Evidenze di utilità, limiti dello screening organizzato e prospettive future

Lauro Bucchi

Prove d'efficacia e raccomandazioni

Benefits and harms of annual, biennial, or triennial breast cancer mammography screening for women at average risk of breast cancer: a systematic review for the European Commission Initiative on Breast Cancer (ECIBC)

Carlos Canelo-Aybar[1,2,3]✉, Margarita Posso[1,4], Nadia Montero[1], Ivan Solà[1,2], Zuleika Saz-Parkinson[5]✉, Stephen W. Duffy[6], Markus Follmann[7], Axel Gräwingholt[8], Paolo Giorgi Rossi[9] and Pablo Alonso-Coello[1,2]

British Journal of Cancer; https://doi.org/10.1038/s41416-021-01521-8

CONCLUSIONS: In women of average BC risk, screening intervals have different trade-offs for each age group. The balance probably favours biennial screening in women 50–69. In younger women, annual screening may have a less favourable balance, while in women aged 70–74 years longer screening intervals may be more favourable.

Prove d'efficacia e raccomandazioni

Screening for breast cancer with mammography (Review)

Olsen O, Gøtzsche PC

Cochrane Database of Systematic Reviews 2001, Issue 4. Art. No.: CD001877.

Main results

The best trials failed to show a significant reduction in breast cancer mortality with a relative risk of 0.97 (95% CI 0.82-1.14). If data from all eligible trials (excluding flawed studies) are considered then the relative risk for breast cancer mortality after 13 years is 0.80 (95% CI 0.71-0.89). However, breast cancer mortality is considered to be an unreliable outcome and biased in favour of screening. Flaws are due to differential exclusion of women with breast cancer from analysis and differential misclassification of cause of death.

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Olsen O, Gøtzsche PC

Cochrane Database of Systematic Reviews 2001, Issue 4. Art. No.: CD001877.

Authors' conclusions

The currently available reliable evidence does not show a survival benefit of mass screening for breast cancer (and the evidence is inconclusive for breast cancer mortality). Women, clinicians and policy makers should consider these findings carefully when they decide whether or not to attend or support screening programs.

Prove d'efficacia e raccomandazioni

Breast-Cancer Screening — Viewpoint of the IARC Working Group

Béatrice Lauby-Secretan, Ph.D., Chiara Scoccianti, Ph.D., Dana Loomis, Ph.D., Lamia Benbrahim-Tallaa, Ph.D., Véronique Bouvard, Ph.D., Franca Bianchini, Ph.D., and Kurt Straif, M.P.H., M.D., Ph.D., for the International Agency for Research on Cancer Handbook Working Group

N ENGL J MED 372;24 NEJM.ORG JUNE 11, 2015

Table 1. Evaluation of Evidence Regarding the Beneficial and Adverse Effects of Different Methods of Screening for Breast Cancer in the General Population and in High-Risk Women.*

Method	Strength of Evidence†
Mammography	
Reduces breast-cancer mortality in women 50–69 yr of age	Sufficient
Reduces breast-cancer mortality in women 70–74 yr of age‡	Sufficient
Reduces breast-cancer mortality in women 40–44 yr of age§	Limited
Reduces breast-cancer mortality in women 45–49 yr of age§	Limited¶

Prove d'efficacia e raccomandazioni

Breast Cancer Screening for Women at Average Risk
2015 Guideline Update From the American Cancer Society

Kevin C. Oeffinger, MD; Elizabeth T. H. Fontham, MPH, DrPH; Ruth Etzioni, PhD; Abbe Herzig, PhD; James S. Michaelson, PhD; Ya-Chen Tina Shih, PhD; Louise C. Walter, MD; Timothy R. Church, PhD; Christopher R. Flowers, MD, MS; Samuel J. LaMonte, MD; Andrew M. D. Wolf, MD; Carol DeSantis, MPH; Joannie Lortet-Tieulent, MSc; Kimberly Andrews; Deana Manassaram-Baptiste, PhD; Debbie Saslow, PhD; Robert A. Smith, PhD; Otis W. Brawley, MD; Richard Wender, MD

JAMA. 2015;314(15):1599-1614.

Recommendation 1

Women with an average risk of breast cancer should undergo regular screening mammography starting at age 45 years. (*Strong Recommendation*)

Recommendation 1a: Women aged 45 to 54 years should be screened annually. (*Qualified Recommendation*)

Recommendation 1b: Women 55 years and older should transition to biennial screening or have the opportunity to continue screening annually. (*Qualified Recommendation*)

Recommendation 1c: Women should have the opportunity to begin annual screening between the ages of 40 and 44 years. (*Qualified Recommendation*)

Prove d'efficacia e raccomandazioni

The benefits and harms of breast cancer screening: an independent review

*Independent UK Panel on Breast Cancer Screening**

***Lancet* 2012; 380: 1778–86**

	Overall RR (95% CI)
This review	
13-year follow-up in trials reported in the Cochrane Review[5] random-effects meta-analysis	0·80 (0·73–0·89)
Cochrane review[5]	
Fixed-effect meta-analysis of the above trials	0·81 (0·74–0·87)
As above, but excluding women <50 years	0·77 (0·69–0·86)
Trials considered adequately randomised (Canada, Malmö, and UK Age trial) had RR 0·90 (95% CI 0·79–1·02); trials deemed suboptimally randomised gave RR 0·75 (0·67–0·83). As a compromise between these two estimates, the authors concluded that an RR of 0·85 was plausible	0·85
US Task Force[9]	
RR 0·86 (95% CI 0·75–0·99) for women aged 50–59 years, and RR 0·68 (0·54– 0·87) for those aged 60–69 years. These estimates have an inverse-variance weighted average RR of 0·81	0·81
Canadian Task Force[4]	
Routinely screening for breast cancer with mammography every 2–3 years for women aged 50–69 years was rated as a weak recommendation based on moderate-quality evidence according to GRADE criteria[11]	0·79 (0·68–0·90)
Duffy et al, 2012[10]	
Review of all trials and age groups	0·79 (0·73–0·86)

Prove d'efficacia e raccomandazioni

Screening for breast cancer with mammography (Review)

Gøtzsche PC, Jørgensen KJ

Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD001877.

Main results

Eight eligible trials were identified. We excluded a trial because the randomisation had failed to produce comparable groups.The eligible trials included 600,000 women in the analyses in the age range 39 to 74 years. Three trials with adequate randomisation did not show a statistically significant reduction in breast cancer mortality at 13 years (relative risk (RR) 0.90, 95% confidence interval (CI) 0.79 to 1.02); four trials with suboptimal randomisation showed a significant reduction in breast cancer mortality with an RR of 0.75 (95% CI 0.67 to 0.83). The RR for all seven trials combined was 0.81 (95% CI 0.74 to 0.87).

Authors' conclusions

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If we assume that screening reduces breast cancer mortality by 15% and that overdiagnosis and overtreatment is at 30%, it means that for every 2000 women invited for screening throughout 10 years, one will avoid dying of breast cancer and 10 healthy women, who would not have been diagnosed if there had not been screening, will be treated unnecessarily. Furthermore, more than 200 women will experience important psychological distress including anxiety and uncertainty for years because of false positive findings. To help ensure that the women are fully informed before they decide whether or not to attend screening, we have written an evidence-based leaflet for lay people that is available in several languages on www.cochrane.dk. Because of substantial advances in treatment and greater breast cancer awareness since the trials were carried out, it is likely that the absolute effect of screening today is smaller than in the trials. Recent observational studies show more overdiagnosis than in the trials and very little or no reduction in the incidence of advanced cancers with screening.

Prove d'efficacia e raccomandazioni

The impact of mammographic screening on breast cancer mortality in Europe: a review of observational studies

Mireille Broeders, Sue Moss, Lennarth Nyström, Sisse Njor, Håkan Jonsson, Ellen Paap, Nathalie Massat, Stephen Duffy, Elsebeth Lynge and Eugenio Paci, for the EUROSCREEN Working Group

J Med Screen 2012;**19 Suppl 1**:14–25

Results Twelve of the 17 trend studies quantified the impact of population-based screening on breast cancer mortality. The estimated breast cancer mortality reductions ranged from 1% to 9% per year in studies reporting an annual percentage change, and from 28% to 36% in those comparing post- and prescreening periods. In the IBM studies, the pooled mortality reduction was 25% (relative risk [RR] 0.75, 95% confidence interval [CI] 0.69–0.81) among invited women and 38% (RR 0.62, 95% CI 0.56–0.69) among those actually screened. The corresponding pooled estimates from the CC studies were 31% (odds ratio [OR] 0.69, 95% CI 0.57–0.83), and 48% (OR 0.52, 95% CI 0.42–0.65) adjusted for self-selection.

Prove d'efficacia e raccomandazioni

Overdiagnosis in mammographic screening for breast cancer in Europe: a literature review

Donella Puliti, Stephen W Duffy, Guido Miccinesi, Harry de Koning, Elsebeth Lynge, Marco Zappa, Eugenio Paci and the EUROSCREEN Working Group (members listed at the end of the paper)

J Med Screen 2012;**19 Suppl 1**:42–56

Conclusions The most plausible estimates of overdiagnosis range from 1% to 10%. Substantially higher estimates of overdiagnosis reported in the literature are due to the lack of adjustment for breast cancer risk and/or lead time.

Prove d'efficacia e raccomandazioni

Screening for breast cancer with mammography (Review)

Gøtzsche PC, Jørgensen KJ

Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD001877.

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La controversia in 15 parole

“Lo screening mammografico
non è sotto attacco
perché è inefficace.
E’ sotto attacco perché è *poco* efficace”

Marco Zappa
Convegno annuale Gisma, Salerno, 2014*

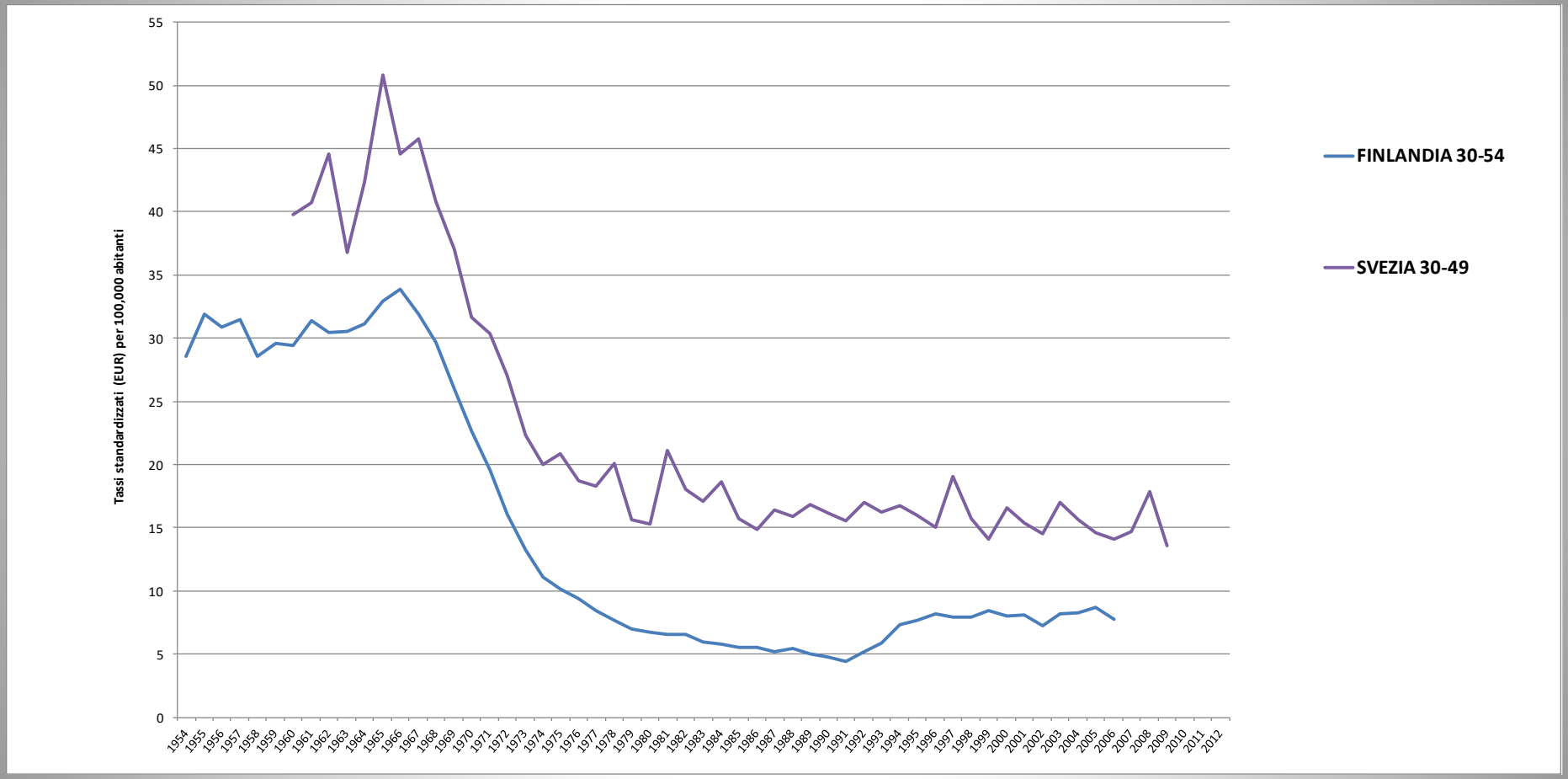
(mi sembra …, NdR)

Pensiamo allo screening cervicale …

- Un trial di screening cervicale non è mai stato condotto
- Lo screening cervicale è associato con un vasto e universalmente riconosciuto fenomeno di sovradiagnosi delle malattie preinvasive
- I programmi di screening cervicale coinvolgono una popolazione bersaglio che è circa 2 volte più ampia dei programmi di screening mammografico

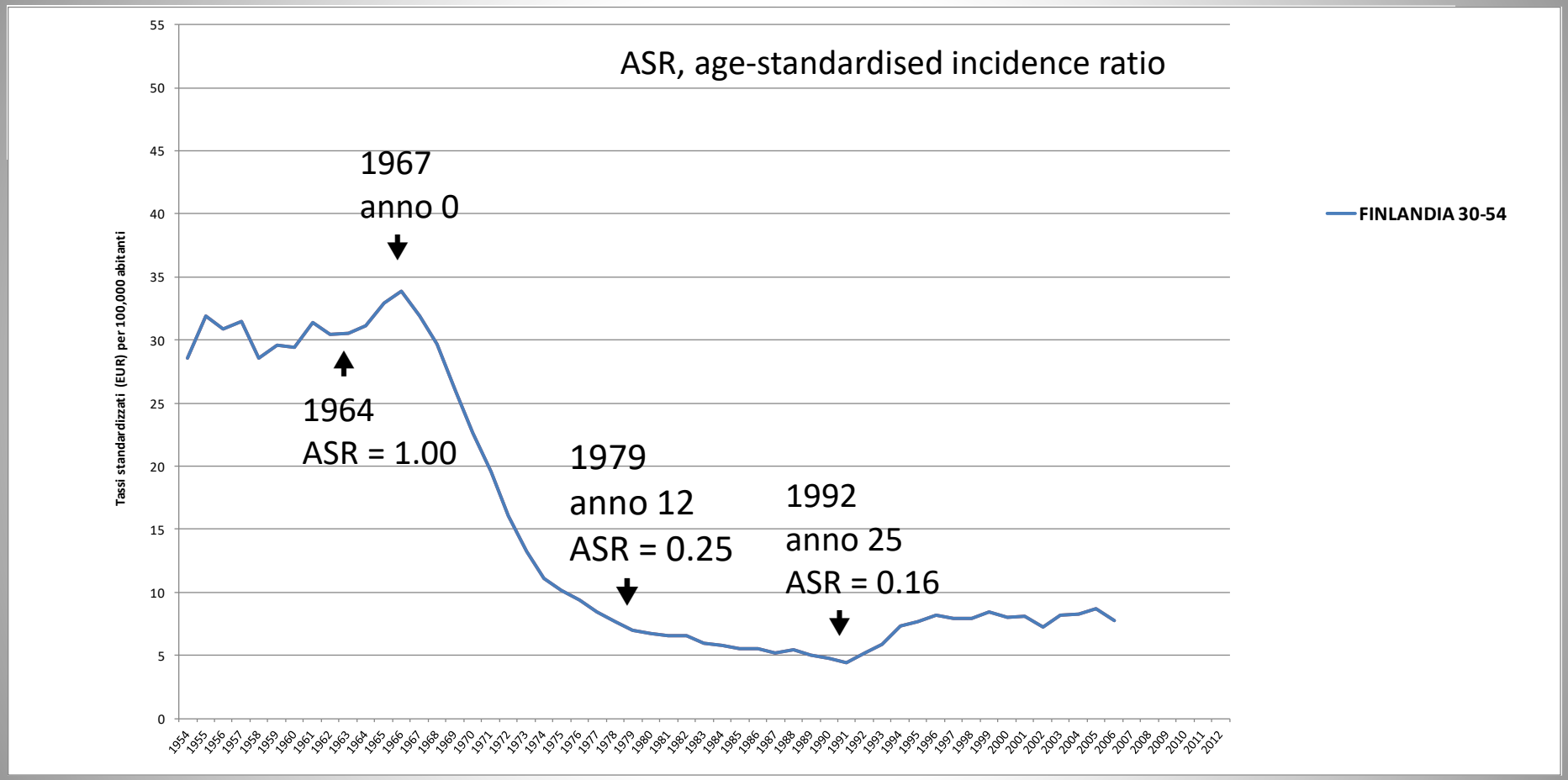
Ma, allora,
perché i programmi organizzati di screening cervicale
non sono mai stati contestati?

Pensiamo allo screening cervicale …



Curva dei tassi d'incidenza del cancro cervicale, standardizzati per età, nella popolazione bersaglio dei programmi di screening cervicale in Finlandia e Svezia, 1954-2009 (*fonte: IARC NORDCAN*).

Pensiamo allo screening cervicale …



Curva dei tassi d'incidenza del cancro cervicale, standardizzati per età, nella popolazione bersaglio del programma di screening cervicale in Finlandia, 1954-2007 (*fonte: IARC NORDCAN*) e rapporti d'incidenza post-screening verso pre-screening.

Il ruolo dello screening nel controllo del cancro della mammella in Italia

18.3%

In Italia, nel 2017,
i cancri della mammella screen-detected in donne di 50-69 anni (9.255) sono stati il 18.3% di tutti i cancri della mammella incidenti in donne di ogni età (50.500)

Fonti: **Osservatorio Nazionale Screening, AIRTUM**

Il ruolo dello screening nel controllo del cancro della mammella in Italia

18.3%: e il restante 81.7%

- donne in età non eleggibile
- donne in età eleggibile ma non invitate per inefficienza dei programmi
- donne non invitate per storia di cancro della mammella
- donne non invitate perché a rischio eredo-familiare
- donne invitate che hanno rifiutato l'invito
- donne aderenti che hanno rifiutato gli approfondimenti
- donne aderenti che hanno avuto un cancro d'intervallo

Il ruolo dello screening nel controllo del cancro della mammella in Italia

81.7%: che cosa si sta facendo?

- donne in età non eleggibile
- donne in età eleggibile ma non invitate per inefficienza dei programmi
- donne non invitate per storia di cancro della mammella
- donne non invitate perché a rischio eredo-familiare
- donne invitate che hanno rifiutato l'invito
- donne aderenti che hanno rifiutato gli approfondimenti
- donne aderenti che hanno avuto un cancro d'intervallo

81.7%: allargamento dell’età eleggibile

OSSERVATORIO
NAZIONALE
SCREENING

Inviti nelle fasce di età 45-49 anni e 70-74 anni nel 2019

45-49 anni: 15% della popolazione bersaglio, in gran parte in 3 regioni
70-74 anni: 34% della popolazione bersaglio

81.7%: allargamento dell'età eleggibile

Estensione dell'età bersaglio del programma di screening mammografico e governo della pratica mammografica in Emilia-Romagna

Priscilla Sassoli de Bianchi,[1] Alessandra Ravaioli,[2] Stefano Ferretti,[1] Alba Carola Finarelli,[1] Adriana Giannini,[1] Carlo Naldoni,[1] Piera Sanna,[1] Lauro Bucchi[2]

CAUSA D'ACCESSO	NUMERO DI DONNE SOTTOPOSTE A MAMMOGRAFIA	
	2008	2014
SCREENING ORGANIZZATO		
50-69 anni	140.822	180.520
Classi d'età eleggibili*	140.822	319.394
SCREENING SPONTANEO		
35-39 anni**	6.517	2.600
40-44 anni	33.895	27.991
45-49 anni	37.391	9.002
50-69 anni	46.801	38.021
70-74 anni	14.359	7.673
75-79 anni**	8.722	11.097
Totale	147.685	96.384
MAMMOGRAFIA DIAGNOSTICA (35-79 ANNI)	12.774	12.040
TUTTE LE CAUSE (35-79 ANNI)	305.755	431.850

81.7%: un ruolo nel follow-up

Recommendations for breast imaging follow-up of women with a previous history of breast cancer: position paper from the Italian Group for Mammography Screening (GISMa) and the Italian College of Breast Radiologists (ICBR) by SIRM

Lauro Bucchi[1] · Paolo Belli[2] · Eva Benelli[3] · Daniela Bernardi[4] · Beniamino Brancato[5] · Massimo Calabrese[6] · Luca A. Carbonaro[7] · Francesca Caumo[8] · Beatrice Cavallo-Marincola[9] · Paola Clauser[10,11] · Chiara Fedato[12] · Alfonso Frigerio[13] · Vania Galli[14] · Livia Giordano[15] · Paola Golinelli[16] · Giovanna Mariscotti[17] · Laura Martincich[18] · Stefania Montemezzi[19] · Doralba Morrone[5] · Carlo Naldoni[20] · Adriana Paduos[15] · Pietro Panizza[21] · Federica Pediconi[9] · Fiammetta Querci[22] · Antonio Rizzo[23] · Gianni Saguatti[24] · Alberto Tagliafico[25] · Rubina M. Trimboli[7] · Chiara Zuiani[11] · Francesco Sardanelli[7,26]

Radiol med (2016) 121:891–896

ASSOCIAZIONE SENONETWORK ITALIA ONLUS
IL NETWORK DEI CENTRI ITALIANI DI SENOLOGIA

Indagine sull'integrazione e collaborazione tra i Programmi di Screening Mammografico e i Centri aderenti a Senonetwork

Four centres (5%) reported that the screening programme was responsible for actively initiating follow-up during the 10-year period after diagnosis.

81.7%: screening ed eredo-familiarità

A regional population-based hereditary breast cancer screening tool in Italy: First 5-year results

Laura Cortesi[1] | Bruna Baldassarri[2] | Stefano Ferretti[2] | Elisabetta Razzaboni[1] | Mariangela Bella[3] | Lauro Bucchi[4] | Debora Canuti[5] | Pierandrea De Iaco[6] | Giorgio De Santis[7] | Fabio Falcini[4,8] | Vania Galli[9] | Lea Godino[10] | Maurizio Leoni[11] | Anna Myriam Perrone[6] | Marco Pignatti[7] | Gianni Saguatti[12] | Donatella Santini[13] | Priscilla Sassoli de'Bianchi[2] | Federica Sebastiani[1] | Mario Taffurelli[14] | Giovanni Tazzioli[15] | Daniela Turchetti[10] | Claudio Zamagni[16] | Carlo Naldoni[2]

Conclusions: To our knowledge, this is the first regional population-based multistep model that is aimed to identify individuals with *BRCA1/2* mutations and to offer an intensive surveillance program for hereditary-high risk women. This tool is feasible and effective, even if more efforts must be performed to increase the acceptance of multiple assessments by the study population.

81.7%: screening personalizzato

STUDY PROTOCOL Open Access

The ANDROMEDA prospective cohort study: predictive value of combined criteria to tailor breast cancer screening and new opportunities from circulating markers: study protocol

Livia Giordano[1*], Federica Gallo[1], Elisabetta Petracci[2], Giovanna Chiorino[3], Nereo Segnan[1] and the Andromeda working group

81.7%: test di screening

Novel Approaches to Screening for Breast Cancer

Ritse M. Mann, MD, PhD • Regina Hooley, MD • Richard G. Barr, MD, PhD • Linda Moy, MD

Radiology 2020; 297:266–285

Novel techniques in the field of breast imaging may soon play a role in breast cancer screening:

- digital breast tomosynthesis,
- Contrast material–enhanced spectral mammography,
- US (automated three-dimensional breast US),
- transmission tomography,
- elastography,
- optoacoustic imaging,
- MRI (abbreviated and ultrafast, diffusion-weighted imaging),
- molecular breast imaging,
- artificial intelligence,
- radiomics,
- nonimaging-based screening tests (liquid biopsy and breathing tests)

Il ruolo dello screening nel controllo del cancro della mammella in Italia

81.7%: che cosa NON si sta facendo

- donne in età non eleggibile
- donne in età eleggibile ma non invitate per inefficienza dei programmi
- donne non invitate per storia di cancro della mammella
- donne non invitate perché a rischio eredo-familiare
- donne invitate che hanno rifiutato l'invito
- donne aderenti che hanno rifiutato gli approfondimenti
- donne aderenti che hanno avuto un cancro d'intervallo

Screening e centri di senologia

Lo screening mammografico non è solo mammografia.
E' anche:

- **protocolli basati sull'evidenza (appropriatezza)**
- **visione di popolazione**
- **responsabilità definita**
- **responsabilità per un risultato**
- **valutazione di processo e di efficacia**
- **pubblicazione dei risultati (trasparenza)**
- **lavoro multidisciplinare <u>autentico</u>**

A tutto questo devono avere accesso tutte le donne,
non solo quelle di 50-69 anni con cancro screen-detected.

Come?

Screening e centri di senologia

Come?

Portando lo screening e i suoi principi fondanti all'interno dei centri di senologia

Screening e centri di senologia

The requirements of a specialist Breast Centre

A.R.M. Wilson [a,*], L. Marotti [b], S. Bianchi [c], L. Biganzoli [d], S. Claassen [e], T. Decker [f], A. Frigerio [g], A. Goldhirsch [h], E.G. Gustafsson [i], R.E. Mansel [j], R. Orecchia [k], A. Ponti [g], P. Poortmans [l], P. Regitnig [m], M. Rosselli Del Turco [n], E.J.Th. Rutgers [o], C. van Asperen [p], C.A. Wells [q], Y. Wengström [i], L. Cataliotti [r]

European Journal of Cancer 49 (2013) 3579–3587

Alcuni dei principi fondanti dello screening mammografico fanno già parte del modello EUSOMA dei Centri di senologia

Conclusione

I centri di senologia sono l’evoluzione della specie Screening