

# TUMORE OVARICO E BRCA: CAMBIARE IL FUTURO SI PUO'



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**Torino**

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**Ruolo della prevenzione:  
terapia medica e  
chirurgica—mammella**



***STIMA DEL  
RISCHIO***



***GESTIONE DEL  
RISCHIO***



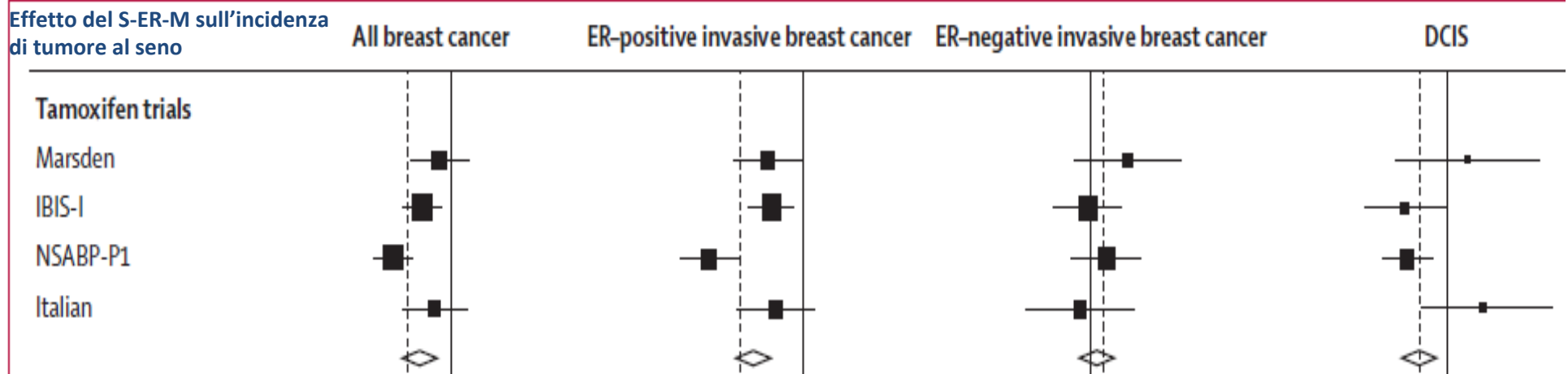
***STRATEGIE DI  
PREVENZIONE***

**Sorveglianza  
e stile di vita**

**Farmacoprevenzione**

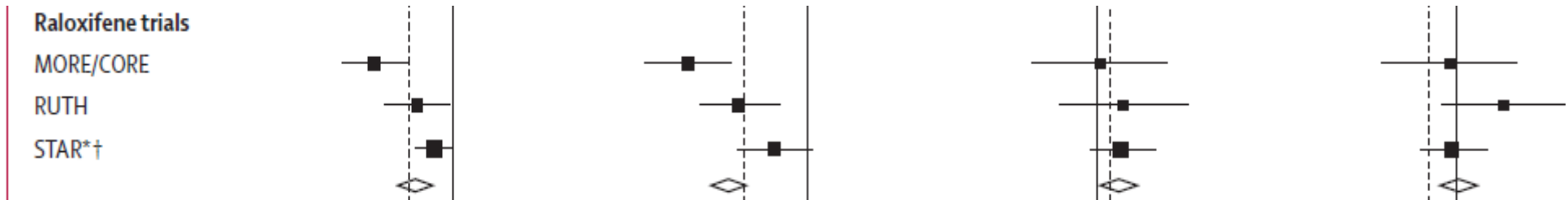
**Chirurgia  
profilattica**

Effetto del S-ER-M sull'incidenza di tumore al seno



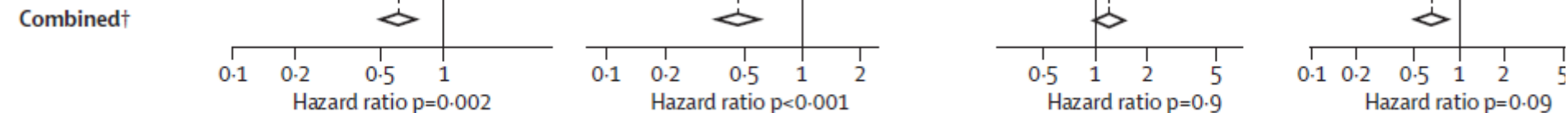
#### NEI TRIAL CHE HANNO VALUTATO TAM Vs PLACEBO:

- Riduzione significativa dell'incidenza di tutti i tumori rispetto al placebo del 33% ( $p < 0.0001$ ).
- Riduzione del 44% dei tumori ER-positivi ( $p < 0.0001$ ) valida anche per l'insorgenza di DCIS ( $p = 0.009$ )
- MA nessuna riduzione dei tumori ER-negativi



#### NEI TRIAL CHE HANNO RALOXIFENE Vs PLACEBO.

- Riduzione significativa dell'incidenza di tutti i tumori ( $p < 0.0001$ ) dovuta a forte riduzione s90due to a reduction in invasive ER-positive breast cancers, with a non-significant increase in the incidence of invasive ER-negative breast cancers and no effect on DCIS (table 2 and figure 3)



When we compared raloxifene with tamoxifen, the only significant difference in effect size was a greater effect for tamoxifen in DCIS (HR 0.78, 95% CI 0.61–0.99;  $p = 0.04$ )

# Tamoxifen and Breast Cancer Incidence Among Women With Inherited Mutations in *BRCA1* and *BRCA2* in the *NSABP-P1* Study

	Placebo	Tamoxifen	Risk Ratio (95% Confidence Interval)
<i>BRCA1</i> mutation	3	5	1.67 (0.32-10.70)
<u><i>BRCA2</i> mutation</u>	8	3	<u>0.38 (0.06-1.56)</u>
Wild type	182	87	0.48 (0.37-0.61)

- Tamoxifen reduced breast cancer incidence among *BRCA2* carriers by 62%, similar to the reduction in incidence of ER-positive breast cancer among all women in the Breast Cancer Prevention Trial.

King et al *JAMA*. 2001

# Healthy BRCA Mutation Carrier and Breast Risk Reducing Surgery

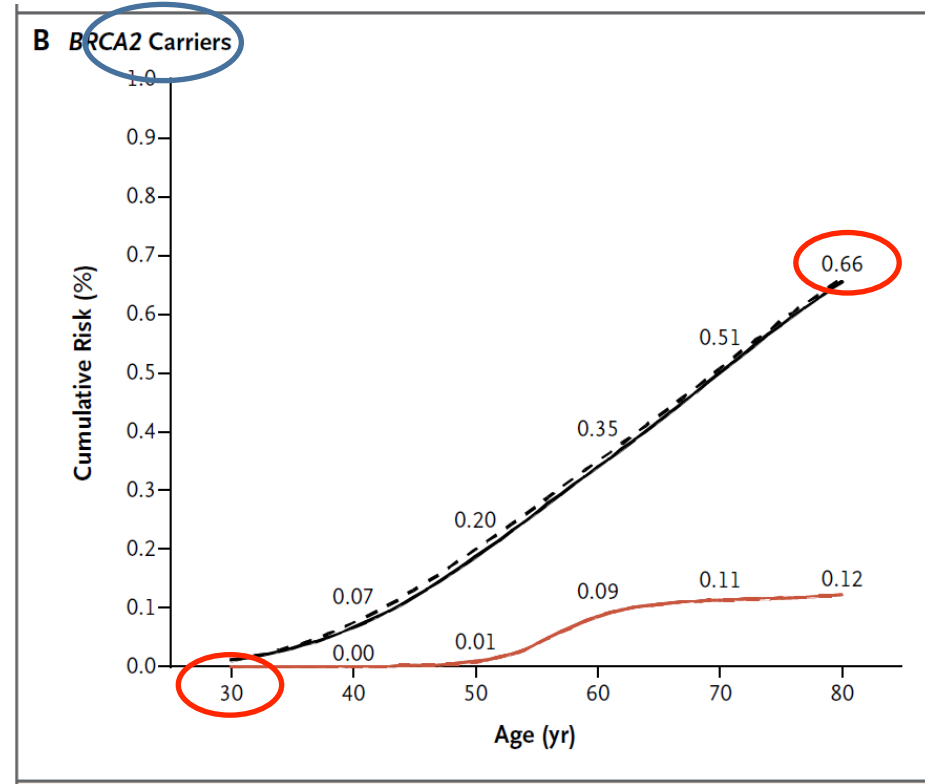
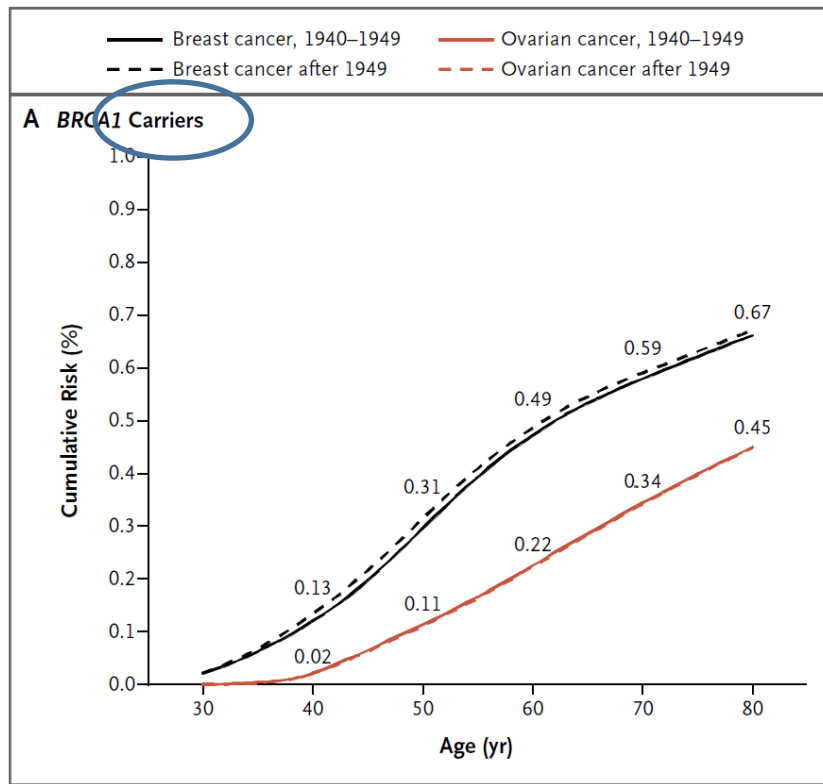
- 1) Oncological Outcome
- 2) Quality of Life
- 3) Cost-effectiveness of Breast Surgery
- 4) Timing
- 5) Kind of Surgery
- 6) Technical Consideration

# Oncological Outcome

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

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

N ENGL J MED 374;5 NEJM.ORG FEBRUARY 4, 2016



Cumulative risk of breast cancer (black) and ovarian cancer (red) for BRCA mut. carr. 1 and 2.

Ex. An unaffected 30 years old BRCA2 carrier has a 66% cumulative risk of BC developing by 80 years. The risk decrease by age.

# Oncological Outcome

## The New England Journal of Medicine

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

LYNN C. HARTMANN, M.D., DANIEL J. SCHAIID, PH.D., JOHN E. WOODS, M.D., THOMAS P. CROTTY, M.D.,

**TABLE 6.** EXPECTED AND ACTUAL NUMBERS OF DEATHS FROM BREAST CANCER  
AMONG THE HIGH-RISK WOMEN WHO UNDERWENT PROPHYLACTIC MASTECTOMY.\*

EVENTS IN SISTERS USED TO CALCULATE RATE	PERSON-YEARS OF FOLLOW-UP		DEATH FROM BREAST CANCER		REDUCTION IN DEATHS (95% CI)  percent
	SISTERS	PROBANDS	NO. EXPECTED	NO. OBSERVED	
All deaths from breast cancer from age 18 to end of follow-up					
Unadjusted	14,896	2970	30.6	2	93.5 (76.4–99.2)
Adjusted†	13,569	2970	19.4	2	89.7 (62.3–98.8)
Deaths from breast cancer after prophylactic mastectomy to end of follow-up	3,356	2970	10.5	2	80.9 (31.4–97.7)

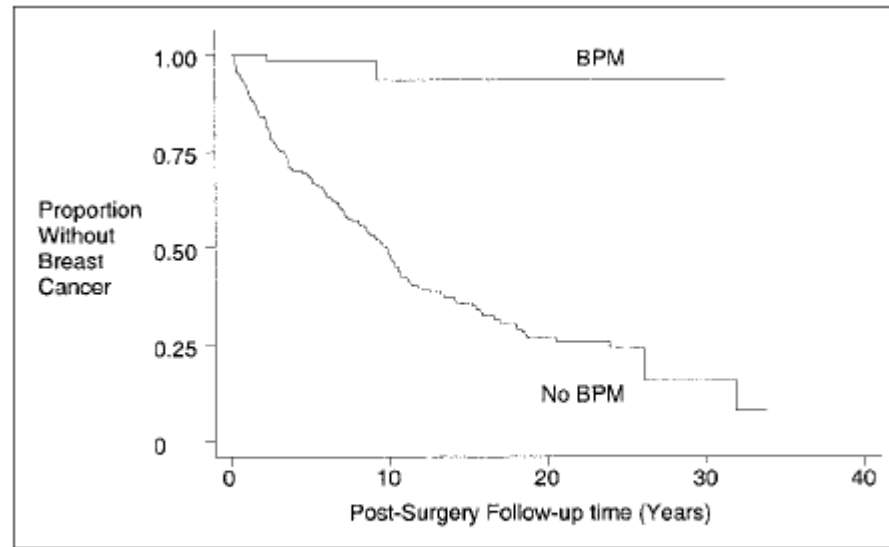
Mayo Clinic first study reported reduction of risk by more than 90% on a large cohort of women with a family history of BC. (reduction in death)

# Oncological Outcome

Bilateral Prophylactic Mastectomy Reduces Breast Cancer Risk in *BRCA1* and *BRCA2* Mutation Carriers:  
The PROSE Study Group

VOLUME 22 • NUMBER 6 • MARCH 15 2004

JOURNAL OF CLINICAL ONCOLOGY



**Fig 1.** Time to breast cancer diagnosis in female *BRCA1* mutation carriers with and without bilateral prophylactic mastectomy (BPM).

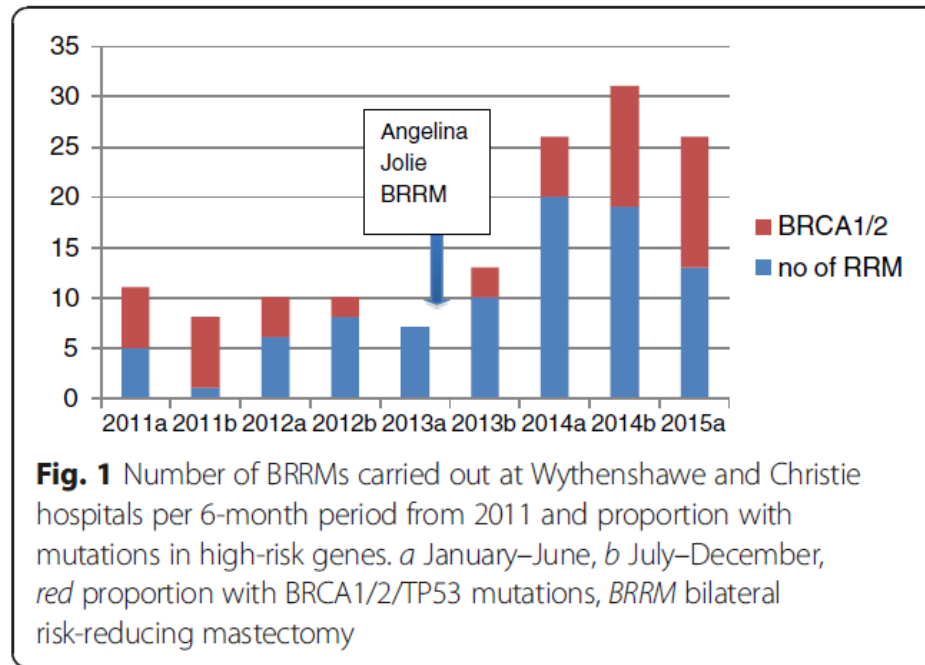
PROSE Study group with a both prospective and historical cohort study of 247 and 483 women with *BRCA* 1-2 mutation.

105 who underwent to prophylactic mastectomy were matched with 378 control who had intact breast. Prophylactic mastectomy was associated with a reduction in risk of breast cancer of about 95%.



# Quality of Life

Longer term effect of the “Angelina Jolie Effect” from May 2013



# Quality of Life

## Psychological Reactions, Quality of Life, and Body Image After Bilateral Prophylactic Mastectomy in Women At High Risk for Breast Cancer: A Prospective 1-Year Follow-Up Study

*Yvonne Brandberg, Kerstin Sandelin, Staffan Erikson, Göran Jurell, Annelie Liljegren, Annika Lindblom, Ann Lindén, Anna von Wachenfeldt, Marie Wickman, and Brita Arver*

20 2008

JOURNAL OF CLINICAL ONCOLOGY

- Prospective study,
- Data from patient questionnaire before, 6 month and 1 year later BPM,
- 90 healthy women with BRCA 1-2 mutation

# Quality of Life

## Impact of Areas of Life

(before bilateral prophylactic mastectomy, 6 months and 1 year later)

**Table 2.** No. and Proportion of Women Reporting Negative or Positive Expectations Preoperatively and Negative or Positive Reactions Postoperatively for All Respondents at Each Point of Assessment and for Those Who Responded at All Assessments

Parameter	All Respondents at Each Assessment Point												Women Responding at All Points of Assessment											
	Expectations Before BPM (n = 79-80)				Reactions 6 Months After BPM (n = 69-71)				Reactions 1 Year After BPM (n = 63-64)				Expectations Before BPM (n = 53-54)				Reactions 6 Months After BPM (n = 53-54)				Reactions 1 Year After BPM (n = 53-54)			
	Negative		Positive		Negative		Positive		Negative		Positive		Negative		Positive		Negative		Positive		Negative		Positive	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Change of life	7	9	51	64	11	16	36	51	8	13	39	61	4	7	33	61	9	17	30	56	7	13	31	57
Femininity	19	24	18	23	19	27	22	31	17	27	17	27	13	25	14	26	14	26	18	34	14	26	15	28
Intimate situation	33	42	13	16	29	41	11	15	29	46	10	16	22	42	9	17	23	43	8	15	23	43	9	16
Physical activity	19	24	18	23	26	37	13	19	15	23	13	20	15	28	14	26	19	35	11	20	13	24	10	19
Social activity	8	10	22	27	5	7	18	26	2	3	21	33	7	13	17	31	4	7	15	28	2	4	17	31
Working capacity	12	15	21	27	15	21	14	20	12	19	13	20	10	19	16	30	12	22	11	20	10	19	10	19

NOTE: No. and proportions of women reporting a neutral response with respect to expectations or reactions (score = 4) are not presented.  
Abbreviation: BPM, bilateral prophylactic mastectomy.

No statistically significant differences were found between the assessment before BPM and the 6-month assessment or between the 6-month and the 1-year assessments.

# Quality of Life

## Body Image

(before bilateral prophylactic mastectomy, 6 months and 1 year later)

Measure	All Respondents at Each Assessment Point (n = 62-69)																Women Responding at All Points of Assessment (n = 53-54)															
	6-Month Assessment								1-Year Assessment								6-Month Assessment								1-Year Assessment							
	Not at All		Quite a Little		Very Bit		Very Much		Not at All		Quite a Little		Very Bit		Very Much		Not at All		Quite a Little		Very Bit		Very Much		Not at All		Quite a Little		Very Bit		Very Much	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Self-conscious	31	45	28	41	7	10	3	4	33	52	25	40	5	8	0	0	25	46	23	43	5	9	1	2	28	52	22	41	4	7	0	0
Less physically attractive	41	59	20	29	6	9	2	3	37	60	18	29	7	11	0	0	34	63	15	28	5	9	0	0	31	59	16	30	6	11	0	0
Dissatisfied with appearance	54	78	10	15	3	4	2	3	52	83	11	17	0	0	0	0	45	83	6	11	2	4	1	2	46	85	8	15	0	0	0	0
Less feminine	49	71	13	19	7	10	0	0	41	65	19	30	3	5	0	0	40	74	10	19	4	7	0	0	35	65	17	31	2	4	0	0
Difficult to see self naked	45	66	18	27	3	4	2	3	48	76	12	19	2	3	1	2	38	70	12	22	3	6	1	2	41	76	10	18	2	4	1	2
Less sexually attractive	33	48	27	39	7	10	2	3	33	52	24	38	5	8	1	2	27	50	20	37	6	11	1	2	29	54	20	37	4	7	1	2
Avoid people	63	93	4	6	0	0	1	1	62	98	1	2	0	0	0	0	50	93	4	7	0	0	0	0	53	98	1	2	0	0	0	0
Body less whole	46	67	19	27	2	3	2	3	45	71	18	29	0	0	0	0	38	70	14	26	2	4	0	0	40	74	14	26	0	0	0	0
Dissatisfied with body	41	59	17	25	8	12	3	4	47	74	13	21	3	5	0	0	36	67	12	22	4	7	2	4	29	54	19	35	6	11	0	0
Dissatisfied with scar	45	65	21	31	2	3	1	1	35	56	21	33	6	9	1	2	38	70	14	26	2	4	0	0	40	74	11	20	3	6	0	0

There was no statistical significant difference in summated BIS mean scores between the 6-month (mean, 4.57; SE, 0.56) and the 1-year assessments (mean, 3.71; SE, 0.45). Wilcoxon signed rank sum test for each of the BIS items revealed no statistical differences over time.

# Quality of Life

## Sexuality

(before bilateral prophylactic mastectomy, 6 months and 1 year later)

More than 80% reported having an intimate relationship at all three points of assessment.

At the first assessment, 62% reported being sexually active.

Corresponding figures 6 months and 1 year after BPM were 77% and 79%, respectively.

Frequencies of sexual activity during the last month for the three assessment points revealed no statistically significant differences over time.

Pleasure decreased statistically significantly from the assessment before BPM to the 1-year assessment (P .005).

# Quality of Life

## Anxiety and Depression

(before bilateral prophylactic mastectomy, 6 months and 1 year later)

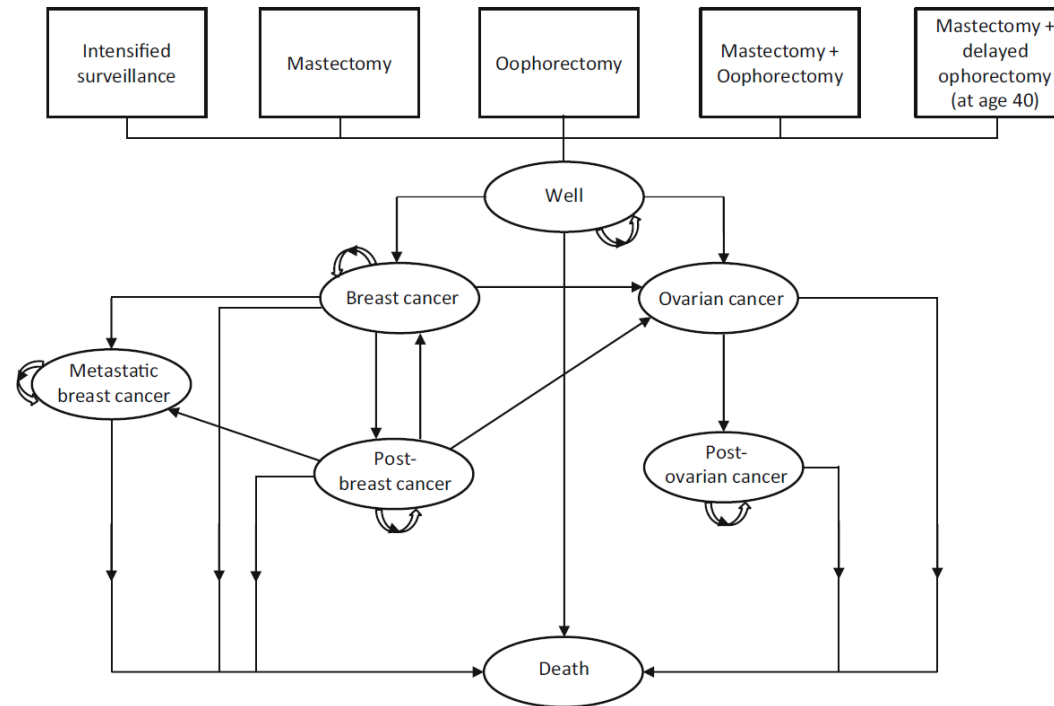
Anxiety decreased over time (df (2, 53); F, 8.53; P, .0004).

No statistical significant difference was found for depression.

# Cost-Effectiveness

## Cost-effectiveness of different strategies to prevent breast and ovarian cancer in German women with a BRCA 1 or 2 mutation

Dirk Müller<sup>1</sup> · Marion Danner<sup>1</sup> · Kerstin Rhiem<sup>2</sup> · Björn Stollenwerk<sup>3</sup>



**Fig. 1** Model overview using a tunnel state, women were kept in the post-breast cancer states for five cycles. From year 6, no further treatment costs and increments in utility incurred and women remained in this state unless a further event occurred

This economic modeling study evaluated different preventive intervention for 30-year-old women with BRCA 1-2 mutation.

This model consider costs and benefits of all conditions statistically reported for 30y old w.

# Cost-Effectiveness

Cost-effectiveness of different strategies to prevent breast and ovarian cancer in German...

**Table 3** Results of the base-case analysis

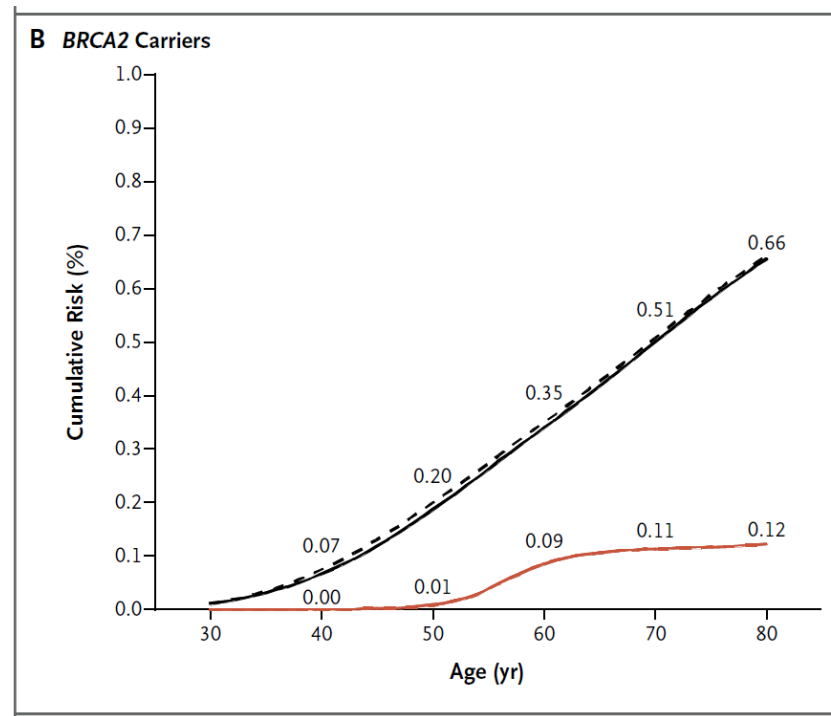
Strategy	Costs (€)	$\Delta$ costs (€)	QALYs	$\Delta$ QALYs	LYG	$\Delta$ LYG	ICER	
							Cost (€)/QALY	Cost (€)/LYG
Mastectomy + oophorectomy at age 30	29,434		17.66		19.86		(reference)	(reference)
Mastectomy + oophorectomy at age 40	30,810	1375	17.28	−0.38	19.53	0.33	dominated	dominated
Oophorectomy alone	34,802	5368	16.71	−0.94	19.32	0.54	dominated	dominated
Mastectomy alone	37,307	7872	16.27	−1.39	18.49	1.37	dominated	dominated
Surveillance	45,480	16,045	14.96	−2.70	17.65	2.21	dominated	dominated

*QALY* quality-adjusted life years, *ICER* incremental cost-effectiveness ratio, *LYG* life year gained

- With total costs of €29,434, the provision of BM plus BSO at age 30 for women with BRCA 1 or 2 was less expensive than all other strategies.
- In addition to this, the strategy achieved the highest gain in Quality Adjusted Life Years (17.7) or additional life-years (19.9) compared to the other strategies.
- BM plus immediate BSO dominated all other strategies.
- Women choosing the surveillance strategy had the highest costs at the lowest gain in Quality Adjusted Life Years.



# Timing



Cumulative risk of breast cancer (black) and ovarian cancer (red) for BRCA mut. carr. 1 and 2. decrease by age.

# Technical Considerations

## Oncological safety of nipple-sparing prophylactic mastectomy: A review of the literature on 3716 cases Annales de chirurgie plastique esthétique (2017)

**Table 3** Overall complication rates, necrosis rates (NAC and skin), types of reconstruction: global perspective on the different studies.

Author	Patients (n)	Mastectomies (n)	Overall complication rates n (%)	NAC necrosis rates n (%)	Skin necrosis rates n (%)	Reconstruction by MP (%)	Reconstruction by flap (%)
Hartmann [18]	639	1278	ND	ND	ND	ND	ND
Yiacoumettis [19]	52	104	4 (4)	1 (1)	2 (1.9)	100	0
Sacchini [35]	123	192	43 (22)	22 (11)	ND	80.7	19.3
Wijayanayagam [32]	43	64	27 (42)	3 (5)	11 (17)	46.9	53.1
Garcia-Etienne [20]	25	42	ND	12 (29)	ND	100	0
Babiera [31]	ND	54	ND	(7.2)	ND	ND	ND
Maxwell [23]	98	186	ND	ND	ND	98.2	1.8
Alcantara Filho [21]	200	353	75 (21)	ND	69 (20)	99.7	0.3
Harness [22]	43	60	12 (20)	9 (15)	ND	100	0
Spear [24]	101	162	46 (28)	11 (6.8)	3 (1.9)	96.3	3.7
Warren Peled [34]	428	657	274 (42)	23 (3.5)	78 (12)	85.7	14.3
Camp [25]	ND	438	ND	ND	ND	ND	ND
Eisenberg [26]	215	325	ND	ND	ND	ND	ND
Peled [27]	106	212	39 (18)	3 (1.4)	9 (4.2)	84.4	13.6
Yao [36]	201	397	33 (8.3)	4 (1)	10 (2.5)	5.5	94.5
Manning [28]	89	177	37 (21)	6 (3.4)	7 (4)	98.9	1.1
Manning [29]	413	728	105 (14)	ND	47 (6.5)	97	1.7
Orzalesi [33]	913	1006	44 (4.4)	44 (4.8)	23 (2.3)	ND	ND
Donovan [30]	201	351	73 (21)	56 (16)	22 (6.3)	93.4	5.1
<b>Total</b>	<b>3890</b>	<b>6786</b>	<b>812 (20.5)</b>	<b>194 (8.1)</b>	<b>281 (7.1)</b>	<b>85</b>	<b>15</b>

n: number; %: percentage; NAC: nipple-areolar complex; MP: mammary prosthesis, FL: flap; ND: no data.

- Systematic review of the literature considering 3716 cases of PBM
- The average overall complication rate was 20.5%.
- The average NAC necrosis rate was 8.1%,
- The average cutaneous necrosis was 7.1%.

# Advances in Surgical Technique

## Robotic nipple-sparing mastectomy for the treatment of breast cancer: Feasibility and safety study

Antonio Toesca <sup>a,\*</sup>, Nickolas Peradze <sup>a</sup>, Andrea Manconi <sup>b</sup>, Viviana Galimberti <sup>a</sup>,  
Mattia Intra <sup>a</sup>, Marco Colleoni <sup>c</sup>, Bernardo Bonanni <sup>d</sup>, Giuseppe Curigliano <sup>e</sup>,  
Mario Rietjens <sup>b</sup>, Giuseppe Viale <sup>f,g</sup>, Virgilio Sacchini <sup>a,g</sup>, Paolo Veronesi <sup>a,g</sup>



**Fig. 2.** Two-month postoperative outcome of the third patient. Comparison between RNSM for contralateral delayed risk reducing surgery (right side) and classical open technique (left side). It is still visible a small blistering from internal electrocautery in the upper quadrant.



**Fig. 3.** Two-month postoperative outcome of the third patient. Lateral view. The 3 cm incision remains hidden in the axilla. It is still visible a small blistering from internal electrocautery in the upper quadrant.

# Advances in Surgical Technique

## Reverse Expansion with Fat Grafting

BREAST SURGERY

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### Total Breast Reconstruction With Fat Grafting After Internal Expansion and Expander Removal

*Andrea Manconi, MD, Francesca De Lorenzi, PhD, Badir Chahuan, MD, Valeria Berrino, MD, Pietro Berrino, MD, Gustavo Zucca-Matthes, PhD, Jean Yves Petit, MD, and Mario Rietjens, MD*

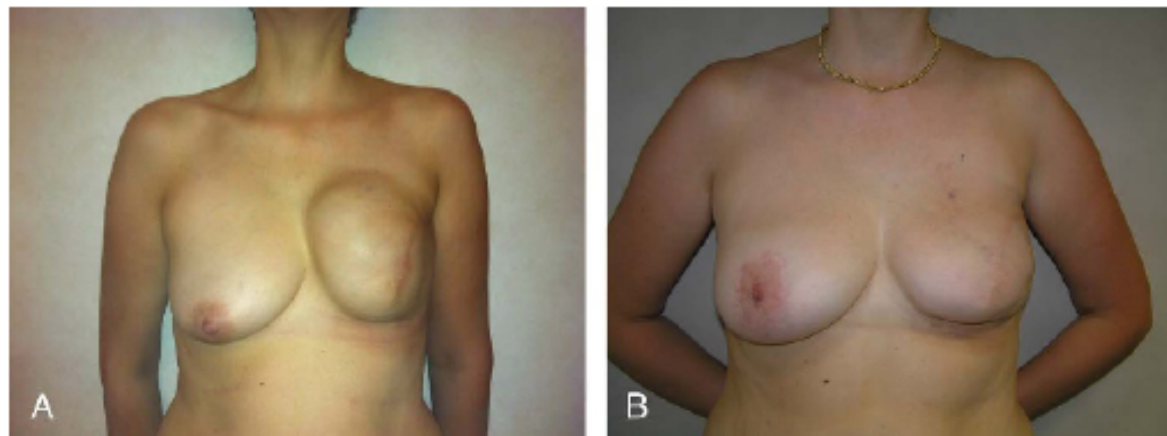


FIGURE 4. Preoperative view (A) and postoperative view after 6 months (B) of case 9.



**Robotic Nipple Sparing Mastectomy and  
Immediate Robotic Reconstruction with «Reverse  
Expansion» with Fat Grafting**



**Dont' Forget**

**Thank You**

**Antonio Toesca**