

# Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

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Guidelines Breast  
Version 2009.1.0

## Breast Cancer Risk and Prevention



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- **Version 2003:**  
**Kiechle, Schmutzler**
- **Version 2004–2008:**  
**Maass / Schmutzler / Thomssen**
- **Version 2009:**  
**Schmutzler, Blohmer**

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# Principles in Prevention

- **Women at increased risk for breast cancer are not considered *patients* but *healthy women* or *counselees***
- **A comprehensive informed consent taking into consideration all potential side effects and risks is warranted prior to offering preventive measures**
- **Highest priority: „First, do no harm!“  
(*Primum nil nocere*)**

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# Who Should be Tested for BRCA1/2 Mutations?

**Oxford LoE: 2b**

**GR: B**

**AGO: ++**

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## **Families with\*,#**

**at least 3 women with breast cancer independent of age in one line**

**at least two women with breast cancer, one < 51 yrs in one line**

**at least one woman affected by breast and one by ovarian cancer in one line**

**at least one woman affected by breast and ovarian cancer in one line**

**at least two women affected by ovarian cancer in one line**

**at least one woman affected by bilateral breast cancer < 51 yrs in one line**

**at least one woman affected by breast cancer < 36 yrs in one line**

**at least one man affected by breast cancer and one additional relative  
affected by breast or ovarian cancer in one line**

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**\*one side of the family**

**#Inclusion criteria of the German Consortium of Hereditary Breast and Ovarian Cancer (GCHBOC) based on a mutation detection rate  $\geq 10\%$**

# Other Risk Genes

**Based on the hypothesis that cancer susceptibility is largely transmitted by a polygenic trait, new susceptibility genes (eg ATM, CHEK2, PALB, FGFR2, TNAC9...) that confer low to moderate risk have been identified by association studies.**

**However, risk profiles of the known variants do not yet allow risk stratification for the provision of clinical prevention or surveillance strategies**

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LoE / GR

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**Clinical genetic testing for low risk variants**

**3b D --**

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# Surveillance Programm for Women at High Risk\*

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LoE / GR

## Multimodal intensive surveillance program\*

➤ For the detection of early stage breast cancers		<b>2a</b>	<b>B</b>	<b>++</b>
➤ Clinical breast exam	≥25 years	semi-annually		
➤ Sonography	≥25 years	semi-annually		
➤ Mammography	≥30 years	annual		
➤ Breast MRI	≥30 years	annual		
➤ For mortality reduction		<b>5</b>	<b>D</b>	<b>+</b>

\*Definition of high risk: deleterious mutation in the BRCA1 or BRCA2 gene or heterozygous risk of ≥ 20% or remaining life time risk of ≥30% acc. to a validated standard risk prediction model; surveillance protocol of the GCHBOC for women with a deleterious BRCA mutation or a high mutation probability; referral to specialized centers for tertiary care is recommended

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# Surgical Prevention for Healthy BRCA1/2 Mutation Carriers

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- |   |   |
|---|---|
| <ul style="list-style-type: none"> <li>➤ <b>Prophylactic bilateral salpingo-oophorectomy (PBSO)</b><br/>reduces BrCa incidence and mortality<br/>reduces OvCa incidence and mortality<br/>reduces overall mortality</li> <br/> <li>➤ <b>Prophylactic bilateral mastectomy (PBM)</b><br/>reduces BrCa incidence and mortality</li> </ul> | <p><b>2a    B    ++*</b></p><br><p><b>2a    B    +*</b></p> |
|---|---|

**PBSO is evidence based only  $\geq 40$  yrs and completion of family planning; PBM revealed an increase of premalignant lesions  $\geq 40$  yrs**

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# Therapy of BRCA1/2-associated Breast Cancer

## Limited prospective cohort studies with short follow-up time

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➤ <b>Breast conserving therapy:</b>			
➤ Adequate local tumor control (10 years observation)	2a	B	+
➤ <b>Contra-lateral (cl) mastectomy<sup>+</sup> :</b>			
➤ Reduction of cl BrCa incidence	2b	B	+/-
➤ <b>PBSO<sup>+</sup>:</b>			
➤ Reduction of ovarian cancer incidence	2b	B	+
➤ Reduction of cl BrCa incidence if performed around the age of 40	2b	B	+
➤ <b>Systemic therapy according to sporadic breast cancer</b>	2b	B	++
➤ <b>Platinum-based regimens</b>	4	C	+/-*
➤ <b>PARP inhibitor</b>	4	C	+/-**

+ Overall prognosis has to be considered

\* Study participation recommended

\*\* Phase II studies only

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# Medical Prevention for Women at Increased Risk

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- **Tamoxifen for women > 35 years**  
Reduction of invasive BrCA, DCIS, and LN 1a A +\*
- **Raloxifen for postmenopausal women**  
Reduction of invasive BrCa only 1b A +\*
- **Aromatase inhibitors for postmenopausal women** 5 D +/-\*\*

**Chemopreventive regimes should only be offered after individual and comprehensive counseling. The net benefit strongly depends on risk status, age and pre-existing risk factors for side effects.**

\*Risk situation as defined in NSABP P1-trial (1.66% in 5 years)

\*\* Study participation recommended

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# Risk Reduction for Ipsi- and Contralateral Breast Cancer

**Rationale: Women with breast cancer have an increased risk for a second primary**

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	<hr/>		
➤ <b>Tamoxifen*</b>	<b>1a</b>	<b>A</b>	<b>+</b>
➤ <b>Aromatase inhibitors*</b>	<b>1a</b>	<b>A</b>	<b>+</b>
➤ <b>Suppression of ovarian function* + Tamoxifen</b>	<b>1b</b>	<b>B</b>	<b>+</b>

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**\*only proven for ER/PgR-positive primary sporadic BrCa**