



PNEUMOLOGIA 2016

Milano, 16 – 18 giugno 2016 · Centro Congressi Palazzo delle Stelline

DIAGNOSI PRECOCE O PREVENZIONE NELLE MALATTIE POLMONARI CRONICHE

Ugo Pastorino

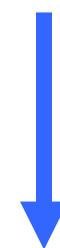
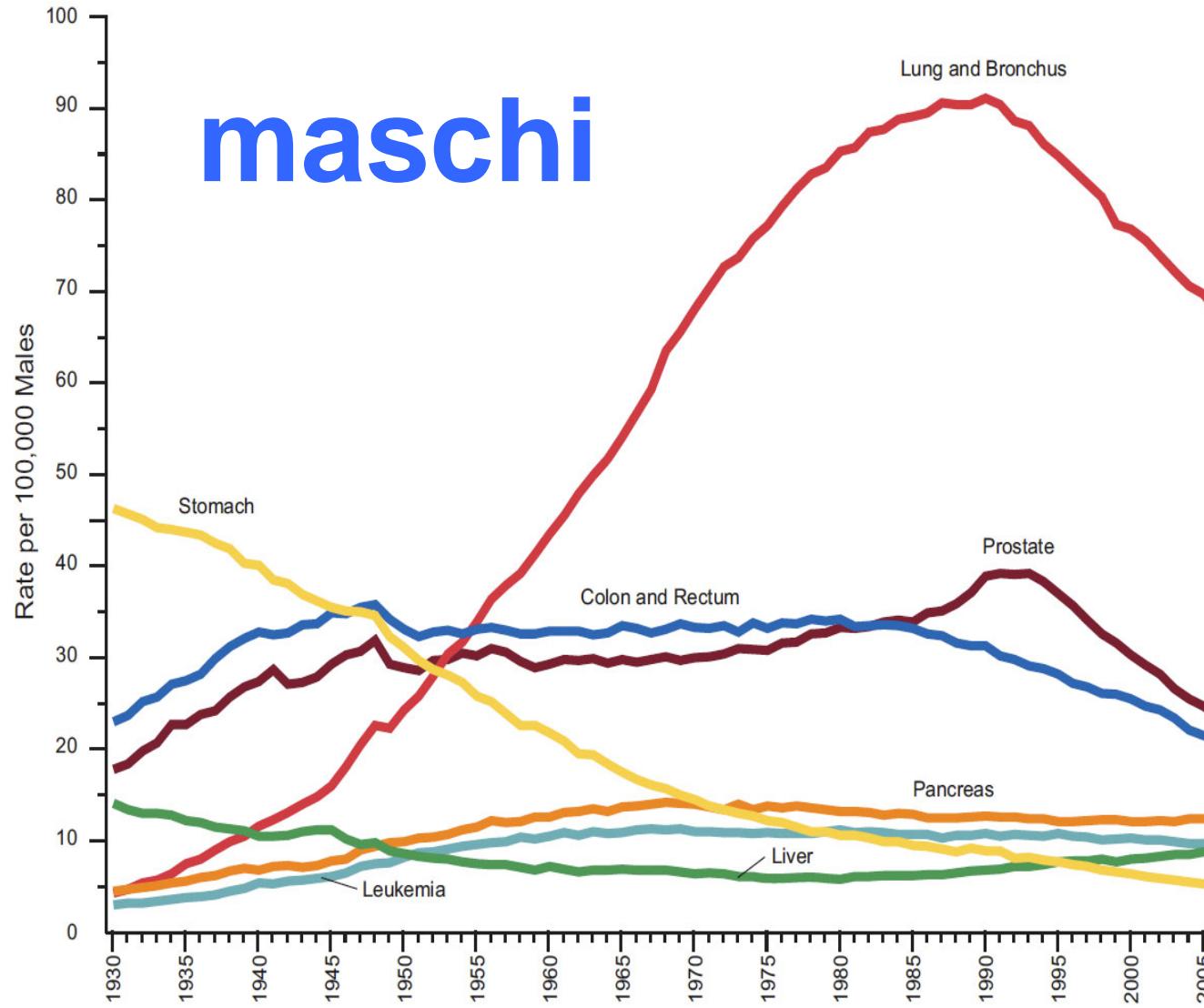
Chirurgia Toracica, Istituto Nazionale Tumori, Milano

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mortalità per cancro negli USA

1930 → 2005

maschi



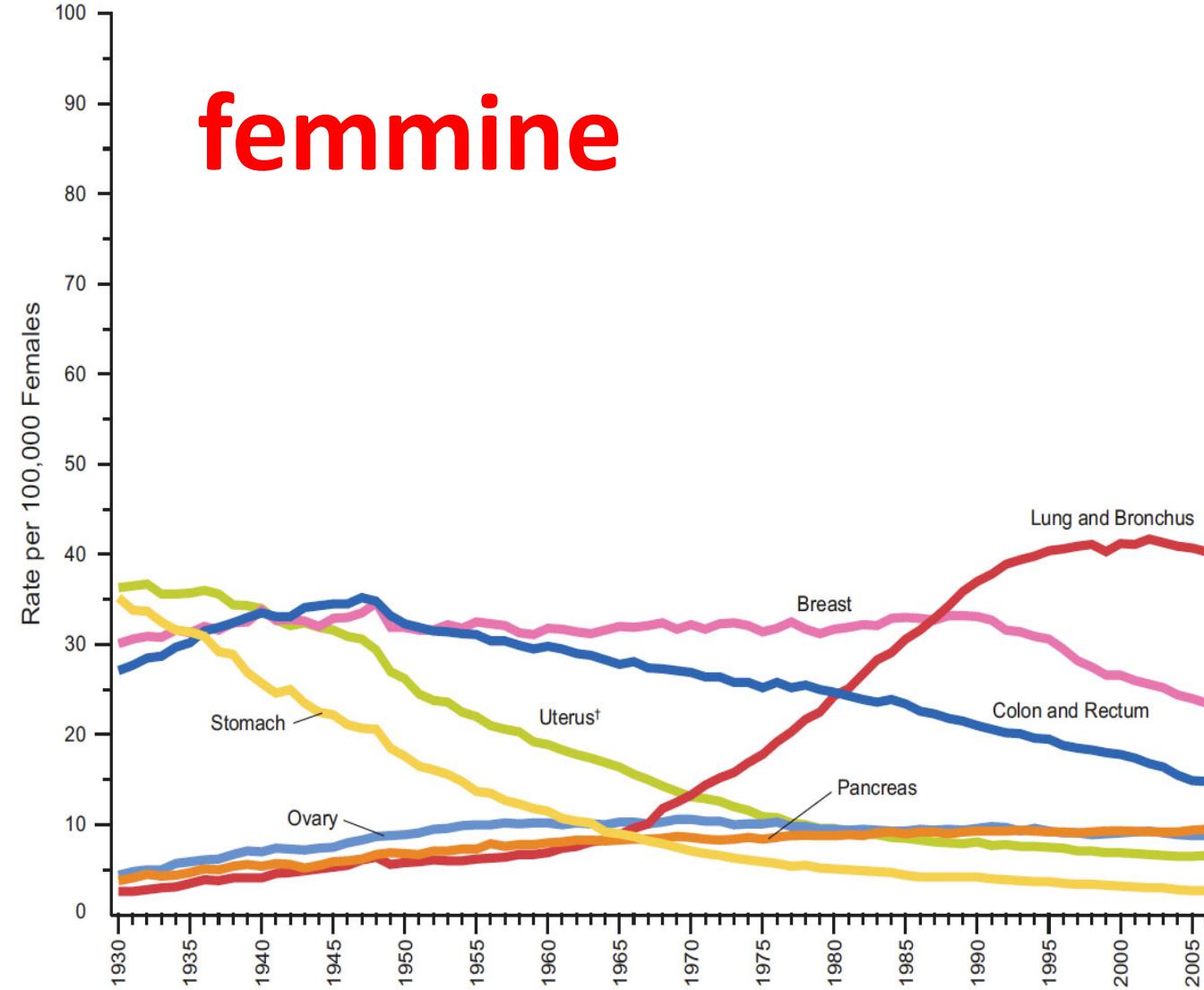
Jemal, CA Can J
Clin
60:277, 2010

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mortalità per cancro negli USA

1930 → 2005

femmine



Jemal, CA Can J Clin
60:277, 2010

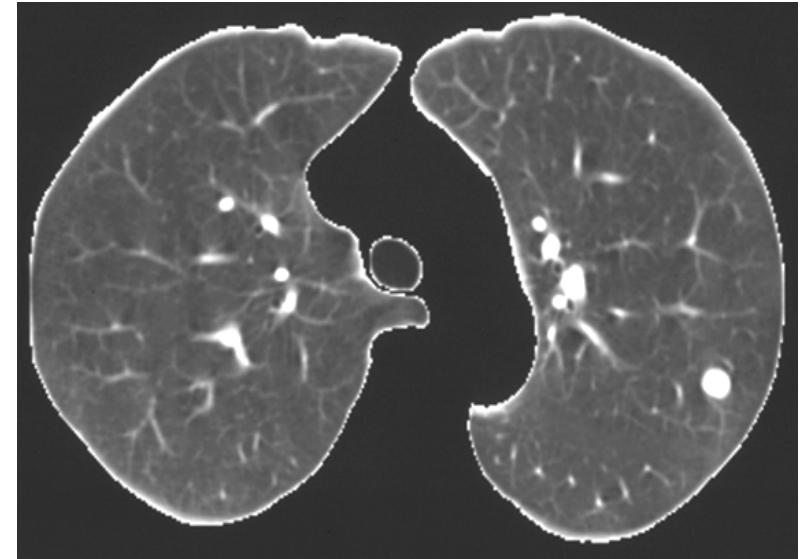
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perche la TAC spirale è importante ?

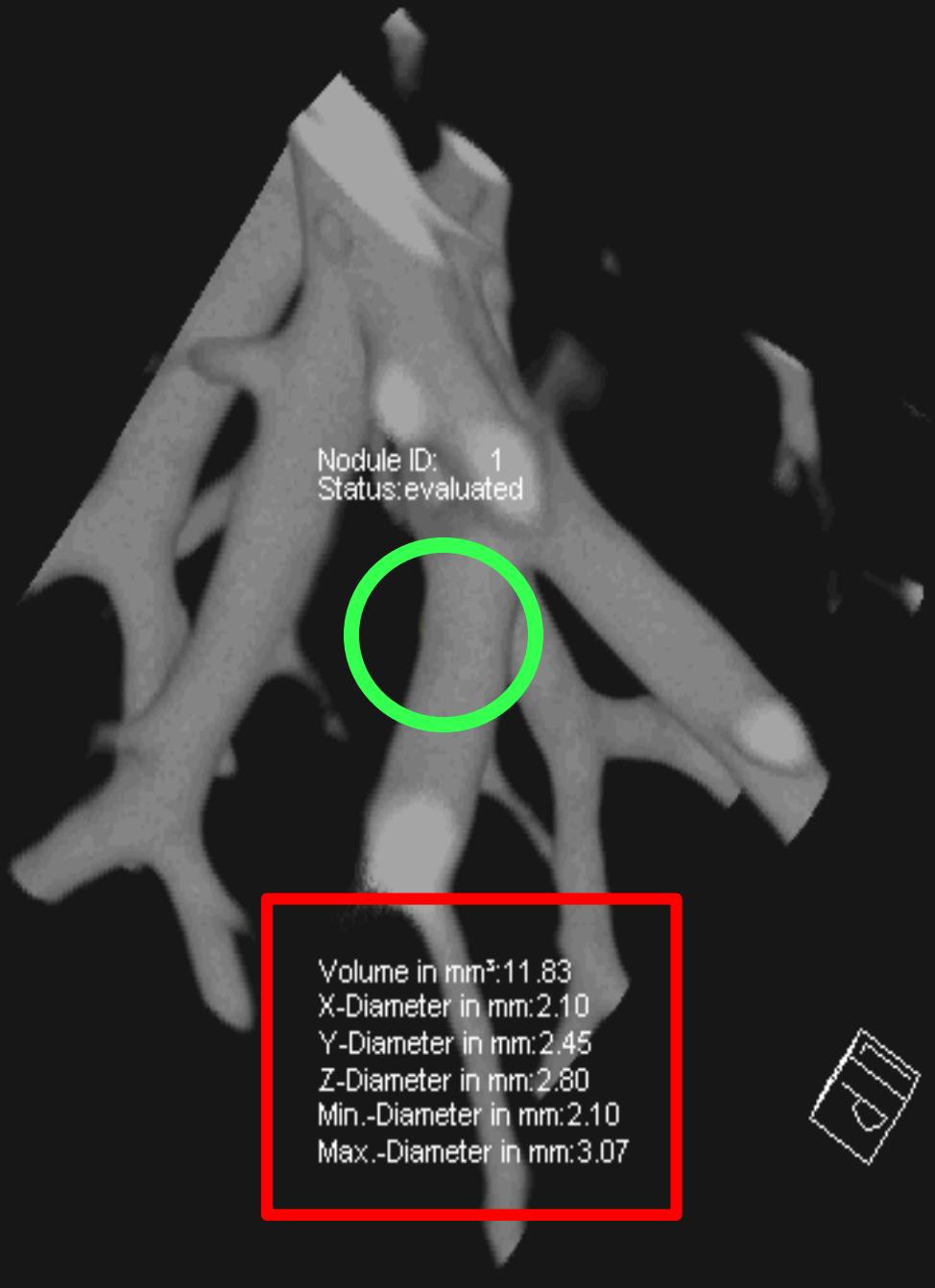


**volume totale
in < 10 sec**

**ottima sensibilità
per noduli > 3 mm**



**bassa dose di radiazioni
niente contrasto in vena**



MILD

nuova
TAC spirale
16-slice:
migliore
accuratezza
diagnostica

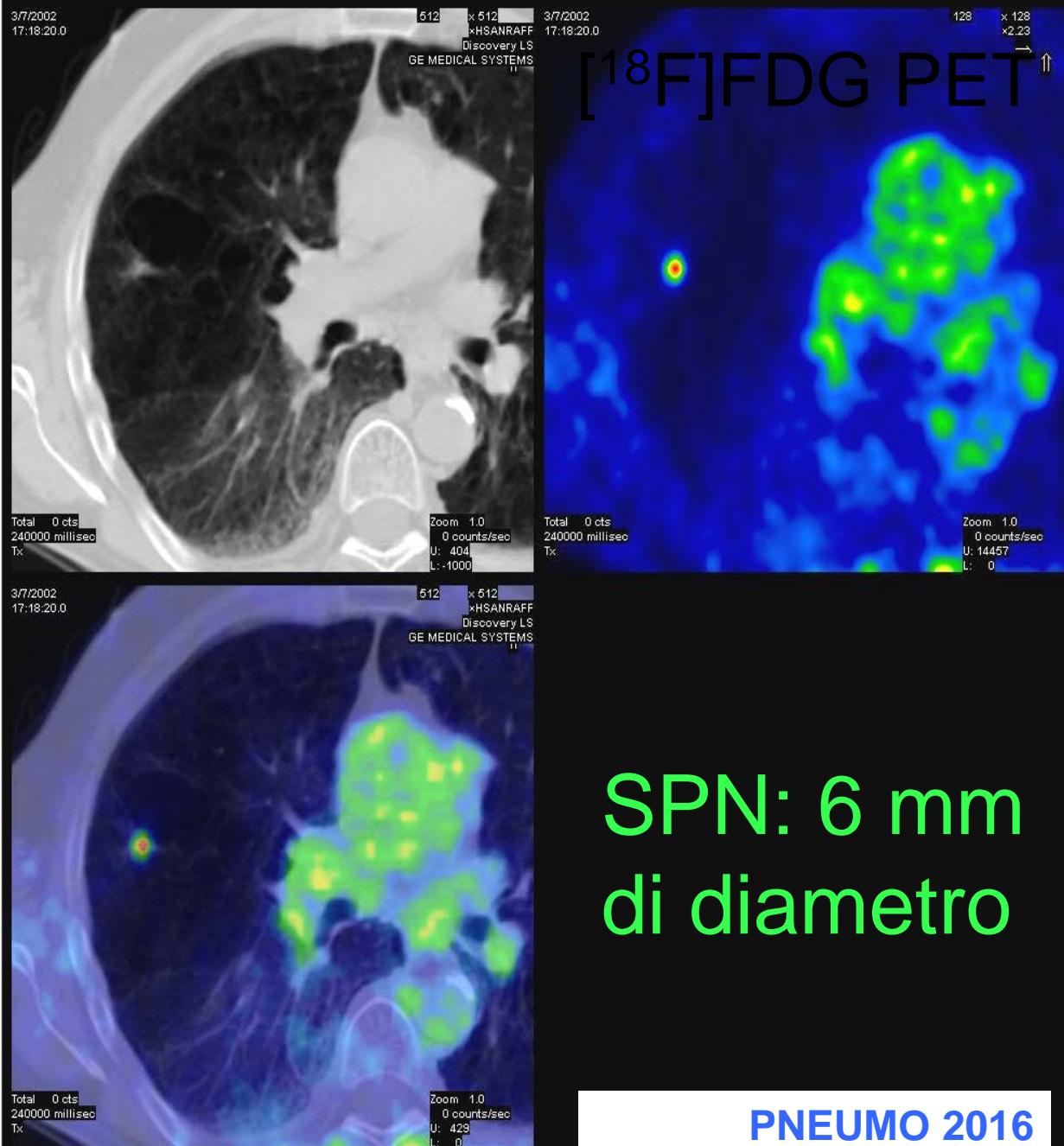
+ CAD

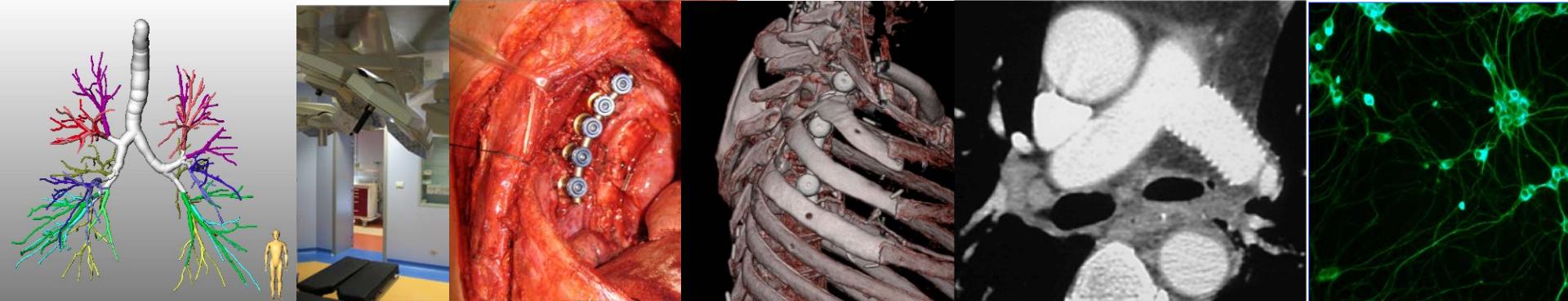
N LUI

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MILD

fusione
CT / PET





30 anni di chirurgia: **suturatrici meccaniche**

PKS 1961



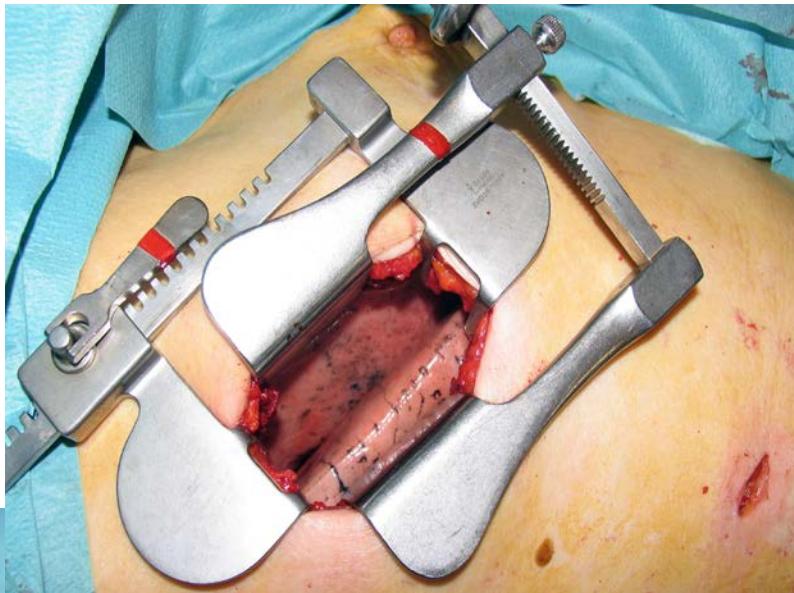
1991

2015



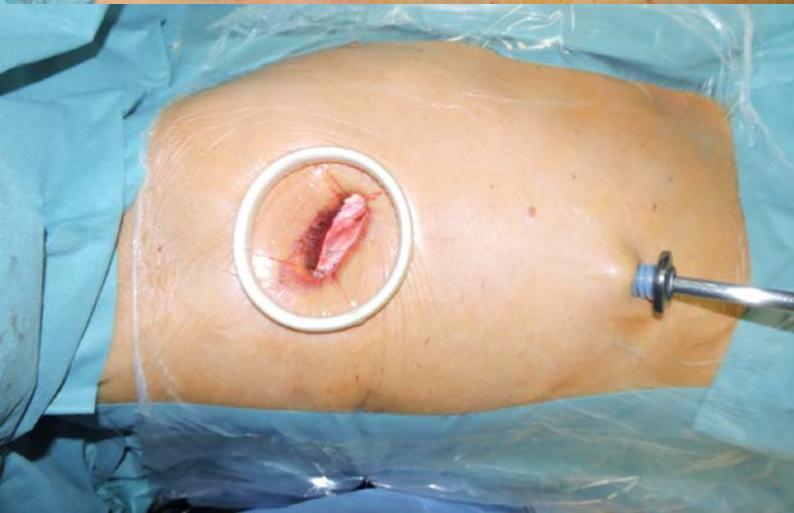
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30 anni di chirurgia: APPROCCIO MINI-INVASIVO



1995

> 90% DEGLI
INTERVENTI
IN CHIRURGIA
TORACICA

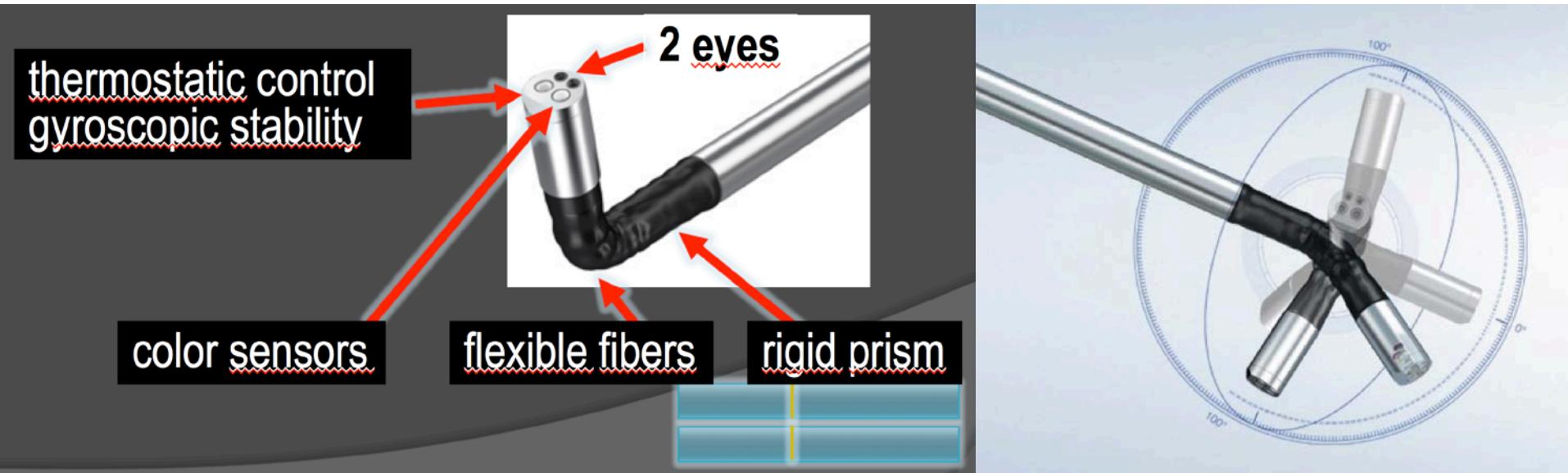


2015

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DIAGNOSI PRECOCE E CHIRURGIA

- approccio mini-invasivo come standard
- lobectomia in VATS fattibile > 90% dei casi
- linfadenectomia essenziale (3N1 + 3N2)
- nuova tecnologia 3D = migliore efficacia



15 ANNI DI SCREENING CON TC SPIRALE

ELEVATA ACCURATEZZA DIAGNOSTICA
STADIO + INIZIALE DELLA MALATTIA
CHIRURGIA MENO INVASIVA

	soggetti	TC positive	LC	stadio I
non RCT	16	71,935	21%	1.0%
all RCTs	8	44,629	23%	1.1%

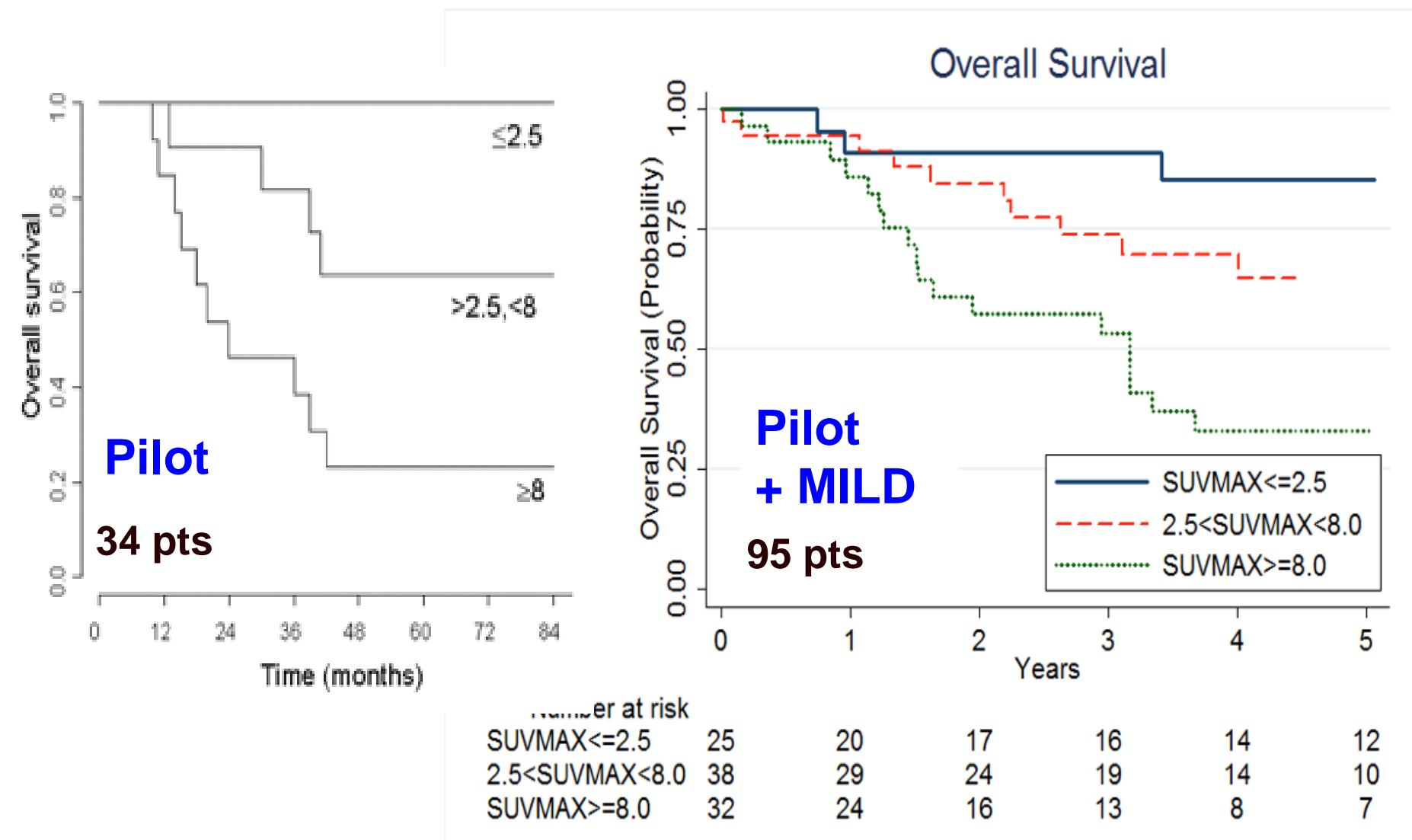
115,000 fumatori valutati

DIAGNOSI DIFFERENTIALE : LA PET E' UTILE ?

chirurgia per lesioni benigne

DLCST 2012	32%
LUSI 2012	29%
NELSON 2009	27%
DANTE 2009	24%
NLST 2011	24%
MILD 2012	8%

PET e diagnosi precoce: profilo metabolico



DIAGNOSI PRECOCE: CON QUALE FREQUENZA ?

Eur Radiol

DOI 10.1007/s00330-016-4228-3



CHEST

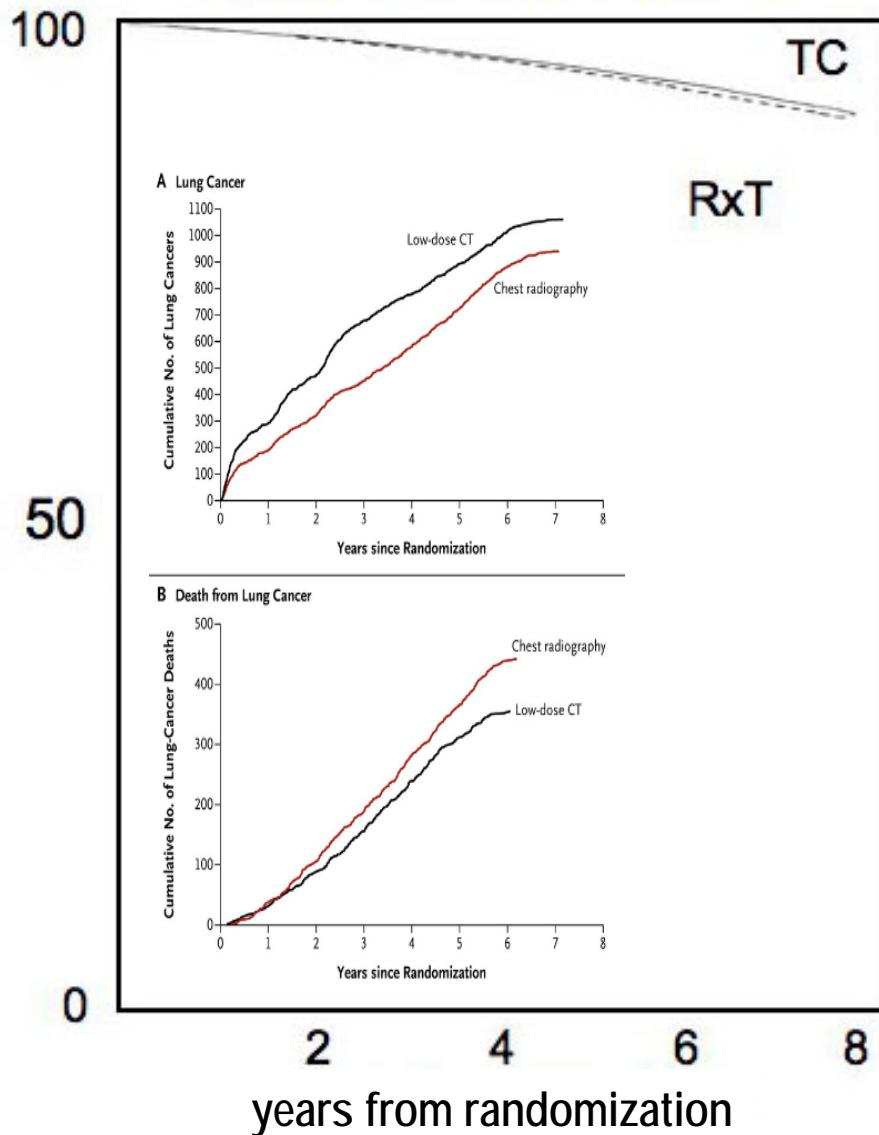
Low-dose computed tomography for lung cancer screening: comparison of performance between annual and biennial screen

Nicola Sverzellati¹ • M. Silva¹ • G. Calareso² • C. Galeone³ • A. Marchianò² • S. Sestini⁴ •
G. Sozzi⁵ • U. Pastorino⁴

va bene anche ogni 2 anni

- Biennial LDCT screening may be as efficient as the annual screening.
- Annual and biennial LDCT screening have similar frequency of interval lung cancers.
- Biennial screening may save about one third of LDCT scans.

STUDIO NLST: QUANTO SI RIDUCE LA MORTALITA' ?



53,454 persons: 3 rounds of LDCT screening vs CXR

- 20% reduction of lung cancer mortality
7% reduction all cause mortality
 - 24.2% positive subjects
96.4% false positive = **PPV 3.6%**
 - overdiagnosis by LDCT : > 18% overall
up to 79% for indolent cancers
- 1% / per anno

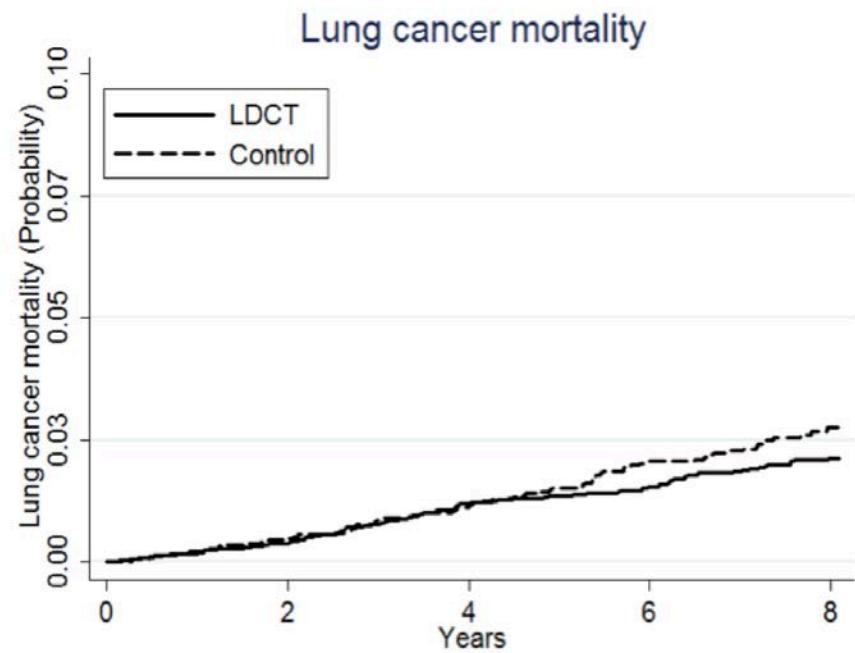
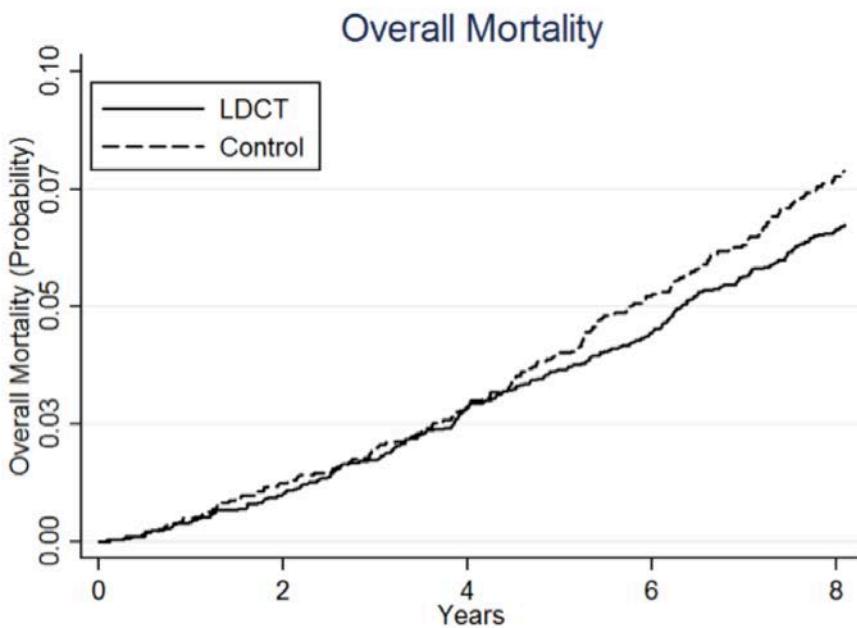
Aberle DR., N Engl J Med 2011
Patz EF., JAMA 2013

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RISULTATI IN ITALIA: ANALISI COMBINATA DI DANTE E MILD

6,549 partecipanti, 52,637 anni/uomo, 520 morti

riduzione -11% della mortalità nel braccio di diagnosi precoce
rispetto al braccio di controllo, HR = 0.89 (95% CI: 0.74-1.06)



LESIONI NON SOLIDE : E' NECESSARIO ASPORTARLE ?

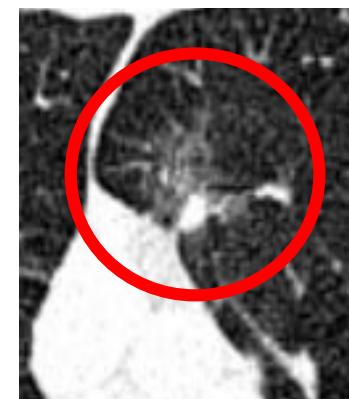
Long-Term Surveillance of Ground-Glass Nodules *Evidence from the MILD Trial*

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

solo uno (1.3%) progredito (ADC stadio Ia)

3 hanno sviluppato un cancro in altre zone del polmone



si possono valutare nel tempo

J Thor Oncol 7:1541, 2012

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analisi dell' enfisema con TAC spirale

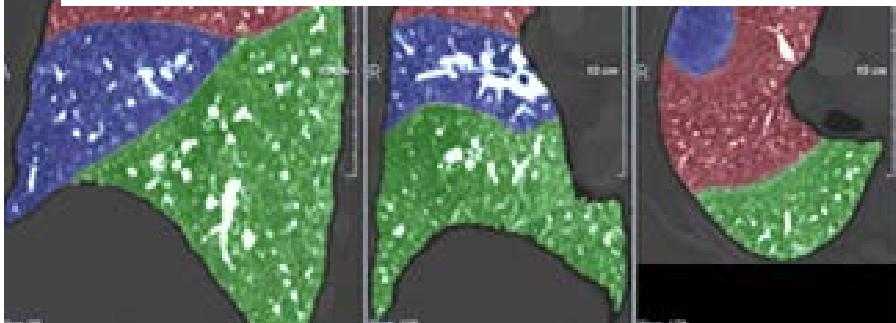


Eur Respir J 2010; 35: 146–151
DOI: 10.1183/09031936.00049909
Copyright ©ERS Journals Ltd 2010

Lung function predicts lung cancer risk in smokers: a tool for targeting screening programmes

E. Calabrò*, G. Randi#, ¶, C. La Vecchia#, ¶, N. Sverzellati+, A. Marchianò§, M. Villani†,
M. Zompatori**, R. Cassandro##, S. Harari## and U. Pastorino*

- densità polmonare media
- pixel, “bulla index”
- sede anatomica enfisema



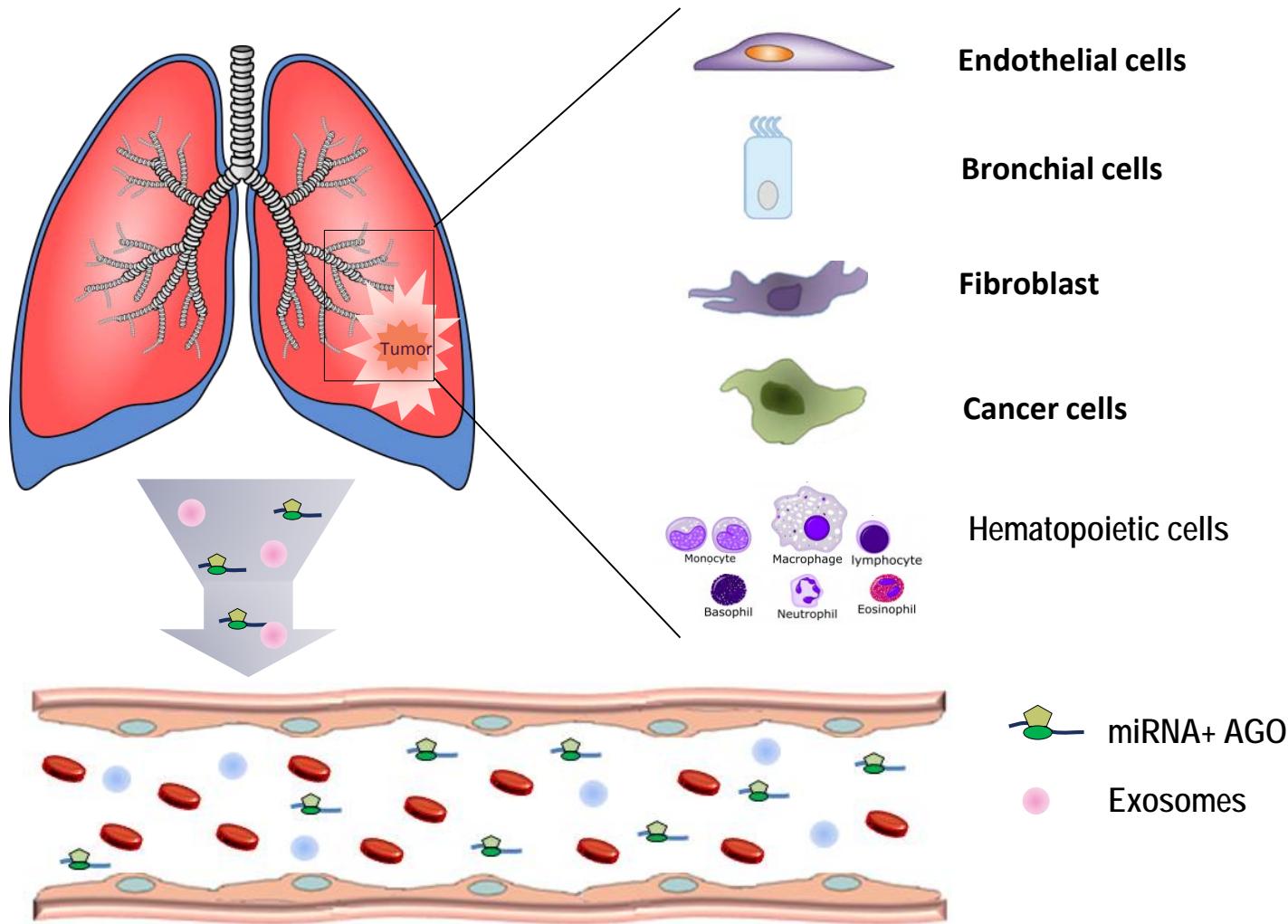
DIAGNOSI PRECOCE E RICERCA TRASLAZIONALE

studi di screening in corso all'INTM

2000	INT-IEO pilota:	1,035	14,000 AU
2005	MILD randomizzato:	2,376	20,000 AU
2013	bioMILD miRNA + LDCT:	4,100	6,000 AU
N. totale partecipanti		7,500	40,000 AU

campioni di sangue e tessuti
congelati - 80° > 100,000

Origine e rilascio dei miRNA nel sangue dei pazienti con tumore polmonare



miRNA più frequenti nel plasma

miR-499 miR-15b let-7d
miR-221 miR-378a miR-432 miR-27a miR-22 miR-145 miR-379
miR-140-3p miR-154-3p miR-484 miR-133b miR-133a miR-320
miR-21 miR-140-5p miR-197 miR-30c miR-32
miR-30e-3p **miR-17-5p** miR-30b miR-106a miR-374
miR-139-5p miR-31 miR-574-5p **miR-486-5p** miR-342
miR-92a miR-155 miR-200b-5p
miR-29a let-7f miR-660
miR-28-3p **miR-142-3p** miR-148a miR-328 miR-30d
miR-210 miR-30a-3p miR-151a-5p
miR-146b miR-148b miR-223 miR-26a miR-182 miR-376a
miR-629 miR-29c miR-100 miR-16 miR-103
miR-331 miR-566 miR-19b miR-451 miR-1
miR-101 miR-191
let-7b

I BIOMARCATORI POSSONO MIGLIORARE LA DIAGNOSI ?

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

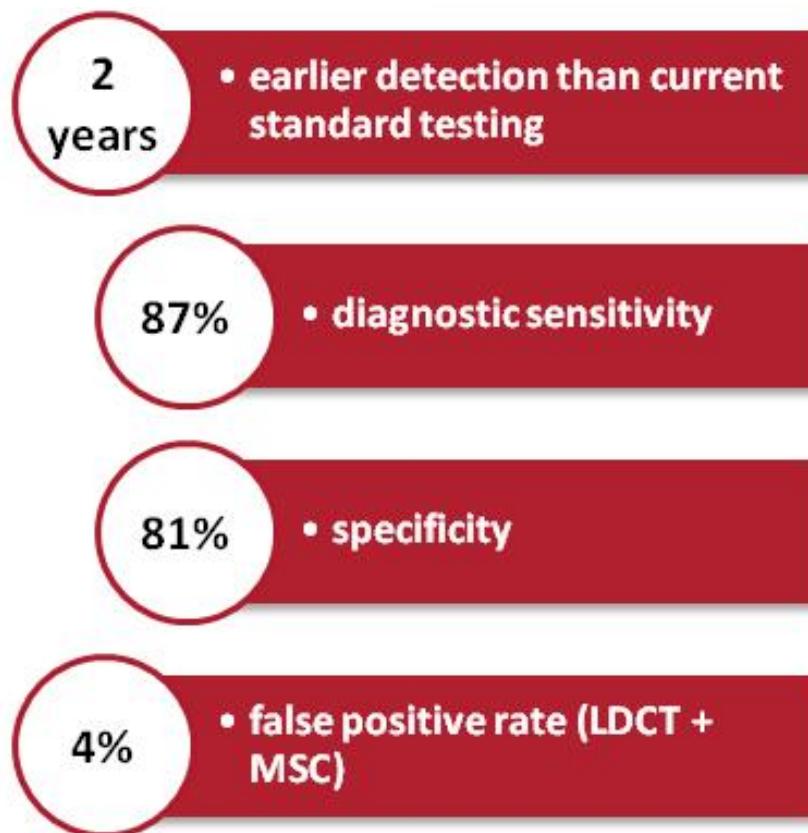
falsi positivi:

solo TC

96%

TC + miRNA

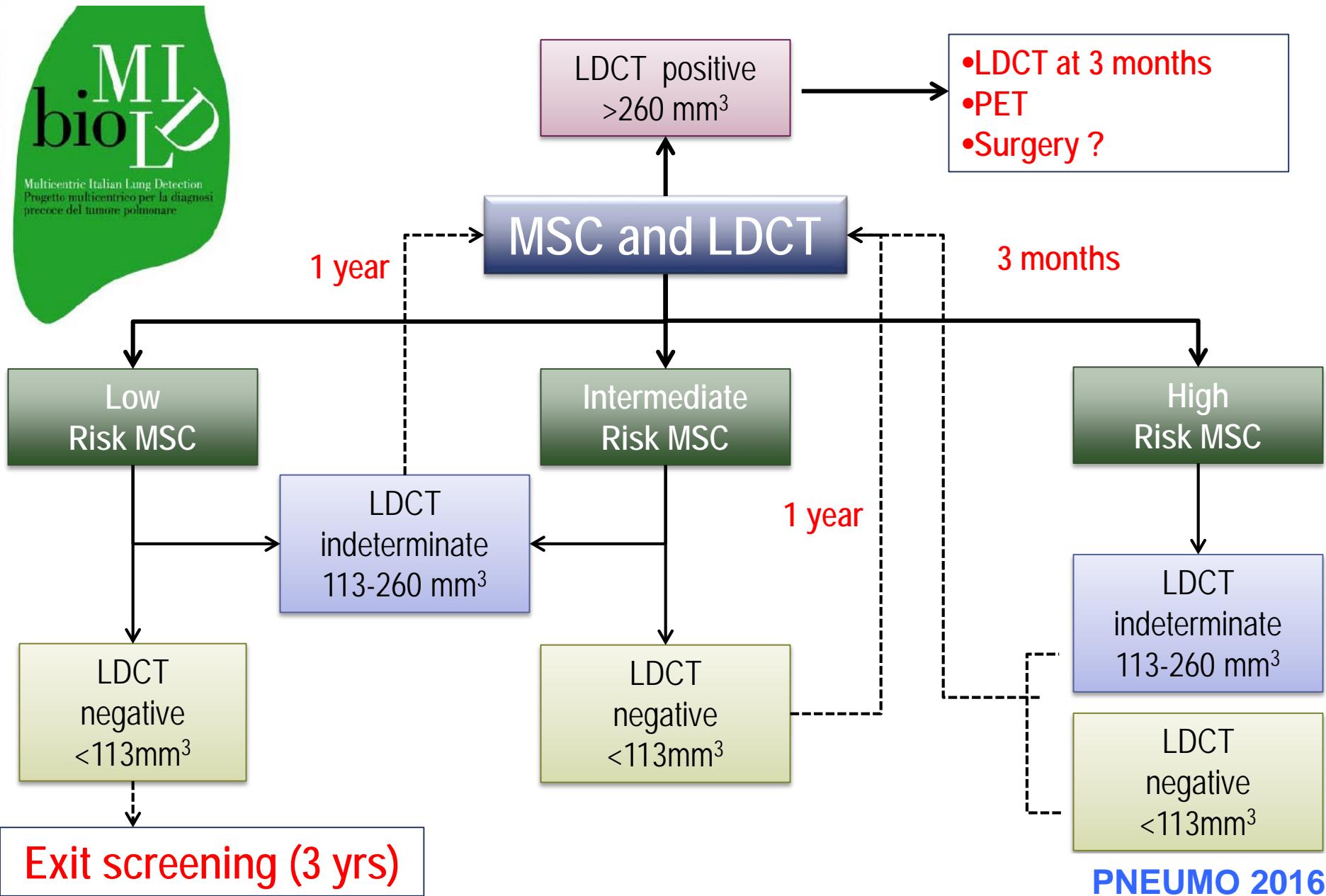
4%



J Clin Onol 10;32:768

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MIRNA + TC: STUDIO BIOMILD SU 4,000 SUGGETTI



PERCHE' LA DIAGNOSI PRECOCE NON E' PIU' EFFICACE ?

50-Year Trends in Smoking-Related Mortality in the United States

Michael J. Thun, M.D., Brian D. Carter, M.P.H., Diane Feskanich, Sc.D.,
Neal D. Freedman, Ph.D., M.P.H., Ross Prentice, Ph.D., Alan D. Lopez, Ph.D.,
Patricia Hartge, Sc.D., and Susan M. Gapstur, Ph.D., M.P.H.

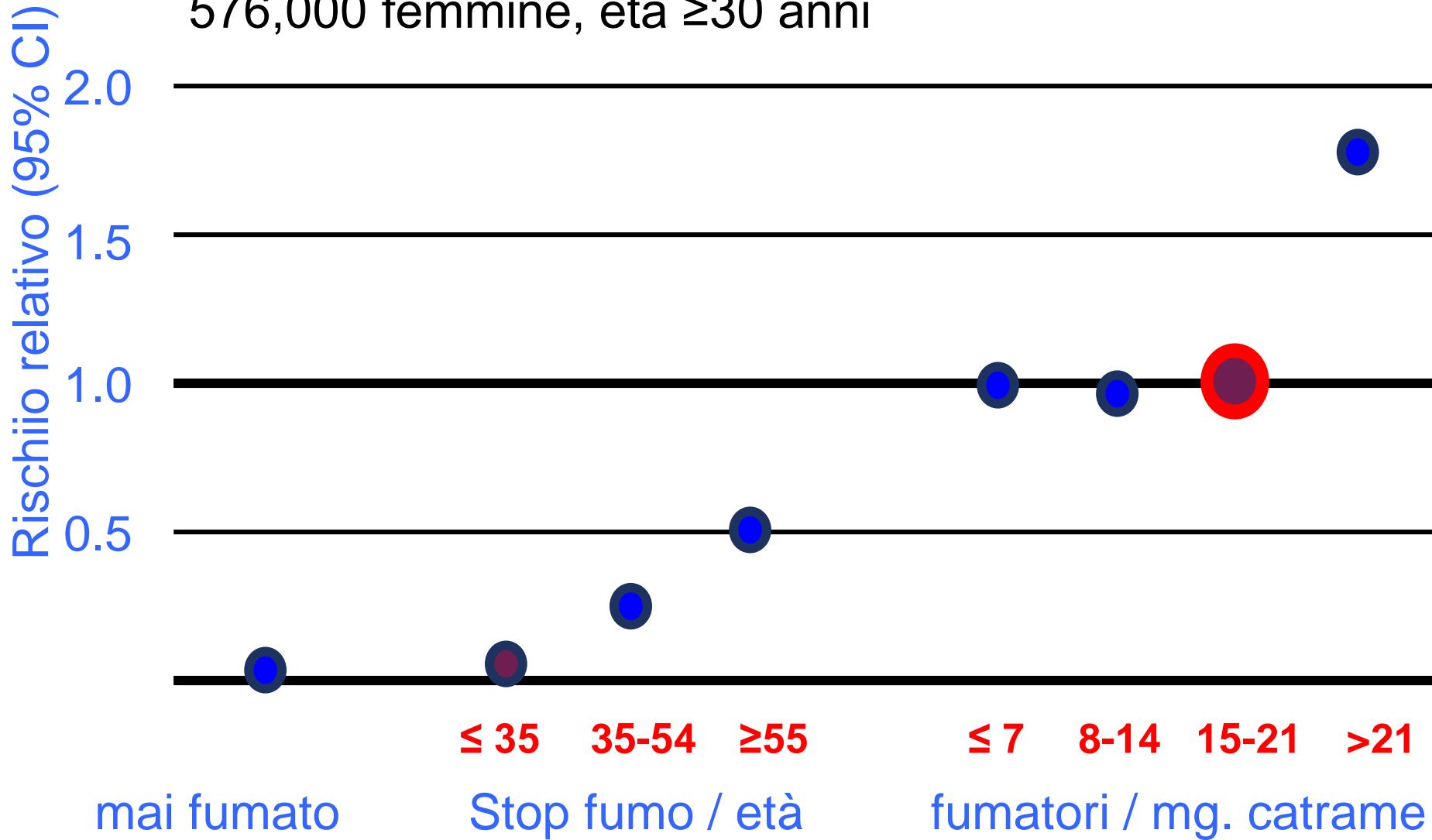
956,761 soggetti età 55-85, 56% fumatori

% DEATHS	maschi	femmine
fumatori	21%	20%
ex	10%	9%

sigarette leggere: il rischio non cambia

Harris, BMJ 2004;328:72

576,000 femmine, età ≥ 30 anni



NUOVI RISULTATI: SMETTERE DOPO 40 ANNI E' POSSIBILE

TJ

ISSN 0300-8916

Tumori 2015; 101(3): 306-311
DOI: 10.5301/tj.5000282

ORIGINAL ARTICLE

efficacia della varenicline

187 MILD subjects, on LDCT screening > 5 yrs

A combined smoking cessation intervention within a lung cancer screening trial: a pilot observational study

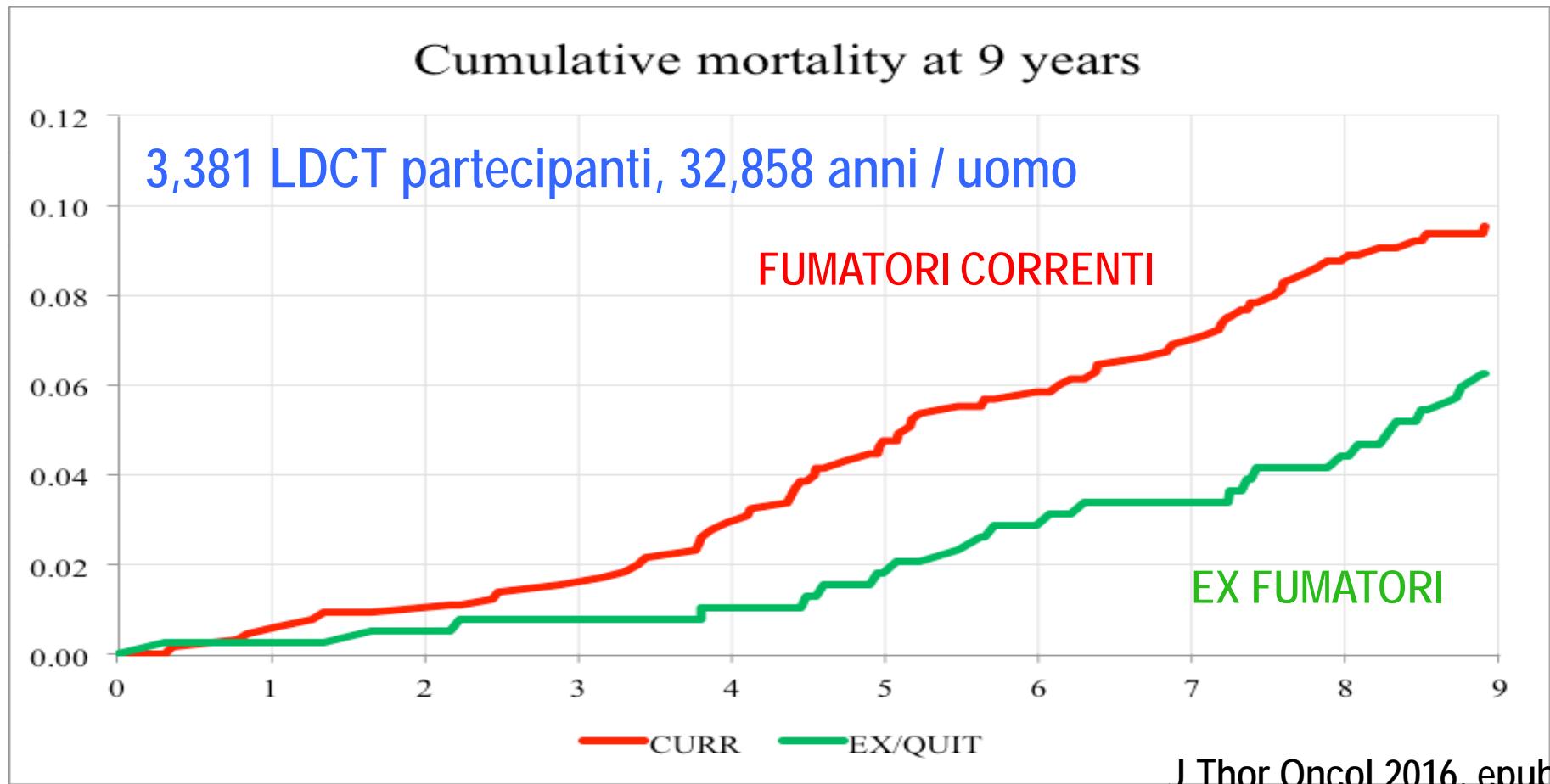
Paolo Pozzi¹, Elena Munarini¹, Francesca Bravi², Marta Rossi^{2,3}, Carlo La Vecchia^{2,3}, Roberto Boffi¹, Ugo Pastorino⁴

cessazione dopo
un solo trattamento:

3 mesi	12 mesi
49%	20%

NUOVI RISULTATI: SMETTERE E' PIU' EFFICACE DELLA TC

Stopping Smoking Reduces Mortality in Low-Dose Computed Tomography Screening Participants



NUOVI RISULTATI: SMETTERE E' PIU' EFFICACE DELLA TC

Stopping Smoking Reduces Mortality in Low-Dose Computed Tomography Screening Participants

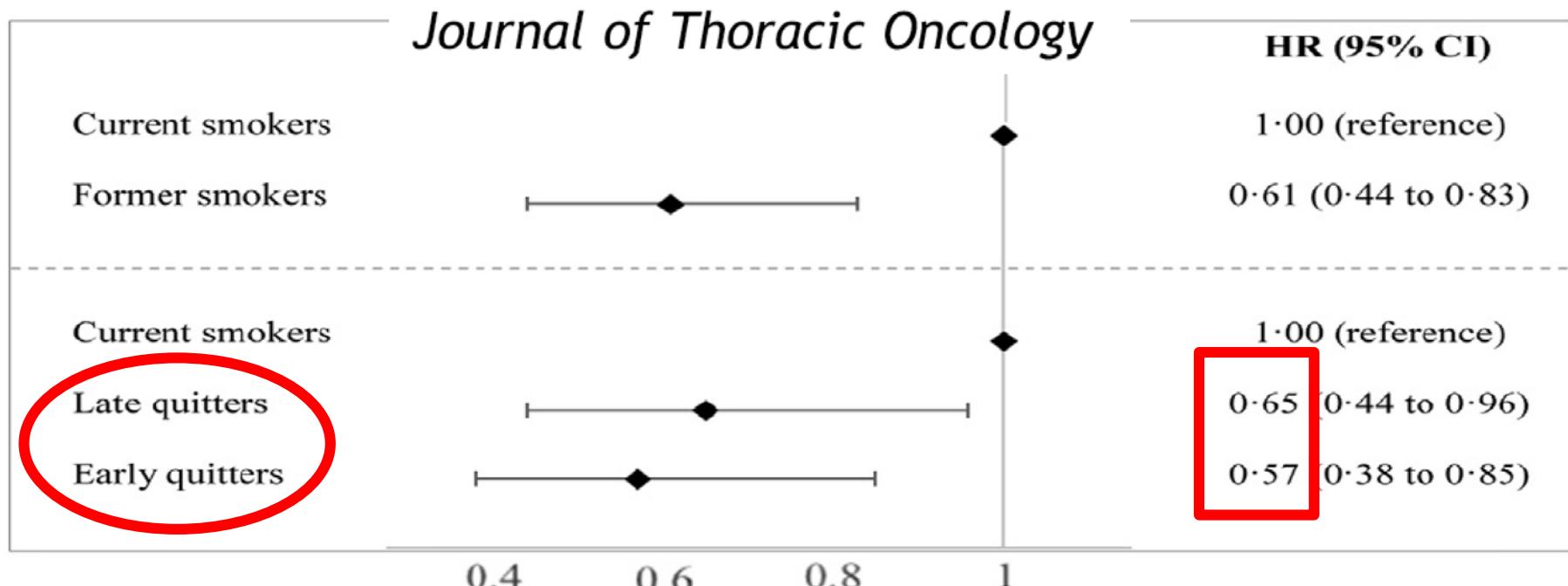


Figure 3. Effect of smoking cessation on overall mortality. Hazard ratios (Cox model) and corresponding 95% confidence intervals estimating the effect of smoking cessation on mortality. Estimates are adjusted for covariates measured at baseline (sex, age, predicted forced expiratory volume in the first second of expiration, and average number of pack-years during follow-up).

DIAGNOSI PRECOCE DEI TUMORI POLMONARI

- tecnica efficace ma migliorabile
- risultati degli studi Europei fondamentali
- ottimizzare la selezione dei soggetti a rischio
- migliorare l'algoritmo diagnostico
- validre i biomarcatori
- combinare diagnosi precoce e prevenzione

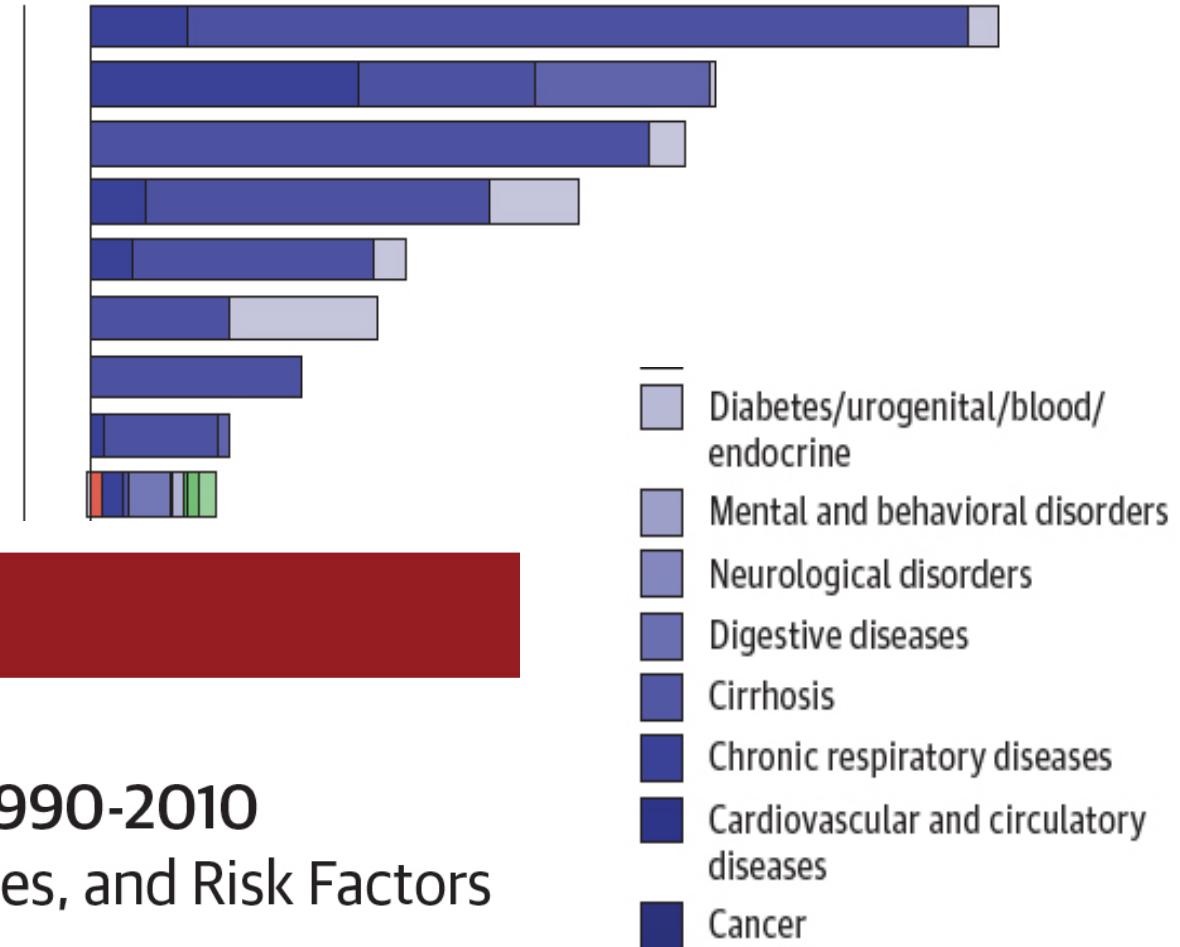
QUESTIONI APERTE: PER UNA MEDICINA SOSTENIBILE

- terapie biologiche per tutti i pazienti ???
- costo per anno di vita salvata > 150,000 €
- mortalità per BPCO e cardiovascolare
- efficace trattamento della dipendenza
- più anziani = più bisogno di prevenzione

A Risk factors and related deaths

Risk Factors

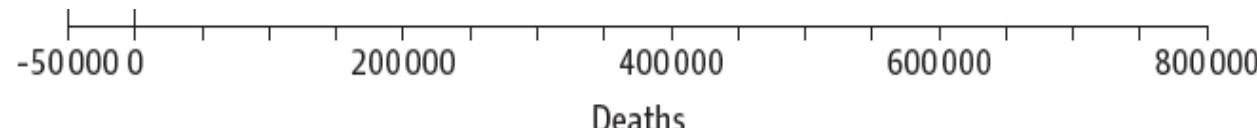
- Dietary risks
- Tobacco smoking
- High blood pressure
- High body mass index
- Physical inactivity and low physical activity
- High fasting plasma glucose
- High total cholesterol
- Ambient particulate matter pollution
- Alcohol use



Original Investigation

The State of US Health, 1990-2010
Burden of Diseases, Injuries, and Risk Factors

US Burden of Disease Collaborators



Baseline C-reactive protein level predicts survival of early-stage lung cancer: evidence from a systematic review and meta-analysis

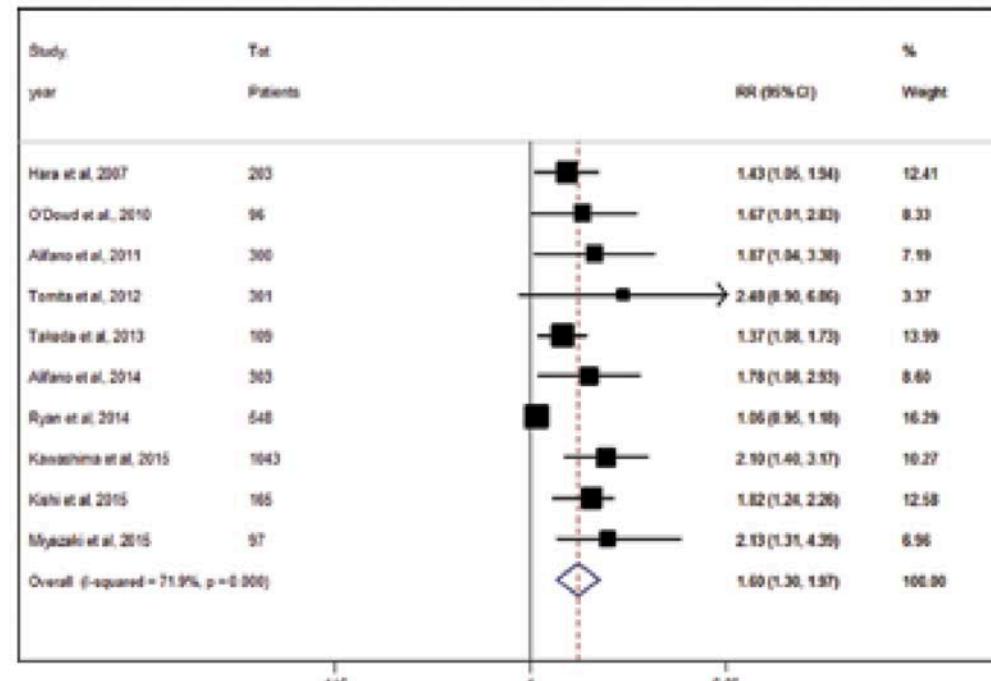
Giovanni Leuzzi¹, Carlotta Galeone², Mara Gisabella¹,
Daniele Morelli⁴, Ugo Pastorino¹

¹ Thoracic Surgery Unit, IRCCS Istituto Nazionale dei Tumori

² Department of Clinical Sciences and Community Health, Ur

³ Immunohematology and Transfusion Medicine Service, IRC

⁴ Department of Pathology and Laboratory Medicine, IRCCS



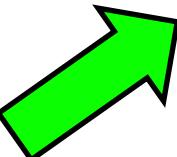
diagnosi precoce + prevenzione: studio SMILE



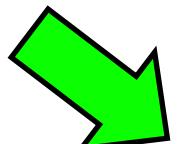
fase pilota 2016 - 2018
fattibilità e compliance

Popolazione:
2000 soggetti
55-75 anni
≥ 30 pacchi / anno

Random
1:1



counselling (Eurocode)
+ LDCT annuale o biennale



counselling (Eurocode)
+ LDCT annuale o biennale
+ **prevenzione integrata :**
• Farmaci (varenicline, cardioASA)
• Dieta bilanciata
• Esercizio fisico



stop smoking



start smiling