Options for Primary Prevention: Modifiable Lifestyle Factors
Prevention

- **Version 2011:** Gerber / Thomssen
- **Versions 2012–15:** Dall / Diel / Gerber / Maass / Mundhenke
- **Version 2016:** Dall / Maass
Non-modifiable Risk Factors for Breast Cancer

- Older age
- Genetic risk factors
- Family cancer history
- Personal history of breast lesions
  - Non-proliferative lesions
  - Proliferative lesions w/o atypia
  - High risk lesions (ADH, LIN)
  - Breast cancer (DCIS, InvBC)
- Breast density
- Chest irradiation
- Lifetime number of menstrual cycles
  - Early menarche, late menopause, mat. pregnancy factors (e.g. preeclampsia (risk reduction), gestational diabetes (risk increase))

Reproductive risk factors

- Lower number of births or no pregnancy
- Higher age at first full term delivery
Modifiable Risk Factors for Breast Cancer

- Less breast feeding
- BMI < 18.5 and > 25 and especially > 40 (obesity)
- Diabetes mellitus Type II
- Food content
- Steroid hormone therapy
  - Recent oral contraceptive use
  - Hormone therapy in postmenopausal women
- Alcohol intake
- Smoking
- Light exposure at night (night shifts)
- Low physical activity
- Toxic agents in fetal and early childhood development (DES, polyfluoroalkyls)
  - So far, there is no evidence for a correlation between aluminium containing antiperspirants and breast cancer
  - So far, there is no evidence for Glyphosate herbicide use and breast cancer
High Proportion of Postmenopausal Breast Cancer Attributable to Lifestyle Factors

population attributable fractions (PAFs) of modifiable risk factors

Risk factors: obesity, physical inactivity, alcohol, low-fibre intake, smoking

Results: retrospective cohort study (Netherlands Cancer Registry)

2000: subpopulations of obese women, inactive women, alcohol drinkers, smokers etc.
2010: breast cancer incidence as compared to background incidence in these subgroups

25.7% of postmenopausal breast cancer cases in the Netherlands in 2010 are attributable to lifestyle factors

8.8% for obesity
6.6% for alcohol
5.5% for physical inactivity
3.2% for low fibre intake
4.6% for smoking

van Germert et al., Int J Cancer 2015; 152: 155-162
Secondary Prevention, Lifestyle and TNBC Subgroup

TNBC subgroup:

N = 518 pat., population-based prospective cohort study, FU 9.1 yrs.

factor: risk of recurrence

phys. activity HR 0.58 (0.39-0.86)

BMI no differences

Bao et al., Epidemiology 2015, 26:909-16
Secondary Prevention, Lifestyle and ER-positive Subgroup

ER-positive subgroup:

n = 6295 pat., prospective pooling study, 5 yrs. after Dx

- no weight gain: HR 1.00
- >10% weight gain: HR 1.24 (1.00-1.53)
- BMI 30-34.99: HR 1.40 (1.05-1.86)
- BMI >35: HR 1.41 (1.02-1.62)

- no alcohol: HR 1.00
- daily alcohol: HR 1.28 (1.091-1.62)

- phys. activity
  - none: HR 1.00
  - < 17.4 MET-h/wk: HR 0.81 (0.71-0.93)
  - > 17.4 MET-h/wk: HR 0.71 (0.61-0.82)

Nechuta et al., Int J Cancer, DOI 10.1002 (Epub ahead of print)
Prevention by Changing Pregnancy Related Factors

- Any full term pregnancy
- Number of pregnancies
- First full term pregnancy before age of 30 years
- Breast feeding
  (protective if total breast feeding time exceeds 1.5–2 years)

Oxford / AGO LoE / GR

<table>
<thead>
<tr>
<th>Prevention Factor</th>
<th>Oxford</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any full term pregnancy</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>First full term pregnancy before 30 yrs</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>Breast feeding</td>
<td>3a</td>
<td>B</td>
</tr>
</tbody>
</table>
Prevention by Changing Lifestyle Factors: Body Mass Index / Diet

- Maintaining normal weight (BMI at 18.5 – 25 kg/m²)
  - Premenopausal
  - Postmenopausal

- Prevention/Screening and treatment of diabetes mellitus type II (reduction of breast cancer incidence and mortality)

<table>
<thead>
<tr>
<th>Oxford / AGO</th>
<th>LoE / GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2a B ++</td>
<td></td>
</tr>
<tr>
<td>3a B ++</td>
<td></td>
</tr>
<tr>
<td>2a B ++</td>
<td></td>
</tr>
<tr>
<td>2b B ++</td>
<td></td>
</tr>
</tbody>
</table>
## Prevention by Changing Lifestyle Factors: Diet

<table>
<thead>
<tr>
<th>Oxford / AGO LoE / GR</th>
<th>Preference of a healthy diet</th>
<th>Dietary components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2b B +</td>
<td>Fat reduced food (unsaturated &gt; saturated fatty acids) 2a B +</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Reduced consumption of red meat 2a B +</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Supplementation of vitamins, minerals, tracer elements 2a B -</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vitamin D substitution for prevention 3a B +/-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vegetables / fruits 2a B +/-*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phytoestrogens / soya 2a B +/-</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fiber containing food 1b A +</td>
</tr>
</tbody>
</table>

* Recommended as a part of healthy nutrition
Prevention by Modifying Lifestyle Risk Factors: Alcohol

- Reduction of alcohol intake reduces risk of breast cancer
  - Particularly for ER+/PgR+ tumors
  - Invasive lobular tumors

Oxford / AGO LoE / GR

2b B
Prevention by Modifying Lifestyle Risk Factors: Smoking

- Never smoking reduces risk of breast cancer (~15-24% reduction of lifetime risk)

- Young women smoking have a 60% increased risk of bc, when smoking > 10 years before the first childbirth (vs. never smokers)
Prevention by Modifying Lifestyle Risk Factors: Physical Activity

- Physical exercise

(Metabolic equivalents to 3–5 hrs moderate pace walking per week)
Prevention by Modifying Lifestyle Risk Factors: Hormone Therapy in Postmenopausal Women

- Avoiding hormonal therapy in postmenopausal women
  - Avoiding estrogen / progestin combinations
  - Avoiding estrogens only

Oxford / AGO
LoE / GR

1b A +
1b A +/-
## Prevention

### Hormones in Postmenopausal Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>MC-RR (95% CI)</th>
<th>Further information</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WHI</strong></td>
<td>~ 27,000</td>
<td>1.3 (1.0-1.6)</td>
<td>1.3 (1.1-1.6) coronaric events, 1.4 (1.1-1.9) insults, 2.1 (1.4-3.3) pulmonary embolism, 2.1 (1.5-2.9) deep vein thrombosis</td>
</tr>
<tr>
<td><strong>HERS</strong></td>
<td>I 2763</td>
<td>1.2 (0.95-1.5)</td>
<td>Med. age 67 J, no secondary prevention, side effects as compared to WHI + cholcystectomy</td>
</tr>
<tr>
<td></td>
<td>II 2321</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Million Women</strong></td>
<td>~ 50% HRT, ~ 1.084,110 person-years</td>
<td>1.66 (1.6-1.8)</td>
<td>EPC &gt; E, mode of applic. not relevant, duration &gt; 5 yrs, Tibolone RR 1.45 (1.2-1.7)</td>
</tr>
<tr>
<td><strong>EPIC</strong></td>
<td>1.153,747 person-years</td>
<td>1.4 (1.2-1.6), 1.8 (1.4-2.2)</td>
<td>E-Mono, EPC &gt; E</td>
</tr>
<tr>
<td><strong>Metaanalyse</strong></td>
<td>16 Studien</td>
<td>1.21-1.40</td>
<td>Side effects as compared to WHI +</td>
</tr>
</tbody>
</table>

**Further References**

- [Chlebowski et al., Climacteric 2015, 18:336-8](#)
- [Chlebowski et al., J Natl Compr Canc Netw 2015, 13:917-24](#)
**Prevention**

**Hormones (EGC) in Postmenopausal Patients**

<table>
<thead>
<tr>
<th>CLEAR-study (NSW)</th>
<th>N</th>
<th>MC-RR (95%CI)</th>
<th>Further statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case-Control-Study, retrospect. Australia</td>
<td>1236 BC cases</td>
<td>2.09 (1.57-2.78)</td>
<td>current user</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.03 (0.82-1.28)</td>
<td>past user</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.62 (1.56-4.38)</td>
<td>E/P combination</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.80 (1.21-2.68)</td>
<td>E only</td>
</tr>
</tbody>
</table>

Salagame et al., Int J Cancer 2015. DOI 10.1002 Epub ahead of print
Prevention by Modifying Lifestyle Risk Factors: Oral Contraception (OC)

- Overall, OC does not significantly increase risk of cancer

- Risk of breast cancer may be slightly increased, risk of ovarian, endometrial cancer is decreased

Oxford LoE

1a

1a(−)
Further information and references:

Screened data bases:

Screened guidelines:
ASCO (American Association of Clinical Oncology, Practice Guidelines, 2015)
CMA (Canadian Medical Association, 2015): http://www.cmaj.ca/cgi/content/full/158/3/DC1
NCCN (National Comprehensive Cancer Network, 2015):
Non Modifiable Risk Factors for Breast Cancer (3/17)

No further information

References:

Modifiable Risk Factors for Breast Cancer Risk (4/17)

No further information

References:

5. Nechuta et al., Int J Cancer, DOI 10.1002 (Epub ahead of print)
6. Bao et al., Epidemiology 2015, 26:909-16
High Proportion of Postmenopausal Breast Cancer Attributable to Lifestyle Factors (5/17)

No further information

No references:
No further information

No references
Secondary Prevention, Lifestyle and ER-positive Subgroup (7/17)

No further information

No references
Prevention by Changing Pregnancy Related Factors (8/17)

No further information

References:


Prevention by Changing Life Style Factors: Body Mass Index / Diet (9/17)

No further information

References:

Prevention by Changing Life Style Factors: Diet (10/17)

No further information

References:

Prevention by Modifying Life Style Risk Factors: Alcohol (11/17)

No further information

References:

Prevention by Modifying Life Style Risk Factors: Smoking (12/17)

No further information

References:

Prevention by Modifying Life Style Risk Factors: Physical Activity (13/17)

No further information

References:

Prevention by Modifying Life Style Risk Factors: Hormone Therapy in Postmenopausal Women (14/17)

No further information

References:

7. Manson JE: Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. JAMA. 2013 Oct 2;310(13):1353-68.
9. Chlebowski et al., Climacteric 2015, 18:336-8
No further information

No references
Prevention - Hormones (EGC) in Postmenopausal Patients (16/17)

No further information

No references
Prevention by Modifying Life Style Risk Factors: Oral contraception (17/17)

No further information

References: