


Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Optionen der primären Prävention: Veränderbare Lifestyle-Faktoren



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Prävention

- **Versionen 2011–2019:**
Dall / Diel / Gerber / Hanf / Maass / Mundhenke / Solbach / Solomayer / Thomssen / von Minckwitz
- **Version 2020:**
Dall / Mundhenke

Screened data bases

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



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Risikofaktoren für Brustkrebs 1

- **Höheres Alter**
- **Genetisches Risiko**
- **Familiäre Krebsanamnese**
- **Persönliche Brustanamnese**
 - Nicht-proliferative Läsionen
 - Proliferative Läsionen +/- Atypien
 - Hochrisikoläsionen (ADH, LIN)
 - Brustkrebs (DCIS, Inv. MaCa)
- **Brustdichte**
- **Thoraxbestrahlung**
- **Typ II Diabetes mellitus**

- **Anzahl der Menstruationszyklen im Laufe des Lebens**
 - frühe Menarche, späte Menopause
- **Mütterliche Schwangerschaftsfaktoren (z.B. Präeklampsie => Risikoreduktion) und geringe körperliche Aktivität während der Schwangerschaft (Risikoerhöhung)**

Sozial definierte Risikofaktoren

- Geringe Geburtenzahl oder keine Schwangerschaft
- Höheres Alter bei erster Geburt


1. Collaborative Group on Hormonal Factors in Breast Cancer: Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. Lancet Oncol. 2012 Nov;13(11):1141-51.
2. Ritte R, Tikk K, Lukanova A et al. Reproductive factors and risk of hormone receptor positive and negative breast cancer: a cohort study. BMC Cancer 2013 Dec 9;13:584.
3. Powe CE, Tobias DK, Michels KB et al, History of gestational diabetes mellitus and risk of incident invasive breast cancer among parous women in the Nurses' Health Study II prospective cohort. Cancer Epidemiol Biomarkers Prev. 2017 Mar; 26(3): 321–327

Risikofaktoren für Brustkrebs 2

- Keine / kurze Stillperioden
- BMI < 18,5 und > 25 und besonders > 40 (Adipositas)
- Nahrungszusammensetzung
- Hormontherapie
 - Kürzlicher Gebrauch oraler Kontrazeptiva
 - Hormontherapie (Östrogen/Gestagen-Kombination) in der Postmenopause
- Alkoholkonsum
- Nikotin
- Schlafmangel (Nacht / Schichtarbeit) *widersprüchlich*
- Verminderte körperliche Aktivität
- Endokrine Disruptoren während der fetalen und frühkindl. Entwicklung (z.B. DES, Bisphenol-A, DDT)
- Einwirkung kanzerogener Substanzen / Arbeitsstoffe
- Exposition gegenüber ionisierender Strahlung


1. Gaudet MM, Gapstur SM, Sun J et al. Active smoking and breast cancer risk: original cohort data and meta-analysis. J Natl Cancer Inst. 2013 Apr 17;105(8):515-25.
2. Willhite CC, Karyakina NA, Yokel RA et al. Systematic review of potential health risks posed by pharmaceutical, occupational and consumer exposures to metallic and nanoscale aluminium, aluminium oxides, aluminium hydroxide and its soluble salts. Crit Rev Toxicol. 2014;44 Suppl 4:1-80.
3. Van Germert, Lanting CI, Goldbohm RA et al. The proportion of postmenopausal breast cancer cases in the Netherlands attributable to lifestyle-related risk factors. Breast Cancer Res Treat. 2015 Jul;152(1):155-162.
4. Bao PP, Zhao GM, Shu XO et al. Modifiable Lifestyle Factors and Triple-negative Breast Cancer Survival: A Population-based Prospective Study. Epidemiology. 2015 Nov;26(6):909-16.
5. Nechuta S, Chen WY, Cai H et al. A pooled analysis of post-diagnosis lifestyle factors in association with late estrogen-receptor-positive breast cancer prognosis. Int J Cancer. 2016 May 1;138(9):2088-97.
6. Masala G, Bendinelli B, Assedi M et al. Up to one-third of breast cancer cases in post-menopausal Mediterranean women might be avoided by modifying lifestyle habits: the EPIC Italy study. Breast Cancer Res Treat. 2017 Jan;161(2):311-320.
7. Nunez C, Bauman A, Egger S3 et al. Obesity, physical activity and cancer risks: Results from the Cancer, Lifestyle and Evaluation of Risk Study (CLEAR); Cancer Epidemiol 2017; 47: 56-63.
8. American Cancer Society 2019 <https://www.cancer.org/cancer/breast-cancer/risk-and-prevention.html>

9. Rodgers KM, Udesky JO, Rudel RA et al. Environmental chemicals and breast cancer: An updated review of epidemiological literature informed by biological mechanisms. *Environ Res.* 2018 Jan;160:152-182. doi: 10.1016/j.envres.2017.08.045. Epub 2017 Oct 6.
10. Gray JM, Rasanayagam S, Engel C et al. State of the evidence 2017: an update on the connection between breast cancer and the environment. *Environ Health.* 2017 Sep 2;16(1):94. doi: 10.1186/s12940-017-0287-4.
11. James P, Bertrand KA, Hart JE et al. Outdoor Light at Night and Breast Cancer Incidence in the Nurses' Health Study II. *Environ Health Perspect.* 2017 Aug 17;125(8):087010. doi: 10.1289/EHP935.
12. Lin X, Chen W, Wie F et al. Night-shift work increases morbidity of breast cancer and all-cause mortality: a meta-analysis of 16 prospective cohort studies. *Sleep Med.* 2015 Nov;16(11):1381-1387. doi: 10.1016/j.sleep.2015.02.543. Epub 2015 May 11.



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Deodorant-Gebrauch und Risiko


Breast Cancer and Deodorants/Antiperspirants: a Systematic Review.

Allam MF¹: Cent Eur J Public Health. 2016 Sep;24(3):245-247. doi: 10.21101/cejph.a4475.

Bisher gibt es keine Evidenz für eine Korrelation zwischen Aluminium-enthaltenden Deodorants und Brustkrebsrisiko

- 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.
- There was no risk of antiperspirants use in the pooled risk (odds ratio 0.40, 95% confidence interval 0.35-0.46).
- 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.

1. Allam MF. Breast Cancer and Deodorants/Antiperspirants: a Systematic Review. Cent Eur J Public Health. 2016 Sep;24(3):245-247. doi: 10.21101/cejph.a4475.



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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

Update 2019: Tamimi et al, 2016
USA: more than a third of postmenopausal breast cancers are preventable through changes in modifiable risk factors

van Germert et al., Int J Cancer 2015; 152: 155-162

1. Van Germert, Lanting CI, Goldbohm RA et al.. The proportion of postmenopausal breast cancer cases in the Netherlands attributable to lifestyle-related risk factors. Breast Cancer Res Treat. 2015 Jul;152(1):155-162.
2. Tamini RM, Spiegelman D, Smith-Warner SA et al.: Population Attributable Risk of Modifiable and Nonmodifiable Breast Cancer Risk Factors in Postmenopausal Breast Cancer. Am J Epidemiol. 2016 Dec 15;184(12):884-893. Epub 2016 Dec 6.

Präventiver Einfluss durch Reproduktionsfaktoren			
	Oxford		
	LoE	GR	AGO
■ Zahl voll ausgetragener Geburten	2b	B	
■ Anzahl der Schwangerschaften	2b	B	
■ Erste ausgetragene Schwangerschaft ≤ 30 Jahre	2b	B	
■ Stillen (schützt, wenn Gesamtstilldauer 1,5–2 Jahre)	3a	B	
■ Assistierte Reproduktion (keinen Einfluss)	2b	B	
■ Geringeres Geburtsgewicht des Erstgeborenen (3000–3500g vs. > 4500g, RR = 1,53)	2b	B	
■ Geringere Schwangerschaftsdauer Erstgeborene (26-31. SSW vs. 40-41. SSW; RR = 2,38, p = 0,03)	2b	B	
■ Polycystic Ovarian Syndrome PCO (keinen Einfluss auf MaCa)	3b	C	

1. Li CI, Beaber EF, Tang MT et al.. Reproductive factors and risk of estrogen receptor positive, triple-negative, and HER2-neu overexpressing breast cancer among women 20-44 years of age. Breast Cancer Res Treat. 2013;137:579-87.
2. Del Pup L, Peccatori FA, Levi-Setti PE et al. Risk of cancer after assisted reproduction: a review of the available evidences and guidance to fertility counselors.Eur Rev Med Pharmacol Sci. 2018 Nov;22(22):8042-8059. doi: 10.26355/eurrev_201811_16434.
3. Swerdlow AJ, Wright LB, Schoemaker MJ et al. Maternal breast cancer risk in relation to birthweight and gestation of her offspring. Breast Cancer Res. 2018 Oct 5;20(1):110. doi: 10.1186/s13058-018-1035-6.
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5. Al-Ajmi K, Lophatananon A, Ollier W et al. Risk of breast cancer in the UK biobank female cohort and its relationship to anthropometric and reproductive factors. PLoS One. 2018 Jul 26;13(7):e0201097. doi: 10.1371/journal.pone.0201097. eCollection 2018.



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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 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]



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Prävention durch Änderung von Lifestyle-Faktoren: Gewicht / Glucosestoffwechsel

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ■ Einhaltung Normalgewicht (BMI 18,5 – 25 kg/m²)* <ul style="list-style-type: none"> ■ Prämenopausal ■ Postmenopausal ■ Vermeidung bzw. Früherkennung und Einstellung eines Typ II Diabetes mellitus (Reduktion der Brustkrebsinzidenz und -mortalität) 	2a 3a 2a 2b	B B B B	++ ++ ++ ++

* die Menge an Körperfett kann auch bei normalem BMI erhöht sein und korreliert mit dem Brustkrebsrisiko.

1. Cheraghi Z, Poorolajal J, Hashem T et al.. Effect of body mass index on breast cancer during premenopausal and postmenopausal periods: a meta-analysis. PLoS One. 2012;7(12):e51446.
2. Pierobon M, Frankenfeld CL. Obesity as a risk factor for triple-negative breast cancers: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013 Jan;137(1):307-14.
3. Simpson ER, Brown KA. Obesity and breast cancer: role of inflammation and aromatase. J Mol Endocrinol. 2013 Nov 26;51(3):T51-9.
4. Brinton LA, Cook MB, McCormack V et al.. Anthropometric and hormonal risk factors for male breast cancer: male breast cancer pooling project results. J Natl Cancer Inst. 2014 Mar;106(3):djt46.
5. Chan DS, Vieira AR, Aune D et al. Body mass index and survival in women with breast cancer-systematic literature review and meta-analysis of 82 follow-up studies. Ann Oncol. 2014 Oct;25(10):1901-14.
6. Jiralerspong S, Goodwin PJ. Obesity and Breast Cancer Prognosis: Evidence, Challenges, and Opportunities JCO 2016, 34:4203-4216.
7. Penniecook-Sawyers JA, Jaceldo-Siegl K, Fan J et al. Vegetarian dietary patterns and the risk of breast cancer in a low-risk population, Br J Nutr. 2016; 115(10): 1790-1797.
8. Pizot C, Boniol M, Mullie P et al. Physical activity, hormone replacement therapy and breast cancer risk: A meta-analysis of

prospective studies, Eur J Cancer. 2016; 52:138-54.

9. Daraei A, Izadi P, Khorasani G et al. Epigenetic changes of the ESR1 gene in breast tissue of healthy women: A missing link with breast cancer risk factors? Genet Test Mol Biomarkers 2017; 21: 464-470.

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).



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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.

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

- **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 ≥ 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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Prävention durch Änderung von Lifestyle-Faktoren: Ernährung

* s. Empfehlungen der Dt. Gesellschaft f. Ernährung (DGE)

** Empfohlen als Bestandteil einer gesunden Ernährung

- **Bevorzugung einer ausgewogenen Ernährung***
- **mediterrane Kost**
- **Nahrungszusammensetzung**

- Olivenöl (Natives O. extra) i. Rahmen mediterr. Diät
- Fettreduzierte Nahrung
- Verminderter Konsum an rotem Fleisch
- Ergänzung von Vitaminen, Mineralien, Spurenelem.
- Vitamin-D-Substitution zur Prävention (MaCa RR1,02)
- Gemüse / Obst **
- Phytoöstrogene / Soja
- Ballaststoffreiche Ernährung
- Vegetarische/Vegane Diät (keine sign. Risikoreduktion)
- Kaffee reduziert das MaCa Risiko (bes. Rezeptor-neg)
- Nüsse/Erdnüsse (> 10g/d) (Erdnussbutter ohne Effekt)

	Oxford		
	LoE	GR	AGO
■ Bevorzugung einer ausgewogenen Ernährung*	2b	B	+
■ mediterrane Kost	2a	B	+
■ Nahrungszusammensetzung			
■ Olivenöl (Natives O. extra) i. Rahmen mediterr. Diät	2b	B	+
■ Fettreduzierte Nahrung	2a	B	+
■ Verminderter Konsum an rotem Fleisch	2b	C	+
■ Ergänzung von Vitaminen, Mineralien, Spurenelem.	2a	B	-
■ Vitamin-D-Substitution zur Prävention (MaCa RR1,02)	1b	B	+
■ Gemüse / Obst **	2a	B	+/-
■ Phytoöstrogene / Soja	2a	B	+/-
■ Ballaststoffreiche Ernährung	2a	B	+
■ Vegetarische/Vegane Diät (keine sign. Risikoreduktion)	2b	C	+/-
■ Kaffee reduziert das MaCa Risiko (bes. Rezeptor-neg)	2a	B	+/-
■ Nüsse/Erdnüsse (> 10g/d) (Erdnussbutter ohne Effekt)	2b	B	+

1. Zamora-Ros R, Ferrari P, González CA et al. Dietary flavonoid and lignan intake and breast cancer risk according to menopause and hormone receptor status in the European Prospective Investigation into Cancer and Nutrition (EPIC) Study. Breast Cancer Res Treat. 2013 May;139(1):163-76.
2. Zheng JS, Hu XJ, Zhao YM et al. Intake of fish and marine n-3 polyunsaturated fatty acids and risk of breast cancer: meta-analysis of data from 21 independent prospective cohort studies. BMJ. 2013 Jun 27;346:f3706.
3. Chlebowski RT. Nutrition and physical activity influence on breast cancer incidence and outcome. Breast. 2013 Aug;22 Suppl 2:S30-7.
4. Brinton LA, Cook MB, McCormack V et al.: Anthropometric and hormonal risk factors for male breast cancer: male breast cancer pooling project results. J Natl Cancer Inst. 2014 Mar;106(3):djt465.
5. Farvid MS, Cho E, Chen WY et al. Dietary protein sources in early adulthood and breast cancer incidence: prospective cohort study. BMJ. 2014 Jun 10;348:g3437.
6. Rossi RE, Pericleous M, Mandair D et al. The Role of Dietary Factors in Prevention and Progression of Breast Cancer. Anticancer Res. 2014 Dec;34(12):6861-6875.
7. Penniecook-Sawyers JA, Jaceldo-Siegl K, Fan J et al. Vegetarian dietary patterns and the risk of breast cancer in a low-risk population, Br J Nutr. 2016; 115(10): 1790-1797.

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11. Schwingshackl L, Schwedhelm C, Galbete C et al. Adherence to Mediterranean Diet and Risk of Cancer: An Updated Systematic Review and Meta-Analysis. *Nutrients.* 2017 Sep 26;9(10). pii: E1063. doi: 10.3390/nu9101063.
12. Toledo, E.; Salas-Salvado, J.; Donat-Vargas, C. et al. Mediterranean diet and invasive breast cancer risk among women at high cardiovascular risk in the PREDIMED trial: A randomized clinical trial. *JAMA Intern. Med.* 2015, 175, 1752–1760.
13. Jiang X, Dimou NL, Al-Dabhani K et al. Circulating vitamin D concentrations and risk of breast and prostate cancer: a Mendelian randomization study. *N Engl J Med.* 2019 Jan 3;380(1):33-44. doi: 10.1056/NEJMoa1809944. Epub 2018 Nov 10.
14. Manson JE, Cook NR, Lee IM et al; VITAL Research Group. Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease. *Int J Epidemiol.* 2018 Nov 8. doi: 10.1093/ije/dyy238. [Epub ahead of print]
15. Key TJ, Angela B, Bradbury KE et al. Foods, macronutrients and breast cancer risk in postmenopausal women: a large UK cohort. *Chiropr Med.* 2018 Jun; 17(2): 90–96. Published online 2018 Jun 14. doi: 10.1016/j.jcm.2017.12.001
16. Marc P. McRae. The Benefits of Dietary Fiber Intake on Reducing the Risk of Cancer: An Umbrella Review of Meta-analyses. *Nutr J.* 2018 Sep 21;17(1):87. doi: 10.1186/s12937-018-0394-2.
17. Xiao Y, Ke Y, Wu S et al. Association between whole grain intake and breast cancer risk: a systematic review and meta-analysis of observational studies. *Asian Pac J Cancer Prev.* 2017 Sep 27;18(9):2309-2328.
18. Sak K. Epidemiological Evidences on Dietary Flavonoids and Breast Cancer Risk: A Narrative Review. *Asian Pac J Cancer Prev.* 2017 Sep 27;18(9):2309-2328.
19. Li XJ, Ren ZJ, Qin JW, et al. Coffee consumption and risk of breast cancer: an up-to-date meta-analysis. *PLoS One* 2013;8:e52681 doi:10.1371/journal.pone.0052681 pmid:23308117
20. Poole R, Kennedy OJ, Roderick P et al. Coffee consumption and health: umbrella review of meta-analyses of multiple health

outcomes. BMJ 2017 Nov 22;359:j5024. doi: 10.1136/bmj.j5024.

21. Grosso G, Godos J, Galvano F et al. Coffee, Caffeine, and Health Outcomes: An Umbrella Review. Annu Rev Nutr. 2017 Aug 21;37:131-156. doi: 10.1146/annurev-nutr-071816-064941.



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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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Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease

N Engl J Med. 2019 Jan 3;380(1):33-44. doi: 10.1056/NEJMoa1809944. Epub 2018 Nov 10.

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

1. Manson JE, Cook NR, Lee IM, et al. VITAL Research Group. Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease. N Engl J Med. 2019 Jan 3;380(1):33-44. doi: 10.1056/NEJMoa1809944. Epub 2018 Nov 10.




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Epidemiological Evidences on Dietary Flavonoids and Breast Cancer Risk: A Narrative Review

Sak, K.: [Asian Pac J Cancer Prev. 2017 Sep 27;18\(9\):2309-2328.](#)


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 womencompared 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.”

1. Sak K. Epidemiological Evidences on Dietary Flavonoids and Breast Cancer Risk: A Narrative Review. Asian Pac J Cancer Prev. 2017 Sep 27;18(9):2309-2328.



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Prävention durch Änderung von Lifestyle-Faktoren: Alkohol


Oxford		
LoE	GR	AGO
2a	B	+
2a	B	
2a	B	

- **Reduktion des Alkoholkonsums vermindert Brustkrebsrisiko (ideal < 10g/d, class II evidence)**
- Insbesondere für**
 - ER+/PgR+ Tumoren
 - Invasiv lobuläre Tumoren

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Nature, Nurture and cancer risks: Genetic and nutritional contributions to cancer

Theodoratou, E.: Annu Rev Nutr. 2017 August 21; 37: 293–320.
doi:10.1146/annurev-nutr-071715-051004

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** (≥ 30 g/d of alcohol consumption versus non-drinkers
RR (95% CI): 1.35 (1.23, 1.48, p-value = 5.2×10^{-10} , I² = 26%,
Psmall effect bias = 0.184, P excess significance bias = 4×10^{-8})

1. Theodoratou, E. Nature, Nurture and cancer risks: Genetic and nutritional contributions to cancer. Annu Rev Nutr. 2017 August 21; 37: 293–320. doi:10.1146/annurev-nutr-071715-051004



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Prävention durch Änderung von Lifestyle-Faktoren: Rauchen

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> ■ Frauen, die nie geraucht haben, haben ein verringertes Lebenszeitrisko für einen Brustkrebs (~ 15–24% Reduktion) 	2a	B	++
<ul style="list-style-type: none"> ■ Junge Frauen haben ein 60% höheres Risiko für ein Mammakarzinom, wenn sie > 10 Jahre vor der Geburt des ersten Kindes geraucht haben (vs. Nichtraucherinnen) 			

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Smoking and risk of breast cancer in the Generations Study cohort

Jones, M.E.: Breast Cancer Res. 2017 Nov 22;19(1):118. doi: 10.1186/s13058-017-0908-4.


102,927 women recruited 2003–2013

average of 7.7 years of follow-up

The HR (reference group was never smokers) was
1.14 (95% CI 1.03–1.25; $P = 0.010$) for ever smokers,
1.24 (95% CI 1.08–1.43; $P = 0.002$) for starting smoking at ages < 17 years
1.23 (1.07–1.41; $P = 0.004$) for starting smoking 1–4 years after menarche

Women with a family history of breast cancer (ever vs never smokers HR 1.35; 95% CI 1.12–1.62; $P = 0.002$) had a significantly larger HR ... than women without (ever smoker vs never smoker HR 1.07; 95% CI 0.96–1.20; $P = 0.22$).

1. Jones ME, Schoemaker MJ, Wright LB et al. Smoking and risk of breast cancer in the Generations Study cohort. Breast Cancer Res. 2017 Nov 22;19(1):118. doi: 10.1186/s13058-017-0908-4.



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Prävention durch Änderung von Lifestyle-Faktoren: Körperliche Aktivität

Oxford		
LoE	GR	AGO
2a ⁽⁻⁾	B	++


■ **Körperliche Aktivität**
**Metabolisches Equivalent zu 3–5 Std. Spaziergänge
 pro Woche mit moderater Schrittgeschwindigkeit**

Diese Effekte gelten auch für BRCA1/2-Mutationsträgerinnen und für
 Frauen mit erhöhtem familiärem Risiko.

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Recreational Physical Activity Is Associated with Reduced Breast Cancer Risk in Adult Women at High Risk for Breast Cancer: A Cohort Study of Women Selected for Familial and Genetic Risk.

Kehm RD et al.: Cancer Res. 2020 Jan 1;80(1):116-125. doi: 10.1158/0008-5472.CAN-19-1847. Epub 2019 Oct 2.

- **Prospective cohort study**
- **N=15550, women with fam. Hx of breast cancer**
- **multiplicative interactions of physical activity with predicted absolute breast cancer familial risk based on pedigree data and with BRCA1 and BRCA2 mutation status**
- **Higher physical activity => 20% reduction of breast cancer incidence**
- **(HR0.80, CI 0.68-0.93), independent of BRCA-status or pedigree risk**

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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Prävention durch Lifestyle-Faktoren: Hormontherapie in der Postmenopause

■ Vermeidung von Hormontherapie in der Postmenopause

- Vermeidung von Östrogen-/Gestagen-Kombinat.
- Vermeidung von alleiniger Östrogentherapie
(kein erhöhtes, evt. sogar verringertes Brustkrebsrisiko bei
alleiniger Östrogentherapie, aber erhöhtes EM Ca Risiko)

Oxford		
LoE	GR	AGO
1b	A	+
1b	A	+/-

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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, $P = 3 \times 10^{-12}$) 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 + cholecystectomy?
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

Prevention of Hormones (EGC) in Postmenopausal Patients

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

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



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Prävention durch Änderung von Lifestyle-Faktoren: Orale Kontrazeption (OC)

- Insgesamt erhöht die OC nicht das Risiko an Brustkrebs zu versterben
- Risiko für Mammakarzinom leicht erhöht, Risiko für Ovarial- und Endometriumkarzinom wird erniedrigt

Oxford
LoE

1a

1a⁽⁻⁾

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