



**iPAAC**  
INNOVATIVE PARTNERSHIP  
FOR ACTION AGAINST CANCER

# Potential of new cancer screening programmes: updated evidence on lung and prostate cancer

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**Marco Zappa**

Prospettive e priorità di intervento nel controllo del cancro - Local Stakeholder Forum Italiano della Joint Action iPAAC” 13 Ottobre 2021



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**ISPRO**  
Istituto per lo studio, la prevenzione  
e la rete oncologica

# LE ATTIVITÀ DI DIAGNOSI PRECOCE HANNO DETERMINATO L'EPIDEMIA DEL TUMORE DELLA PROSTATA (NEL BENE E NEL MALE...)

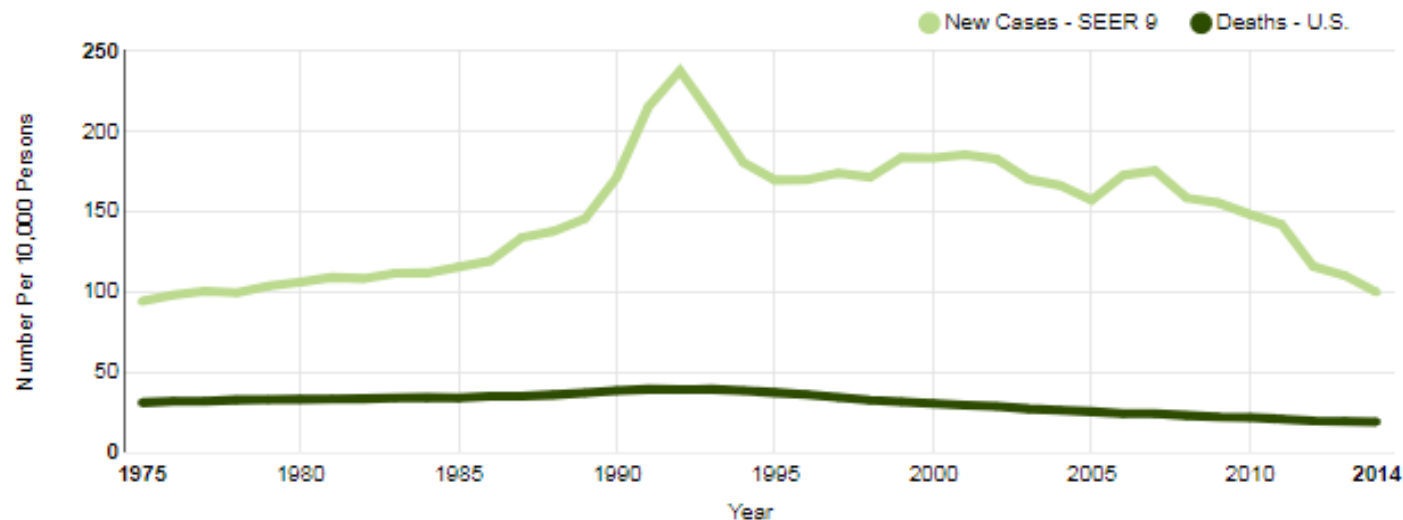


- dagli anni 80 → Enorme aumento di incidenza con uso PSA
- Diminuzione Mortalità e aumento enorme sopravvivenza
- Grandi trial che confermano (ERSPC) l'efficacia del PSA nel ridurre la mortalità per tumore della prostata ma a costo di una notevole sovradiagnosi
- Nessun programma organizzato
- Agenzie Regolatorie (USPTF 2012) che raccomandano contro (livello D) utilizzo PSA a fini di prevenzione . Posizione cambiata nel 2018 in livello C
- Grande diminuzione Incidenza ma anche tendenza a un aumento della mortalità



# SEER 9- Prostate Cancer incidence mortality survival

## New Cases, Deaths and 5-Year Relative Survival

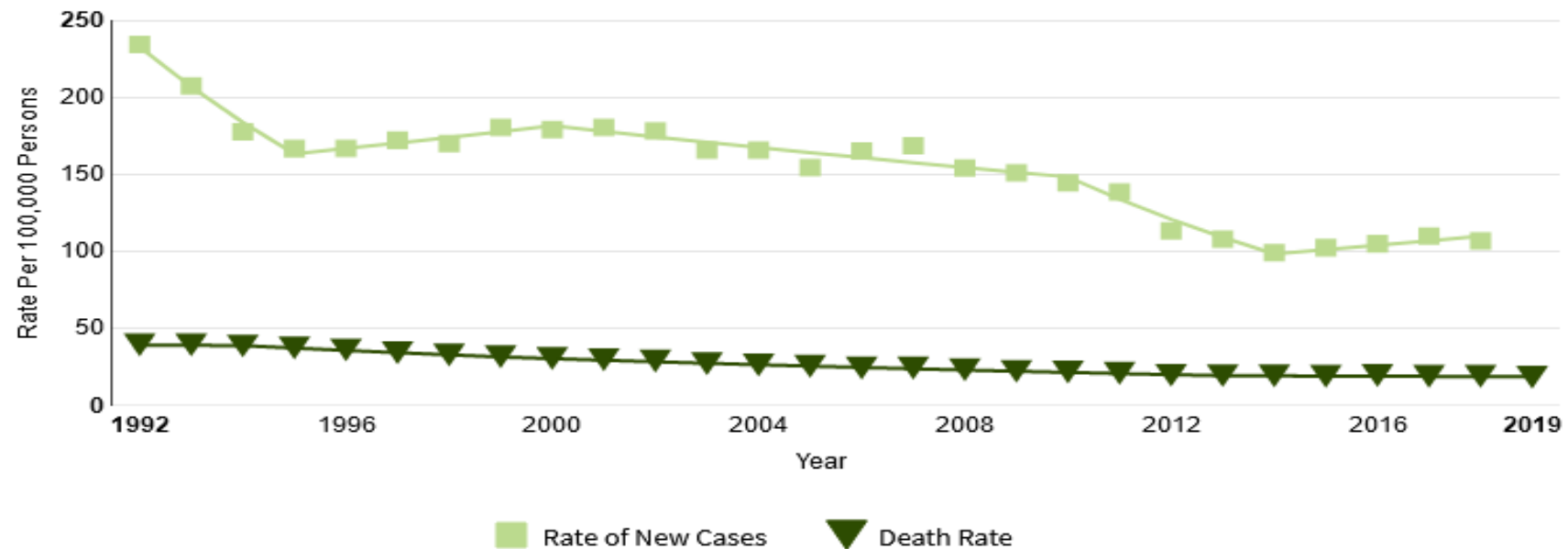


[View Data Table](#)

Year	1975	1980	1985	1990	1995	2000	2005	2009
5-Year Relative Survival	66.0%	70.2%	75.0%	88.5%	95.7%	98.8%	99.1%	99.3%



## Cancer Stat Facts: Prostate Cancer



New cases come from SEER 13. Deaths come from U.S. Mortality.

All Races, Males. Rates are Age-Adjusted.

Modeled trend lines were calculated from the underlying rates using the [Joinpoint Trend Analysis Software](#).

New cases are also referred to as incident cases in other publications. Rates of new cases are also referred to as incidence rates.

# US PC MORTALITÀ 1950 – 2019

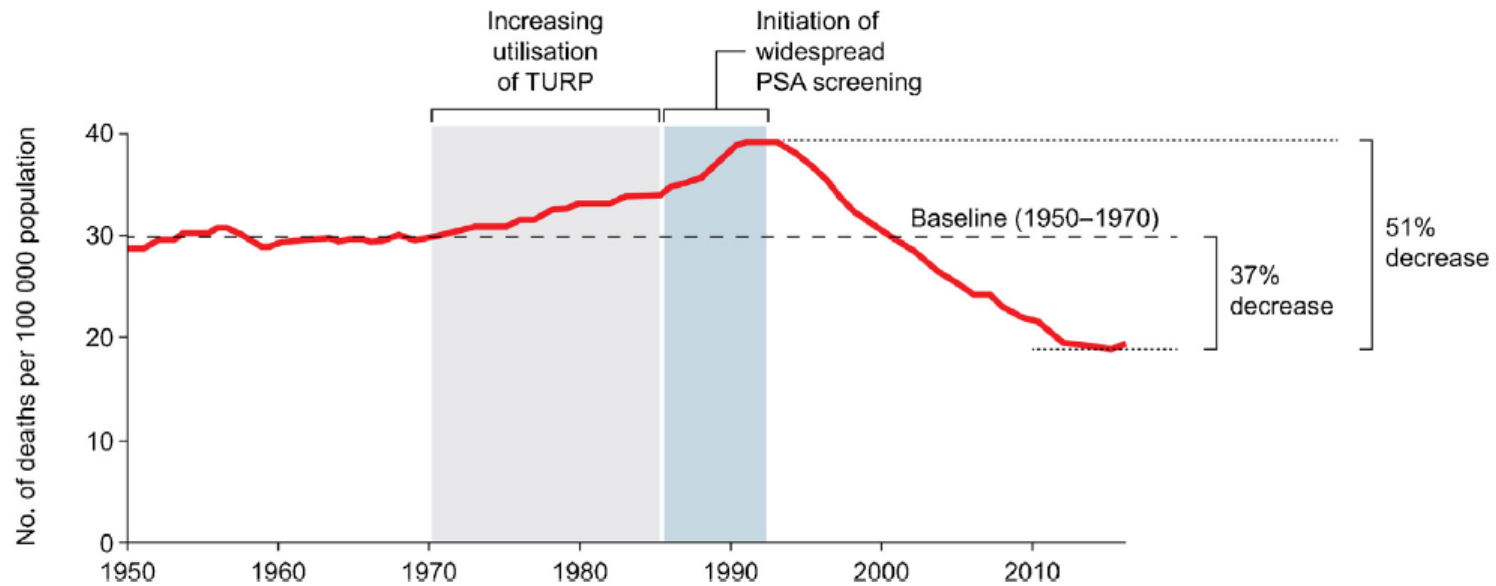


Fig. 2 – Prostate cancer-specific mortality rates in the USA from 1950 to 2019 [8].  
PSA = prostate-specific antigen; TURP = transurethral resection of the prostate.  
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# TUMORE DELLA PROSTATA LE ATTIVITÀ PREVENTIVE DETERMINANO L'EPIDEMIA DEL TUMORE (NEL BENE E NEL MALE...)

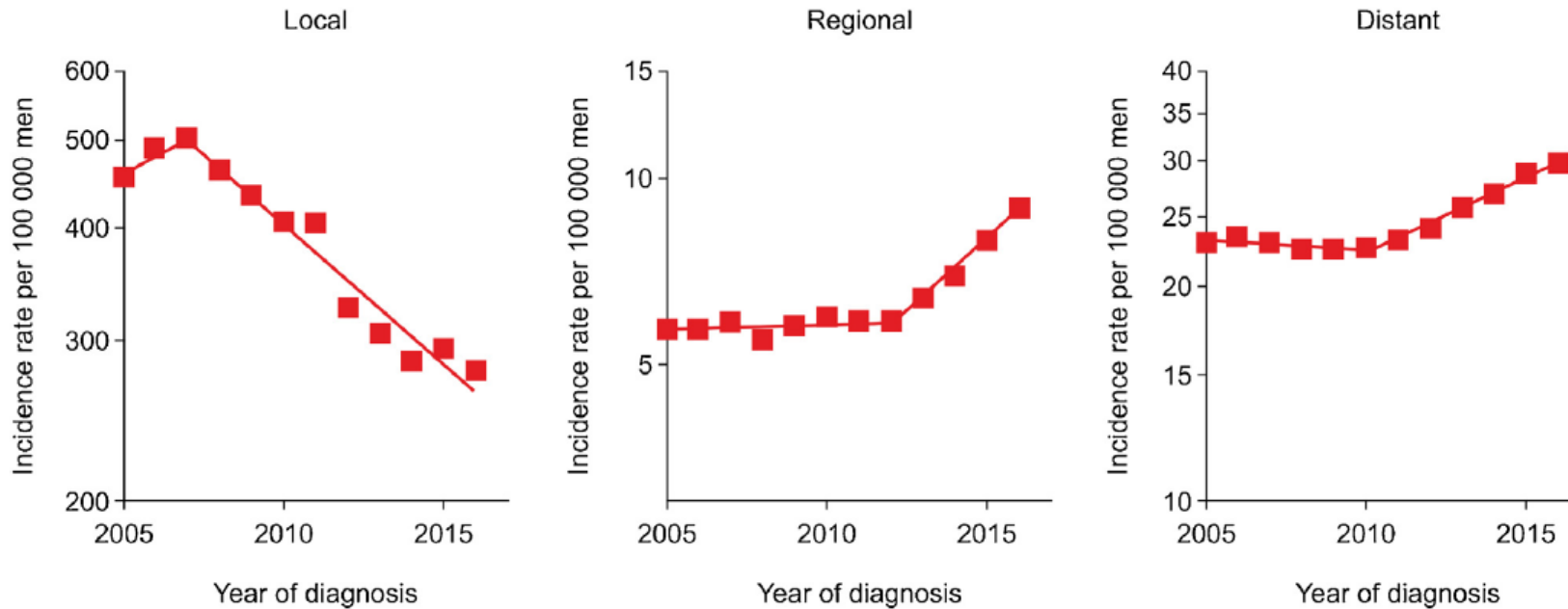


Fig. 3 – Stage migration in prostate cancer diagnoses in the USA after the USPSTF recommendations against PSA screening in 2012 [14].  
PSA = prostate-specific antigen; USPSTF = United States Preventive Service Task Force.  
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# USPTF FINAL RECOMMENDATION STATEMENT

## PROSTATE CANCER SCREENING

### MAY 08, 2018



#### Recommendation Summary

Population	Recommendation	Grade
Men aged 55 to 69 years	For men aged 55 to 69 years, the decision to undergo periodic prostate-specific antigen (PSA)-based screening for prostate cancer should be an individual one. Before deciding whether to be screened, men should have an opportunity to discuss the potential benefits and harms of screening with their clinician and to incorporate their values and preferences in the decision. Screening offers a small potential benefit of reducing the chance of death from prostate cancer in some men. However, many men will experience potential harms of screening, including false-positive results that require additional testing and possible prostate biopsy; overdiagnosis and overtreatment; and treatment complications, such as incontinence and erectile dysfunction. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the balance of benefits and harms on the basis of family history, race/ethnicity, comorbid medical conditions, patient values about the benefits and harms of screening and treatment-specific outcomes, and other health needs. Clinicians should not screen men who do not express a preference for screening.	C
Men 70 years and older	The USPSTF recommends against PSA-based screening for prostate cancer in men 70 years and older.	D



# Reconsidering the Trade-offs of Prostate Cancer Screening

Jonathan E. Shoag, M.D., Yaw A. Nyame, M.D., M.B.A., Roman Gulati, M.S., Ruth Etzioni, Ph.D.,  
and Jim C. Hu, M.D., M.P.H.

N ENGL J MED 382;25 NEJM.ORG JUNE 18, 2020

**Table 1.** Estimates of the Number Needed to Screen and the Number of Excess Prostate Cancer Diagnoses to Prevent One Death from Prostate Cancer during the Indicated Follow-up Interval.\*

Variable	No. Needed to Screen (95% CI)	No. of Excess Diagnoses (95% CI)
16 Yr of follow-up: empirical estimate from ERSPC	570 (380–1137)	18 (12–35)
25 Yr of follow-up: conservative model estimate	385 (273–687)	11 (8–20)





# COSA DICE IL DOCUMENTO DI IPAAC



- «Analysis of studies with lower risk of bias demonstrated a 21% decrease in prostate specific mortality».
- Efforts are underway in form of new trials trying to find screening strategies to detect particularly high-grade prostate cancers and avoid detection of low grade cancers
- Use of Multiparametric magnetic Resonance (mpMRI) before biopsy could improve diagnosis and reduce number of men needing biopsy



## MRI has transformed the PCa diagnostic pathway

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Foundational studies include the verification PROMIS study [1], the randomised international PRECISION and multicentre Canadian trials [2,3], and head-to-head systematic versus MRI-directed biopsy studies [4].

Taken together, the evidence indicates that MRI before biopsy can allow **one-third of men to avoid an immediate biopsy** and **reduce overdiagnosis, with 40% fewer clinically unimportant cancers** and approximately **15% more clinically important cancers detected** [5].

- 1) Ahmed HU et al, Lancet 2017
- 2) Ahmed HU et al, Lancet 2017
- 3) Klotz I et al, Jama Oncology 2021
- 4) Van der Leest M, Eur Urol 2019
- 5) Drost FH et al, Cochrane database system rev 2019

available at [www.sciencedirect.com](http://www.sciencedirect.com)

journal homepage: [www.europeanurology.com](http://www.europeanurology.com)



European Association of Urology



## Review – Prostate Cancer

# Prostate-specific Antigen Testing as Part of a Risk-Adapted Early Detection Strategy for Prostate Cancer: European Association of Urology Position and Recommendations for 2021

*Hendrik Van Poppel<sup>a,\*</sup>, Monique J. Roobol<sup>b</sup>, Christopher R. Chapple<sup>c</sup>, James W.F. Catto<sup>d,e</sup>, James N'Dow<sup>f,g</sup>, Jens Sønksen<sup>h,i</sup>, Arnulf Stenzl<sup>j</sup>, Manfred Wirth<sup>k</sup>*



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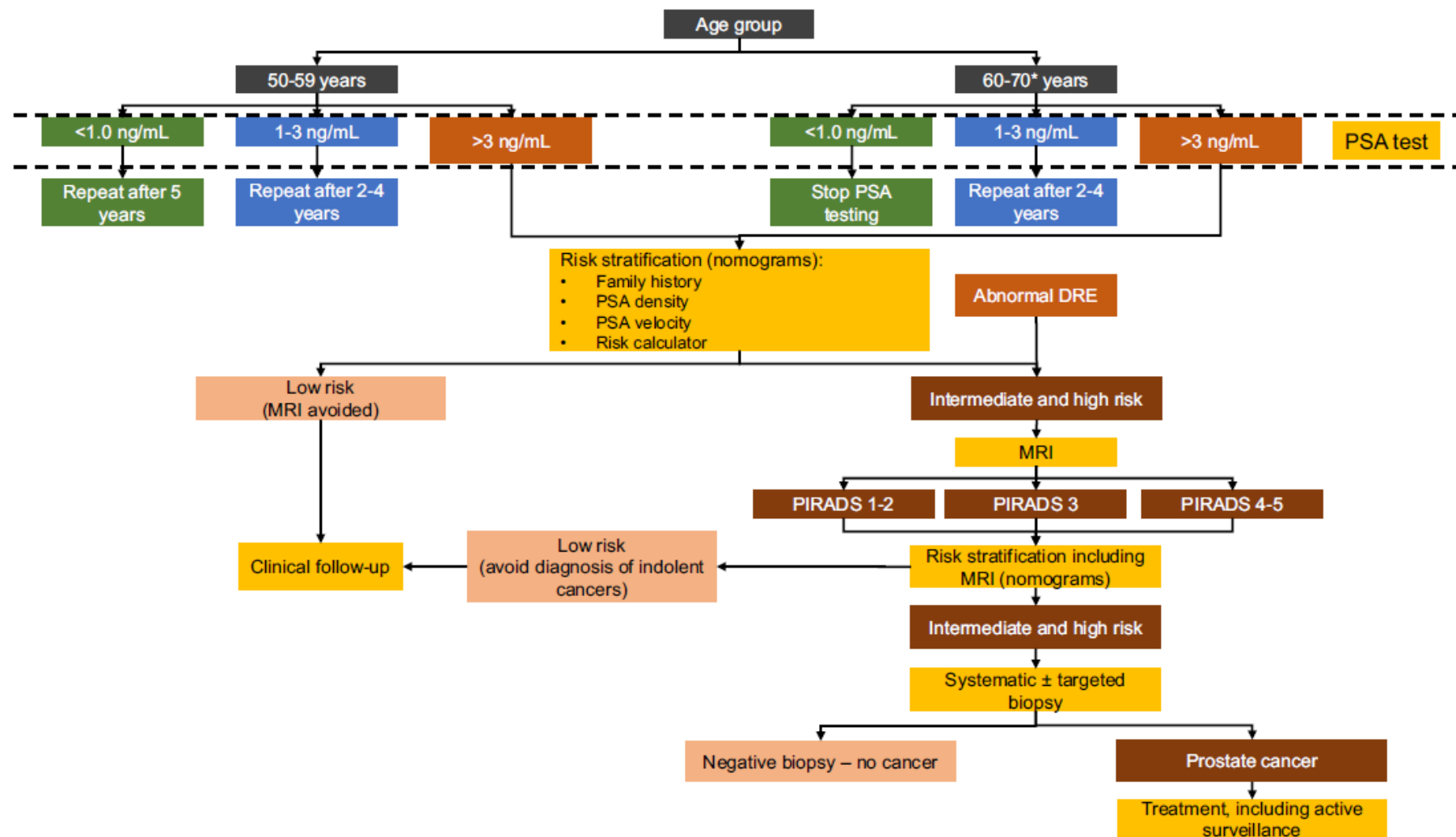


Fig. 4 – Risk-adapted algorithm for the early detection of prostate cancer, adapted based on prostate cancer guidelines published by the EAU [21]. The patient's values and preferences should always be taken into account as part of a shared decision-making process [21].

DRE = digital rectal examination; EAU = European Association of Urology; MRI = magnetic resonance imaging; PIRADS = Prostate Imaging Reporting and Data System; PSA = prostate-specific antigen.

\*Healthy men >70 yr without important comorbidities and a life expectancy of >10-15 yr may continue PSA testing.



- Although not confirmed by the highest level of evidence, current literature and guidelines point towards an algorithm for early detection of PCa that starts with risk-based prostate-specific antigen (PSA) testing, followed by multivariable risk stratification with Risk Calculators (RCs). All men who are classified to be at intermediate and high risk are then offered prostate MRI. The combined data from RCs and MRI results can be used to select men for prostate biopsy. Low-risk men return to a risk-based safety net that includes individualised PSA-interval tests and, if necessary, repeated MRI.

# SCREENING DEL POLMONE MEDIANTE LOW DOSE CT

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- Ampia dimostrazione di efficacia (9 RCTs)
- Prioritaria la prevenzione mediante smoking cessation (possibile integrazione positiva)
- Protocolli diversi utilizzati nei vari trial



Research paper

# Lung cancer mortality reduction by LDCT screening: UKLS randomised trial results and international meta-analysis

John K. Field<sup>a,\*</sup>, Daniel Vulkan<sup>b</sup>, Michael P.A. Davies<sup>a</sup>, David R. Baldwin<sup>c</sup>, Kate E. Brain<sup>d</sup>,

## Mortality from Lung Cancer

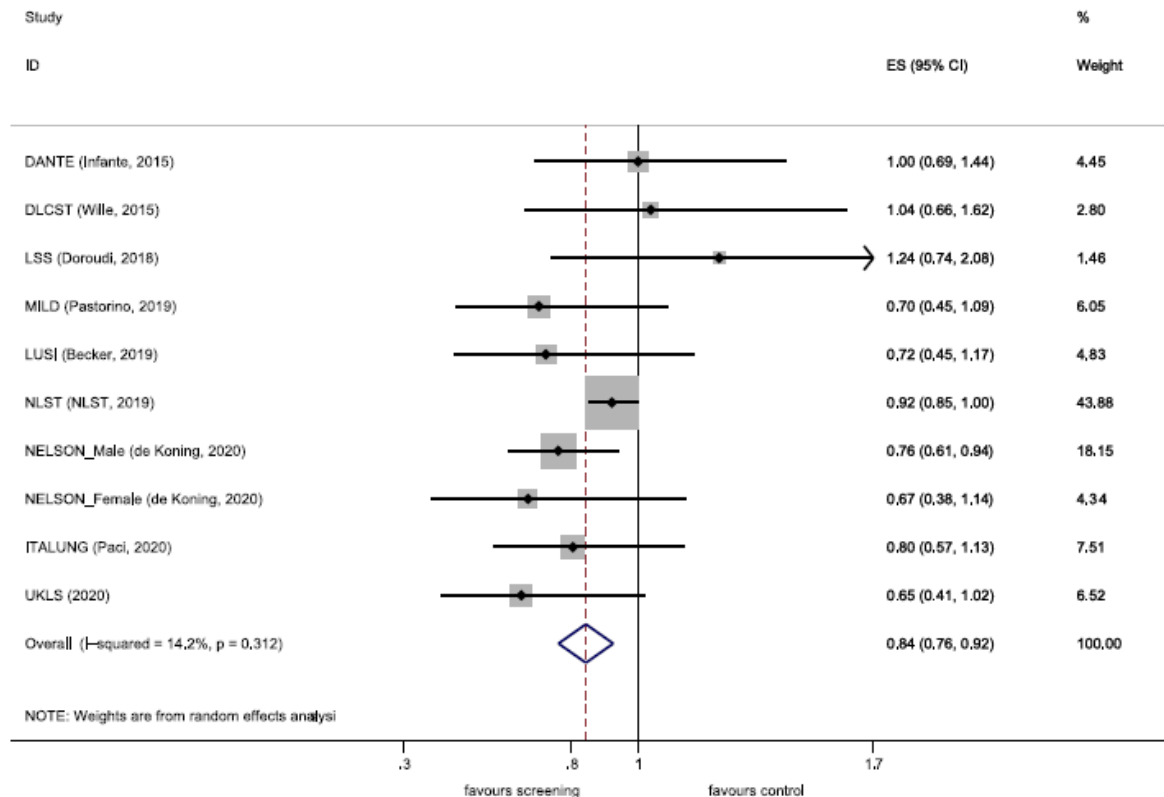


Fig. 7. Forest plot, lung cancer mortality.

**Pooled Overall RR**  
**0.86 (95%CI .76-.92)**

Research paper

# Lung cancer mortality reduction by LDCT screening: UKLS randomised trial results and international meta-analysis

John K. Field<sup>a,\*</sup>, Daniel Vulkan<sup>b</sup>, Michael P.A. Davies<sup>a</sup>, David R. Baldwin<sup>c</sup>, Kate E. Brain<sup>d</sup>

## Overall Mortality

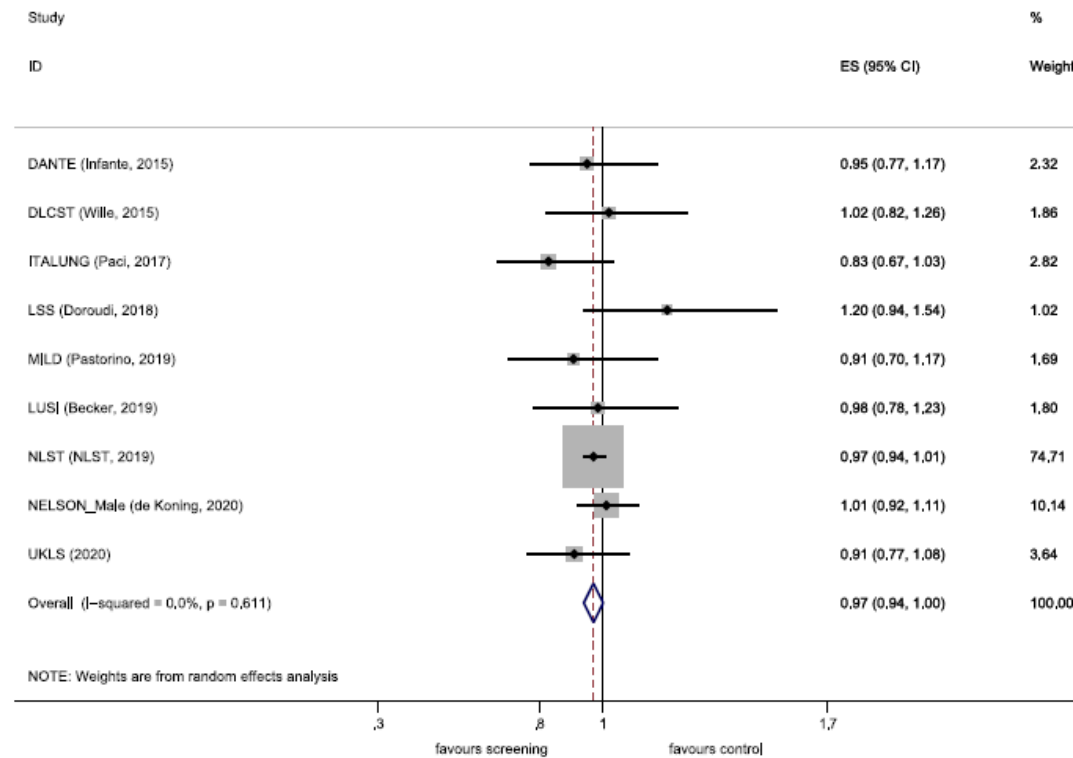


Fig. 8. Forest plot, mortality from all causes.

**Pooled Overall RR**  
**0.97(95%CI.94- 1.00)**



# STIMA CONSERVATIVA

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- Almeno uno studio «negativo» ha riconosciuto errori di randomizzazione
- Si riportano i dati del trial americano (NLST il primo e il più numeroso) molti anni dopo la fine dello screening

# HARMS OF LUNG CANCER SCREENING (IPAAC)

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- False positive results
  - Complications from invasive follow up
  - Overdiagnosis and overtreatment (?)
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- ➔ Specificity of screening and number of false positive are associated with the algorithms and protocols
  - ➔ Availability of technology , resources and skilness

# KEY ASPECTS OF IMPLEMENTATION STUDIES (IPAAC)

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- Availability of CT scanners
- Clinical validation ,training and accreditation of the novel diagnostic and management services
- How to select target population
- How to reach the target population
- How to best integrated intervention on smoking cessation with screening
- To further investigate the mortality benefits by gender
- To understand aspects related to other findings than on lung cancer mortality (i.e. reduction from cardiovascular mortality)

