Options for Primary Prevention: Modifiable Lifestyle Factors
Prevention

- **Version 2011-2017**
  Dall / Diel / Gerber / Maass / Mundhenke Thomssen / von Minckwitz

- **Version 2018:**
  Dall / Solbach
Non-modifiable Risk Factors for Breast Cancer

- Older age
- Genetics
- Family history of cancer
- 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, complications of pregnancy

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

- Short duration or absence of 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)
  - To date there is no evidence for a correlation between aluminium containing antiperspirants and breast cancer
  - To date 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-fiber 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 were attributable to lifestyle factors

- 8.8% attributed to obesity
- 6.6% attributed to alcohol
- 5.5% attributed to physical inactivity
- 3.2% attributed to low fiber intake
- 4.6% attributed to 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 Modifying 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)

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### 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)

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BMI and epigenetics link between obesity and breast cancer?

Changing the ESR1-promoter activity by methylation of CpG-islands

n=120 breast tissue samples of cancer free patients

ESR1-promoter methylation

BMI $\geq 30$ > BMI 25-29 > BMI 25 kg/m$^2$ (p<0.001 resp.)

postmenopausal > premenopausal (p=0.046)

[multivariate analysis]

BMI and epigenetics link between obesity and breast cancer?

Walker, CL, SABCS 2011
Prevention by Changing Lifestyle Factors: Diet

- Preference of a balanced diet*
- Dietary components
  - Fat reduced food
  - Reduced consumption of red meat
  - Supplementation of vitamins, minerals, trace elements
  - Vitamin D substitution for prevention
  - Vegetables / fruits
  - Phytoestrogens / soy
  - Fiber containing food
  - Vegetarian diet (no risk reduction)
  - Vegan diet (no significant risk reduction)
  - nuts/peanuts (>10g/d)

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* As recommended by German Society of Nutrition (DGE)
** Recommended as a part of healthy nutrition
Tree nut, peanut, and peanut butter intake and risk of postmenopausal breast cancer: The Netherlands Cohort Study

n = 62573 women, aged 55-69

Follow up: 20.3 Years

2321 breast cancers and 1665 healthy subcohort members

Case cohort analysis

Tree nut or peanut intake >10g/day reduces HR-negative BC incidence

(HR 0.55 (CI 0.33-0.93), p=0.025)

No effect for peanut butter

Prevention by Modifying Lifestyle Risk Factors: Alcohol

- Reduction of alcohol intake reduces risk of breast cancer

Particularly for
- ER+/PgR+ tumors
- Invasive lobular tumors

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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)

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## Prevention by Modifying Lifestyle Risk Factors: Physical Activity

- **Physical exercise**

  (Metabolic equivalents to 3–5 hrs moderate pace walking per week)

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## Prevention by Modifying Lifestyle Risk Factors: Hormone Therapy in Postmenopausal Women

- **Avoiding hormonal therapy in postmenopausal women**
  - Avoiding estrogen / progestin combinations
    - Oxford: 1b, A, +
  - Avoiding estrogens only
    - (Estrogen alone 5 years after menopause does not show an increase in breast cancer risk)
    - Oxford: 1b, A, +/-
# Prevention of Hormones in Postmenopausal Patients

<table>
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<tr>
<th>Study</th>
<th>N</th>
<th>MC-RR (95%CI)</th>
<th>Further information</th>
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<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) coronary events</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</td>
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<td></td>
<td>II 2321 open-label 2.7J</td>
<td></td>
<td>no secondary prevention</td>
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<td>side effects as comp. to WHI + cholcystectomy</td>
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<tr>
<td><strong>Million Women</strong></td>
<td>1.084 110</td>
<td>1.66 (1.6-1.8)</td>
<td>EPC &gt; E</td>
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<tr>
<td></td>
<td>~ 50% HRT 4.1 J J 4.1 J. follow-up</td>
<td></td>
<td>mode of applic. not relevant</td>
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<td>duration &gt; 5 yrs.</td>
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<td>Pulmonary embolism 2.1 (1.5-2.9)</td>
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<td>Deep vein thrombosis 2.1 (1.4-2.9)</td>
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<tr>
<td><strong>EPIC</strong></td>
<td>1.153 747 person-years</td>
<td>1.4 (1.2-1.6)</td>
<td>E-Mono</td>
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<td></td>
<td></td>
<td>1.8 (1.4-2.2)</td>
<td>EPC &gt; E</td>
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<tr>
<td><strong>Metaanalyse</strong></td>
<td>16 Studies</td>
<td>1.21-1.40</td>
<td>side effects as compared to WHI +</td>
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- WHI: JAMA 2002, JAMA 2017
- WHI: JAMA 2002, JAMA 2017
- EPIC: Int J Cancer 2010
- EPIC: Int J Cancer 2010

Chlebowski et al., Climacteric 2015, 18:336-8
Chlebowski et al., J Natl Compr Canc Netw 2015, 13:917-24
Manson JE et al., JAMA 2017; 318: 927-938
### Prevention of Hormones (EGC) in Postmenopausal Patients

<table>
<thead>
<tr>
<th>Study Description</th>
<th>N</th>
<th>MC-RR (95% CI)</th>
<th>Further statements</th>
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<tbody>
<tr>
<td>CLEAR-study (NSW)</td>
<td>1236 BC cases</td>
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<tr>
<td>Case-Control-Study, retrospect. Australia</td>
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<td>2.09 (1.57-2.78)</td>
<td>current user</td>
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<td>1.03 (0.82-1.28)</td>
<td>past user</td>
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<td>2.62 (1.56-4.38)</td>
<td>E/P combination</td>
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<td>1.80 (1.21-2.68)</td>
<td>E only</td>
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<td>Salagame et al., Int J Cancer. 2016;138(8):1905-14</td>
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Prevention by Modifying Lifestyle Risk Factors: Oral Contraception (OC)

- OC does not increase the risk of mortality from breast cancer

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

Oxford LoE

1a

1a(-)