

# CÁNCER DE MAMA HEREDITARIO:

## *Cirugía preventiva*

Dra. T.Ramón y Cajal

[tramon@santpau.cat](mailto:tramon@santpau.cat)

Oncología Médica

Hospital Sant Pau

## CIRUGÍA PREVENTIVA: RACIONAL

Five- and 10-year risks of ovarian cancer after breast cancer

	Annual risk <sup>a</sup>	Actuarial 5-year cumulative risk	Actuarial 10-year cumulative risk
BRCA1	1.3%	4.5%	12.7%
BRCA2	0.8%	5.3%	6.8%

<sup>a</sup> Calculated over 10 years.

Deaths: breast and ovarian cancers

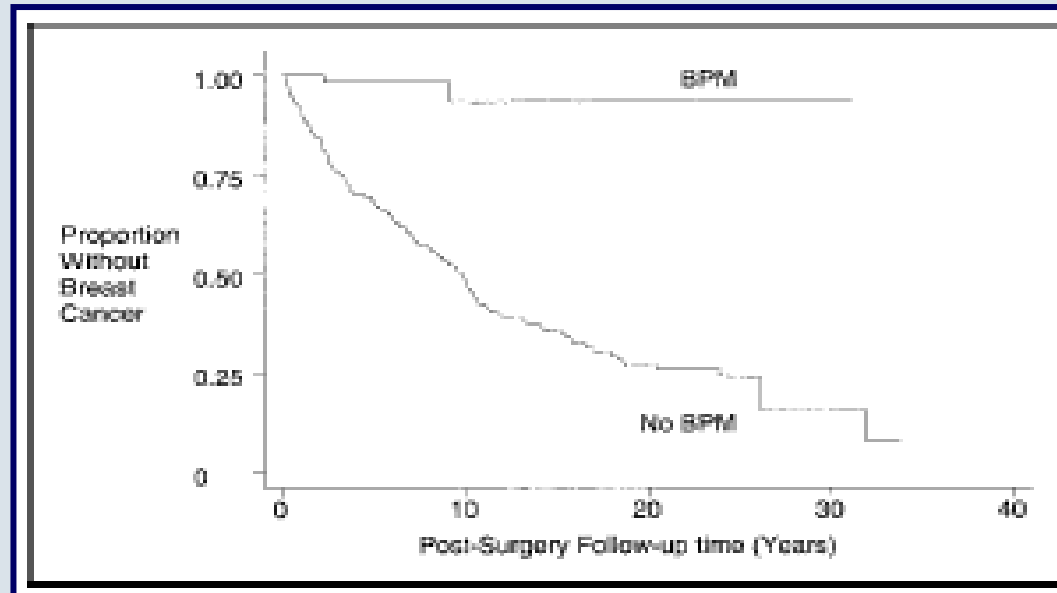
	Cause of death		Total deaths
	Breast cancer	Ovarian cancer	
Stage I breast cancer (n = 201)	21	7	28
Stage II breast cancer (n = 248)	54	1	55
Total deaths	75	8	83

*Gynecologic Oncology 96 (2005) 222–226*

Table 4. Synopsis of management strategies available to BRCA1 and BRCA2 mutation carriers<sup>a</sup>

Management option	Strategy	Advantage	Limitation	
Gynecologic cancer	Chemoprevention	Oral contraceptive pills	Likely 30%–60% reduction in ovarian cancer risk (21,22)	Potential increase risk of breast cancer (23,24)
	Screening	Transvaginal ultrasound, serum CA-125	Avoids BRSO	Unproven efficacy (25)
	Risk-reducing surgery	Bilateral salpingo-oophorectomy	Substantial decrease in risks of ovarian and fallopian tube cancers (this study)	Premature menopause and iatrogenic infertility
Breast cancer	Chemoprevention	Selective estrogen receptor modulators (tamoxifen, raloxifene)	May reduce risk of ER-positive breast cancer (26,27)	Very limited data in BRCA1/2 mutation carriers
	Screening	Yearly MRI		Issues of specificity (false positives)
		Yearly mammogram Self breast examination, clinical breast examination	≈80% sensitive for detection of malignancy (28,29)	Does not prevent cancer, goal is early detection
	Risk-reducing surgery	Bilateral salpingo-oophorectomy	Substantial decrease in breast cancer risk (this study)	Premature menopause, iatrogenic infertility
Mastectomy, with or without breast reconstruction		Highly effective (30)	Body image and quality-of-life issues	

## MASTECTOMÍA PROFILÁCTICA



### RACIONAL

- Reducción R de CM 90- 95% estudios retrospectivos y prospectivos no controlados
- MPx permite el diagnóstico de lesiones premalignas (x12) y cánceres ocultos  
**Hartmann, JNCI 2001, Meijers-Heijboer, NEJM 2001, Rebbeck, JCO 2004**

### CIFRAS

- 27% portadoras con CM (49% en USA-Canada y 15% en Europa): edad media joven (39 años vs 43), cirugía radical previa (40 vs 12%) y antec. de OOPX (33 vs 18%)
- 18% portadoras sanas (29% en USA-Canada y 6% en Europa)

**Metcalfe, JCO 2008**

## MASTECTOMÍA PROFILÁCTICA

Autor/Publicación	Casos	Selección	Resultado
<b>Hartmann et al. New Engl J Med 1999</b>	639 (214 AR y 425 RM)	Hx familiar	14 años seg medio 7 MPx / 37 control Reducción R 90%
<b>Hartmann et al. J Natl Cancer Inst 2001</b>	26	BRCA 1 BRCA 2	Reducción R 89.5-100%
<b>Meijers-Heijboer et al. N Engl J Med 2001</b>	139 (66 vs 63)	BRCA 1 BRCA 2	3 años seguimiento 0 MPx/ 8 control p=0.003
<b>Rebbeck et al. J Clin Oncol 2004</b>	483 (105 vs 378)	BRCA 1 BRCA 2	6.4 años seg medio 2 MPx /184 control Reducción R 95%

## TIPOS DE INTERVENCIÓN

### ***Mastectomía subcutánea***

### ***Mastectomía total simple con conservación de piel +/- reconstrucción***

- Diferencias entre técnicas quirúrgicas y volumen de tejido mamario residual
- Falta de datos de estudios comparativos
- Pros/cons de la mastectomía subcutánea determinantes de la decisión paciente, oncólogo y cirujano

Metcalfe, Lancet 2005

# MASTECTOMÍA PROFILÁCTICA

PROGRAMA DE FORMACIÓN MULTIDISCIPLINAR EN CÁNCER DE MAMA

**Estrategia profiláctica  
más efectiva**

**Implicaciones  
psicológicas positivas**

**No eliminación del Riesgo**

**No evita seguimiento**

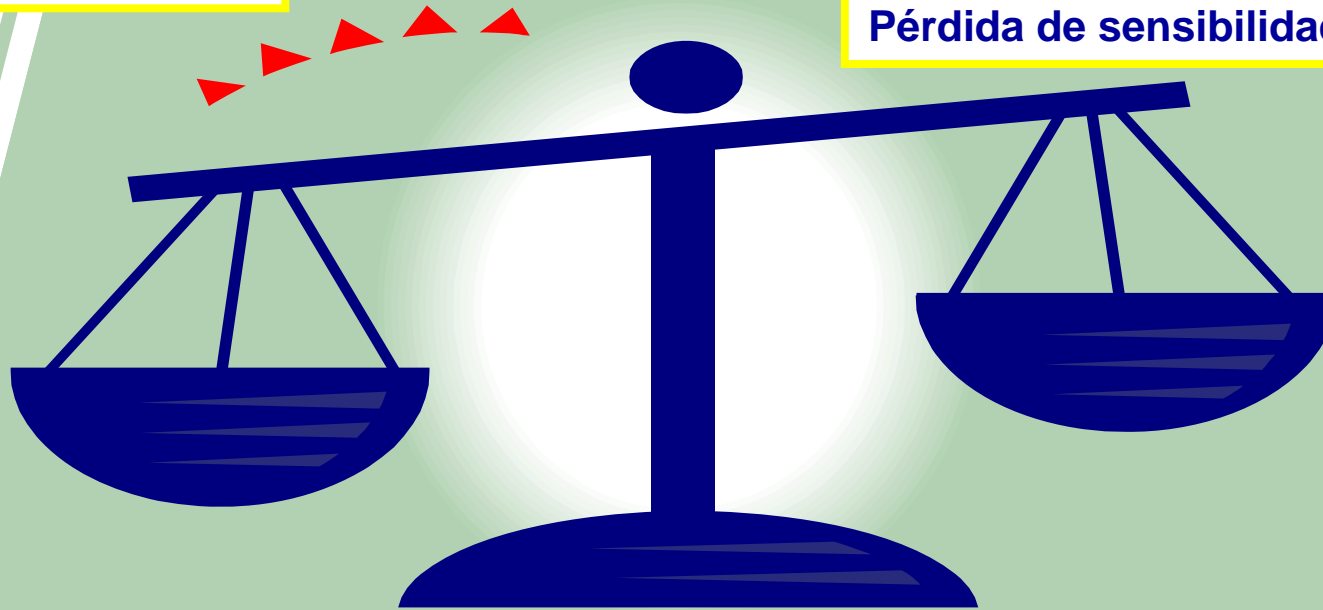
**Procedimiento irreversible**

**Morbilidad quirúrgica**

**Implicaciones psicológicas**

**Impacto sexualidad**

**Pérdida de sensibilidad**



## ESTUDIOS DE SATISFACCIÓN

- **Clinica Mayo:** 583 mujeres MPx en 30 años de seguimiento (244 MS y 384 MS +/- reconstrucción :98% implantes y 2% TRAM)
  - 83% mujeres satisfechas
  - Satisfacción MS < MT mas reconstrucción por reoperaciones en MS
  - Insatisfacción relacionada con la reconstrucción, alteración de apariencia y aumento del estrés vital

Hartmann, JCO 2005

- **Rotterdam:** 114 mujeres MPx + reconst. (prótesis) a 3 años
  - 60% mujeres satisfechas
  - Relación significativa entre insatisfacción y falta de información, complicaciones, falta de reconocimiento corporal y tipo de reconstrucción

Tibben, Plast Reconstr Surg, 2006

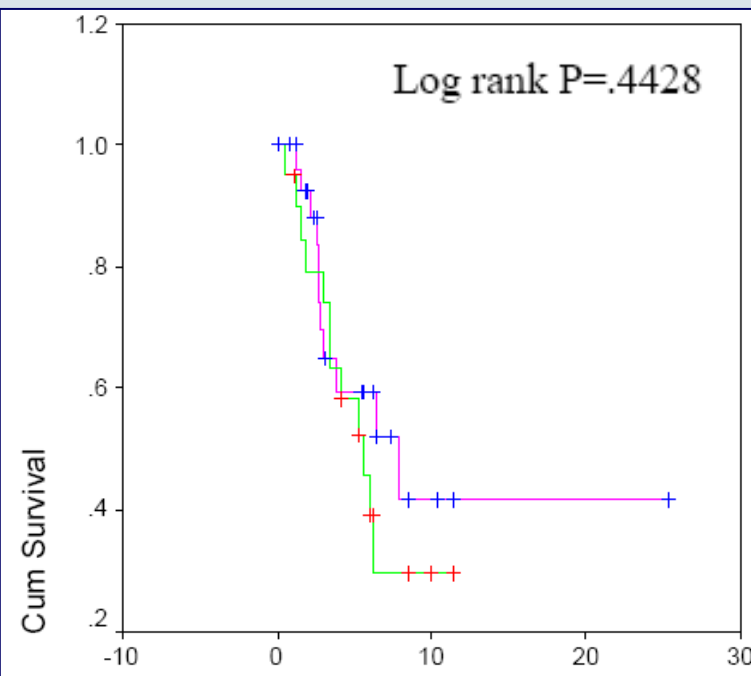
## PREDICTORES MPx

Autor/Publicación	Población	MPX	Factores predictores decisión MPx
<b>Metcalfé</b> <b>JCO 2008</b>	927 Portadoras con CM	27%	MRM previa DAP previa Edad (jóvenes)
<b>Meijers-Heijboer</b> <b>JCO 2003</b>	220 Alto riesgo con CM	35%	Edad <50 Portadoras mutación
<b>Meijers-Heijboer</b> <b>Lancet 2000</b>	75 Portadoras sanas	51%	Edad <55
<b>Friebel</b> <b>Clin.Breast.Can 2007</b>	537 Portadoras sanas	21%	Paridad Antecedente CO

JMG

## Screening for Familial Ovarian Cancer: Poor survival of BRCA1/2 related cancers

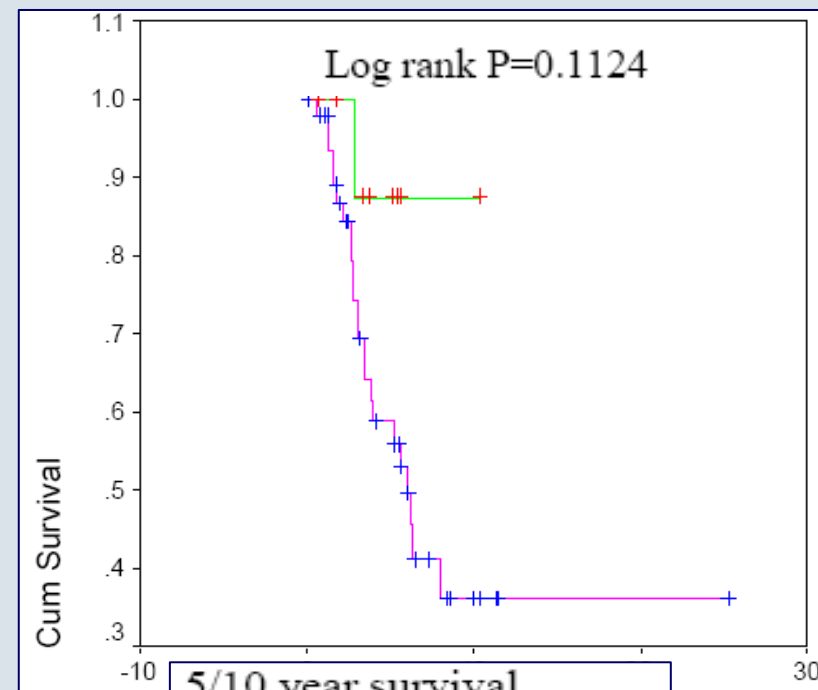
Gareth R Evans, Katja N Gaarenstroom, Diane Stirling, Andrew Shenton, Iovise Maehle, Ann Dørum, Michael Steel, Fiona Laloo, Jaran Apold, Mary Porteous, Hans F.A. Vasen, Christi van Asperen and Pal Møller



5/10 year survival

1-Prevalence 0.62/0.32

2-Incidence/interval 0.64/0.45



5/10 year survival

1. Carriers 0.59/0.36

0. Non-carriers 0.84/0.84

# DOBLE ANEXECTOMIA PROFILÁCTICA

J Natl Cancer Inst 2009;

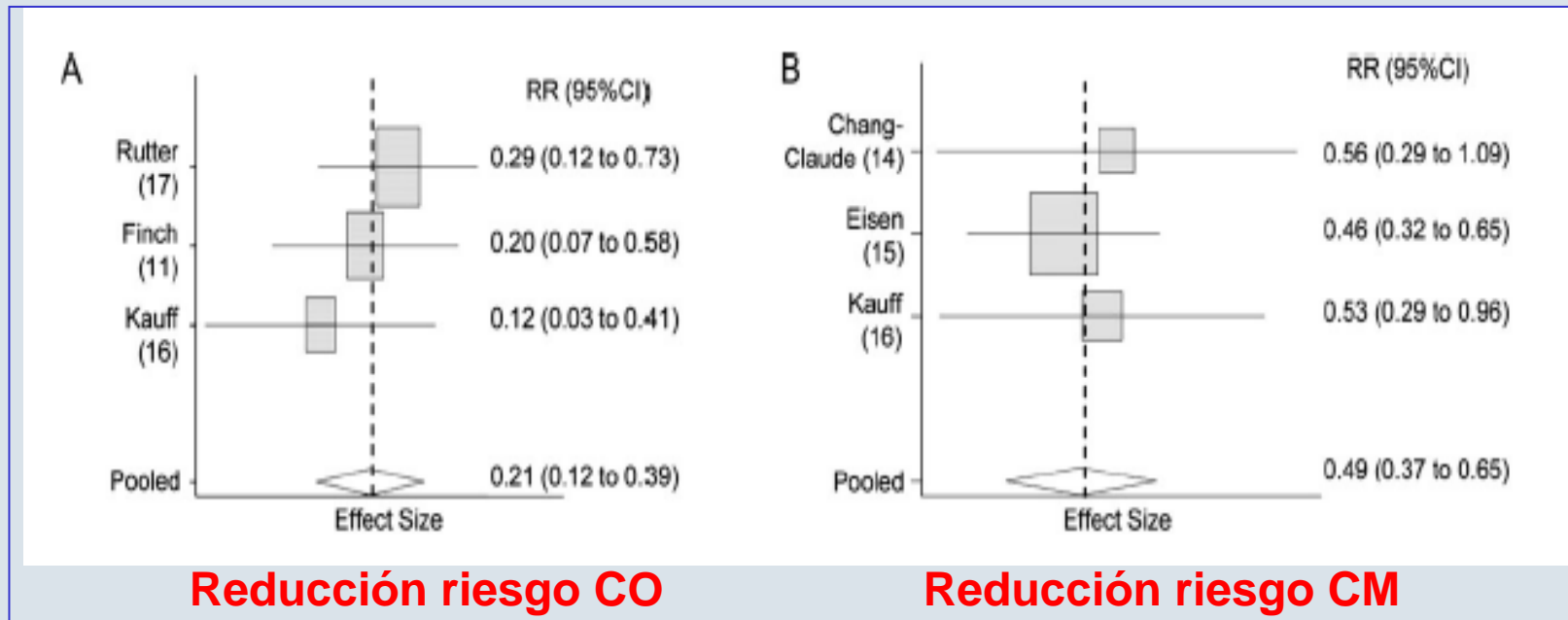


Table 4. Hazard Ratio for the Development of *BRCA*-Associated Breast Cancer After RRSO

Mutation	No. of Patients	No. of Women Electing RRSO	Mean FU (months)	No. of Breast Cancers After RRSO	No. of Women Electing Surveillance	Mean FU (months)	No. of Breast Cancers During Surveillance	Hazard Ratio	95% CI	P
<i>BRCA1</i> and <i>BRCA2</i>	597	303	36.4	19	294	33.2	28	0.53	0.29 to 0.96	.036
<i>BRCA1</i>	368	190	36.3	15	178	34.0	19	0.61	0.30 to 1.22	.16
<i>BRCA2</i>	229	113	36.6	4	116	31.9	9	0.28	0.08 to 0.92	.036

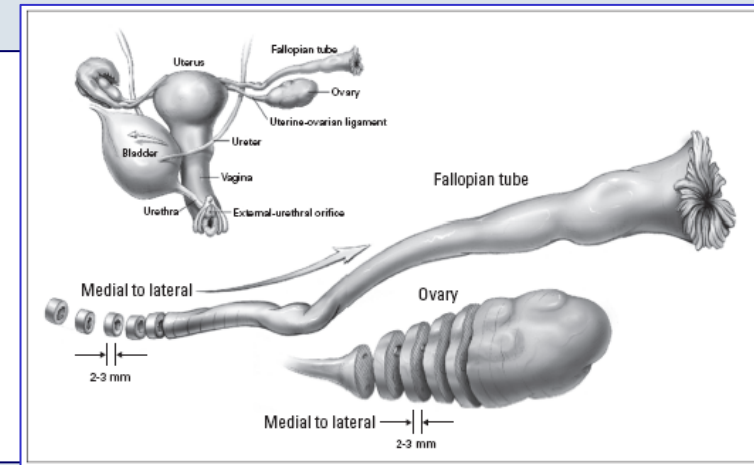
## DOBLE ANEXECTOMIA PROFILÁCTICA

Riesgo cáncer trompas en BRCA1 x120 población general

(Brose, JNCI 2002)

Cohorte prospectiva de 1828 portadoras de 32 centros:

- mediana seguimiento 3,5 años
- 32 tumores incidentes (29 ovario, 2 trompa y 1 prim periton)
- 11 tumores ocultos:



**Table 2.** Description of Cancers Diagnosed at Prophylactic Oophorectomy

Case No.	Mutation	Age at Prophylactic Oophorectomy, y	Site	Surgical Stage	Previous Breast Cancer	Vital Status and Age at Follow-up, y
1	BRCA1	49	Ovary	IIIC	Yes	Alive at 50
2	BRCA1	43	Ovary	IIIC	Yes	Alive at 46
3	BRCA1	51	Ovary	NA	Yes	Alive at 56
4	BRCA1	38	Ovary	IIIC	Yes	Alive at 39
5	BRCA2	68	Tubal	IA	Yes	Alive at 69
6	BRCA1	45	Malignant cytology	NA	No	Alive at 46
7	BRCA1	40	Ovary	IA	Yes	Dead of disease at 44
8	BRCA2	51	Tubal	IA	No	Alive at 57
9	BRCA1	49	Tubal	IIIC	No	Alive at 51
10	BRCA1	45	Ovary	NA	Yes	Alive at 46
11	BRCA1	46	Ovary	NA	Yes	Alive at 47

## DOBLE ANEXECTOMIA PROFILÁCTICA

American Journal of Obstetrics and Gynecology (2004) 191, 1113–23

- Riesgo primario peritoneal del 2% de 1 a 30 años post cirugía

- Tasa de cáncer ovario oculto del 2.5% (3-4%) según estudios

**Table V** Incidence of PPC after PO

Study	Patients (n)	Patients with PPC (n)
Rebbeck et al <sup>29</sup>	259	2 (0.8%)
Kauff et al <sup>28</sup>	191	1 (0.5%)
Struewing et al <sup>16</sup>	44	2 (4.5%)
Piver et al <sup>27</sup>	324	6 (1.8%)
Tobacman et al <sup>15</sup>	28	3 (10.7%)
TOTAL	846	14 (1.7%)

**Table VI** Incidence of occult ovarian cancer at PO

Study	Patients (n)	Patients with occult ovarian carcinoma (n)
Rebbeck et al <sup>29</sup>	259	6 (2.3%)
Kauff et al <sup>28</sup>	98	3 (3.1%)
Leeper et al <sup>31</sup>	30	5 (16.7%)
Colgan et al <sup>30</sup>	60	5 (8.3%)
Lu et al <sup>32</sup>	50	2 (4.0%)
TOTAL	497	21 (4.2%)

## Effect of Short-Term Hormone Replacement Therapy on Breast Cancer Risk Reduction After Bilateral Prophylactic Oophorectomy in *BRCA1* and *BRCA2* Mutation Carriers: The PROSE Study Group

### Methods

We identified a prospective cohort of 462 women with disease-associated germline *BRCA1/2* mutations at 13 medical centers to evaluate breast cancer risk after BPO with and without HRT. We determined the incidence of breast cancer in 155 women who had undergone BPO and in 307 women who had not undergone BPO on whom we had complete information on HRT use. Postoperative follow-up was 3.6 years.

### Results

Consistent with previous reports, BPO was significantly associated with breast cancer risk reduction overall (hazard ratio [HR] = 0.40; 95%CI, 0.18 to 0.92). Using mutation carriers without BPO or HRT as the referent group, HRT of any type after BPO did not significantly alter the reduction in breast cancer risk associated with BPO (HR = 0.37; 95% CI, 0.14 to 0.96).

**Table 3.** Breast Cancer Risk Reduction After BPO Stratified by Postsurgical HRT Use

Variable		Total Sample			BPO Before Age 50		
		No.	HR	95% CI*	No.	HR	95% CI*
No surgery	No HRT	286	1.0	—	286	1.0	—
BPO	No HRT	62	0.38	0.09 to 1.59	50	0.59	0.14 to 2.52
BPO	Any HRT	93	0.37	0.14 to 0.96	89	0.30	0.11 to 0.85
BPO	E2 only	50	0.44	0.12 to 1.61	50	0.44	0.12 to 1.61
BPO	PROG ± E2	34	0.43	0.07 to 2.68	34	0.43	0.07 to 2.68

## Hormone Therapy and the Risk of Breast Cancer in *BRCA1* Mutation Carriers

Andrea Eisen, Jan Lubinski, Jacek Gronwald, Pal Moller, Henry T. Lynch, Jan Klijn, Charmaine Kim-Sing, Susan L. Neuhausen, Lucy Gilbert, Parviz Ghadirian, Siranoush Manoukian, Gad Rennert, Eitan Friedman, Claudine Isaacs, Eliot Rosen, Barry Rosen, Mary Daly, Ping Sun, Steven A. Narod, and the Hereditary Breast Cancer Clinical Study Group

J Natl Cancer Inst 2008;100:1361-1367

**Results** In this group of *BRCA1* mutation carriers, the adjusted OR for breast cancer associated with ever use of HT compared with never use was 0.58 (95% CI = 0.35 to 0.96;  $P = .03$ ). In analyses by type of HT, an inverse association with breast cancer risk was observed with use of estrogen only (OR = 0.51, 95% CI = 0.27 to 0.98;  $P = .04$ ); the association with use of estrogen plus progesterone was not statistically significant (OR = 0.66, 95% CI = 0.34 to 1.27;  $P = .21$ ).

**Conclusion** Among postmenopausal women with a *BRCA1* mutation, HT use was not associated with increased risk of breast cancer; indeed, in this population, it was associated with a decreased risk.

### CONSIDERACIONES:

- Seguimiento limitado del efecto del THS sobre el R CM en portadoras  
(Rebeck JCO'05, Eisen JNCI'08)
- Desconocido el efecto del THS en portadoras con antecedente CM RH negativo

## PREDICTORES DAP

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