Il test di screening

Eugenio Paci

Epidemiologo, già ISPRO, Istituto per lo Studio, la Prevenzione e la Rete Oncologica, Firenze

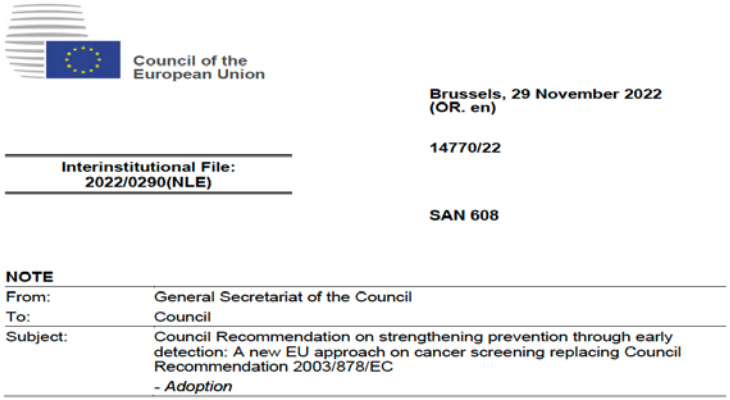
Coordinatore regionale LILT - Toscana

Il sottoscritto Eugenio Paci
ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 17 del Reg. Applicativo dell'Accordo Stato-Regione del 5 novembre 2009,

dichiara

che negli ultimi due anni NON ha avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario

- Bari, 17 Aprile 2023.



Council of the European Union

Brussels, 29 November 2022
(OR. en)

14770/22

Interinstitutional File:
2022/0290(NLE)

SAN 608

NOTE

From:	General Secretariat of the Council
To:	Council
Subject:	Council Recommendation on strengthening prevention through early detection: A new EU approach on cancer screening replacing Council Recommendation 2003/878/EC - *Adoption*

All of Wilson and Jungner's criteria for responsible screening, as well as the additional criteria set out by the WHO, should be used to assess the feasibility of a screening programme.

Breast cancer:
Considering the evidence presented in the European guidelines, breast cancer screening for women aged 50 to 69 with mammography is recommended.

A lower age limit of 45 years and an upper age limit of 74 years is suggested.
The use of either digital breast tomosynthesis or digital mammography is suggested.

The use of magnetic resonance imaging (MRI) should be considered when medically appropriate.

DOCUMENTO INTERSOCIETARIO PER LA DEFINIZIONE DEGLI INDICATORI DEGLI SCREENING ONCOLOGICI

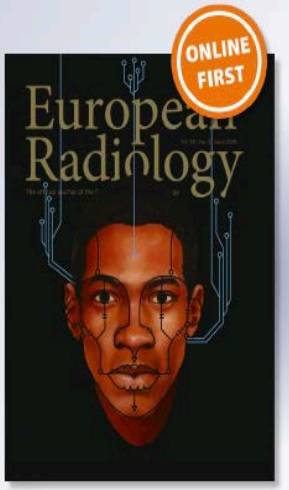
A cura di: Silvia Deandrea[1,2], Samuele Rivolta[3], Diego Baiocchi[4], Alessandra Barca[4], Eva Benelli[5], Lauro Bucchi[6], Cinzia Campari[7], Alfonso Frigerio[8], Livia Giordano[8], Daniela Giorgi[9], Paolo Giorgi Rossi[7], Cesare Hassan[10], Paola Mantellini[11,12], Gessica Martello[13], Paola Mosconi[14], Carlo Naldoni[15], Eugenio Paci[16], Antonio Ponti[8], Priscilla Sassoli De Bianchi[17], Nereo Segnan[8], Carlo Senore[8], Mariano Tomatis[8], Marco Zappa[11,12] e Manuel Zorzi[18]

Figura 1: Framework per la selezione degli indicatori di screening

Annual mammography at age 45–49 years and biennial mammography at age 50–69 years: comparing performance measures in an organised screening setting

on behalf of the Emilia-Romagna Region Workgroup for Mammography Screening Evaluation

European Radiology
ISSN 0938-7994
Eur Radiol
DOI 10.1007/s00330-019-06050-w



Springer

Mammogrammi

Richiami

Non-Invasivi

Invasivi (FNA, VAB)

Referral chirurgici

Biopsie chirurgiche

Table 2 Recall rate, assessment rate by type, surgical referral and surgical biopsy rates, and detection rate of breast cancer at the first screen and homologous cumulative rates at the second and subsequent screens, by woman's age group. All rates are per 1000 screening mammograms. Emilia-Romagna Region mammography screening programme (2011–2015)

	Rate at the first screen			Cumulative rate at the second and subsequent screens		
	45–49	50–54	55–69	45–49	50–54	55–69
Recall rate	103.6	93.5	93.2	208.9	99.7	75.5
Assessment rates						
Non-invasive assessment	78.6	66.0	63.3	171.0	76.6	51.5
Invasive assessment						
FNA	12.5	14.6	11.8	17.9	10.3	11.3
NCB, VAB	10.5	9.9	12.8	17.9	11.7	11.7
Total invasive assessment	23.0	24.5	24.6	35.8	22.0	23.0
Surgical referral rate	6.2	9.2	14.1	12.2	9.3	13.7
Surgical biopsy rate	5.9	8.6	13.2	11.5	8.5	13.0
Detection rate of benign breast lesion	1.4	1.5	1.4	2.2	1.4	0.8
Detection rates of breast cancer						
DCIS	1.3	2.0	2.1	2.2	1.7	2.0
Invasive cancer						
pT1mic-a-b	1.0	1.8	3.4	2.3	1.8	4.1
pT1c	1.3	1.9	3.6	2.8	2.3	4.0
pT2–4	0.6	0.9	2.2	1.1	0.9	1.4
pN-negative	2.0	3.3	6.2	4.6	3.6	7.6
pN-positive	0.9	1.2	3.0	1.6	1.4	1.9
Total invasive cancer*	3.0	4.8	9.6	6.7	5.2	10.0
Total breast cancer*	4.3	6.7	11.7	8.9	6.8	12.0

FNA fine-needle aspiration; *NCB* needle core biopsy; *VAB* vacuum-assisted biopsy; *DCIS* ductal carcinoma in situ

Recall indicates recall for further assessment. Non-invasive assessment indicates one or more among ultrasound, diagnostic mammography, breast physical examination, and other tests without pathologic evaluation. Surgical referral indicates referral for excisional biopsy or definitive surgical treatment. Surgical biopsy indicates excisional biopsy or definitive surgical treatment. Second and subsequent screens indicate the second, third, fourth, and fifth annual screen for women aged 45–49 years, and the second and third biennial screen for women aged 50–54 years and 55–69 years

*Including pTX and pNX invasive cancers and invasive cancers with missing pT and pN information

UICC global cancer control
IJC International Journal of Cancer

Performance indicators in breast cancer screening in the European Union: A comparison across countries of screen positivity and detection rates

Paola Armaroli[1], Emilia Riggi[1], Partha Basu[2], Ahti Anttila[3], Antonio Ponti[1], Andre L. Carvalho[2], Joakim Dillner[4], Miriam K. Elfström[4], Livia Giordano[1], Stefan Lönnberg[5], Guglielmo Ronco[1,6], Carlo Senore[1], Isabelle Soerjomataram[2], Mariano Tomatis[1], Diama B. Vale[7], Katja Jarm[8], Rengaswamy Sankaranarayanan[9] and Nereo Segnan[1]

Comparable performance indicators for breast cancer screening in the European Union (EU) have not been previously reported. We estimated adjusted breast cancer screening positivity rate (PR) and detection rates (DR) to investigate variation across EU countries. For the age 50–69 years, the adjusted EU-pooled PR for initial screening was 8.9% (cross-programme variation range 3.2–19.5%) while DR of invasive cancers was 5.3/1,000 (range 3.8–7.4/1,000) and DR of ductal carcinoma *in situ* (DCIS) was 1.3/1,000 (range 0.7–2.7/1,000). For subsequent screening, the adjusted EU-pooled PR was 3.6% (range 1.4–8.4%), the DR was 4.0/1,000 (range 2.2–5.8/1,000) and 0.8/1,000 (range 0.5–1.3/1,000) for invasive and DCIS, respectively. Adjusted performance indicators showed remarkable heterogeneity, likely due to different background breast cancer risk and awareness between target populations, and also different screening protocols and organisation. Periodic reporting of the screening indicators permits comparison and evaluation of the screening activities between and within countries aiming to improve the quality and the outcomes of screening programmes. Cancer Screening Registries would be a milestone in this direction and EU Screening Reports provide a fundamental contribution to building them.

Int. J. Cancer: 147, 1855–1863 (2020)

UICC
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Even though we adjusted for different covariates, our current EU-pooled estimates for initial and subsequent screening are still higher than this desirable level (8.9 and 4.4%, respectively).

These current findings could be useful to update the European standard. It would make sense also advice ranges of values rather than only the upper limits.

Furthermore, we also observed a less than perfect correlation of DRs and PRs where some programmes have high PRs and low DRs or vice versa

- ***A perfect correlation of PRs with DRs would mean that uniform and reproducible screening and diagnostic criteria are used across European countries. The interpretation of these results remains difficult because in some screening programmes (e.g. in the Netherlands) referral for final diagnostic assessmen is based on immediate clinical evaluation after positive mammography.***

UICC
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	Malattia		Totale
Test	**Presente**	**Assente**	**Tot.**
Pos.	**Vero Positivo (TP) a=464** Tumori Screen Detected	**Falso Positivo (FP) c= 2462**	**Richiami a+c**
Neg.	**Falso Negativo (FN) b=227** Tumori di intervallo (1,2,3 anni)	**Vero Negativo (TN) d=90213**	**b+d**
Tot.	**a+b** Num. Donne con tumore al seno	**c+d** Num. Donne senza malattia	**a+b+c+d Totale donne screening**

- *Of importance, high probability of test positivity and low detection rate indicate poor specificity and positive predictive value, and the variability in these measures may suggest that the screening harms may be different from one programme to another. The consequences of the variability of the reported screening performance data on the outcomes, however, are not yet known.*

- *Alta probabilità di positività al test=alto tasso di richiami (a+c)*
- *Basso tasso di identificazione di tumori Screen detected (a/a+b+c+d)*

Int. J. Cancer: 147, 1855–1863 (2020) © 2020 UICC

UICC global cancer control

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	Falsi Positivi (%) Iniziale/Successivi	Carcinomi invasivi TEST Iniziale/Successivi (Tasso identificazione x 1000)
EU- pooled	8.9 / 3.6	5.3/ 4.0
Italia	10.0/4.8	4.0/3.5
Olanda	6.4/2.0	5.3/4.6
Francia	13.4 /8.4	7.1/5.4

- Oggi non esiste una raccomandazione particolare per queste donne, l'unica pratica che in qualche modo modifica la procedura corrente (che è 2 anni di intervallo nelle 50-74enni, e 1 anno nelle 45-49enni) è quello che viene chiamato *early recall*, un richiamo precoce rispetto all'intervallo programmato. Valutato negli anni scorsi dal Gisma, non è mai stata una pratica suggerita**. Si tratta, in breve, di una indecisione diagnostica da evitare, non di un indicatore di rischio futuro. (Gisma)**

Ravaioli *et al. BMC Medicine* 2010, 8:11
http://www.biomedcentral.com/1741-7015/8/11

BMC Medicine

RESEARCH ARTICLE Open Access

Incidence, detection, and tumour stage of breast cancer in a cohort of Italian women with negative screening mammography report recommending early (short-interval) rescreen

Alessandra Ravaioli[1], Flavia Foca[1], Americo Colamartini[1], Fabio Falcini[1], Carlo Naldoni[2], Alba C Finarelli[2], Priscilla Sassoli de Bianchi[2], Lauro Bucchi[1*]

Table 2 Proportional incidence of first-year interval breast cancers by type of previous negative mammography report.

	Mammography report	
	Standard negative	Negative with RES
Woman-years at risk, *n**	272,710	3286
OBS, *n* (rate)†	96 (35.3)	4 (121.7)
EXP, *n*	640.4	7.6
OBS:EXP ratio (95% CI)	0.15 (0.12-0.18)	0.53 (0.14-1.35)
Ratio‡ of the OBS:EXP ratios (95% CI)	1.00 (referent)	3.51 (0.94-9.29)

* Adjusted for general mortality and rounded to the whole-number value.
† Per 100,000 woman-years at risk.
‡ Adjusted for woman's age (5-year groups).
RES, recommendation for early (<24 months) rescreen; OBS:EXP ratio, observed:expected ratio or proportional incidence of interval cancers; CI, confidence interval.

After the mammogram: The use of tomosynthesis for further assessment (summary information for women)

PAGE CONTENTS

Recommendation

After mammography screening, if you need further assessment, what test should be used?

> **Digital breast tomosynthesis (DBT) rather than mammography, as suggested by the ECIBC's Guidelines Development Group (GDG).**

Who is this recommendation for?

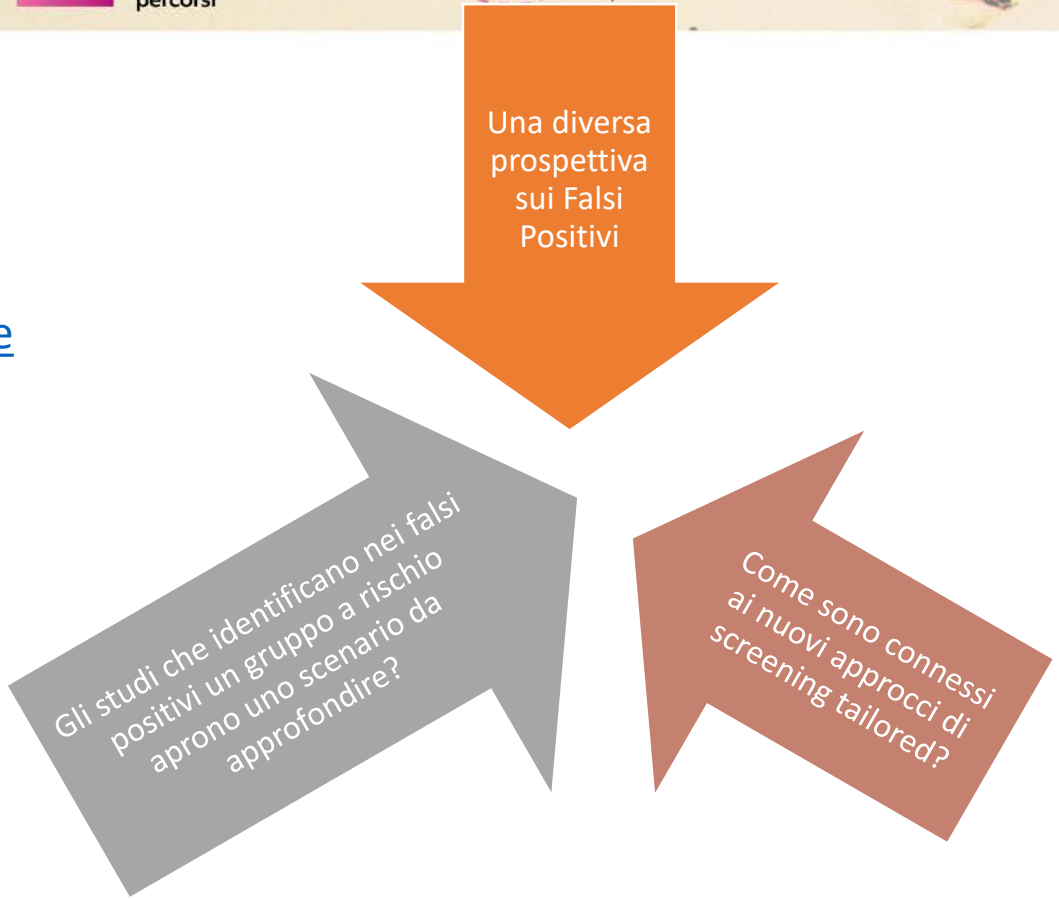
- You do not have a high risk of developing breast cancer
- You had a mammogram or other screening test and the results were unclear
- You were recalled for further assessment following this unclear result

What would following this recommendation mean for you?

It might be important to speak with your healthcare professional about the unclear results of your mammogram or other screening test.

[Sito Osservatorio nazionale Screening, 2019]

https://www.osservatorionazionalescreening.it/content/la-lunga-strada-uno-screening-personalizzato-il-tumore-al-seno



[Sito Osservatorio nazionale Screening, 2019]

https://www.osservatorionazionalescreening.it/content/la-lunga-strada-uno-screening-personalizzato-il-tumore-al-seno

- Dati di screening della Norvegia (1996-2008), Danimarca (1991-2010 e Spagna (1994-2010)
- Aumentato rischio di un tumore Screen-detected o intervallo nelle donne che avuto un Falso Positivo

BJC British Journal of Cancer www.nature.com/bjc

ARTICLE
Epidemiology

Long-term risk of screen-detected and interval breast cancer after false-positive results at mammography screening: joint analysis of three national cohorts

Marta Román[1,2], Solveig Hofvind[3,4], My von Euler-Chelpin[5] and Xavier Castells[1,2]

BACKGROUND: We assessed the long-term risk of screen-detected and interval breast cancer in women with a first or second false-positive screening result.
METHODS: Joint analysis had been performed using individual-level data from three population-based screening programs in Europe (Copenhagen in Denmark, Norway, and Spain). Overall, 75,513 screened women aged 50–69 years from Denmark (1991–2010), 556,640 from Norway (1996–2008), and 517,314 from Spain (1994–2010) were included. We used partly conditional Cox hazards models to assess the association between false-positive results and the risk of subsequent screen-detected and interval cancer.
RESULTS: During follow-up, 1,149,467 women underwent 3,510,450 screening exams, and 10,623 screen-detected and 5700 interval cancers were diagnosed. Compared to women with negative tests, those with false-positive results had a two-fold risk of screen-detected (HR = 2.04, 95% CI: 1.93–2.16) and interval cancer (HR = 2.18, 95% CI: 2.02–2.34). Women with a second false-positive result had over a four-fold risk of screen-detected and interval cancer (HR = 4.71, 95% CI: 3.81–5.83 and HR = 4.22, 95% CI: 3.27–5.46, respectively). Women remained at an elevated risk for 12 years after the false-positive result.
CONCLUSIONS: Women with prior false-positive results had an increased risk of screen-detected and interval cancer for over a decade. This information should be considered to design personalised screening strategies based on individual risk.

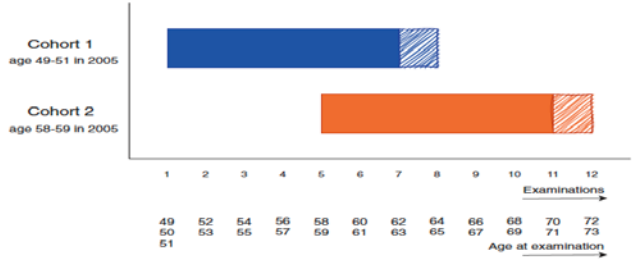
British Journal of Cancer (2019) 120:269–275; https://doi.org/10.1038/s41416-018-0358-5

Table 4. Adjusted and unadjusted hazard ratios (HR) of screen-detected cancer and interval breast cancer for women with false-positive screening results compared to women with negative results

	Women-years at risk	Number of cases	Unadjusted HR (95% CI)	Adjusted HR (95% CI)[a]
Screen-detected cancer				
Negative test	4,595,260	9229	Ref.	Ref.
False-positive result	360,439	1308	1.97 (1.86–2.09)	2.04 (1.93–2.16)
Second false-positive result	15,186	86	3.62 (2.92–4.47)	4.71 (3.81–5.83)
Interval breast cancer				
Negative test	6,630,989	4815	Ref.	Ref.
False-positive result	569,334	826	2.06 (1.92–2.22)	2.18 (2.02–2.34)
Second false-positive result	30,072	59	2.92 (2.26–3.78)	4.22 (3.27–5.46)

[a]Hazard ratios from partly conditional Cox proportional hazards model were adjusted by age at screen (continuous), type of attendance (regular or irregular), mammography type (SFM or FFDM), and country (random effect)

FIGURE 1 Construction of cohorts. [Color figure can be viewed at wileyonlinelibrary.com]



	Cohort 1 First-time invitees in 2005	Cohort 2 Fifth or sixth invitation in 2005
Age range	49-51	58-59
n	92 902	66 472
Average number of invitations received between 2005 and 2019	6.9 (SD 1.1) (range 1-10)	6.8 (SD 1.1) (range 1-12)
Times participated	6.2 (SD 1.7) (range 1-9)	6.3 (SD 1.5) (range 1-9)
Result screening examination in 2005		
TP	464 (5.0 per 1000)	288 (4.3 per 1000)
FP	1998 (21.5 per 1000)	435 (6.5 per 1000)
TN	90 213 (971.1 per 1000)	65 588 (986.7 per 1000)
Interval cancer (FN)	227 (2.4 per 1000)	161 (2.4 per 1000)
FP/TP ratio	4.3	1.5

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CANCER EPIDEMIOLOGY
IJC INTERNATIONAL JOURNAL of CANCER

Cumulative risks of false positive recall and screen-detected breast cancer after multiple screening examinations

Lindy M. Kregting[1] | Nicolien T. van Ravesteyn[1] | Sarocha Chootipongchaivat[1] | Eveline A. M. Heijnsdijk[1] | Johannes D. M. Otten[2] | Mireille J. M. Broeders[2,3] | Harry J. de Koning[1]

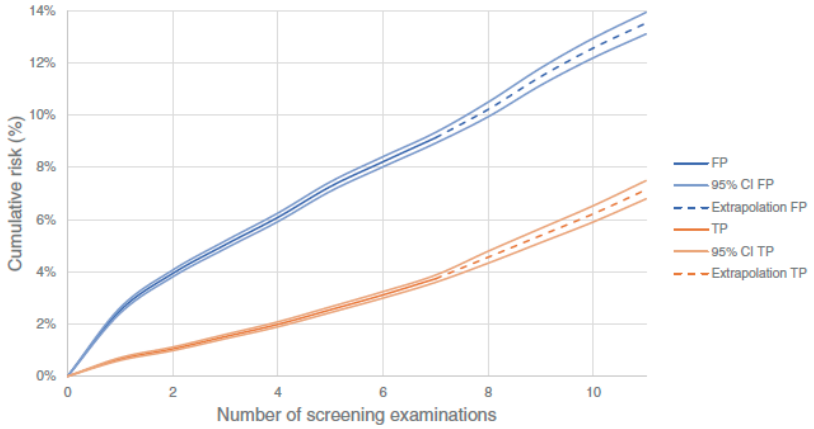

FIGURE 2 Cumulative risk of FP and TP screening results over 11 screening examinations. The dashed lines represent the extrapolation of results based on data from cohort 2. [Color figure can be viewed at wileyonlinelibrary.com]

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CANCER EPIDEMIOLOGY

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TABLE 1 Population characteristics.

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I tassi sono riportati x 1000 donne screenate	Età 48-51 1 test, 2005	Età 59 - 61 Test successivo (5 o 6, 2005)	Rapporto Coorte 1 vs Coorte 2
VPP (TP/(TP+FP)	18,85%	39,8%	
FP	21,5	6,5	3.3
TP	5,0	4,3	1,2
FN	2,4	2,4	1,0
BC(TP+FN)	7.4	6.7	1,1
Rapporto FP / BC (TP+FN)	4,3	1,5	

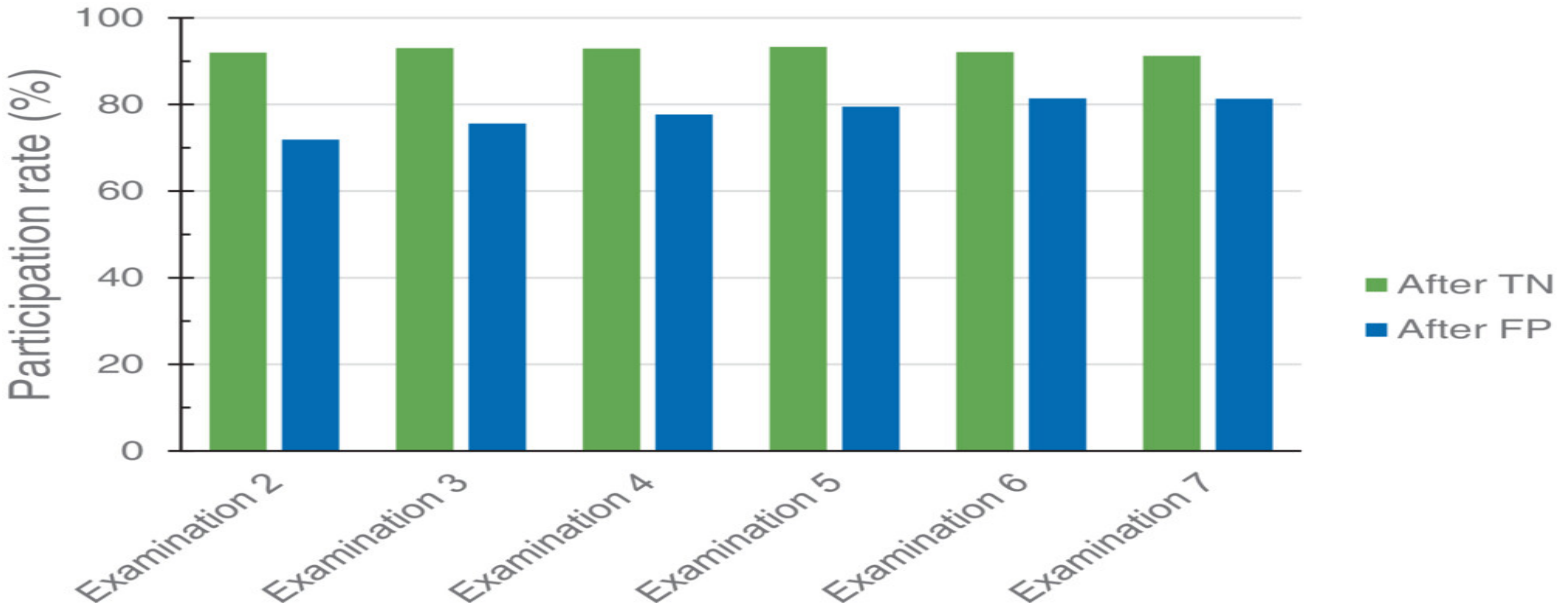
Rischio cumulativo di Falsi Positivi (FP), veri positivi (TP), Falsi negativi (t. di intervallo, FN), prevalenza di tumori al seno (BC=TP+FN). Per 1000 screening.
Follow-up : 7 esami di screening.

Numero /pop screenata , x1000 donne	AFTER TN (DOPO UN VERO NEGATIVO) (N=516.918)	AFTER FP (DOPO UN FALSO POSITIVO) (N=7.406)	Rapporto tra After FP e After TN
FP	34.6	67.8	+96%
TP	16.5	26.1	+59%
FN	5	8.2	+66%
BC(TP+FN)	21.5	34.3	+60%

I numeri di donne

	Primo Test			Repeated (6 exam, coorte 2)	
	coh 1	coh 2		Afer TN	After TP
Screenate	92902	66472		516918	7406
TP	464	288		8529	193
FP	1998	435		17871	502
TN	90213	65588		487954	6650
FN	227	161		2564	61

Diminuita partecipazione dopo un Falso Positivo



Intl Journal of Cancer, First published: 10 April 2023, DOI: (10.1002/ijc.34530)

Breast cancer risk is increased in the years following false-positive breast cancer screening

Mathijs C. Goossens[a,c], Isabel De Brabander[b], Jacques De Greve[a], Evelien Vaes[b], Chantal Van Ongeval[d], Koen Van Herck[c,e] and Eliane Kellen[c,d]

A small number of studies have investigated breast cancer (BC) risk among women with a history of false-positive recall (FPR) in BC screening, but none of them has used time-to-event analysis while at the same time quantifying the effect of false-negative diagnostic assessment (FNDA). FNDA occurs when screening detects BC, but this BC is missed on diagnostic assessment (DA). As a result of FNDA, screenings that detected cancer are incorrectly classified as FPR. Our study linked data recorded in the Flemish BC screening program (women aged 50–69 years) to data from the national cancer registry. We used Cox proportional hazards models on a retrospective cohort of 298 738 women to assess the association between FPR and subsequent BC, while adjusting for potential confounders. The mean follow-up was 6.9 years. Compared with women without recall, women with a history of FPR were at an increased risk of developing BC [hazard ratio = 2.10 (95% confidence interval: 1.92–2.31)]. However, 22% of BC after FPR was due to FNDA. The hazard ratio dropped to 1.69 (95% confidence interval: 1.52–1.87) when FNDA was excluded. Women with FPR have a subsequently increased BC risk compared with women without recall. The risk is higher for women who have a FPR BI-RADS 4 or 5 compared with FPR BI-RADS 3. There is room for improvement of diagnostic assessment: 41% of the excess risk is explained by FNDA after baseline screening. *European Journal of Cancer Prevention* 26:396–403

European Journal of Cancer Prevention 2017, 26:396–403

Keywords: breast neoplasms, false-positive recall, mammographic screening, risk

[a]Vrije Universiteit Brussel, [b]Belgian Cancer Registry, [c]Centrum voor Kankeropsporing (Center for Cancer Detection), [d]University Hospital Leuven and [e]Ghent University

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Received 20 May 2016 Revised 29 July 2016

- FNDA
- False-negative Diagnostic Assessement

Riflessione 1

- *Il risultato conferma un maggior rischio nei FP che è stato documentato Spagna, Danimarca e Irlanda, paesi che seguono un modello di tipo inglese e europeo, cioè con un screening/assessment eseguiti nella stessa fase e, spesso, senza il coinvolgimento di un centro di senologia clinica se non dopo la fase di imaging.*
- *Lo studio mette in evidenza il rapporto tra i Falsi Positivi e Veri Positivi (FP/ (BC=SD+INV)) in Olanda è migliore rispetto a quello osservato in altri paesi.*
- *Il dato Olandese è sempre stato diverso sia riguardo al tasso di richiamo che nella gestione perché ha distinto test di screening e assessment, procedure affidate a un centro clinico. Può essere utile anche in Italia rivalutare le pratiche correnti e i rapporti tra centri di screening e di senologia?*

Implicazioni per la comunicazione

- Una donna che ha aderito all'invito deve essere chiaramente informata che la pratica dello screening riguarda un periodo lungo della sua vita e e che benefici e danni dello screening mammografico non si valutano su un unico test ma nell'arco di esami multipli di screening nel corso della vita.
- La donna ha diritto a una informazione che riguarda il suo personale livello di rischio ed è importante che sappia, se i dati fossero confermati in Italia, che un risultato Falso Positivo a un test di screening può essere un indicatore aggiuntivo del suo rischio di ammalare negli anni successivi e che quindi è importante continuare a partecipare con regolarità.
- In una prospettiva di screening basato sul rischio («tailored») conoscere che la donna ha una storia di un risultato Falso Positivo potrebbe esser considerato un modificatore del rischio di ammalare di cui tenere conto nella sorveglianza, forse adottando specifici protocolli di monitoraggio.
- L'identificazione di un Falso Positivo può essere considerato un evento favorevole perché permette una migliore sorveglianza futura e non solo uno sfavorevole determinato dallo screening?

- Modificate da IJC, 2023

- Nat Rev Clin Oncol. 2020 Nov;17(11):687-705. doi: 10.1038/s41571-020-0388-9. Epub 2020 Jun 18.

La possibilità di uno screening personalizzato è oggi oggetto di ricerca e innovazione.

OPEN

Check for updates

Personalized early detection and prevention of breast cancer: ENVISION consensus statement

Nora Pashayan[1], Antonis C. Antoniou[2], Urska Ivanus[3], Laura J. Esserman[4], Douglas F. Easton[2], David French[5], Gaby Sroczynski[6,7], Per Hall[8,9], Jack Cuzick[10], D. Gareth Evans[11], Jacques Simard[12], Montserrat Garcia-Closas[13], Rita Schmutzler[14], Odette Wegwarth[15], Paul Pharoah[2,16], Sowmiya Moorthie[17], Sandrine De Montgolfier[18], Camille Baron[19], Zdenko Herceg[20], Clare Turnbull[21], Corinne Balleyguier[22], Paolo Giorgi Rossi[23], Jelle Wesseling[24], David Ritchie[25], Marc Tischkowitz[26], Mireille Broeders[27], Dan Reisel[28], Andres Metspalu[29], Thomas Callender[1], Harry de Koning[30], Peter Devilee[31], Suzette Delaloge[32], Marjanka K. Schmidt[24] and Martin Widschwendter[28,33,34] ✉

Abstract | The European Collaborative on Personalized Early Detection and Prevention of Breast Cancer (ENVISION) brings together several international research consortia working on different aspects of the personalized early detection and prevention of breast cancer. In a consensus conference held in 2019, the members of this network identified research areas requiring development to enable evidence-based personalized interventions that might improve the benefits and reduce the harms of existing breast cancer screening and prevention programmes. The priority areas identified were: 1) breast cancer subtype-specific risk assessment tools applicable to women of all ancestries; 2) intermediate surrogate markers of response to preventive measures; 3) novel non-surgical preventive measures to reduce the incidence of breast cancer of poor prognosis; and 4) hybrid effectiveness–implementation research combined with modelling studies to evaluate the long-term population outcomes of risk-based early detection strategies. The implementation of such programmes would require health-care systems to be open to learning and adapting, the

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Breast Cancer Research

RESEARCH ARTICLE Open Access

Volumetric breast density and risk of advanced cancers after a negative screening episode: a cohort study

Donella Puliti[1*], Marco Zappa[1], Paolo Giorgi Rossi[2], Elena Pierpaoli[3], Gianfranco Manneschi[1], Daniela Ambrogetti[3], Leonardo Ventura[1], Paola Mantellini[3] and the DENSITY Working Group

Abstract

Background: We evaluated the association between volumetric breast density (BD) and risk of advanced cancers after a negative screening episode.

Methods: A cohort of 16,752 women aged 49–54 years at their first screening mammography in the Florence screening programme was followed for breast cancer (BC) incidence until the second screening round. Volumetric BD was measured using fully automated software. The cumulative incidence of advanced cancer after a negative screening episode (including stage II or more severe cancer during the screening interval – on average 28 months – and at the subsequent round) was calculated separately for Volpara density grade (VDG) categories.

Results: BC incidence gradually increased with the increas in BD: 3.7‰, 5.1‰, 5.4‰ and 9.1‰ in the VDG categories 1–4, respectively (p trend < 0.001). The risk of advanced cancers after a negative screening episode was 1.0‰, 1.3‰, 1.1‰, and 4.2‰ (p trend = 0.003). The highest BD category, compared with the other three together, has double the invasive BC risk (RR = 2.0; 95% CI 1.5–2.8) and almost fourfold risk of advanced cancer (RR = 3.8; 95% CI 1.8–8.0).

Conclusion: BD has a strong impact on the risk of advanced cancers after a negative screening episode, the best early surrogate of BC mortality. Therefore, our results suggest that screening effectiveness is quite different among BD categories.

Keywords: Breast density, Breast cancer, Mammography sensitivity, Advanced stage

Donne in età 49-54 anni seguire per due anni e allo screening ripetuto (Tumori di intervallo + screen detected al secondo). Coorte Firenze, Puliti, 2018. N=16752

Table 3 Screening performance measurements and relative risks (95% CI) among Volpara density grade categories

BC incidence rate (only invasive)

	Cases/person-years	Rate	RR (95% CI)
VDG1–3	110/30390	3.6‰	reference
VDG 4	56/7513	7.5‰	2.0 (1.5–2.8)

Interval cancer rate

	Cases/negative screened	Rate	RR (95% CI)
VDG1–3	18/12709	1.4‰	reference
VDG 4	22/3129	7.0‰	5.0 (2.7–9.2)

Advanced cancers rate among negative screened

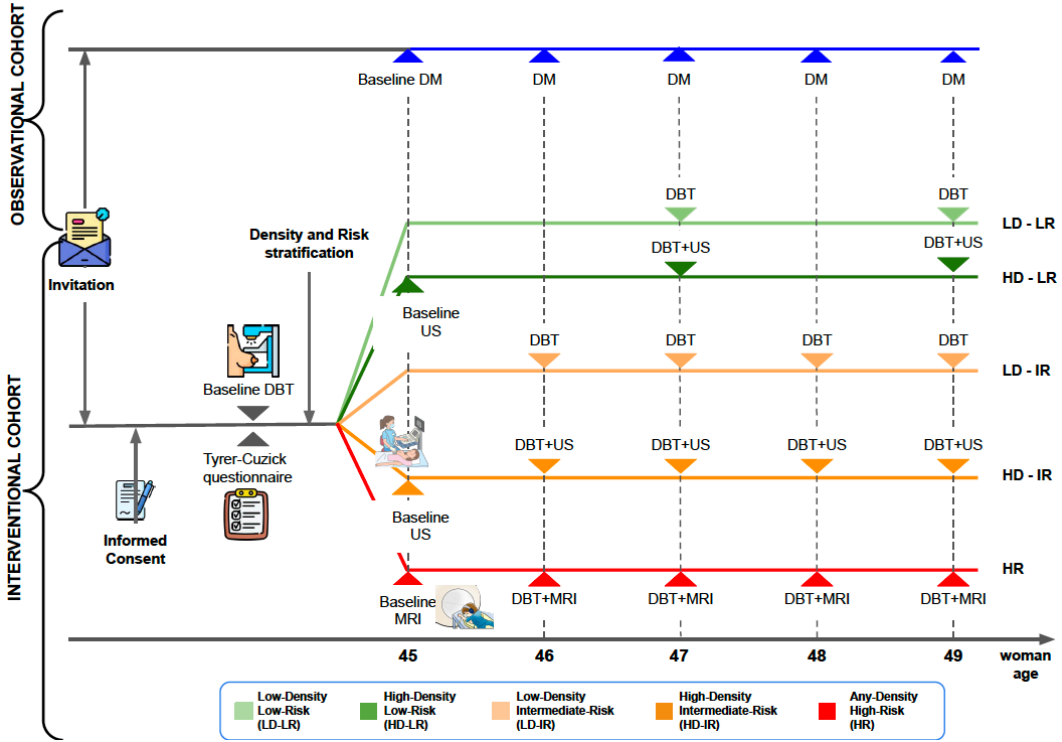
	Cases/negative screened	Rate	RR (95% CI)
VDG1–3	14/12709	1.1‰	reference
VDG 4	13/3129	4.2‰	3.8 (1.8–8.0)

VDG Volpara density grade, *BC* breast cancer, *RR* relative risk

Aumento del rischio relativo per l'alta densità (VDG 4)

Esiste un rapporto con FP?

Lo studio RIBBS: protocolli basati sul livello di rischio individuale e densità del seno



Cortesia di Francesca Caumo

Strategie di intervento basate sul livello di rischio e processo di screening per il cancro. Una riflessione da sviluppare?

Comment

Polygenic risk scores in cancer screening: a glass half full or half empty?

Current cancer screening programmes use age and sex to define the individuals most likely to benefit. However, cancer risk also varies widely between people according to their genetics, lifestyle, and other risk factors. The principle of risk-stratified screening, beyond age and sex, is already incorporated into guidelines by the National Institute for Health and Care Excellence (NICE)[1] and others, for example through offering enhanced breast cancer screening to women with a family history of breast cancer. Polygenic risk scores (PRSs) represent the combined effect of multiple genetic variants on cancer risk, identified through genome-wide

cancer. In practice, stratification can also be considerably improved by combining PRS with other risk factors (notably, family history and, for breast cancer, breast imaging markers).[4]

Huntley and colleagues focused on providing additional screening to the PRS-defined high-risk group, but there are several other ways in which risk-stratified screening might be used—most importantly, by providing less intensive screening to low-risk individuals (to reduce the unnecessary harms and costs of overscreening) and tailoring screening age range, frequency, and method to each risk group. The benefit-harm balance.

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Utility of polygenic risk scores in UK cancer screening: a modelling analysis

Catherine Huntley*, Bethany Torr*, Amit Sud, Charlie F Rowlands, Rosalind Way, Katie Snape, Helen Hanson, Charles Swanton, John Broggio, Anneke Lucassen, Margaret McCartney, Richard S Houlston, Aroon D Hingorani, Michael E Jones, Clare Turnbull

Summary

Background It is proposed that, through restriction to individuals delineated as high risk, polygenic risk scores (PRSs) might enable more efficient targeting of existing cancer screening programmes and enable extension into new age ranges and disease types. To address this proposition, we present an overview of the performance of PRS tools (ie, models and sets of single nucleotide polymorphisms) alongside harms and benefits of PRS-stratified cancer screening for eight example cancers (breast, prostate, colorectal, pancreas, ovary, kidney, lung, and testicular cancer).

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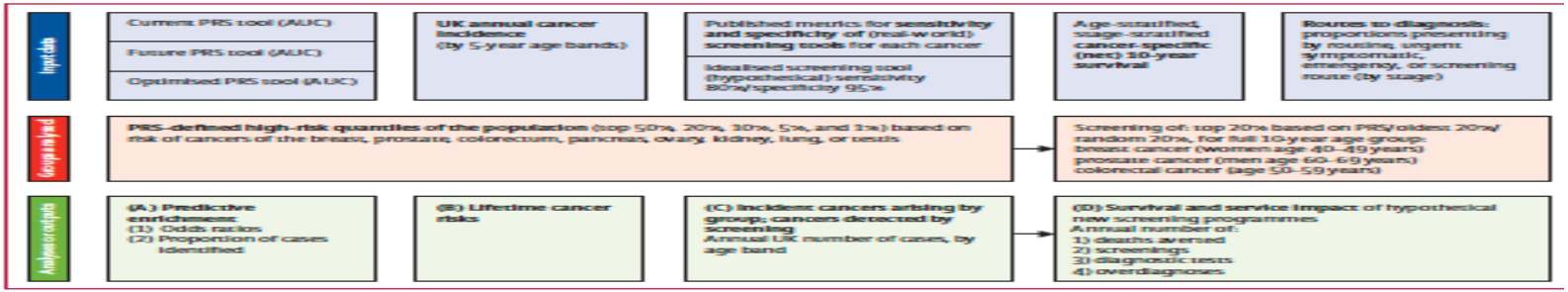


Figure 1: Overview of analyses, data sources, and screening scenarios
AUC=area under the receiver operating characteristic curve. PRS=polygenic risk score.

JAMA Network | Open

Original Investigation | Oncology

Development and Validation of a Multivariable Lung Cancer Risk Prediction Model That Includes Low-Dose Computed Tomography Screening Results

A Secondary Analysis of Data From the National Lung Screening Trial

Martin C. Tammemägi, PhD; Kevin ten Haaf, PhD; Iakovos Toumazis, PhD; Chung Yin Kong, PhD; Summer S. Han, PhD; Jihyoun Jeon, PhD; John Commins, BSc; Thomas Riley, BSc; Rafael Meza, PhD

Abstract

IMPORTANCE Low-dose computed tomography lung cancer screening is most effective when applied to high-risk individuals.

OBJECTIVES To develop and validate a risk prediction model that incorporates low-dose computed tomography screening results.

DESIGN, SETTING, AND PARTICIPANTS A logistic regression risk model was developed in National Lung Screening Trial (NLST) Lung Screening Study (LSS) data and was validated in NLST American College of Radiology Imaging Network (ACRIN) data. The NLST was a randomized clinical trial that recruited participants between August 2002 and April 2004, with follow-up to December 31, 2009. This secondary analysis of data from the NLST took place between August 10, 2013, and November 1, 2018. Included were LSS (n = 14 576) and ACRIN (n = 7653) participants who had 3 screens, adequate follow-up, and complete predictor information.

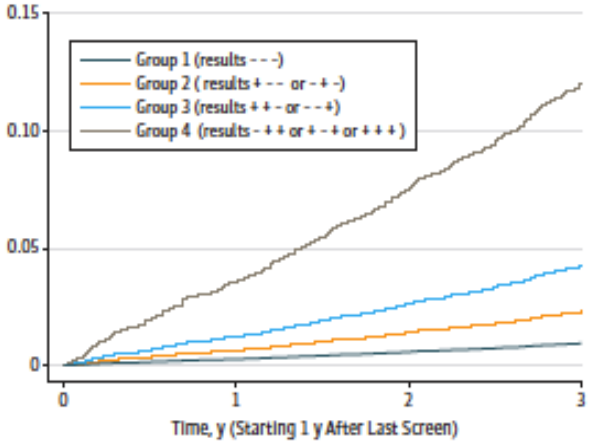
Key Points

Question In this study of data from the National Lung Screening Trial (NLST), can a lung cancer risk model's prediction be improved by inclusion of lung cancer screening results?

Findings In this secondary analysis of NLST data including 22 229 participants,

Radiomics+
baseline screening characteristics + biomarkers?

ıcidence of Lung Cancer in the National Lung Screening Trial Low-Dose Computed
ːurring 1 to 4 Years After the Last Low-Dose Computed Tomography Screen Among



sk

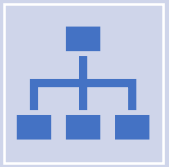
l	18 770	18 581	18 294	16 417
!	3048	2998	2932	2586
3	974	944	908	774
l	435	405	388	323

Stratified by Lung CT Scr
System screen results (p
baseline, 1-year, and 2-ye
categorized into 4 group

* Competing risks (ie, no
taken into account acc
and Gray.[24] Included in
incident lung cancer ca
deaths during the 3-ye

2019;2(3):e190204. doi:10.1001/jamanetworkopen.2019.0204

Riflessione 2



Modelli di rischio individuale, densità mammografica o biomarker permettono l'attribuzione a un livello di rischio. L'identificazione, attraverso lo screening di un possibile «evento di rischio» come avviene con alcuni segni di diagnostica per immagine o test biomolecolari (biopsia liquida) apre alla valutazione utilizzando «diagnostic biomarkers» che possono essere indicatori di un rischio incombente.

E' necessario con altri mezzi (per esempio AI nella diagnostica per immagine) identificare questi indicatori e orientare a una diversa sorveglianza queste persone che hanno una modificazione del loro livello di rischio? In questo contesto un approfondimento sui falsi positivi può fornire informazioni per una stratificazione basata non solo sul «livello di rischio» ma anche sui « diagnostic biomarkers»