MASTECTOMIA CONTRALATERAL EM PACIENTES BRCA MUTADAS
- IMPACTO NA SOBREVIDA -

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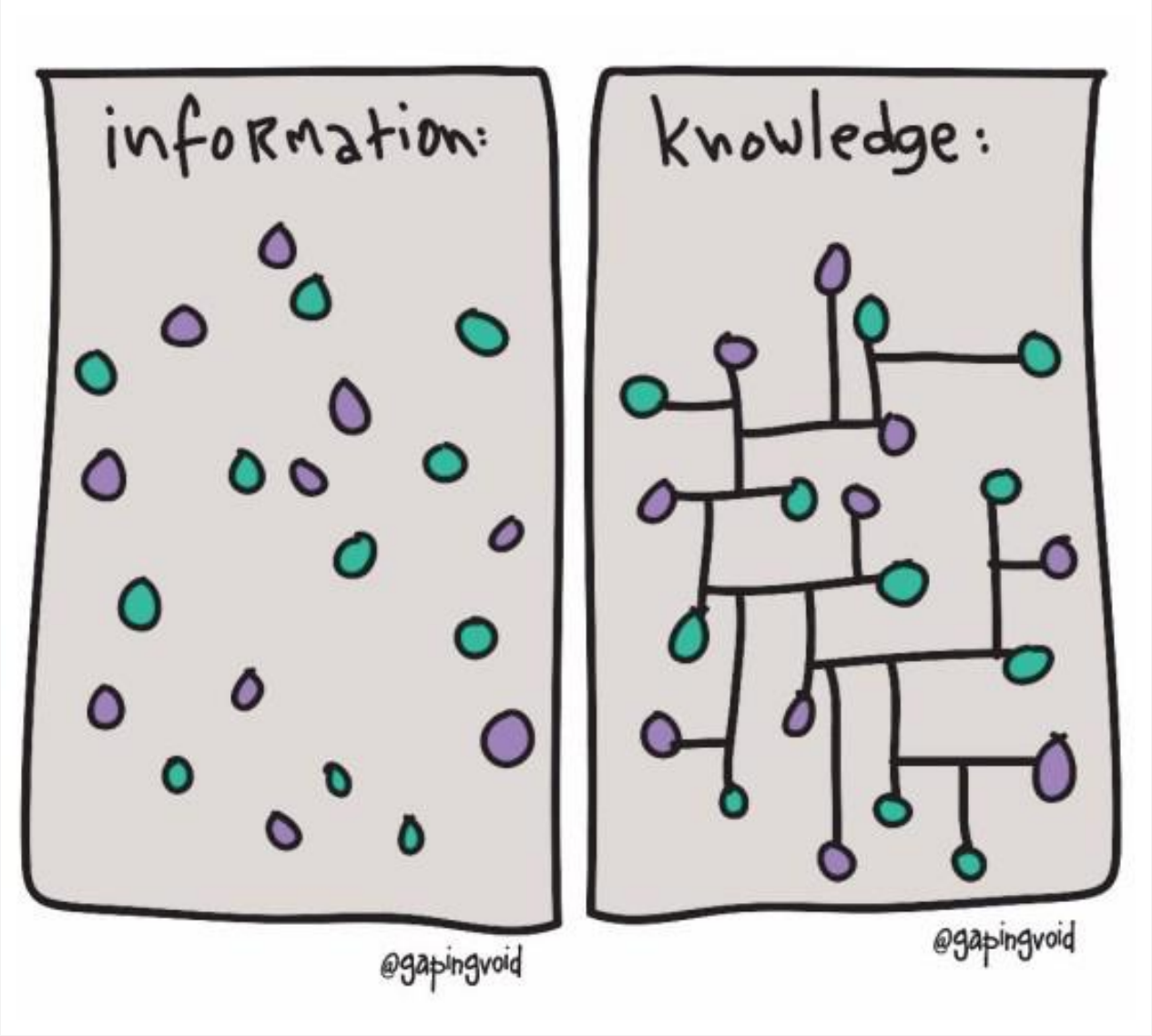
2019

MASTECTOMIA PROFILÁTICA CONTRALATERAL

- Testes genéticos
- Medo de morrer pelo câncer
- Medo de ter de lidar novamente!
- Simetrizacão
- Elevada Eficácia

MASTECTOMIA PROFILÁTICA CONTRALATERAL

- Diagn CA (BRCA+) – CURA – ter novo CA contralateral – morte (LEVA TEMPO)
- Risco de recorrência (frente a outras terapias)
- Risco de câncer contralateral (frente a outras terapias)
- Ponderação dos prejuízos
- Impacto da informação



Multi-gene testing is a new and rapidly growing field, but there is currently a **lack of evidence** regarding proper procedures and risk management strategies that should follow testing, especially when pathogenic or likely pathogenic variants are found for moderate-penetrance genes and when a VUS is found

NCCN 2019

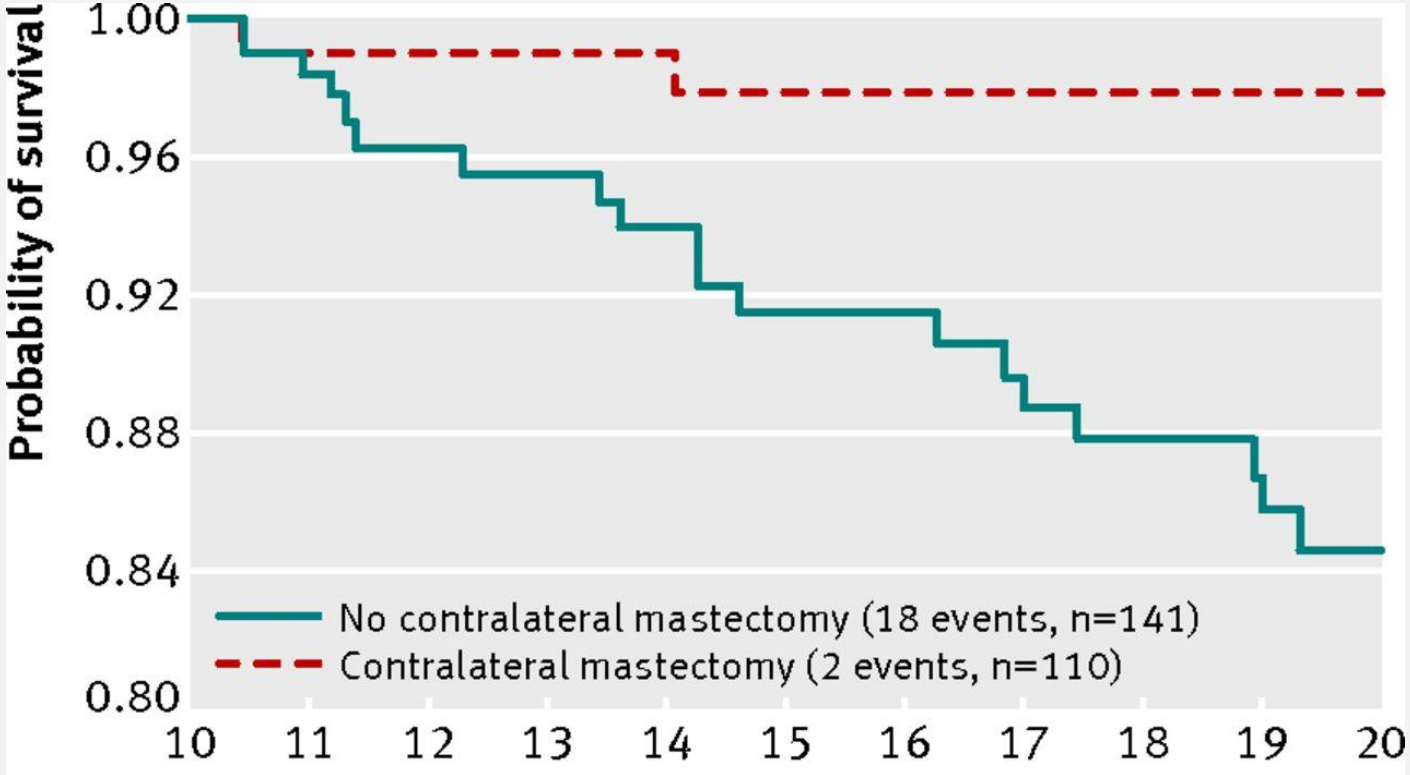
RESEARCH Contralateral mastectomy and survival after breast cancer in carriers of BRCA1 and BRCA2 mutations: retrospective analysis

BMJ 2014; 348 doi: https://doi.org/10.1136/bmj.g226 (Published 11 February 2014)Cite this as: *BMJ* 2014;348:g226

1.Kelly Metcalfe, professor[1], adjunct scientist[2],
2.Shelley Gershman, registered nurse[12],
3.Parviz Ghadirian, professor[3],
4.Henry T Lynch, professor[4],
5.Carrie Snyder, registered nurse[4],
6.Nadine Tung, associate professor[5],

Characteristics	Unilateral mastectomy (n=209)	Bilateral mastectomy (n=181)	P value
Age at diagnosis (years)	43.6	41.3	0.01
Year of diagnosis	1987	1994	<10 to 4
Size of tumour (cm):			
0-2	114 (55.9)	114 (65.1)	0.07
2.1-5	90 (44.1)	61 (34.9)	
Mean (range) size	2.3 (0.2-5.0)	1.9 (0.1-5.0)	0.006
Positive lymph nodes	89 (43.0)	70 (38.7)	0.39
Chemotherapy	115 (57.5)	121 (68.4)	0.03
O			
Ta			
C ca			
Died from breast cancer	61 (29.2)	18 (9.9)	<10 to 4
Radiotherapy	41 (20.5)	30 (16.6)	0.33
BRCA1	123 (60.0)	103 (57.5)	0.63
BRCA2	82 (40.0)	76 (42.5)	

Contralateral breast câncer 70 (33.5) x 1 (0.6)<10 to 4
Died from breast câncer 61 (29.2) x 18 (9.9)<10 to 4



No in study

Contralateral mastectomy	110	104	95	92	83	71	61	58	45	42	39
No contralateral mastectomy	141	134	127	122	116	108	101	94	87	83	72

Contralateral mastectomy was associated with a **48%** reduction in death from breast cancer (hazard ratio 0.52, 95% confidence interval 0.29 to 0.93; P=0.03).

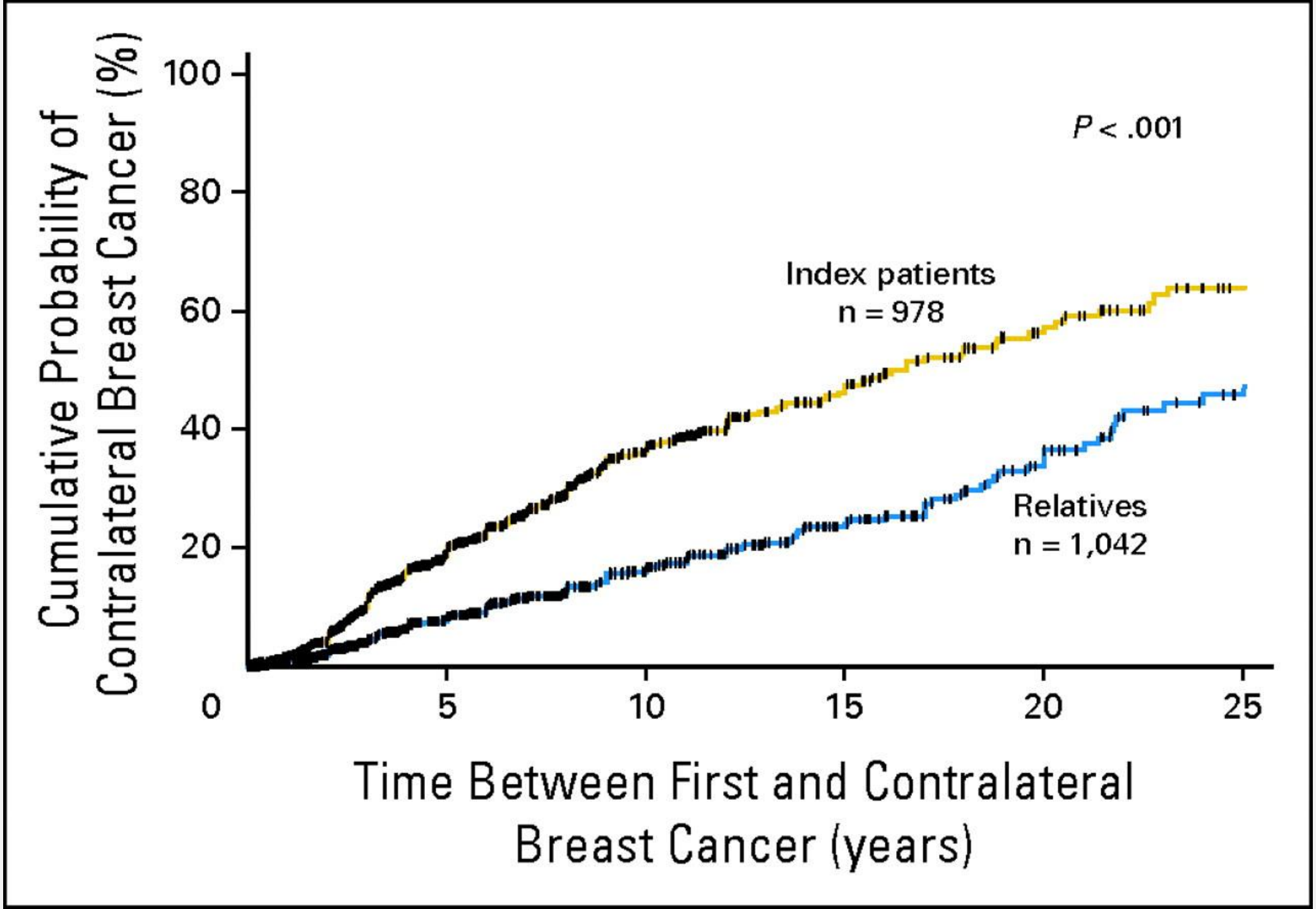
In a propensity score adjusted analysis of 79 matched pairs, the association **was not significant** (0.60, 0.34 to 1.06; P=0.08)

J Clin Oncol. 2009 Dec 10;27(35):5887-92. doi: 10.1200/JCO.2008.19.9430. Epub 2009 Oct 26.

Contralateral breast cancer risk in BRCA1 and BRCA2 mutation carriers.

Graeser MK[1], Engel C, Rhiem K, Gadzicki D, Bick U, Kast K, Froster UG, Schlehe B, Bechtold A, Arnold N, Preisler-Adams S, Nestle-Kraemling C, Zaino M, Loeffler M, Kiechle M, Meindl A, Varga D, Schmutzler RK.

A retrospective, multicenter, cohort study was performed from 1996 until 2008 and comprised 2,020 women with unilateral breast cancer (index patients, n = 978; relatives, n = 1.42) from 978 families who had a BRCA1 or BRCA2 mutation.


Cumulative Probability of Contralateral Breast Cancer (%)
100
80
60
40
20
0
5
10
15
20
25
P < .001
Index patients
n = 978
Relatives
n = 1,042
Time Between First and Contralateral Breast Cancer (years)

Pacientes BRCA 1,2 mutadas com câncer de mama

- 10y risk **31%** (<40y)
- 10y risk **8%** (>50y)

Pacientes BRCA 1,2 mutadas com câncer de mama

- 25y risk **63%** (<40y)
- 25y risk **19,6%** (>50y)

MASTECTOMIA PROFILÁTICA CONTRALATERAL

Improved overall survival after contralateral risk-reducing mastectomy in BRCA1/2 mutation carriers with a history of unilateral breast cancer: A prospective analysis

Bernadette A.M. Heemskerk-Gerritsen
Matti A. Rookus
Cora M. Aalfs
... See all authors

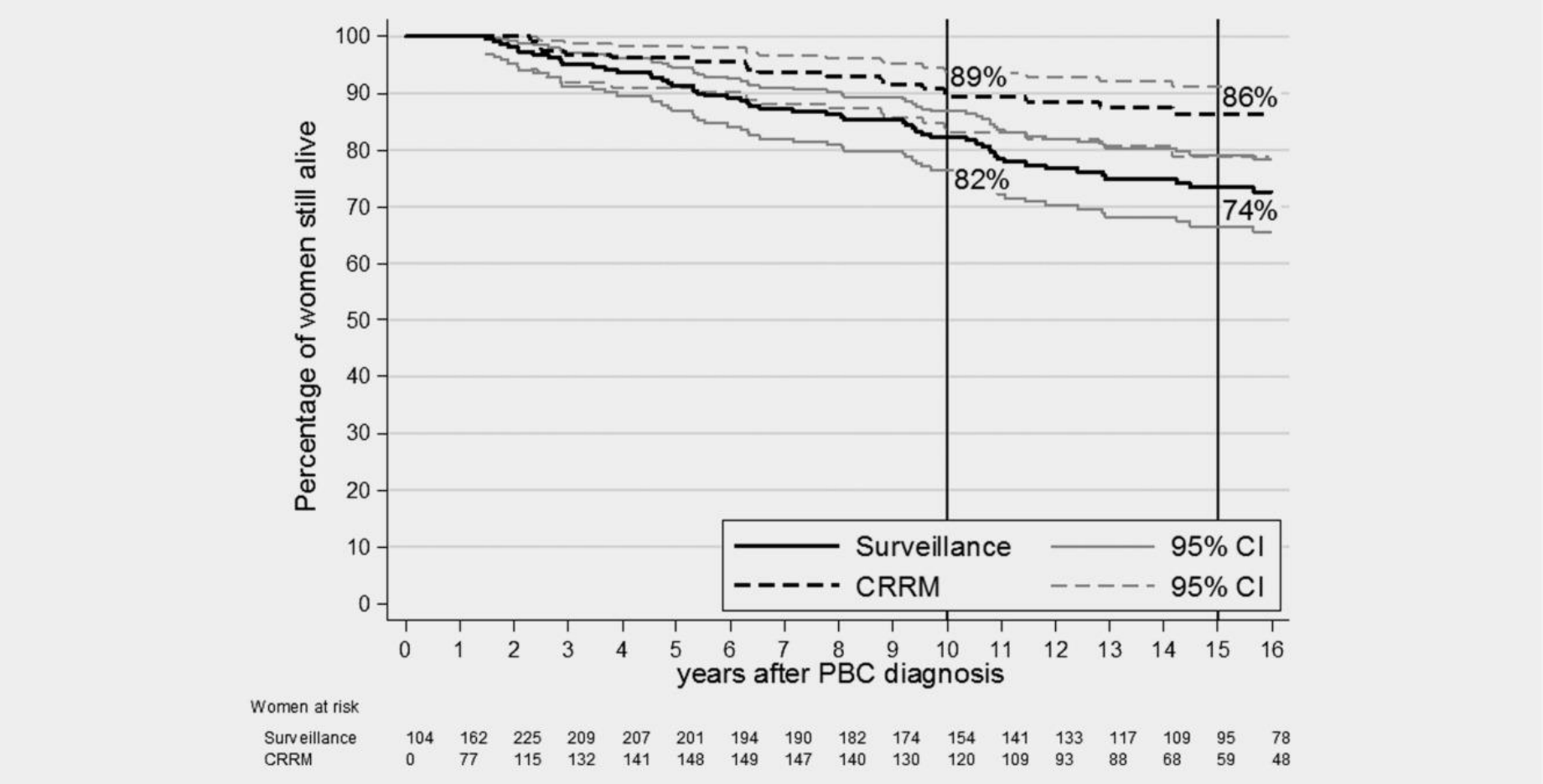
Int J Cancer. 2015

https://doi.org/10.1002/ijc.29032

Table 3. Efficacy of contralateral risk-reducing mastectomy on overall survival

Analysis[a]	Group	Person years of observation	Deaths	Mortality[b] (95 % CI)	HR (95% CI)
(a)	Surveillance	3007	65	**21.6** (16.9–27.6)	Ref.
	CRRM	1975	19	**9.6** (6.1–15.1)	0.43 (0.26–0.72)[c]
					0.49 (0.29–0.82)[d]
(b)	Surveillance	2673	56	21.0 (16.1–27.2)	Ref.
	CRRM	1837	18	9.8 (6.2–15.5)	0.46 (0.27–0.79)[c]
					0.55 (0.32–0.95)[d]

Improved overall survival after contralateral risk-reducing mastectomy in BRCA1/2 mutation carriers with a history of unilateral breast cancer: A prospective analysis



International Journal of Cancer, Volume: 136, Issue: 3, Pages: 668-677, First published: 20 June 2014, DOI: (10.1002/ijc.29032)

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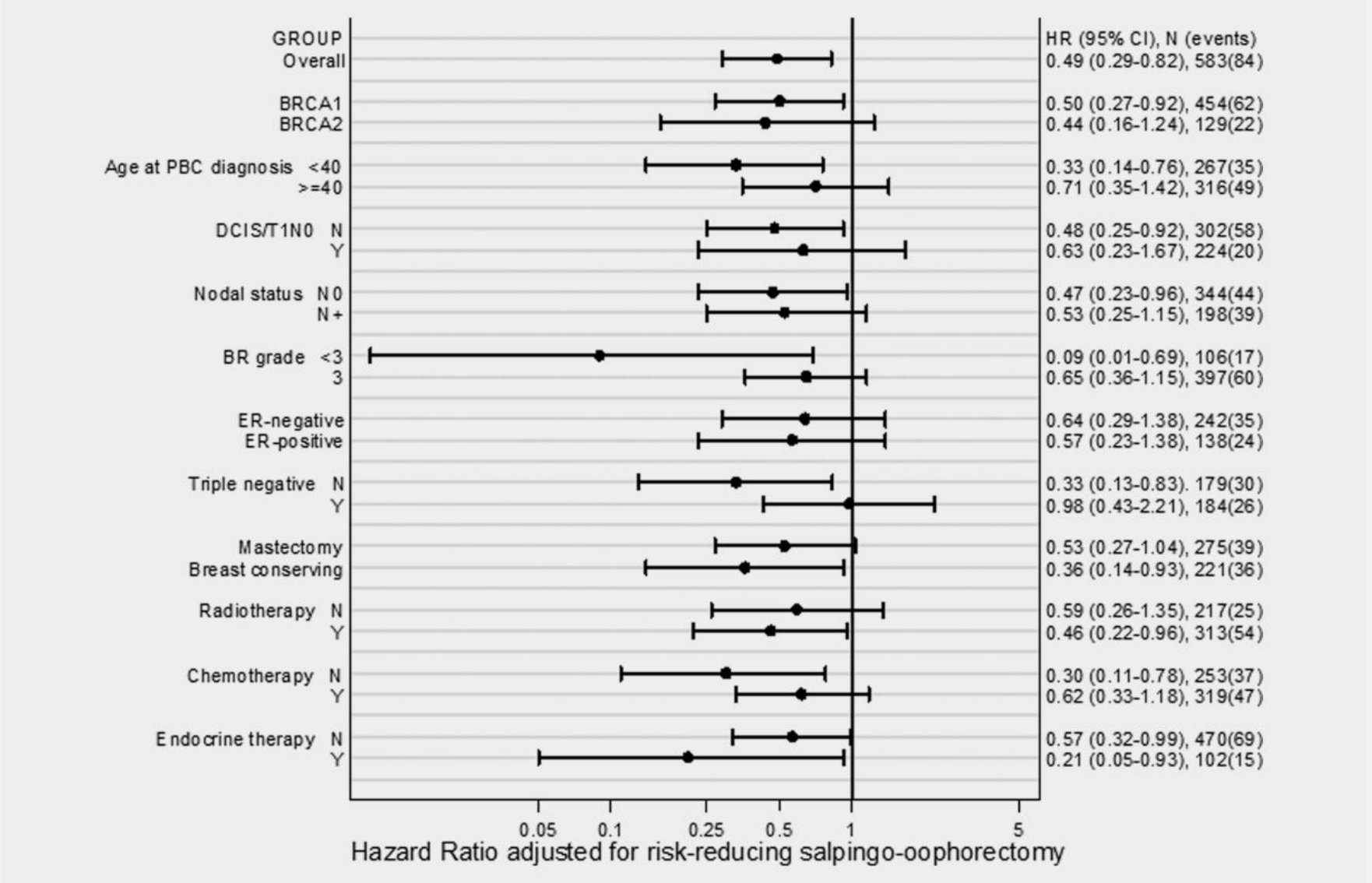

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Of note, the risk of developing CBC is not the same for all PBC patients, and may depend on age at PBC diagnosis, ER-status, and given adjuvant systemic therapy

Greatest survival benefits after CRRM are expected in subgroups of patients at **high risk of CBC** and low risk of primary BC-specific **mortality.**

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

Ideally, one should offer CRRM to PBC patients with a high CBC risk and a low risk of dying from PBC

Breast Cancer Res Treat. 2011

The impact of contralateral mastectomy on mortality in BRCA1 and BRCA2 mutation carriers with breast cancer.

Narod SA[1].

Author information:

1. Womens College Research Institute and Dalla Lana School of Public Health, University of Toronto

The cumulative mortality from the first breast cancer will be 9.6% at 5 years, 18.3% at 10 years, and 33.3% at 20 years.

The cumulative mortality from new contralateral breast cancers will be 0.4% at 5 years, 1.7% at 10 years, and 6.8% at 20 years.

At 20 years, the probability of dying of contralateral breast cancer is 6.8%

Am J Surg. 2016 Oct;212(4):660-669. doi: 10.1016/j.amjsurg.2016.06.010. Epub 2016 Jul 18.

Risk reduction and survival benefit of prophylactic surgery in BRCA mutation carriers, a systematic review.

Ludwig KK[1], Neuner J[2], Butler A[3], Geurts JL[4], Kong AL[5].
Author information

1Department of Surgery, Indiana University School of Medicine, Carmel, IN, USA.2Division of General Internal Medicine, Department of Medicine, Medical College of Wisconsin, Milwaukee, WI, USA.3Division of Surgical Oncology,

Results Bilateral risk-reducing mastectomy provides a **90% to 95%** risk reduction in BRCA mutation carriers, although the data do not demonstrate improved mortality.

DIRETRIZES INTERNACIONAIS

THE AMERICAN SOCIETY OF
Breast Surgeons

- Official Statement -

Consensus Guideline on Genetic Testing for Hereditary Breast Cancer

1.Breast surgeons, genetic counselors, and other medical professionals knowledgeable in genetic testing can provide patient education and counseling and make recommendations to their patients regarding genetic testing and arrange testing

2. Genetic testing should be made available to all patients with a personal history of breast cancer.

3.Patients who had genetic testing previously may benefit from updated testing.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

Breast Cancer

Version 3.2019 — September 6, 2019

NCCN.org

CLINICAL STAGE	WORKUP[a]		
T0-3,N1,M0 T1-3,N0-1,M0 →	• History and physical exam • Diagnostic bilateral mammogram; ultrasound as necessary • Axillary assessment with exam; ultrasound or other imaging as necessary, and percutaneous biopsy of suspicious nodes • Pathology review[c] • Determination of tumor estrogen/progesterone receptor (ER/PR) status and HER2 status[d] • Genetic counseling if patient is at risk[e] for hereditary breast cancer • Breast MRI[f] (optional), with special consideration for mammographically occult tumors • Counseling for fertility concerns if premenopausal; pregnancy test in all women of childbearing potential[g] • Assess for distress[h]	Consider additional studies only if directed by signs or symptoms:[i] • Complete blood count (CBC) • Comprehensive metabolic panel, including liver function tests and alkaline phosphatase • Bone scan indicated if localized bone pain or elevated alkaline phosphatase or sodium fluoride PET/CT[j] (category 2B) • Abdominal ± pelvic diagnostic CT with contrast or MRI with contrast indicated if elevated alkaline phosphatase, abnormal liver function tests, abdominal symptoms, or abnormal physical examination of the abdomen or pelvis • Chest diagnostic CT with contrast (if pulmonary symptoms present) • FDG PET/CT[k,l] (optional)	→ See Locoregional Treatment (BINV-2)

If considering preoperative systemic therapy[b] for T0-4,N1-3,M0 or T2-4,N0,M0 → See Workup Prior to Preoperative Systemic Therapy (BINV-11)

Recurrent or Stage IV (M1) → See Workup for Recurrent or Stage IV (M1) Disease (BINV-18)

TESTING CRITERIA FOR HIGH-PENETRANCE BREAST AND/OR OVARIAN CANCER SUSCEPTIBILITY GENES

(This often includes *BRCA1, BRCA2, CDH1, PALB2, PTEN,* and *TP53* among others. See GENE-A for a more complete list.)[a,b,c,d]

Testing is clinically indicated in the following scenarios:

1. Individuals with any blood relative with a known pathogenic/likely pathogenic variant in a cancer susceptibility gene
2. Individuals meeting the criteria below but with previous limited testing (eg, single gene and/or absent deletion duplication analysis) interested in pursuing multi-gene testing
3. *Personal history of cancer*
   - Breast cancer with at least one of the following:
     - Diagnosed at age ≤45 y; or
     - Diagnosed at age 46–50 y with:
       - Unknown or limited family history; or
       - A second breast cancer diagnosed at any age; or
       - ≥1 close blood relative[e] with breast, ovarian, pancreatic, or high-grade (Gleason score ≥7) or intraductal prostate cancer at any age
     - Diagnosed at age ≤60 y with triple-negative breast cancer;
   - Metastatic or intraductal prostate cancer at any age[h]
   - High-grade (Gleason score ≥7) prostate cancer with:
     - Ashkenazi Jewish ancestry; or
     - ≥1 close relative[e] with breast cancer at age ≤50 y or ovarian, pancreatic, or metastatic or intraductal prostate cancer at any age; or
     - ≥2 close relatives[e] with breast or prostate cancer (any grade) at any age.
   - A mutation identified on tumor genomic testing that has clinical implications if also identified in the germline
   - To aid in systemic therapy decision-making, such as for HER2-negative metastatic breast cancer[i]
4. *Family history of cancer*
   - An affected or unaffected individual with a first- or second-degree blood relative meeting any of the criteria listed

Criteria met → See GENE-1

If testing criteria not met, consider testing for other hereditary syndromes → If criteria for other hereditary syndromes not met, then cancer screening as per NCCN Screening Guidelines

Studies have reported *BRCA1* mutations in 7% to 28% of patients with triple-negative breast cancer.[75,113,146-153]

triple-negative disease, *BRCA* mutation carriers were diagnosed at a younger age compared with non-carriers,

39 years

60a

T1N0M0

TNBC

BRCA 1

MASTECTOMIA CONTRALATERAL?