Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Guidelines Breast
Version 2020.1

FORSCHEN
LEHREN
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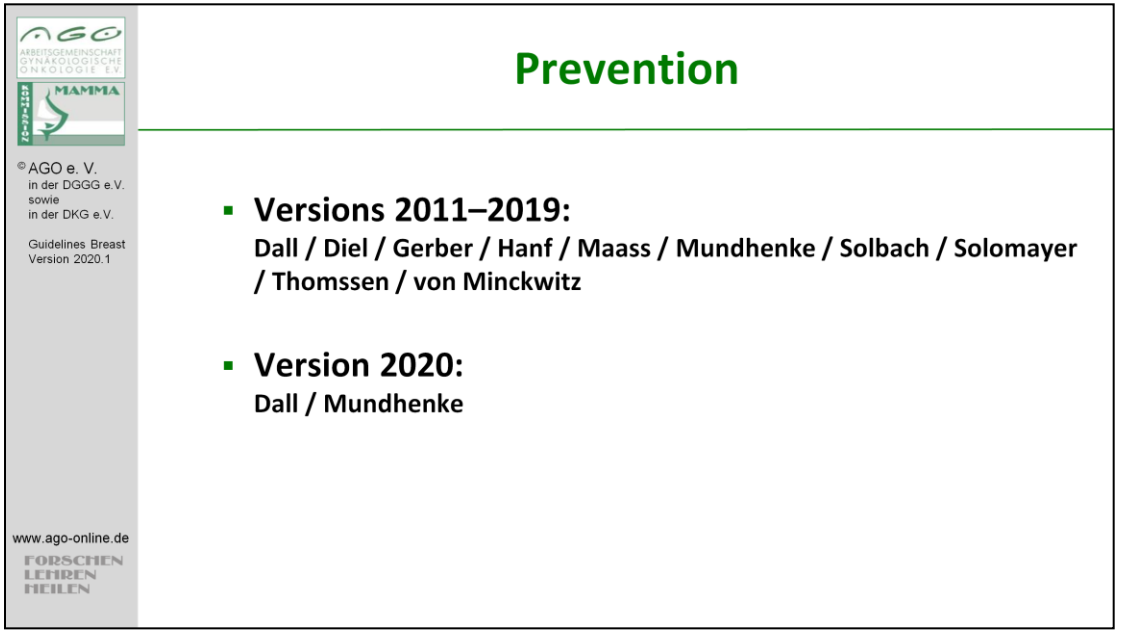
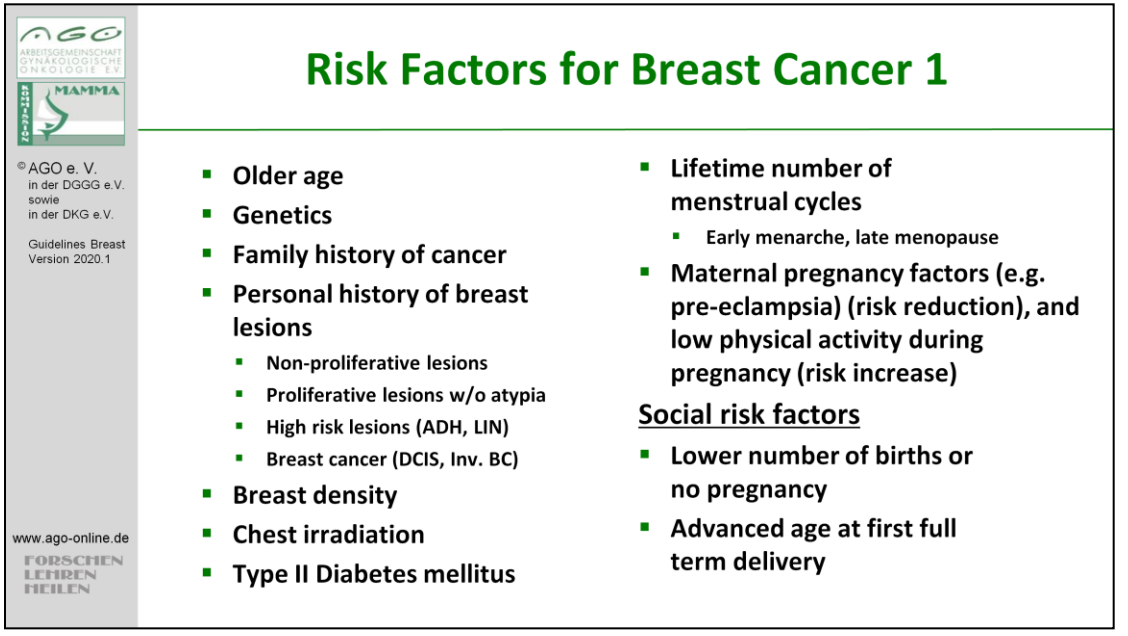
Options for Primary Prevention: Modifiable Lifestyle Factors



Screened data bases

Pubmed 2005 – 2019, ASCO 2012 – 2019, SABCS 2012 – 2019, Cochrane data base 2019



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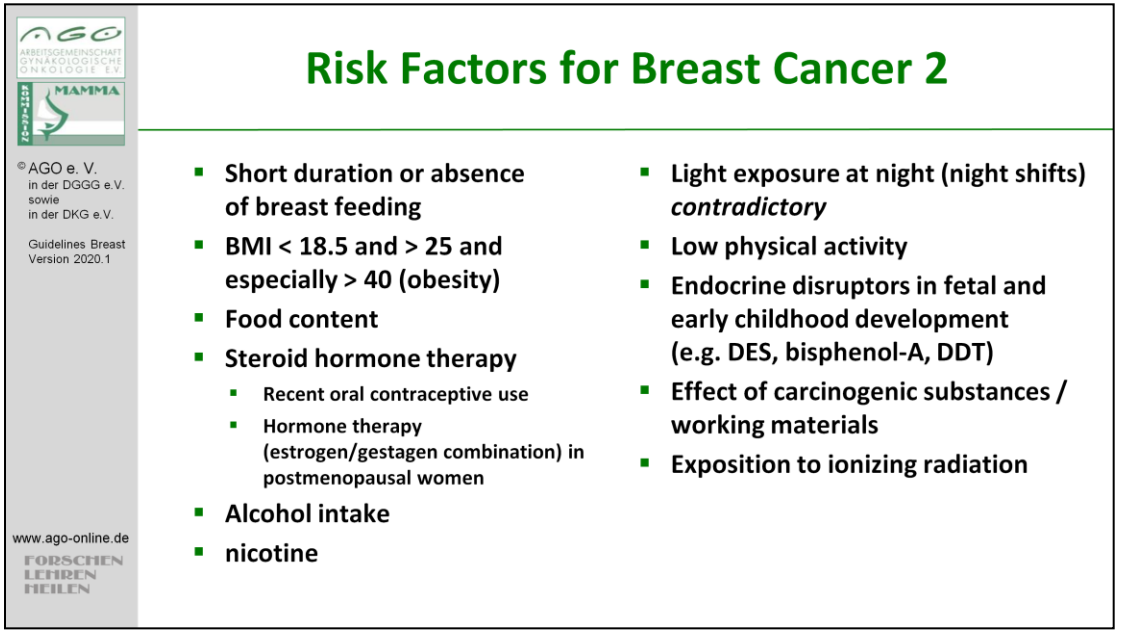

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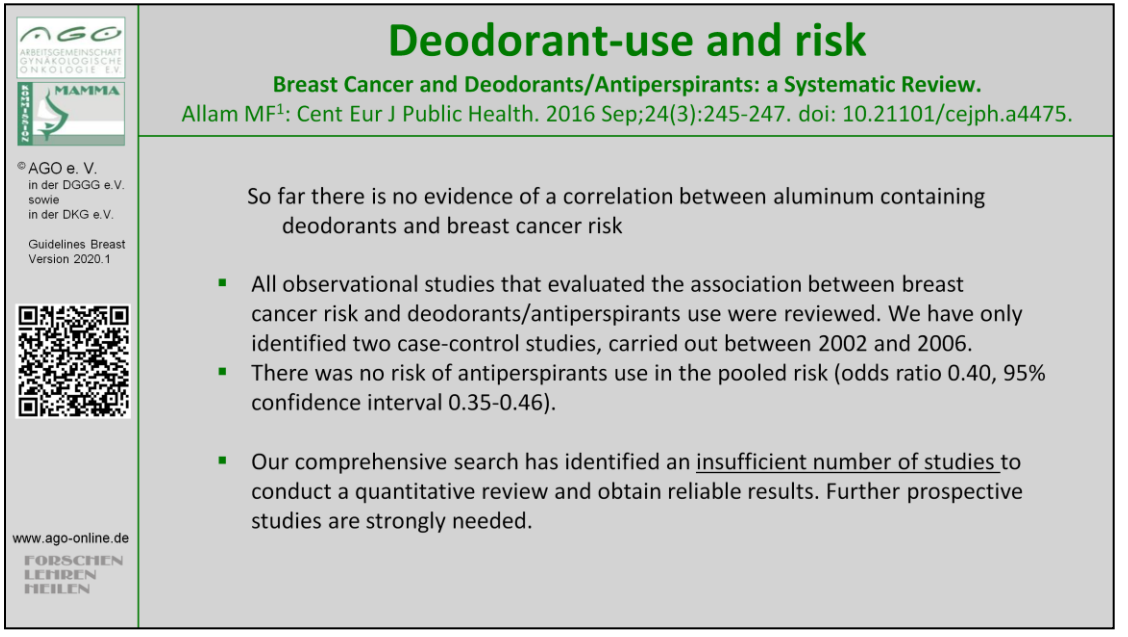

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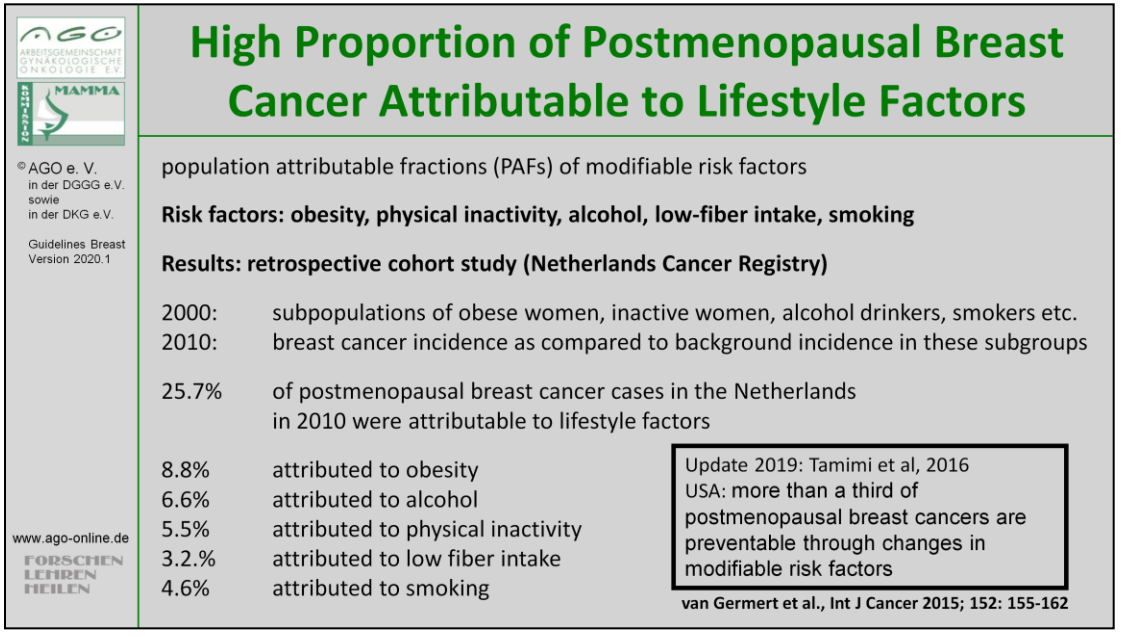

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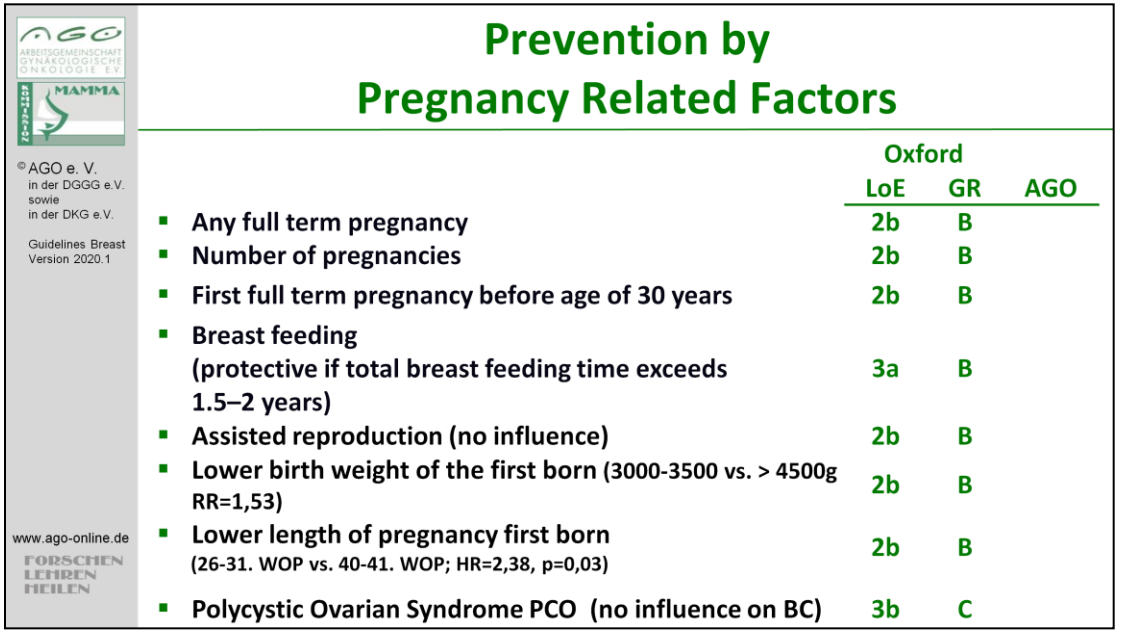

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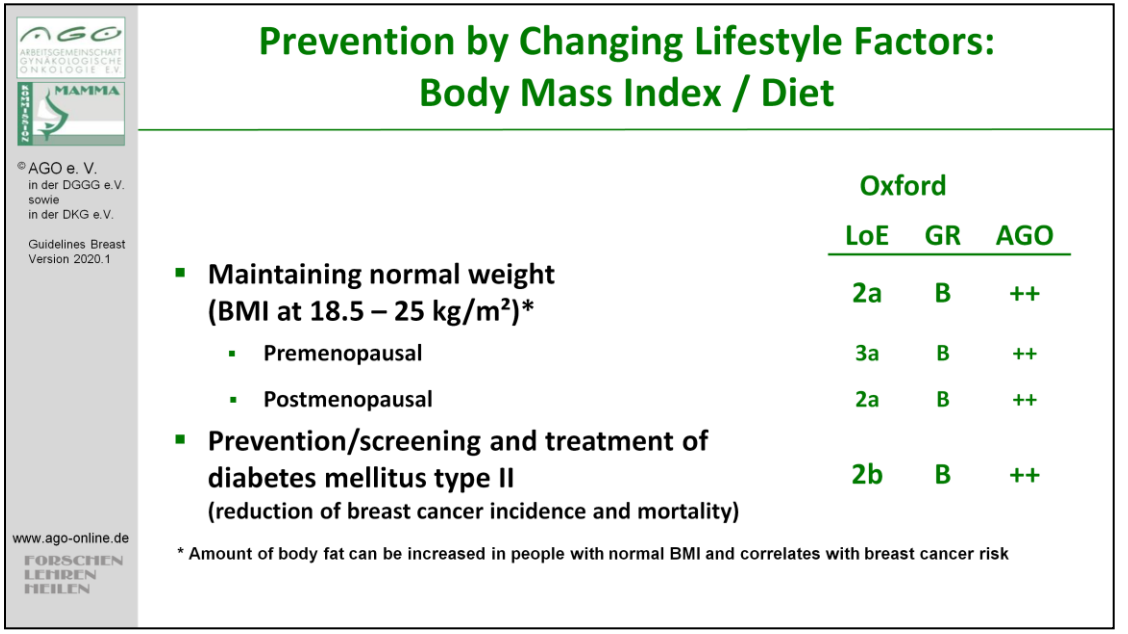
Medical Prevention

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. 18;21(1):52

Prospective multinational cohort study, n=5606, healthy women questionaire, 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]



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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).

Association of Body Fat and Risk of Breast Cancer in Postmenopausal Women With Normal Body Mass Index: A Secondary Analysis of a Randomized Clinical Trial and Observational Study.

Iyengar NM et al.: JAMA Oncol. 2019 Feb 1;5(2):155-163

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- **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.**

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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 ≥ 30 > BMI 25–29 > BMI 25 kg/m² **(p < 0.001 resp.)**

postmenopausal > premenopausal **(p = 0.046)**

[multivariate analysis]

Daraei A., Genet Test Mol Biomarkers 2017, 21:464-470

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**

Walker, CL, SABCS 2011

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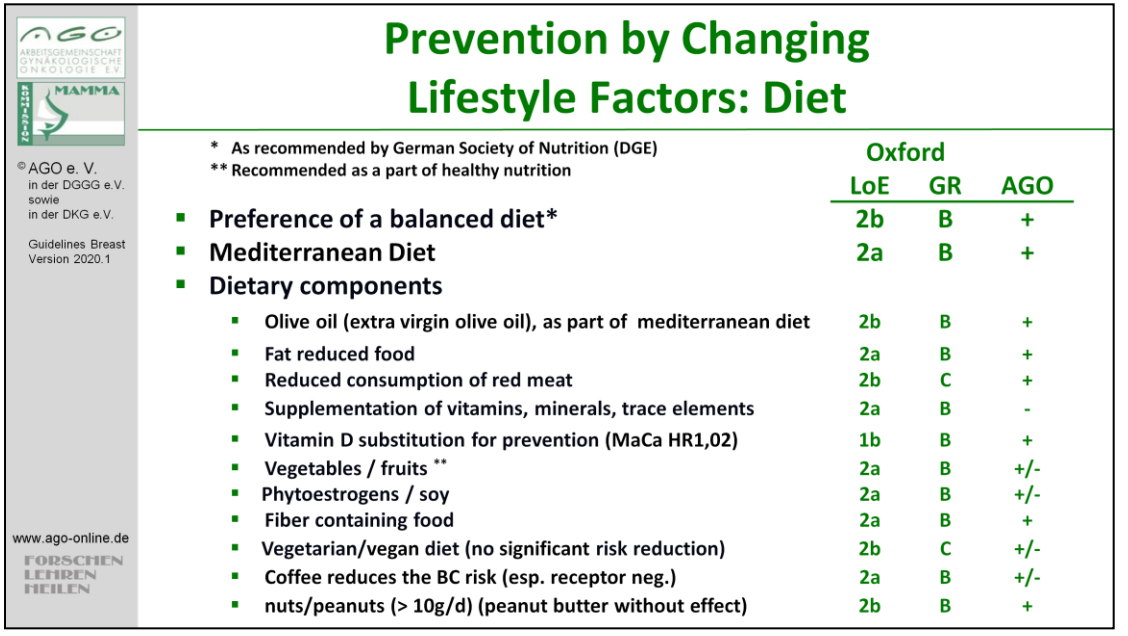

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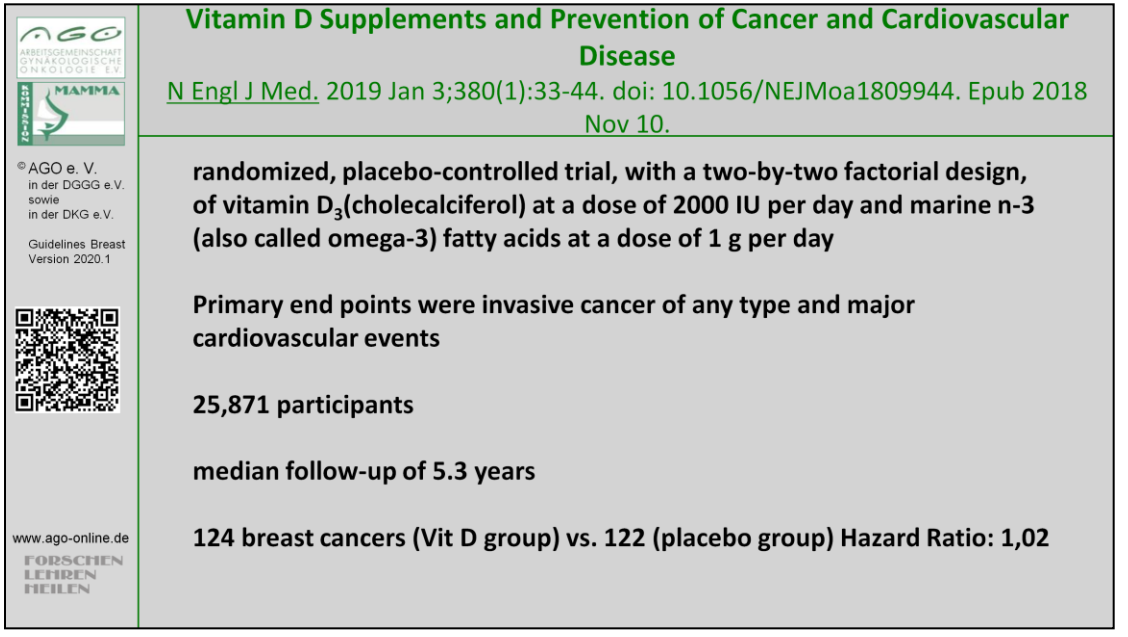
Coffee Consumption and Risk of Breast Cancer: An Up- To-Date Meta-Analysis

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.



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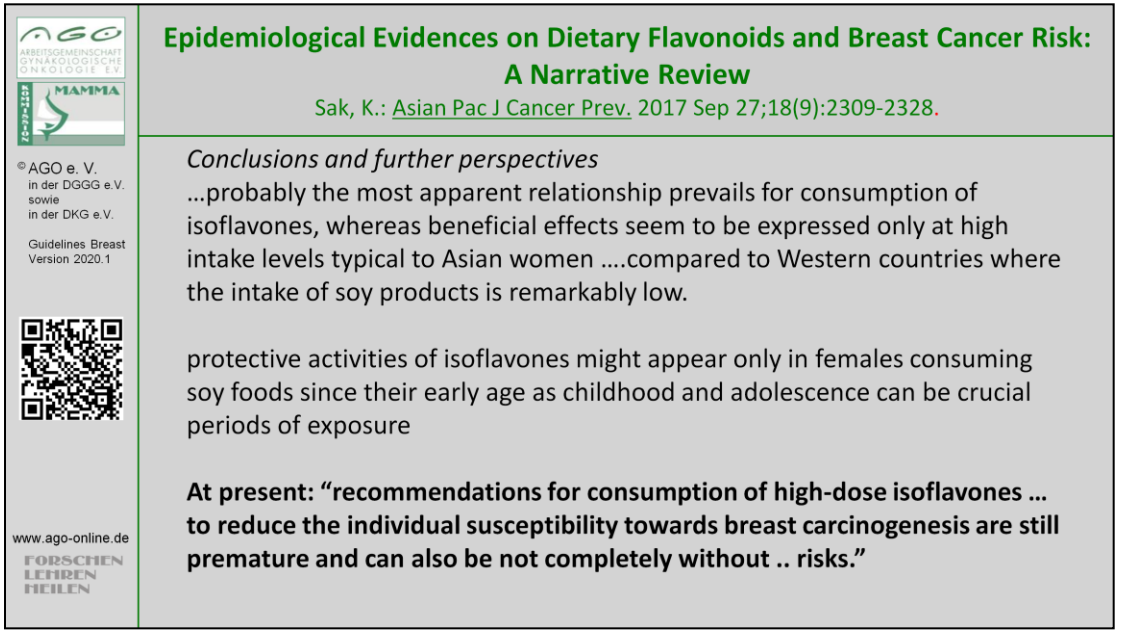

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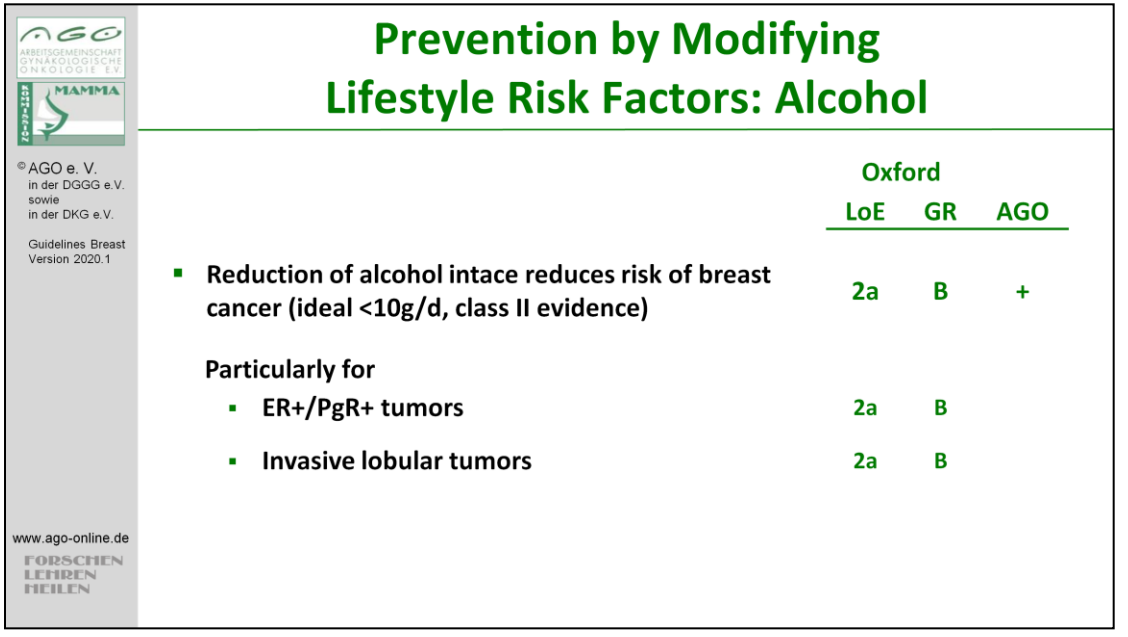

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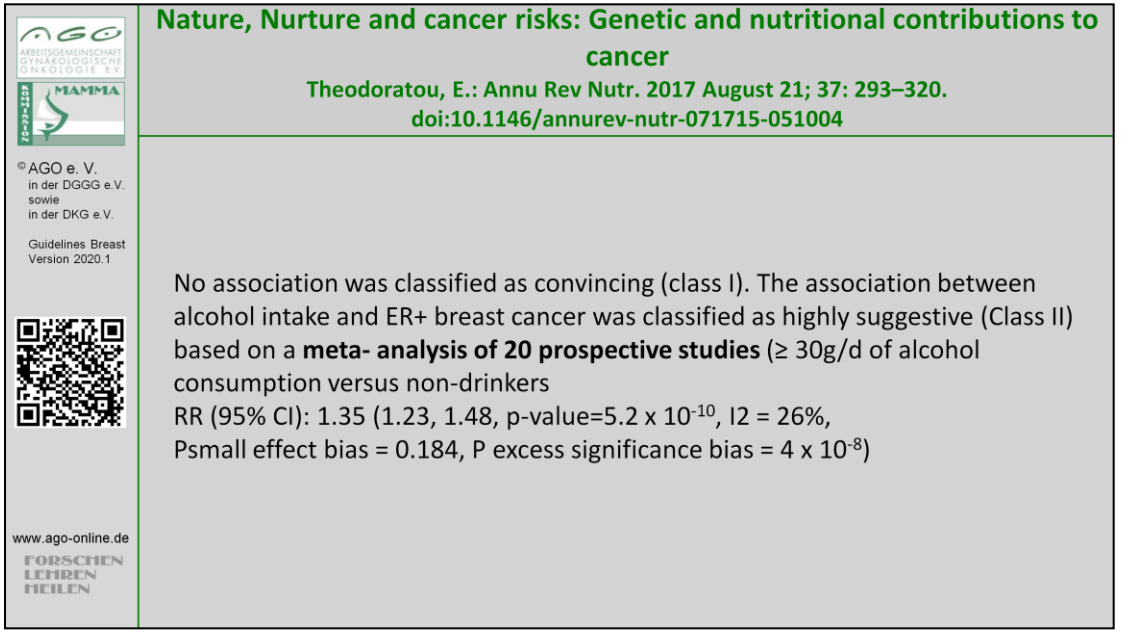

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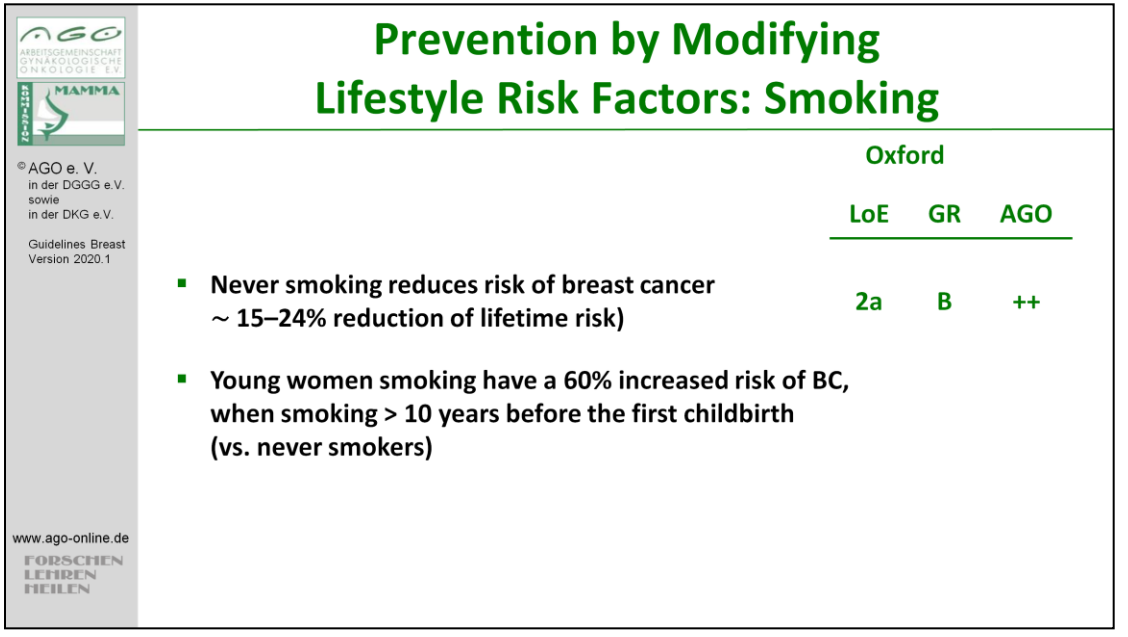

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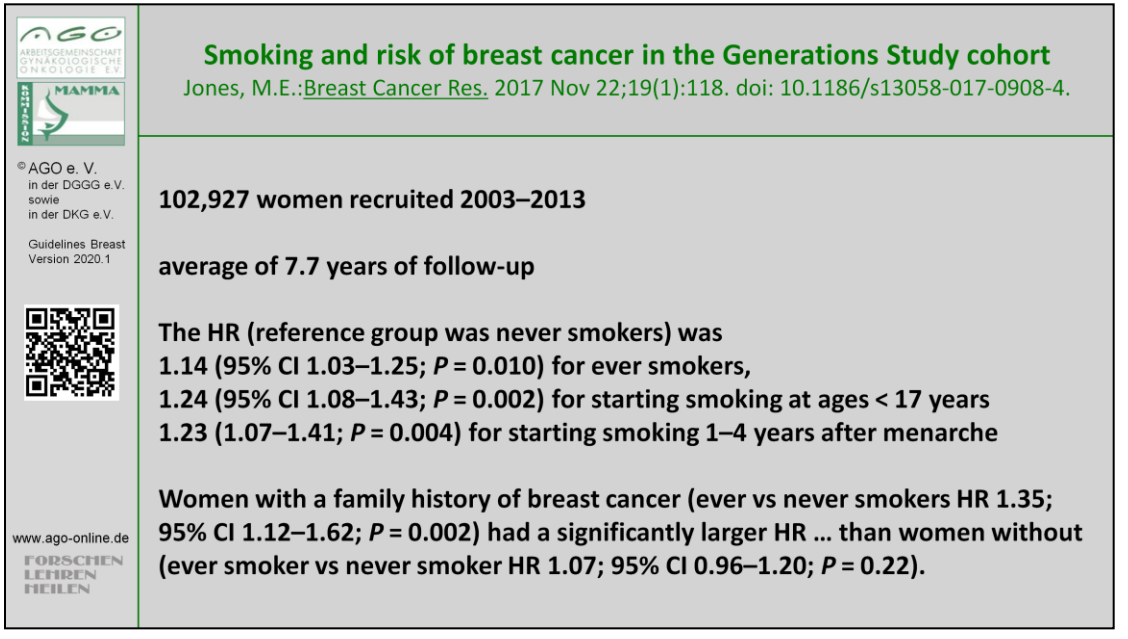

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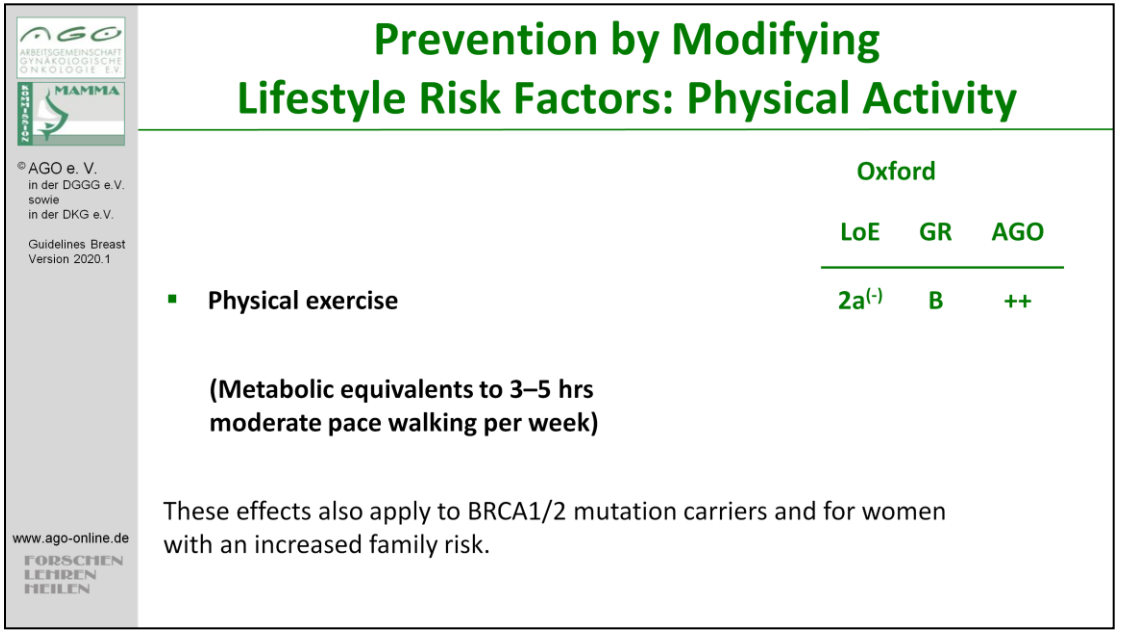

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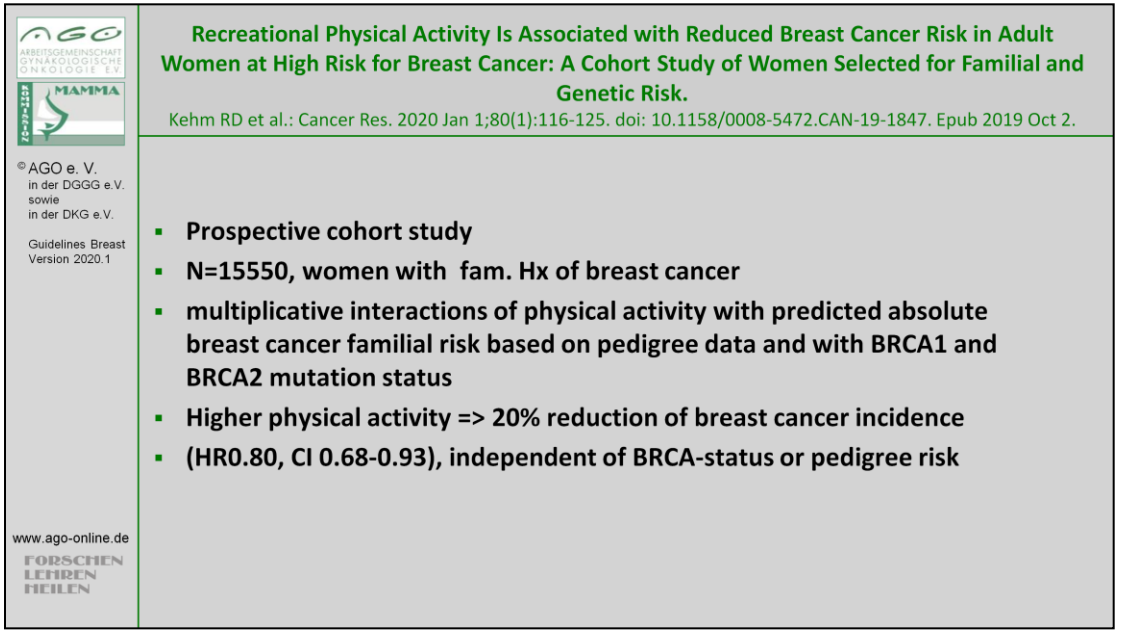
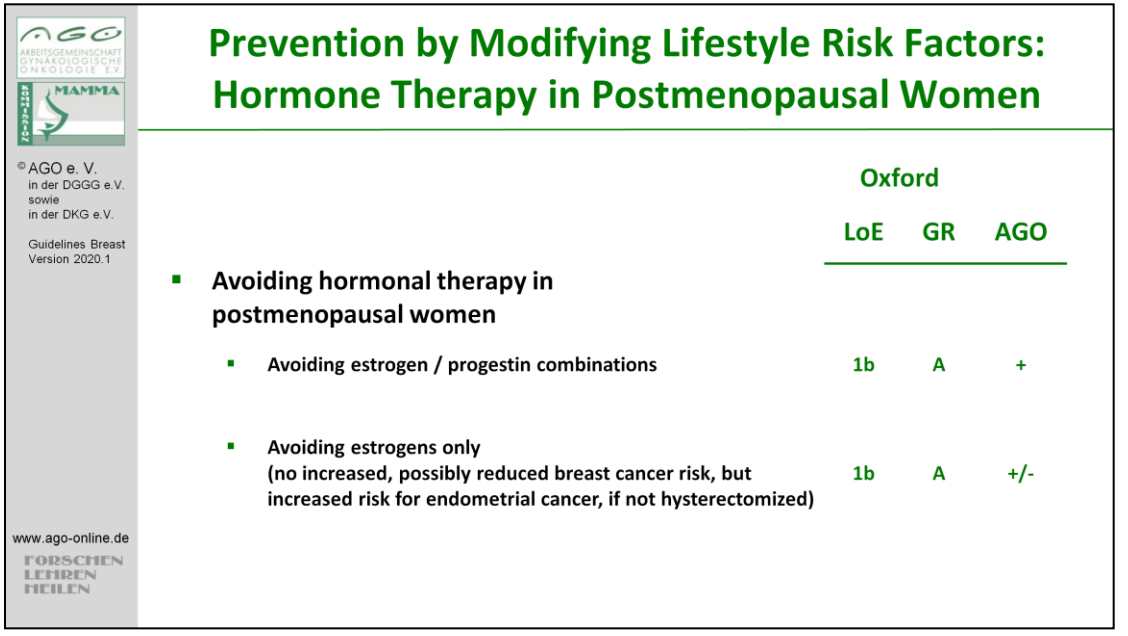


We examined associations of adult and adolescent recreational physical activity (quintiles of age-adjusted total metabolic equivalents per week) with breast cancer risk using multivariable Cox proportional hazards regression, adjusted for demographics, lifestyle factors, and body mass index. We tested 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.



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Epigenome-wide association study for lifetime estrogen exposure identifies an epigenetic signature associated with breast cancer risk.

Johansson A et al.: Clin Epigenetics. 2019 Apr 30;11(1):66.

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

	N	MC-RR (95%CI)	Further information
WHI WHI: JAMA 2002, JAMA 2017	~ 27 000	1.3 (1,0-1,6)	1.3 (1.1-1,6) coronary 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
HERS Hulley S: JAMA 2002	I 2763 RCT, med. 4.1 J II 2321 open-label, 2.7J	1.2 (0.95-1.5)	med. age 67 J no secondary prevention side effects as comp. to WHI + cholcystectomy↗
Million Women Beral V: Lancet 2003	1.084 110 ~ 50% HRT 4.1 J. follow-up	1.66 (1.6-1.8)	EPC > E mode of applic. not relevant duration > 5 yrs. Tibolon RR 1.45 (1.2-1.7)
EPIC Int J Cancer 2010	1.153 747 person-years	1.4 (1.2-1.6) 1.8 (1.4-2.2)	E-Mono EPC > E
Metaanalyse Nelson HD: JAMA 2002	16 Studies	1.21-1.40	side effects as compared to WHI +

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

Guidelines Breast
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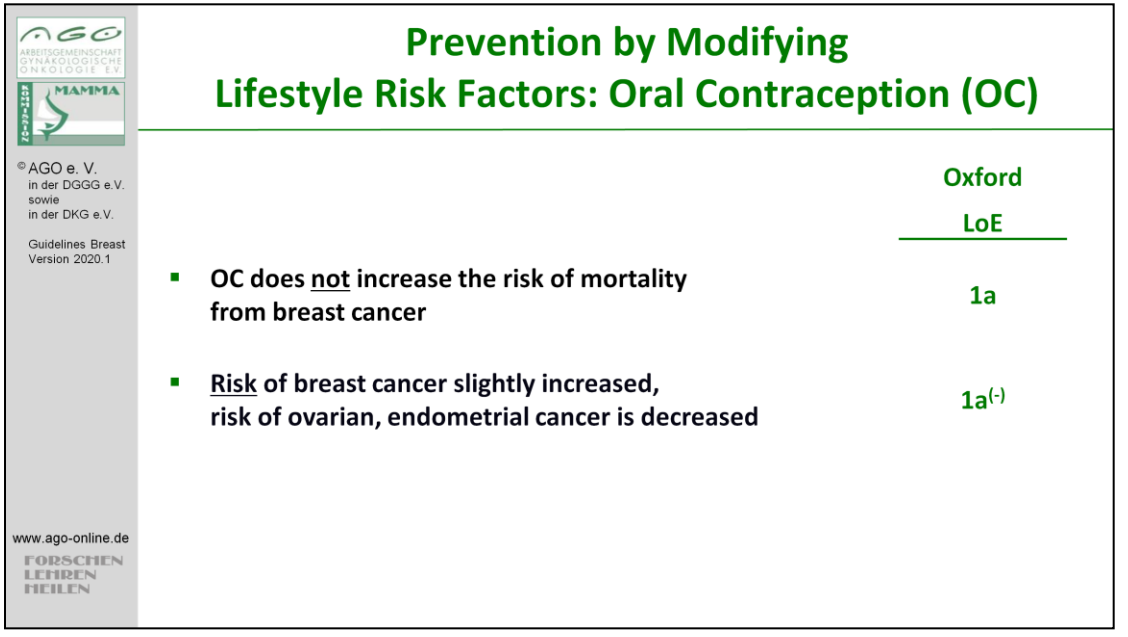
Prevention of Hormones (EGC) in Postmenopausal Patients

	N	MC-RR (95% CI)	Further statements
CLEAR-study (NSW) **Case-Control-Study, retrospect. Australia**	**1236 BC cases**	2.09 (1,57-2.78) 1.03 (0.82-1.28) 2.62 (1.56-4.38) 1.80 (1.21-2.68)	current user past user E/P combination E only

Salagame et al., Int J Cancer. 2016;138(8):1905-14



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