Options for Primary Prevention: Modifiable Lifestyle Factors
Prevention

- **Versions 2011–2019:**
  Dall / Diel / Gerber / Hanf / Maass / Mundhenke / Solbach / Solomayer / Thomssen / von Minckwitz

- **Version 2020:**
  Dall / Mundhenke

**Screened data bases**


**Deodorant-use and risk**

*Breast Cancer and Deodorants/Antiperspirants: a Systematic Review.*

<table>
<thead>
<tr>
<th>Deodorant-use and risk</th>
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<tbody>
<tr>
<td>So far there is no evidence of a correlation between aluminum containing deodorants and breast cancer risk</td>
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<tr>
<td>▪ All observational studies that evaluated the association between breast cancer risk and deodorants/antiperspirants use were reviewed. We have only identified two case-control studies, carried out between 2002 and 2006.</td>
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<tr>
<td>▪ There was no risk of antiperspirants use in the pooled risk (odds ratio 0.40, 95% confidence interval 0.35-0.46).</td>
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<tr>
<td>▪ Our comprehensive search has identified an insufficient number of studies to conduct a quantitative review and obtain reliable results. Further prospective studies are strongly needed.</td>
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Medical Prevention

Kehm RD et al. Regular use of aspirin and other non-steroidal anti-inflammatory drugs and breast cancer risk for women at familial or Genetic risk: a cohort study, Breast Cancer Res. 2019 Apr;21(1):52

Prospective multinational cohort study, n=5606, healthy women, questionnaire, regular intake of ASS, NSAID, COX2-inhibitors

Regular ASS-intake: HR 0.61, CI 0.33-1.14, breast cancer incidence
Regular COX2-inhibitors: HR 0.39, CI 0.15-0.97, breast cancer incidence other NSAIDs: n.s.
[independent of BRCA-status]


8. Pizot C, Boniol M, Mullie P et al. Physical activity, hormone replacement therapy and breast cancer risk: A meta-analysis of

The risk of breast, ovarian and endometrial cancer in obese women submitted to bariatric surgery: A meta-analysis
SABCS 2019, B Ishihara, D Farah, M Fonseca and A Nazário.

- Meta-analysis, of a total of 150,528 patients in the bariatric surgery arm and 1,461,938 women in the control arm.
- The risk of breast cancer was reduced by 61% [RR: 0.39 (95%CI [0.24 to 0.64]); I² = 90%; 6 studies).
- The risk of ovarian cancer was reduced by 53% [RR: 0.47 (95%CI [0.27 to 0.81]); I² = 0%; 3 studies).
- The risk of endometrial cancer was reduced by 67% [RR: 0.33 (95%CI [0.21 to 0.51]); I² = 88%; 7 studies).
- WHI substudy
- Among the 3460 women included in the analysis (mean [SD] age, 63.6 [7.6] years), multivariable-adjusted hazard ratios for the risk of invasive breast cancer were 1.89 (95% CI, 1.21-2.95) for the highest quartile of whole-body fat and 1.88 (95% CI, 1.18-2.98) for the highest quartile of trunk fat mass.
- The corresponding adjusted hazard ratios for ER-positive breast cancer were 2.21 (95% CI, 1.23-3.67) and 1.98 (95% CI, 1.18-3.31), respectively.
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/m² (p < 0.001 resp.)

postmenopausal > premenopausal (p = 0.046)

[multivariate analysis]

BMI and epigenetics link between obesity and breast cancer?

- The epigenetic code (methyl marks) determines how the genome functions, dictating which genes are turned on and which genes are turned off.
- Development is the critical period when this programming occurs, directing cell and organ development.

Waller, CL, SABCS 2011


Coffee Consumption and Risk of Breast Cancer: An Up-To-Date Meta-Analysis
Xiu Juan Li: PlosOne, January 2013 | Volume 8 | Issue 1 | e52681

49497 breast cancer cases
26 studies (16 cohort and 10 case-control studies)

The pooled RR showed a borderline significant influence of highest coffee consumption (RR = 0.96; 95% CI 0.93–1.00), low-to moderate coffee consumption (RR = 0.99; 95% CI 0.95–1.04), or an increment of 2 cups/day of coffee consumption (RR = 0.98; 95% CI 0.97–1.00) on the risk of breast cancer.

In stratified analysis, a significant inverse association was observed in ER-negative subgroup. However, no significant association was noted in the others.
randomized, placebo-controlled trial, with a two-by-two factorial design, of vitamin D₃ (cholecalciferol) at a dose of 2000 IU per day and marine n-3 (also called omega-3) fatty acids at a dose of 1 g per day

Primary end points were invasive cancer of any type and major cardiovascular events

25,871 participants

median follow-up of 5.3 years

124 breast cancers (Vit D group) vs. 122 (placebo group) Hazard Ratio: 1.02

Conclusions and further perspectives

...probably the most apparent relationship prevails for consumption of isoflavones, whereas beneficial effects seem to be expressed only at high intake levels typical to Asian women ... compared to Western countries where the intake of soy products is remarkably low.

Protective activities of isoflavones might appear only in females consuming soy foods since their early age as childhood and adolescence can be crucial periods of exposure.

At present: “Recommendations for consumption of high-dose isoflavones ... to reduce the individual susceptibility towards breast carcinogenesis are still premature and can also be not completely without .. risks.”


No association was classified as convincing (class I). The association between alcohol intake and ER+ breast cancer was classified as highly suggestive (Class II) based on a **meta-analysis of 20 prospective studies** (≥30g/d of alcohol consumption versus non-drinkers)

RR (95% CI): 1.35 (1.23, 1.48, p-value=5.2 x 10^{-10}, I^2 = 26%, Psmall effect bias = 0.184, P excess significance bias = 4 x 10^{-8})


We examined associations of adult and adolescent recreational physical activity (quintiles of age-adjusted total metabolic equivalents per week) with breast cancer risk using multivariable Cox proportional hazards regression, adjusted for demographics, lifestyle factors, and body mass index. We tested for multiplicative interactions of physical activity with predicted absolute breast cancer familial risk based on pedigree data and with BRCA1 and BRCA2 mutation status. Baseline recreational physical activity level in the highest four quintiles compared with the lowest quintile was associated with a 20% lower breast cancer risk (HR, 0.80; 95% confidence interval, 0.68-0.93). The association was not modified by familial risk or BRCA mutation status (P interactions >0.05). No overall association was found for adolescent recreational physical activity. Recreational physical activity in adulthood may lower breast cancer risk for women across the spectrum of familial risk.


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

<table>
<thead>
<tr>
<th>Avoiding hormonal therapy in postmenopausal women</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
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</thead>
<tbody>
<tr>
<td>Avoiding estrogen / progestin combinations</td>
<td>1b</td>
<td>A</td>
<td>+</td>
</tr>
<tr>
<td>Avoiding estrogens only</td>
<td>1b</td>
<td>A</td>
<td>+/-</td>
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</table>

(no increased, possibly reduced breast cancer risk, but increased risk for endometrial cancer, if not hysterectomized)


epidemiological data from EPIC-Italy (n = 31,864)

Study: estimated lifetime estrogen exposure

Method: epigenome-wide association study, blood DNA samples, N=216, and 440 healthy controls

Results: an estimated 5% increase in breast cancer risk per 1-year longer ELEE (OR = 1.05, 95% CI 1.04-1.07, P = 3 × 10^-12) in EPIC-Italy. 694 CpG sites were associated with ELEE (FDR Q < 0.05)
# Prevention of Hormones in Postmenopausal Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>MC-RR (95%CI)</th>
<th>Further information</th>
</tr>
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<tbody>
<tr>
<td>WHI</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></td>
<td></td>
<td></td>
<td>1.4 (1.1-1.9) ischemics</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.1 (1.4-3.1) pulmonary embolism</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2.1 (1.5-3.9) deep vein thrombosis</td>
</tr>
<tr>
<td>HERS</td>
<td>2 763</td>
<td>1.2 (0.95-1.5)</td>
<td>med. age 67</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>side effects as comp. to WHI + cholecystectomy</td>
</tr>
<tr>
<td>Million Women</td>
<td>1,084,110</td>
<td>1.66 (1.4-1.9)</td>
<td>EPC + E mode of applic, not relevant duration &gt; 3 yrs.</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>TItox RR 1.45 (1.2-1.7)</td>
</tr>
<tr>
<td>EPIC</td>
<td>1,153,747</td>
<td>1.4 (1.2-1.6)</td>
<td>E-Mono</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.8 (1.4-2.2)</td>
<td>EPC + E</td>
</tr>
<tr>
<td>Metaanalyse</td>
<td>16 Studies</td>
<td>1.21-1.40</td>
<td>side effects as compared to WHI +</td>
</tr>
</tbody>
</table>

Chlebowksi 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</th>
<th>N</th>
<th>MC-RR (95% CI)</th>
<th>Further statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLEAR-study (NSW)</td>
<td>1236 BC cases</td>
<td>2.09 (1.57-2.78)</td>
<td>current user</td>
</tr>
<tr>
<td>Case-Control-Study, retrospect. Australia</td>
<td></td>
<td>1.03 (0.83-1.38)</td>
<td>past user</td>
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<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>
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Salagame et al., Int J Cancer. 2016;138(8):1905-14

