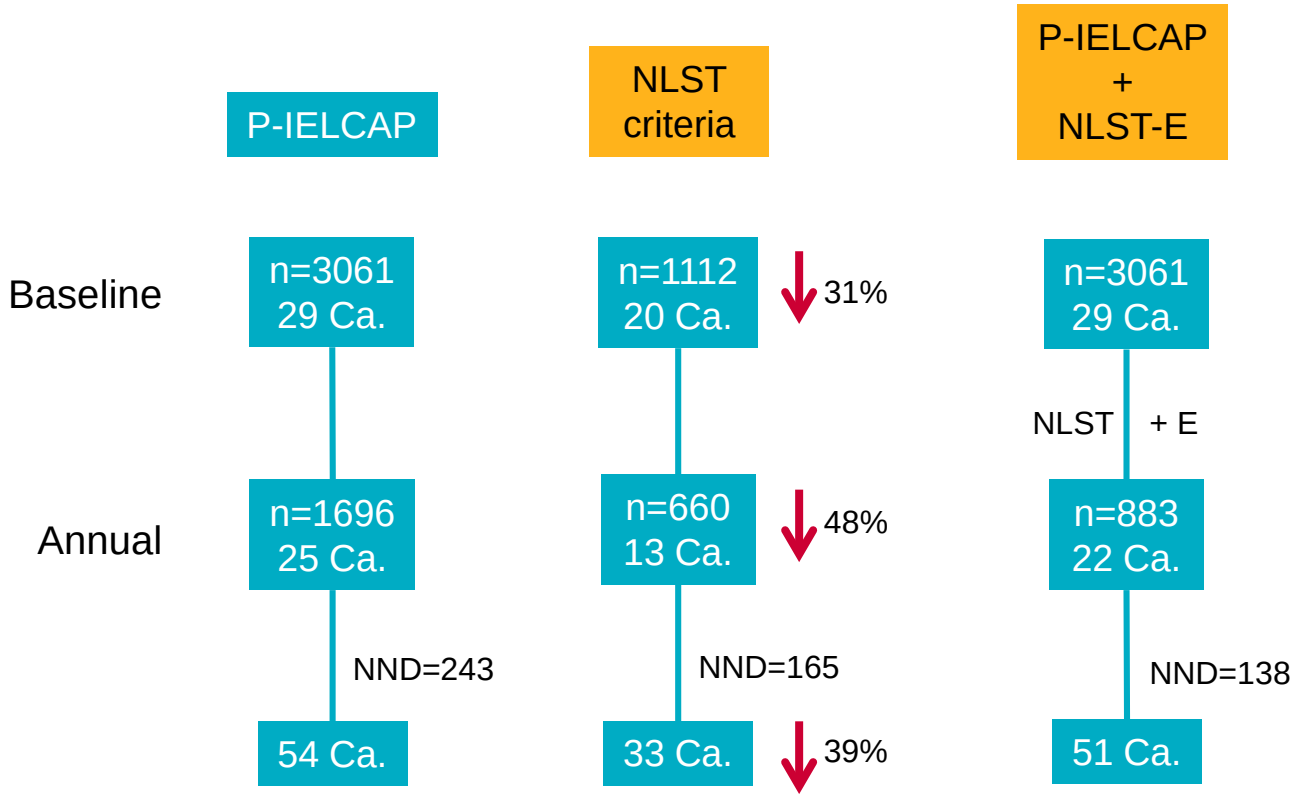
Improving Selection Criteria for Lung Cancer Screening. The Potential Role of Emphysema

Pablo Sanchez-Salcedo[1], David O. Wilson[2], Juan P. de-Torres[1], Joel L. Weissfeld[3], Juan Berto[1], Arantzazu Campo[1], Ana B. Alcaide[1], Jesús Pueyo[4], Gorka Bastarrika[4], Luis M. Seijo[5], Maria J. Pajares[6,7], Ruben Pio[6,8], Luis M. Montuenga[6,7], and Javier J. Zulueta[1]

Sanchez-Salcedo P et al. Am J Respir Crit Care Med 2015;191:924-31

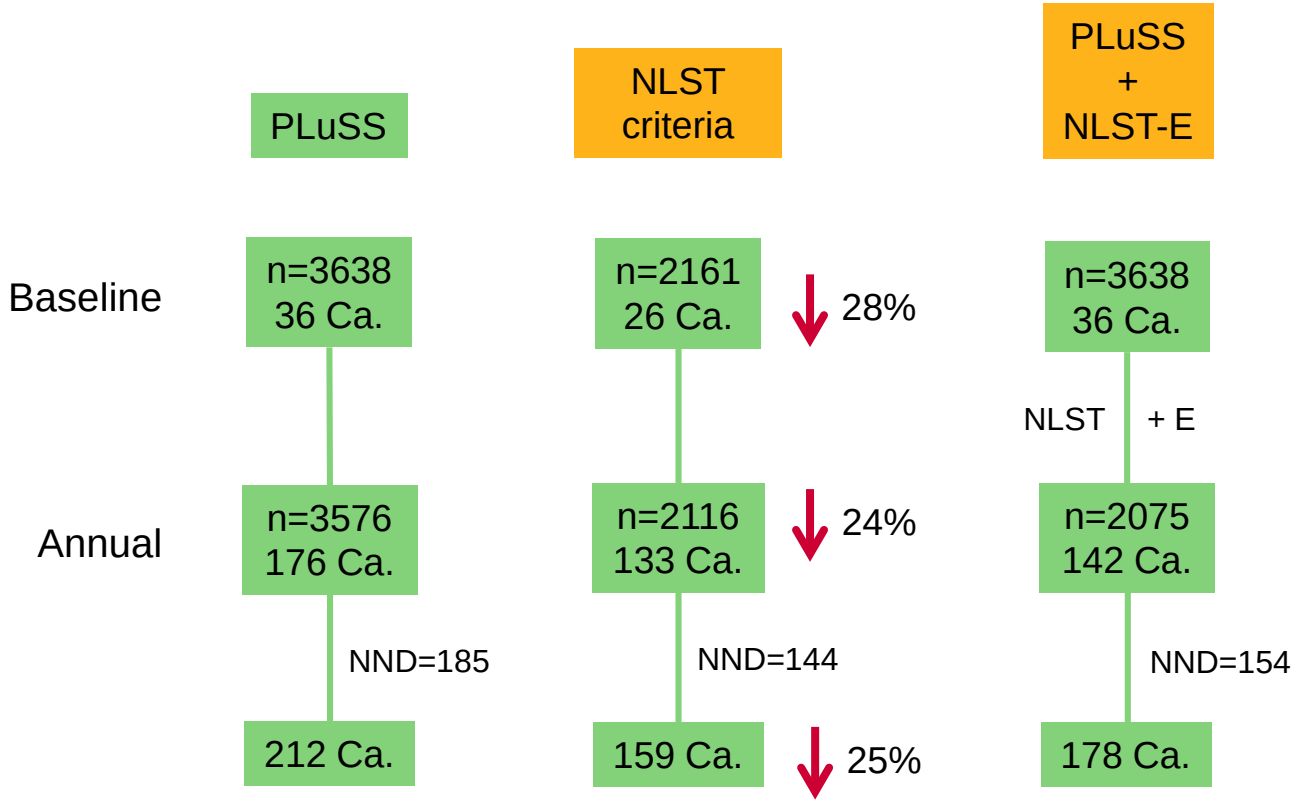
P-IELCAP



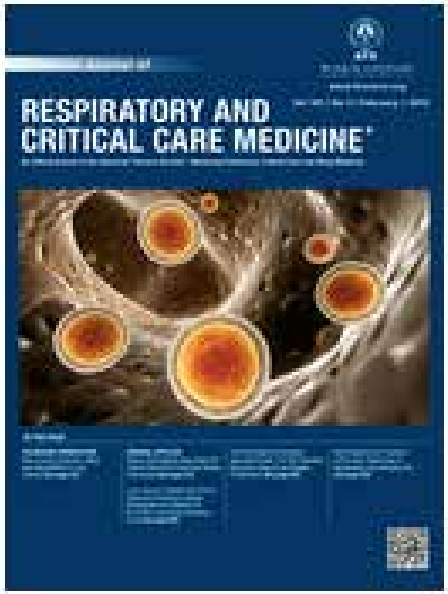
Ca., cancer;
NND, the number needed to screen in a year to detect one lung cancer

Sanchez-Salcedo P et al. Am J Respir Crit Care Med 2015;191:924-31

PLuSS



Sanchez-Salcedo P et al. Am J Respir Crit Care Med 2015;191:924-31



Lung Cancer in Patients with Chronic Obstructive Pulmonary Disease. Development and Validation of the COPD Lung Cancer Screening Score

Juan P. de-Torres[1], David O. Wilson[2], Pablo Sanchez-Salcedo[1], Joel L. Weissfeld[3], Juan Berto[1], Arantzazu Campo[1], Ana B. Alcaide[1], Marta García-Granero[4], Bartolome R. Celli[5], and Javier J. Zulueta[1]

de Torres et al. Am J Respir Crit Care Med 2015;191:285-91

Lung Cancer in COPD patients: development and validation of the COPD LUng Cancer Screening Score

Panel A			
	p value	HR	95% CI
Age: > 60 vs < 60	0.001	2.5	1.6, 3.7
Sex: male vs female	0.88	0.9	0.7, 1.4
BMI: < 25 vs > 25	0.026	2.1	1.1, 4.1
Pack-years: > 60 vs < 60	0.001	1.9	1.3, 2.6
Active smoker	0.37	1.2	0.8, 1.6
Years of former smoker	0.47	1.6	0.5, 5.0
Family History LC: yes vs no	0.29	1.2	0.8, 1.8
GOLD I-II vs III-IV	0.04	1.4	1.04, 1.6
Emphysema: yes vs no	0.001	3.5	2.3, 5.2
Panel B			
	p value	HR	95% CI
Age: > 60 vs < 60	0.005	2.3	1.5, 3.5
BMI: < 25 vs > 25	0.15	1.2	0.9, 1.8
Pack-years: > 60 vs < 60	0.001	1.5	1.1, 2.2
Emphysema: yes vs no	0.001	2.7	1.7, 4.3

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BMI, body mass index

de Torres et al. Am J Respir Crit Care Med 2015;191:285-91

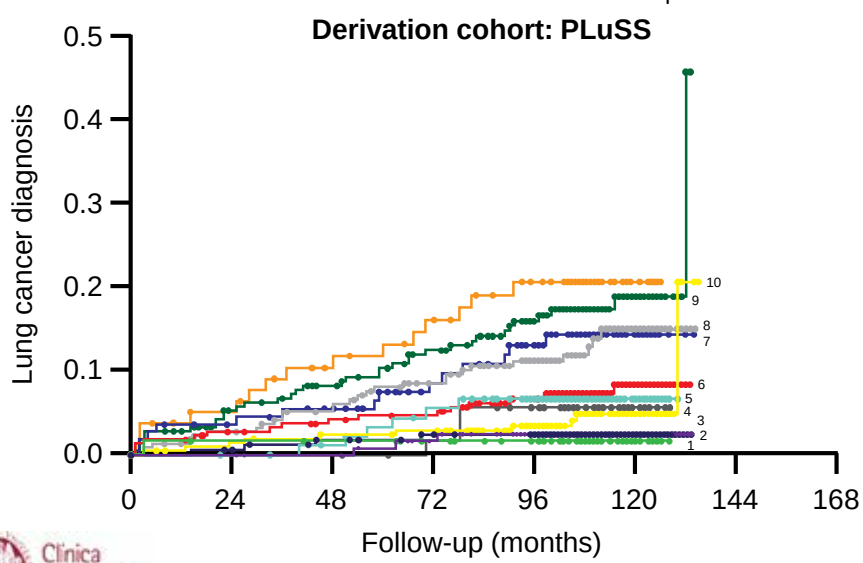
Lung cancer in COPD patients: development and validation of the COPD LUng Cancer Screening Score

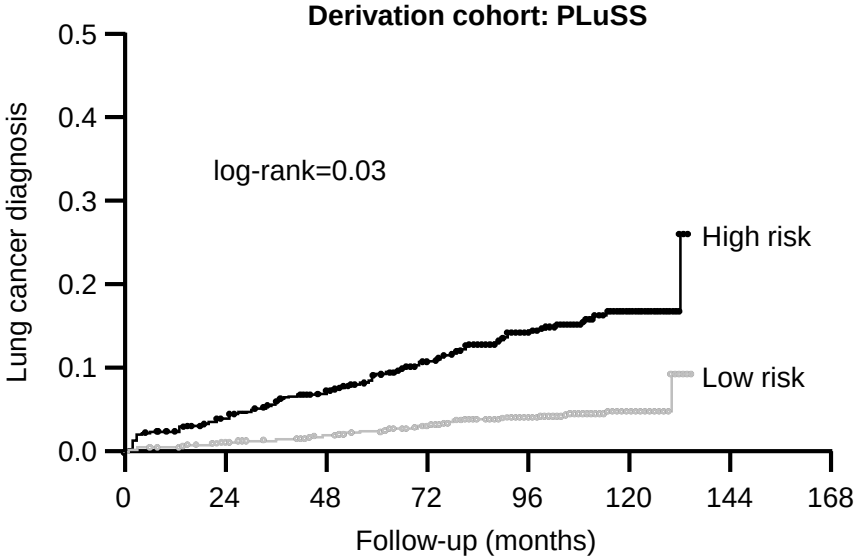
COPD lung cancer screening score (COPD-LUCSS)

BMI: < 25	1 point
Pack-years history: > 60	2 points
Age: > 60	3 points
Radiological emphysema: yes	4 points
Total	10 points

COPD lung cancer screening score (COPD-LUCSS) categories

Low-risk category:	0-6 points
High-risk category:	7-10 points





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LUCSS, lung cancer screening score

de Torres et al. Am J Respir Crit Care Med 2015;191:285-91

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Original Research: COPD

Identification of COPD Patients at High Risk for Lung Cancer Mortality Using the COPD-LUCSS-DLCO

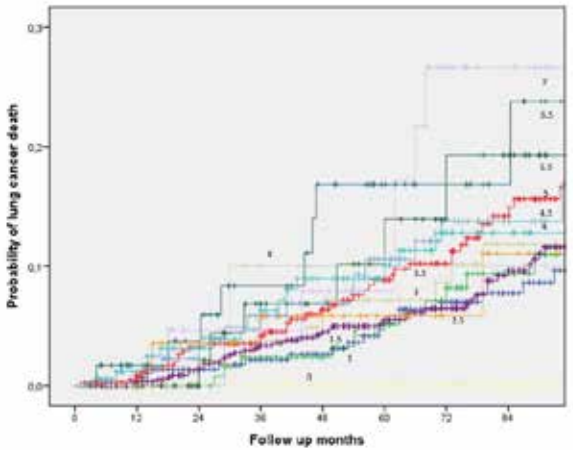
Juan P. de-Torres, MD[a], Jose M. Marín, MD[b], Ciro Casanova, MD[c, d], Victor Pinto-Plata, MD[f], Miguel Divo, MD[f], Claudia Cote, MD[e, †], Bartolome R. Celli, MD[f], Javier J. Zulueta, MD[a]

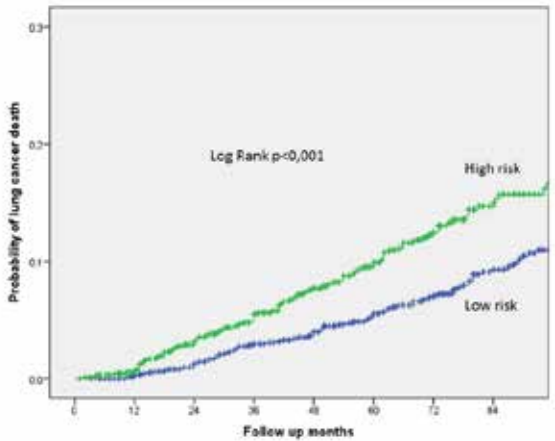
Sanchez-Salcedo P et al. Am J Respir Crit Care Med 2015;191:924-31

Prediction of lung cancer mortality in COPD patients using the new COPD-LUng Cancer Screening Score DLCO

COPD lung cancer screening score (COPD-LUCSS) categories

Low risk Category: 0 – 3 points
High risk Category: 3.5 -8 points





	p value	HR	95% CI
Low-risk vs high-risk category	0.001	2.4	2.0, 2.7

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Zulueta et al. Chest (in press)

Resumen

- El cribado con TCBD reduce la mortalidad por cáncer de pulmón ***al menos*** un 20%
- El sobrediagnóstico no tiene el peso suficiente para anular la reducción de mortalidad
- Los falsos positivos se pueden manejar sin pruebas diagnósticas invasivas
- El cribado de cáncer de pulmón es coste-efectivo

Resumen

- El enfisema es quizás el biomarcador que mejor predice el riesgo de cáncer de pulmón
- COPD LUCSS puede ser útil en la selección de pacientes con EPOC con el mayor riesgo