The Breast Surgeon and the High Risk Individual

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Pink Hope Vic Information Day 2018

Jane O'Brien
Specialist Oncoplastic Breast Surgeon
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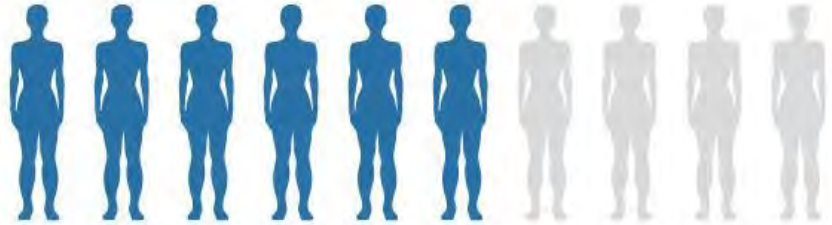
CHANCES OF DEVELOPING BREAST CANCER BY AGE 70

Specific inherited mutations in the BRCA1 and BRCA2 genes increase the risk of breast and ovarian cancers. Testing for these mutations is usually recommended in women without breast cancer only when the person's individual or family history suggests the possible presence of a harmful mutation in BRCA1 or BRCA2. Testing is often recommended in younger women newly diagnosed with breast cancer because it can influence treatment decisions and have implications for their family members.



MUTATED BRCA1

55-65%

MUTATED BRCA2

45%

NORMAL BRCA

12%

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"Every breast or ovarian cancer patient with a BRCA1 or BRCA2 mutation detected after diagnosis is a missed opportunity to prevent a cancer. No woman with a BRCA1 or BRCA2 mutation should die from breast or ovarian cancer"

Mary Claire King

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Previvor

n. 1. A survivor of a predisposition (or increased risk) for a disease such as cancer

PREVIVOR POWER

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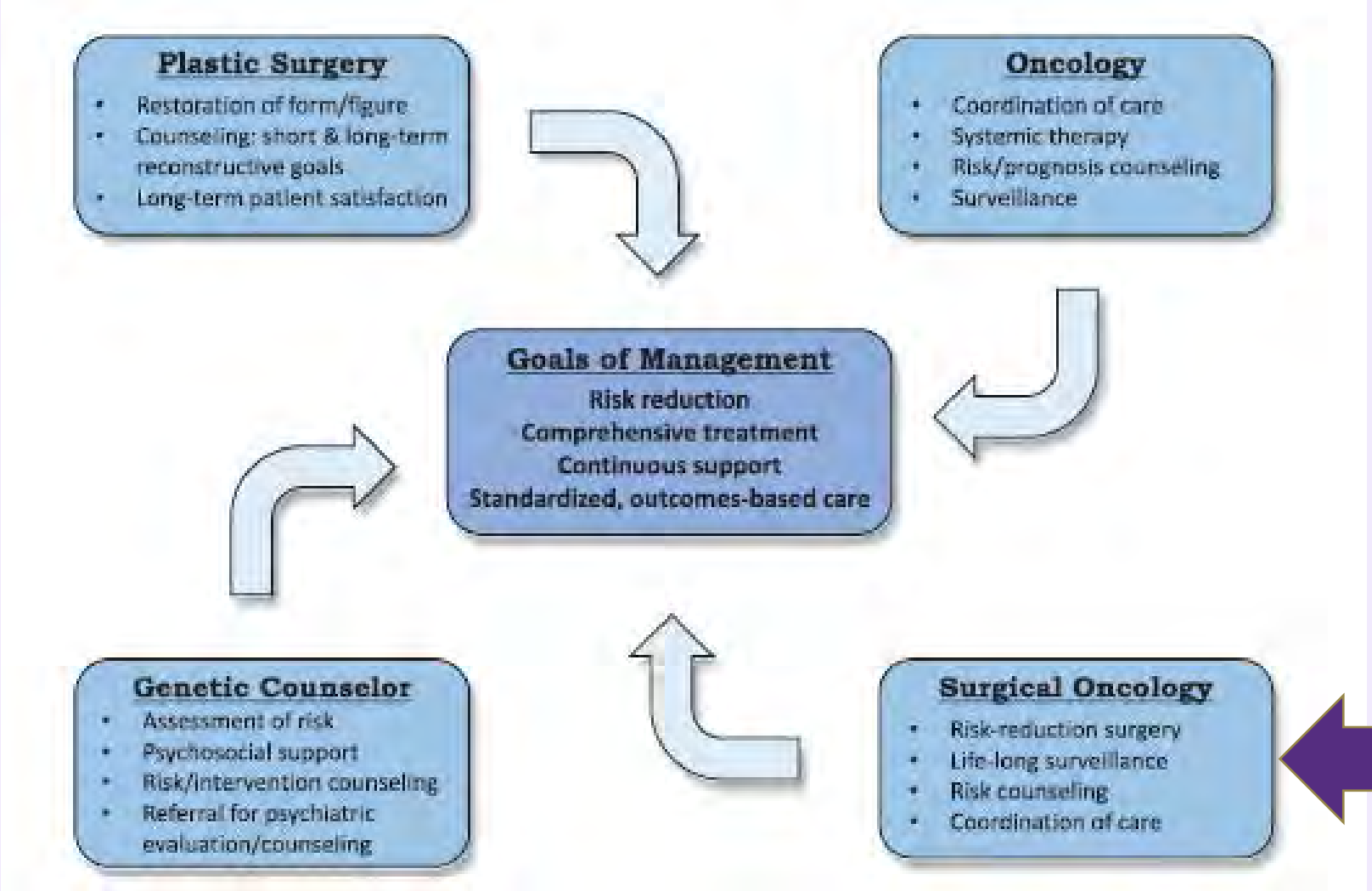
Role of the Breast Surgeon



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RISK ASSESSMENT

- Basic Risk assessment

RISK MANAGEMENT

- High Risk Screening

- Risk-Reduction Surgery

- Treatment of Breast Cancer in the patient with a known or suspected BRCA mutation

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RISK ASSESSMENT

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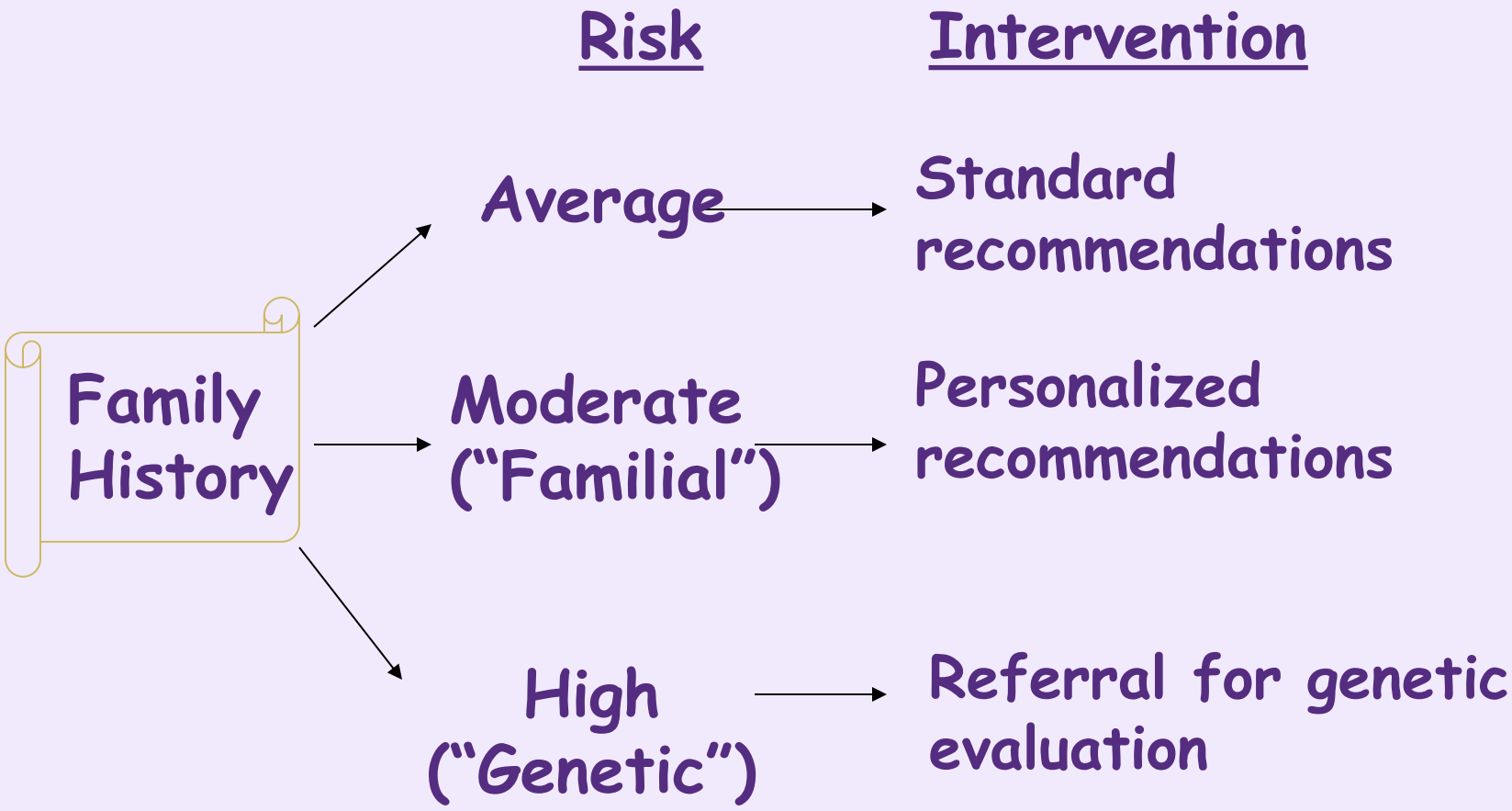

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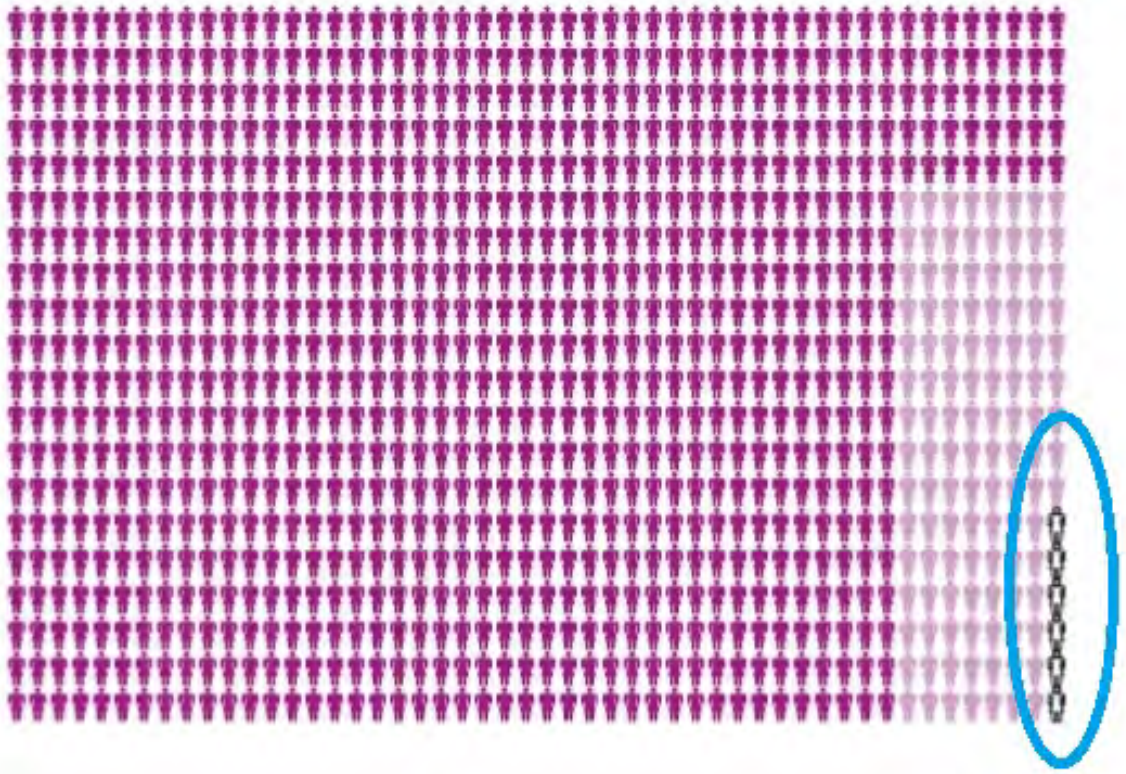
The diagram below shows that of 1000 Australian women, about 120 (12%) will develop breast cancer some time in their life. Most of these women will develop cancer after turning 60 years old.

About six of the 120 women (5%) will have a strong family health history of breast cancer, which suggests that there is a faulty cancer protection gene specific to the family.

Key:

880 will not develop breast cancer at any time

120 will develop breast cancer sometime in their lifetime



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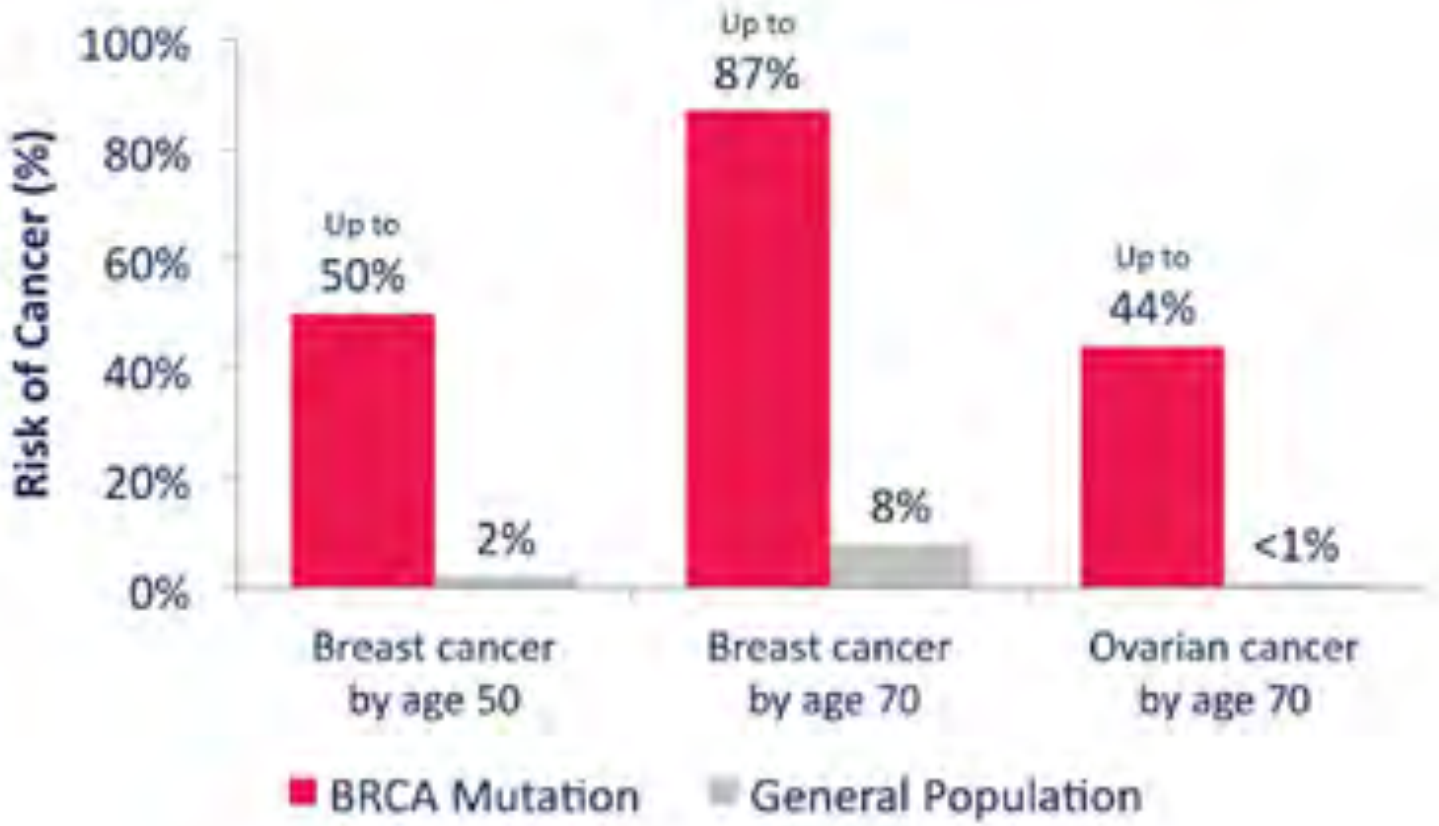
BRCA MUTATIONS INCREASE BREAST AND OVARIAN CANCER RISKS



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Breast Cancer Risk

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Once cancer risks have been estimated, the focus shifts to developing a risk management strategy that considers:

- the magnitude of the risk
- the risks and effectiveness of possible interventions
- individual risk tolerance and preferences.

RISK MANAGEMENT

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EARLY DETECTION

- High Risk Screening

PREVENTION

- Lifestyle Factors
- Risk-Reducing Medication
- Risk-Reducing Surgery

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LIFESTYLE STRATEGIES

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- Regular exercise
- Limiting alcohol intake
- Weight control
- Limit use of HRT

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RISK REDUCING MEDICATIONS

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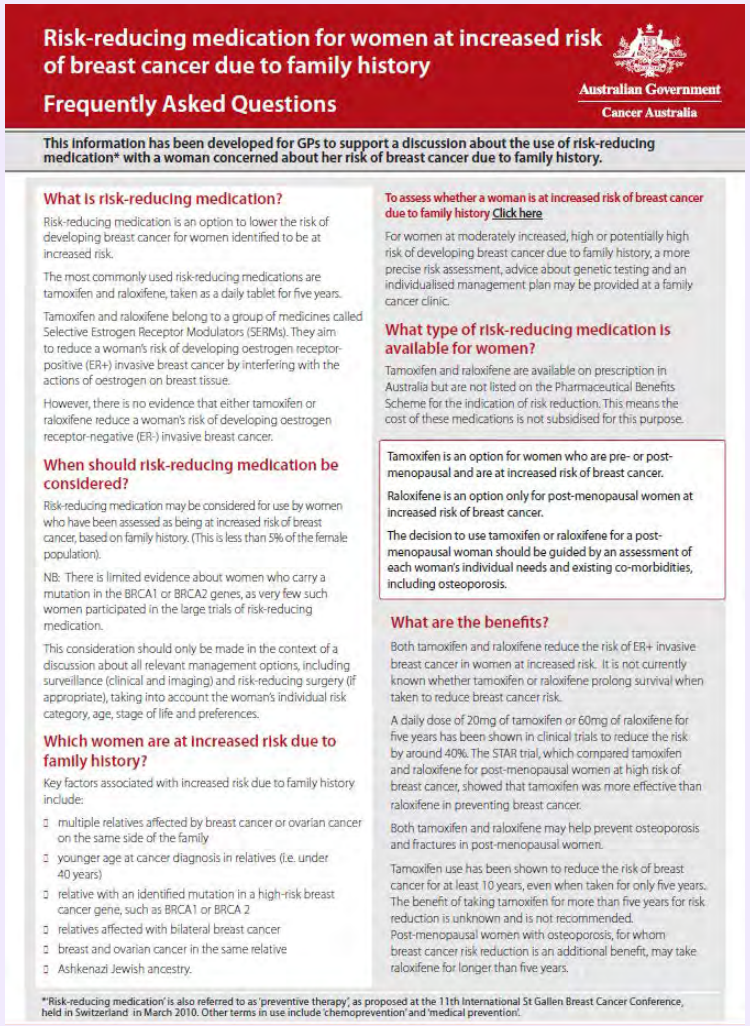

Risk-reducing medication for women at increased risk of breast cancer due to family history

Frequently Asked Questions

Australian Government
Cancer Australia

This information has been developed for GPs to support a discussion about the use of risk-reducing medication* with a woman concerned about her risk of breast cancer due to family history.

What is risk-reducing medication?

Risk-reducing medication is an option to lower the risk of developing breast cancer for women identified to be at increased risk.

The most commonly used risk-reducing medications are tamoxifen and raloxifene, taken as a daily tablet for five years.

Tamoxifen and raloxifene belong to a group of medicines called Selective Estrogen Receptor Modulators (SERMs). They aim to reduce a woman's risk of developing oestrogen receptor-positive (ER+) invasive breast cancer by interfering with the actions of oestrogen on breast tissue.

However, there is no evidence that either tamoxifen or raloxifene reduce a woman's risk of developing oestrogen receptor-negative (ER-) invasive breast cancer.

When should risk-reducing medication be considered?

Risk-reducing medication may be considered for use by women who have been assessed as being at increased risk of breast cancer, based on family history. (This is less than 5% of the female population).

NB: There is limited evidence about women who carry a mutation in the BRCA1 or BRCA2 genes, as very few such women participated in the large trials of risk-reducing medication.

This consideration should only be made in the context of a discussion about all relevant management options, including surveillance (clinical and imaging) and risk-reducing surgery (if appropriate), taking into account the woman's individual risk category, age, stage of life and preferences.

Which women are at increased risk due to family history?

Key factors associated with increased risk due to family history include:

- multiple relatives affected by breast cancer or ovarian cancer on the same side of the family
- younger age at cancer diagnosis in relatives (i.e. under 40 years)
- relative with an identified mutation in a high-risk breast cancer gene, such as BRCA1 or BRCA 2
- relatives affected with bilateral breast cancer
- breast and ovarian cancer in the same relative
- Ashkenazi Jewish ancestry.

To assess whether a woman is at increased risk of breast cancer due to family history Click here

For women at moderately increased, high or potentially high risk of developing breast cancer due to family history, a more precise risk assessment, advice about genetic testing and an individualised management plan may be provided at a family cancer clinic.

What type of risk-reducing medication is available for women?

Tamoxifen and raloxifene are available on prescription in Australia but are not listed on the Pharmaceutical Benefits Scheme for the indication of risk reduction. This means the cost of these medications is not subsidised for this purpose.

Tamoxifen is an option for women who are pre- or post-menopausal and are at increased risk of breast cancer.

Raloxifene is an option only for post-menopausal women at increased risk of breast cancer.

The decision to use tamoxifen or raloxifene for a post-menopausal woman should be guided by an assessment of each woman's individual needs and existing co-morbidities, including osteoporosis.

What are the benefits?

Both tamoxifen and raloxifene reduce the risk of ER+ invasive breast cancer in women at increased risk. It is not currently known whether tamoxifen or raloxifene prolong survival when taken to reduce breast cancer risk.

A daily dose of 20mg of tamoxifen or 60mg of raloxifene for five years has been shown in clinical trials to reduce the risk by around 40%. The STAR trial, which compared tamoxifen and raloxifene for post-menopausal women at high risk of breast cancer, showed that tamoxifen was more effective than raloxifene in preventing breast cancer.

Both tamoxifen and raloxifene may help prevent osteoporosis and fractures in post-menopausal women.

Tamoxifen use has been shown to reduce the risk of breast cancer for at least 10 years, even when taken for only five years. The benefit of taking tamoxifen for more than five years for risk reduction is unknown and is not recommended.
Post-menopausal women with osteoporosis, for whom breast cancer risk reduction is an additional benefit, may take raloxifene for longer than five years.

*'Risk-reducing medication' is also referred to as 'preventive therapy', as proposed at the 11th International St Gallen Breast Cancer Conference, held in Switzerland in March 2010. Other terms in use include 'chemoprevention' and 'medical prevention'.

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RISK-REDUCING SURGERY

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The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

The Role of Risk-Reducing Surgery in Hereditary Breast and Ovarian Cancer

Lynn C. Hartmann, M.D., and Noralane M. Lindor, M.D.

NEJM, 2016

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- Why ?
- For Whom ?
- If ?
- When ?
- By Whom ?
- What ?
- Where ?

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WHY ?

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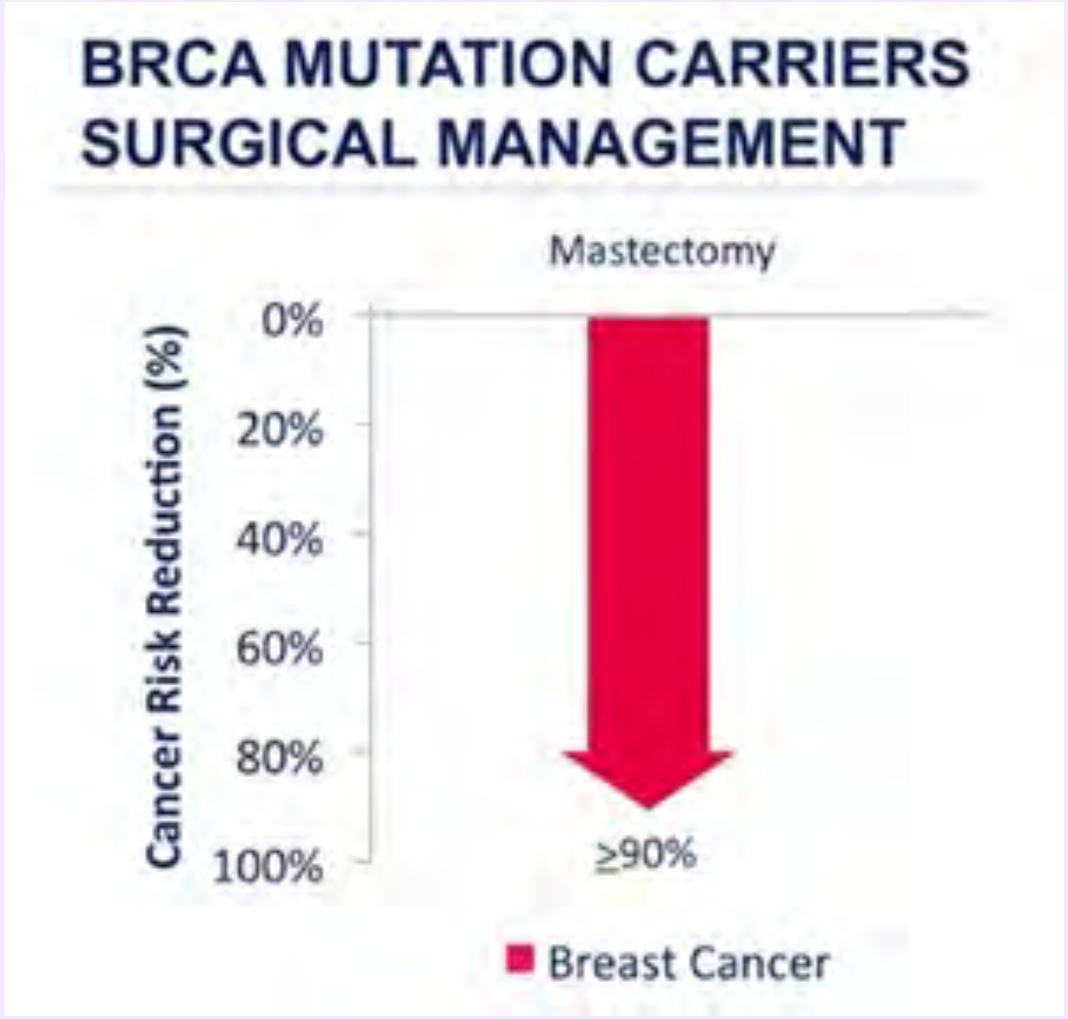
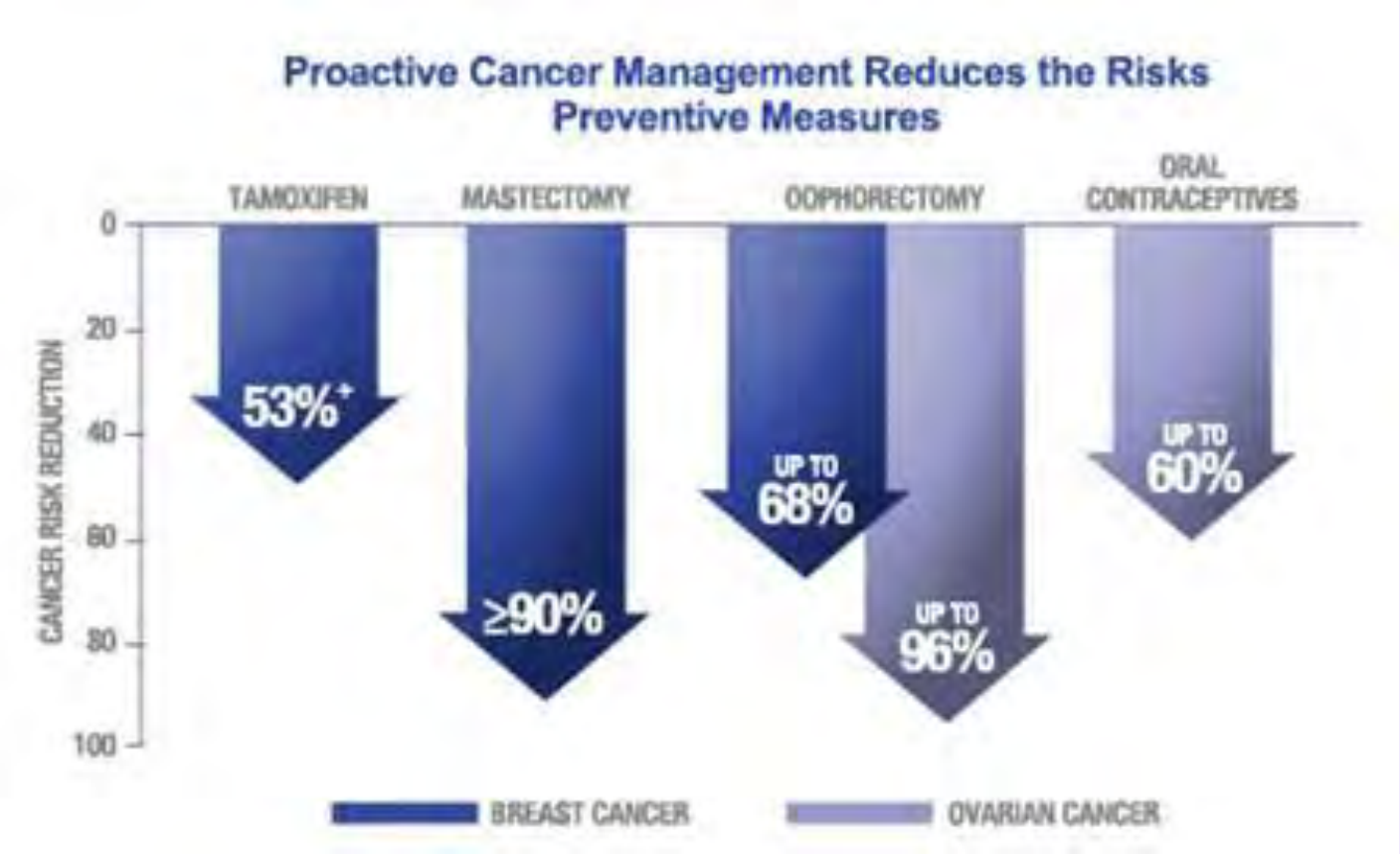


Because it works……



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- Studies of high risk women show bilateral risk-reduction mastectomy (RRM) offers a 90-95% risk reduction in the development of breast cancer
- 81-94% risk reduction in death from breast cancer

Hartmann et al NEJM 1999

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Preventing breast and ovarian cancers in high-risk *BRCA1* and *BRCA2* mutation carriers

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1 Risk management strategies for breast and ovarian* cancers in *BRCA1* and *BRCA2* mutation carriers

Strategy	Relative risk reduction	
	Breast cancer	Ovarian cancer
Risk-reducing mastectomy	> 90%	—
Risk-reducing bilateral salpingo-oophorectomy	Up to 50% (if premenopausal)	> 90%
Risk-reducing medication	38%† (tamoxifen/raloxifene)	About 50%‡ (oral contraceptive pill)
Screening	0 (mammography/MRI)	0 (ultrasound/Ca125)§
Tubal ligation	—	About 40%

* High-grade serous cancers of the ovary, fallopian tube or peritoneum. † Estimate from meta-analysis of multiple randomised controlled trials in high-risk women; limited data suggest a similar benefit in mutation carriers. ‡ The effects of the oral contraceptive pill on breast cancer risk are uncertain. § Ineffective and not recommended.[2]

MJA, 2013

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Bilateral Risk-Reducing Mastectomy (RRM).

Table 1. Bilateral Risk-Reducing Mastectomy (BRRM).*

Study and Focus	Design	Eligibility	Participants	Follow-up	Outcomes
				yr	
Cancer risk reduction					
Mayo Clinic; Hartmann et al.[2]	Retrospective cohort	Women with high familial risk of breast cancer	214 with BRRM, 403 sisters without BRRM	14	3 breast cancers in BRRM group, 38 breast cancers in no-BRRM group; hazard ratio for development of breast cancer, 0.08 (95% CI, 0.02–0.33)
Mayo Clinic; Hartmann et al.[21]	Subcohort of carriers identified among original 214 women with BRRM	*BRCA1* or *BRCA2* carriers	18 with BRRM	13.4	0 breast cancers in BRRM group†‡
Rotterdam; Meijers-Heijboer et al.[22]	Prospective cohort	*BRCA1* or *BRCA2* carriers	76 with BRRM, 63 without BRRM	2.9	0 breast cancers in BRRM group, 8 breast cancers in no-BRRM group†
Rotterdam; Heemskerk-Gerritsen et al.[23]	Prospective cohort	*BRCA1* or *BRCA2* carriers and noncarriers with hereditary risk of breast cancer	177 with BRRM	4.5	1 breast cancer in BRRM group‡
PROSE Study Group; Rebbeck et al.[24]	Retrospective cohort	*BRCA1* or *BRCA2* carriers	102 with BRRM, 378 without BRRM	6.4	2 breast cancers in BRRM group, 184 breast cancers in no-BRRM group; hazard ratio for development of breast cancer, 0.05–0.09 (95% CI, 0.01–0.38)
PROSE; Domchek et al.[25]	Prospective cohort	*BRCA1* or *BRCA2* carriers	247 with BRRM, 1372 without BRRM	3	0 breast cancers in BRRM group, 98 breast cancers in no-BRRM group†
Multicenter European collaboration; Evans et al.[19]	Ascertainment both retrospective and prospective; follow-up prospective	Women with a lifetime risk of breast cancer >25%	114 with BRRM	NR	0 breast cancers in women with BRRM; authors estimated that 21 breast cancers would have occurred in these women from person-years at-risk analysis based on mutation status or family history†§
Denmark; Skytte et al.[26]	Retrospective national cohort	*BRCA1* or *BRCA2* carriers	96 with BRRM, 211 without BRRM	NR	3 breast cancers in BRRM group, 16 breast cancers in no-BRRM group; hazard ratio for development of breast cancer, 0.39 (95% CI, 0.12–1.36); P=0.14
Psychosocial effects					
Mayo Clinic; Frost et al.[20]	Retrospective cohort; data from patient questionnaire	Women with family history of breast cancer who had BRRM, 1960–1993	609 eligible, 572 responded	14.5	Satisfaction: 70% satisfied, 11% neutral, 19% dissatisfied; 74% had decreased concern about breast-cancer risk; percentages of women who reported favorable effects, no change, or negative effects, respectively, in the following quality-of-life measures were: emotional stability: 23%, 68%, and 9%; stress: 28%, 58%, and 14%; self-esteem: 13%, 69%, and 18%; satisfaction with sexual relationships: 4%, 73%, and 23%; feelings of femininity: 8%, 67%, and 25%; and physical appearance: 16%, 48%, and 36%
University of Sydney; Heiniger et al.[1]	Prospective cohort; data from patient questionnaires at baseline and 3-yr follow-up	Women with high familial risk of breast cancer	17 with BRRM, 39 matched controls	3	BRRM group had significant reduction in perceived risk of breast cancer and cancer-related anxiety; no change from baseline in measures of general anxiety, depression, body image, and sexual activity
Karolinska Institutet; Brandberg et al.[27]	Prospective study; data from patient questionnaire at baseline and 1 yr postoperatively	Women at high risk for breast cancer considering BRRM, 1997–2005	Of 90 consecutive women, 83 completed questionnaire 1 yr after surgery (58% *BRCA* carriers, 42% other high-risk patients)	1	Measures of anxiety decreased significantly; preoperatively to 1 yr postoperatively, no change on measures of physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health; percentages of women who reported favorable effects or negative effects, respectively, in the following quality-of-life measures were: overall "satisfaction in life": 61% and 13%, femininity: 27% and 27%, and intimate situations: 16% and 46%; with respect to body image, women who reported that they were, respectively, "not at all," "a little," "quite a bit," or "very much" self-conscious were 52%, 40%, 8%, and 0%, less physically attractive: 60%, 29%, 11%, and 0%, dissatisfied with their appearance: 83%, 17%, 0%, and 0%, less feminine: 65%, 30%, 5% and 0%, avoiding people: 98%, 2%, 0%, and 0%, feeling that their body was less whole: 71%, 29%, 0%, and 0%, dissatisfied with their body: 74%, 21%, 5%, and 0%, and dissatisfied with their scar: 56%, 33%, 9%, and 2%; women who reported that they were, respectively, "not at all," "a little," "quite a bit," or "very much" having difficulty seeing themselves naked

Hartmann LC, Lindor NM. N Engl J Med 2016;374:454-468

PROSE Study Group; Rebbeck et al.[24]	Retrospective cohort	*BRCA1* or *BRCA2* carriers	102 with BRRM, 378 without BRRM	6.4	2 breast cancers in BRRM group, 184 breast cancers in no-BRRM group; hazard ratio for development of breast cancer, 0.05–0.09 (95% CI, 0.01–0.38)
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Ann Surg Oncol (2017) 24:375–397
DOI 10.1245/s10434-016-5688-z

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

CrossMark

CONTINUING EDUCATION– BREAST ONCOLOGY

Society of Surgical Oncology Breast Disease Working Group Statement on Prophylactic (Risk-Reducing) Mastectomy

Kelly K. Hunt, MD[1], David M. Euhus, MD[2], Judy C. Boughey, MD[3], Anees B. Chagpar, MD[4], Sheldon M. Feldman, MD[5], Nora M. Hansen, MD[6], Swati A. Kulkarni, MD[6], David R. McCready, MD[7], Eleftherios P. Mamounas, MD[8], Lee G. Wilke, MD[9], Kimberly J. Van Zee, MD[10], and Monica Morrow, MD[10]

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- From the published data it is clear that bilateral prophylactic mastectomy (BPM) confers a reduction in the risk of developing a primary breast cancer approaching **100%** when meticulous surgical technique is used to remove the vast majority of breast tissue.
- The breast cancer risk reduction from BPM is greatest in healthy, unaffected women with a known genetic predisposition or a strong family history of breast and ovarian cancer.
- Almost all new breast cancers after BPM occur in patients who had significant breast tissue remaining, such as those who underwent subcutaneous mastectomy and those who had residual breast tissue in the axillary tail after surgery.
- Often, BPM is combined with risk-reducing bilateral salpingo-oophorectomy (BSO), which can further decrease breast cancer risk.

Annals of Surgical Oncology, 2017

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FOR WHOM?

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Informed decision-making is the key in women at high risk of breast cancer

A. Taylor [a], M. Tischkowitz [a,b,*]

[a] East Anglian Medical Genetics Service, Addenbrooke's Hospital, Cambridge CB2 0QQ, UK
[b] Academic Department of Medical Genetics, University of Cambridge, UK

EJSO, 2014

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"First, do no harm"

- Fundamental principle underlying medical ethics and practice
- RRM is currently "offered" rather than "recommended"
- Women opt for surgery of their own volition
- There is no single risk threshold above which RRM is clearly indicated
- All women considering cancer risk-reduction procedures in the absence of a cancer diagnosis should receive formal genetic counselling—and testing when deemed appropriate—prior to undergoing major and irreversible surgery.

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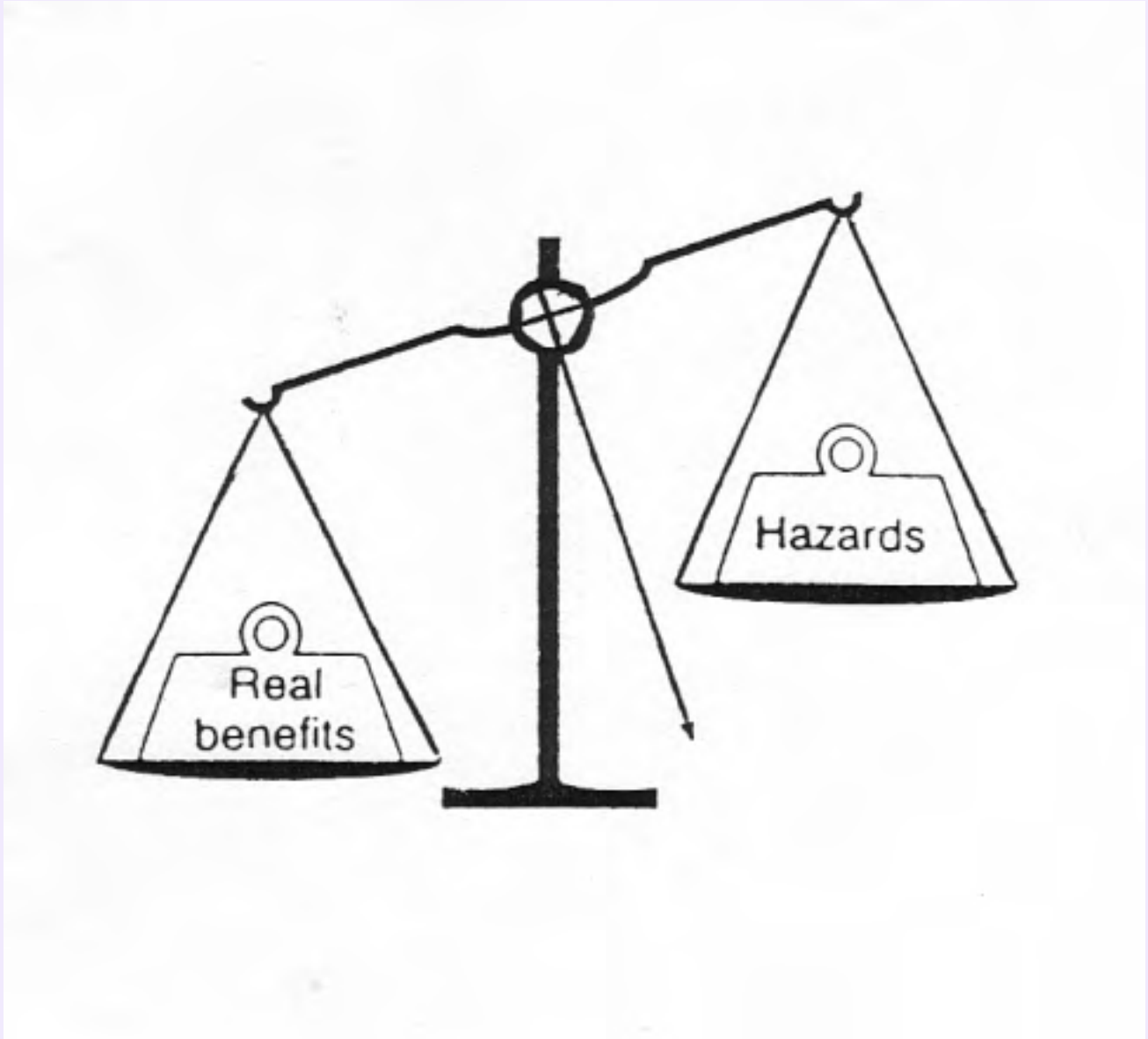

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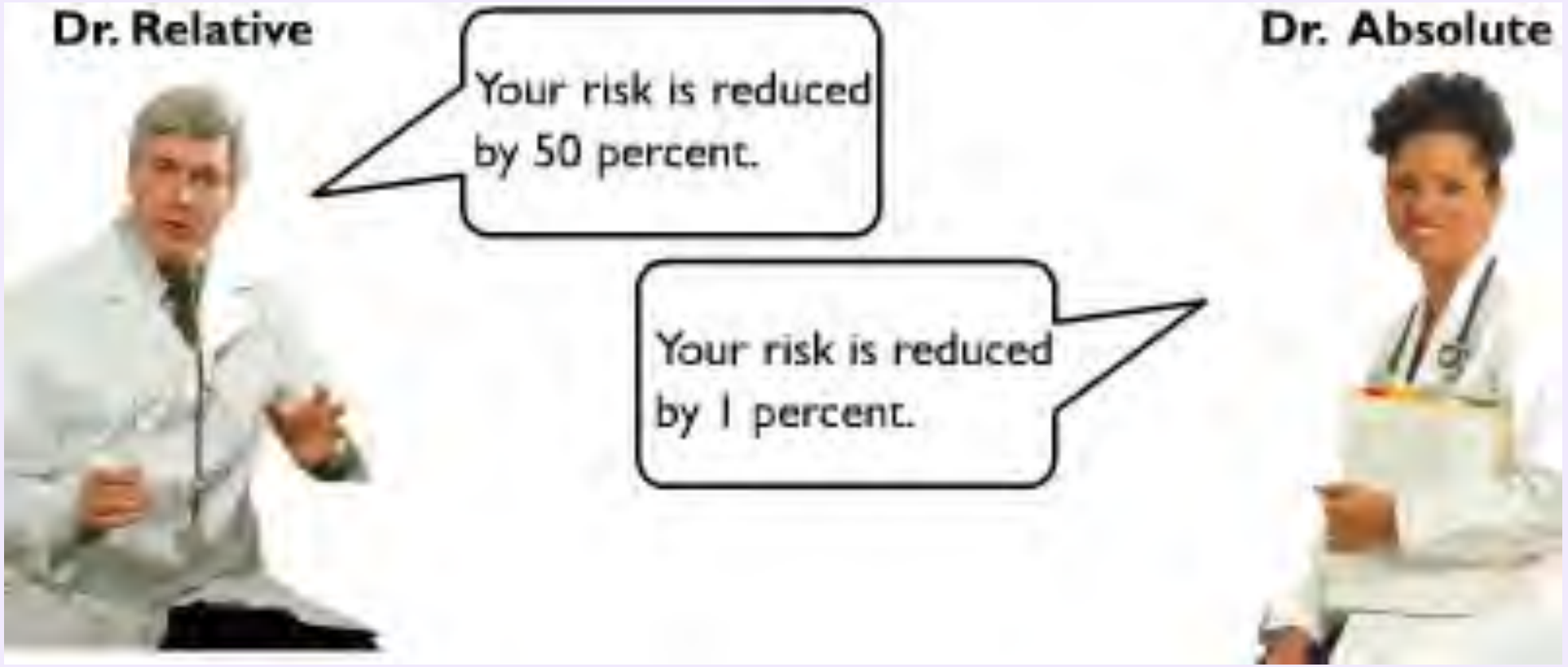

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Assuming 95% risk reduction

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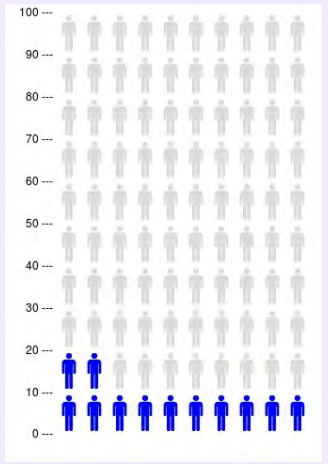
Average Risk



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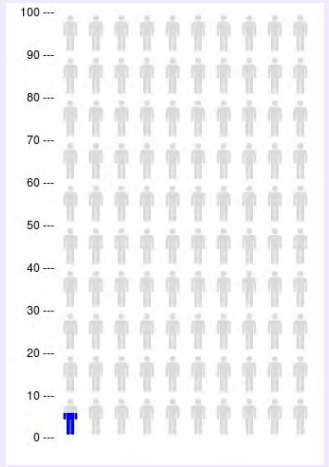
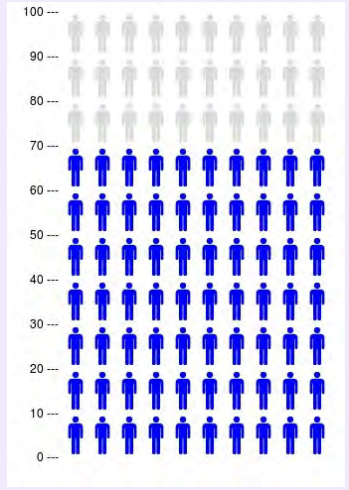


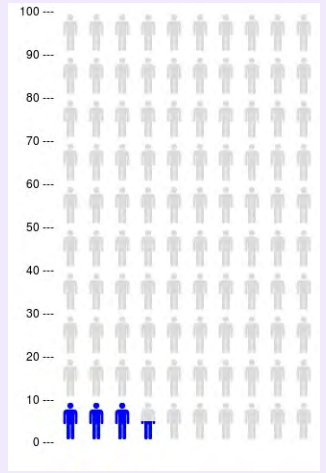
0.6/100

11.4 % absolute risk reduction

BRCA



70/100



3.5/100

67.5% absolute risk reduction

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Guidelines Regarding Candidates for Risk-Reducing Mastectomy

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Professional/academic organizations' guidelines regarding candidates for risk-reducing mastectomy

I. Society of Surgical Oncology Position Statement on Prophylactic Mastectomy
- A. Potential indications for bilateral prophylactic mastectomies (high risk patients with no prior breast cancer diagnosis)
  1. BRCA mutation or mutation in other hereditary susceptibility gene
  2. Strong family history of breast and/or ovarian cancer (especially if breast cancer was bilateral or premenopausal)
  3. Histological risk factors (atypical ductal hyperplasia; atypical lobular hyperplasia; lobular carcinoma in situ)
  4. Difficult surveillance (extremely dense fibronodular tissue that is difficult monitor with conventional screening modalities, especially if associated with a history of multiple diagnostic biopsies)
- B. Potential indications for contralateral prophylactic mastectomy (patients with unilateral breast cancer)
  1. Risk reduction (see potential indications noted for bilateral prophylactic mastectomy)
  2. Difficult surveillance (see potential indications noted for bilateral prophylactic mastectomy)
  3. Reconstructive or chest wall symmetry issues (patients undergoing mastectomy and reconstruction for unilateral breast cancer in whom symmetry can be improved with bilateral mastectomy and bilateral reconstruction; or patients undergoing mastectomy without reconstruction in whom a large, pendulous, and/or ptotic contralateral breast would result in substantial symptomatic imbalance)

II. National Comprehensive Cancer Network breast cancer risk reduction guideline
- A. Candidates in whom bilateral risk-reducing mastectomy may be considered
  1. BRCA 1/2 mutation carrier
  2. Carriers of other "strongly predisposing" gene mutations
  3. Patients with lobular carcinoma in situ
  4. "Compelling" family history
  5. Patients with prior thoracic radiation therapy delivered at age younger than 30 y

Curr Breast Cancer Rep (2013)

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- BRCA or other high risk mutation
- "Compelling" family history
- Histological risk factors (eg LCIS)
- Prior thoracic radiation therapy delivered at age younger than 30-35 yrs
- Contralateral Prophylactic Mastectomy(CPM) in patients with Unilateral Breast Cancer

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Multidisciplinary Team Approach Essential

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31-Jul-19

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- Multidisciplinary approach to help in decision making
- Alternatives of surveillence and chemoprevention should be discussed
- Risk/benefit discussion including not 100% protection
- Patient selection must be individualized
- Decision making should not be rushed

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Multidisciplinary Team

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- Clinical Geneticist
- Specialist Breast Surgeon
- Plastic Surgeon
- Medical Oncologist
- Gynaecological Oncologist
- Fertility Specialist
- Endocrinologist
- General Practitioner
- Psychiatrist
- Pathologist

PATIENT

- Radiologist
- Genetics Counsellor
- Breast Care Nurse
- Genetics Nurse
- Other Specialist Nurses
- Social Worker
- Clinical Psychologist
- Physiotherapist
- Dietician
- Radiographer
- Research Staff

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Risk-Reducing surgery should not be undertaken under the following circumstances:

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- Individual risk cannot be substantiated
- Factitious family history
- Munchausen's syndrome
- Gene test result imminent
- Surgery is not the woman's own choice
- Choice of surgery is for cosmetic rather than oncological reasons
- Psychiatric disorder, clinical depression, cancer phobia, dysmorphic syndrome
- Co-morbidity outweighs potential clinical benefit
- Immoveable unrealistic expectation of outcome

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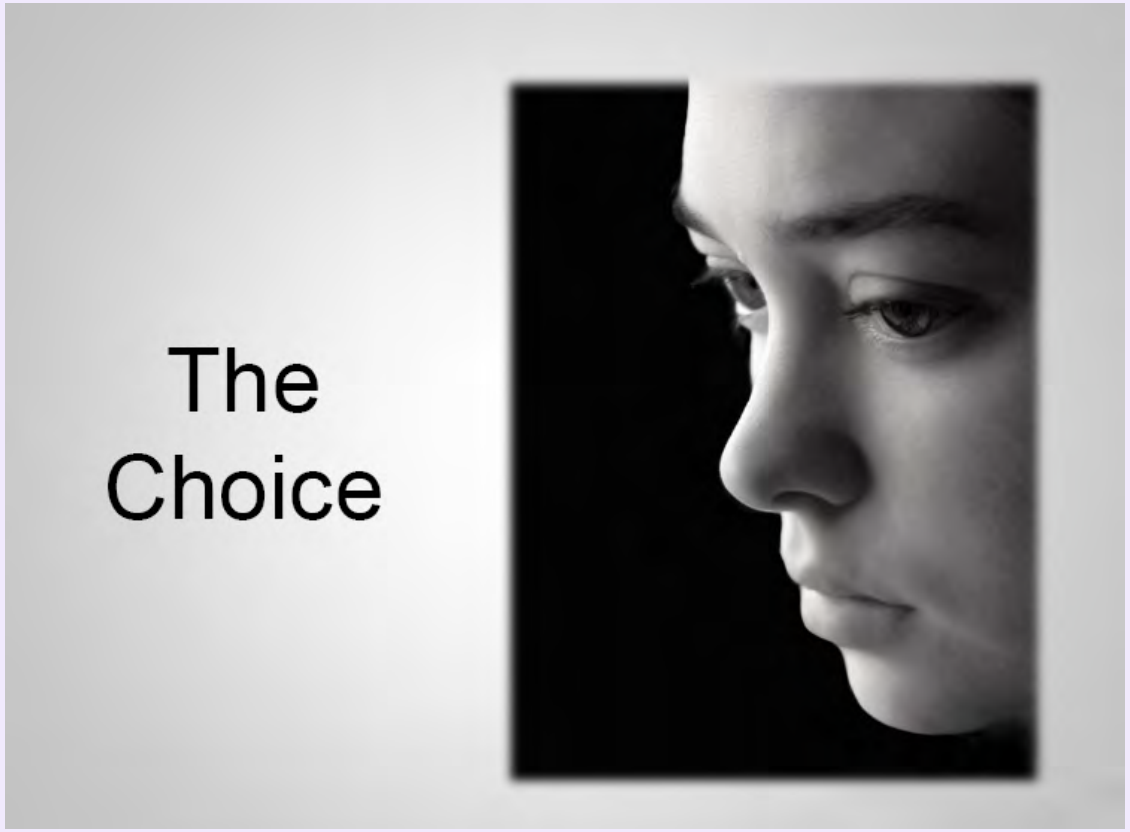
IF ?



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Risk Reducing Mastectomy Uptake Rates

International variation in rates of uptake of preventive options in *BRCA1* and *BRCA2* mutation carriers

Kelly A. Metcalfe[1,2], Daphna Birenbaum-Carmeli[3], Jan Lubinski[4], Jacek Gronwald[4], Henry Lynch[5], Pal Moller[6], Parviz Ghadirian[7], William D. Foulkes[8,9,10], Jan Klijn[11], Eitan Friedman[12,13], Charmaine Kim-Sing[14], Peter Ainsworth[15], Barry Rosen[16], Susan Domchek[17,18], Teresa Wagner[19], Nadine Tung[20], Siranoush Manoukian[21], Fergus Couch[22], Ping Sun[2], Steven A. Narod[2*] and the Hereditary Breast Cancer Clinical Study Group

Austria	Canada	France	Israel	Italy	Holland	Norway	Poland	USA
20%	22.4%	25%	4.2%	10%	32.7%	4.5%	2.7%	36.3%

Int J Cancer 2008

- Enormous variation worldwide 3-36%
- >50% of women rely on screening alone
- 20-30% do not have recommended regular screening tests

Australian Figures

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Risk-reducing surgery, screening and chemoprevention practices of *BRCA1* and *BRCA2* mutation carriers: a prospective cohort study

Clinical Genetics 2006

kConFab

11% - RRM
29% - BSO

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Preventing breast and ovarian cancers in high-risk *BRCA1* and *BRCA2* mutation carriers

3 Uptake of risk-reducing interventions among 325 women who were aware that they carried a ***BRCA1*** or ***BRCA2*** mutation

Risk-reducing intervention	Number	Age at intervention (years)	
		Median	Range
RRM*	69 (21%)	40	26–67
RRBSO†	125 (38%)	44	30–77
By age 40‡	16/62		
BRCA1	12/35		
BRCA2	4/27		
By age 50§	29/44		
BRCA1	17/27		
BRCA2	12/17		
Both RRM and RRBSO	38 (12%)	—	—
Risk-reducing medication or placebo (on trial)	9 (3%)	36	35–56
Risk-reducing medication (off trial)	1 (< 1%)	—	—
Tubal ligation¶	71 (22%)	32	20–54

RRBSO = risk-reducing bilateral salpingo-oophorectomy. RRM = risk-reducing mastectomy.
* Seven before cohort entry. † Eight before cohort entry. ‡ Restricted to 62 women who were followed to at least the age of 40 years and knew their genetic result before the age of 40 years. § Restricted to 44 women who were followed to at least the age of 50 years and knew their genetic result before the age of 50 years. ¶ 60 before cohort entry. ◆

MJA May 2013

Table 3: Uptake of risk-reducing interventions among 325 women who were aware they carried a *BRCA1* or *BRCA2* mutation

Risk-reducing intervention	Number	Age at intervention (yrs)	
		Median	Range
RRM (Risk-reducing mastectomy)	69/325 (21%) Seven before cohort entry	40	26–67
RRBSO (Risk-reducing bilateral salpingo-oophorectomy)	125/325 (38%) Eight before cohort entry	44	30–77
By age 40 *Restricted to 62 women who were followed to at least the age of 40 years and knew their genetic result before the age of 40 years*	16/62		
BRCA1	12/35		
BRCA2	4/27		
By age 50 Restricted to 44 women who were followed to at least the age of 50 years and knew their genetic result before the age of 50 years	29/44		
BRCA1	17/27		
BRCA2	12/17		
Both RRM and RRBSO	38/325 (12%)	–	–
Risk-reducing medication or placebo (on trial)	9/325 (3%)	36	35–56
Risk-reducing medication (off trial)	1/325 (< 1%)	–	–
Tubal ligation	71/325 (22%) 60 before cohort entry	32	20–54

Collins IM, et al. Preventing breast and ovarian cancers in high-risk BRCA1 and BRCA2 mutation carriers. *Medical Journal of Australia* 2013; 199(10):680-83.

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Risk-Reducing Intervention	%
RRM	21
RRBSO	38
RRM and RRBSO	12
Risk Reducing Medication (on trial)	3
Risk Reducing Medication (off trial)	<1

MJA May 2013

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Original article

Psychological factors associated with the intention to choose for risk-reducing mastectomy in family cancer clinic attendees

C.M.G. van Driel [a,*], J.C. Oosterwijk [b], E.J. Meijers-Heijboer [c], C.J. van Asperen [d], I.A. Zeijlmans van Emmichoven [e], J. de Vries [f], M.J.E. Mourits [a], L. Henneman [c,g], D.R.M. Timmermans [g,h], G.H. de Bock [i]

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[g] EMGO Institute for Health and Care Research, VU University Medical Center Amsterdam, PO Box 7057, 1007 MB Amsterdam, The Netherlands
[h] Department of Public and Occupational Health, VU University Medical Center Amsterdam, PO Box 7057, 1007 MB Amsterdam, The Netherlands
[i] Department of Epidemiology, University Medical Center Groningen, PO Box 30.001, 9700 RB Groningen, The Netherlands

Risk-reducing mastectomy in *BRCA1/2* mutation carriers: Factors influencing uptake and timing

Catheleine M. van Driel [a,*], Yassir Eltahir [b], Jakob de Vries [c], Jan P. Jaspers [d], Jan C. Oosterwijk [e], Marian J. Mourits [f], Geertruida H. de Bock [a]

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What influences uptake of RRM?

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- Risk perception
- Anxiety
- Family history
- Patient knowledge
- Patient demographic and socioeconomic factors
- Health care professionals' recommendation
- Access to care (cost and availability)
- Mutation type influence on uptake of RRBSO

Metcalfe, K, et al. Int. J. Cancer(2008)
Meiser et al J Womens Health (Larchmt). 2003
Madalinska et al J Clin Oncol. 2007 Jan 20;25(3):301-7.
Metlcalfe et al J Clin Oncol. 2008

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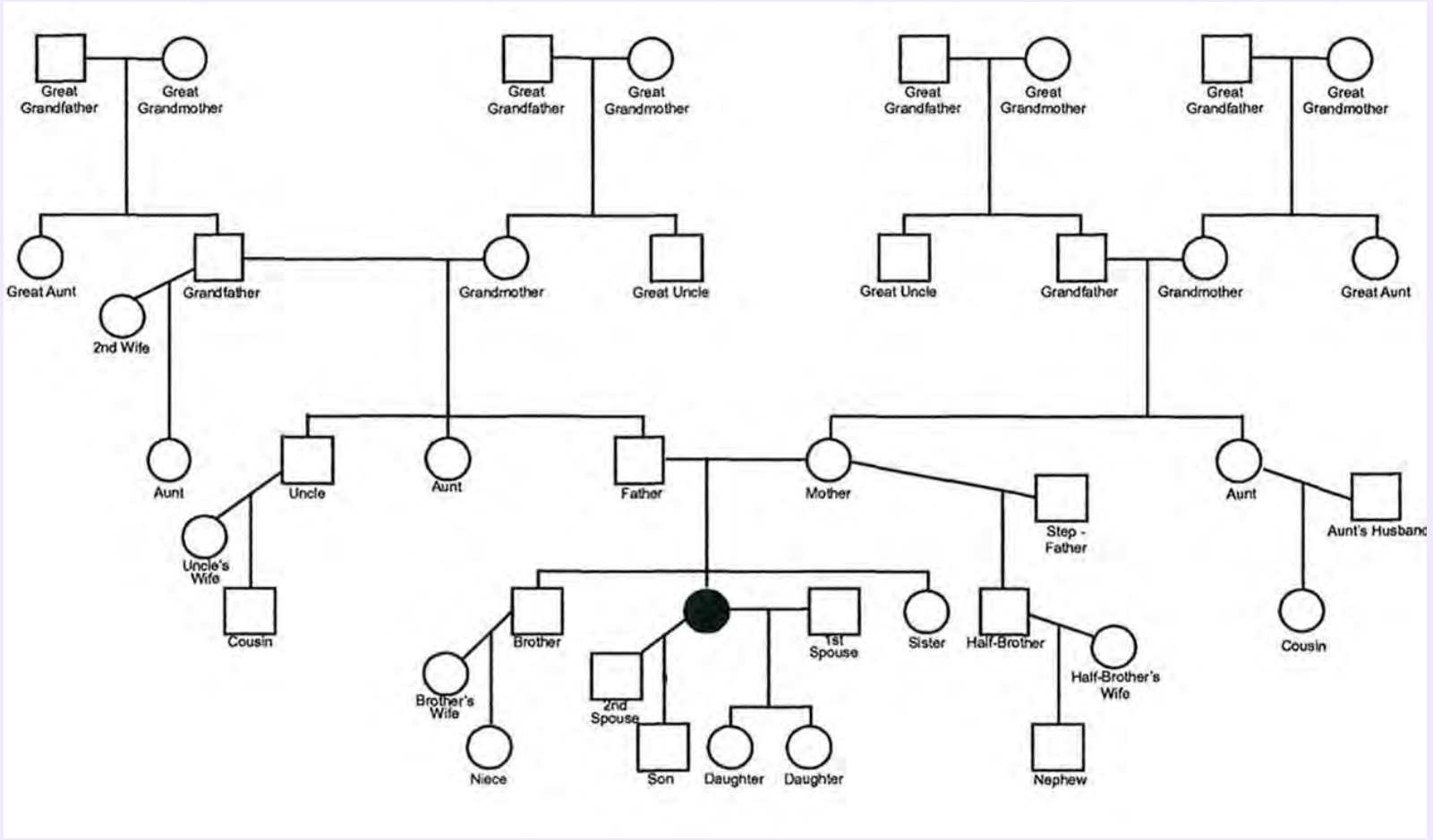

Living With the BRCA Gene: One Family's Story

Generations of the Price family have been affected by a mutation in the BRCA1 gene that significantly raises the risk of breast and ovarian cancer. A parent who carries the defective gene has a 50 percent chance of passing it on to his or her children. In 2002, Christie Veale became the first family member to get a DNA test that revealed she had inherited the mutation from her mother. As many of her relatives followed, they have made different choices about how to manage their genetic predisposition to the life-threatening condition.

Robert Milton Price
Died of colon cancer at age 50.

Two of Robert and Eleanor's sisters died of breast cancer. Another sister died of ovarian cancer.

Eleanor Price Veith, 87
Has not been tested for the gene, but is assumed to be positive because her daughter has it. Ovarian cancer was diagnosed.

Robert Neville Price
Died of pancreatic cancer. One of his daughters died of breast cancer.

Rosalyn Price Pierce
Had never been tested for the gene, but must have passed it to her daughter. First developed breast cancer at age 34. Died of breast cancer in July at age 67.

Janice Price Brown
Had never been tested for the gene, but must have passed it to her daughters. Ovarian and breast cancer were first diagnosed at age 33. Died of breast cancer at age 57 in 2001.

Joan Veith Lindner, 64
Learned she had breast cancer at age 48, underwent chemotherapy and had her breasts and ovaries removed. She later tested positive for the gene.

"When I tested positive I knew my daughters needed to be tested as well."

Gloria Veith Spurlock, 59
Has not been tested.

"There's no real need to know because it is a situation where we would just continue to take care of ourselves extremely well."

Dana Pierce, 47
Tested negative for the gene.

Brenda Russo, 41
Tested positive for the gene, and had her ovaries removed. Goes for frequent mammograms and M.R.I.'s.

"I know some women have their breasts removed. To me that's a little drastic... I'm not safe from getting cancer, but I'm pretty confident that we would catch it early if we ever did catch it."

Jodi Dembeck, 41
After her sister learned she had cancer, she tested positive for the gene. She gets regular mammograms and is waiting to decide whether to have a fourth child before considering surgery.

"You can have everything taken out and a few cells maybe weren't caught. There's no foolproof way to avoid cancer."

Christie Veale, 39
After breast cancer was diagnosed, she tested positive for the gene. She then had a bilateral mastecomy and later had her ovaries removed.

"I've gotten rid of the areas where it can come. I'd rather be proactive than have something chasing me."

Lori French, 37
Tested negative for the gene.

"When they explained that that means my daughter would not get it either, I was elated."

Deborah Lindner, 33
Tested positive for the gene and had a prophylactic mastectomy this summer at age 33. She is planning to have her ovaries removed before she turns 40.

"I just feel really happy that I don't have to worry about this anymore."

Lisa Spurlock's brother has not been tested for the gene. He requested that his name and picture be withheld because of the potential for discrimination based on his genetic risk.

Lisa Spurlock, 24
Has not been tested.

"Since cancer runs in my family it makes me more aware of my lifestyle. I eat a lot of raw fruits and vegetables and try to be healthier."

THE NEW YORK TIMES

The Breast Centre
thebreastcentre.com.au

- Decisions regarding preventive surgery are influenced by much more than the actual risk figure
- Individual life experience, and in particular the loss of a mother significantly impacts decision making regardless of age or risk
- Shared decision-making leads to higher levels of patient satisfaction, but physicians struggle to gauge patient preference for paternalism vs. autonomy
- While some women feel disappointed that a physician was not more directive, others reject doctors' input as too forceful or definitive

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- An important predictor of a patient later regretting having had RRM is when the physician was the one to introduce this option into the discussion of treatment

- This emphasizes that physicians must be well aware of how much they may influence a woman's decision to have prophylactic surgery, and they must remain alert when giving advice about possible treatment and monitoring options and verify whether the choice for prophylactic surgery is based on the patients' own decision.

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Incidence of regret low (6%)

More common in women who were :

- dissatisfied with their cosmetic result
- those who felt misinformed about their options preoperatively

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CLINICAL PSYCHOLOGY

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- The decision to undergo risk-reducing surgery can be a complex one. There are many issues to consider.
- Even after a decision has been made, the process, including surgery and beyond, can be physically and emotionally challenging.
- For these reasons, many women find it helpful to have one or more consultations with a psychologist who is knowledgeable and familiar with the impact of risk-reducing surgery.
- Consultation with a psychologist is not an assessment of suitability for surgery or about competence in making decisions. It is an opportunity to discuss the decision.

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THE ANGELINA EFFECT

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OP-ED CONTRIBUTOR

My Medical Choice

By ANGELINA JOLIE
Published: May 14, 2013 | 1712 Comments

LOS ANGELES

Enlarge This Image

Loren Capelli

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Jolie's Disclosure of Preventive Mastectomy Highlights Dilemma (May 15, 2013)

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Letters: Angelina Jolie's Preventive Surgery (May 15, 2013)

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MY MOTHER fought cancer for almost a decade and died at 56. She held out long enough to meet the first of her grandchildren and to hold them in her arms. But my other children will never have the chance to know her and experience how loving and gracious she was.

We often speak of "Mommy's mommy," and I find myself trying to explain the illness that took her away from us. They have asked if the same could happen to me. I have always told them not to worry, but the truth is I carry a "faulty" gene, BRCA1, which sharply increases my risk of developing breast cancer and ovarian cancer.

My doctors estimated that I had an 87 percent risk of breast cancer and a 50 percent risk of ovarian cancer, although the risk is different in the case of each woman.

Only a fraction of breast cancers result from an inherited gene mutation. Those with a defect in BRCA1 have a 65 percent risk of getting it, on average.

NY Times, May 14 2013

The Breast Centre

thebreastcentre.com.au

The number of Australian women aged 20-39 who had a mastectomy for reducing their breast cancer risk more than doubled from 99 in 2012/13 to 227 in 2013/14, according to a report by the Australian Institute of Health and Welfare (AIHW).

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WHEN ?

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Research

JAMA | Original Investigation

Risks of Breast, Ovarian, and Contralateral Breast Cancer for *BRCA1* and *BRCA2* Mutation Carriers

Karoline B. Kuchenbaecker, PhD; John L. Hopper, PhD; Daniel R. Barnes, PhD; Kelly-Anne Phillips, MD; Thea M. Mooij, MSc; Marie-José Roos-Blom, MSc; Sarah Jervis, PhD; Flora E. van Leeuwen, PhD; Roger L. Milne, PhD; Nadine Andrieu, PhD; David E. Goldgar, PhD; Mary Beth Terry, PhD; Matti A. Rookus, PhD; Douglas F. Easton, PhD; Antonis C. Antoniou, PhD; and the *BRCA1* and *BRCA2* Cohort Consortium

JAMA June 20, 2017
Volume 317, Number 23

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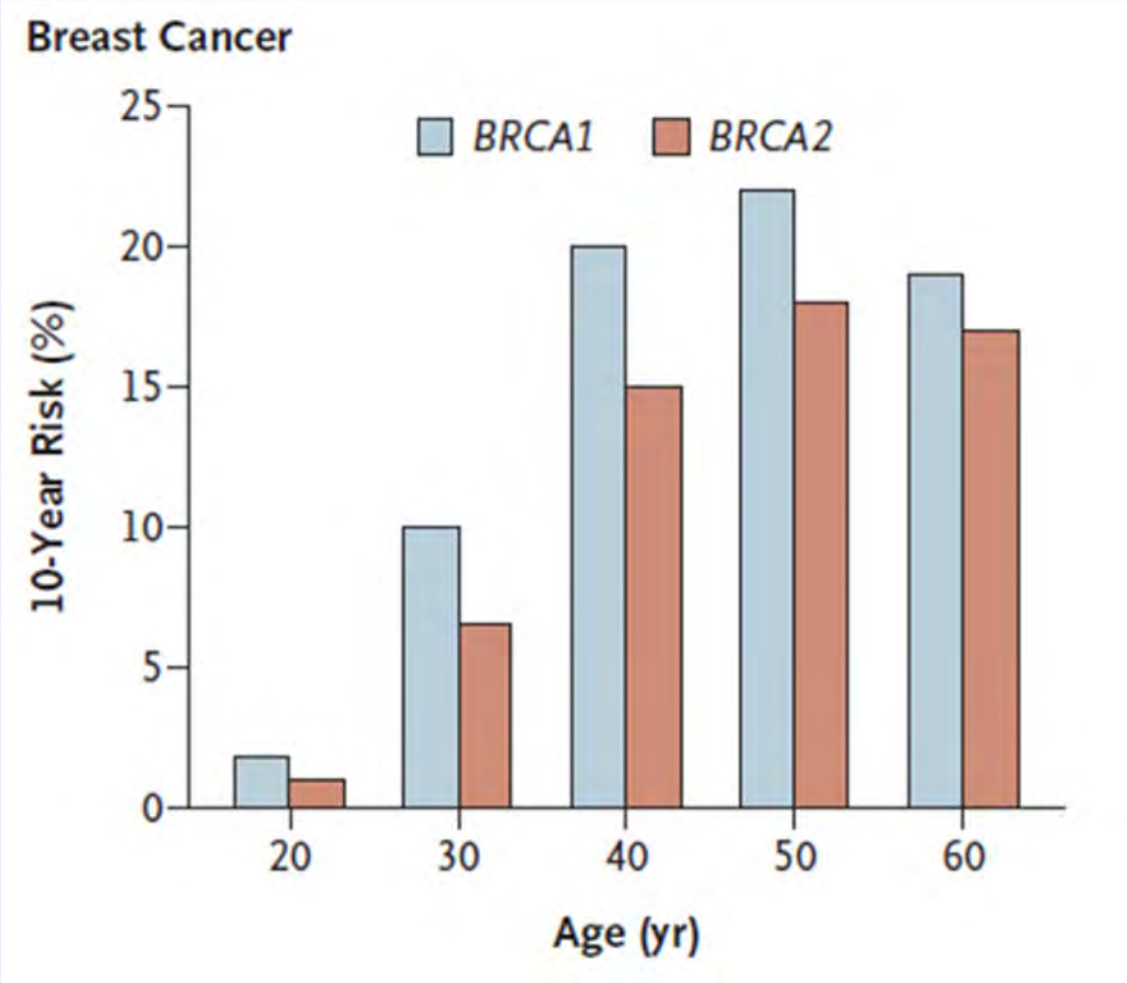
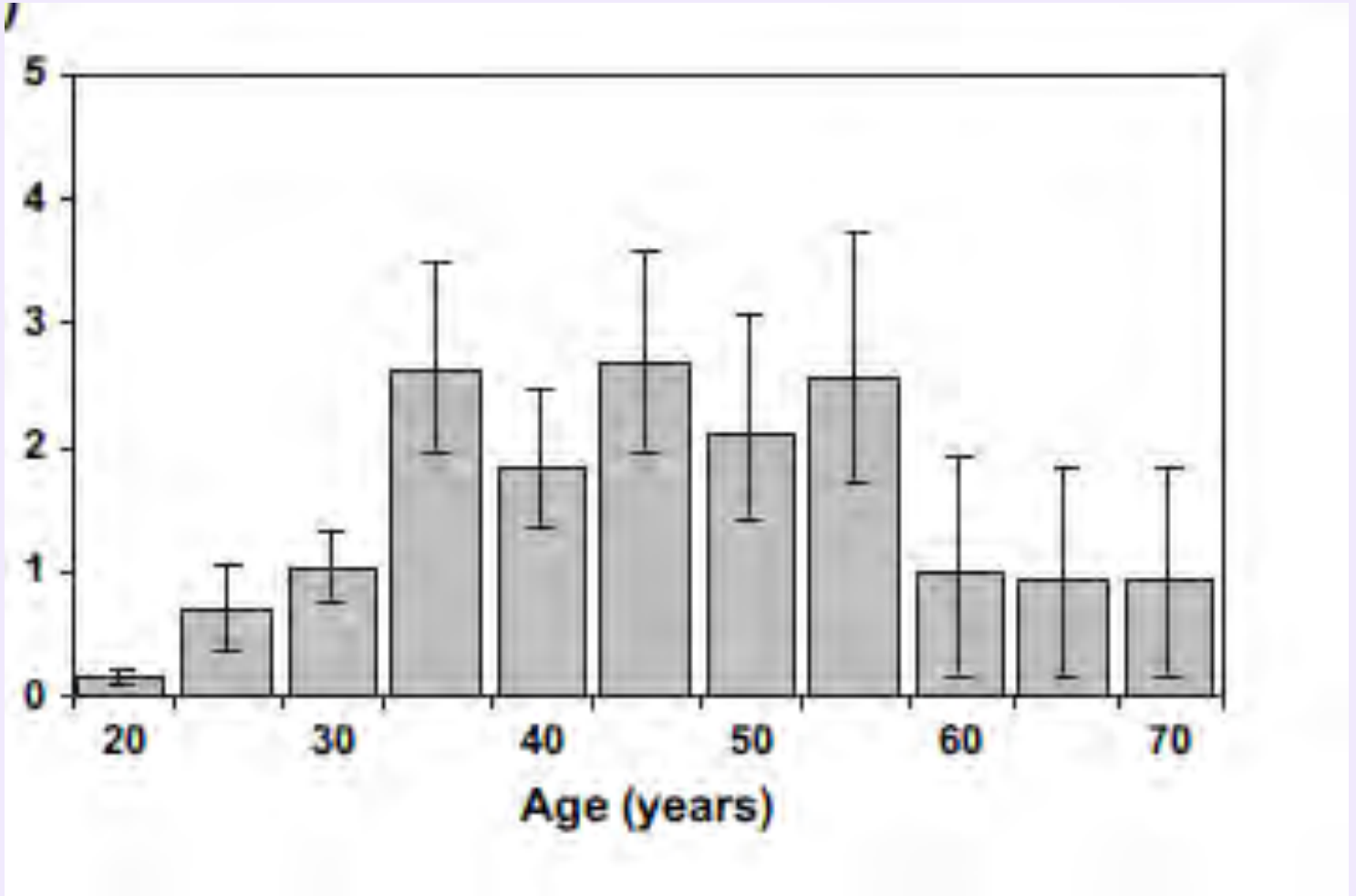
Timing of Risk Reducing Mastectomy



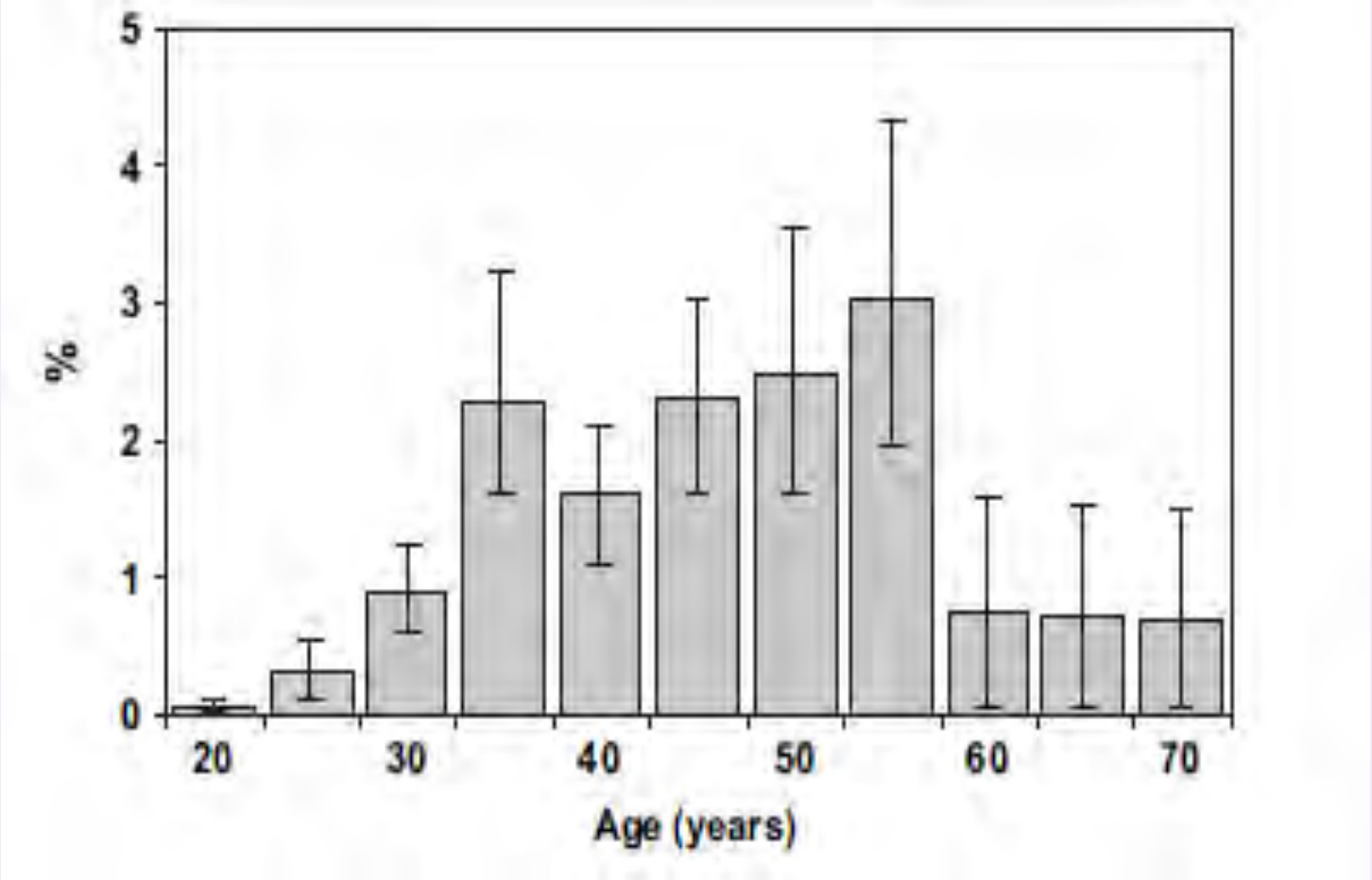
Robson & Offit NEJM 2007

Age Specific Annual Risk of Breast Cancer BRCA1 carrier



Suthers, ANZ J Surg 2007

Age Specific Annual Risk of Breast Cancer BRCA 2 carrier



Suthers, ANZ J Surg 2007

BRCA Mutation Carriers

- For the older woman, risk of breast cancer is falling
- Therefore may be less benefit from RRM

Table 2. Predicted Mean Cancer Risk to Currently Unaffected *BRCA1/2* Mutation Carriers

	Risk (%) of Developing Cancer by Age									
	30 Years		40 Years		50 Years		60 Years		70 Years	
Current Age	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Breast cancer: *BRCA1*										
20 years	1.8	1.4 to 2.2	12	9.5 to 14	29	24 to 35	44	37 to 52	54	46 to 63
30 years	—		10	8.2 to 13	28	23 to 34	44	36 to 52	54	45 to 63
40 years	—		—		20	16 to 25	38	31 to 45	49	41 to 58
50 years	—		—		—		22	18 to 27	37	30 to 44
60 years	—		—		—		—		19	15 to 24
Breast cancer: *BRCA2*										
20 years	1	0.78 to 1.4	7.5	5.8 to 9.8	21	17 to 26	35	28 to 42	45	38 to 53
30 years	—		6.6	5.1 to 8.6	20	16 to 26	35	28 to 42	45	38 to 53
40 years	—		—		15	12 to 19	30	24 to 36	42	34 to 49
50 years	—		—		—		18	15 to 22	32	26 to 38
60 years	—		—		—		—		17	14 to 20
Ovarian cancer: *BRCA1*										
20 years	1	0.68 to 1.8	3.2	2.3 to 5.1	9.5	7.3 to 13	23	18 to 28	39	34 to 44
30 years	—		2.2	1.6 to 3.4	8.7	6.7 to 12	22	18 to 27	39	34 to 43
40 years	—		—		6.7	5.2 to 8.9	20	17 to 24	38	33 to 41
50 years	—		—		—		15	12 to 17	34	29 to 36
60 years	—		—		—		—		22	20 to 23
Ovarian cancer: *BRCA2*										
20 years	0.19	0.09 to 0.47	0.7	0.37 to 1.5	2.6	1.5 to 4.5	7.5	5.1 to 11	16	12 to 20
30 years	—		0.52	0.28 to 1	2.4	1.5 to 4.2	7.4	5.1 to 11	16	12 to 20
40 years	—		—		1.9	1.2 to 3.2	7	4.8 to 10	16	12 to 20
50 years	—		—		—		5.2	3.7 to 7.2	14	11 to 17
60 years	—		—		—		—		9.8	7.8 to 11

NOTE. The CI is provided for the mean risk, not the risk itself.

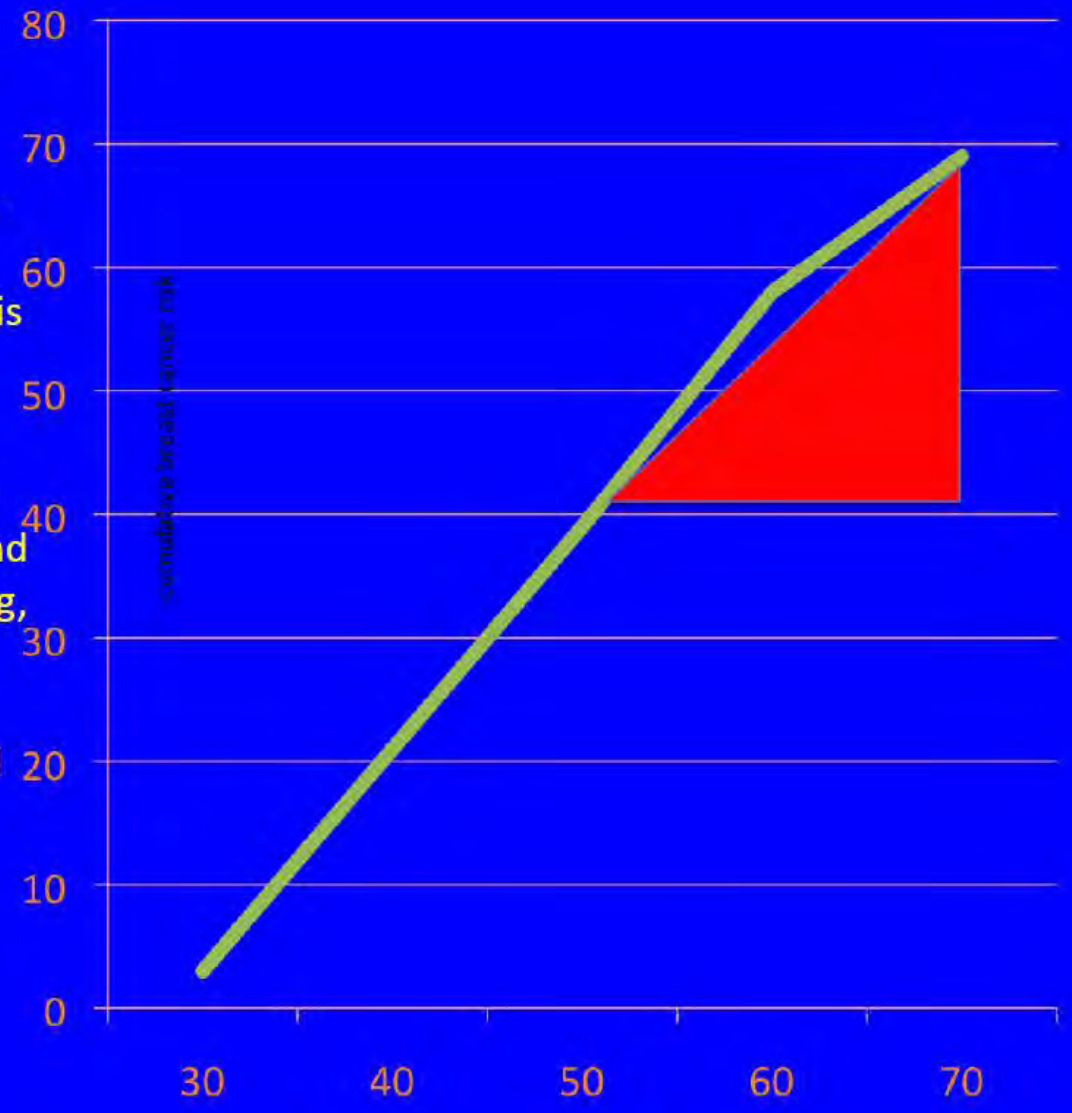
Chen et al, JCO. 2007

Women "outlive" some of their lifetime risk as they age

Area Under the Curve Concept of Future Risk

For a 30 year old woman just found to be a BRCA 1 carrier the entire lifetime risk curve is applied

For a 50 year old who has no personal history of cancer, and completed negative screening, her risk is estimated as the area under the curve of remaining risk a 30% residual risk



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The expected benefit of preventive mastectomy on breast cancer incidence and mortality in BRCA mutation carriers, by age at mastectomy

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Table 2 Proportions of all deaths by various causes, according to age at mastectomy, for a 25 year old woman. Deaths before age 80

Age at mastectomy (years)	Death from breast cancer (%)	Death from ovarian cancer (%)	Death from other causes (%)
No mastectomy	25.6	42.3	32.1
25	0	56.6	43.4
30	1.5	55.6	42.9
35	6.4	52.9	40.6
40	10.8	50.8	38.4
45	15.2	47.9	36.9
50	18.4	46.4	35.1
55	21.3	44.5	34.2
60	23.2	43.2	33.5
65	24.5	42.9	32.6

Deaths before age 80

Narod et al,Breast Cancer Res Treat (2018) 167:263-267

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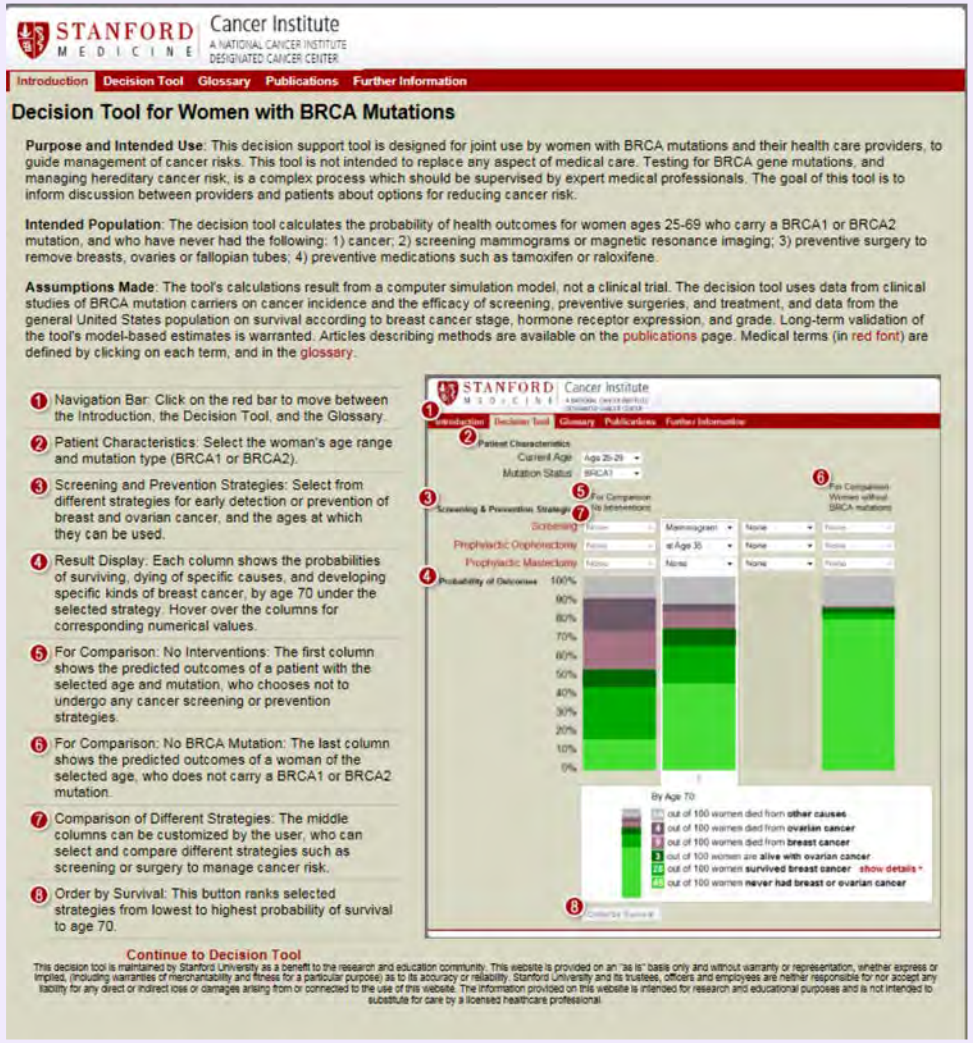
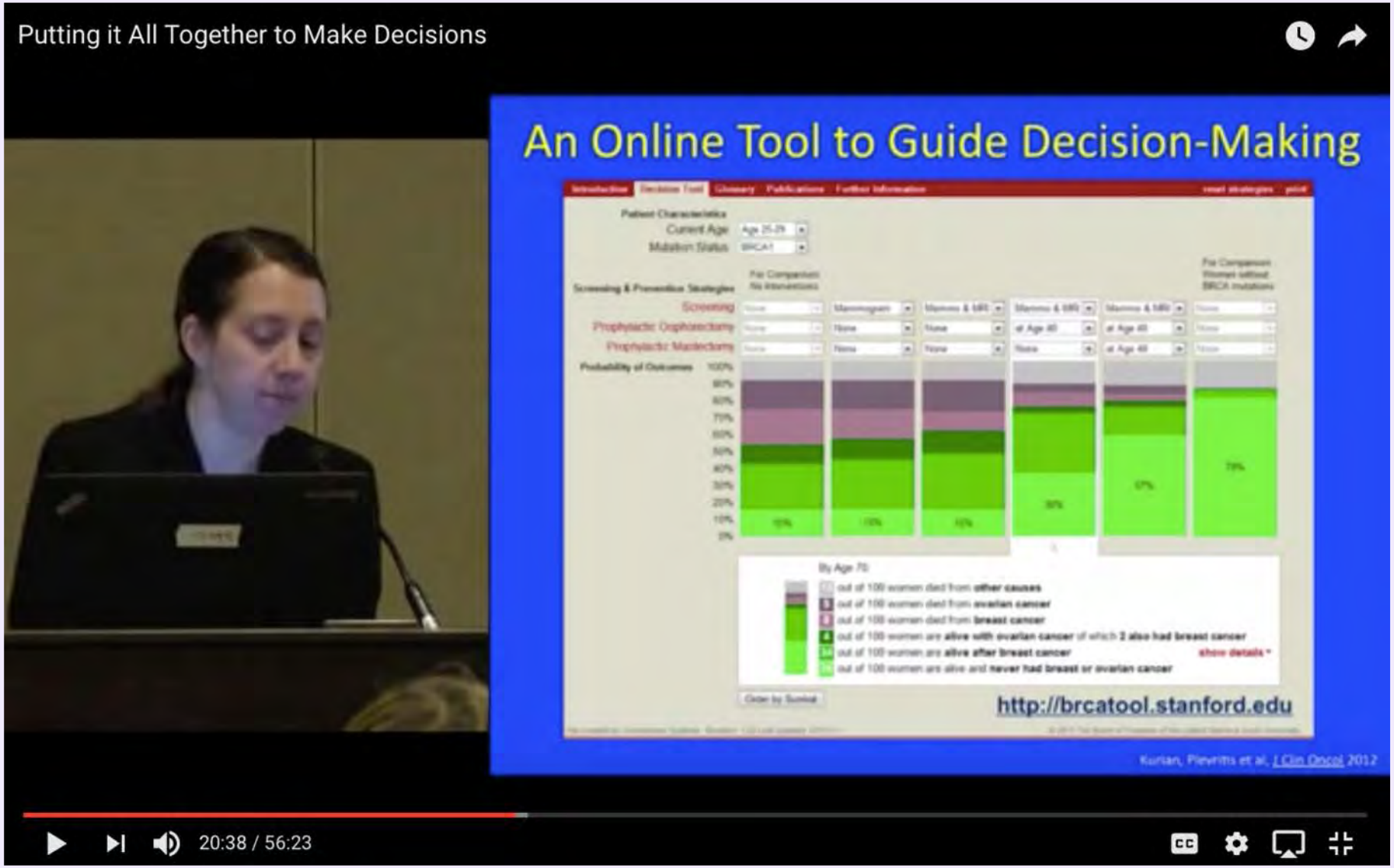
Online Decision Tool



http://brcatool.stanford.edu/



https://www.youtube.com/watch?v=74z6yMukORE

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BY WHOM ?

CHOOSING YOUR BREASTSURGEON

CHOOSING YOUR BREASTSURGEON

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- Gender
- Style / manner
- Age / Experience
- Degree of Specialisation
- Work environment
- eg ? multidisciplinary team member,
- site of practice –location, public or private sector

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GENDER

- 1998 Scottish Study
- Patient preferences for male or female breast surgeons
- 68% - no preference
- 32% - preferred female
- NIL – preferred male
- Patients preferring female surgeon generally younger

STYLE

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"Dr. Hedley, lose the polka-dot tie ... the patients hate that sort of thing."

"Dr. Swift, we prefer that our practitioners not take fashion risks with their jackets."

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MANNER

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"So, let's catch a wellness wave!"

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AGE

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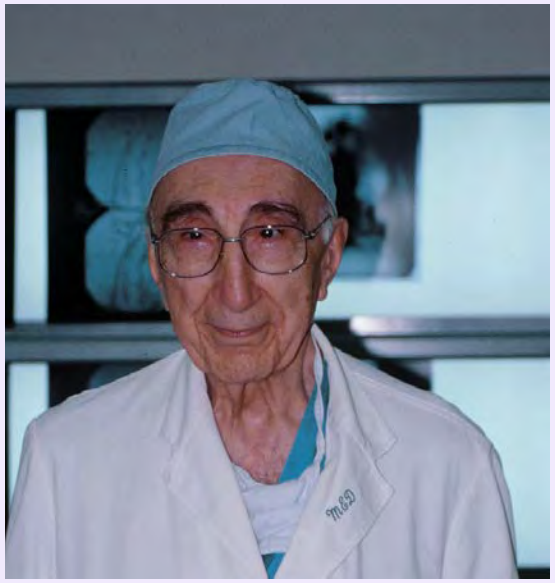

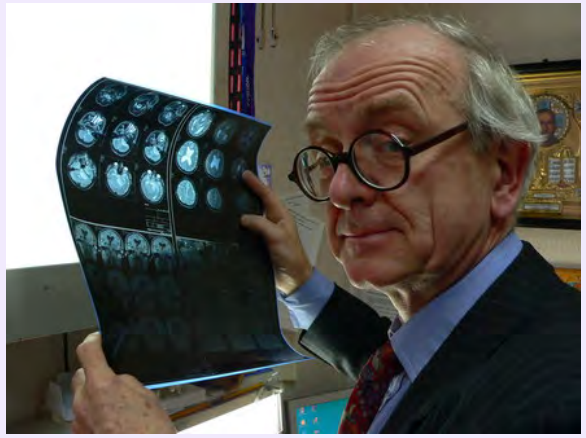

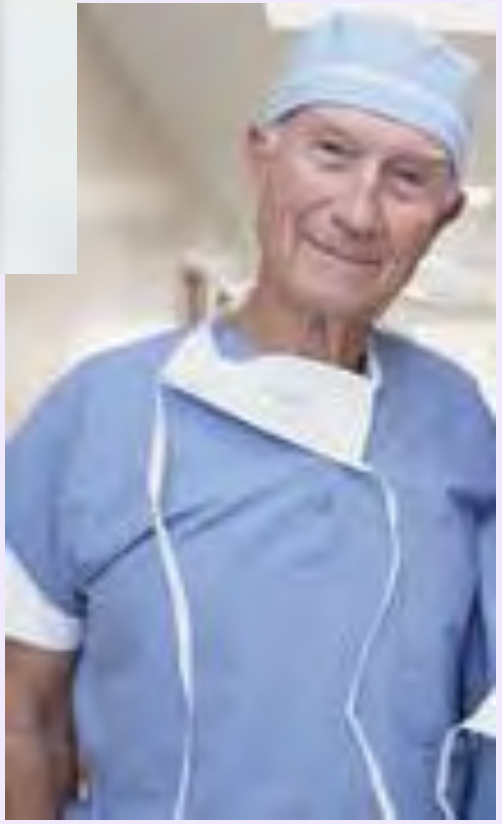

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Experience / Expertise

"No, I haven't performed the procedure myself, but I've seen it done successfully on 'E.R.' and 'Chicago Hope.' "

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WHAT ?

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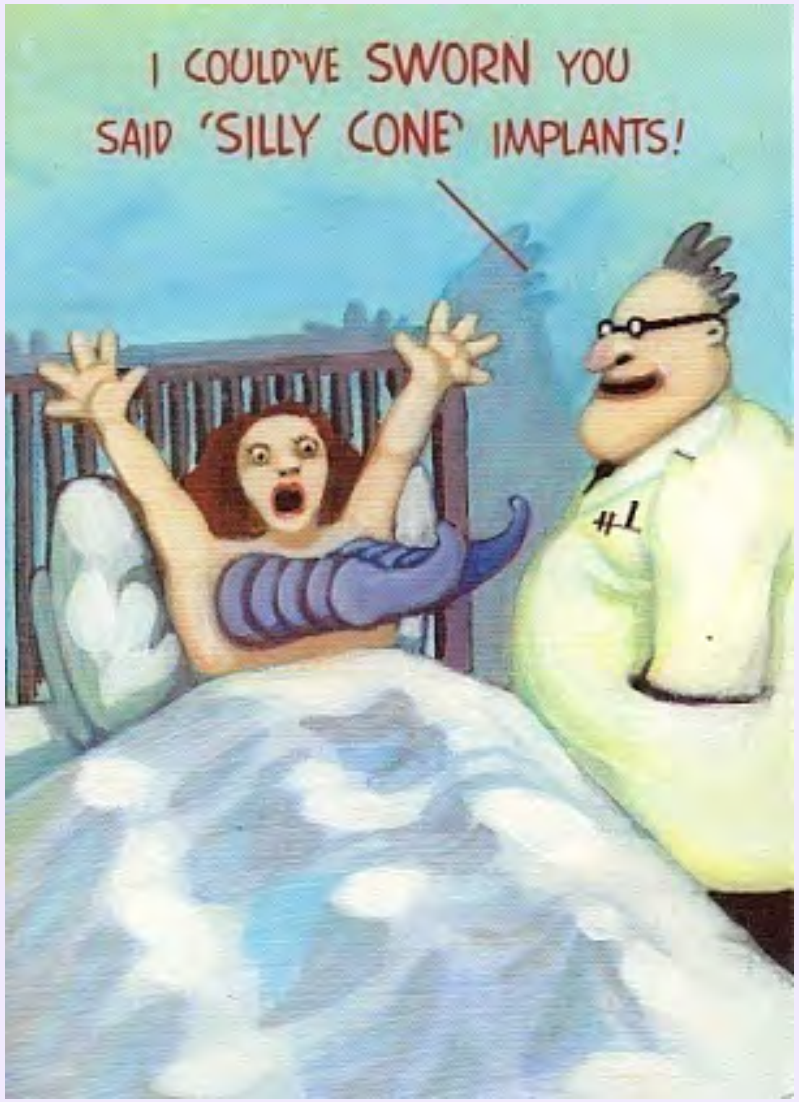

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Expectations need to be be realistic and achievable

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Recent Advances

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- Nipple-Sparing Mastectomy (NSM)
- Mesh Products (biological and synthetic)
- Direct-to-Implant Reconstruction (DTI)
- Prepectoral IBBR

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Types of Risk Reducing Mastectomy

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- Simple
- Skin-Sparing (SSM)
- Nipple-Sparing (NSM)

Type of mastectomy depends on:
- Whether there is to be immediate reconstruction
- Patient preference

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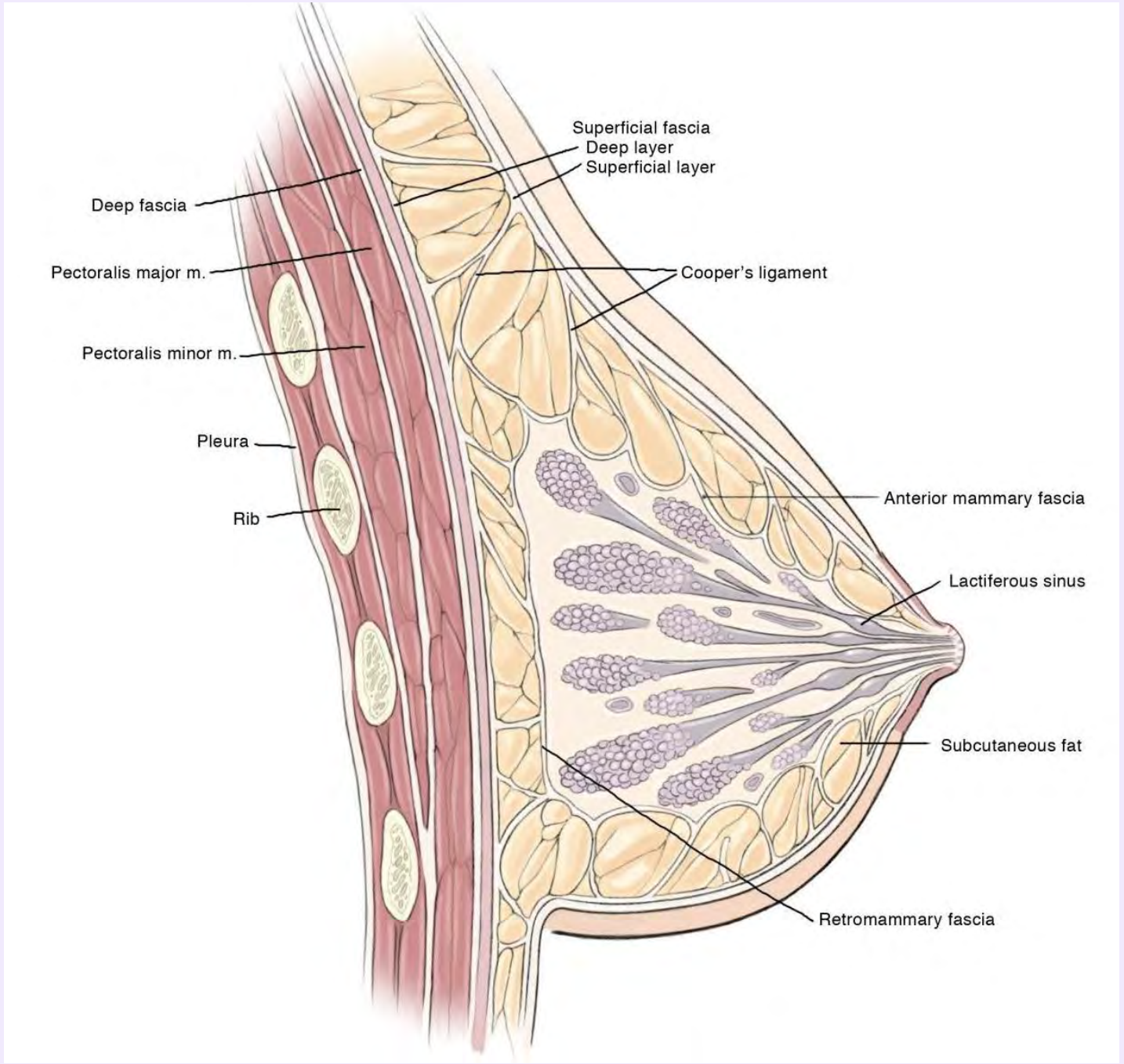

International Reconstruction Rates Post Risk Reducing Mastectomy

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Ann Surg Oncol (2013) 20:3817–3822
DOI 10.1245/s10434-013-3040-4

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

ORIGINAL ARTICLE – BREAST ONCOLOGY

International Rates of Breast Reconstruction After Prophylactic Mastectomy in *BRCA1* and *BRCA2* Mutation Carriers

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Ann Surg Onc 2013

- 70 % BRCA 1/ 2 mutation carriers have reconstruction after prophylactic mastectomy
- Compared to 5-29% of women having a mastectomy for breast cancer

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Rates of Breast Reconstruction after Prophylactic Mastectomy in BRCA 1 and 2 carriers

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TABLE 1 Reconstruction by country and groups

Country	Total no.	Subject groups *n* (%)			Reconstructions, *n* (%)
		Bilateral PM (no cancer)	Contralateral PM after mastectomy	Contralateral PM after lumpectomy	
Austria	26	10 (38.5)	8 (30.8)	8 (30.8)	15 (57.5)
Canada	664	293 (44.1)	217 (31.8)	154 (23.2)	444 (66.9)
France	7	1 (14.3)	2 (28.6)	4 (57.1)	6 (85.7)
Hong Kong, China	6	1 (14.9)	5 (83.3)	0	3 (50)
Italy	17	3 (17.7)	10 (58.8)	4 (23.5)	14 (82.4)
Norway	10	8 (80.0)	2 (20.0)	0	8 (80.0)
Poland	63	19 (30.2)	40 (63.5)	4 (6.4)	42 (66.7)
United States	842	310 (36.8)	392 (46.6)	140 (16.6)	605 (71.9)
Total	1,635	645	676	314	
Total no. of reconstructions	1,137	514 (79.7 %)	387 (57.1 %)	236 (75.2 %)	1,137 (69.1)

PM prophylactic mastectomy

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International Immediate Reconstruction Rates in Patients with Breast Cancer

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EJSO
the Journal of Cancer Surgery

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Review

Uptake and predictors of post-mastectomy reconstruction in women with breast malignancy – Systematic review

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EJSO 2013

- USA- 30 %
- Stockholm – 30%
- UK- 11%
- Australia – 10%

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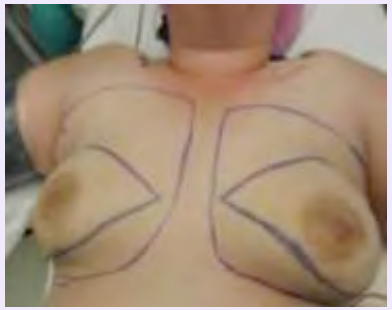
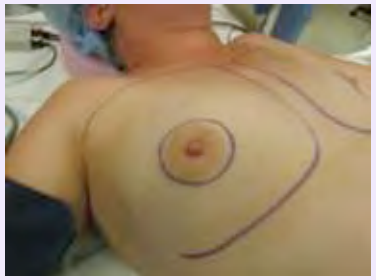
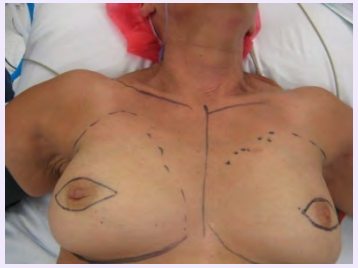
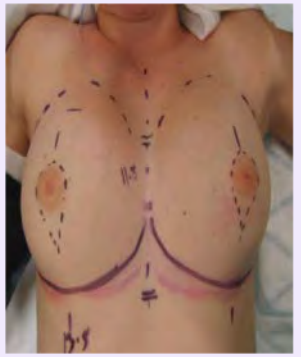
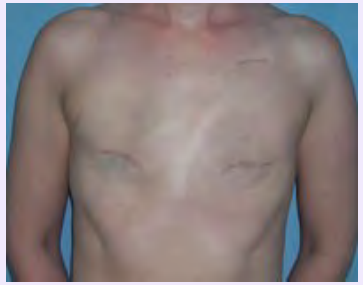
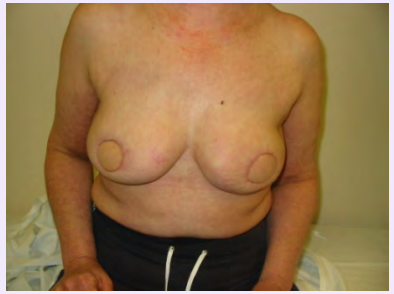
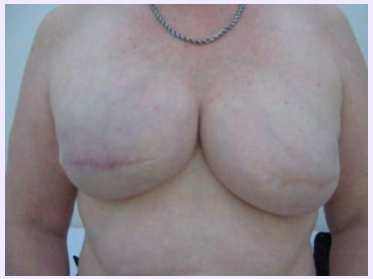
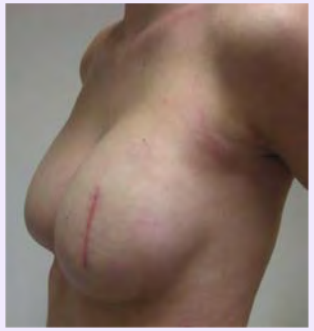
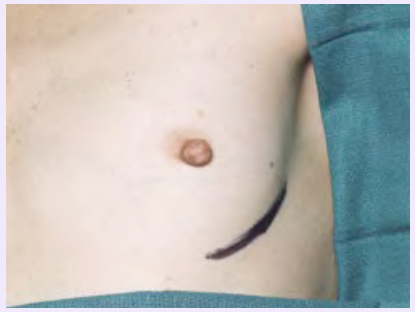
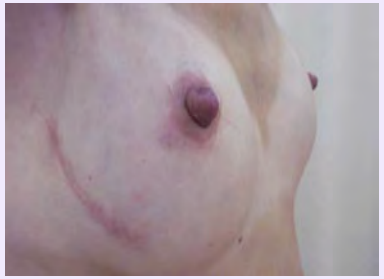
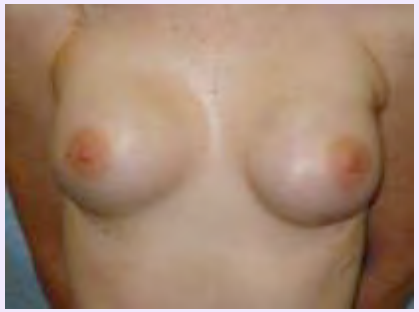
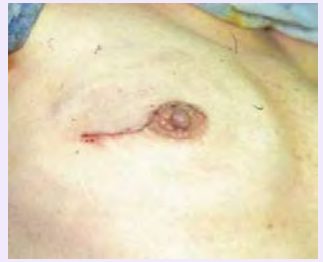









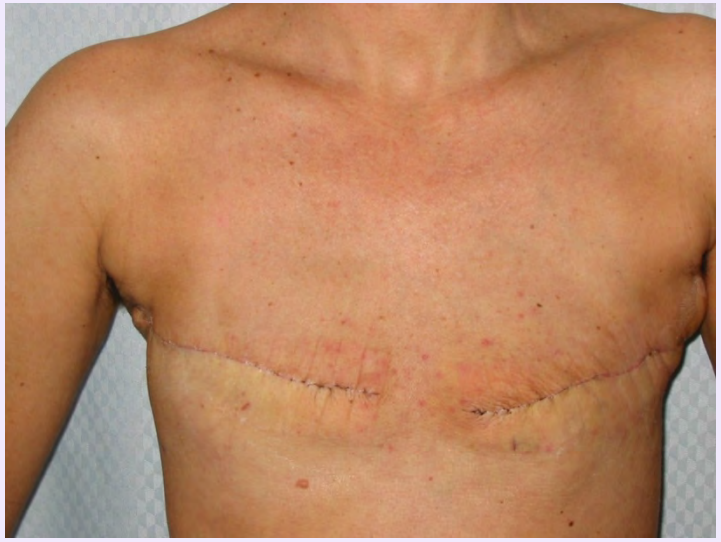
Simple Mastectomy

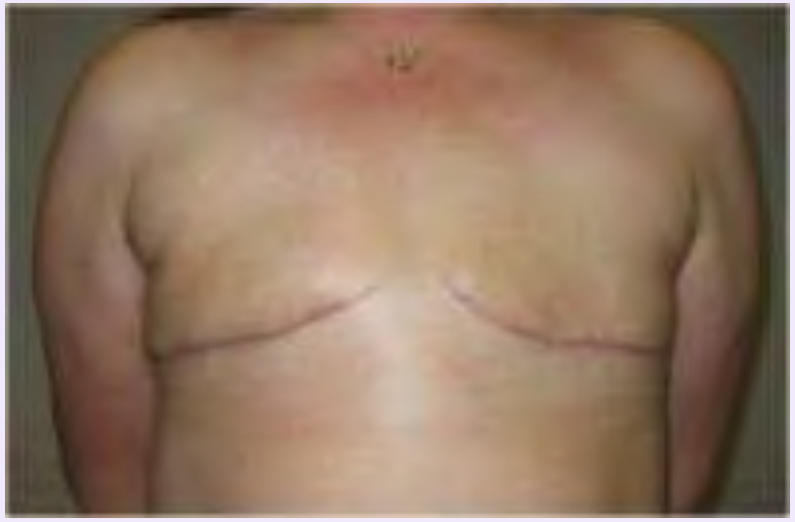
Skin-Sparing Mastectomy

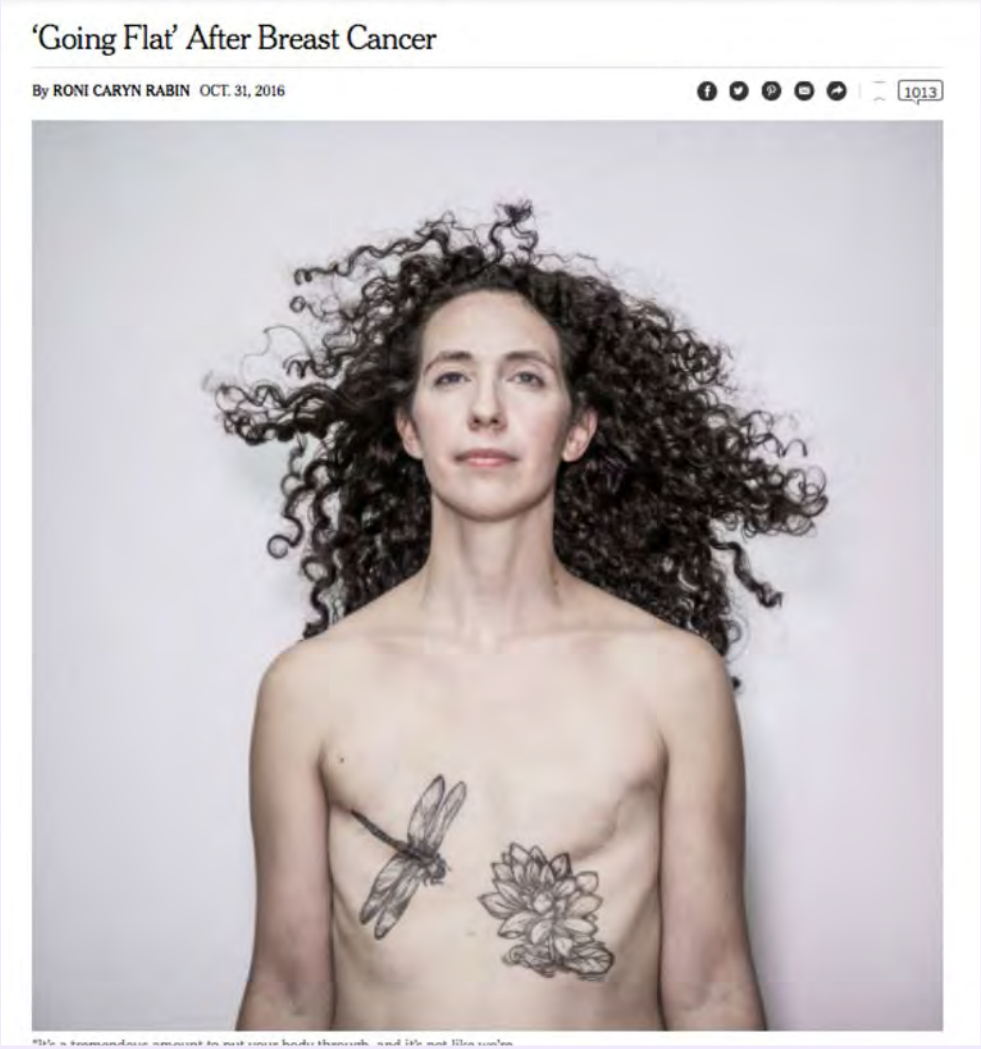
Nipple-Sparing Mastectomy

Simple Mastectomy





"Going Flat"



'Going Flat' After Breast Cancer

By RONI CARYN RABIN OCT. 31, 2016

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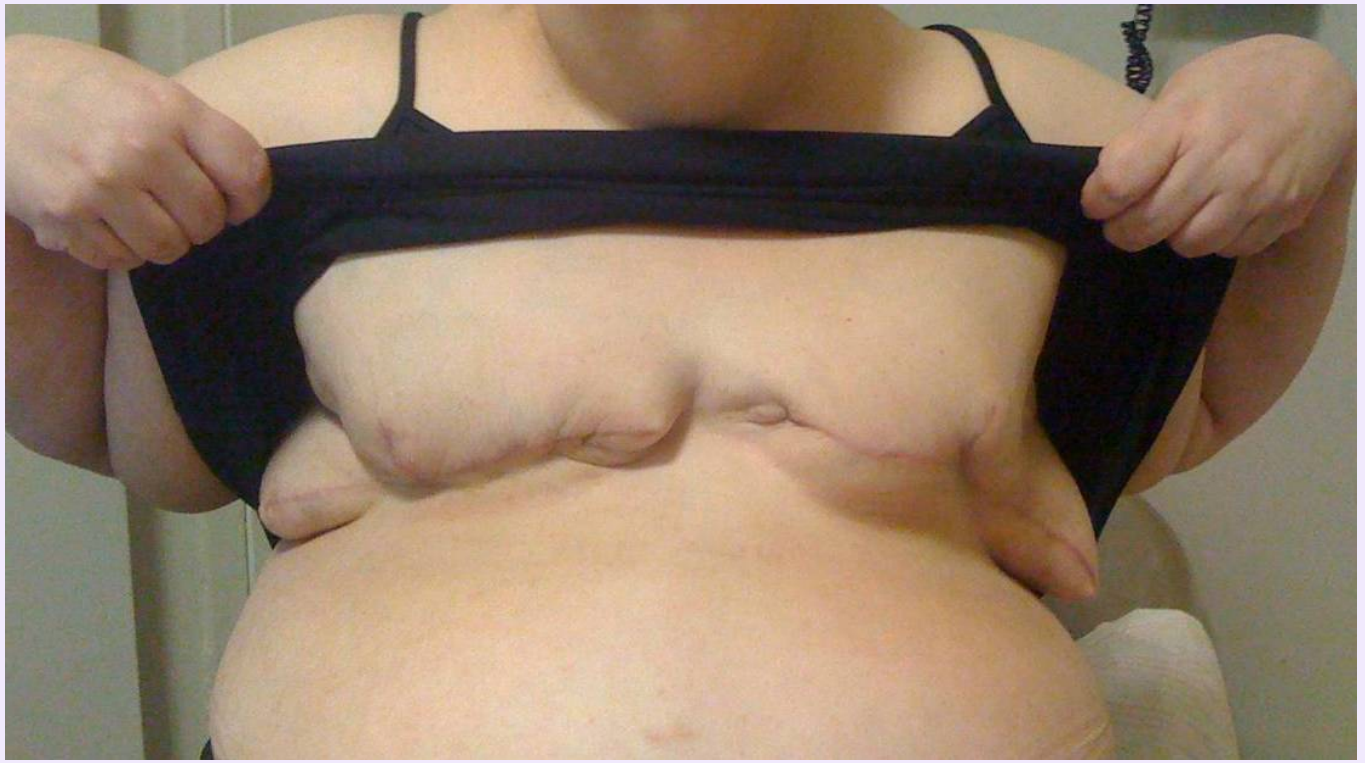
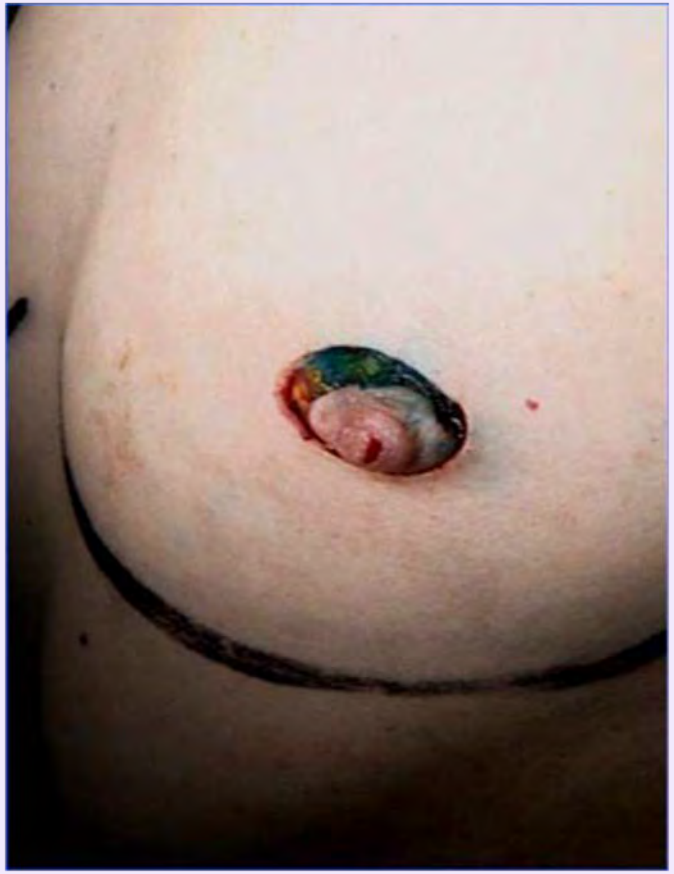
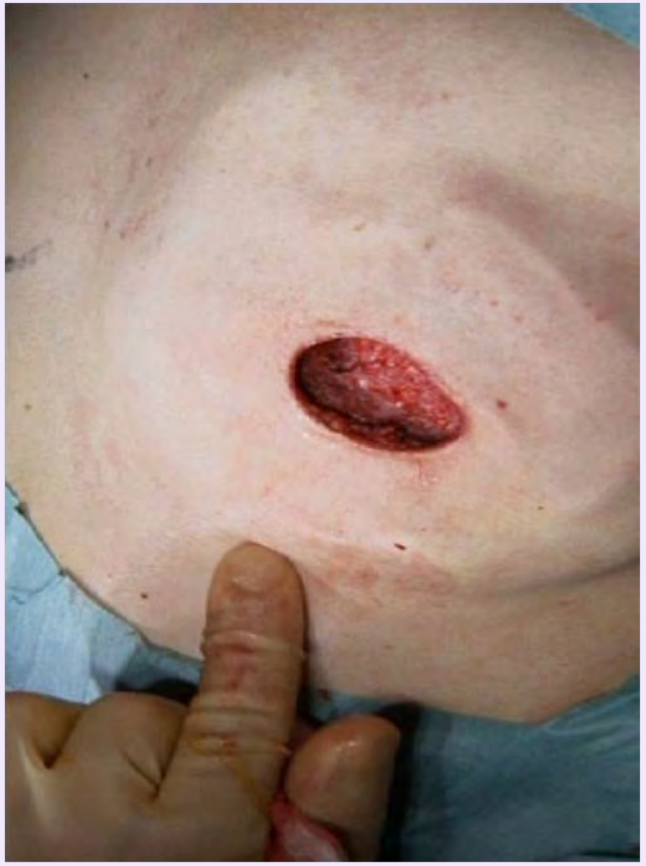
New York Times, Oct 2016

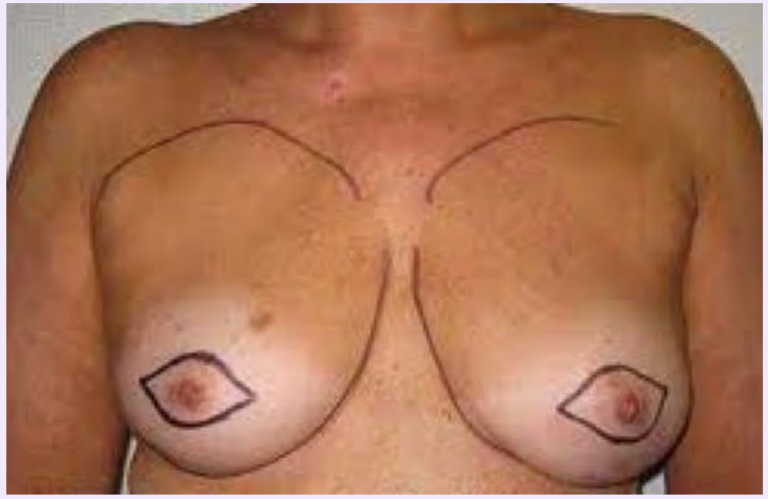
http://www.flatandfabulous.org

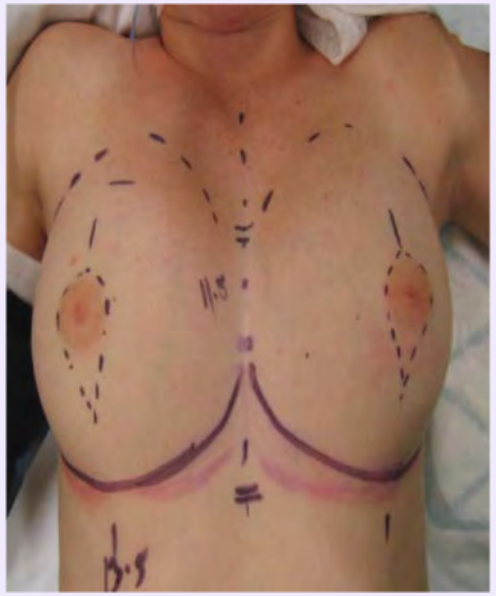


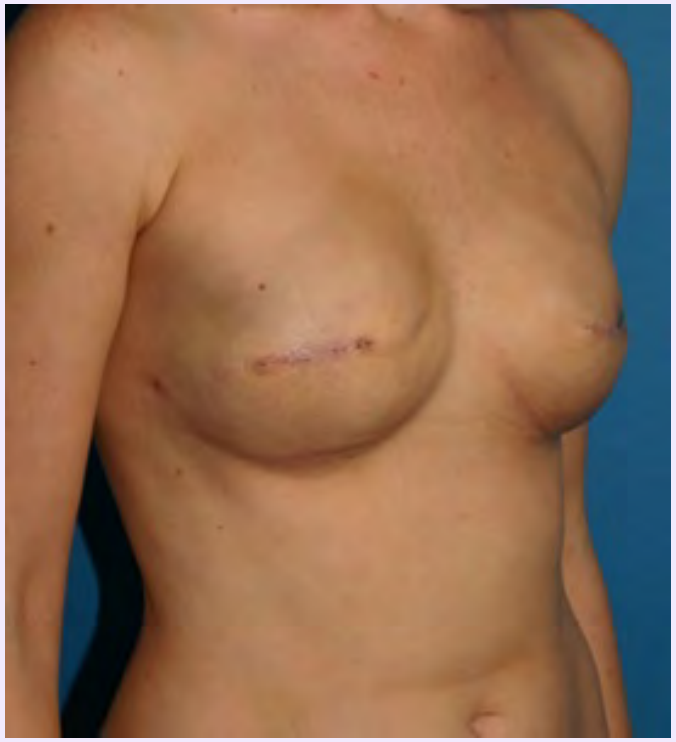
Skin-Sparing Mastectomy (SSM)

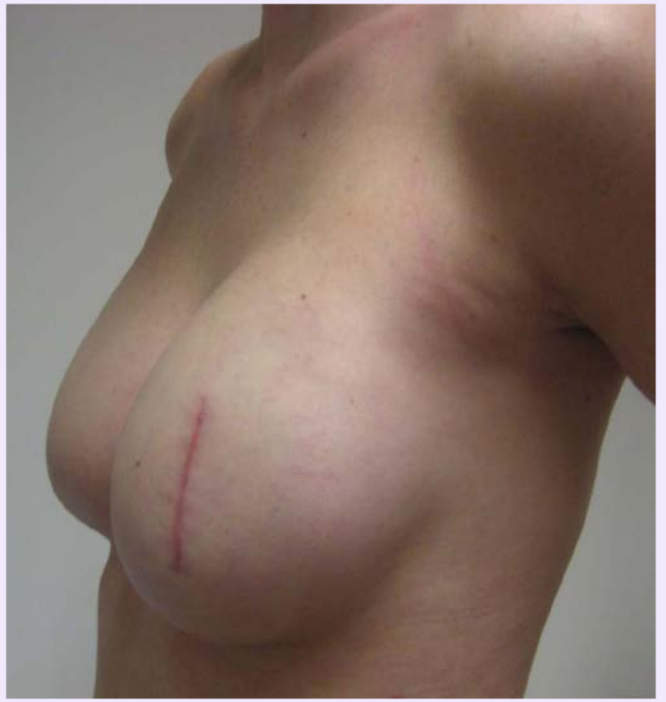












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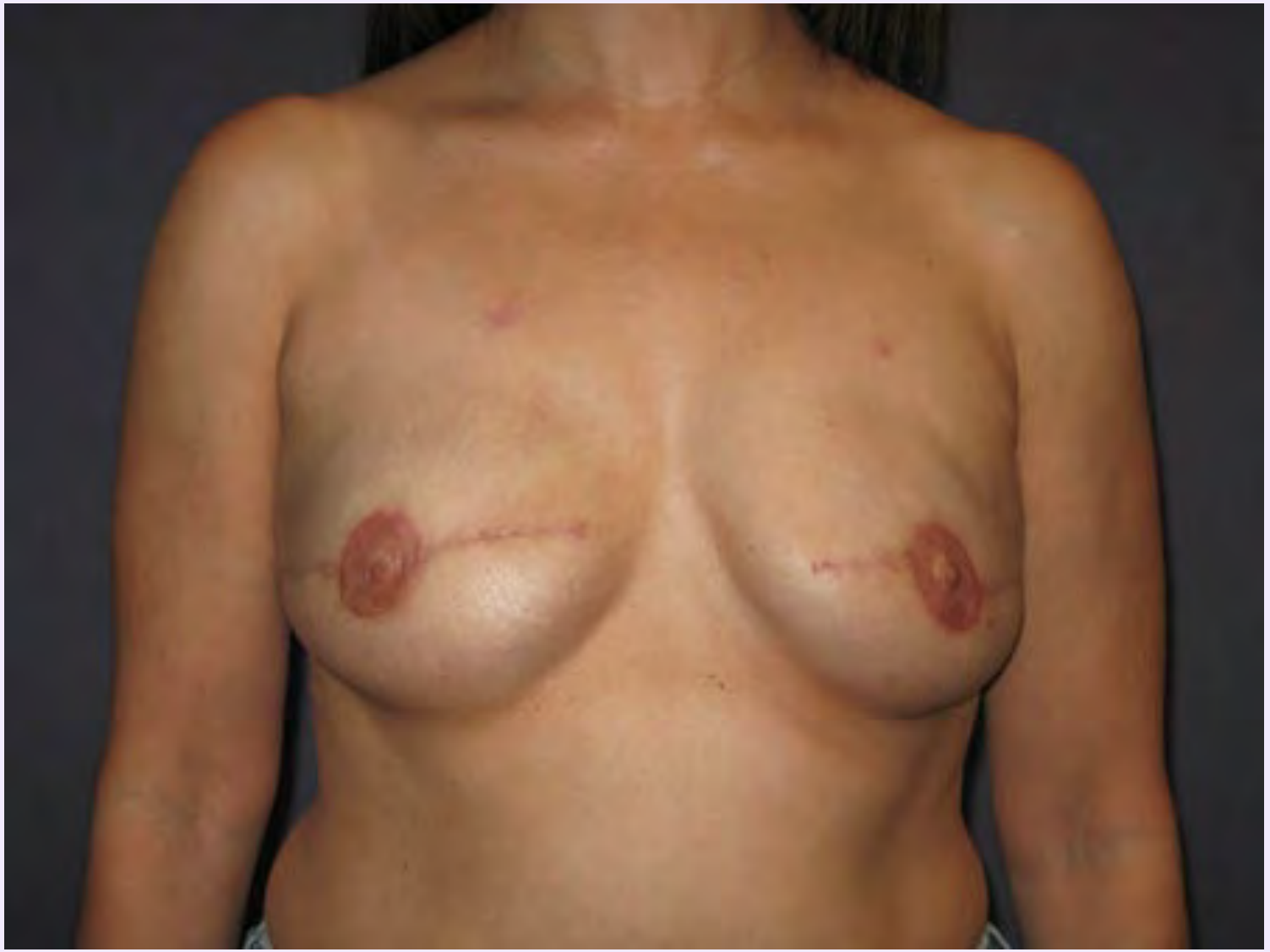

Nipple-Sparing Mastectomy (NSM)

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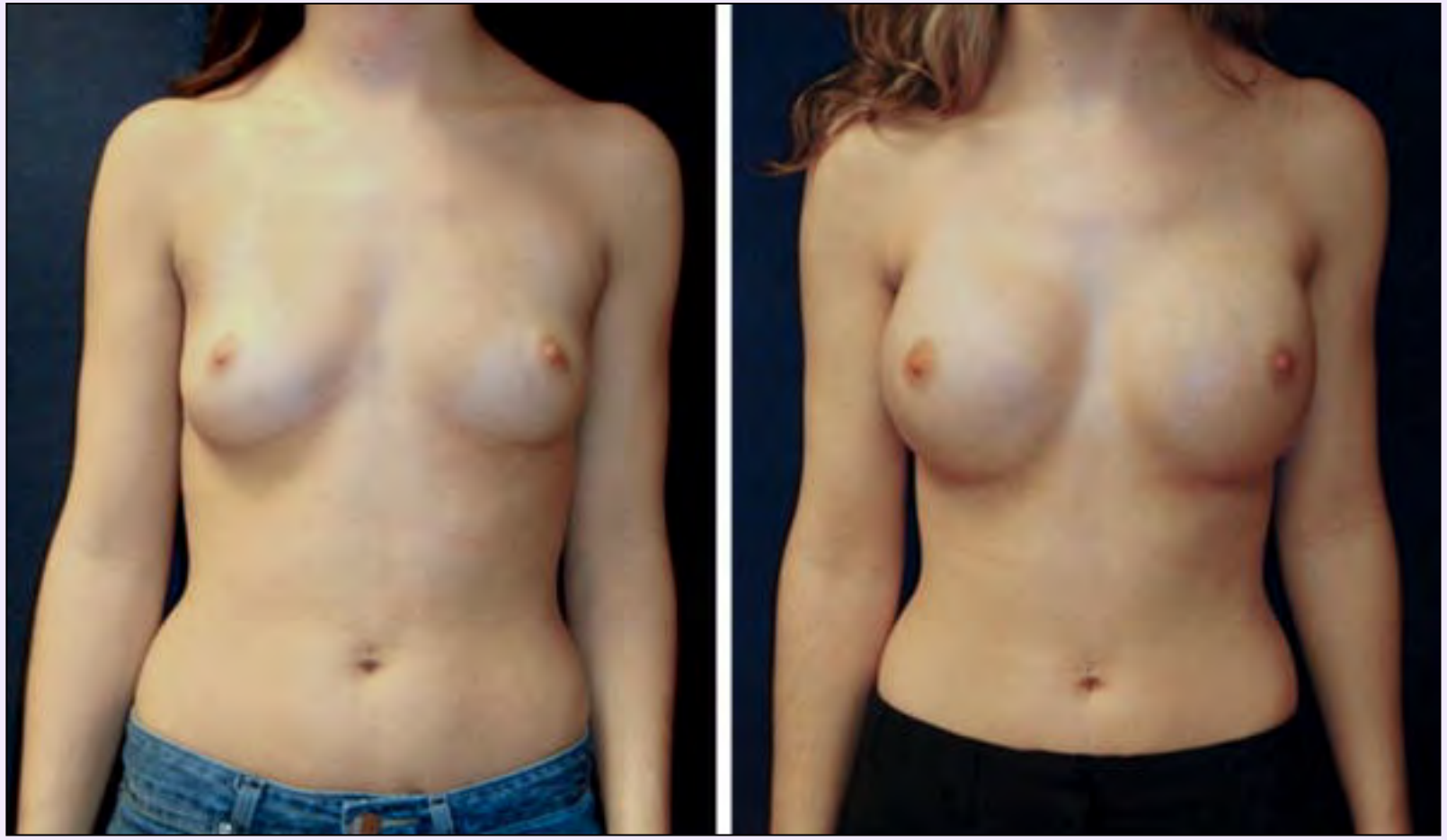

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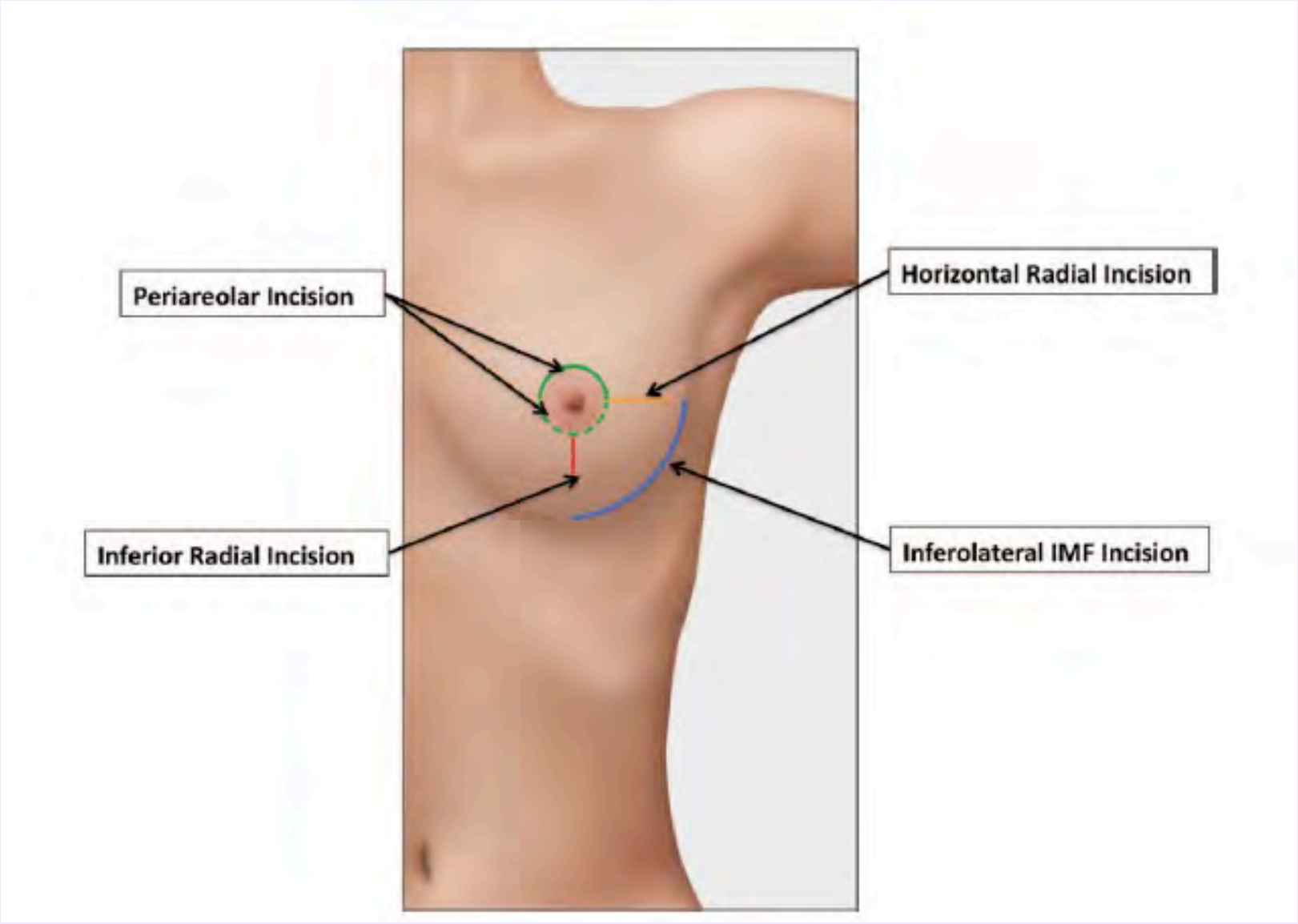

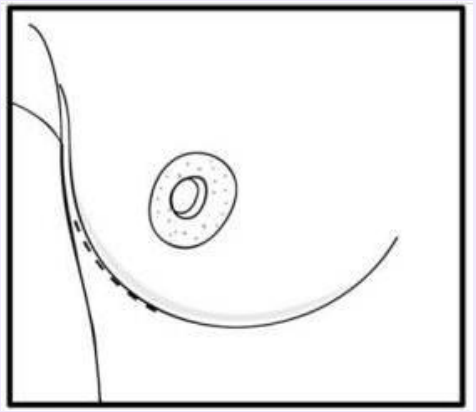

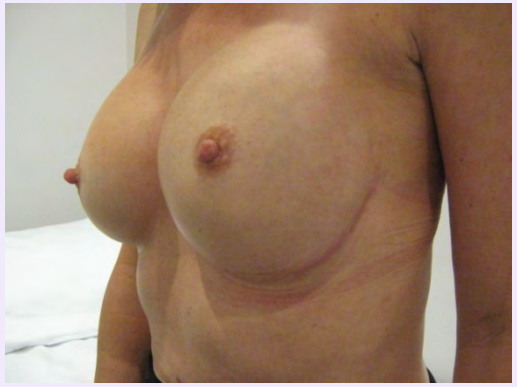

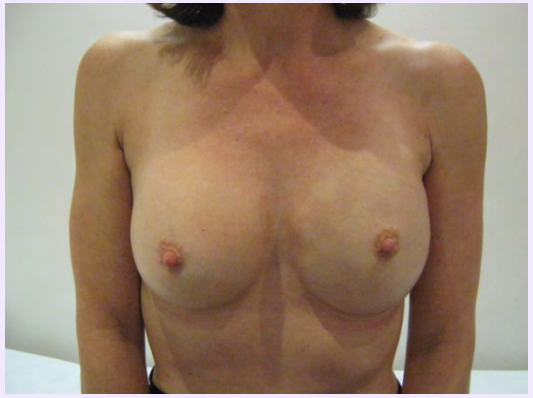

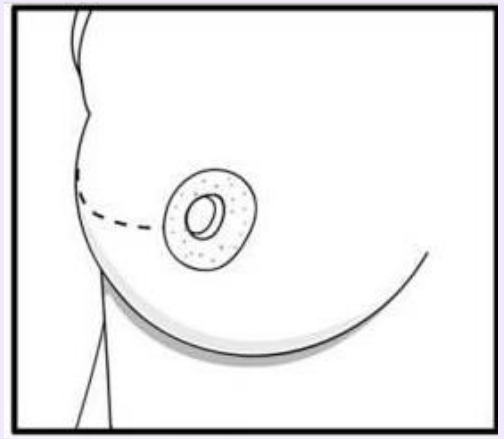

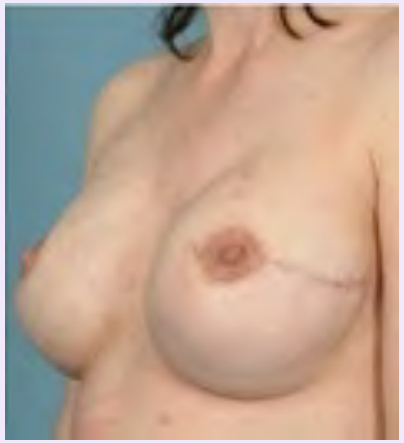

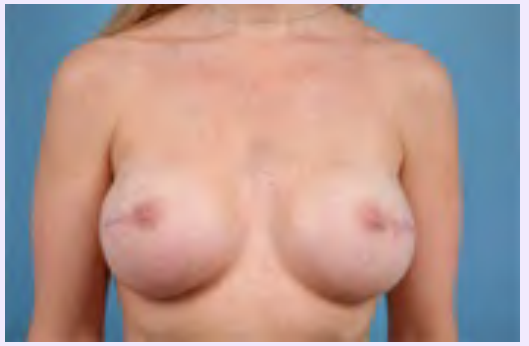

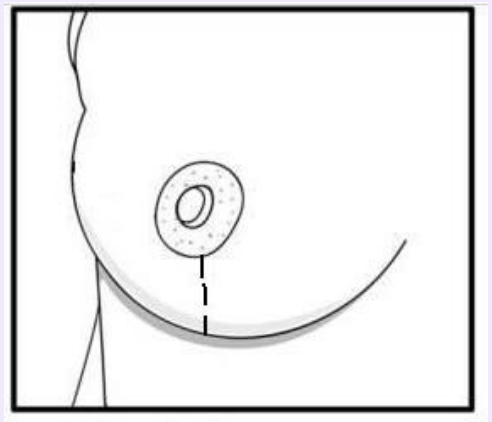

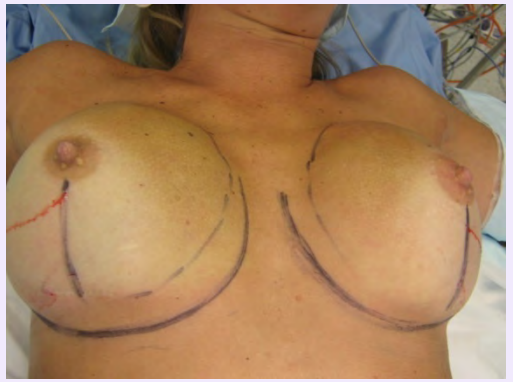

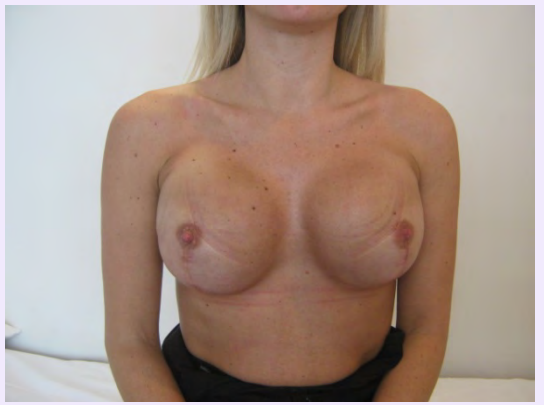

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Breast Reconstruction

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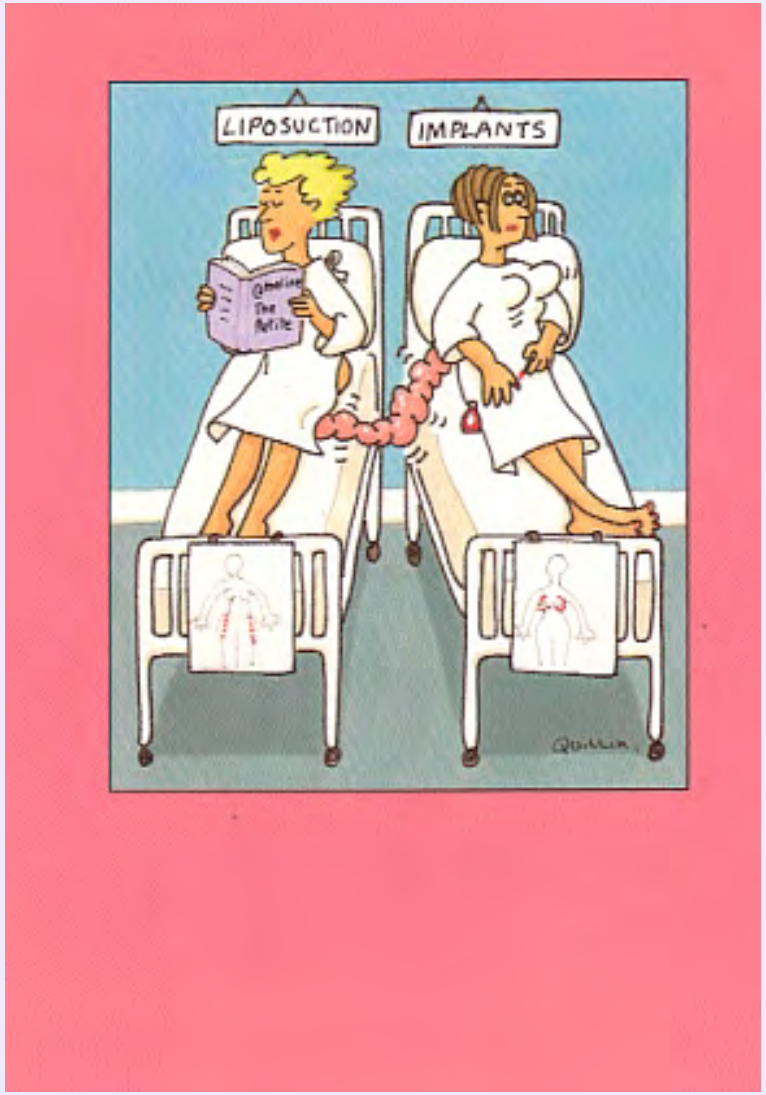

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Implant Based Breast Reconstruction (IBBR)

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- Tissue Expander/ Implant Reconstruction (Two Stage)

- Direct-to-Implant (DTI) (One Stage) Reconstruction with Acellular Dermal Matrix (ADM)

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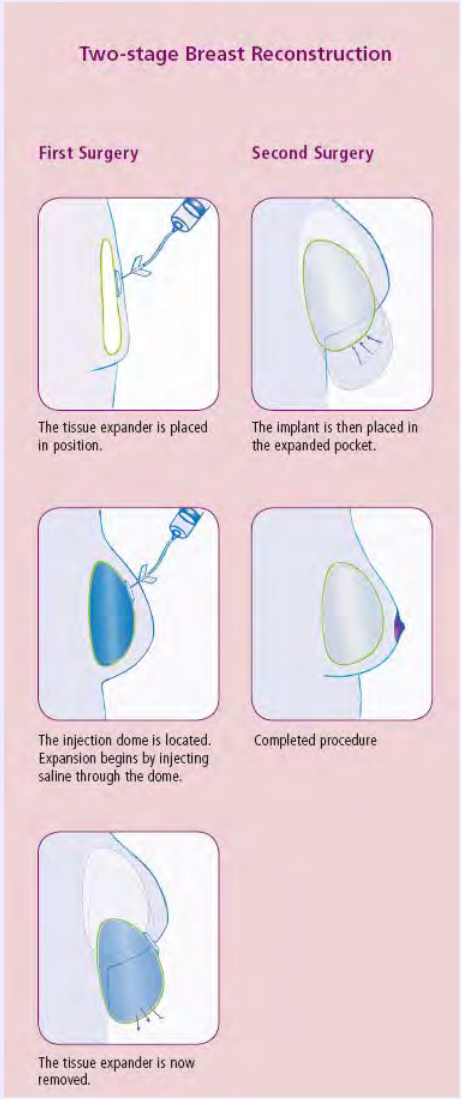
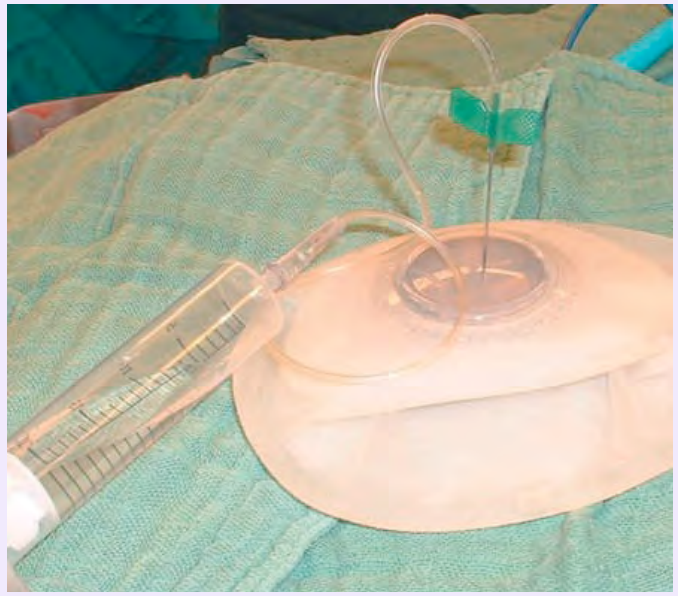
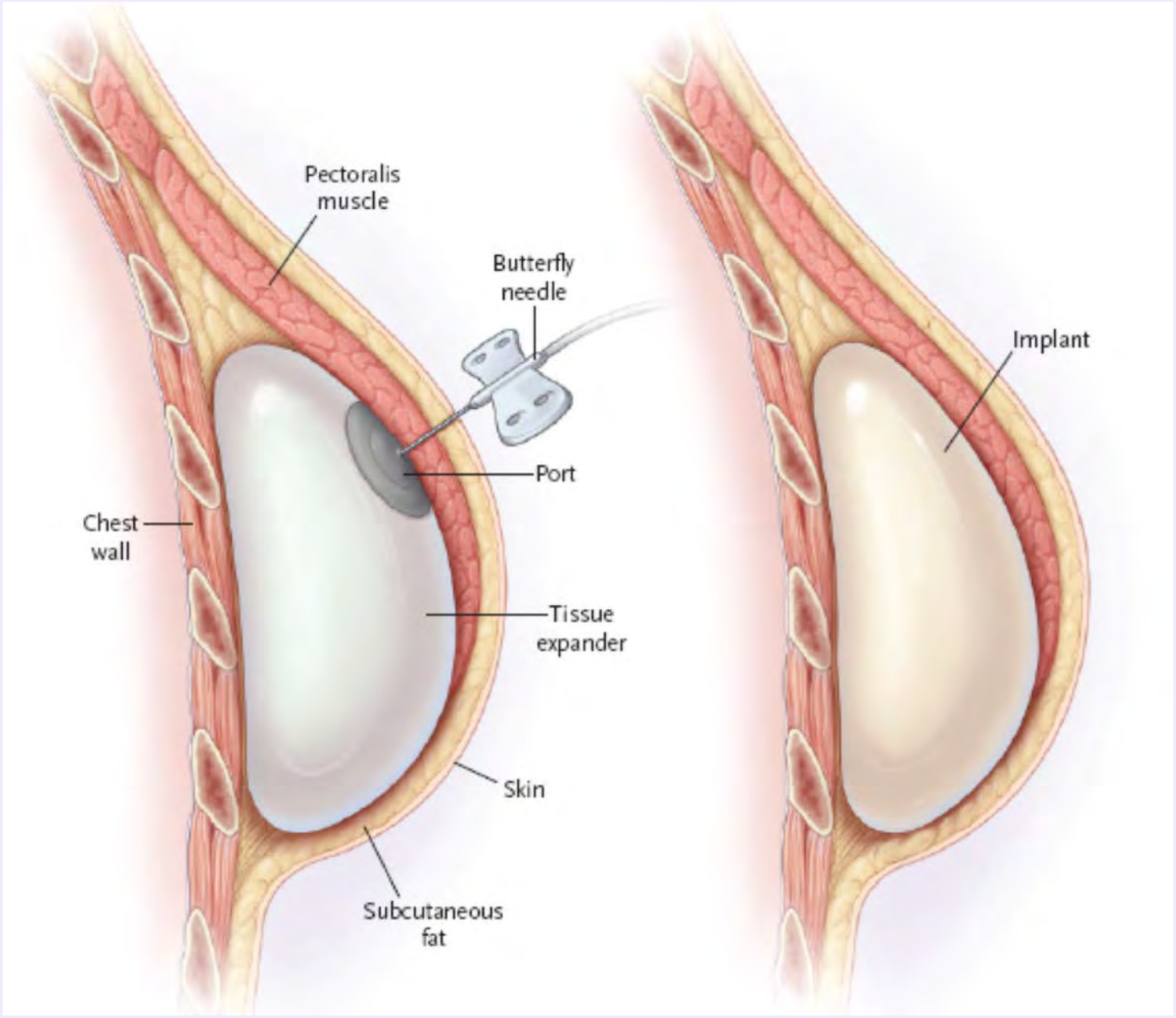
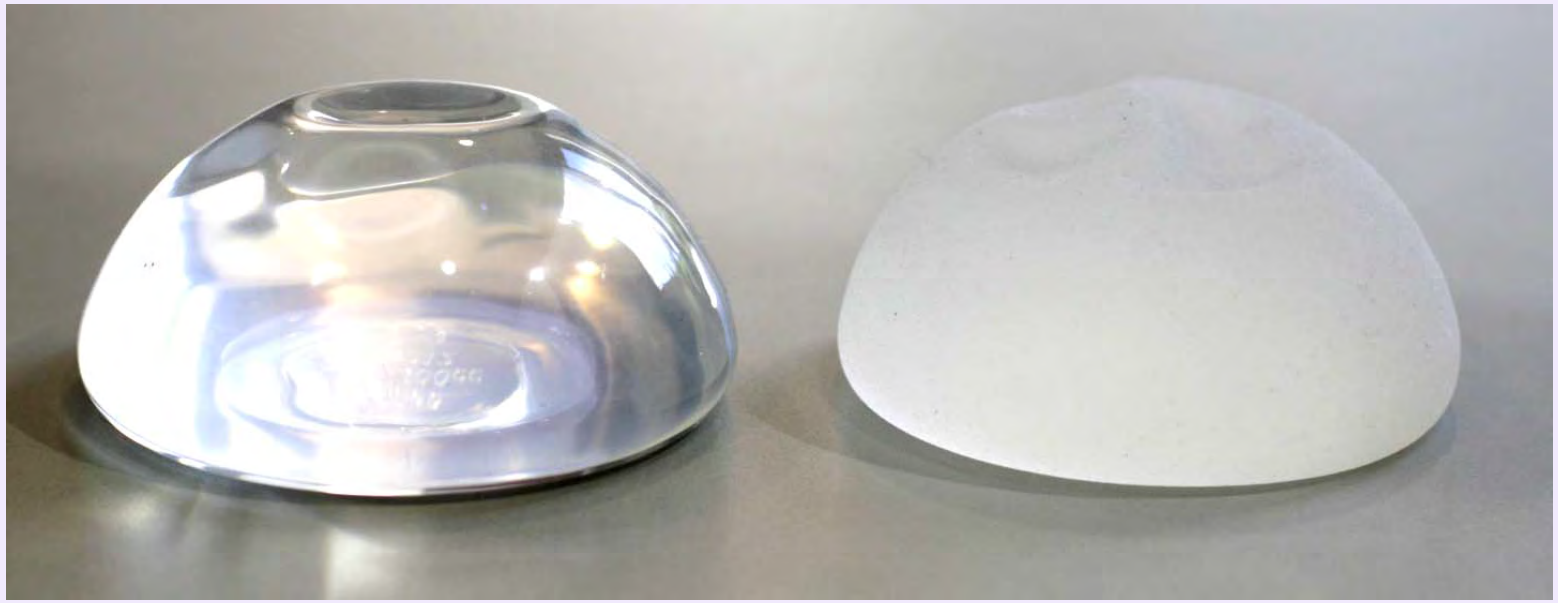
Tissue Expander/ Implant Reconstruction (Two Stage)






Pectoralis muscle
Butterfly needle
Port
Chest wall
Tissue expander
Skin
Subcutaneous fat
Implant



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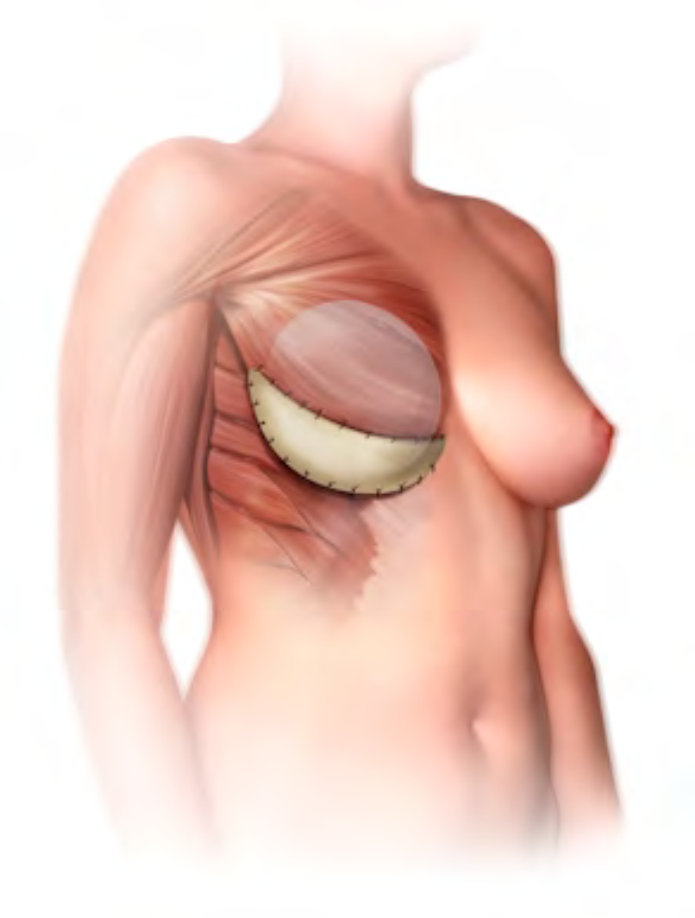
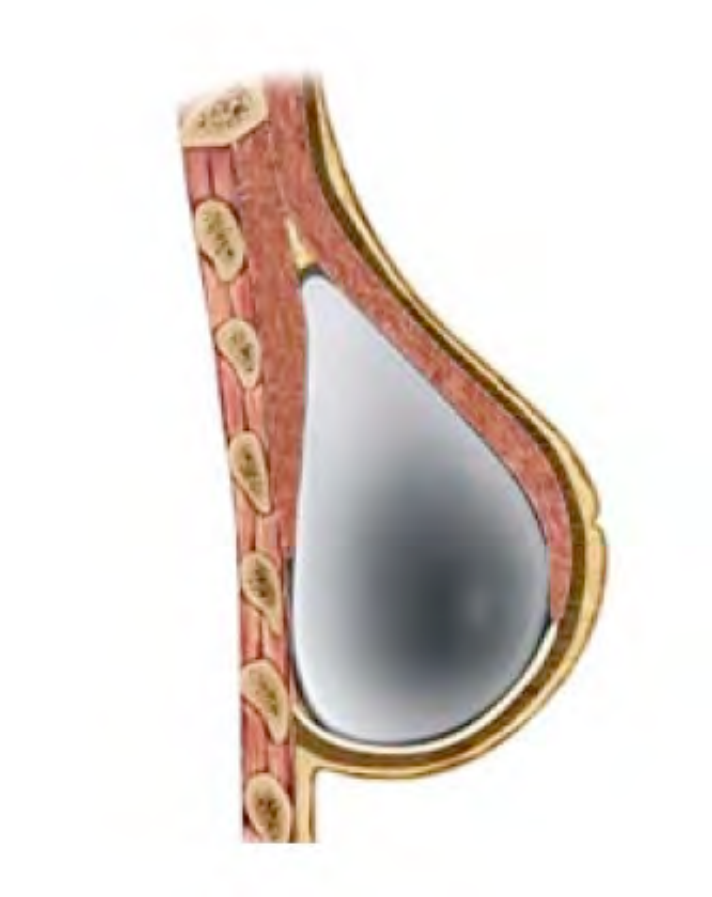
Single Stage Direct-to-Implant (DTI) Reconstruction





Embrace the Change: Incorporating Single-Stage Implant Breast Reconstruction into Your Practice

Jose Rodriguez-Feliz, M.D.
Mark A. Codner, M.D.
Atlanta, Ga.

Background: Multiple studies have reported on the safety of nipple-sparing mastectomy and low complication rates associated with single-stage implant breast reconstruction. Yet many plastic surgeons continue to be resistant to change. This article presents the senior author's (M.A.C.) experience during his transition period from the latissimus dorsi flap with adjustable implants to a "one-and-done" approach using shaped implants and fetal bovine acellular dermal matrix.

Methods: A literature review was performed selecting articles discussing single-stage implant reconstruction, indications, outcomes, technique, and complications. Additional articles were selected after review of the references of identified articles. Clinical pearls discussed include patient selection, implant selection, and mastectomy incision choices, with a detailed description of the senior author's operative technique.

Results: Twenty-seven single-stage implant reconstructions were performed. Average mastectomy weight was 343.82 g. The average implant volume was 367 cc. Shaped implants were most commonly used. Acellular dermal matrix was used in all breasts. Complications included erythema requiring intravenous antibiotics (three patients), skin ischemia caused by methylene blue (one patient), seroma (one patient), unilateral partial nipple necrosis (one patient), mastectomy skin necrosis (one patient), and exposed/infected implants that were salvaged using a sequential irrigation protocol described by Sforza et al. in 2014 (two patients).

Conclusions: Breast reconstruction after mastectomy has evolved toward less invasive, single-stage procedures. Aesthetic refinements include nipple-sparing mastectomy, use of acellular dermal matrix, shaped implants, and fat grafting. Selected patients will benefit from a one-and-done breast implant reconstruction with no additional oncologic risk. Surgeons must embrace the change and provide their patients with a procedure that will offer the best aesthetic outcomes. (*Plast. Reconstr. Surg.* 136: 221, 2015.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

4
THERAPEUTIC

PRSJ, Aug 2015

"Breast in a Day": Examining Single-Stage Immediate, Permanent Implant Reconstruction in Nipple-Sparing Mastectomy

Mihye Choi, M.D.
Jordan D. Frey, M.D.
Michael Alperovich, M.D.
Jamie P. Levine, M.D.
Nolan S. Karp, M.D.

New York, N.Y.

Background: Nipple-sparing mastectomy with immediate, permanent implant reconstruction offers patients a prosthetic "breast in a day" compared to tissue expander techniques requiring multiple procedures.
Methods: Patients undergoing nipple-sparing mastectomy with immediate, permanent implant reconstruction were reviewed with patient demographics and outcomes analyzed.
Results: Of 842 nipple-sparing mastectomies from 2006 to June of 2015, 160 (19.0 percent) underwent immediate, permanent implant reconstruction. The average age and body mass index were 46.5 years and 23.3 kg/m^2. The majority of implants were either Allergan Style 20 (48.1 percent) or Style 15 (22.5 percent). The average implant size was 376.2 ml, and 91.3 percent of reconstructions used acellular dermal matrix. The average number of reconstructive operations was 1.3. Follow-up was 21.9 months. The most common major complication was major mastectomy flap necrosis (8.1 percent). The rate of reconstructive failure was 5.6 percent and implant loss was 4.4 percent. The most common minor complication was minor mastectomy flap necrosis (14.4 percent). The rates of full-thickness and partial-thickness nipple necrosis were 4.4 and 7.5 percent, respectively. Age older than 50 years ($p = 0.0276$) and implant size greater than 400 ml ($p = 0.0467$) emerged as independent predictors of overall complications. Obesity ($p = 0.4073$), tobacco use ($p = 0.2749$), prior radiation therapy ($p = 0.4613$), and acellular dermal matrix ($p = 0.5305$) were not associated with greater complication rates.
Conclusion: Immediate, permanent implant reconstruction in nipple-sparing mastectomy provides patients with a breast in a day in less than two procedures, with a low complication rate. (*Plast. Reconstr. Surg.* 138: 184e, 2016.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

PRSJ, Aug 2016

31% reoperation rate

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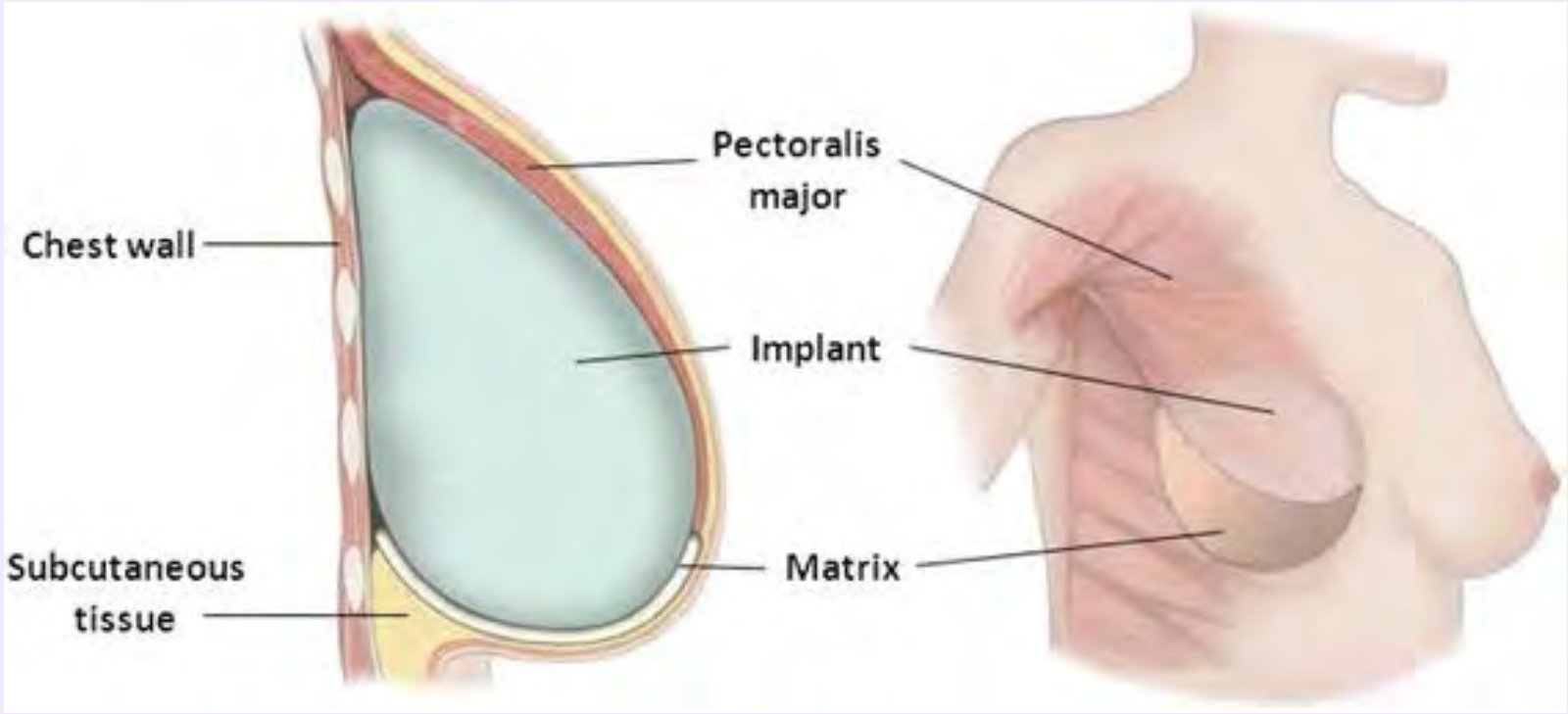

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Acellular Dermal Matrices (ADM)

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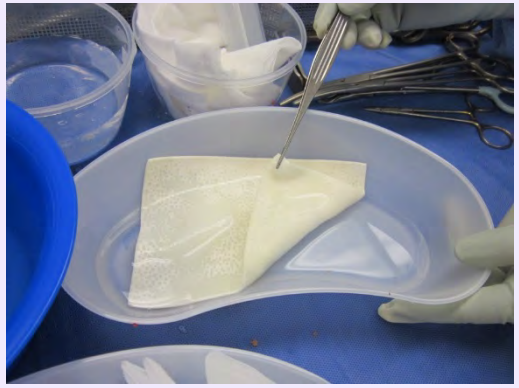

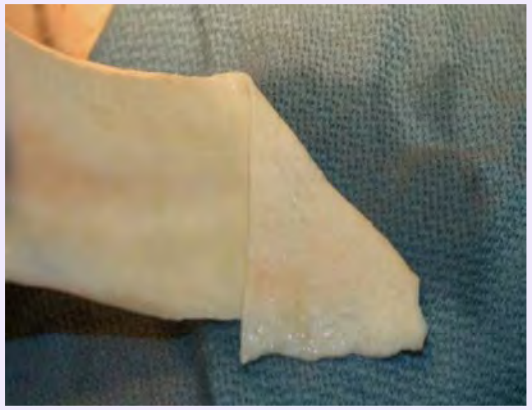

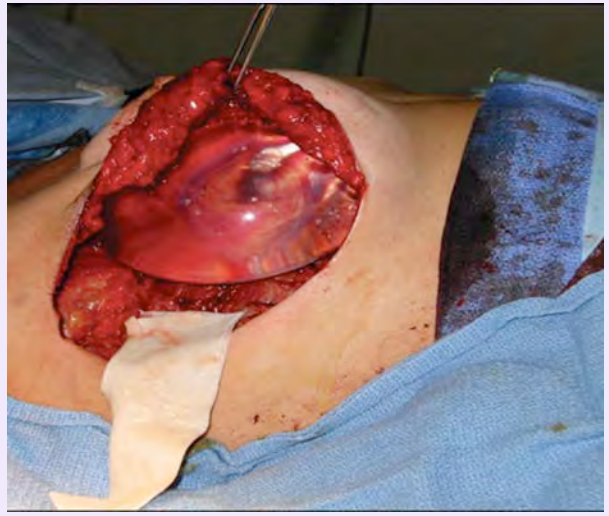

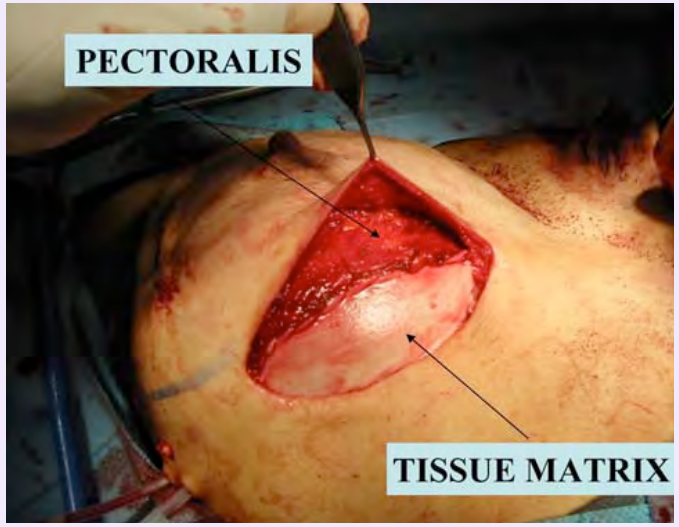

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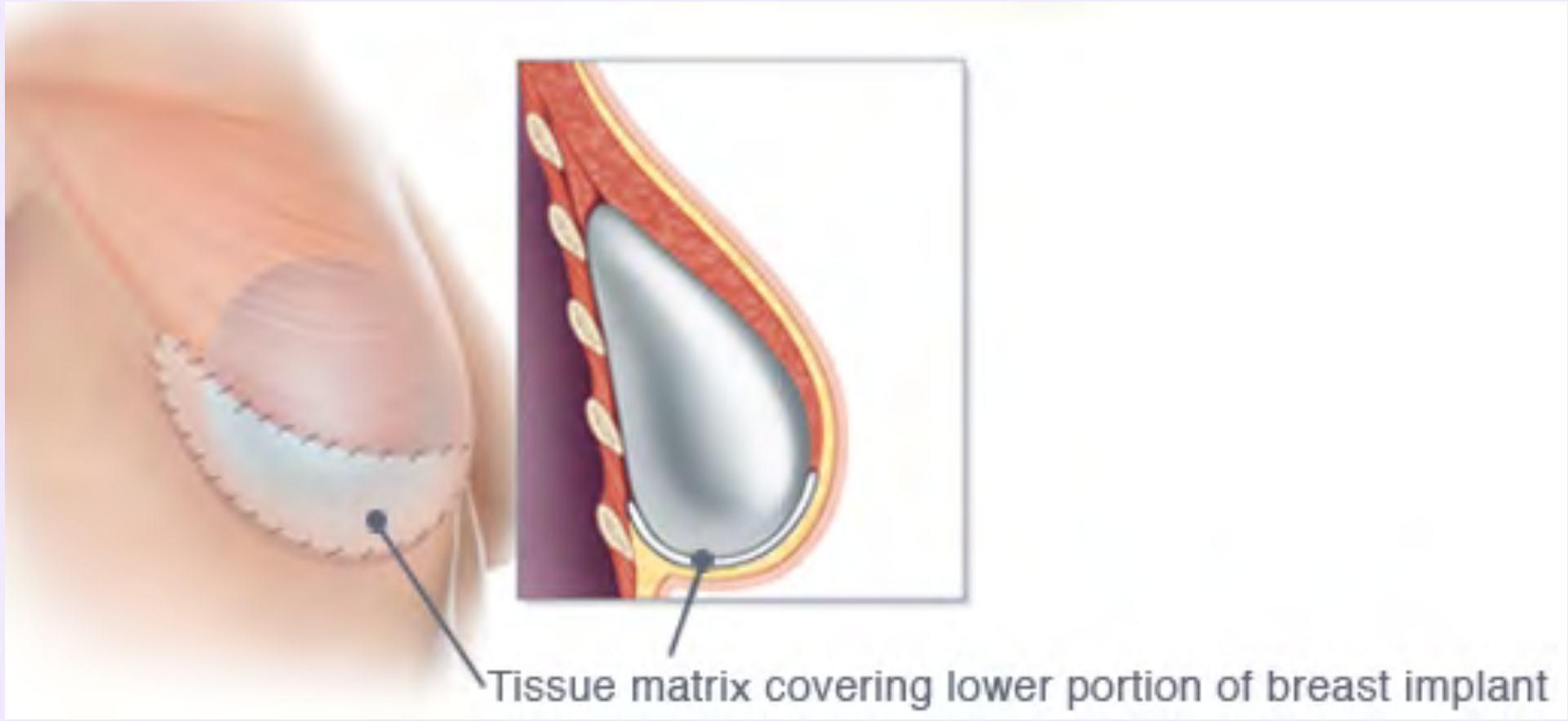
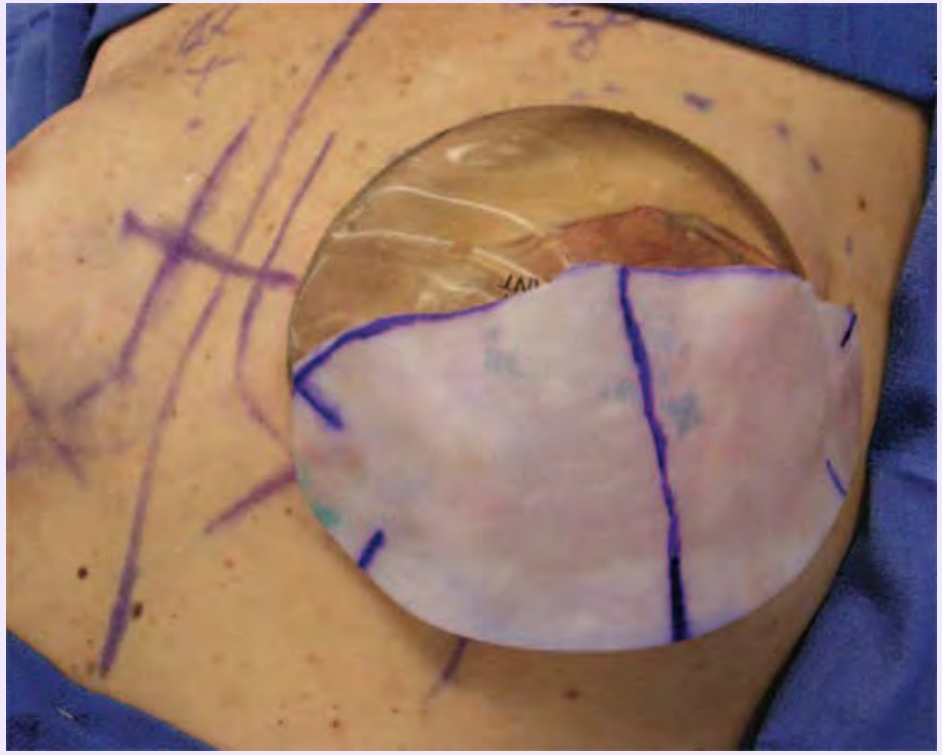
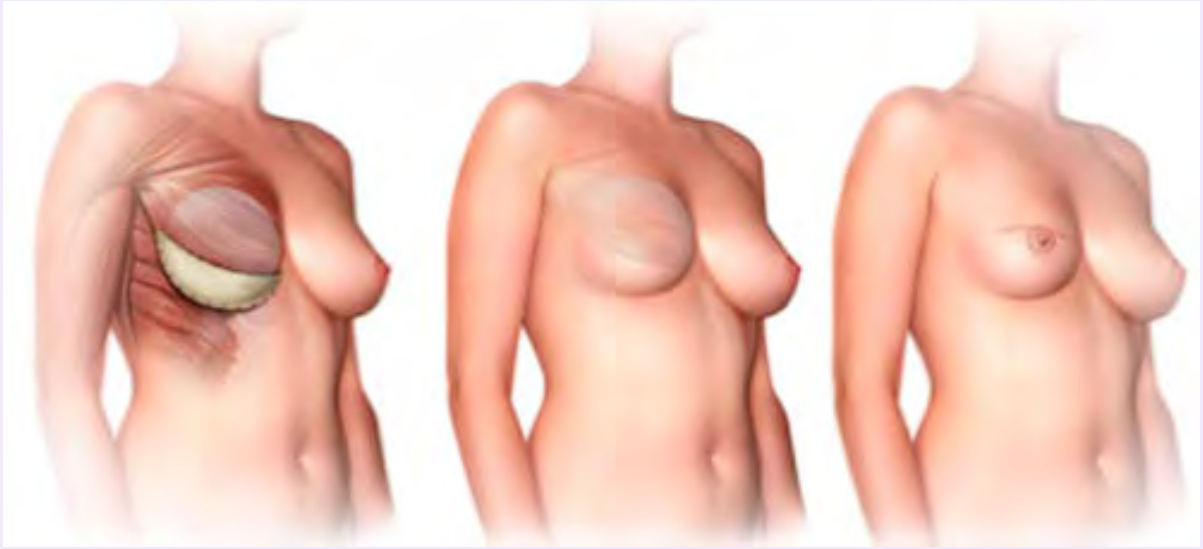

Tissue matrix covering lower portion of breast implant





Ideal Candidate for DTI Reconstruction:

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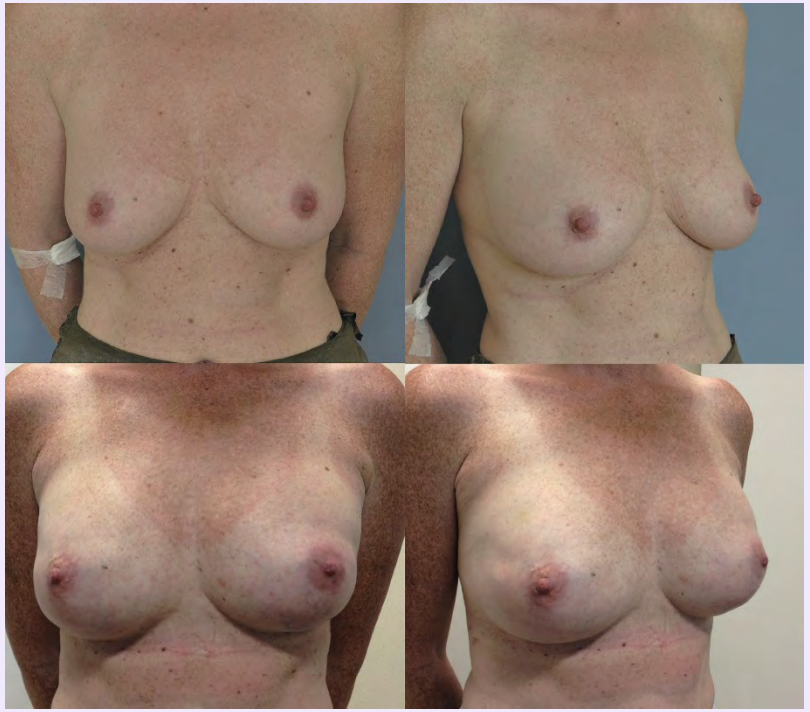
- Healthy, non-smoker
- Small to moderate sized breast
- Undergoing NSM
- Desires to be a similar breast size



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Autologous Tissue Based Reconstruction

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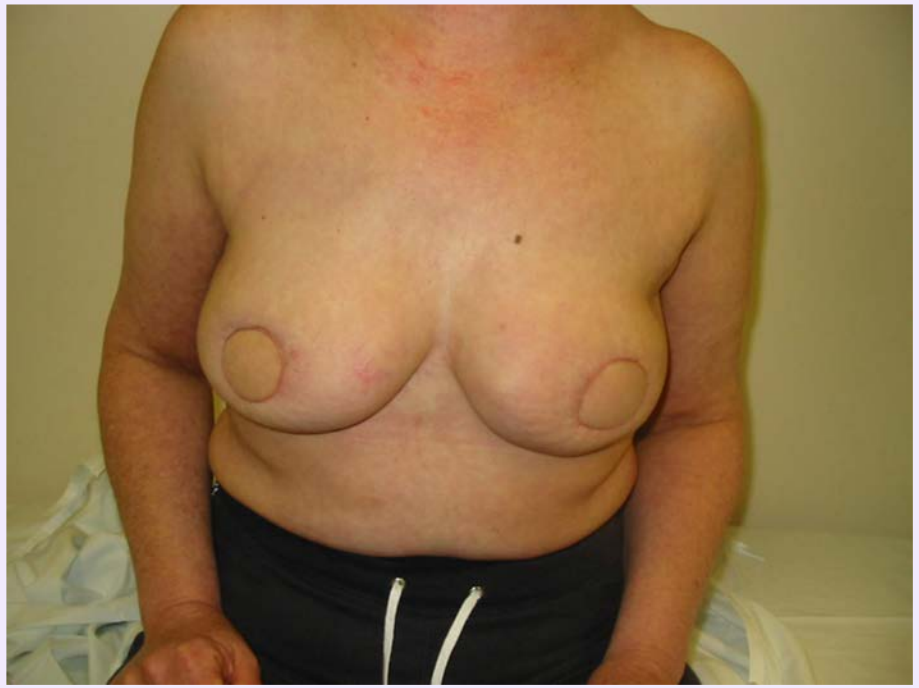

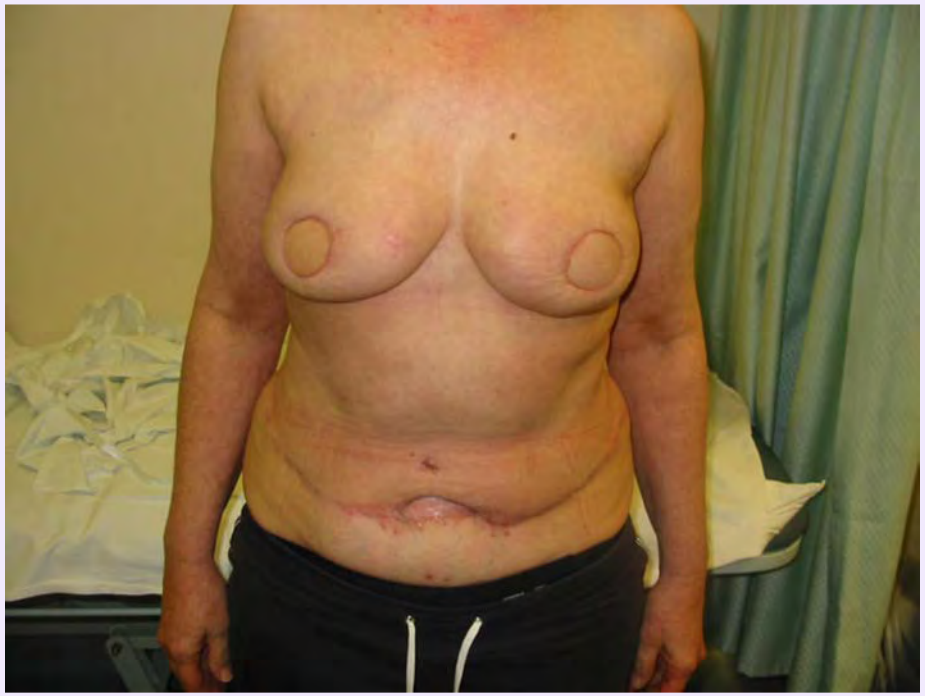

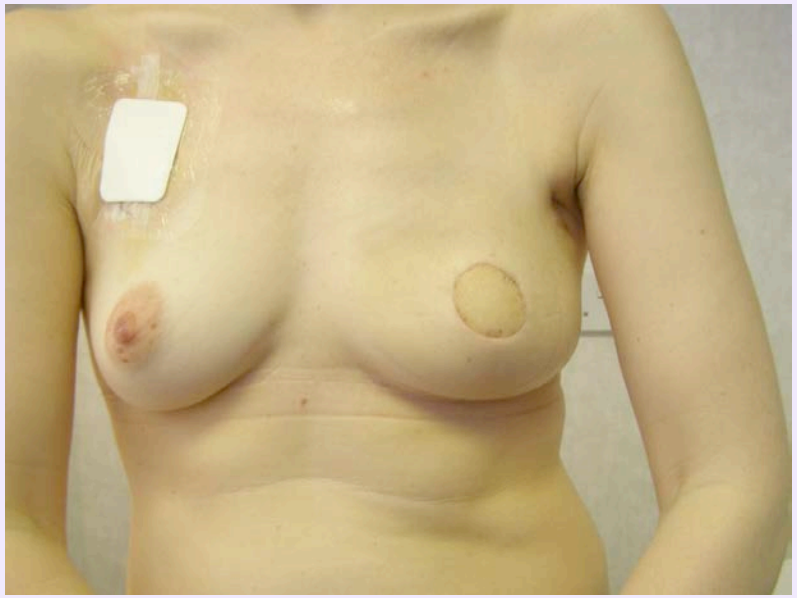

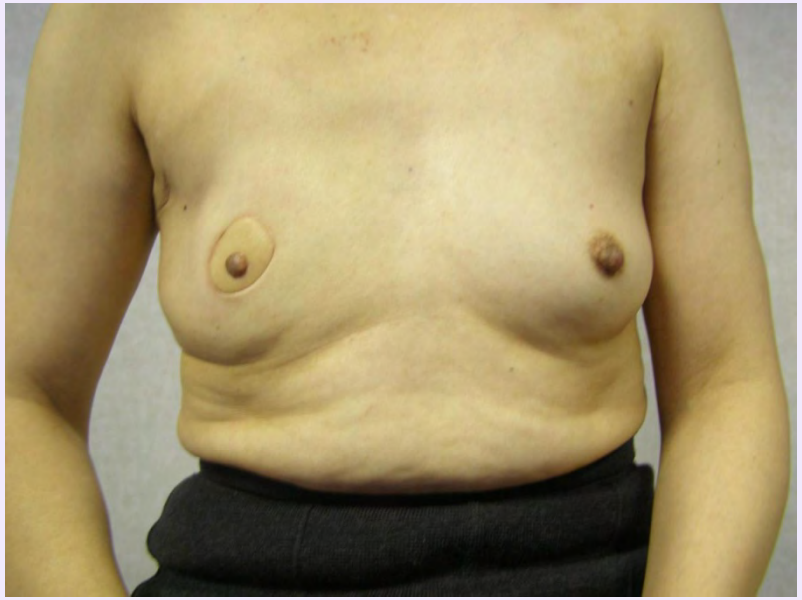

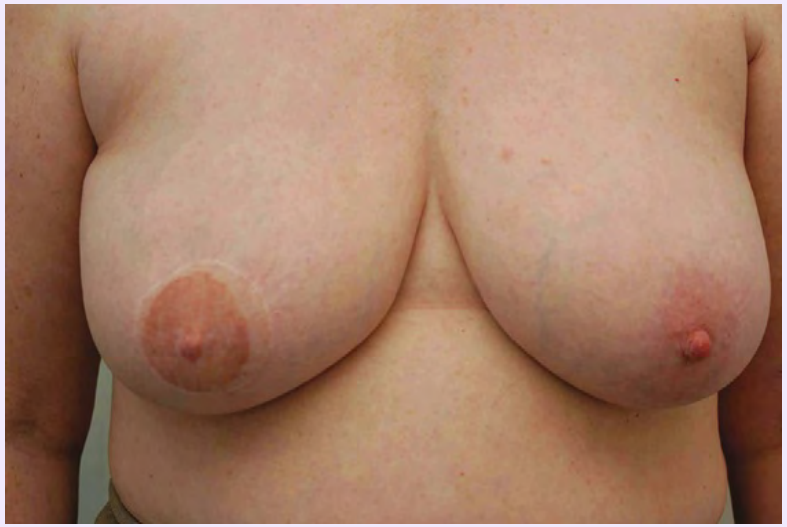

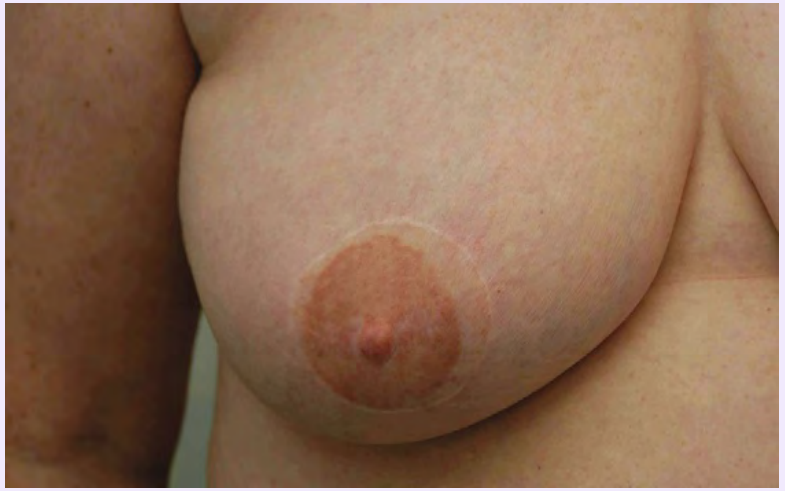

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ST VINCENT'S PRIVATE HOSPITAL EAST MELBOURNE

How Did NSM Regain Acceptance?

The New England
Journal of Medicine

VOLUME 340 JANUARY 14, 1999 NUMBER 2

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

LYNN C. HARTMANN, M.D., DANIEL J. SCHAID, PH.D., JOHN E. WOODS, M.D., THOMAS P. CROTTY, M.D., JEFFREY L. MYERS, M.D., P.G. ARNOLD, M.D., PAUL M. PETTY, M.D., THOMAS A. SELLERS, PH.D., JOANNE L. JOHNSON, R.N., SHANNON K. MCDONNELL, M.S., MARLENE H. FROST, PH.D., R.N., AND ROBERT B. JENKINS, M.D., PH.D.

Hartmann, L.C. et al, Efficacy of Bilateral Prophylactic Mastectomy in Women with a Family History of Breast Cancer. *N Engl J Med*, 340: 77-84, 1999

Time to reconsider subcutaneous mastectomy for breast-cancer prevention?

Kelly A Metcalfe, John L Semple, Steven A Narod

Lancet Oncol 2005; 6: 431–34

Faculty of Nursing, University of Toronto, Ontario, Canada (K A Metcalfe PHD); Division of Plastic Surgery, Department of Surgery, Sunnybrook and Women's College Hospital, Toronto, Ontario, Canada (K A Metcalfe PHD, J L Semple MD); and Centre for Research in Women's Health, Toronto, Ontario, Canada (Prof S A Narod MD)

Correspondence to: Prof Steven Narod, Centre for Research in Women's Health, 790 Bay Street, 7th Floor, Toronto, Ontario, M5G 1N8, Canada

stevennarod@ow.ca

Genetic testing for women at increased risk of developing breast cancer has moved from the research setting to become part of established clinical practice. By testing for inherited mutations in *BRCA1* and *BRCA2*, we are identifying more and more women who have an 80% or more lifetime risk of developing breast cancer. Since the discovery of *BRCA1* in 1994, several clinical studies have led to strategies for reducing the risk of developing breast cancer, including prophylactic mastectomy, prophylactic oophorectomy, and preventive tamoxifen. We believe that in 2005, all prophylactic options, including subcutaneous and total mastectomy should be discussed and made available to women who find themselves unfortunate enough to have inherited a BRCA mutation.

For women with a *BRCA1* or *BRCA2* mutation, prophylactic mastectomy offers the greatest protection against the development of breast cancer. Initially, the effectiveness of prophylactic mastectomy (figure) was unknown and it was regarded as an extreme technique. The procedure has been described as a desperate measure[1] and a drastic option,[2] and many investigators did not recommend the procedure because its benefit was not proven. However, many women felt that they had seen enough cancer in their families and had the operation anyway—these women were later enrolled onto several research studies (table) that showed the effectiveness of prophylactic mastectomy in prevention of breast cancer.[3–5,10]

In the first study, Hartmann and colleagues[3] at the Mayo clinic location reported on cancer risk in a large cohort of women with a family history of breast cancer who had undergone bilateral prophylactic mastectomy. The researchers estimated that the risk of breast cancer was reduced by more than 90% with bilateral prophylactic mastectomy. In a subsequent study[9] on a subcohort of these women the investigators identified 26 women who had a *BRCA1* or *BRCA2* mutation. In this small sample of women, prophylactic mastectomy was associated with a risk reduction of between 89·5% and 100%. Researchers[10] in the Netherlands followed up 139 women with *BRCA1* and *BRCA2* mutations; after about 3 years of follow-up, no woman who had had a prophylactic mastectomy had developed breast cancer, compared with eight women who underwent regular breast surveillance (p=0·003). Although follow-up was short, updated data supports the preliminary result.[10] Finally, in a historical cohort study[5] of 483 women who were carriers of *BRCA1* and *BRCA2* mutations (105 patients who underwent bilateral prophylactic mastectomy were matched with 378 control who had intact breasts), prophylactic mastectomy was associated with a reduction in risk of breast cancer of about 95%.

Acceptance of prophylactic surgery

Many factors determine the rates of prophylactic surgery, including social and cultural context, physician willingness, and the patient and doctor's belief in the effectiveness of the procedure (and of alternate preventive measures). Rates of prophylactic mastectomy in mutation carriers differ widely by country. The highest reported frequency is in the Netherlands, where 54% of eligible women have had a prophylactic mastectomy.[10] Two US studies surveyed women who had received genetic test results and reported much fewer prophylactic mastectomies than in the Netherlands. In an early study, Lerman and co-workers[11] reported that only 3% of carriers underwent prophylactic mastectomy within 1 year, and Botkin and colleagues[12] reported that no women had prophylactic mastectomy within 2 years of receiving her result. In Canada, 20% of carriers of the

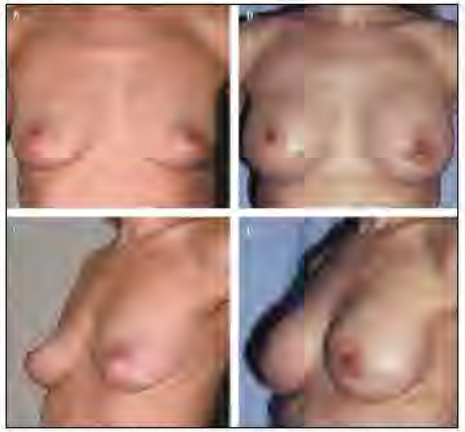


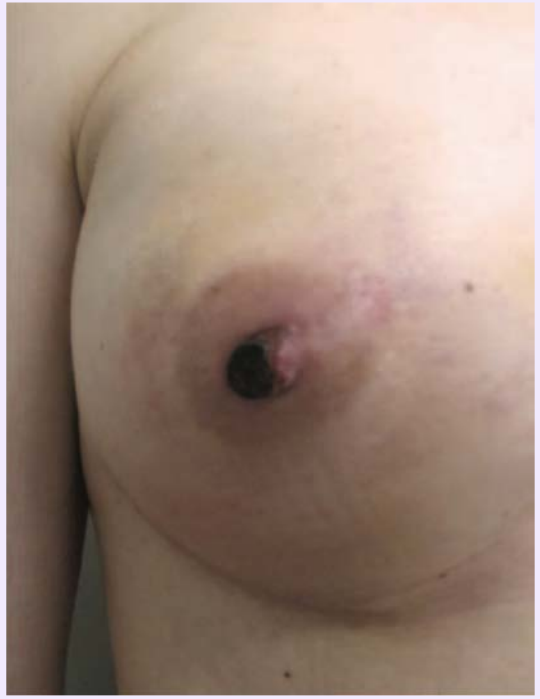
Figure: 45-year-old woman who had prophylactic bilateral subcutaneous mastectomy and immediate reconstruction with tissue expanders placed under the pectoralis muscle
(A, C) Preoperative appearance. (B, D) 3 months' follow-up. Tissue expanders have been exchanged for implants. Mastectomy was done through an inframammary incision.

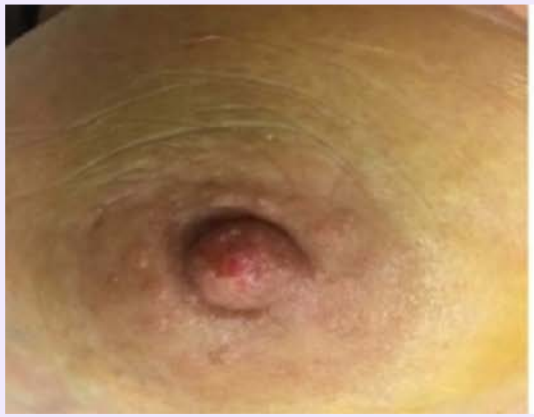
Lancet Oncology 2005

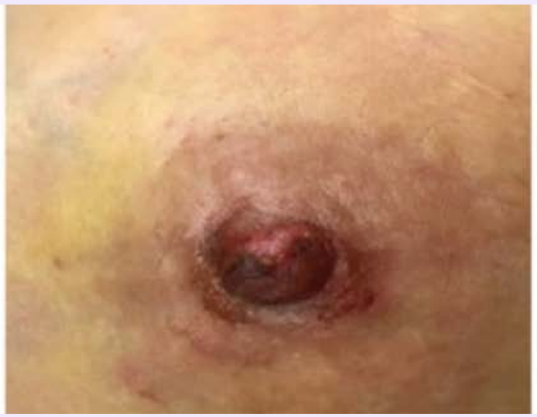
Authors predicted that predict that the number of women requesting the procedure will rise from 20% to 50% if subcutaneous mastectomy were offered

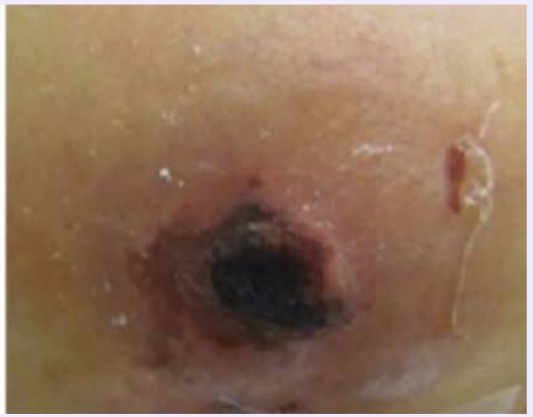
Surgical Complications

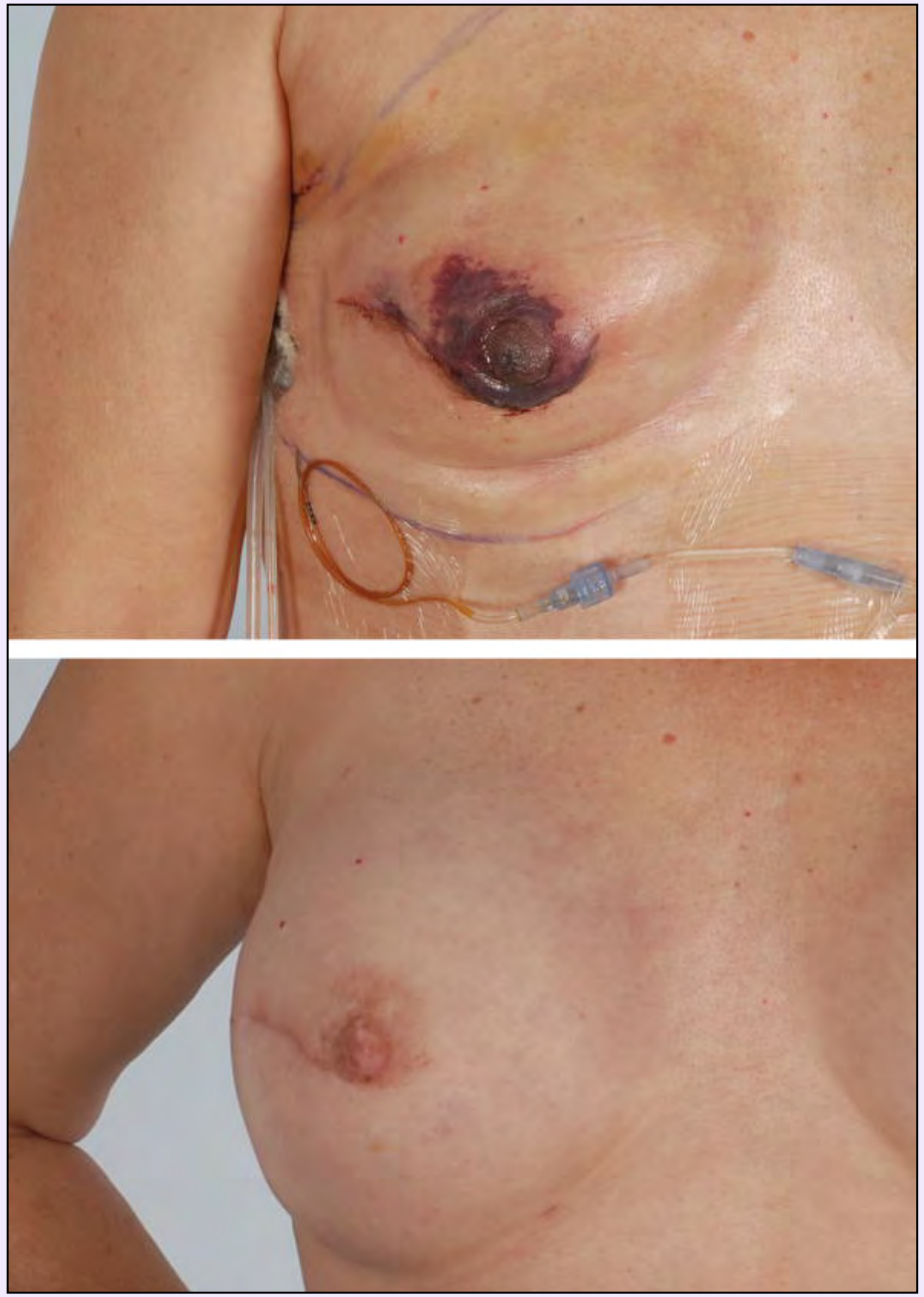
-skin flap /nipple necrosis











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Ann Surg Oncol (2012) 19:3171–3176
DOI 10.1245/s10434-012-2528-7

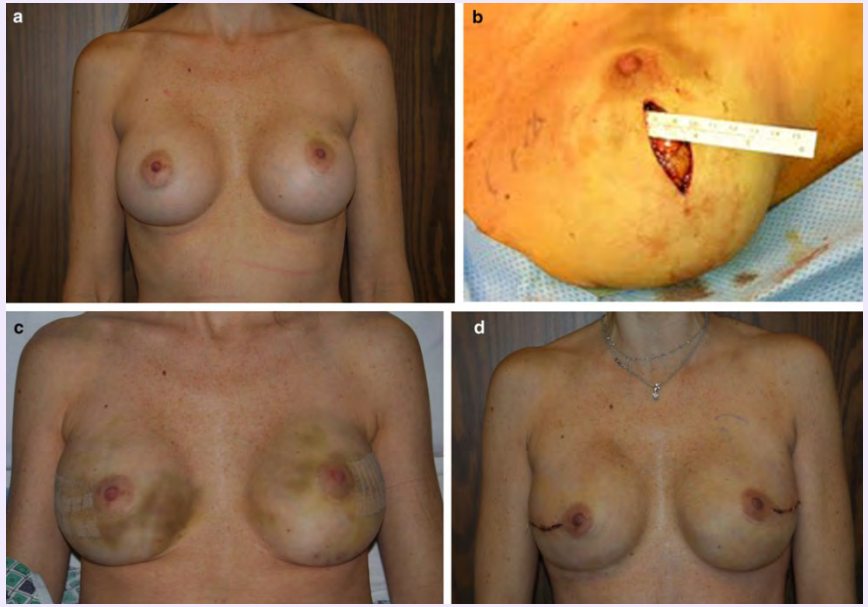
Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – BREAST ONCOLOGY

Surgical Delay of the Nipple–Areolar Complex: A Powerful Technique to Maximize Nipple Viability Following Nipple-Sparing Mastectomy

J. Arthur Jensen, MD[1,2], Jennifer H. Lin, MD[2], Nimmi Kapoor, MD[2,3], and Armando E. Giuliano, MD[2,4]

[1]Division of Plastic Surgery, Geffen School of Medicine at U.C.L.A., Los Angeles, CA; [2]Division of Surgical Oncology, John Wayne Cancer Institute at Saint John's Health Center, Santa Monica, CA; [3]Division of Surgery, Cedars Sinai Medical Center, Los Angeles, CA; [4]Division of Surgical Oncology, Cedars-Sinai Medical Center, Los Angeles, CA



Ann Surg Onc 2012

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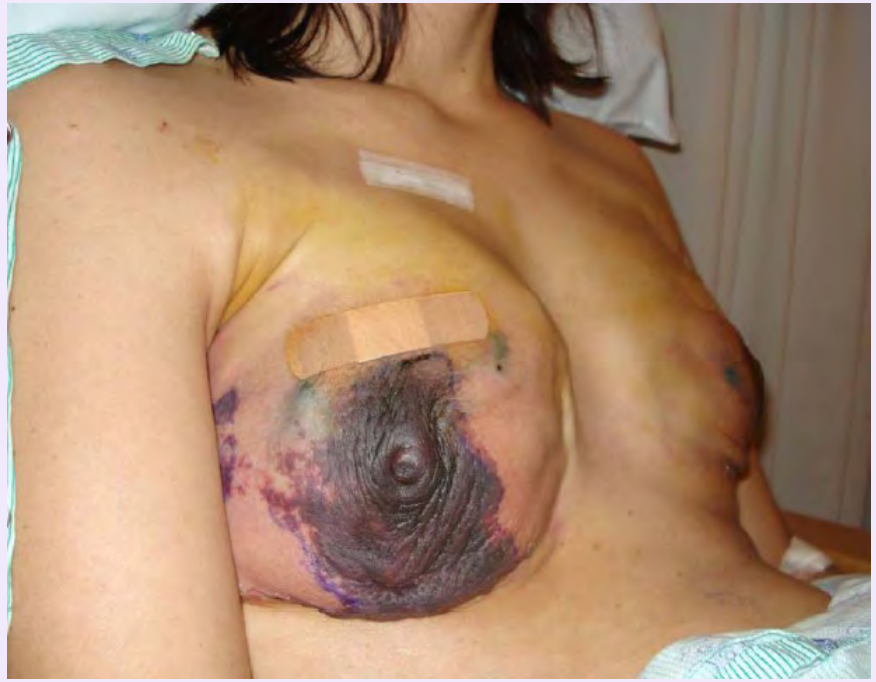
Skin Flap/ Nipple/Areolar Necrosis

- Larger breasts
- Volume of implant
- Smoking
- Obesity
- Incision type
- Age



Risk Analysis and Stratification of Surgical Morbidity after Immediate Breast Reconstruction

John P Fischer, MD, Ari M Wes, BA, Charles T Tuggle, MD, Joseph M Serletti, MD, FACS, Liza C Wu, MD, FACS

BACKGROUND: Surgical complications after breast reconstruction can be associated with significant morbidity, dissatisfaction, and cost. We used the ACS-NSQIP datasets from 2005 to 2011 to derive predictors of morbidity and to stratify risk after immediate breast reconstruction (IBR).

STUDY DESIGN: Surgical complications after implant and autologous reconstruction were assessed using the ACS-NSQIP 2005 to 2011 datasets. Patient demographics, clinical characteristics, and operative factors were associated with the likelihood of experiencing a surgical complication. A "model cohort" of 12,129 patients was randomly selected from the study cohort to derive predictors. Weighted odds ratios derived from logistic regression analysis were used to create a composite risk score and to stratify patients. The remaining one-third of the cohort (n = 6,065) were used as the "validation cohort" to assess the accuracy value of the risk model.

RESULTS: On adjusted analysis, autologous reconstruction (odds ratio [OR] 1.41, $p < 0.001$), American Society of Anesthesiologists physical status ≥ 3 (OR 1.25, $p = 0.004$), class I obesity (OR 1.38, $p < 0.001$), class II obesity (OR 1.91, $p < 0.001$), class III obesity (OR 1.70, $p < 0.001$), and active smoking (OR 1.46, $p < 0.001$) were associated with complications. Risk factors were weighted and patients were stratified into low (0 to 2, n = 9,133, risk = 7.14%), intermediate (3 to 4, n = 1,935, risk = 10.90%), high (5 to 7, n = 1,024, risk = 16.70%), and very high (8 to 9, n = 37, risk = 27.02%) risk categories based on their total risk score ($p < 0.001$). Internal validation of the "model cohort" using the "validation cohort" was performed demonstrating accurate prediction of risk across groups: low (7.1% vs 7.1%, respectively, $p = 0.9$), intermediate (10.9% vs 12.0%, respectively, $p = 0.38$), high (16.7% vs 16.8%, respectively, $p = 0.95$), and very high (27.0% vs 30.0%, respectively, $p = 1.0$).

CONCLUSIONS: Surgical complications after IBR are related to preoperatively identifiable factors that can be used to accurately risk stratify patients, which may assist with counseling, selection, and perioperative decision-making. (J Am Coll Surg 2013;217:780–787.

J Am Coll Surg 2013

- Obesity
- Smoking

EJSO 2002; **28**: 815–820
doi:10.1053/ejso.2002.1308, available online at http://www.idealibrary.com on IDEAL®

EJSO
European Journal of Surgical Oncology

Smoking as a risk factor for wound healing and infection in breast cancer surgery

L. T. Sørensen*, J. Hørby*, E. Friis*, B. Pilsgaard* and T. Jørgensen†

*Department of Surgical Gastroenterology K, Bispebjerg University Hospital, Copenhagen Hospital Corporation, Denmark and †Centre for Preventive Medicine, Glostrup University Hospital, Copenhagen County, Denmark

- Pts with a smoking history have a 6.5 times greater risk of complications following breast surgery
- Wound infection increased by 3.46 in heavy smokers and 2.95 in light smokers
- Flap necrosis- 9.22 times in heavy and 6.85 in light smokers

The Larger or Ptotic Breast

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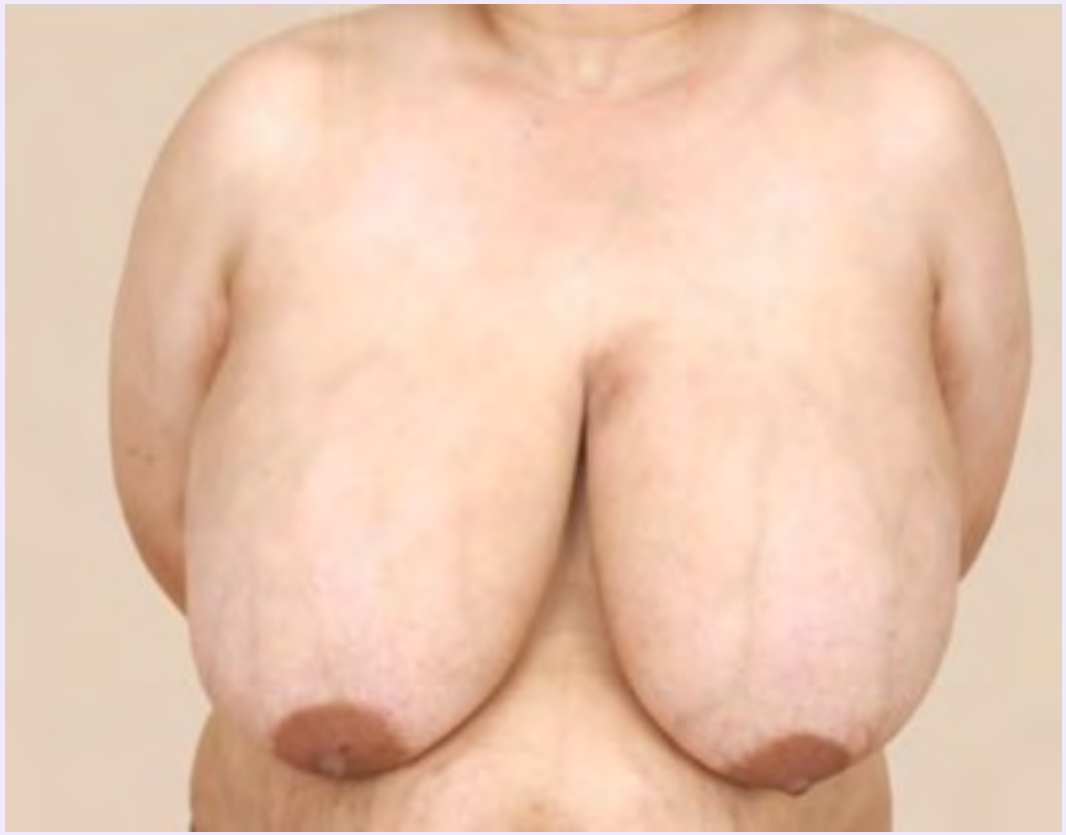
- Skin Reducing Mastectomy
- Staged NSM following mastopexy or reduction



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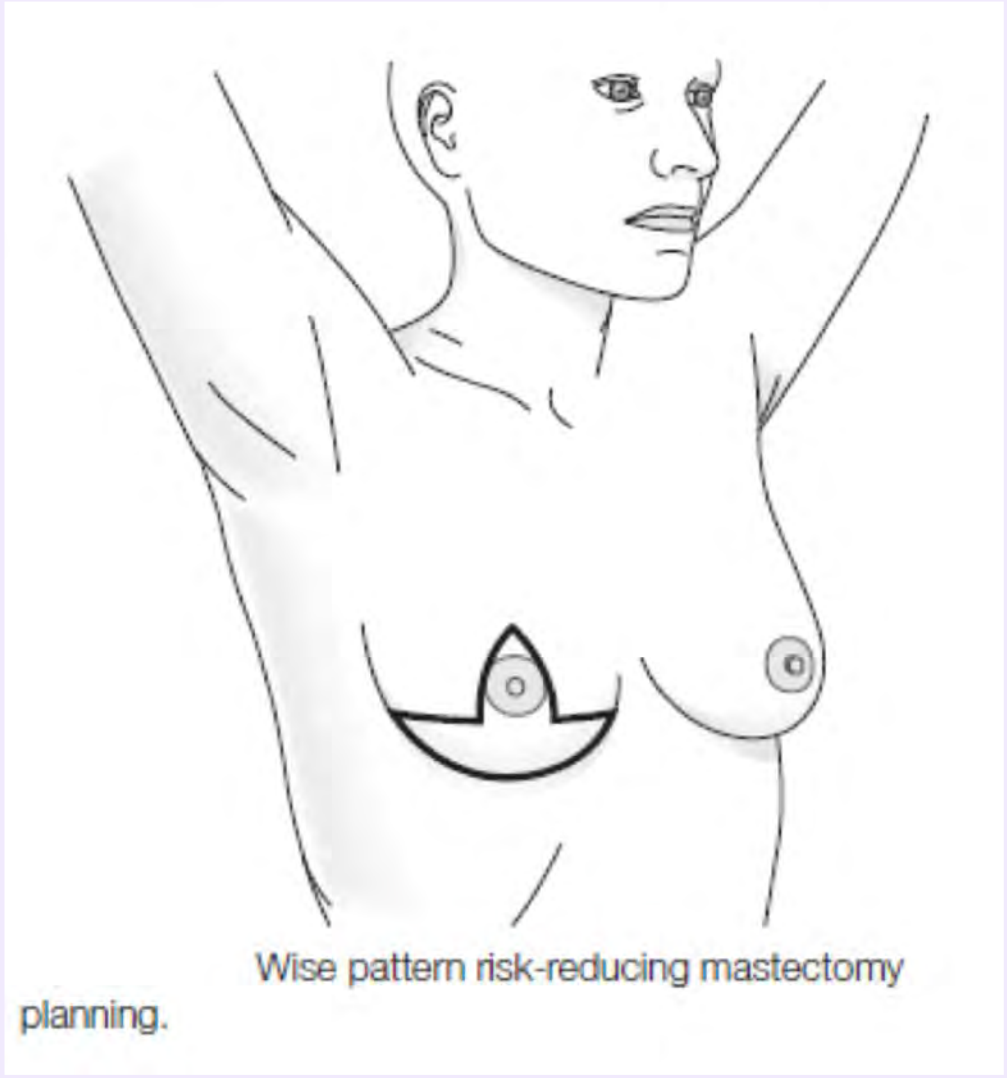
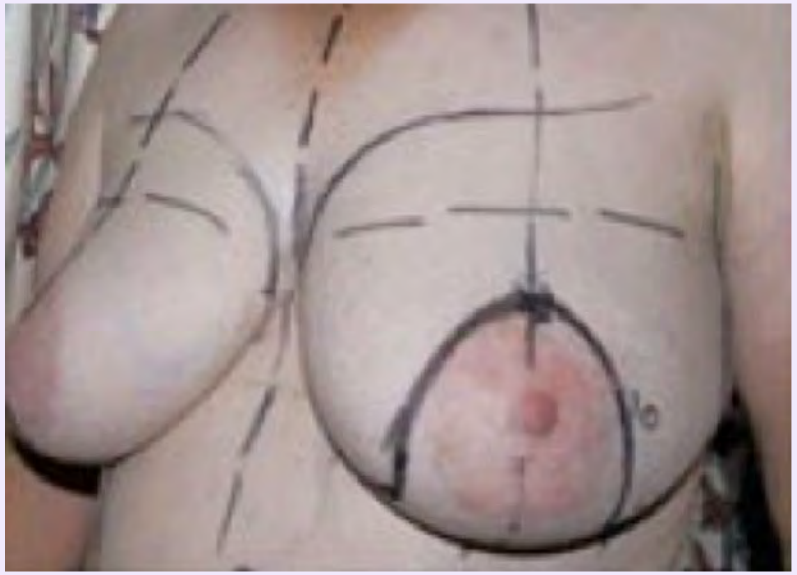
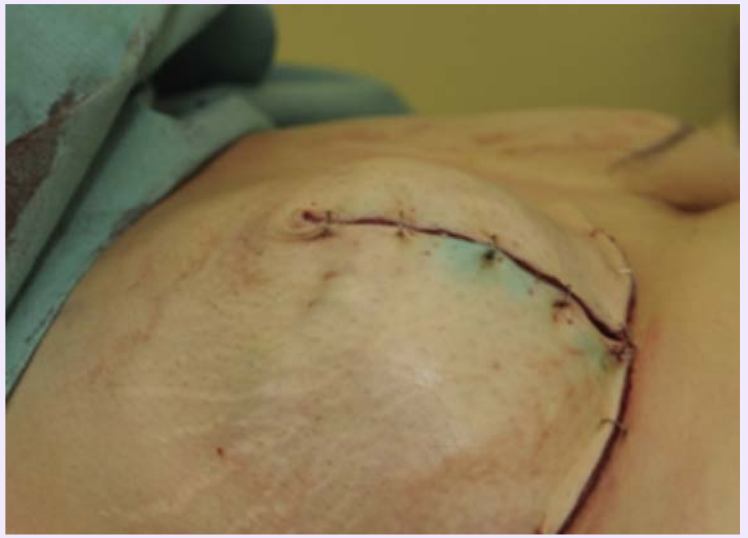
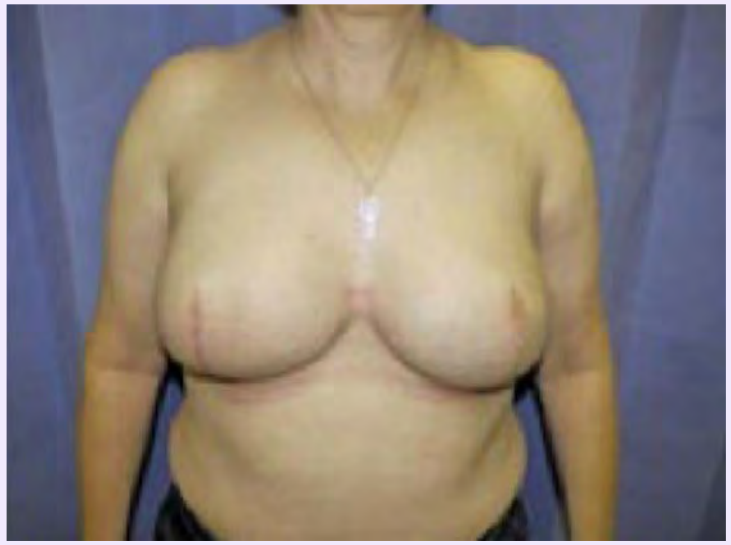
Skin Reducing Mastectomy
"Wise Pattern"

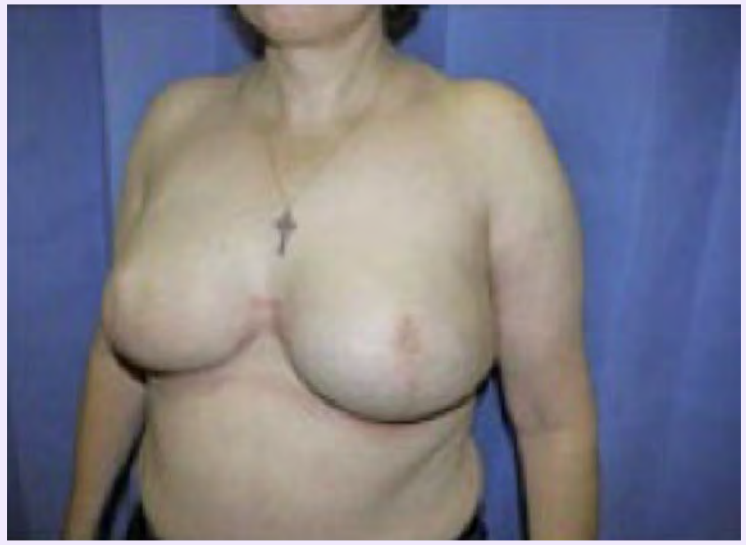


Wise pattern risk-reducing mastectomy planning.









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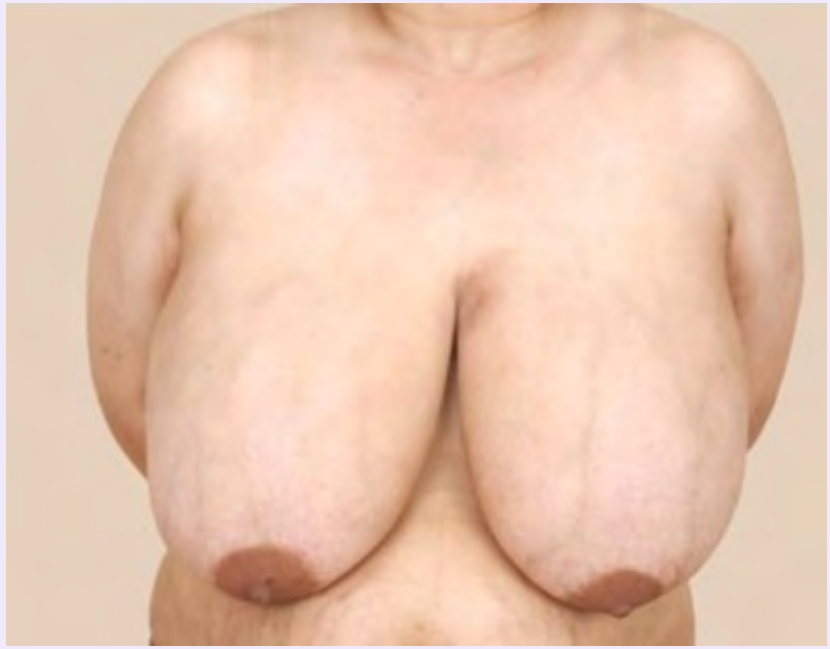

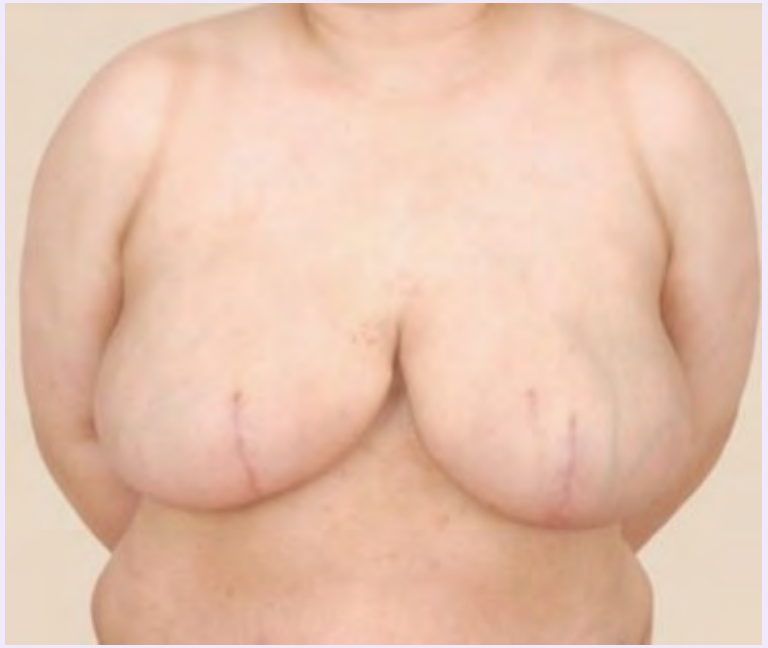

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Skin Reducing Mastectomy
"Hemibatwing Pattern"

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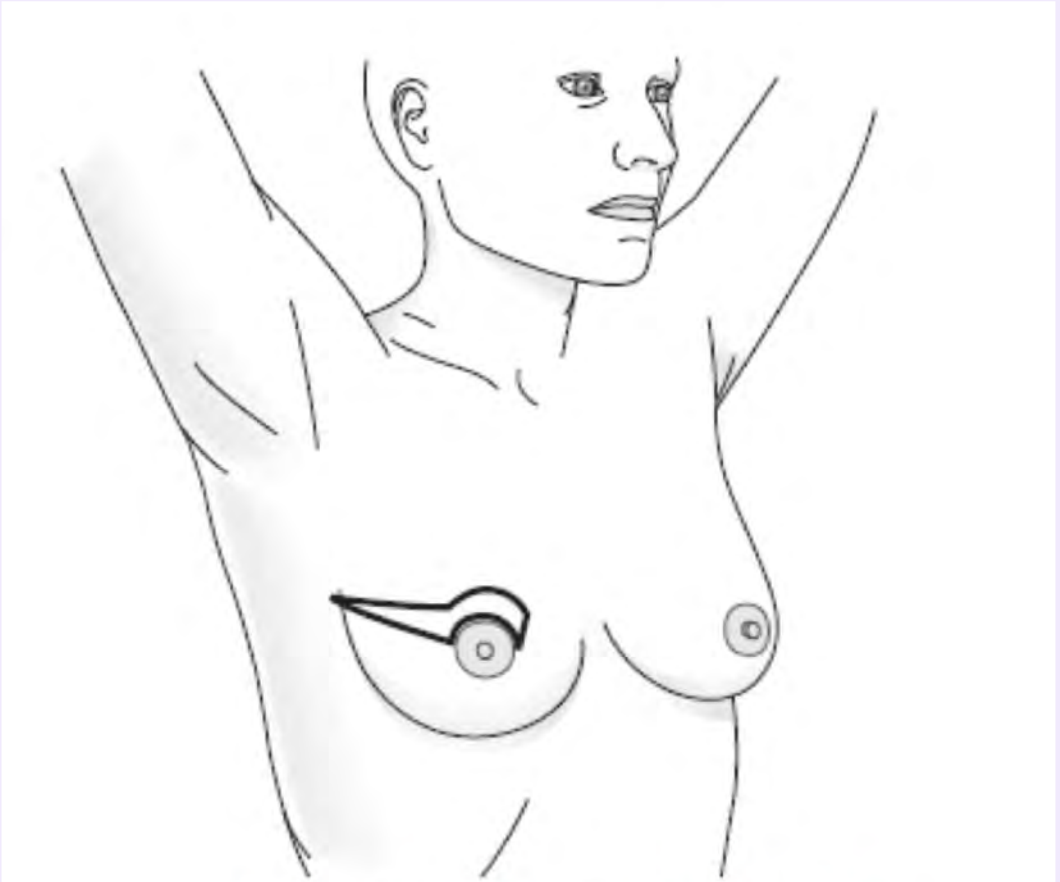

Batwing incision to reduce the upper skin and elevate the nipple.

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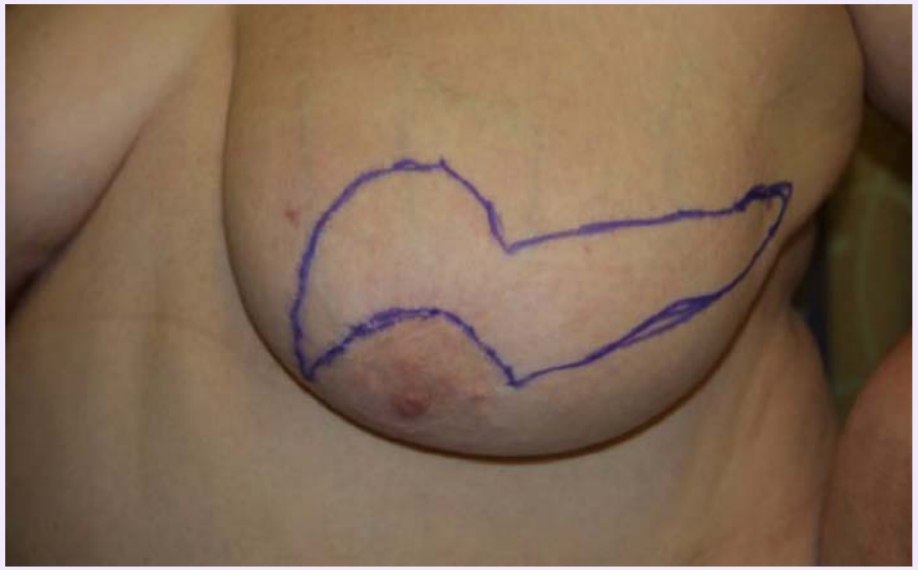
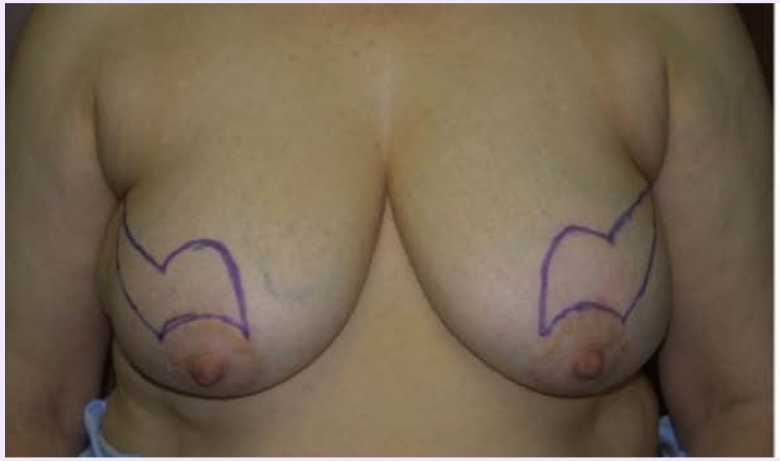
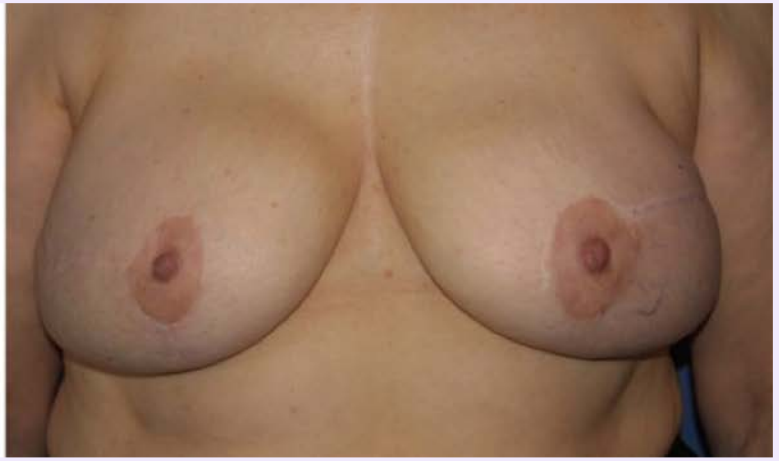






Extending NSM Eligibilty

The Larger or Ptotic Breast

BREAST

Breast Reconstruction Using a Staged Nipple-Sparing Mastectomy following Mastopexy or Reduction

Scott L. Spear, M.D.
Steven J. Rottman, M.D.
Laura A. Seiboth, M.D.
Catherine M. Hannan, M.D.
Washington, D.C.

Background: To address those patients who do not meet anatomical criteria for nipple-sparing mastectomy, the authors use a staged approach: (1) mastopexy or breast reduction, (2) nipple-sparing mastectomy through the mastopexy incisions after a minimum of 3 to 4 weeks, and (3) the final reconstruction.

Methods: Fifteen patients underwent nipple-sparing mastectomy at Georgetown University Hospital between 2007 and 2010 after planned or unrelated mastopexy or reduction. An institutional review board–approved retrospective chart review recorded demographic information and outcomes such as skin necrosis and device failure.

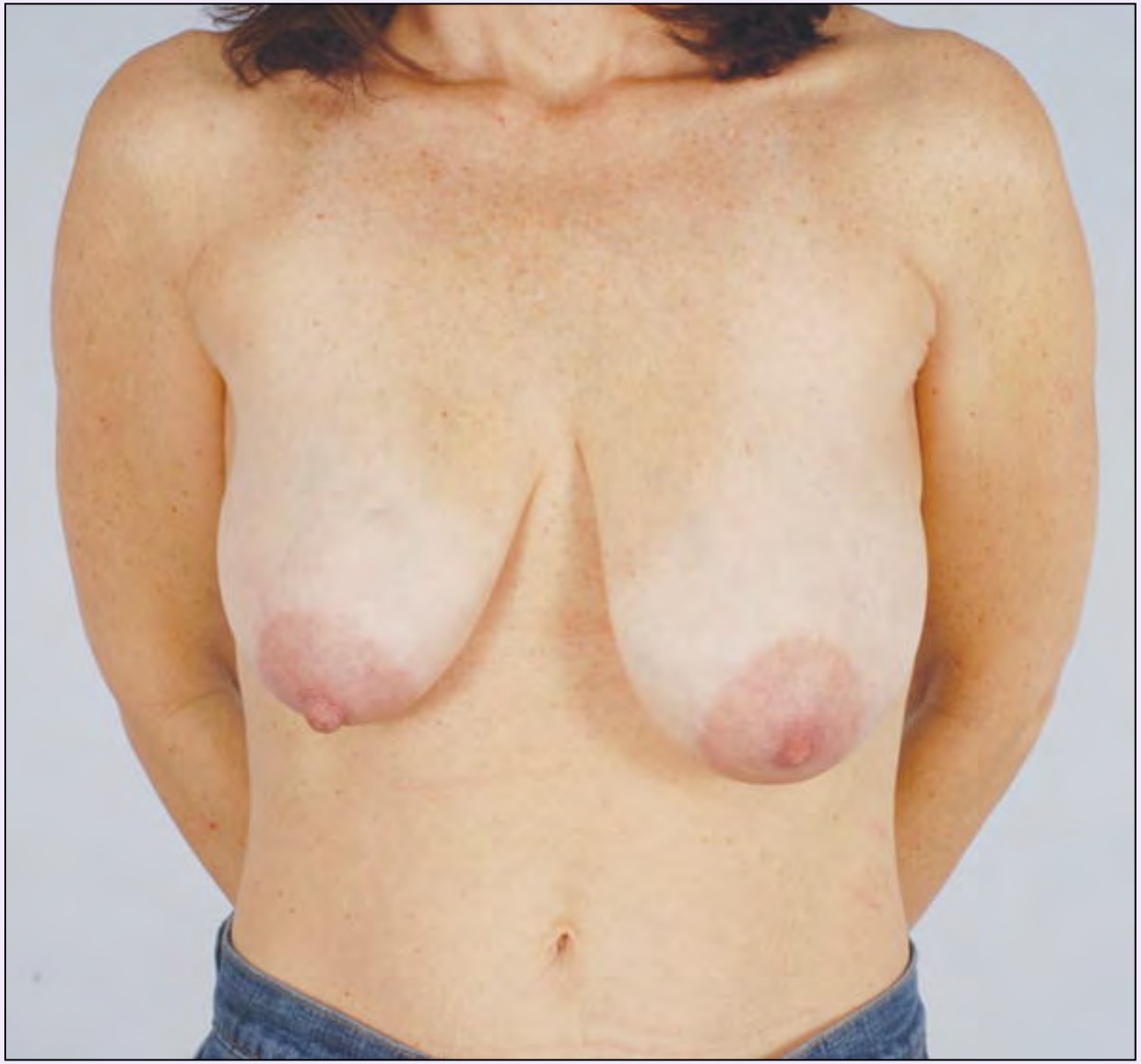
Results: Fifteen patients (24 breasts) underwent nipple-sparing mastectomy after mastopexy or reduction with an average follow-up of 13 months. The staged procedure was planned in 10 patients [19 breasts (79 percent)] and unplanned, or coincidental, in five [five breasts (21 percent)]. The mastectomy was prophylactic in 17 breasts (71 percent) and therapeutic in seven (29 percent). Four of the 24 operated breasts (17 percent) experienced a complication. Two patients [two breasts (8 percent)] developed skin flap necrosis. Two patients [three breasts (13 percent)] developed minimal partial nipple-areola complex necrosis. One patient [one breast (4 percent)] had an expander explanted for infection related to skin flap necrosis. Fourteen patients [23 breasts (96 percent)] successfully recovered following nipple-sparing mastectomy and prior mastopexy or reduction without residual effects of nipple-areola complex or skin flap necrosis.

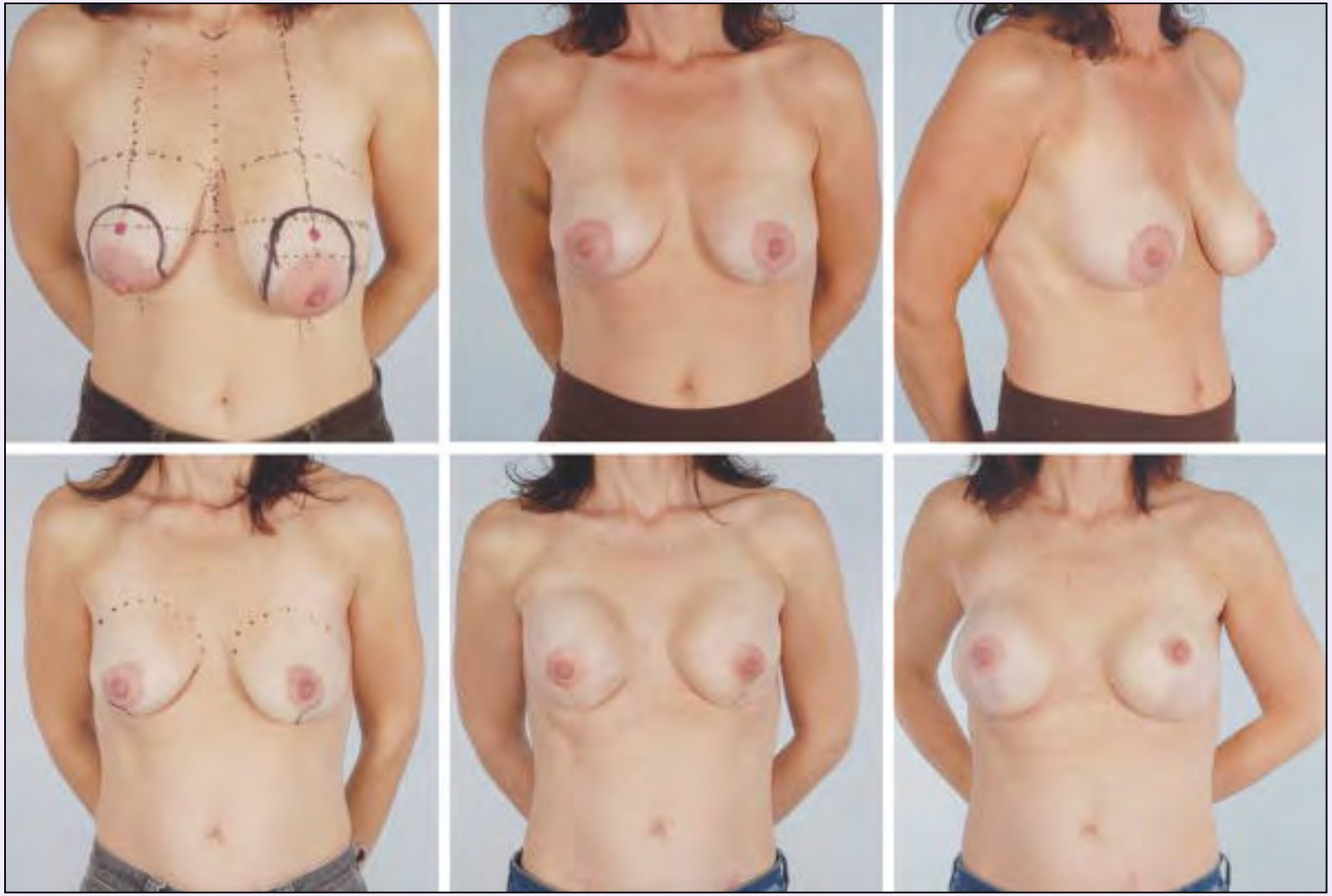
Conclusions: The authors are comfortable offering the staged approach to nipple-sparing mastectomy to patients with moderately large or ptotic breasts. It may not be suitable for the very large or ptotic breast. (*Plast. Reconstr. Surg.* 129: 572, 2012.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Therapeutic, IV.

THERAPEUTIC

Plastic and Reconstructive Surgery 2012





Personal Practice Audit
Risk-Reduction Mastectomy 2015-2018

The Breast Centre
thebreastcentre.com.au

- Patient undergoing bilateral risk reduction mastectomy were aged 22-57 years
- Average age 39, but increasing numbers in their 20s- 22, 27, 27, 28, 28, 29

	%
Overseas	6
Interstate	24
Regional Victoria	41
Melbourne	29

- All but 1 patient underwent immediate reconstruction

Personal Practice Audit
Bilateral Risk-Reduction Mastectomy 2015-2018

The Breast Centre
thebreastcentre.com.au

- All but 2 patients proven BRCA mutation carriers

- All but 3 pts underwent bilateral NSM
- * Bilat simple mastectomy
- * Bilat skin reducing mastectomy with two stage tissue expander/implant recon
- * Bilat skin reducing mastectomy with DIEP flap recon

- 86% pts undergoing NSM underwent prior "nipple delay"

- All but 1 pt undergoing NSM –one stage DTI reconstruction

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The Breast Centre

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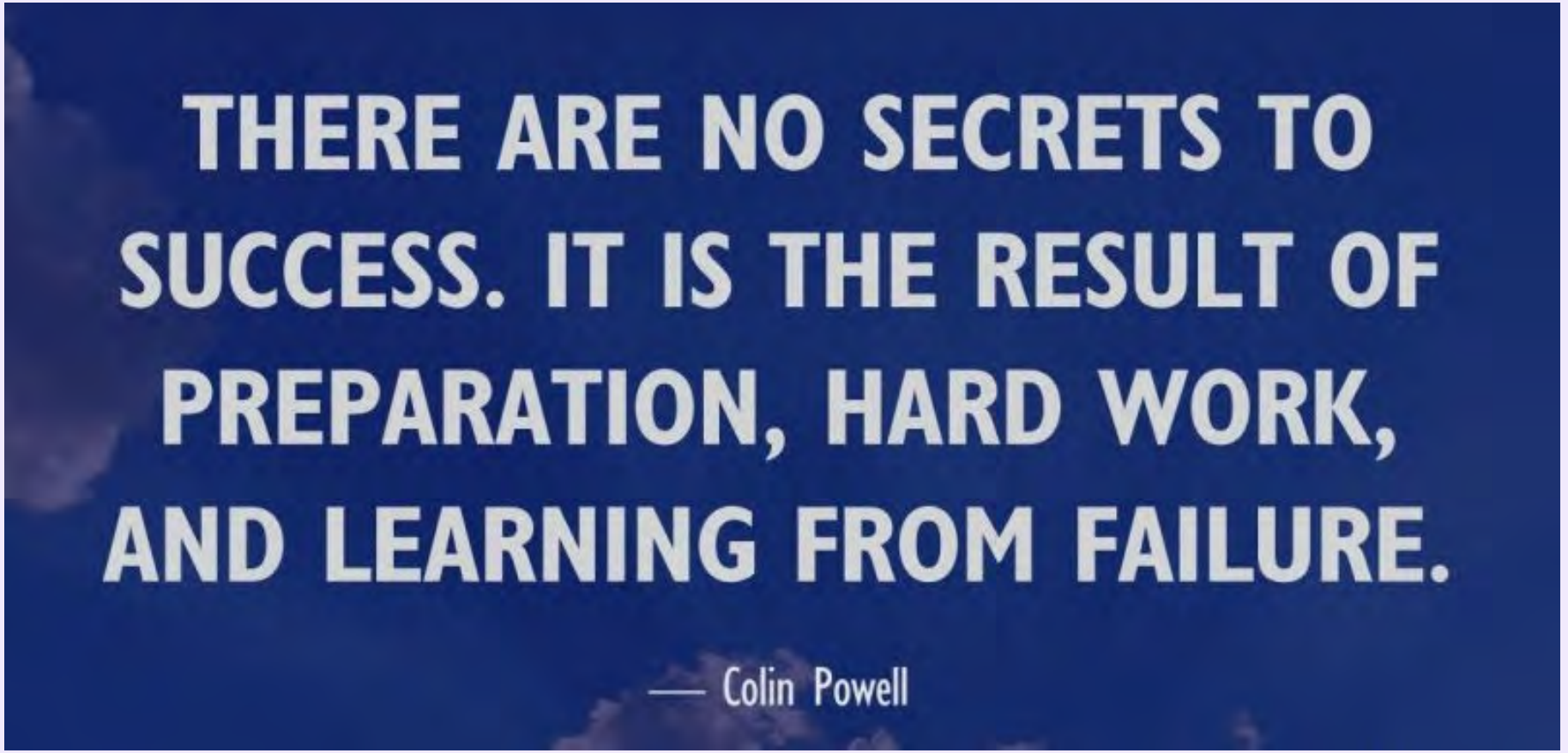

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WHERE?

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Private vs Public Sector

The Breast Centre

thebreastcentre.com.au

"Ok, we'll let the patient choose her own doctor, but only with the blindfold on."

"Please pick a doctor and take a seat"

Choice of Doctor

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Private Sector

The Breast Centre
thebreastcentre.com.au

- Ability to select surgeon who will perform the operation
- Availability of theatre time
- Greater flexibility to easily coordinate operations involving more than one surgeon eg immediate breast reconstruction
- Advance scheduling
- No cancellation of elective procedures
- Access to expensive prosthetic products eg ADMs

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Preparation for Risk-Reducing Surgery

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thebreastcentre.com.au

- No Smoking
- Healthy weight (BMI 20-25)
- Core Strength eg pilates

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Occult Malignancy in Prophylactic Mastectomy

The Breast Centre

thebreastcentre.com.au

- The chance of finding an occult synchronous invasive tumour during prophylactic mastectomy is low -about 5%
- Higher in CPM compared to Bilat RRM
- **Routine use of SLNB in this setting is not recommended**

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Follow up after RRM

The Breast Centre
thebreastcentre.com.au

- New lifetime risk 3-5%
  - ie 90-95% reduction of 60-85% lifetime risk
- Tumours detectable by clinical examination
- No role for routine surveillance imaging of reconstructed breast

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RESOURCES

- Books
- Organisations
- Online Groups
- Social Media

The Breast Centre

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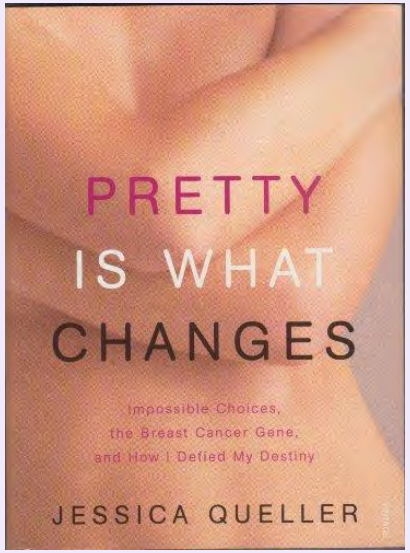
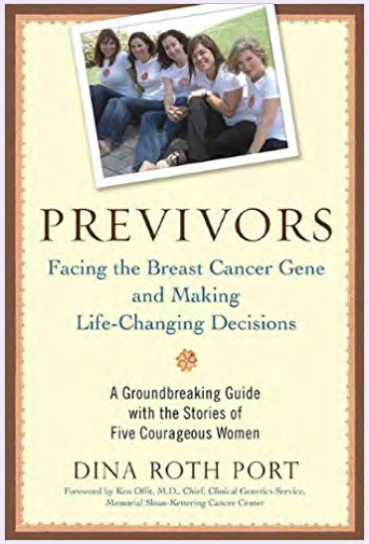
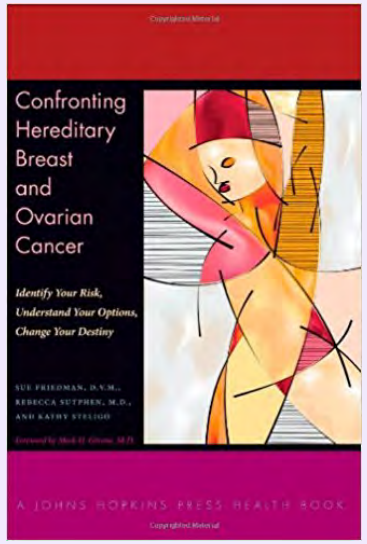
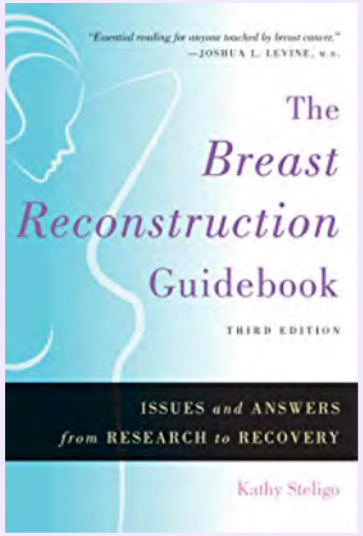
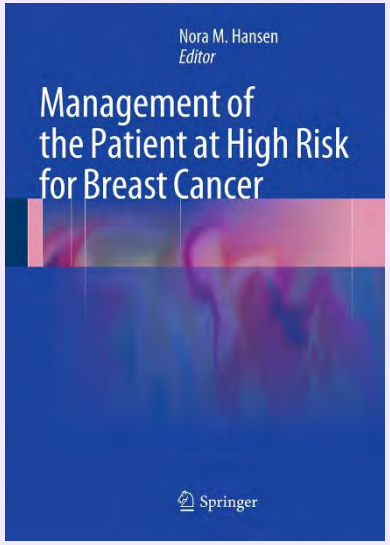
A story of courage, hope and bright pink lipstick
The LUCKY ONE
KRYSTAL BARTER


PRETTY IS WHAT CHANGES
Impossible Choices, the Breast Cancer Gene, and How I Defied My Destiny
JESSICA QUELLER


PREVIVORS
Facing the Breast Cancer Gene and Making Life-Changing Decisions
A Groundbreaking Guide with the Stories of Five Courageous Women
DINA ROTH PORT


Confronting Hereditary Breast and Ovarian Cancer
Identify Your Risk, Understand Your Options, Change Your Destiny
A JOHNS HOPKINS PRESS HEALTH BOOK


"Essential reading for anyone touched by breast cancer."
—JOSHUA L. LEVINE, M.D.
The Breast Reconstruction Guidebook
THIRD EDITION
ISSUES and ANSWERS from RESEARCH to RECOVERY
Kathy Steligo


Nora M. Hansen
Editor
Management of the Patient at High Risk for Breast Cancer
Springer

Books

Organisations

The Breast Centre
thebreastcentre.com.au

- Pink Hope

http://pinkhope.org.au

- Force

http://www.facingourrisk.org/index.php

- Bright Pink

https://www.brightpink.org/high-risk-support/high-risk-resources/

- Basser Center for BRCA

https://www.basser.org

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The Breast Centre
thebreastcentre.com.au

- "Every breast or ovarian cancer patient with a BRCA1 or BRCA2 mutation detected after diagnosis is a missed opportunity to prevent a cancer. No woman with a BRCA1 or BRCA2 mutation should die from breast or ovarian cancer"

Mary Claire King

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The Breast Centre
thebreastcentre.com.au

For debate

Bilateral risk-reducing mastectomy is the safest strategy in *BRCA1* carriers

S. Pilgrim*, S. Pain

Department of General Surgery, Norfolk & Norwich University Hospital, Colney Lane, Norwich, United Kingdom

Commentary: Bilateral risk-reducing mastectomy is the safest strategy in *BRCA1* carriers

Rachael Glassey[1], Christobel Saunders[1] and Sarah J. Hardcastle[2]*

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[2] Health Psychology and Behavioural Medicine Research Group, Faculty of Health Sciences, School of Psychology and Speech Pathology, Curtin University, Perth, WA, Australia

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The types of breast cancer that occur in *BRCA1* carriers differ considerably from those that occur in *BRCA2* carriers.

BRCA1 carriers

- More than 75% of breast cancers are oestrogen-receptor (ER)–negative, high-grade cancers
- 69% are ER-negative, progesterone-receptor–negative, and human epidermal growth factor receptor 2–negative, or "triple-negative," breast cancers

BRCA2 carriers

- Breast cancers mirror those seen in the general population
- 77% are ER-positive and only 16% are triple-negative breast cancers.

Ovarian cancer typically occurs earlier and with greater frequency among *BRCA1* carriers than among *BRCA2* carriers

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The Breast Centre

at St Vincent's Private Hospital East Melbourne

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