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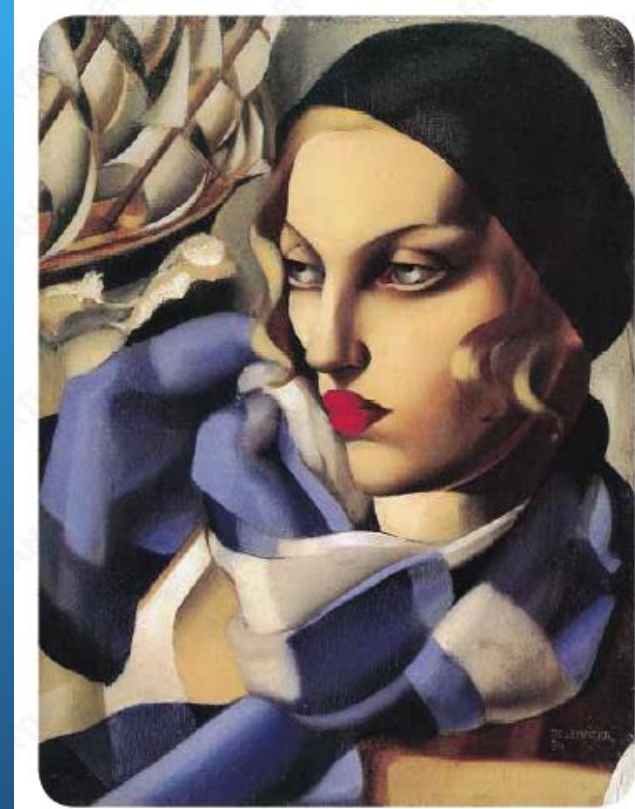
TINTERRI CORRADO BREAST UNIT MILAN



BRCA MUTATION PATIENTS : WHAT SURGERY ?

NEGRAR (VERONA) 13.10.2015

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ROZZANO-MILAN





The Washington Post

Breast cancer: genetic testing soars after Angelina Jolie's double mastectomy

After Jolie, women less shy to investigate mastectomies

RISK REDUCING SURGERY

Great media impact that sometimes dominates the scientific aspects

Los Angeles Times | HEALTH

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More women choose prophylactic mastectomy [Updated]

September 28, 2009 | 8:00 am

The choice to remove a healthy breast in order to avoid breast cancer is a deeply personal decision that appears to be on the upswing in one group of women, according to a study published today in the journal *Cancer*.



Among women who had cancer in one breast, the number who opted to have the other breast removed, called contralateral prophylactic mastectomy, increased from 1995 to 2005 in New York state. During the same time period, however, the number of healthy women who chose to have a prophylactic mastectomy of both breasts because of a higher-than-average risk of developing cancer held steady. The research is among the first to examine the choice of prophylactic

ASPS Recommended Insurance Coverage Criteria for Third-Party Payers

Prophylactic Mastectomy

Diagnosis	ICD-9
A. Family history of malignant neoplasm of breast	V16.3
B. Personal history of malignant neoplasm of breast	V10.3
C. Fibrocystic breast disease	610.1
D. Malignant neoplasm of female breast	1740-1749
E. Malignant neoplasm of male breast	1750-1759
F. Carcinoma in situ of the breast	233.0
G. Neoplasm of uncertain behavior of the breast	238.3

Procedure	CPT Code
A. Mastectomy, simple, complete	19100
B. Mastectomy, simple, complete, bilateral	19100-50
C. Mastectomy, subcutaneous	19182
D. Mastectomy, subcutaneous, bilateral	19182-50

DEFINITION: COSMETIC AND RECONSTRUCTIVE SURGERY

For reference, the following definitions of cosmetic and reconstructive surgery were adopted by the American Medical Association in 1989.

Cosmetic surgery is performed to reshape normal structures of the body in order to improve the patient's appearance and self-esteem.

Reconstructive surgery is performed on abnormal structures of the body, caused by congenital defects, developmental abnormalities, trauma, infection, tumors or disease. It is generally performed to improve function, but may also be done to approximate a normal appearance.

DEFINITION: PROPHYLACTIC MASTECTOMY

Prophylactic mastectomy is the surgical removal of the breast to prevent the occurrence or recurrence of cancer.

POLICY

Prophylactic mastectomy is considered reconstructive surgery and medically necessary when one of the following diagnoses or conditions are present:

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The Jolie effect: Number of women asking about mastectomies quadruples since actress revealed she had her breasts removed to reduce cancer risk

By Sophie Jordan

WELLBEEBEE 11:55 AM GMT on September 20th 2013 | UPDATED: 12:02 PM GMT on September 20th

23 shares

Breast cancer charities have reported a four-fold surge in women enquiring about having their breasts removed since Angelina Jolie announced she'd had the operation to lessen her risk of developing the disease.

Figures from Cancer Research UK show the numbers of calls to its helpline have increased four-fold while there has been a similar rise in visits to its website.

The actress revealed she'd had a double mastectomy in May after learning she carried a faulty gene that gave her an 87 per cent chance of developing breast cancer.

Miss Jolie, 37, said she'd made the decision for the sake of her eight children having witnessed her own mother Marcellina's battle with a



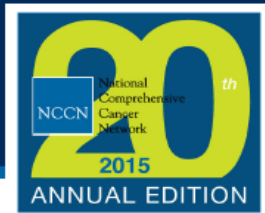
New Details
THE OHIO THREE



HOW THEY
SURVIVED



HARRY
TAKES
AMERICA!



NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Breast Cancer

Version 3.2015

NCCN.org

NCCN Guidelines for Patients® available at www.nccn.org/patients

The Panel recommend that women with breast cancer who are less than or equal 35 yrs or premenopausal or CARRIER of a KNOWN BRCA1/2 mutation consider additional risk reduction strategy. Following appropriate risk assessment and counselling

This process should involve multidisciplinary consultation prior to the surgery

Recommendations for the management of early breast cancer

in women with an identified BRCA1 or BRCA2 gene mutation or at high risk of a gene mutation

FEBRUARY 2014 | Incorporates published evidence to August 2013

A CLINICAL PRACTICE GUIDELINE DEVELOPED BY CANCER AUSTRALIA

RECOMMENDATIONS – SURGERY



Surgical management *on the ipsilateral side* for women diagnosed with breast cancer with a BRCA1/2 mutation

Offer a choice of either breast conserving treatment (breast conserving surgery and radiotherapy) or *mastectomy* to women diagnosed with breast cancer with a BRCA1/2 mutation as both are effective in terms of survival.

- If women diagnosed with breast cancer with a BRCA1/2 mutation are considering a contralateral risk-reducing mastectomy (at the time of the cancer diagnosis or in the future) inform them that therapeutic ipsilateral mastectomy may be preferable to breast conserving treatment.
- Inform women diagnosed with breast cancer with a BRCA1/2 mutation that there is an increased risk of ipsilateral breast cancer after breast conserving treatment compared to mastectomy, but this is reduced by *adjuvant chemotherapy*.[#](see practice points B and F).

STATEMENTS OF EVIDENCE SURGICAL RISK-REDUCING STRATEGIES

CONTRALATERAL RISK-REDUCING MASTECTOMY

Survival outcomes

It is unclear whether contralateral risk-reducing mastectomy (***compared to no contralateral risk-reducing mastectomy***) *improves overall survival or breast cancer-specific survival in women with breast cancer and a BRCA1/2 mutation.*

Contralateral breast cancer

Contralateral risk-reducing mastectomy (**compared to no contralateral risk-reducing mastectomy**) **substantially decreases** (by more than 90%) the risk of contralateral breast cancer, particularly in younger women (less than 50 years) with breast cancer with a BRCA1/2 mutation.

Contralateral mastectomy improves survival in women with *BRCA1/2*-associated breast cancer

D. Gareth R. Evans · Sarah L. Ingham ·
Andrew Baildam · Gary L. Ross · Fiona Lalloo ·
Iain Buchan · Anthony Howell

The survival advantage remained after matching for oophorectomy, gene, grade and stage: HR 0.37 (0.17–0.80, $p = 0.008$) CRRM appeared to act independently of RRBSO.

CRRM appears to confer a survival advantage. If this finding is confirmed in a larger series it should form part of the counselling procedure at diagnosis of the primary tumour.

The indication for CRRM in women who have had RRBSO also requires further research.

Improved overall survival after contralateral risk-reducing mastectomy in brca1/2 mutation carriers with a history of unilateral breast cancer: A prospective analysis

Bernadette A.M. Heemskerk-Gerritsen¹, Matti A. Rookus², Cora M. Aalfs³, Margreet G.E.M. Ausems⁴, Johanna M. Collée⁵, Liesbeth Jansen⁶, C. Marleen Kets⁷, Kristien B.M.I. Keymeulen⁸, Linetta B. Koppert⁹, Hanne E.J. Meijers-Heijboer¹⁰, Thea M. Mooij², Rob A.E.M. Tollenaar¹¹, Hans F.A. Vasen¹², HEBON¹³, Maartje J. Hooning^{1†} and Caroline Seynaeve^{1†}

We examined the efficacy of CRRM on overall survival in mutation carriers with a history of PBC. From a Dutch multicentre cohort, we selected 583 BRCA-associated PBC patients, being diagnosed between 1980 and 2011.

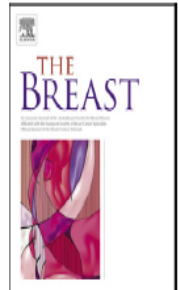
Survival benefit was especially seen in young PBC patients (<40 years), in patients having a PBC with differentiation grade 1/2 and/or no triple-negative phenotype, and in patients not treated with adjuvant chemotherapy



Contents lists available at [ScienceDirect](#)

The Breast

journal homepage: www.elsevier.com/brst



Original article

Optimal surgical management for high-risk populations

Tari A. King^{*}, Melissa Pilewskie, Monica Morrow

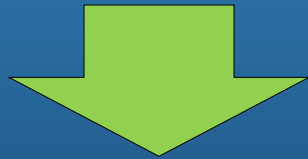
Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, 300 East 66th Street, New York, NY 10065, USA

...and those who harbor a deleterious mutation in BRCA1 or BRCA2 are frequently considered to be at highest risk of local failure, leading to speculation that more-aggressive surgical treatment is warranted in these patients.

For those at inherited risk, **a more-aggressive surgical approach may be preferable**, however; patient age, ER status, stage of the index lesion, and individual patient preferences should all be considered in the surgical decision-making process.

BREAST PROPHYLACTIC SURGERY

- ✓ Most effective if implemented before the age of 40
- ✓ Functional and aesthetic irreversible changes



Inevitable conditioning of the psycho-physical aspects of the women with undeniable implications of the life's relationship



RISK REDUCING SURGERY

*Literature more and more consistent ,
BUT*

- Fragmented and uneven casistics
- No randomized trials
- Small number of patients
- Limited follow-up
- Different surgery
- Different indications (≠ USA/Europa)
- Different reimbursement (USA insurance – Italia /EuropaDRG)

Limitations of Current Studies

- No RCTs
- Difficult since women be reluctant to randomize regarding their decision
- Justifying randomization of women to control group is problematic.
- Long follow up period
- Difficulty blinding participants and investigators

ETHICAL ISSUES

Published Online April 4, 2007

Prophylactic mastectomy: ethical issues

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Main points: First, a risky condition is not a disease and prevention does not improve well-being. The benefits are only statistical and make sense at the population level. Secondly, the cause of the risk is a genetic factor and some might argue about genetic 'exceptionalism'. Thirdly, there is no organ as, connected to femininity, sensuality, sexuality, adulthood and motherhood as the breast. Lastly, making tough and complex choices requires assistance from ethics.

criteria to fulfil, reducing autonomy.

Emerging areas for developing research: It might be expected that this tough issue will be solved, thanks to the improvement of prevention and therapeutic efficacy.

symposium article

Hereditary breast cancer: clinical features and risk reduction strategies

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Prophylactic bilateral mastectomy has resulted in up to 97% risk reduction of CBC [7, 26, 27]. Interestingly, the pattern of utilization of bilateral mastectomy differs widely between countries, reflecting providers' biases in interpreting the evidence, communicating it and offering treatment options. It also reflects the diversity of the value systems affecting medical decision and health care delivery in differing countries [28].

In conclusion, the management of *BRCA* mutation carriers is evolving: it reflects the available evidence as well as the bias of different ethical value systems and structural characteristics of the different health care systems operating worldwide.

RISK REDUCING SURGERY

- WHY ?
- FOR WHOM ?
- WHAT SURGERY ?
- HOW ?
- TIMING ?
- WHICH UPTAKE ?
- WHERE ?



RISK REDUCING SURGERY

WHY?

The New England Journal of Medicine

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NUMBER 2



EFFICACY OF BILATERAL PROPHYLACTIC MASTECTOMY IN WOMEN WITH A FAMILY HISTORY OF BREAST CANCER

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JOANNE L. JOHNSON, R.N., SHAWN K. McDONNELL, M.S., MARLENE H. FROST, Ph.D., R.N.,
AND ROBERT B. JENKINS, M.D., Ph.D.

ABSTRACT

Background Options for women at high risk for breast cancer include surveillance, chemoprevention, and prophylactic mastectomy. The data on the outcomes for surveillance and prophylactic mastectomy are incomplete.

Methods We conducted a retrospective study of all women with a family history of breast cancer who underwent bilateral prophylactic mastectomy at the Mayo Clinic between 1960 and 1993. The women were divided into two groups — high risk and moderate risk — on the basis of family history. A control study of the sisters of the high-risk probands and the Gail model were used to predict the number of breast cancers expected in these two groups in the absence of prophylactic mastectomy.

Results We identified 639 women with a family history of breast cancer who had undergone bilateral prophylactic mastectomy: 214 at high risk and 425 at moderate risk. The median length of follow-up was 14 years. The median age at prophylactic mastectomy was 42 years. According to the Gail model, 37.4 breast cancers were expected in the moderate-risk group; 4 breast cancers occurred (reduction in risk, 89.5 percent; $P < 0.001$). We compared the numbers of breast cancers among the 214 high-risk probands with the numbers among their 403 sisters who had not undergone prophylactic mastectomy. Of these sisters, 38.7 percent (156) had been given a diagnosis of breast cancer (115 cases were diagnosed before the respective proband's prophylactic mastectomy, 38 were diagnosed afterward, and the time of the diagnosis was unknown in 3 cases). By contrast, breast cancer was diagnosed in 14 percent (3 of 214) of the probands. Thus, prophylactic mastectomy was associated with a reduction in the incidence of breast cancer of at least 90 percent.

Conclusions In women with a high risk of breast cancer on the basis of family history, prophylactic mastectomy can significantly reduce the incidence of breast cancer. (N Engl J Med 1999;340:77-84.)

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THE availability of improved means to identify women at high risk for breast cancer such as genetic testing for *BRCA1* and *BRCA2* mutations, intensifies the need to define the benefits and risks of early detection and protective measures for such women.

Prophylactic mastectomy, either total or subcutaneous mastectomy, is one option for the prevention of breast cancer.¹ Specific indications for prophylactic mastectomy include a family or personal history of breast cancer, multiple previous breast biopsies with atypical hyperplasia, findings of dense breast tissue on mammography, mastodynia, and cancerphobia.² Although prophylactic mastectomy has been used for decades, there is little information regarding the effectiveness of this procedure.³⁻⁵ Surgeons long recognized that breast cancer is widely distributed over the entire anterolateral portion of the chest and axilla and that no mastectomy removes all primary disease.⁶ There have been case reports of breast cancer in residual glandular epithelium after total or subcutaneous prophylactic mastectomy.⁷

One study of prophylactic mastectomy included 1500 women who underwent subcutaneous mastectomy.¹¹² Patients were identified by soliciting information from members of the American Board of Plastic Surgery; 165 plastic surgeons contributed

From the Division of Medical Oncology (L.C.H., M.H.F.), Breast Disease, Gynecology, Plastic and Reconstructive Surgery (L.W., R.C.A.), and Clinical Epidemiology (T.A.S., J.L.), and the Departments of Surgery (J.E.W., P.G.A.), and the Departments of Pathology (J.L.M., P.S.), Mayo Clinic and Mayo Foundation, Rochester, Minn., and the Departments of Pathology, St. Vincent Hospital, Dublin, Ireland (T.P.C.). Address reprint requests to Dr. Hartmann at the Department of Oncology, Mayo Clinic, 200 First St. S., Rochester, MN 55905.

Other authors were: John E. Gray, M.D., of the Departments of Surgery and Virginia V. Michalek, M.D., of the Departments of Medical Gynecology and Mayo Foundation, Rochester, Minn.

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BREAST CANCER AFTER PROPHYLACTIC BILATERAL MASTECTOMY IN WOMEN WITH A *BRCA1* OR *BRCA2* MUTATION

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CECILE T.M. BREKELMANS, M.D., Ph.D., AND JAN G.M. KILIN, M.D., Ph.D.

ABSTRACT

Background Women with a *BRCA1* or *BRCA2* mutation have a high risk of breast cancer and may choose to undergo prophylactic bilateral total mastectomy. We investigated the efficacy of this procedure in such women.

Methods We conducted a prospective study of 139 women with a pathogenic *BRCA1* or *BRCA2* mutation who were enrolled in a breast-cancer surveillance program at the Rotterdam Family Cancer Clinic. At the time of enrollment, none of the women had a history of breast cancer. Seventy-six of these women eventually underwent prophylactic mastectomy, and the other 63 remained under regular surveillance. The effect of mastectomy on the incidence of breast cancer was analyzed by the Cox proportional-hazards method in which mastectomy was modeled as a time-dependent covariate.

Results No cases of breast cancer were observed after prophylactic mastectomy after a mean (\pm SE) follow-up of 2.5 ± 1.4 years, whereas eight breast cancers developed in women under regular surveillance after a mean follow-up of 3.0 ± 1.5 years ($P = 0.003$; hazard ratio, 0; 95 percent confidence interval, 0 to 0.36). The actuarial mean five-year incidence of breast cancer among all women in the surveillance group was 17.27 percent. On the basis of an exponential model, the yearly incidence of breast cancer in this group was 2.6 percent. The observed number of breast cancers in the surveillance group was consistent with the expected number (ratio of observed to expected cases, 1.2; 95 percent confidence interval, 0.4 to 3.7; $P = 0.50$).

Conclusions In women with a *BRCA1* or *BRCA2* mutation, prophylactic bilateral total mastectomy reduces the incidence of breast cancer at three years of follow-up. (N Engl J Med 2001;345:159-64.)

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THE identification of the breast-cancer-susceptibility genes *BRCA1*¹ and *BRCA2*² evoked widespread interest in genetic testing among women at risk for a mutation in these genes.^{3,4} We found that 57 percent of women without breast cancer who had a 50 percent chance of carrying a *BRCA1* or *BRCA2* mutation requested genetic testing.⁴ This result indicates the need to determine the efficacy of the various options for reducing the risk of breast cancer and for early detection in women with a *BRCA1* or *BRCA2* mutation.

Women with a *BRCA1* or *BRCA2* mutation have a cumulative lifetime risk of invasive breast cancer (up to the age of 70 years) of 55 to 85 percent and of invasive epithelial ovarian cancer of 15 to 65 percent.^{5,6} In these women the risk of breast cancer begins to increase near the age of 25 years, and their overall survival once breast cancer does develop is similar to that of age-matched patients with sporadic cases of breast cancer: in both, the 10-year survival rate is about 50 percent.^{7,8}

Current risk-reduction strategies for women with a *BRCA1* or *BRCA2* mutation include regular surveillance; prophylactic mastectomy, oophorectomy, or both; and chemoprevention.⁹⁻¹¹ In our experience, 50 percent of women who have a *BRCA1* or *BRCA2* mutation have chosen to undergo prophylactic bilateral mastectomy.⁴ Until now, however, there have been only retrospective studies of the efficacy of the procedure in women with an increased risk of breast cancer.

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Substantial breast cancer risk reduction and potential survival benefit after bilateral mastectomy when compared with surveillance in healthy BRCA1 and BRCA2 mutation carriers: a prospective analysis

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Conclusions: In healthy BRCA1/2 mutation carriers, BRRM when compared with surveillance reduces BC risk substantially, **while longer follow-up is warranted to confirm survival benefits.**

Breast Cancer Res Treat (2013) 142:611–618

DOI 10.1007/s10549-013-2765-x

EPIDEMIOLOGY

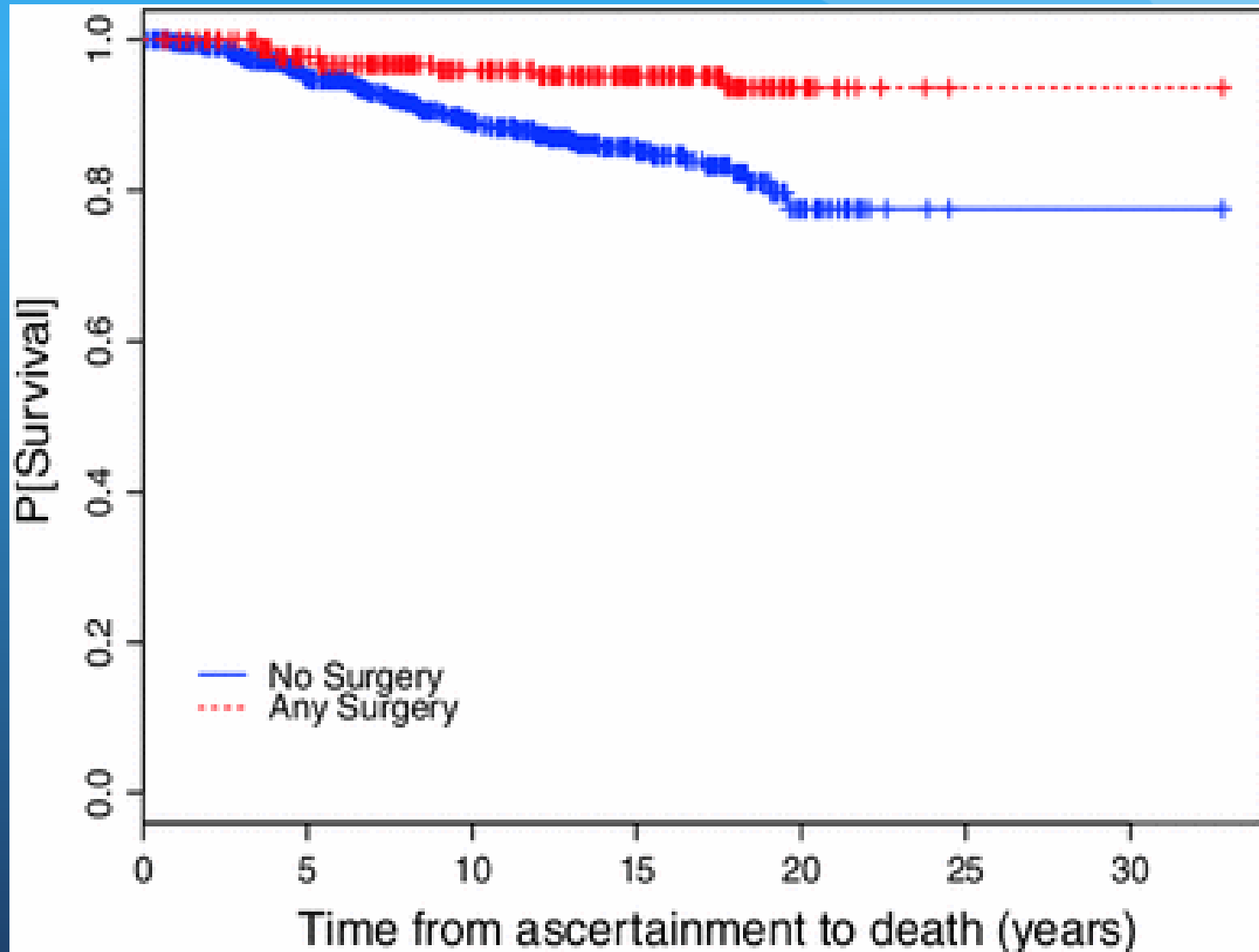
Risk-reducing surgery increases survival in *BRCA1/2* mutation carriers unaffected at time of family referral

Sarah L. Ingham · Matthew Sperrin · Andrew Baildam · Gary L. Ross ·
Richard Clayton · Fiona Lalloo · Iain Buchan · Anthony Howell ·
D. Gareth R. Evans

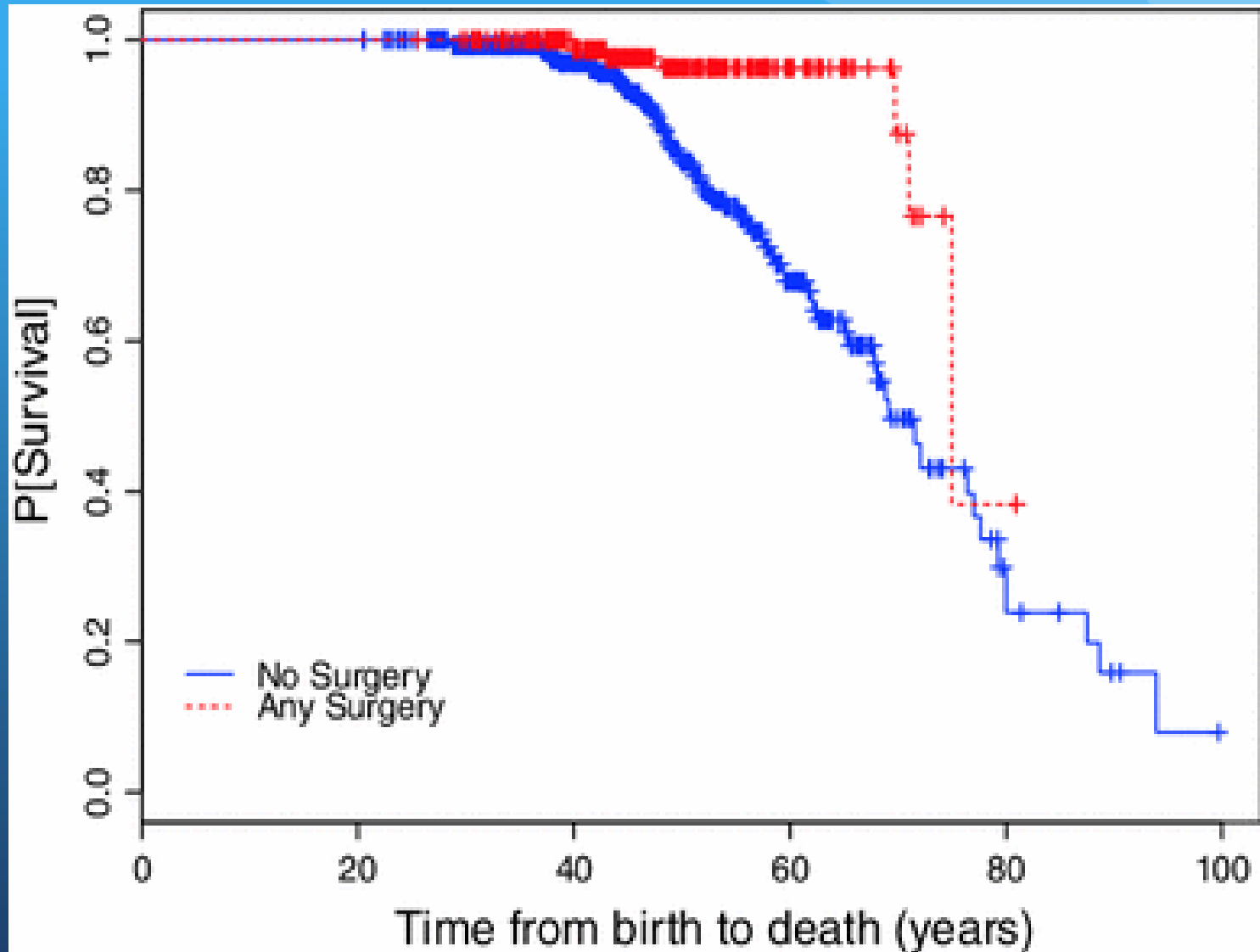
Manchester Genetic Medicine Database

A total of 691 female *BRCA1/2* mutation carriers were identified in the Genetic Medicine database from *BRCA* families ascertained between February 1980 and December 2011. This cohort included 346 *BRCA1* carriers and 345 *BRCA2* carriers

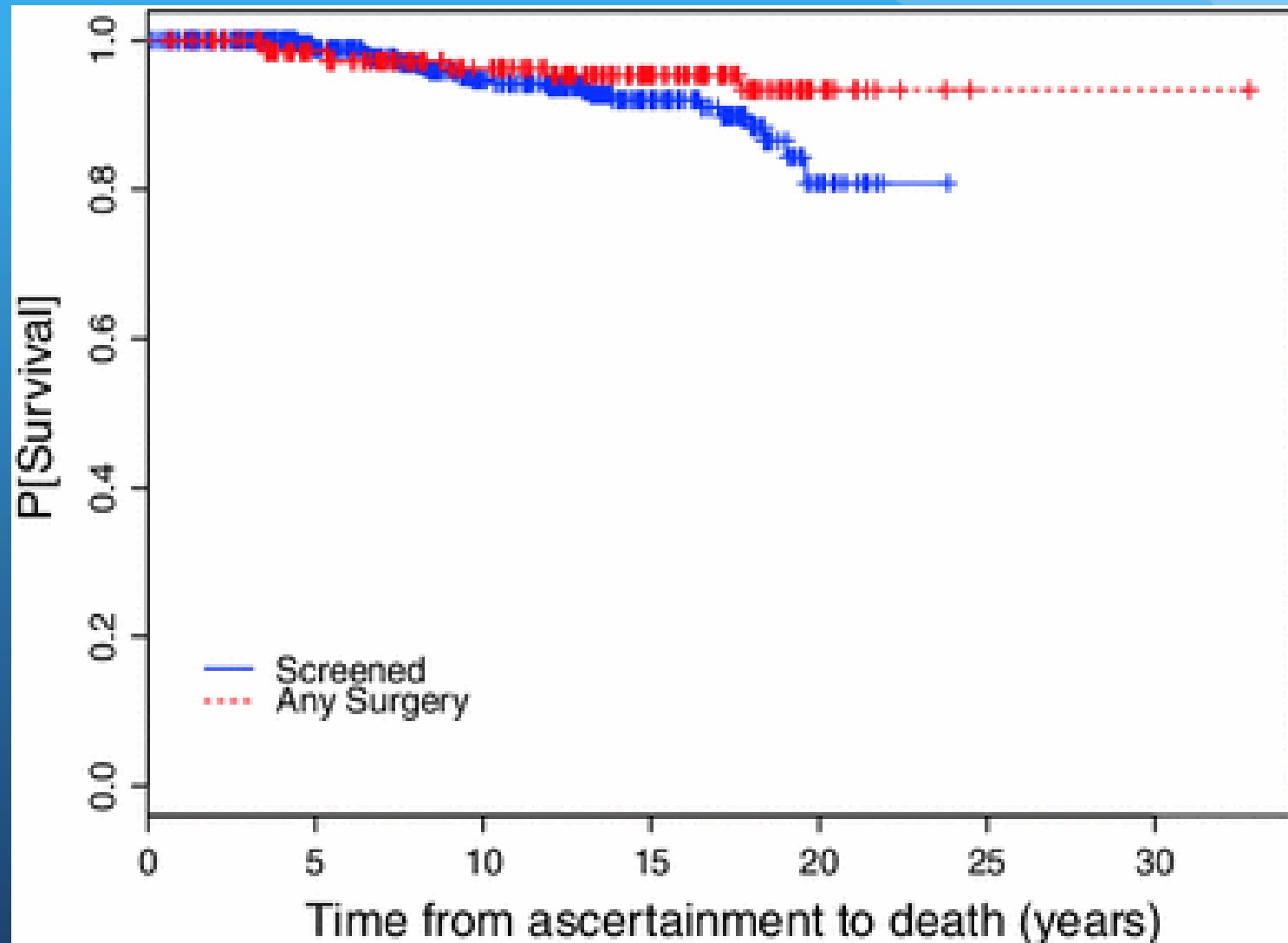
Risk Reducing Surgery Vs Observation



Risk Reducing Surgery by Age



Risk Reducing Surgery Vs Intensively Screened



REVIEW ARTICLE – BREAST ONCOLOGY

Bilateral Risk-Reduction Mastectomy in BRCA1 and BRCA2 Mutation Carriers: A Meta-analysis

Francesca De Felice, MD¹, Claudia Marchetti, MD², Angela Musella, MD², Innocenza Palaia, PhD², Giorgia Perniola, PhD², Daniela Musio, MD¹, Ludovico Muzii, PhD², Vincenzo Tombolini, MD¹, and Pierluigi Benedetti Panici, MD²

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Results. Meta-analysis of four prospective studies, including 2635 patients, demonstrated a significant risk reduction of breast cancer incidence in BRCA1 and BRCA2 mutation carriers receiving BRRM (HR 0.07;95 % CI 0.01–0.44; p = 0.004).

- Their analysis included four prospective studies and estimated a 93 % reduction in breast cancer risk.
- The fact that only 4 of 627 women undergoing risk-reducing mastectomy had a diagnosis of breast cancer could be encouraging, but the median follow-up period for all the included studies was only about 4 years.

.... SOME LIMITATIONS.....

- they found that in patients who underwent BRRM plus RRSO the benefit was confirmed (HR 0.11; $p = 0.03$) but was slightly lower than the one recorded in patients receiving BRRM without RRSO (HR 0.06; $p = 0.005$).
- it was not possible to delineate a correct standardization by age
- they only analyzed studies of a prospective nature because randomized studies have not been published in this setting, probably because they are ethically unacceptable.

clinical practice guidelines

Annals of Oncology 22 (Supplement 6): vi31–vi34, 2011
doi:10.1093/annonc/mdr373

BRCA in breast cancer: ESMO Clinical Practice Guidelines

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On behalf of the ESMO Guidelines Working Group*

¹Medical Oncology Department, Breast Cancer Center; ²Oncogenetics Laboratory, University Hospital Vall d'Hebron, Barcelona, Spain; ³Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; ⁴Breast Cancer Surgical Unit, Breast Cancer Center, University Hospital Vall d'Hebron, Barcelona, Spain; ⁵European School of Oncology, Milan, Italy; ⁶Breast Cancer Unit, Champalimaud Cancer Center, Lisbon, Portugal

BUT...

prophylactic bilateral mastectomy

This is the most effective strategy available for risk reduction of breast cancer in mutation carriers [III, B]. Studies have shown a risk reduction of at least 90% with PBM. In two prospective studies published to date, no breast cancers were diagnosed in the risk-reducing mastectomy group compared with 7–13% breast cancers in women under surveillance with a mean follow-up of 3 years. However, survival benefits have not been demonstrated with risk reduction breast surgery.

RISK REDUCING SURGERY

FOR WHOM ?

Familial Cancer (2008) 7:91–95
DOI 10.1007/s10689-007-9167-3

Genetic counseling and clinical management of newly diagnosed breast cancer patients at genetic risk for *BRCA* germline mutations: perspective of a surgical oncologist

Edibaldo Silva

Published online: 18 October 2007
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Abstract Women with a family history of breast cancer who are diagnosed with breast cancer are often counseled to undergo prophylactic mastectomy as part of their treatment for breast cancer. The majority of such individuals make these decisions in haste and without appropriate genetic counseling or testing. Most of them when tested for *BRCA* or other established mutations find that they are not mutation carriers. In retrospect, this realization leads many to question the wisdom of their prophylactic surgery which is often associated with complications and quality of life problems which they never envisioned. We have designed an algorithm for the management of these patients which minimizes these lifelong problems.

Keywords Breast cancer · Clinical management · Genetic counseling · High risk breast cancer pedigree

Breast cancer remains a disease of older women. Yet, increasing public awareness of the familial predisposition associated with it leads many to overestimate their own individual risk of being potential genetic carriers. Family history is often the source of this exaggerated concern which leads many to regard themselves at high risk for carrying a genetic mutation for breast cancer. In extreme cases all too frequently encountered as referrals to multidisciplinary state of the art breast centers, prior inappropriate risk assessment by clinicians fuels a patient's emotional distress and leads to unnecessary preventive surgical procedures such as prophylactic bilateral

mastectomy while perhaps ignoring the more serious and nearly impossible to effectively screen risk of occult ovarian cancer. Recent reports suggest that as many as 80% of women submitted to prophylactic mastectomy resulting from limited risk assessment and counseling are not *BRCA* carriers or carry an inordinate risk for these mutations [1, 2].

Descriptions abound regarding the phenotype of potential *BRCA* gene carriers who ultimately account for no more than 5–10% of all breast cancers. Hereditary breast ovarian cancer (HBOC) pedigree candidates include patients whose familial pedigree fits within the categories listed in Table 1. Recent attempts by Lakhani et al. [3] to supplement this information with histologic evaluation of the individual's breast cancer show that high histologic grade and a negative ER receptor status in women with early onset breast cancer increase the probability of harboring a *BRCA* mutation from 5 to 27%. Thus, this remarkable finding justifies the use of genetic testing regardless of family history in such individuals. For this reason, in all cases where the HBOC syndrome is invoked counseling must begin before any genetic testing of individual's at risk and certainly well before any prophylactic treatment is enacted.

Four common scenarios can be envisioned which may present to an otherwise busy primary care practitioner. These are as follows: (1) the potential *BRCA* mutation carrier with newly-diagnosed breast cancer; (2) the known *BRCA* mutation carrier without breast cancer; (3) the high-risk pedigree patient with breast or ovarian cancer without an identifiable mutated *BRCA* allele; and (4) the high-risk pedigree patient without breast or ovarian cancer without an identifiable mutated *BRCA* allele. Of these, the first scenario is the most commonly faced by primary care physicians and the one most imbued with emotional

Recent reports suggest that as many as 80% of women submitted to prophylactic mastectomy resulting from limited risk assessment and counseling are not *BRCA* carriers or carry an inordinate risk for these mutations

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Position Statement on Prophylactic Mastectomy

Potential Indications for Bilateral Prophylactic Mastectomies

(In Patients without a Cancer Diagnosis)

1. **A known mutation of BRCA 1 or BRCA2 or other strongly predisposing breast cancer susceptibility genes.**
2. **A family history of breast cancer in multiple first-degree relatives and/or multiple successive generations of family members with breast and/or ovarian cancer (family cancer syndrome).** Additionally a family history of multiple family members with bilateral and/or pre-menopausal and/or male breast cancer may be associated with a familial breast cancer syndrome. Genetic counseling should be strongly considered, although prophylactic surgery is appropriate in women with a family history consistent with genetic predisposition and no demonstrable genetic mutation.
3. **High-risk histology: Atypical ductal or lobular hyperplasia, or lobular carcinoma in situ confirmed on biopsy.** These changes are especially significant if present in a patient with a strong family history of breast cancer.



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Comprehensive
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NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Breast Cancer Risk Reduction

Version 2.2015

NCCN.org

The NCCN Breast Cancer Risk Reduction Panel supports the use of RRM for carefully selected women at high risk for breast cancer who desire this intervention (eg, women with a *BRCA1/2*, *TP53*, *PTEN*, *CDH1*, or *STK11* mutation or, possibly, women with a history of LCIS). Although the consensus of the NCCN Breast Cancer Risk Reduction Panel is that consideration of RRM is an option for a woman with LCIS without additional risk factors, it is not a recommended approach for most of these women. There are no data regarding RRM in women with prior mantle radiation exposure. The value of RRM in women with deleterious mutations in other genes associated with a high risk for breast cancer (based on large epidemiologic studies) in the absence of a compelling family history of breast cancer is unknown.



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CURA
SALUTE
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WHAT RISK REDUCING SURGERY ?



WHAT SURGERY ?

- TOTAL MASTECTOMY (without reconstruction !!!!)



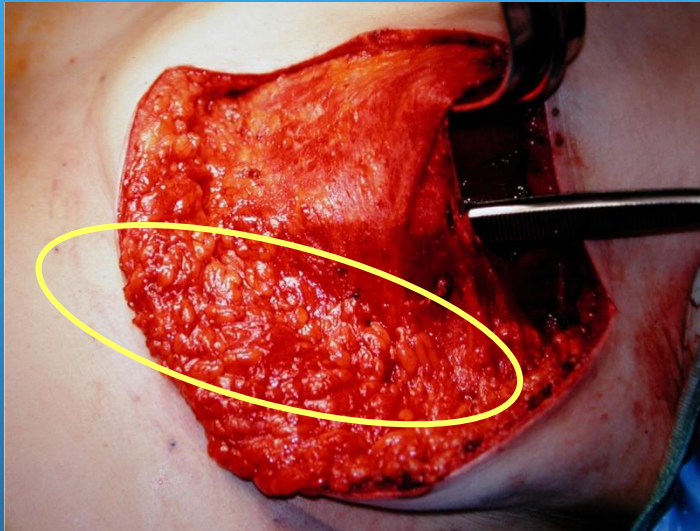
Nipple-Sparing Mastectomy



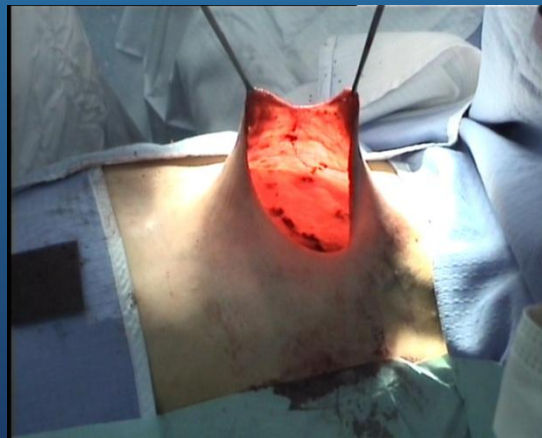
IT'S
REALLY
SAFETY ?

NIPPLE SPARING MASTECTOMY

POSSIBLE LOCATION OF GLANDULAR RESIDUAL



- “BREAST TAIL” AND SUPERIOR AREA
- RETROAREOLAR AND BELOW THE NIPPLE
- INFRAMAMMARY FOLD



WHAT SURGERY ?

Ann Surg Oncol (2011) 18:3102–3109
DOI 10.1245/s10434-011-1908-8

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – AMERICAN SOCIETY OF BREAST SURGEONS

Prophylactic and Therapeutic Mastectomy in *BRCA* Mutation Carriers: Can the Nipple Be Preserved?

Carol Reynolds, MD¹, Jennifer A. Davidson, PA¹, Noralane M. Lindor, MD², Katrina N. Glazebrook, MD³, James W. Jakub, MD⁴, Amy C. Degnim, MD⁴, Nicole P. Sandhu, MD⁵, Molly F. Walsh, MD⁶, Lynn C. Hartmann, MD⁷, and Judy C. Boughey, MD⁴

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Conclusions. The probability of nipple involvement by premalignant or malignant lesions in the NAC of *BRCA* mutation carriers is low at time of prophylactic mastectomy, but higher (10%) in women undergoing therapeutic mastectomy. NSM may be appropriate and oncologically safe for selected women with *BRCA* mutations.

BRCA2) were studied. TDLUs were present in 15 (24%) NAC specimens. No evidence of atypical hyperplasia, carcinoma in situ, or invasive carcinoma was found in any of the 33 prophylactic mastectomy specimens. Among the 29 breasts with cancer and available tissue, 2 (7%) had malignant findings and 1 (3%) had atypia in the NAC. One woman who underwent bilateral mastectomy for bilateral invasive carcinoma had one nipple with tumor within lymphatics, and her contralateral nipple had atypical lobular hyperplasia. A second woman had ductal carcinoma in situ involving a single major lactiferous duct.

Conclusions. The probability of nipple involvement by premalignant or malignant lesions in the NAC of *BRCA* mutation carriers is low at time of prophylactic mastectomy,

prevention, and prophylactic mastectomy and prophylactic oophorectomy are the standard options to consider in this setting. Women with *BRCA1* or *BRCA2* mutation may be monitored closely utilizing self-examination, clinical breast examination, and breast imaging techniques (mammography and magnetic resonance imaging). However, this surveillance is intended for early detection of breast cancer. Cohort studies have shown that mutation carriers enrolled in these intense surveillance programs develop invasive breast carcinoma at an annual rate of 33–41 per 1,000 women.^{1,2} As an alternative to early detection, some women have chosen preventative approaches to reduce their risk of developing breast carcinoma, including prophylactic surgery and chemoprevention. In women with *BRCA1* and *BRCA2* mutation with unilateral breast cancer, a number of studies have consistently demonstrated an increased risk of contralateral cancer, especially in women with *BRCA1* mutation and first cancer diagnosed at young age.^{3–5} Several studies have also shown that mutation status may influence a woman's choice of more aggressive surgical intervention such as unilateral or bilateral

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WHAT SURGERY ?

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Annals of
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ORIGINAL ARTICLE – AMERICAN SOCIETY OF BREAST SURGEONS

Nipple-Sparing Mastectomy for Breast Cancer and Risk-Reducing Surgery: The Memorial Sloan-Kettering Cancer Center Experience

Paulo de Alcantara Filho, MD¹, Deborah Capko, MD¹, John Mitchel Barry, MD¹, Monica Morrow, MD¹, Andrea Pusic, MD², and Virgilio S. Sacchini, MD¹

¹Breast Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY; ²Plastic and Reconstruction Service, Memorial Sloan-Kettering Cancer Center, New York, NY

ABSTRACT

Background. Nipple-sparing mastectomy (NSM) has been gathering increased recognition as an alternative to more traditional mastectomy approaches. Initially, questions concerning its oncologic safety limited the use of NSM. Nevertheless, mounting evidence supporting the practice of NSM for both prophylactic and oncologic purposes is leading to its more widespread use and broadened indications.

Methods. Using a prospectively maintained database, we reviewed our experience of 353 NSM procedures performed in 200 patients, from 2000 to 2009.

metastatic disease to her brain. No other recurrences are attributable to the 353 NSMs.

Conclusions. The trends demonstrate the increasing acceptance of NSM as a prophylactic procedure as well as for therapeutic purposes. Although NSM is not standard, our experience supports the selective use of NSM in both prophylactic and malignant settings.

The surgical management of breast cancer has evolved over the past several decades from the radical mastectomy

Conclusions. The trends demonstrate the increasing acceptance of NSM as a prophylactic procedure as well as for therapeutic purposes. Although NSM is not standard, our experience supports the selective use of NSM in both prophylactic and malignant settings.

clinical practice guidelines

Annals of Oncology 22 (Supplement 6): vi31–vi34, 2011
doi:10.1093/annonc/mdr373

BRCA in breast cancer: ESMO Clinical Practice Guidelines

J. Balmaña¹, O. Díez^{2,3}, I. T. Rubio⁴ & F. Cardoso^{5,6}

On behalf of the ESMO Guidelines Working Group*

¹Medical Oncology Department, Breast Cancer Center; ²Oncogenetics Laboratory, University Hospital Vall d'Hebron, Barcelona, Spain; ³Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; ⁴Breast Cancer Surgical Unit, Breast Cancer Center, University Hospital Vall d'Hebron, Barcelona, Spain; ⁵European School of Oncology, Milan, Italy; ⁶Breast Cancer Unit, Champalimaud Cancer Center, Lisbon, Portugal

There have been no randomized trials comparing the effectiveness of different surgical techniques.

clinical practice guidelines

Annals of Oncology 22 (Supplement 6): vi31–vi34, 2011
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The possibility of finding an occult synchronous invasive tumor during a prophylactic mastectomy is quite low at ~5%.

clinical practice guidelines

Annals of Oncology 22 (Supplement 6): vi31–vi34, 2011
doi:10.1093/annonc/mdr373

BRCA in breast cancer: ESMO Clinical Practice Guidelines

J. Balmaña¹, O. Díez^{2,3}, I. T. Rubio⁴ & F. Cardoso^{5,6}

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At this time, there is insufficient evidence to recommend routine sentinel node biopsy for patients undergoing prophylactic mastectomy.

RISK REDUCING SURGERY

UPTAKE

The Process of Deciding About Prophylactic Surgery for Breast and Ovarian Cancer: Patient Questions, Uncertainties, and Communication

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AMERICAN JOURNAL OF
medical genetics

Little is known about how these individuals in fact make these decisions - particularly, what stresses they face in making these decisions, and what roles, if any, health care providers and others may play

These issues are important since many women who might benefit from prophylactic surgery do not undergo it

TIMING

Review Article

Clinical Considerations of *BRCA1* - and *BRCA2*-Mutation Carriers: A Review

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² Centre for Cancer Therapeutics, Ottawa Hospital Research Institute, The Ottawa Hospital, Ottawa, ON, Canada K1H 8L6

³ The Division of Gynaecologic Oncology, The Ottawa Hospital, Ottawa, ON, Canada K1H 8L6

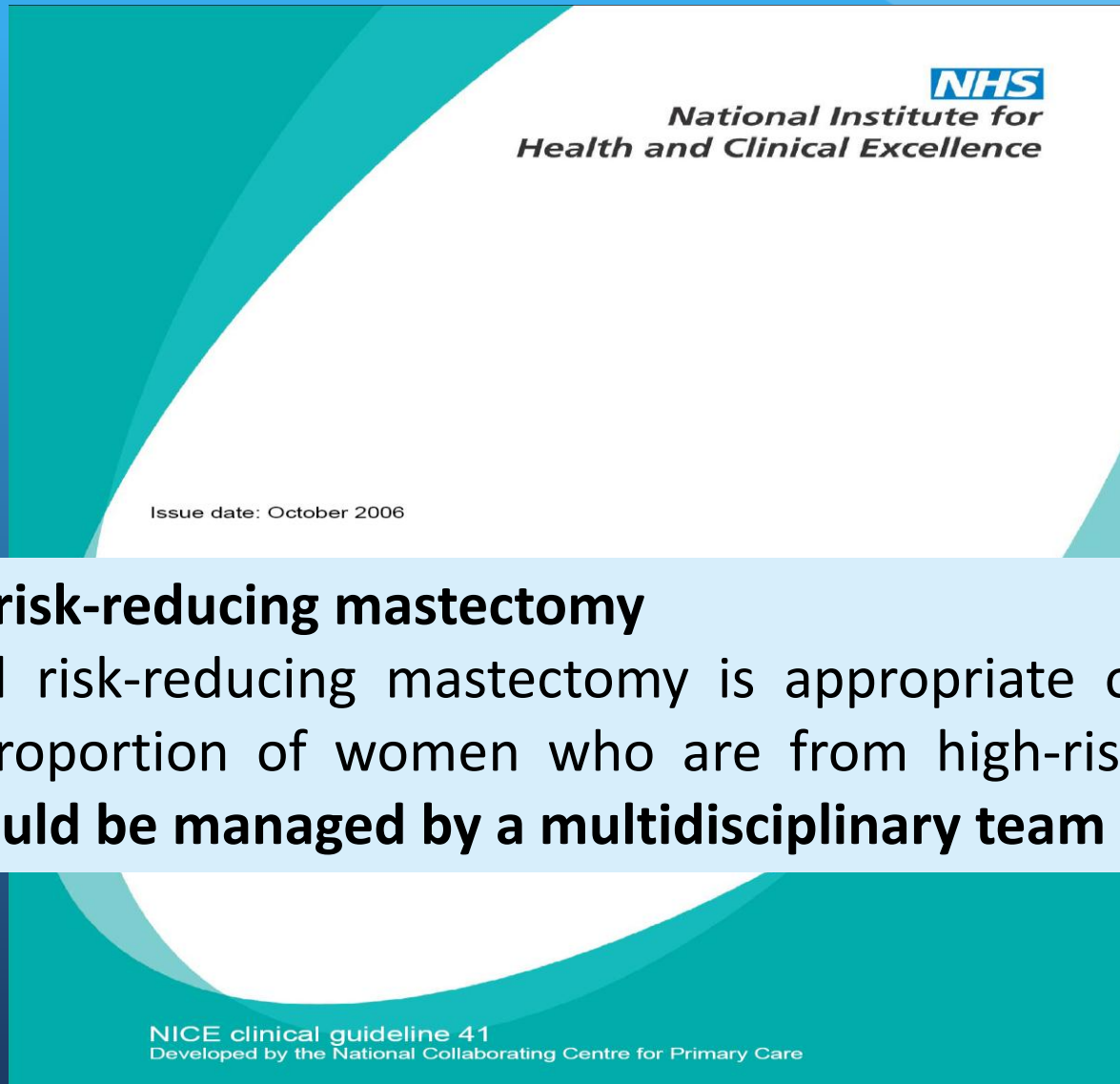
Correspondence should be addressed to J. I. Weberpals, jweberpals@ottawahospital.on.ca

Received 2 April 2011; Accepted 16 June 2011

The most effective single intervention for *BRCA1*-mutation carriers was a BSO at age 40, yielding a 15% absolute survival gain. For *BRCA2*-mutation carriers, the most effective single intervention was a prophylactic mastectomy, yielding a 7% survival gain if performed at age 40. The combination of prophylactic mastectomy and BSO at the age of 40 improved survival more than any single intervention, yielding a 24% and 11% survival gain for *BRCA1*- and *BRCA2*-mutation carriers, respectively.

When choosing a surveillance option, patients must be cautioned that premalignant and malignant changes can occur in spite of normal radiological investigations.

WHERE

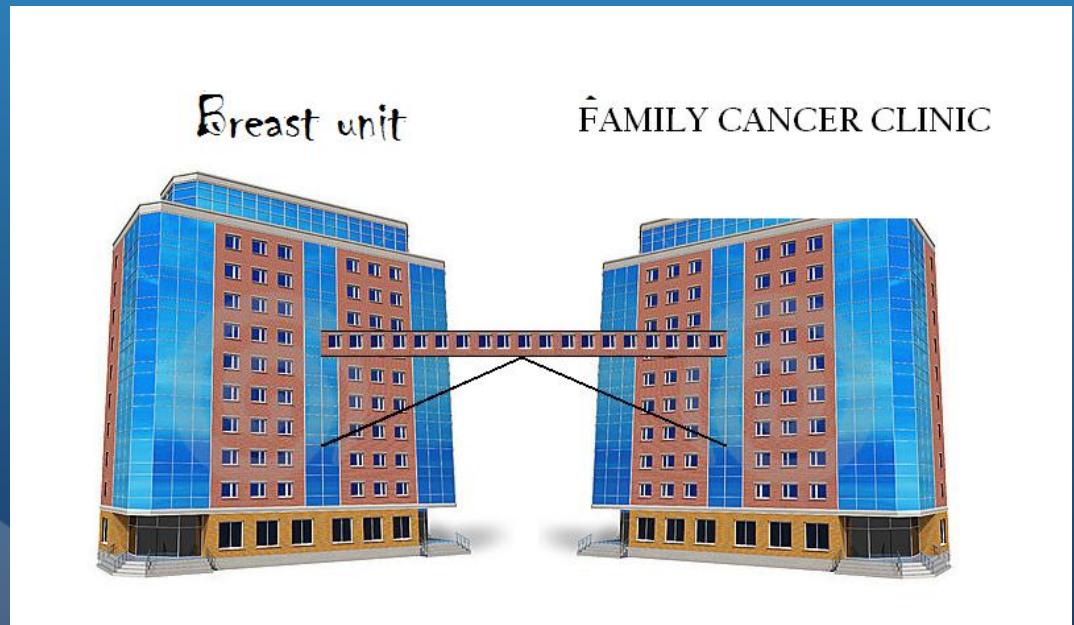


Bilateral risk-reducing mastectomy

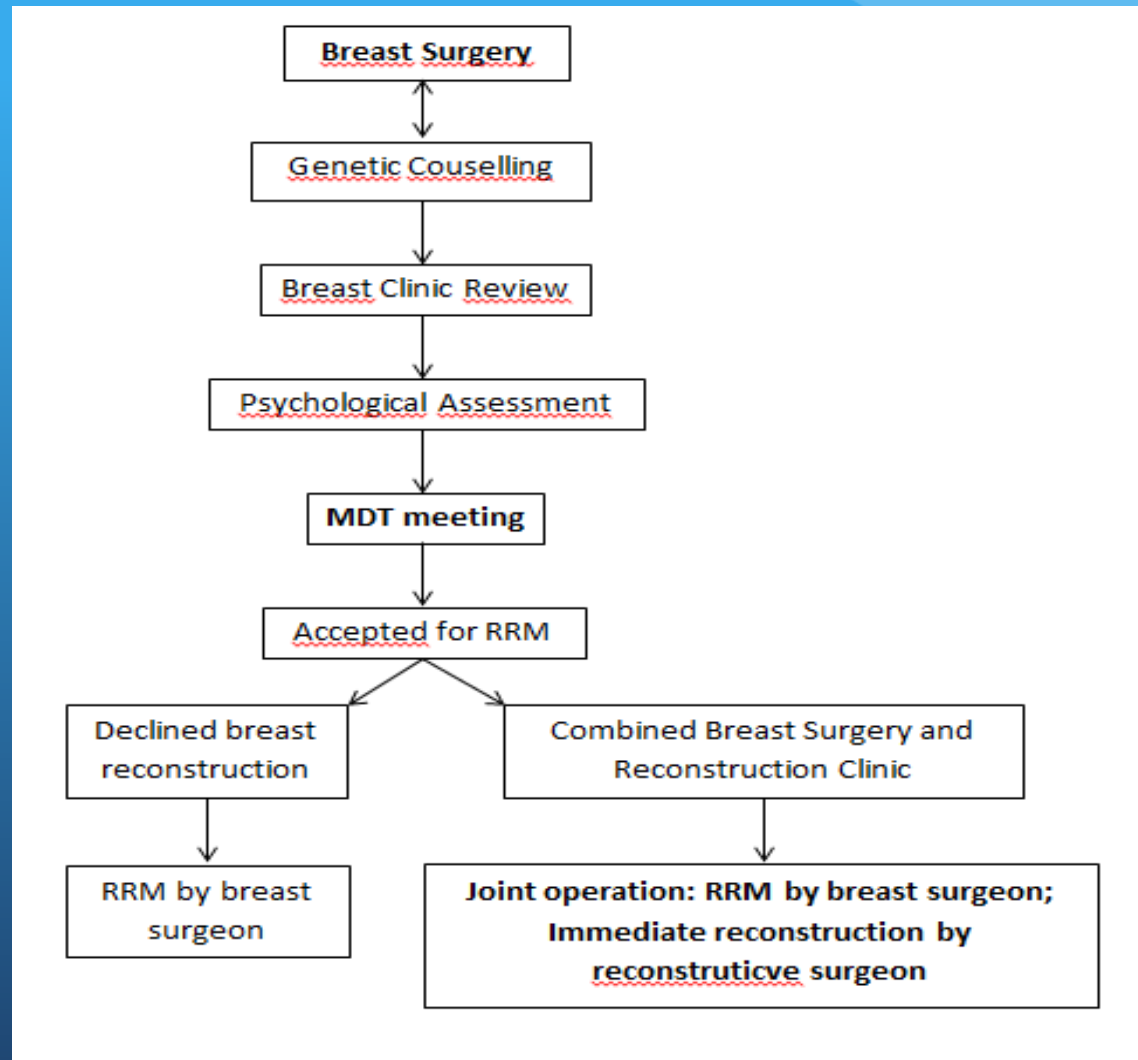
- Bilateral risk-reducing mastectomy is appropriate only for a small proportion of women who are from high-risk families and **should be managed by a multidisciplinary team**

REQUIREMENTS FOR MANAGEMENT OF BRCA MUTATED WOMEN

- Multidisciplinary Dedicated Team
- Time !



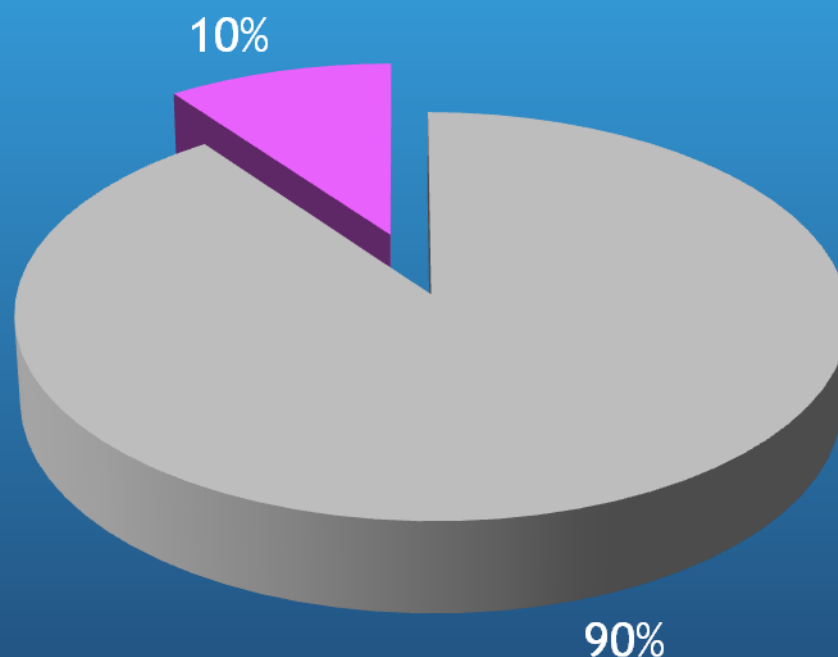
Breast Unit Humanitas: flow chart high risk patients



Breast Unit Humanitas Cancer Center: 2009-2014

Nipple Sparing Mastectomy : total number 273

■ n° of therapeutic mastectomy 246 ■ n° of prophylactic mastectomy 27

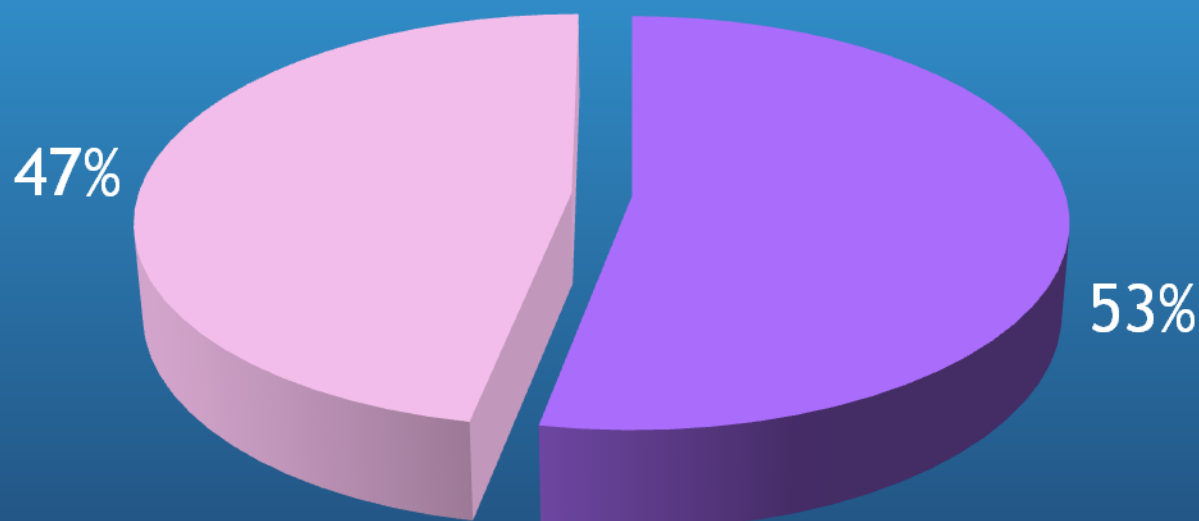


90% of cases was performed a therapeutic mastectomy
10% of cases was performed a prophylactic mastectomy

Breast Unit Humanitas Cancer Center: 2009-2014

Mutation BRCA1/2: 17 patients

- Bilateral Prophylactic Mastectomy (9 patients)
- Monolateral Prophylactic Mastectomy, contralateral Breast cancer (8 patients)



The other 10 patients had monolateral prophylactic mastectomy without genetic test or with negative genetic test, but all of them had history of breast cancer

Malattie ad andamento degenerativo di particolare rilevanza sociale,

con specifico riguardo al tumore della mammella,
alle malattie reumatiche croniche ed alla
sindrome HIV. Documento conclusivo

con cd di testi allegato

indagini conoscitive

Atti dell'indagine
conoscitiva svolta
dalla 12ª commissione
permanente del Senato
(igiene e sanità)

n. 36
giugno 2011

XVI legislatura

ITALIAN PROGRAM FOR BREAST CENTRES.



Presidenza del Consiglio dei Ministri

SEGRETERIA DELLA CONFERENZA PERMANENTE
PER I RAPPORTI TRA LO STATO LE REGIONI
E LE PROVINCE AUTONOME

Codice sito: 4.10/2014/71

Presidenza del Consiglio dei Ministri
CSR 0000067 P-4.23.2.10
del 07/01/2015



10715549

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All'Assessore della Regione Veneto
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Oggetto: Intesa sul documento recante "Linee di indirizzo sulle modalità organizzative ed assistenziali della rete dei centri di senologia"

Si trasmette, per il seguito di competenza, l'atto dell'intesa sancita dalla Conferenza Stato-Regioni, nella seduta del 18 dicembre 2014.



Ministero della Salute

DIPARTIMENTO DELLA PROGRAMMAZIONE E
DELL'ORDINAMENTO DEL SSN
DIREZIONE GENERALE DELLA PROGRAMMAZIONE
EX UFFICIO III DG PROG

**Documento del Gruppo di lavoro per la definizione di specifiche
modalità organizzative ed assistenziali della rete dei centri di
senologia**

Roma, Aprile 2014

- ...must provides specific training and pathway for the prevention and diagnosis for women with genetic risk or high risk family.
- ...must provides specific clinic for risk-reduction options whit all the specialists (onco-genetist, breast and plastic surgeon , psyo-oncologist , nursing ,ginecologyst,radiologist)

Newsweek

December 6, 1993 : \$2.95

If life gives you
lemons, a simple
operation can
give you melons.

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