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Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Optionen der primären Prävention: Veränderbare Lifestyle-Faktoren



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Prävention

- **Versionen 2011–2021:**

Dall / Diel / Gerber / Hanf / Maass / Mundhenke / Rhiem / Solbach /
Solomayer / Thomssen / von Minckwitz

- **Version 2022:**

Dall / Gerber

Screened data bases

Pubmed 2005 – 2021, ASCO 2012 – 2021, SABCs 2012 – 2021, Cochrane data base 2021



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Risikofaktoren für Brustkrebs 1

- | | |
|---|--|
| <ul style="list-style-type: none">▪ Höheres Alter▪ Genetisches Risiko▪ Familiäre Krebsanamnese▪ Persönliche Brustanamnese<ul style="list-style-type: none">▪ Nicht-proliferative Läsionen▪ Proliferative Läsionen +/- Atypien▪ Hochrisikoläsionen (ADH, LIN)▪ Brustkrebs (DCIS, Inv. MaCa)▪ Brustdichte▪ Thoraxbestrahlung▪ Typ II Diabetes mellitus▪ Hyperthyreose | <ul style="list-style-type: none">▪ Anzahl der Menstruationszyklen im Laufe des Lebens<ul style="list-style-type: none">▪ frühe Menarche, späte Menopause▪ Mütterliche Schwangerschaftsfaktoren (z. B. Präeklampsie → Risikoreduktion) und geringe körperliche Aktivität während der Schwangerschaft (Risikoerhöhung) <p><u>Sozial definierte Risikofaktoren</u></p> <ul style="list-style-type: none">▪ Geringe Geburtenzahl oder keine Schwangerschaft▪ Höheres Alter bei erster Geburt |
|---|--|

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3. Coombes,R.C., Tovey, H, Kilburn, L: Effect of Celecoxib vs Placebo as Adjuvant Therapy on Disease-Free Survival Among Patients With Breast Cancer: The REACT Randomized Clinical Trial. *JAMA Oncol.* 2021 Sep 1;7(9):1291-1301. doi: 10.1001/jamaonc.2021.2193.
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- predictors. BMC Medicine (2020) 18:225 <https://doi.org/10.1186/s12916-020-01690-y>
- 9. Wang B, Lu Z, Huang Y et al. Does hypothyroidism increase the risk of breast cancer: evidence from a metaanalysis. . BMC Cancer (2020) 20:733 <https://doi.org/10.1186/s12885-020-07230-4>
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 - 11. Puvanesarajah S, Gapstur SM, Gansler T et al. Epidemiologic risk factors for in situ and invasive ductal breast cancer among regularly screened postmenopausal women by grade in the Cancer Prevention Study-II Nutrition Cohort. Cancer Causes Control. 2020 Jan;31(1):95-103. doi: 10.1007/s10552-019-01253-4.
 - 12. Mukama T, Fallah M, Brenner H et al. Risk of invasive breast cancer in relatives of patients with breast carcinoma in situ: a prospective cohort study. BMC Med. 2020 Nov 5;18(1):295. doi: 10.1186/s12916-020-01772-x.



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Risikofaktoren für Brustkrebs 2

- Keine / kurze Stillperioden
- Postmenopausaler 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 frühkindlichen Entwicklung (z. B. DES, Bisphenol-A, DDT)
- Einwirkung kanzerogener Substanzen / Arbeitsstoffe
- Exposition gegenüber ionisierender Strahlung

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14. 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.
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19. Puvanesarajah S, Gapstur SM, Gansler T et al. Epidemiologic risk factors for in situ and invasive ductal breast cancer among regularly screened postmenopausal women by grade in the Cancer Prevention Study-II Nutrition Cohort. *Cancer Causes Control.* 2020 Jan;31(1):95-103. doi: 10.1007/s10552-019-01253-4.
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Deodorant-Gebrauch und Risiko

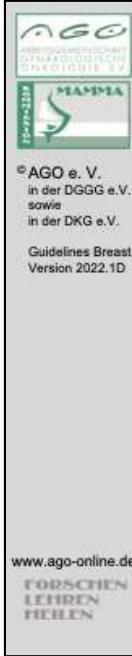
Breast Cancer and Deodorants/Antiperspirants: a Systematic Review.

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.



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

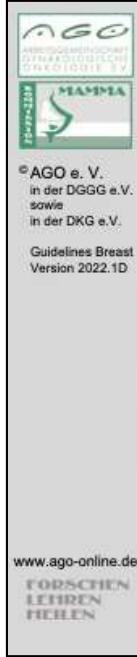
25.7% of postmenopausal breast cancer cases in the Netherlands
in 2010 were attributable to lifestyle factors

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: Tamini 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.



Einfluss durch Reproduktionsfaktoren

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

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- 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.
- 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.
- Ding DC, Chen W, Wang JH et al. Association between polycystic ovarian syndrome and endometrial, ovarian, and breast cancer: A population-based cohort study in Taiwan. *Medicine (Baltimore).* 2018 Sep;97(39):e12608. doi: 10.1097/MD.00000000000012608.
- 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.
- Huang Y, Zhang X, Li W, et al.: A meta-analysis of the association between induced abortion and breast cancer risk among Chinese females. *Cancer Causes Control* 25 (2): 227-36, 2014.
- Guo J, Huang Y, Yang L, et al.: Association between abortion and breast cancer: an updated systematic review and meta-analysis based on prospective studies. *Cancer Causes Control* 26 (6): 811-9, 2015.



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Medikamentöse Primärprävention*

- ASS
- COX2-Inhibitoren
- Bisphosphonate
- Vitamin D
- Statine

Oxford		
LoE	GR	AGO
2a	B	+/-
2a	B	+/-
2b	B	+/-
2b	B	+/-
2b	B	-

* Keine Zulassung, Nebenwirkungsprofil muss berücksichtigt werden

1. Coombes,R.C., Tovey, H, Kilburn, L: Effect of Celecoxib vs Placebo as Adjuvant Therapy on Disease-Free Survival Among Patients With Breast Cancer: The REACT Randomized Clinical Trial. *JAMA Oncol.* 2021 Sep 1;7(9):1291-1301. doi: 10.1001/jamaoncol.2021.2193.
2. Fernandez-Lazaro, CI, Romanos-Nanclares, A, Sánchez-Bayona, R.: Dietary calcium, vitamin D, and breast cancer risk in women: findings from the SUN cohort. *Eur J Nutr* 2021 Oct;60(7):3783-3797. doi: 10.1007/s00394-021-02549-5. Epub 2021
3. Zhou L, Chen B, Sheng L, Turner A.: The effect of vitamin D supplementation on the risk of breast cancer: a trial sequential meta-analysis. *Breast Cancer Res Treat.* 2020 Jul;182(1):1-8. doi: 10.1007/s10549-020-05669-4. Epub 2020 May 13
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Medical Prevention

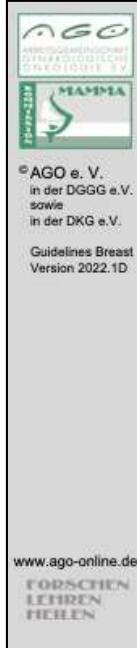
Kehm RD et al. Regular use of aspirin and other non-steroidal anti-inflammatory drugs and breast cancer risk for women at familial or Genetic risk: a cohort study, Breast Cancer Res. 2019 Apr;18(1):52

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]



Prävention durch Änderung von Lifestyle-Faktoren: Gewicht / Glucosestoffwechsel

Oxford		
LoE	GR	AGO
2a	B	++
3a	B	+/-
2a	B	++
2b	B	++

- **Einhaltung Normalgewicht (BMI 18,5-25 kg/m²)***
 - Prämenopausal
 - Postmenopausal
- **Vermeidung bzw. Früherkennung und Einstellung eines Typ II Diabetes mellitus (Reduktion der Brustkrebsinzidenz und -mortalität)**

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

1. Soltani S, Abdollahi S, Aune D, et al. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. *Sci Rep.* 2021 Jan 28;11(1):2479. doi: 10.1038/s41598-021-81671-0
2. Soltani S, Abdollahi S, Aune D, et al. Body mass index and cancer risk in patients with type 2 diabetes: a dose-response meta-analysis of cohort studies. *Sci Rep.* 2021 Jan 28;11(1):2479. doi: 10.1038/s41598-021-81671-0.
3. Ling S, Brown K, Miksza JK, et al. Risk of cancer incidence and mortality associated with diabetes: A systematic review with trend analysis of 203 cohorts. *Nutr Metab Cardiovasc Dis.* 2021 Jan 4;31(1):14-22. doi: 10.1016/j.numecd.2020.09.023. Epub 2020 Sep 25
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5. 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.
6. 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.
7. Jiralerpong S, Goodwin PJ. Obesity and Breast Cancer Prognosis: Evidence, Challenges, and Opportunities *JCO* 2016, 34:4203-4216.
8. Penniecock-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.
9. 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.
10. 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.

11. Escala-Garcia M, Morra A, Canisius S et al. Breast cancer risk factors and their effects on survival: a Mendelian randomisation study. *BMC Med.* 2020 Nov 17;18(1):327. doi: 10.1186/s12916-020-01797-2. PMID: 33198768; PMCID: PMC7670589.
12. Tao W, Santoni G, von Euler-Chelpin M et al. Cancer Risk After Bariatric Surgery in a Cohort Study from the Five Nordic Countries. *Obes Surg.* 2020; 30(10): 3761–3767. Published online 2020 Jun 13. doi: 10.1007/s11695-020-04751-6



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The Risk of Breast, Ovarian and Endometrial Cancer in Obese Women Submitted to Bariatric Surgery: a Meta-Analysis

B Ishihara, D Farah, M Fonseca and A Nazário, Surg Obes Relat Dis 2020;16(10):1596-1602

- **Meta-analysis, of a total of 150,537 patients in the bariatric surgery arm and 1,461,938 women in the control arm.**
- **The risk of breast cancer was reduced by 49 % [RR: 0.39 (95% CI [0.31 to 0.56]; I²= 90%; 7 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).**

1. Ishihara BP, Farah D, Fonseca MCM, et al. The risk of developing breast, ovarian, and endometrial cancer in obese women submitted to bariatric surgery: a meta-analysis. *Surg Obes Relat Dis.* 2020 Oct;16(10):1596-1602. doi: 10.1016/j.sobrd.2020.06.008. Epub 2020 Jun 14. PMID: 32690459.



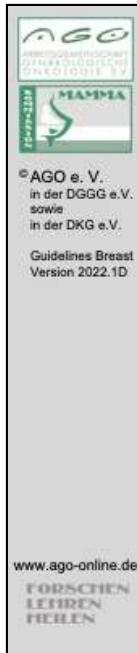
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Association of Body Fat and Risk of Breast Cancer in Postmenopausal Women with Normal Body Mass Index: A Secondary Analysis of a Randomized Clinical Trial and Observational Study

Iyengar 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.



Prävention durch Änderung von Lifestyle-Faktoren: Ernährung

- Bevorzugung einer ausgewogenen Ernährung*
- mediterrane Kost
- Nahrungszusammensetzung
 - Olivenöl (natives O. extra) i. Rahmen mediterraner Diät
 - Fettreduzierte Nahrung
 - Verminderter Konsum an rotem Fleisch
 - Nüsse / Erdnüsse (> 10g/d) (Erdnussbutter ohne Effekt)
 - Ballaststoffreiche Ernährung
 - Vitamin-D-Substitution zur Prävention (MaCa RR1,02)
 - Gemüse / Obst **
 - Phytoöstrogene / Soja
 - Vegetarische / Vegane Diät (keine sign. Risikoreduktion)
 - Kaffee (keine signifikante Risikoreduktion)
 - Ergänzung von Vitaminen, Mineralien, Spurenelementen

Oxford		
LoE	GR	AGO
2b	B	+
2a	B	+
2b	C	+
2b	B	+
2a	B	+
2a	B	+
1b	B	+/-
2a	B	+/-
2a	B	+/-
2b	C	+/-
2a	B	+/-
2a	B	-

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

** Empfohlen als Bestandteil einer gesunden Ernährung

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10.1158/1055-9965.EPI-20-1051. Epub 2020 Aug 14. PMID: 32817071.



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

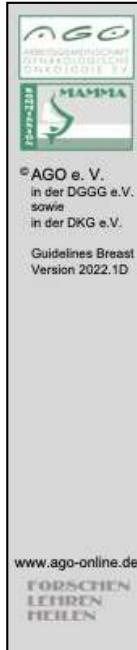
Primary end points were invasive cancer of any type and major cardiovascular events

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.



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+ / PR+ 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} , $I^2 = 26\%$,
 $P_{\text{small effect bias}} = 0.184$, $P_{\text{excess significance bias}} = 4 \times 10^{-8}$)

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



Prävention durch Änderung von Lifestyle-Faktoren: Rauchen

Oxford		
LoE	GR	AGO
2a	B	++

- Frauen, die nie geraucht haben, haben ein verringertes Lebenszeitrisiko für einen Brustkrebs (~ 15-24 % Reduktion)
- Junge Frauen haben ein 60 % höheres Risiko für ein Mammakarzinom, wenn sie > 10 Jahre vor der Geburt des ersten Kindes geraucht haben (vs. Nichtraucherinnen)

1. Poorolajal J, Heidarmoghis F, Karami M, et al. Factors for the Primary Prevention of Breast Cancer: A Meta-Analysis of Prospective Cohort Studies. *J Res Health Sci.* 2021 Jul 20;21(3):e00520. doi: 10.34172/jrhs.2021.57
2. Zhang YB, Pan XF, Chen J, et al. Combined lifestyle factors, incident cancer, and cancer mortality: a systematic review and meta-analysis of prospective cohort studies. *Br J Cancer.* 2020 Mar;122(7):1085-1093. doi: 10.1038/s41416-020-0741-x. Epub 2020 Feb 10
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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.

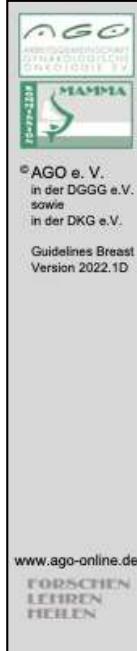
102,927 women recruited 2003–2013

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.



Prävention durch Änderung von Lifestyle-Faktoren: Körperliche Aktivität

Oxford		
LoE	GR	AGO
2a	B	++

- **Körperliche Aktivität**

**Metabolisches Äquivalent 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.

1. Poorolajal J, Heidaramoghis F, Karami M, et al. Factors for the Primary Prevention of Breast Cancer: A Meta-Analysis of Prospective Cohort Studies. *J Res Health Sci.* 2021 Jul 20;21(3):e00520. doi: 10.34172/jrhs.2021.57
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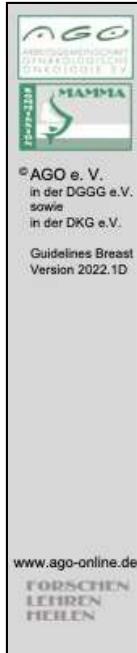
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Recreational Physical Activity is Associated with Reduced Breast Cancer Risk in Adult Women at High Risk for Breast Cancer: A Cohort Study of Women Selected for Familial and Genetic Risk

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. history 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**
- **(HR 0.80, 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.



Prävention durch Lifestyle-Faktoren: Hormontherapie in der Postmenopause

Oxford
LoE GR AGO

■ Vermeidung von Hormontherapie in der Postmenopause

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

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: ELEE (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 x 10⁻¹²) in EPIC-Italy.**

694 CpG sites were associated with ELEE (FDR Q < 0.05)



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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. 4.3 yrs. II 2321 open-label, 2.7 yrs.	1 2763 RCT, med. 4.3 yrs. II 2321 open-label, 2.7 yrs.	1.2 (0.95-1.5)	med. age 67 yrs. no secondary prevention side effects as comp. to WHI + cholecystectomy
Million Women Beral V: Lancet 2003	1.084 110 ~ 50% HRT 4.1J. follow-up	1.66 (1.6-1.8)	EPC > E mode of applic. not relevant duration > 5 yrs. Tibolone 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



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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)	current user
		1.03 (0.82-1.28)	past user
		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



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

Oxford

LoE

1a

1a⁽⁻⁾

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

1. Kanadys W, Barańska A, Malm M, et al. Use of Oral Contraceptives as a Potential Risk Factor for Breast Cancer: A Systematic Review and Meta-Analysis of Case-Control Studies Up to 2010. *Int J Environ Res Public Health.* 2021 Apr 27;18(9):4638. doi: 10.3390/ijerph18094638.
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4. Mørch LS, Skovlund CW, Hannaford PC et al. Contemporary hormonal contraception and the risk of breast cancer. *N Engl J Med.* 2017 Dec 7;377(23):2228-2239.
5. Nur U, El Reda D, Hashim D, Weiderpass E. A prospective investigation of oral contraceptive use and breast cancer mortality: findings from the Swedish women's lifestyle and health cohort. *BMC Cancer* 2019, 19:807



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Risikoreduktion für das ipsi- und kontralaterale Mammakarzinom

Frauen nach Brustkrebs haben ein erhöhtes Risiko für ein kontralaterales Zweitkarzinom.

- Tamoxifen*
- Aromatasehemmer*
- GnRHa + Tamoxifen*

Oxford		
LoE	GR	AGO
1a	A	+
1a	A	+
1b	B	+

* Nur für das HR positive sporadische MaCa belegt

1. Breast International Group 1-98 Collaborative Group, Thurlimann B, Keshaviah A, et al. A comparison of letrozole and tamoxifen in postmenopausal women with early breast cancer. *N Engl J Med.* 2005;353(26):2747-57.
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