

Breast Cancer Screening In High Risk Individuals

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Screening in High Risk Individuals

- Who is a “high risk” individual ?
 - What is the preferred method of screening ?
 - Is there an alternative to screening ?
 - What is the data on outcome after such screening protocol ?
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Who is defined as “high risk” ?

□ Commonly used criteria

- Personal history of breast cancer
 - age at onset

- Personal history of related cancers
 - double primaries

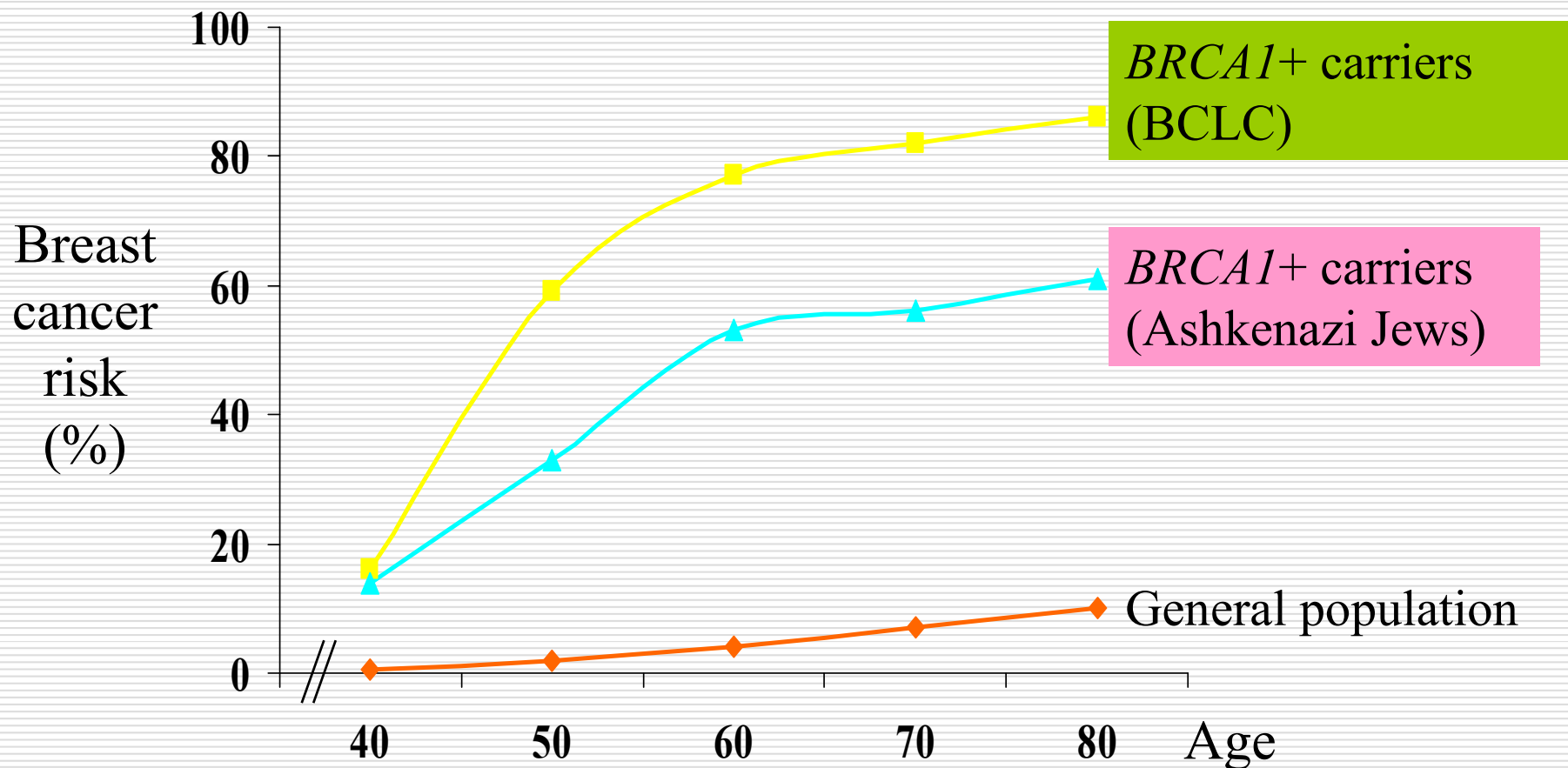
- Family history of breast cancers

- Family history of related cancers

□ High risk due to mutation testing

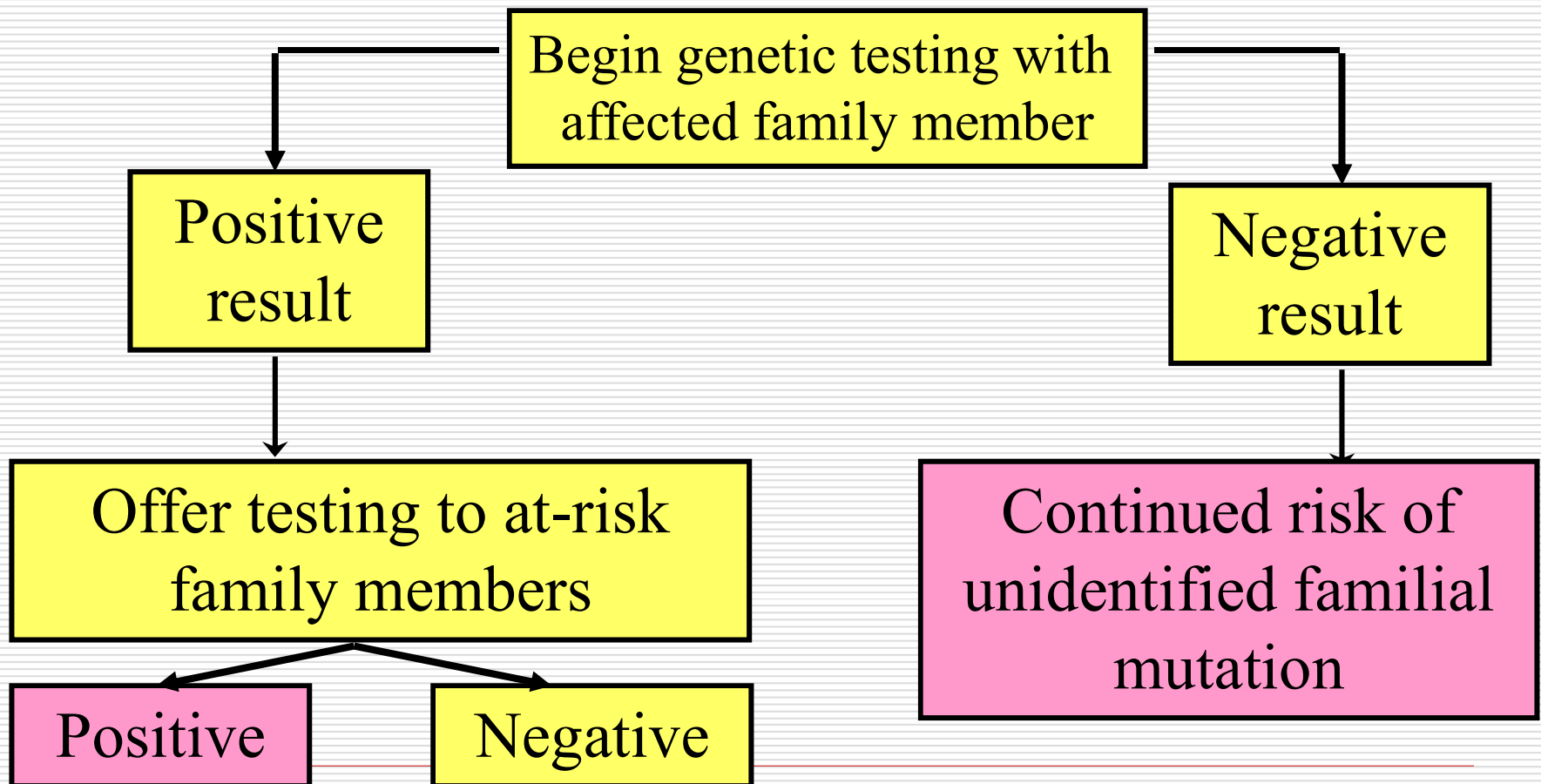
- carrier of a BRCA1 or 2 mutation

Comparing Breast Cancer Risk Estimates in BRCA Mutation Carriers



Easton DF et al. *Am J Hum Genet* 56:265, 1995
Struwing JP et al. *N Engl J Med* 336:1401, 1997

Genetic Testing for Hereditary Cancer in family members



Scoring system for likelihood of being a genetic mutation carrier

- BRCAPRO 2001
 - Myriad model 2002
 - Manchester scoring 2003
 - IBIS 2004
 - BOADICEA 2006
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Manchester scoring system

Cancer and patient age	<i>BRCA1</i>	<i>BRCA2</i>
FBC <30	6	5
FBC 30–39	4	4
FBC 40–49	3	3
FBC 50–59	2	2
FBC >59	1	1
MBC <60	5 (if <i>BRCA2</i> tested); for combined, score = 5 without prior testing	8
MBC >59	5 (if <i>BRCA2</i> tested); for combined, score = 5 without prior testing	5
Ovarian cancer <60	8	5 (if <i>BRCA1</i> tested); for combined, score = 5 without prior testing
Ovarian cancer >59	5	5 (if <i>BRCA1</i> tested); for combined, score = 5 without prior testing
Pancreatic cancer	0	1
Prostate cancer <60	0	2
Prostate cancer >59	0	1

Table 1 Detection rates for *BRCA1* and *BRCA2* mutations in breast ovary double primaries and first degree ovarian (ov) cancer

Group	Number of ovary/ breast in family	Br/ov in index	Manchester score	BRCA1 and BRCA2			
				BRCA1	BRCA2	BRCA2	None
Isolated breast/ovary	1ov 1br	Yes	All	2	1	3/22 (14%)	19/22 (86%)
			>15	2	0	2/11 (18%)	9/11 (82%)
FDR pair*	1ov 1br	No	All	10	7	17/99 (17%)	82/99 (83%)
			>15	10	6	16/84 (19%)	68/84 (81%)
			>19	6	3	9/25 (36%)	16/25 (64%)
Isolated Breast/ovary†	1ov 2br	Yes	All	2	1	3/6 (50%)	3/6 (50%)
Br/ovary + other breast in family	1ov 2br	Yes	All	4	0	4/16 (25%)	12/16 (80%)
Br/ovary double primary	All	Yes	All	36	13	49/100 (49%)	51/100 (51%)
			>19	34	10	44/71 (62%)	27/71 (38%)
			>29	28	9	37/50 (74%)	13/50 (26%)
			>39	19	4	23/28 (82%)	5/28 (18%)

*Sister pair or mother and daughter one with breast cancer the other ovarian cancer.

†Bilateral breast cancer and ovarian cancer in one woman and no family history.

Risk ladder for BRCA1/2 mutation

- ❑ Bilat Br + Ov in 1 upto 50%
 - ❑ Bilat Br in 1 + Ov in 1 25-40%
 - ❑ Br + Ov in 1 + Br or Ov 25%
 - ❑ BR in 1 + Ov in 1 17-35%
 - ❑ Br and Ov in 1 14-18%
 - ❑ Br in young age <40 5-8%
 - ❑ Average age single case <1%
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What to do if being “high risk” ?

- Option 1 Continued surveillance
 - Option 2 Risk reduction surgery
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Preferred screening method

Method	Sens	Spec	Outcome data
Mammo	36	99.8	Y
US	25-59	75-96	N
M+US	49-67	-	Y
MRI	77	95.4	N
M+MRI	86-98	97-98	N

JAMA. 2004 Sep 15;292(11):1317-25.

CA Cancer J Clin 2007;57 and www.cancer.org

Surveillance Options for Breast Cancer in BRCA-Mutation Carriers

- Monthly breast self-exams (begin by age 18) *and*
- Early clinical surveillance (begin at age 25-30)
 - annual clinical breast exams
 - annual mammography
 - Combination mammography + others

ACS recommendation 2008

- Women at high risk (greater than 20% lifetime risk) should get an MRI and a mammogram every year. Women at moderately increased risk (15% to 20% lifetime risk) should talk with their doctors about the benefits and limitations of adding MRI screening to their yearly mammogram. Yearly MRI screening is not recommended for women whose lifetime risk of breast cancer is less than 15%.**
 - Starting age for screening is 30 yrs of age (no clear consensus)**
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Risk reduction surgery

- Mastectomy --→ 93-95% risk reduction
- Oophorectomy → 90% risk reduction

Surveillance Options for Ovarian Cancer in BRCA-Mutation Carriers

- No proven methodology
- Annually or semiannually, starting at 25–35
 - transvaginal ultrasound w/color Doppler imaging
 - CA-125 II

Breast cancer prophylaxis

- **All five randomised prevention trials comparing tamoxifen or raloxifene with placebo were included**
- **Tamoxifen prevention trials showed a 38% (95% CI 28-46; $p < 0.0001$) reduction in breast-cancer incidence**
- **There was no effect for breast cancers negative for oestrogen receptor (ER; hazard ratio 1.22 [0.89-1.67]; $p = 0.21$), but ER-positive cancers were decreased by 48% (36-58; $p < 0.0001$) in the tamoxifen prevention trials**
- **Rates of endometrial cancer were increased in all tamoxifen prevention trials (consensus relative risk 2.4 [1.5-4.0]; $p = 0.0005$)**