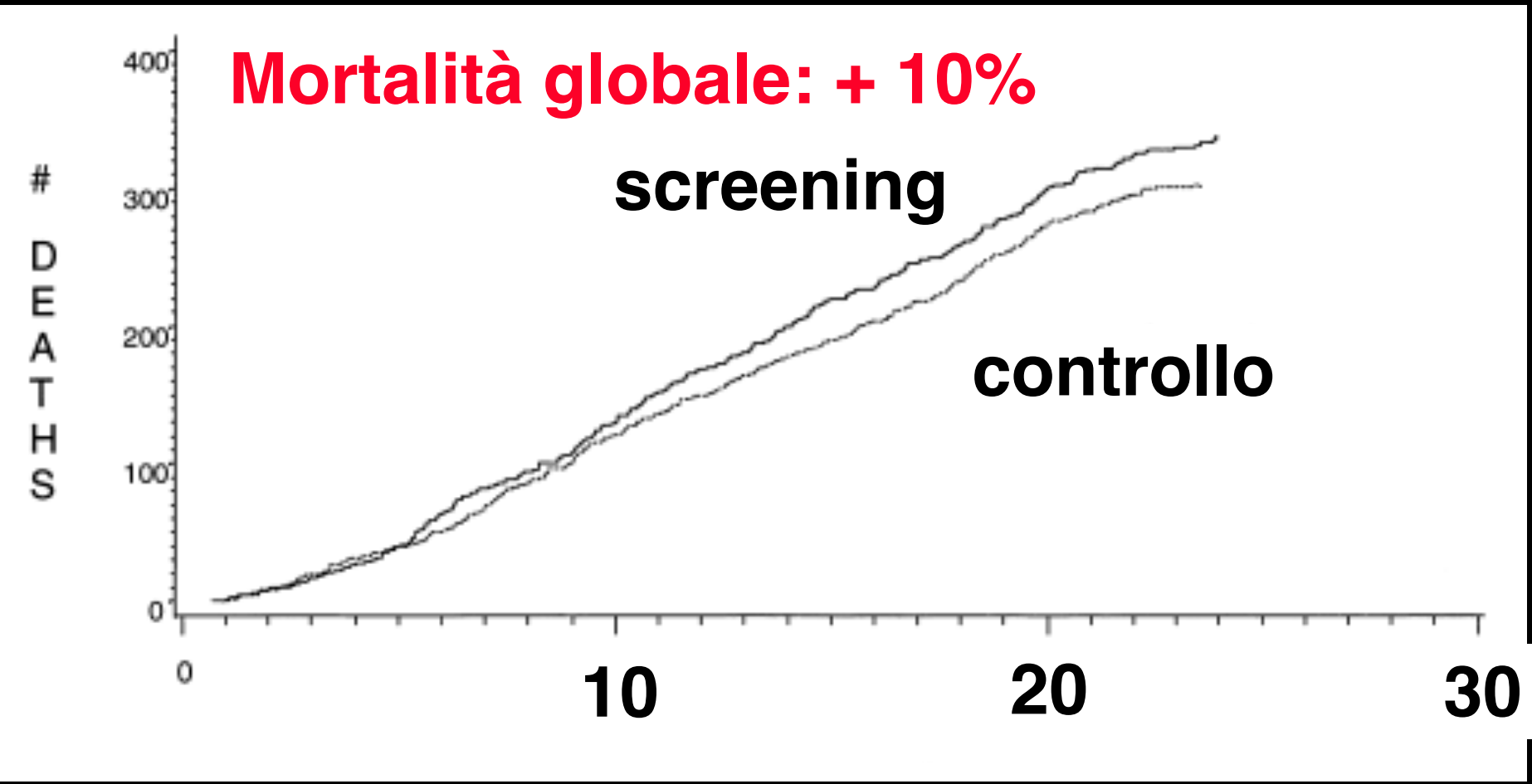
GIORNATA MONDIALE SENZA TABACCO
WORLD NO -TOBACCO DAY 2015
ISS - Roma, 29 maggio 2015

Nuove prospettive per la diagnosi precoce del tumore al polmone

Ugo Pastorino
Chirurgia Toracica, Istituto Nazionale Tumori, Milano

Studio randomizzato NCI - Mayo

RxT ogni 4 mesi vs. controllo
9211 smokers, 1971-1983



JNCI 2000; 92:1308-16

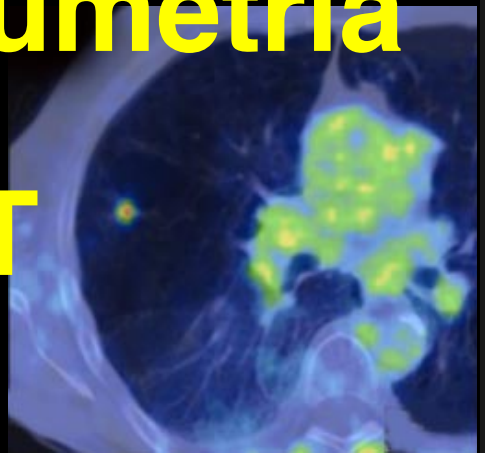
cosa è cambiato ?

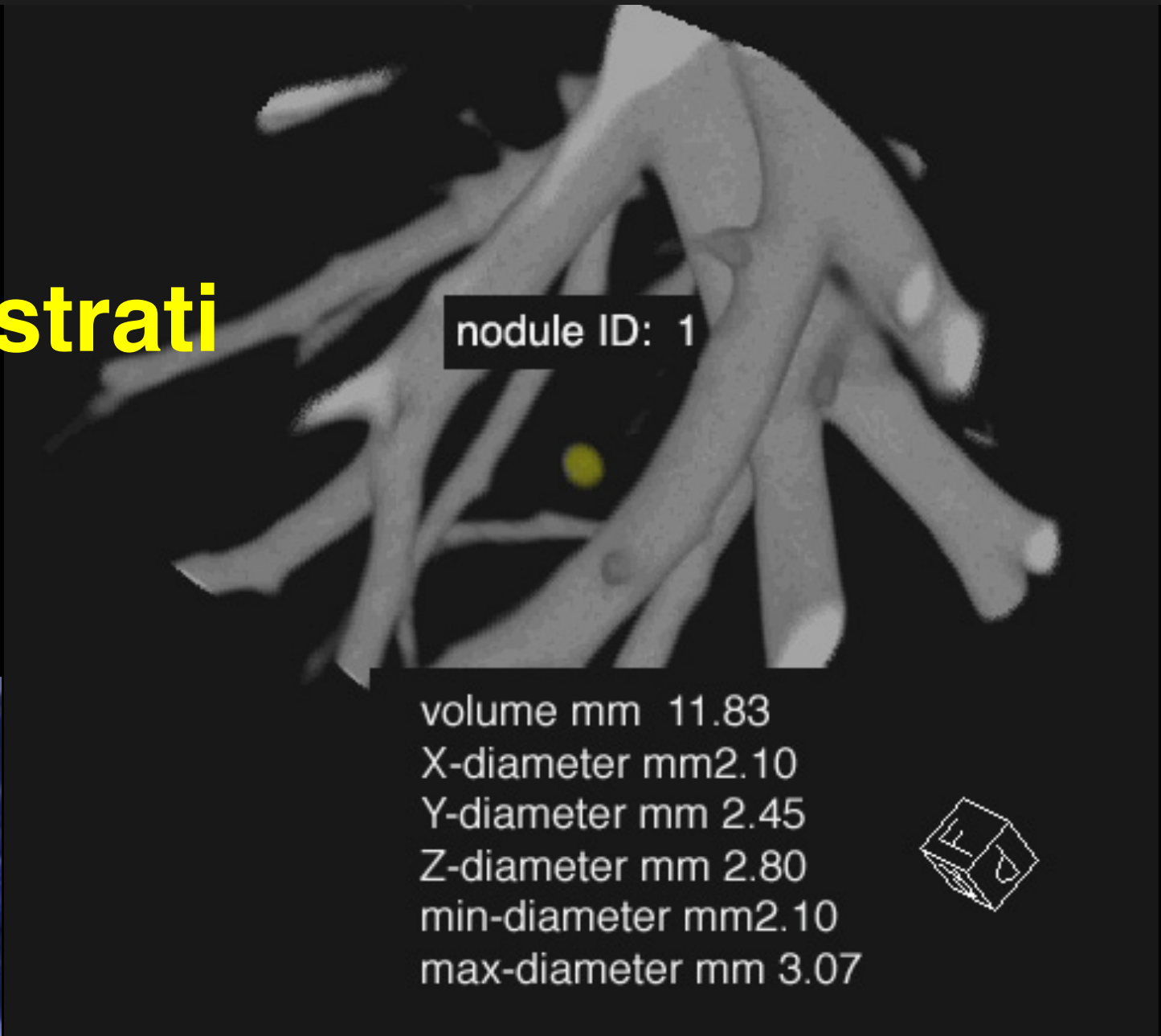
TC 16 - 128 strati

CAD

volumetria

PET





trial randomizzati sullo screening

diagnosi alla 1ª e 2ª TC

	Noduli sospetti		Ca polmone				
			1ª TC		stadio I	2ª TC	
LSS	316	(17)	30	(1.8)	48	8	(.6)
NELSON	1,570	(21)	70	(.9)	64	54	(.7)
DANTE	226	(18)	47	(3.7)	66	13	(1)
ITALUNG	426	(30)	20	(1.5)	48	-	
NLST	6561	(25)	270	(1)	63	168	(.6)
DLCST	179	(9)	17	(.8)	53	11	(.6)
MILD	335	(14)	17	(.7)	57	18	(.8)
LUSI	540	(27)	22	(1.1)	-	-	
Totale	10,153	(23)	493	(1.1)	62	272	(.7)

90,866 soggetti arruolati, 44,629 nel braccio TC

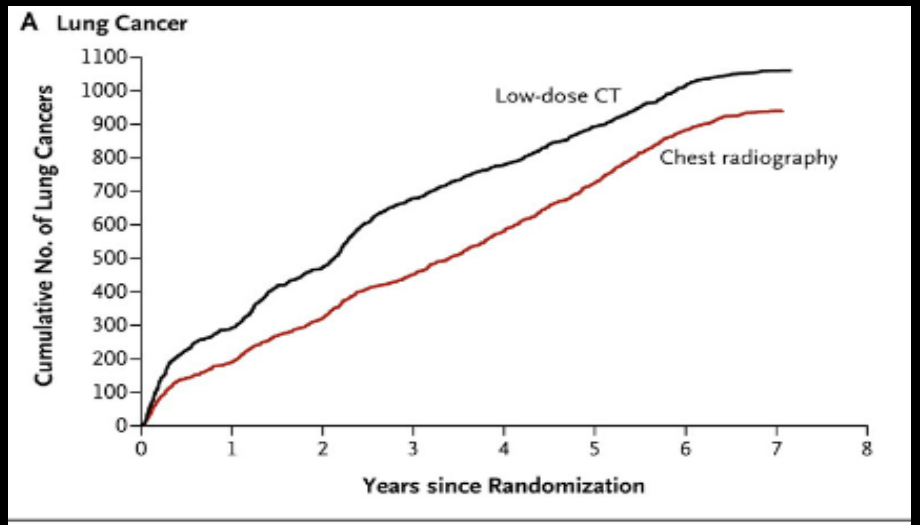
Thorac Surg Clin 2013; 23:129-40

trial randomizzati sullo screening
procedure chirurgiche per lesioni benigne

	soggetti	cancro	benigno	% ben
NELSON	7,557	67	24	27
DANTE	1,276	55	17	24
ITALUNG	1,406	16	1	6
NLST	26,309	509	164	24
DLCST	2,047	41	8	16
MILD	2,376	47	4	8
LUSI	2,029	22	9	29
Totale	76,962	1,229	355	22

Thorac Surg Clin 2013; 23:129-40

NLST: lo studio più grande



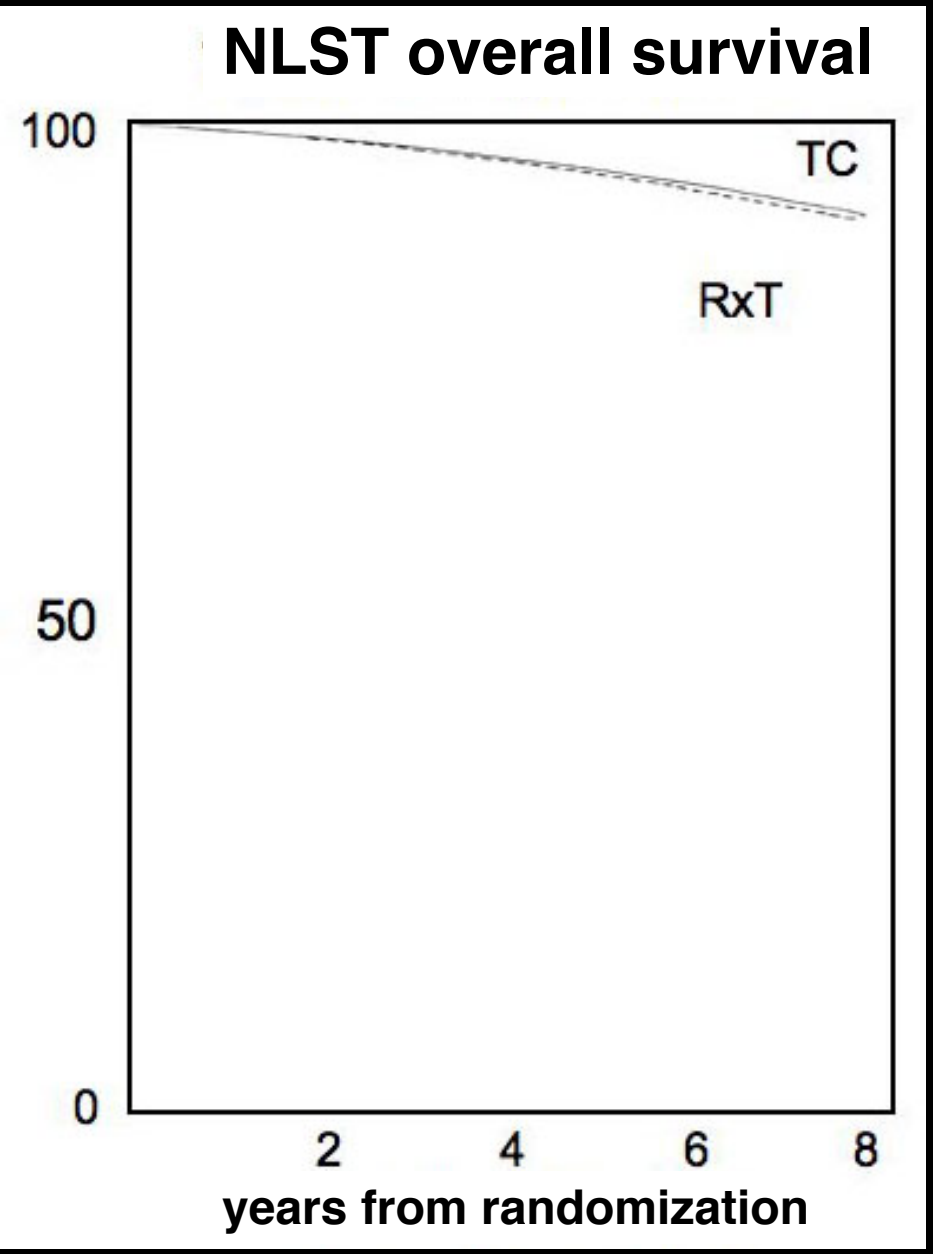
53,454 persone
randomizzate
3 esami annuali
CT vs RxT

- 20% mortalità specifica
- 7% mortalità globale

24.2% TC positive
96.4% di falsi positivi

N Engl J Med 2011;365:395-409

NLST: lo studio più grande



per prevenire 1 morte per ca polmone in 6 anni

- 900 CT
- 18 PET
- 3 broncoscopie / FNABs
- 2 resezioni chirurgiche

per patologia benign

Mortalità - 0.06% / anno

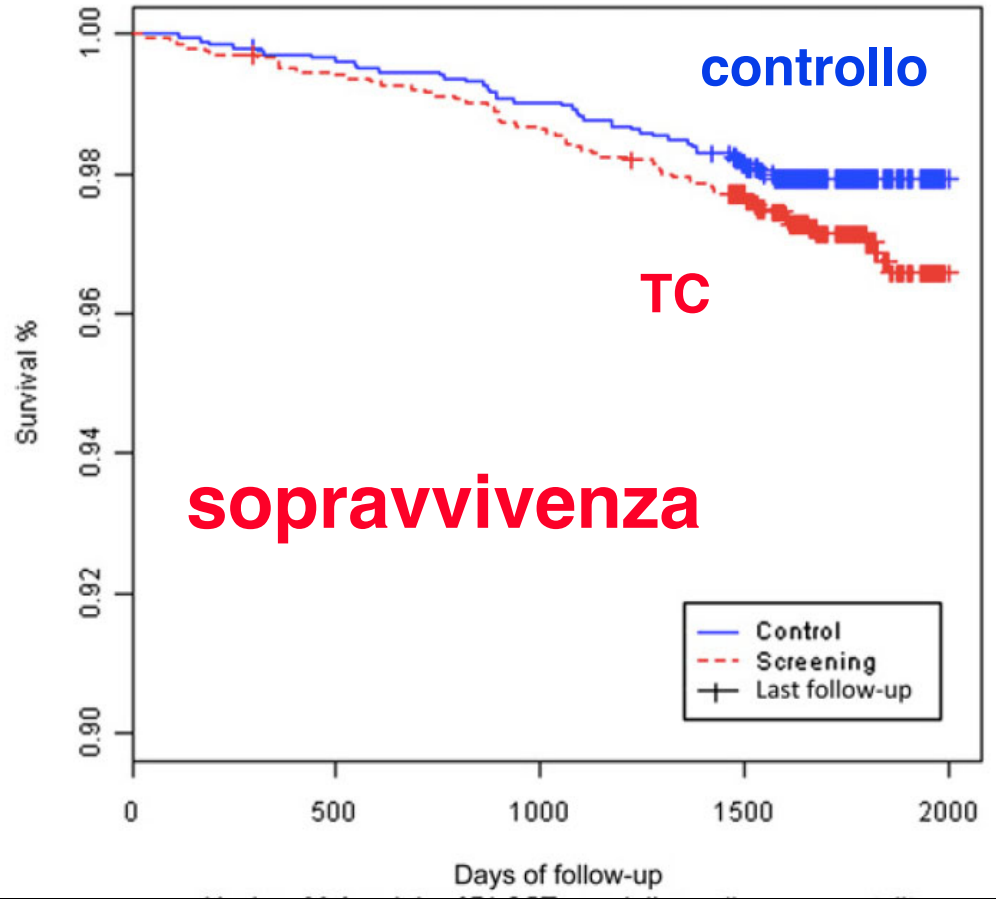
N Engl J Med 2011;365:395-409

Studio danese DLCST : risultati a 5-anni

ORIGINAL ARTICLE

CT screening for lung cancer brings forward early disease. The randomised Danish Lung Cancer Screening Trial: status after five annual screening rounds with low-dose CT

Zaigham Saghir,[1] Asger Dirksen,[1] Haseem Ashraf,[2] Karen Skjøldstru
John Brodersen,[4] Paul Frost Clementsen,[1] Martin Døssing,[5] Hanne
Klaus Fuglsang Kofoed,[7] Klaus Richter Larsen,[8] Jann Mortensen,[9]
Jakob Fraes Rasmussen,[4] Niels Seersholm,[1] Birgit Guldhammer Skov,[1]
Philip Tønnesen,[1] Jesper Holst Pedersen[11]

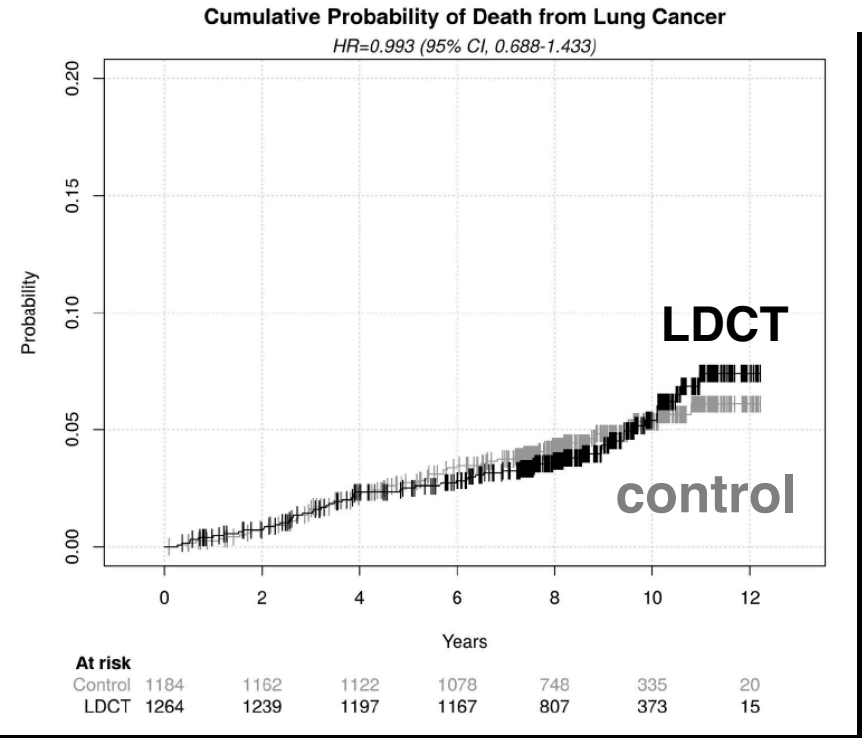


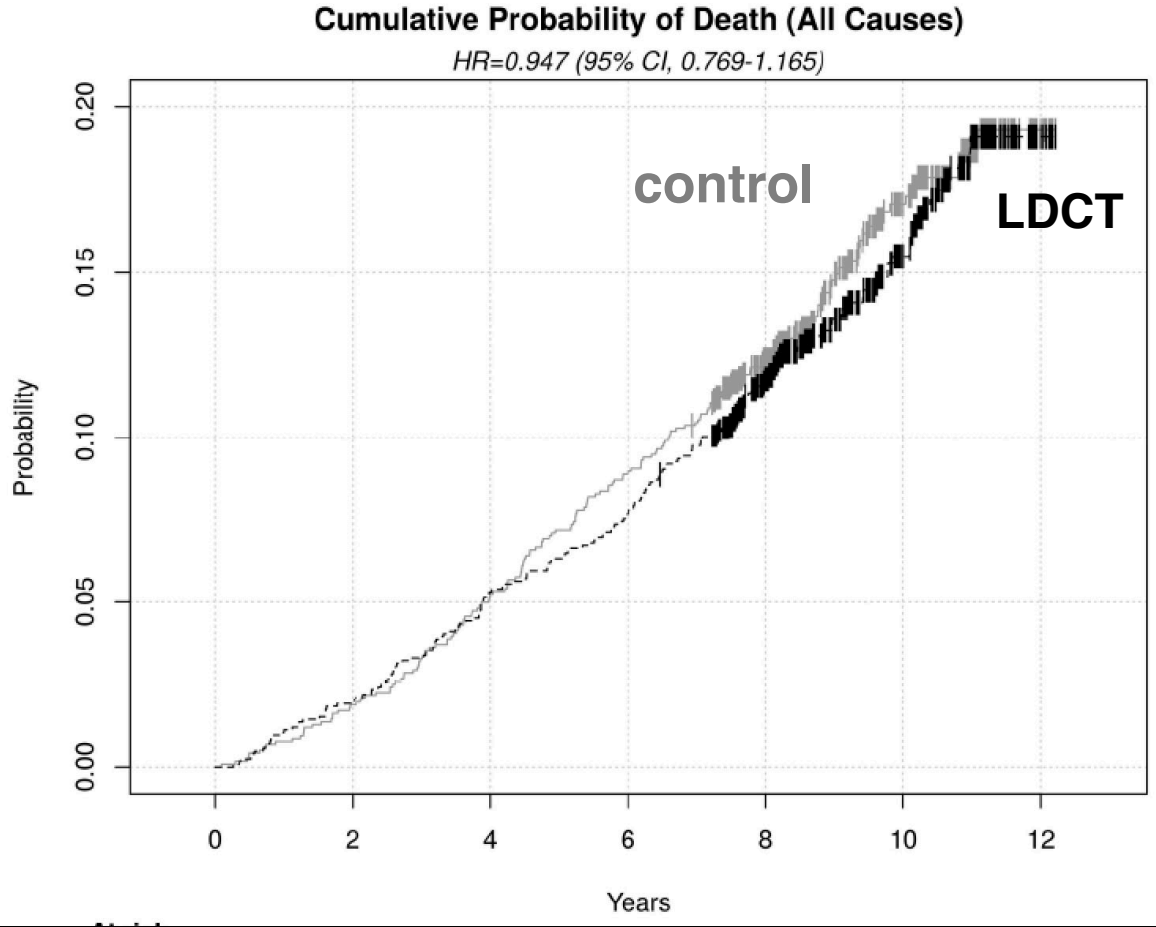
Thorax 2012; 67:296-301

Am J Respir Crit Care Med. First published online 11 Mar 2015 as DOI:
10.1164/rccm.201408-1475OC

Long-term Follow-up Results of the DANTE Trial, a Randomized Study of Lung Cancer Screening with Spiral Computed Tomography

Maurizio Infante , Silvio Cavuto , Fabio Romano Lutman , Eliseo Passera , Maurizio Chiarenza , Giuseppe Chiesa , Giorgio Brambilla , Aranzulla , Arturo Chiti , Marta Scorsetti , Pierina Michele Ciccarelli , Massimo Roncalli , Anna Dest Voulaz , Valentina Errico , Giorgio Ferraroli , Giov Armando Santoro , Marco Alloisio , and for the DA



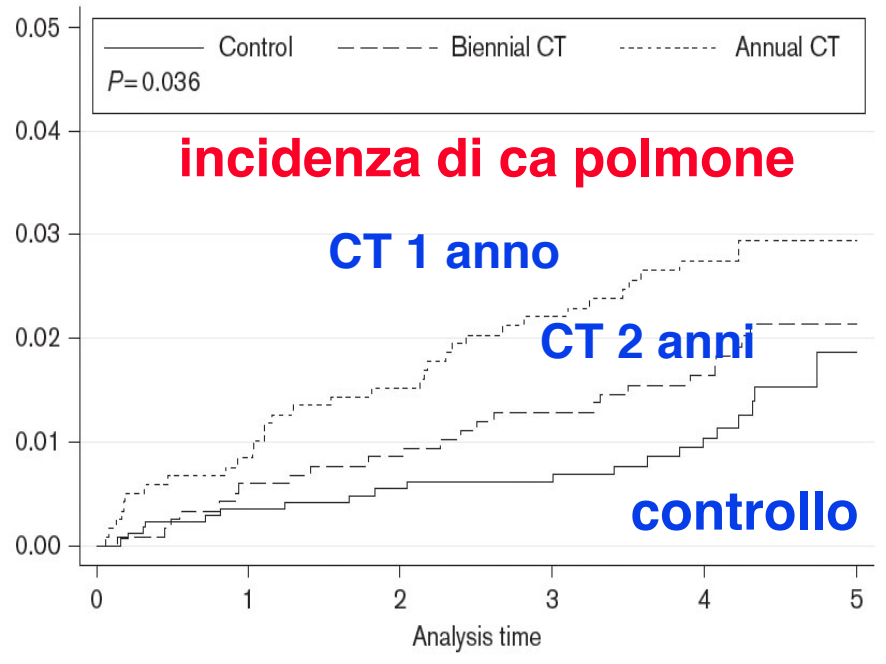


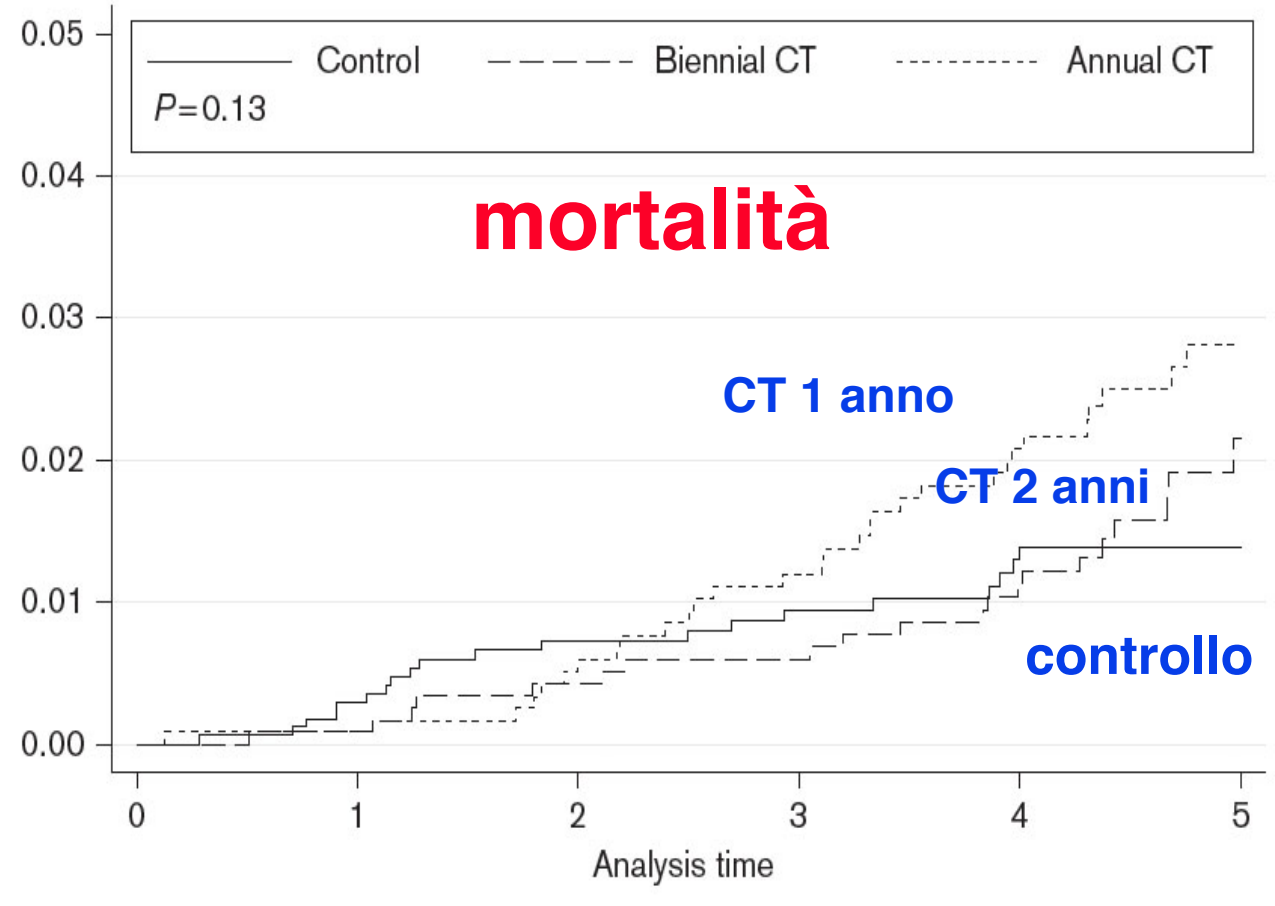
Am J Respir Crit Care Med. 2015 Mar 11. [Epub]

MILD trial: risultati a 5 anni

Annual or biennial CT screening versus observation in heavy smokers: 5-year results of the MILD trial

Ugo Pastorino[a], Marta Rossi[e,f], Valentina Rosato[e,f], Alfonso Marchianò[b], Nicola Sverzellati[g], Carlo Moros
Eva Negri[e], Gabriella Sozzi[d], Gi



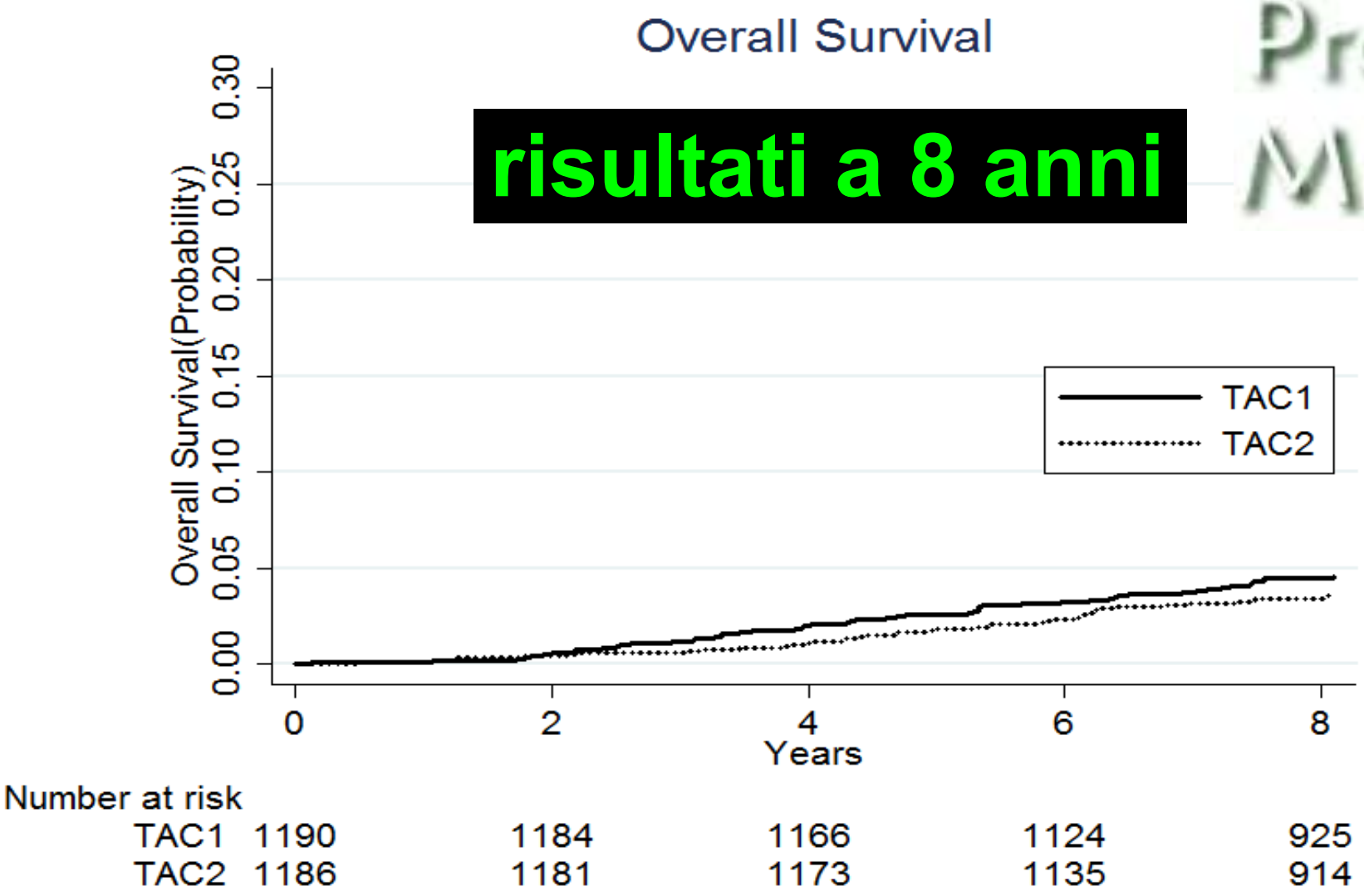


follow-up 17,523 man / year

EJCP 2012; 21:308–315

risultati a 8 anni

Progetto MILD

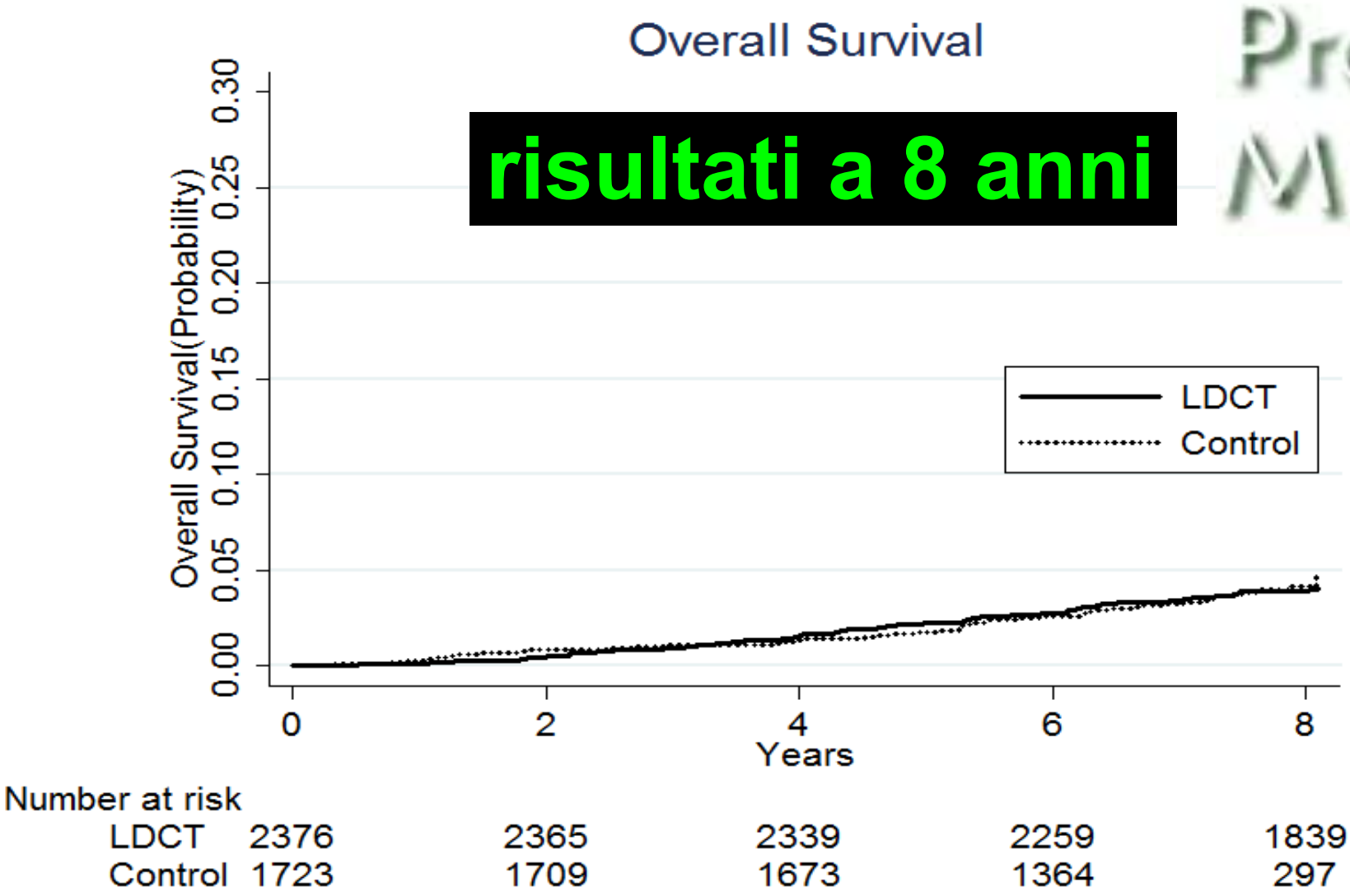


P = 0.23

Arm	OS at 5 years (95% CI)	OS at 8 years (95% CI)
LDCT – Tac 1	97.4% (96.3 – 98.2)	95.6% (94.2-96.6)
LDCT – Tac 2	98.1% (97.2-98.8)	96.6% (95.4-97.5)

risultati a 8 anni

Progetto MILD

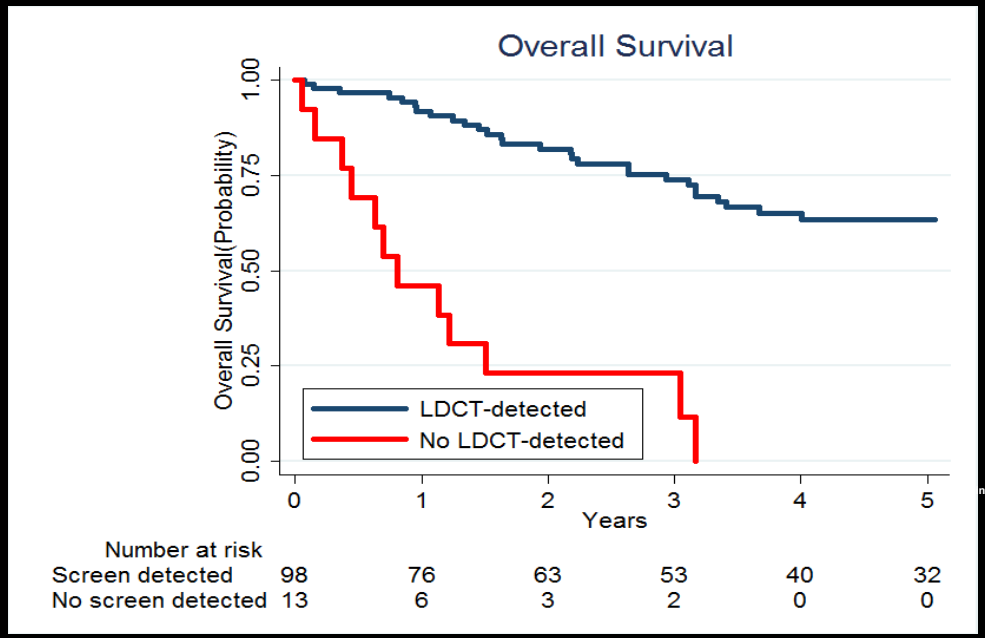


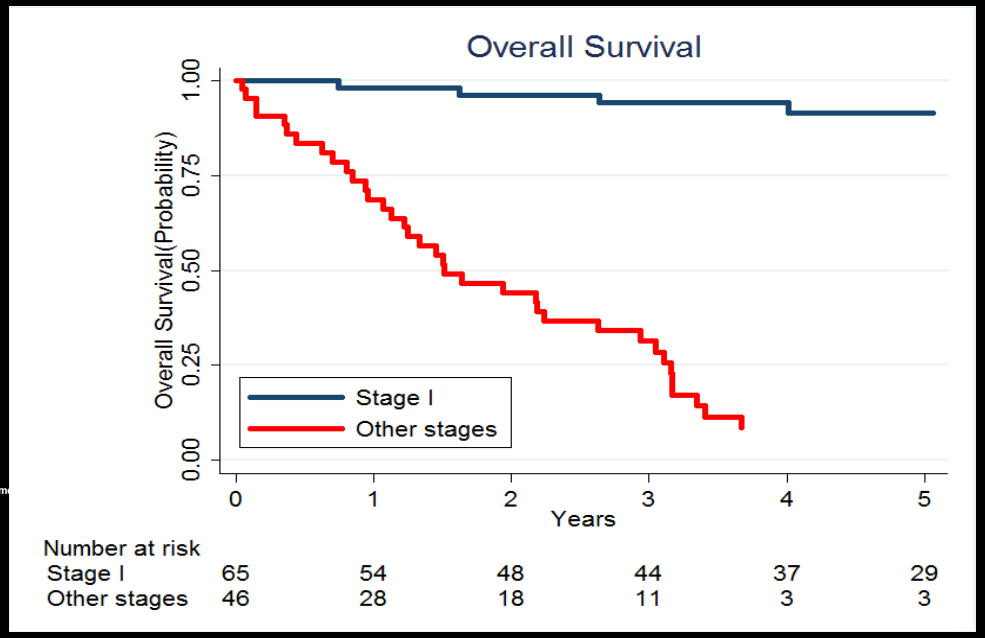
P = 0.70

Arm	OS at 5 years (95% CI)	OS at 8 years (95% CI)
LDCT	97.8% (97.1-98.3)	96.1% (95.2-96.8)
Control	98.2% (97.5-98.8)	95.9% (94.7-96.8)

INT screening trials (pilota + MILD)

3411 smokers, 24,000 p/y, 111 lung cancers





- A major difference in survival was observed between LDCT-detected cases and no LDCT-detected (interval) cancers
- A similar difference in survival was observed between stage I cases and other stages together

Studio USA - ELCAP: come ottimizzare la TC

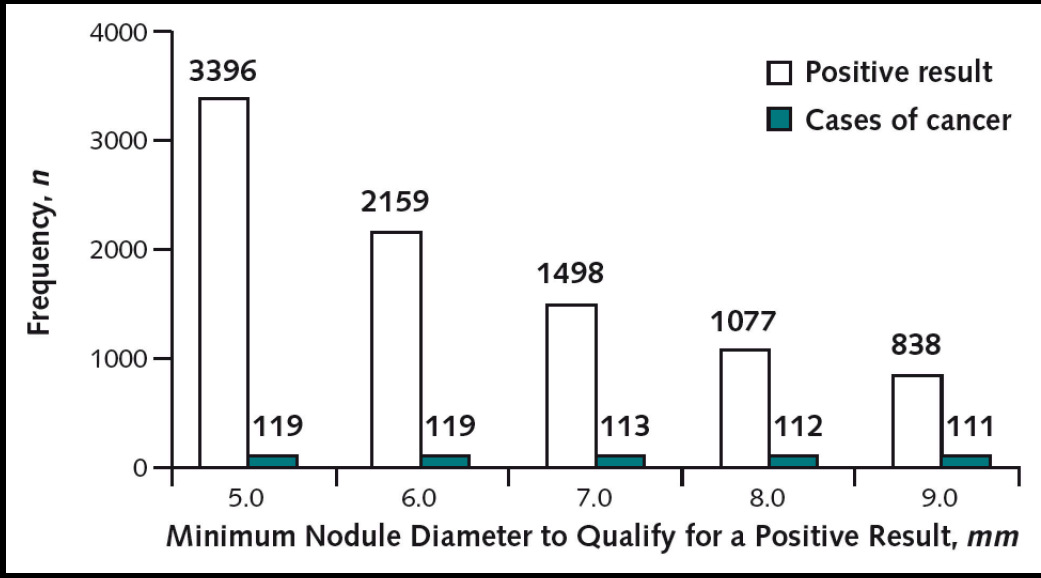
ORIGINAL RESEARCH | Annals of Internal Medicine

Definition of a Positive Test Result in Computed Tomography Screening for Lung Cancer

A Cohort Study

Claudia I. Henschke, PhD, MD; Rowena Yip, MPH; David F. Yankelevitz, MD; and James P. Smith, MD, for the International Early Lung Cancer Action Program Investigators*

Conclusion: These findings suggest that using a threshold of 7 or 8 mm to define positive results in the baseline round of computed tomography screening for lung cancer should be prospectively evaluated to determine whether the benefits of decreasing further work-up outweigh the consequent delay in diagnosis in some patients.

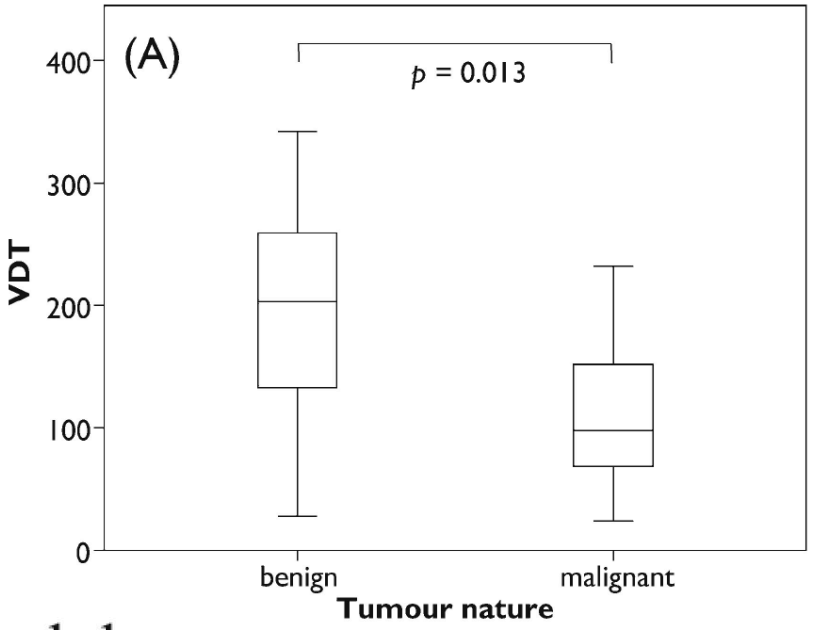


Ann Intern Med 2013;158:246-252

Studio NELSON: come ottimizzare la TC

Optimisation of volume-doubling time cutoff for fast-growing lung nodules in CT lung cancer screening reduces false-positive referrals

Marjolein A. Heuvelmans · Matthijs Oudkerk · Geertruida H. de Bock · Harry J. de Koning · Xueqian Xie · Peter M. A. van Ooijen · Marcel J. W. Greuter · Pim A. de Jong · Harry J. M. Groen · Rozemarijn Vliegenthart



Conclusion All malignant fast-growing lung nodules referred after the 3-month follow-up CT in the baseline lung cancer screening round had VDT ≤232 days. Lowering the VDT cutoff may reduce false-positive referrals.

Eur Radiol 2013; 23:1836–1845

NLST: sovradiagnosi

Original Investigation

Overdiagnosis in Low-Dose Computed Tomography Screening for Lung Cancer

Edward F. Patz Jr, MD; Paul Pinsky, PhD; Constantine Gatsonis, PhD; JoRean D. Sicks, MS; Barnett S. Kramer, MD, MPH; Martin C. Tammemägi, PhD; Caroline Chiles, MD; William C. Black, MD; Denise R. Aberle, MD; for the NLST Overdiagnosis Manuscript Writing Team

CONCLUSIONS AND RELEVANCE More than 18% of all lung cancers detected by LDCT in the NLST seem to be indolent, and overdiagnosis should be considered when describing the risks of LDCT screening for lung cancer.

15% totale, 85% dei BAC

JAMA 2014;174:269-74

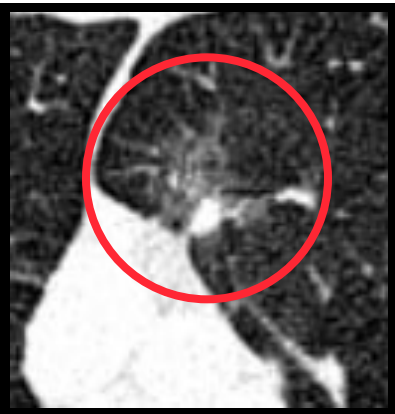
ORIGINAL ARTICLE

Long-Term Surveillance of Ground-Glass Nodules

Evidence from the MILD Trial

Silva Mario, MD, Sverzellati Nicola, MD, PhD,* Manna Carmelinda, MD,* Negrini Giulio, MD,* Marchianò Alfonso, MD,† Zompatori Maurizio, MD,‡ Rossi Cristina, MD,* and Pastorino Ugo, MD§*

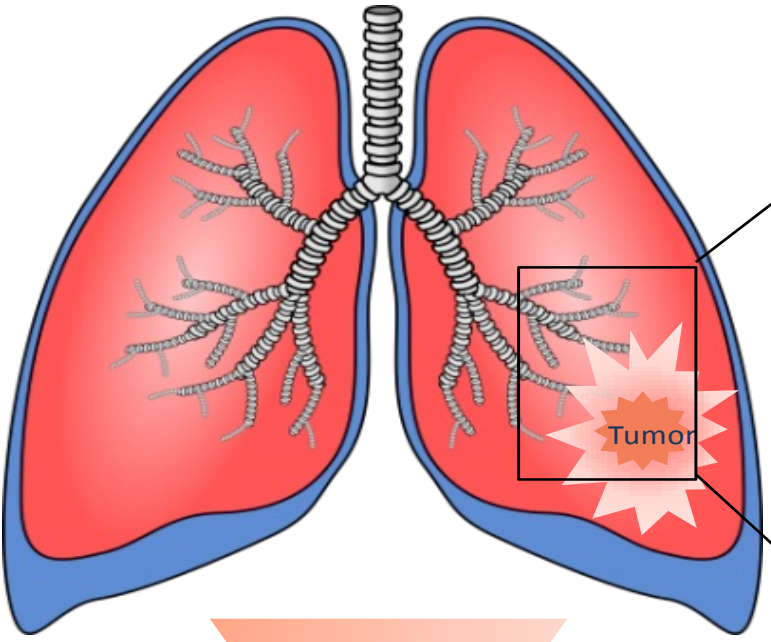
76 lesioni ground-glass (GGNs)
detected in 56 patients at baseline CT
followed for 5 years by CT:

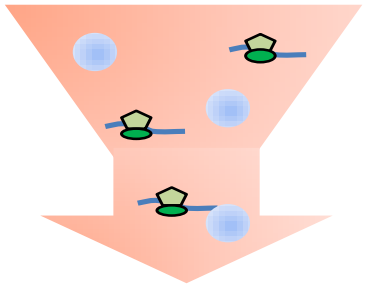


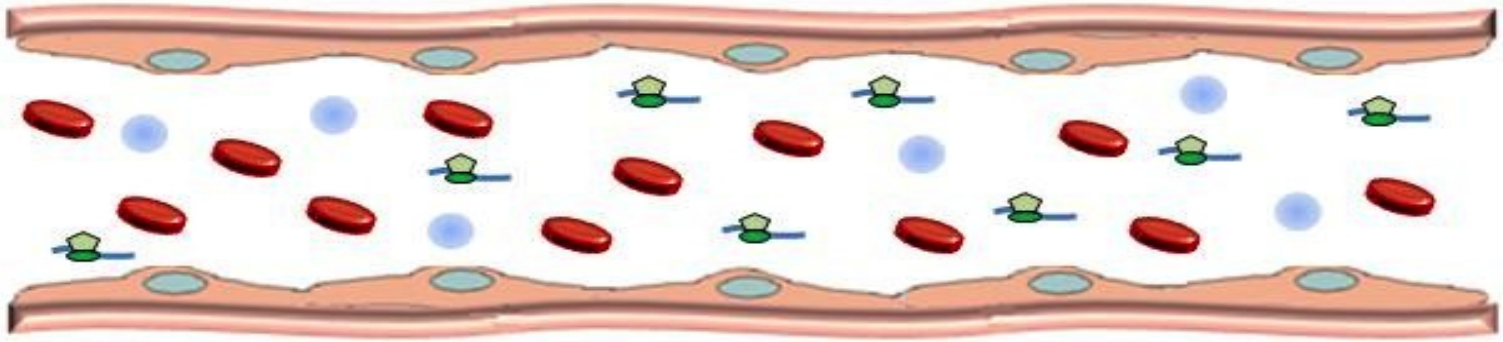
solo una (1.3%) progredita (stadio Ia ADC)
3 hanno sviluppato un cancro
in altre zone del polmone

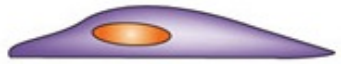
JTO 7:1541, 2012

miRNA nel sangue come biomarcatori







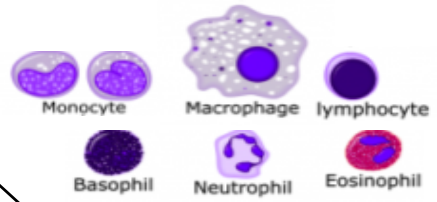


Endothelial cells

Bronchial cells

Fibroblast

Cancer cells



Hematopoietic cells

miRNA+ Ago2

Exosomes

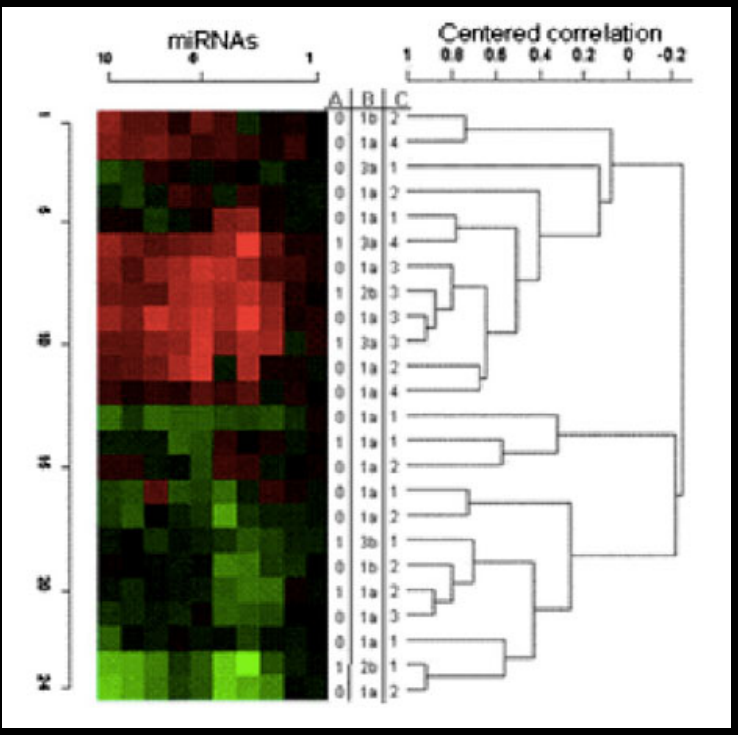
miRNA più frequenti nel sangue

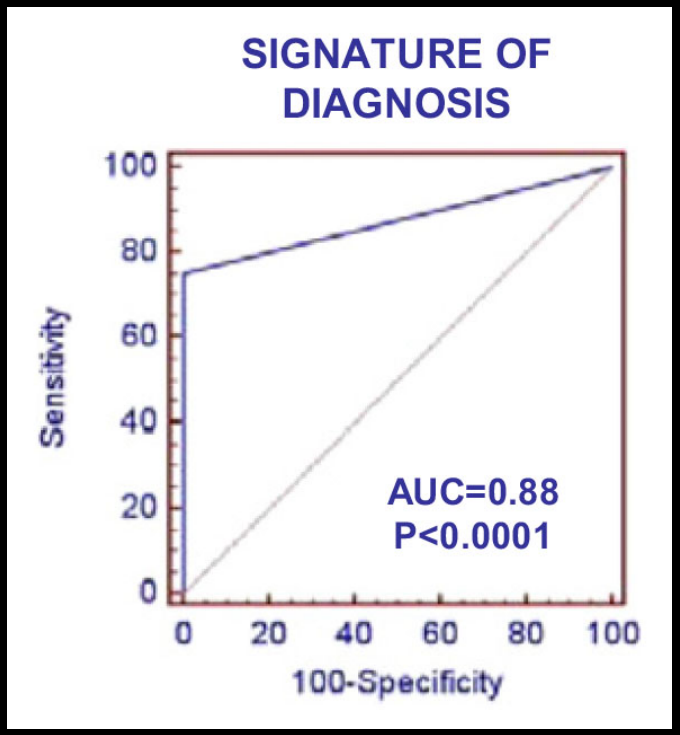
PNAS

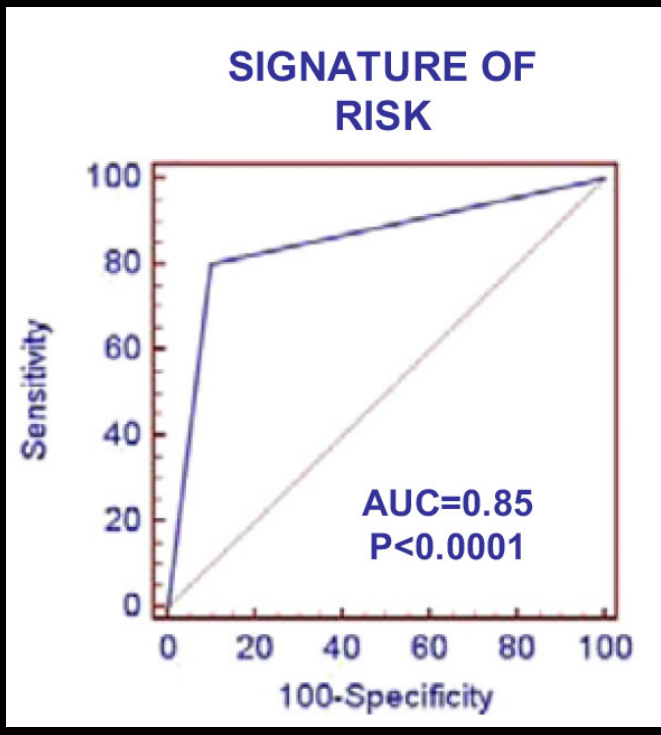
MicroRNA signatures in tissues and plasma predict development and prognosis of computed tomography detected lung cancer

Mattia Boeri[a,1], Carla Verri[a,1], Davide Conte[a,1], Luca Roz[a,1], Piergiorgio Modena[b], Federica Facchinetti[a], Elisa Calabrò[c], Carlo M. Croce[d,2,3], Ugo Pastorino[c,2], and Gabriella Sozzi[a,2,3]

[a]Tumor Genomics Unit, Department of Experimental Oncology and Molecular Medicine, and [c]Unit of Thoracic Surgery, Fondazione IRCCS Istituto Nazionale Tumori, 20133 Milan, Italy; [b]Unit of Experimental Oncology 1, Centro di Riferimento Oncologico, 33081 Aviano (PN), Italy; and [d]Ohio State University Comprehensive Cancer Center, Ohio State University, Columbus, OH 43210







1 - 2 anni prima della TC

PNAS 2011; 108:3713-18

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Clinical Utility of a Plasma-Based miRNA Signature Classifier Within Computed Tomography Lung Cancer Screening: A Correlative MILD Trial Study

Gabriella Sozzi, Mattia Boeri, Marta Rossi, Carla Verri, Paola Suatoni, Francesca Bravi, Luca Roz, Davide Conte, Michela Grassi, Nicola Sverzellati, Alfonso Marchiano, Eva Negri, Carlo La Vecchia, and Ugo Pastorino

Conclusion

This large validation study indicates that MSC has predictive, diagnostic, and prognostic value and could reduce the false-positive rate of LDCT, thus improving the efficacy of lung cancer screening.

J Clin Oncol 32.

Uso combinato di miRNA e LDCT

Aumento della specificità diagnostica nel ca polmonare

Soggetti senza tumore	TOTALE	miRNA	
		+	-
TC	594	116	478
Nessun nodulo	248	49	199
Nodulo ≤ 5 mm	231	45	186
Nodulo > 5 - ≤ 10 mm	94	18	76
Nodulo > 10 mm	21	4	17

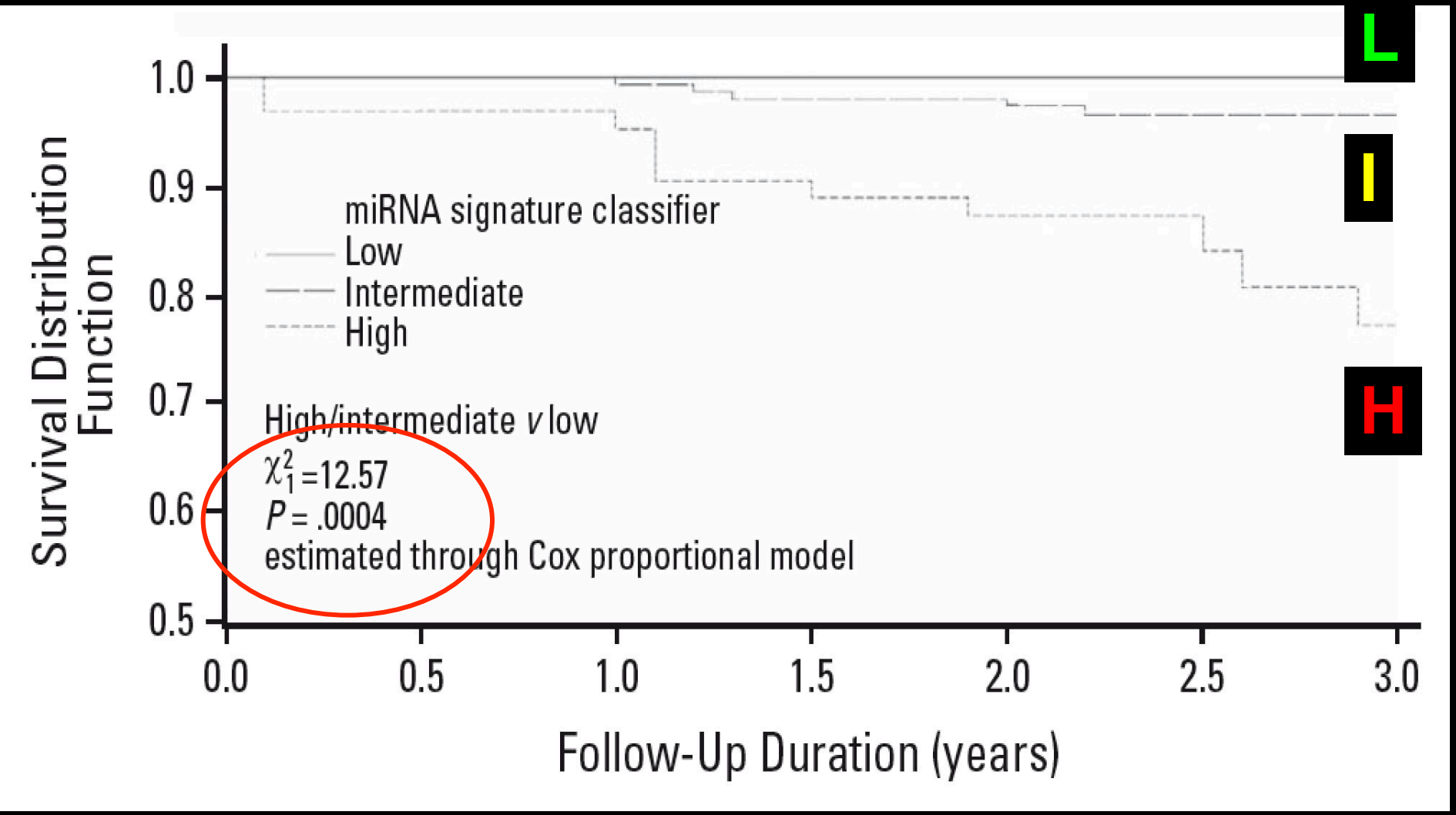
594 soggetti del braccio TC senza tumore

58% con nodulo non calcifico alla TC
Ridotto a 11% con il test miRNA

19.4% con lesioni ≥ 5mm con noduli clinicamente sospetti
Ridotto a 3.7% con il test miRNA

J Clin Oncol 32. © 2014 by American Society of Clinical Oncology

Sopravvivenza a 3 anni secondo il test miRNA
in tutti I soggetti (con o senza cancro, n=939)



efficacia del miRNA test (MSC) nello studio MILD

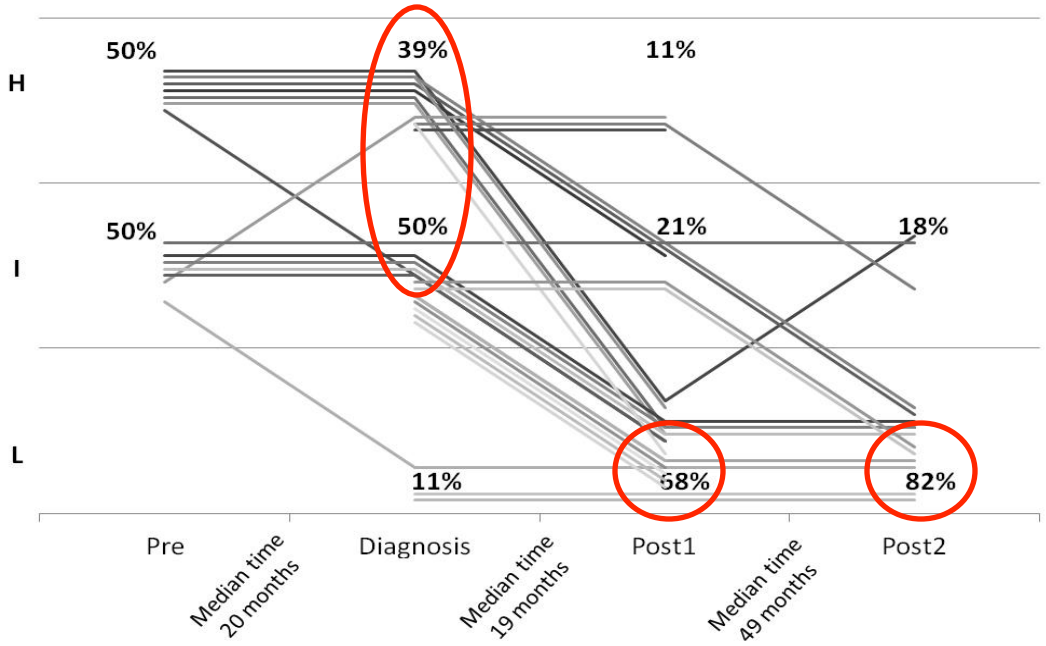
2 anni — **diagnosi anticipata**

87% — **sensibilità diagnostica**

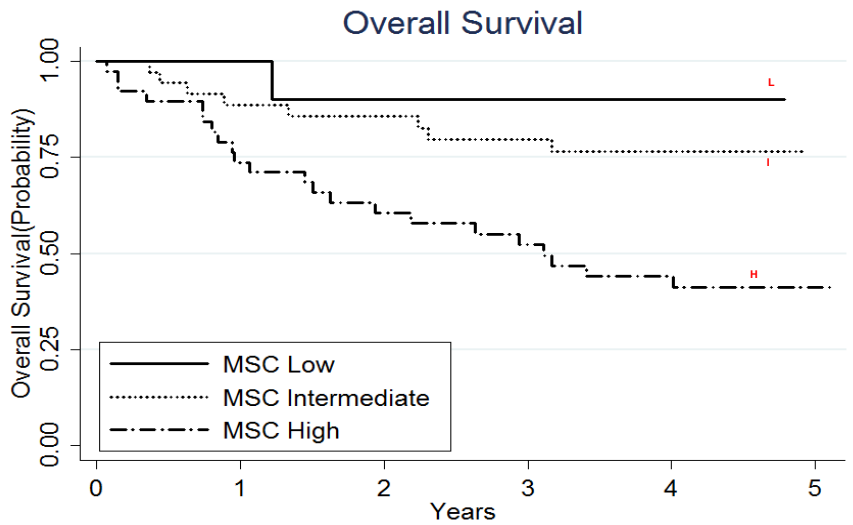
81% — **specificità**

80% — **riduzione dei falsi positivi TC**

monitoraggio della malattia



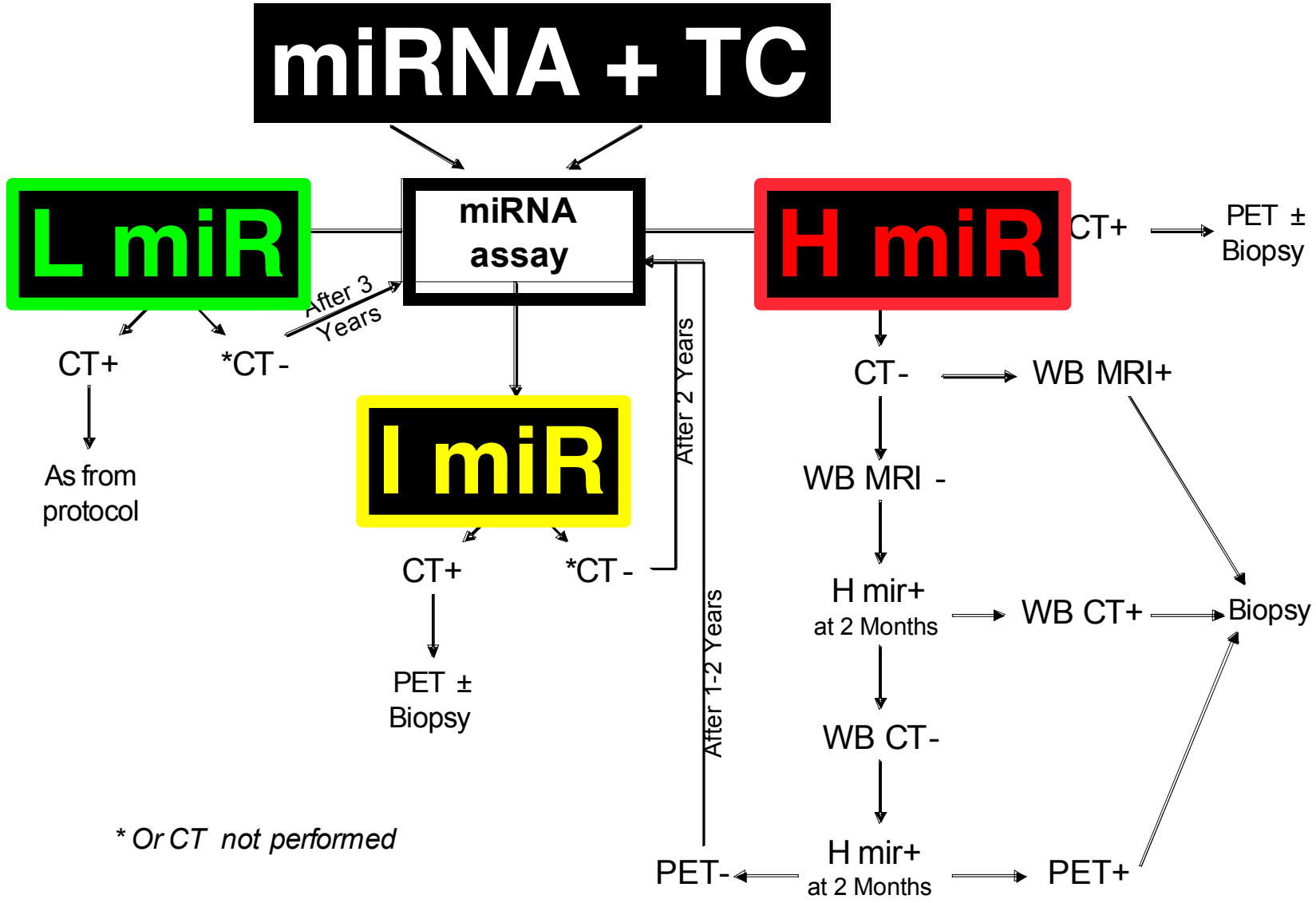
valore prognostico



Number at risk

MSC L	10	10	9	8	5	3
MSC I	36	31	30	25	24	19
MSC H	38	28	22	19	16	15

nuovo studio prospettico bioMILD



nuovo studio bioMILD

03 / 13 – 05 / 15

arruolati	7,725
eligibile	4,619
TC-miR	2,815

risultati:

4000 TC-miR:	12 / 15
analisi efficacia:	12 / 16

4,000 fumatori ≥ 50 anni

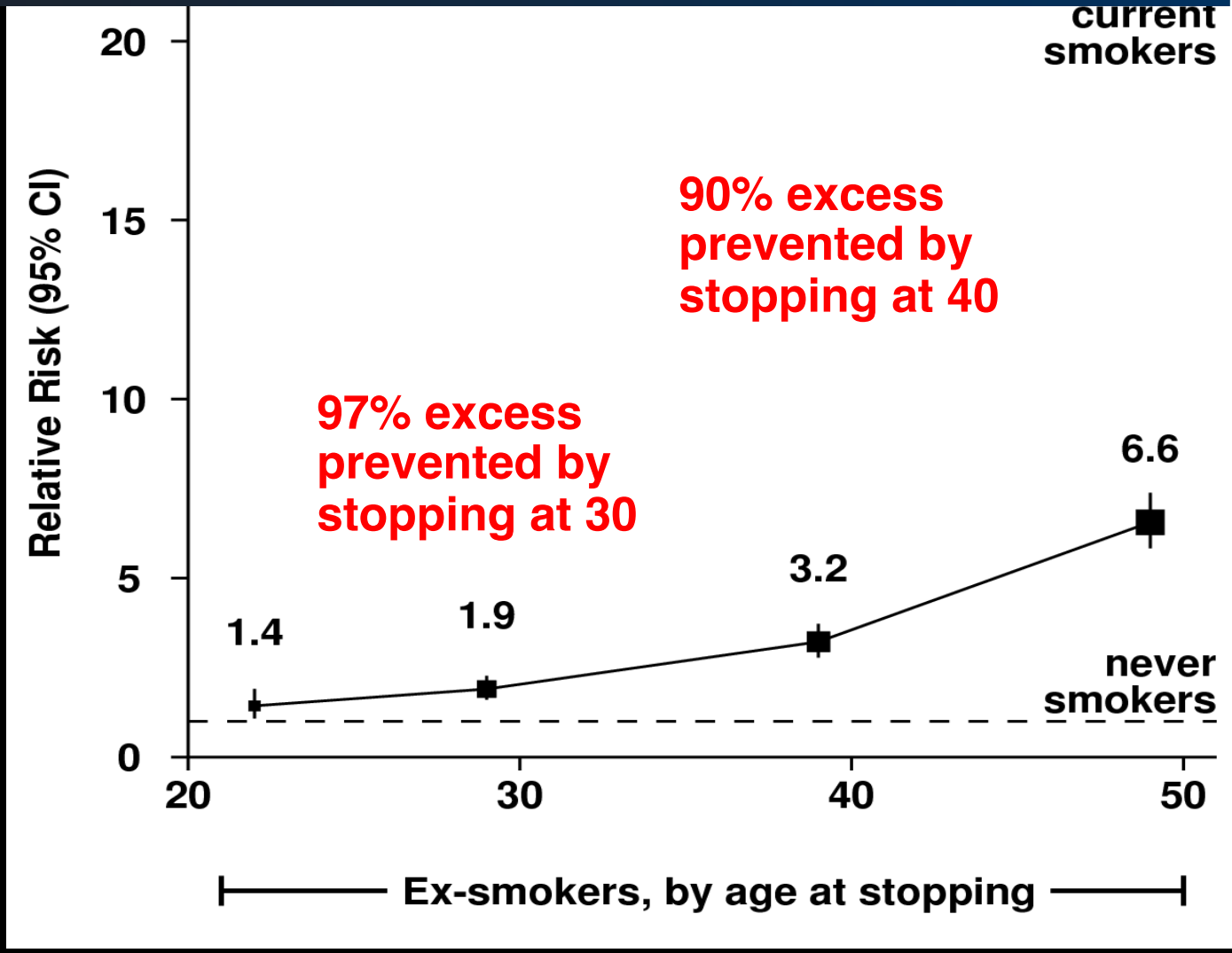
Screening TC: conclusioni (1)

- potrà ridurre la mortalità
- i risultati Europei sono cruciali
- ottimizzare il rischio individuale
- migliorare l'algoritmo diagnostico
- validare i biomarcatori

IASLC
15th World Conference on Lung Cancer
October 27 – October 30, 2013
Sydney, Australia
WCLC.IASLC.ORG

THE MILLION WOMEN STUDY

Reduction in lung cancer incidence by stopping smoking



Unpublished results

PL04.01 – Valerie Beral

Screening TC: conclusioni (2)

- prevenzione primaria come priorità
- smettere di fumare è essenziale in ogni programma di screening TC per ottenere benefici significativi
- farmaci anti-tabacco nei LEA