

# Diagnostik und Therapie von Patientinnen mit primärem und metastasierten Brustkrebs

## Optionen der primären Prävention: Veränderbare Lifestyle-Faktoren

# Prävention

- **Version 2011-2017:**  
Dall / Diel / Gerber / Maass / Mundhenke / Thomssen / von Minckwitz
- **Version 2018:**  
Dall / Solbach

## Screened data bases

Pubmed 2005 – 2017, ASCO 2012 – 2017, SABCS 2012 – 2017, Cochrane data base 2014

## Screened guidelines

NCI (National Cancer Institute , 2017):

<http://www.cancer.gov/cancertopics/pdq/treatment/breast/healthprofessional>

ASCO (American Association of Clinical Oncology, Practice Guidelines, 2015)

<http://www.asco.org/ASCO/Quality+Care+%26+Guidelines/Practice+Guidelines/Clinical+Practice+Guidelines/Breast+Cancer>.

CMA (Canadian Medical Association, 2015):

<http://www.cmaj.ca/cgi/content/full/158/3/DC1>

NCCN (National Comprehensive Cancer Network); NCCN Guidelines Version 3.2017

Breast Cancer: [https://www.nccn.org/professionals/physician\\_gls/PDF/breast.pdf](https://www.nccn.org/professionals/physician_gls/PDF/breast.pdf)

# Nicht-modifizierbare Risikofaktoren für Brustkrebs

- **Höheres Alter**
- **Genetisches Risiko**
- **Familiäre Krebsanamnese**
- **Persönliche Brustanamnese**
  - Nicht-proliferative Läsionen
  - Proliferative Läsionen +/- Atypien
  - Hochrisikoläsionen (ADH, LIN)
  - Brustkrebs (DCIS, InvBC)
- **Brustdichte**
- **Thoraxbestrahlung**
- **Anzahl der Menstruationszyklen im Laufe des Lebens**  
frühe Menarche, späte Menopause, mütterl. SS-Faktoren (z.B. Präeklampsie (Risikored.), Gestationsdiabetes und geringe phys. Aktivität während der SS (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. American Cancer Society 2017. <https://www.cancer.org/cancer/breast-cancer/risk-and-prevention/breast-cancer-risk-factors-you-cannot-change.html>

# Modifizierbare Risikofaktoren für Brustkrebs

- **Wenig Stillen**
- **BMI < 18,5 und > 25 und besonders > 40 (Adipositas)**
- **Typ II Diabetes mellitus**
- **Nahrungszusammensetzung**
- **Hormontherapie**
  - Kürzlicher oraler Kontrazeptivagebrauch
  - Hormontherapie (Östrogen/Gestagen-Kombination) in der Postmenopause
- **Alkoholabusus**
- **Nikotin**
- **Schlafmangel (Nacht / Schichtarbeit)**
- **Verminderte körperliche Aktivität**
- **Chem. Noxen während der fetalen und frühkindl. Entwicklung (DES, Polyfluoroalkyl)**
  - Bisher gibt es keine Evidenz für eine Korrelation zwischen Aluminium-enthaltenden Deodorants und Brustkrebsrisiko
  - Bisher gibt es keine Evidenz für die Glyphosat-Herbizid-Anwendung und eine Erhöhung des Brustkrebsrisikos

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 postmenopausal 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 2017 <https://www.cancer.org/cancer/breast-cancer/risk-and-prevention/lifestyle-related-breast-cancer-risk-factors.htm>

# 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



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Guidelines Breast  
Version 2018.1D

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**FORSCHEN  
LEHREN  
HEILEN**

## 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)

# Präventiver Einfluss durch das Reproduktionsverhalten

	Oxford		
	LoE	GR	AGO
▪ 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	

1. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and breastfeeding: collaborative reanalysis of individual data from 47 epidemiological studies in 30 countries, including 50302 women with breast cancer and 96973 women without the disease. Lancet 2002;360:187-95.
2. Martin RM, Middleton N, Gunnell D et al.. Breast-feeding and cancer: the Boyd Orr cohort and a systematic review with meta-analysis. J Natl Cancer Inst. 2005;97:1446-57.
3. Lord SJ, Bernstein L, Johnson KA et al.. Breast cancer risk and hormone receptor status in older women by parity, age of first birth, and breastfeeding: a case-control study. Cancer Epidemiol Biomarkers Prev. 2008;17(7):1723-30.
4. Ma H, Henderson KD, Sullivan-Halley J et al.. Pregnancy-related factors and the risk of breast carcinoma in situ and invasive breast cancer among postmenopausal women in the California Teachers Study cohort. Breast Cancer Res. 2010;12(3):R35.
5. 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.



## Prävention durch Änderung von Lifestyle-Faktoren: Gewicht / Glucosestoffwechsel

- **Einhaltung Normalgewicht (BMI 18,5 – 25 kg/m<sup>2</sup>)**
  - Prämenopausal
  - Postmenopausal
- **Vermeidung bzw. Früherkennung und Einstellung eines Typ II Diabetes mellitus**  
(Reduktion der Brustkrebsinzidenz und -mortalität)

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

- 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.
- 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.
- Simpson ER, Brown KA. Obesity and breast cancer: role of inflammation and aromatase. J Mol Endocrinol. 2013 Nov 26;51(3):T51-9.
- 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.
- 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.
- Jiralerspong S, Goodwin PJ. Obesity and Breast Cancer Prognosis: Evidence, Challenges, and Opportunities JCO 2016, 34:4203-4216.
- 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.
- 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.
- 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.

# 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<sup>2</sup> (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

# Prävention durch Änderung von Lifestyle-Faktoren: Ernährung

	Oxford		
	LoE	GR	AGO
■ <b>Bevorzugung einer ausgewogenen Ernährung*</b>	<b>2b</b>	<b>B</b>	<b>+</b>
■ <b>Nahrungszusammensetzung</b>			
■ <b>Fettreduzierte Nahrung</b>	<b>2a</b>	<b>B</b>	<b>+</b>
■ <b>Verminderter Konsum an rotem Fleisch</b>	<b>2a</b>	<b>B</b>	<b>+</b>
■ <b>Ergänzung von Vitaminen, Mineralien, Spurenelem.</b>	<b>2a</b>	<b>B</b>	<b>-</b>
■ <b>Vitamin-D-Substitution zur Prävention</b>	<b>3a</b>	<b>B</b>	<b>+/-</b>
■ <b>Gemüse / Obst</b>	<b>2a</b>	<b>B</b>	<b>+/-**</b>
■ <b>Phytoöstrogene / Soja</b>	<b>2a</b>	<b>B</b>	<b>+/-</b>
■ <b>Ballaststoffreiche Ernährung</b>	<b>1b</b>	<b>A</b>	<b>+</b>
■ <b>Vegetarische Diät (keine Risikoreduktion)</b>	<b>1b</b>	<b>B</b>	<b>+/-</b>
■ <b>Vegane Diät (keine signifikante Risikoreduktion)</b>	<b>1b</b>	<b>B</b>	<b>+/-</b>
■ <b>Nüsse/Erdnüsse (&gt;10g/d)</b>	<b>2b</b>	<b>B</b>	<b>+</b>

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

\*\* Empfohlen als Bestandteil einer gesunden Ernährung

1. Trichopoulou A, Bamia C, Lagiou P et al.. Conformity to traditional Mediterranean diet and breast cancer risk in the Greek EPIC (European Prospective Investigation into Cancer and Nutrition) cohort. Am J Clin Nutr. 2010 Sep;92(3):620-5.
2. 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.
3. 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.
4. Chlebowski RT. Nutrition and physical activity influence on breast cancer incidence and outcome. Breast. 2013 Aug;22 Suppl 2:S30-7.
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):djt465.
6. 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.
7. 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.
8. 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.
9. Chajès V, Assi N, Biessy C et al.. A prospective evaluation of plasma phospholipid fatty acids and breast cancer risk in the EPIC study. Ann Oncol 2017;28: 2836-2842.
10. Limon-Miro AT, Lopez-Teros V, Astiazaran-Garcia H. .Dietary Guidelines for Breast Cancer Patients: A Critical Review. Adv Nutr. 2017 Jul 14;8(4):613-623.
11. van den Brandt PA, Nieuwenhuis L.. Tree nut, peanut, and peanut butter intake and risk of postmenopausal breast cancer: The Netherlands Cohort Study. Cancer Causes Control. 2018 Jan;29(1):63-75.

## 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**

van den Brandt PA et al. Cancer Causes Control. 2017 Nov 22. doi: 10.1007/s10552-017-0979-7.

# Prävention durch Änderung von Lifestyle-Faktoren: Alkohol

## ■ Reduktion des Alkoholkonsums vermindert Brustkrebsrisiko

### Insbesondere für

- ER+/PgR+ Tumoren
- Invasiv lobuläre Tumoren

Oxford		
LoE	GR	AGO
2b	B	
2b	B	
2b	B	

1. Suzuki R, Orsini N, Mignone L et al.. Alcohol intake and risk of breast cancer defined by estrogen and progesterone receptor status--a meta-analysis of epidemiological studies. Int J Cancer. 2008 Apr 15;122(8):1832-41.
2. Li CI, Chlebowski RT, Freiberg M et al.. Alcohol Consumption and Risk of Postmenopausal Breast Cancer by Subtype: The Women's Health Initiative Observational Study. J Natl Cancer Inst 2010;102:1422–1431.
3. McDonald JA, Goyal A, Terry MB. Alcohol Intake and Breast Cancer Risk: Weighing the Overall Evidence. Curr Breast Cancer Rep. 2013 Sep;5(3). doi: 10.1007/s12609-013-0114-z.
4. Bagnardi V, Rota M, Botteri E et al.. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. Br J Cancer. 2015 Feb 3;112(3):580-93.

# Prävention durch Änderung von Lifestyle-Faktoren: Rauchen

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

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. Bjerkaas E, Parajuli R, Weiderpass E et al.. Smoking duration before first childbirth: an emerging risk factor for breast cancer? Results from 302,865 Norwegian women. Cancer Causes Control. 2013 Jul;24(7):1347-56.
3. Dossus L, Boutron-Ruault MC, Kaaks R et al.. Active and passive cigarette smoking and breast cancer risk: results from the EPIC cohort. Int J Cancer. 2014 Apr 15;134(8):1871-88.

# Prävention durch Änderung von Lifestyle-Faktoren: Körperliche Aktivität

## ■ Körperliche Aktivität

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

Oxford		
LoE	GR	AGO
2a <sup>(-)</sup>	B	++

1. Friedenreich CM. Physical activity and breast cancer: review of the epidemiologic evidence and biologic mechanisms. Recent Results Cancer Res. 2011;188:125-39.
2. Wu Y, Zhang D, Kang S. Physical activity and risk of breast cancer: a meta-analysis of prospective studies. Breast Cancer Res Treat. 2013 Feb;137(3):869-82.
3. Chlebowski RT. Nutrition and physical activity influence on breast cancer incidence and outcome. Breast. 2013 Aug;22 Suppl 2:S30-7.
4. Kerr J, Anderson C, Lippman SM. Physical activity, sedentary behavior, diet and cancer: an update and emerging new evidence. Lancet Oncol. 2017 Aug;18(8):e457-e471.



# Prävention durch Lifestyle-Faktoren: Hormontherapie in der Postmenopause

	Oxford		
	LoE	GR	AGO
■ <b>Vermeidung von Hormontherapie in der Postmenopause</b>			
■ Vermeidung von Östrogen-/Gestagen-Kombinat.	1b	A	+
■ Vermeidung von alleiniger Östrogentherapie Die alleinige Östrogentherapie 5 Jahre nach der Menopause zeigt kein erhöhtes Brustkrebsrisiko	1b	A	+/-

1. Beral V; Million Women Study Collaborators. Breast cancer and hormone-replacement therapy in the Million Women Study. Lancet 2003; 362: 419 – 27.
2. Chlebowski RT, Hendrix SL, Langer RD et al.. Influence of estrogen plus progestin on breast cancer and mammography in healthy postmenopausal women: the Women's Health Initiative Randomized Trial. JAMA 2003; 289: 3243–3253.
3. Reeves GK, Beral V, Green J et al.. Hormonal therapy for menopause and breast-cancer risk by histological type: a cohort study and meta-analysis. Lancet Oncol 2006; 7: 910–918.
4. De P, Neutel CI, Olivotto I et al.. Breast cancer incidence and hormone replacement therapy in Canada. J Natl Cancer Inst 2010; 102: 1489 – 95.
5. Chlebowski RT, Anderson GL, Gass M et al.. Estrogen plus progestin and breast cancer incidence and mortality in postmenopausal women. JAMA 2010;304: 1684–1692.
6. Sæther S, Bakken K, Lund E. The risk of breast cancer linked to menopausal hormone therapy. Tidsskr Nor Laegeforen 2012;132: 1330–1334.
7. Marjoribanks J, Farquhar C, Roberts H et al.. Long term hormone therapy for perimenopausal and postmenopausal women. Cochrane Database Syst Rev. 2012 Jul 11;7:CD004143.
8. Manson JE, Chlebowski RT, Stefanick ML et al.. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. JAMA. 2013 Oct 2;310(13):1353-68.
9. Chlebowski RT, Anderson GL, Prentice RL et al.. Reliable evidence from placebo-controlled, randomized, clinical trials for menopausal hormone therapy's influence on incidence and deaths from breast cancer. Climacteric. 2015 Jun;18(3):336-8.
10. Chlebowski RT, Aragaki AK, Anderson GL. Menopausal Hormone Therapy Influence on Breast Cancer Outcomes in the Women's Health Initiative. J Natl Compr Canc Netw. 2015 Jul;13(7):917-24.
11. Salagame U, Banks E, Sitas F et al.. Menopausal hormone therapy use and breast cancer risk in Australia: Findings from the New South Wales Cancer, Lifestyle and Evaluation of Risk study. Int J Cancer. 2016 Apr 15;138(8):1905-14.
12. Manson JE, Aragaki AK, Rossouw JE et al.. Menopausal hormone therapy and long-term all-cause and cause-specific mortality, the women's health initiative randomized trials. JAMA 2017; 318: 927-938.

# Prevention of Hormones in Postmenopausal Patients

	N	MC-RR (95%CI)	Further information
<b>WHI</b> WHI: JAMA 2002, JAMA 2017	~ 27 000	<b>1.3</b> (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
<b>HERS</b> Hulley S: JAMA 2002	<b>I 2763</b> RCT, med. 4.1 J <b>II 2321</b> open-label, 2.7J	<b>1.2</b> (0.95-1.5)	med. age 67 J no secondary prevention side effects as comp. to WHI + cholecystectomy 7
<b>Million Women</b> Beral V: Lancet 2003	<b>1.084 110</b> ~ 50% HRT 4.1 J. follow-up	<b>1.66</b> (1.6-1.8)	EPC > E mode of applic. not relevant duration > 5 yrs. Tibolon RR 1.45 (1.2-1.7)
<b>EPIC</b> Int J Cancer 2010	<b>1.153 747</b> person-years	<b>1.4</b> (1.2-1.6) <b>1.8</b> (1.4-2.2)	E-Mono EPC > E
<b>Metaanalyse</b> Nelson HD: JAMA 2002	<b>16 Studies</b>	<b>1.21-1.40</b>	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
<b>CLEAR-study (NSW)</b>	<b>1236 BC cases</b>	2.09 (1.57-2.78)	current user
<b>Case-Control-Study, retrospect. Australia</b>		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
<ul style="list-style-type: none"> <li>■ Insgesamt erhöht die OC <u>nicht</u> das Risiko an Brustkrebs zu versterben</li> </ul>	1a
<ul style="list-style-type: none"> <li>■ <u>Risiko</u> für Mamakarzinom evtl. leicht erhöht, Risiko für Ovarial- und Endometriumkarzinom wird erniedrigt</li> </ul>	1a <sup>(-)</sup>

1. Cibula D, Gompel A, Mueck AO et al.. Hormonal contraception and risk of cancer. Human Reproduction Update, 2010; 16(6): 631–650.
2. Gierisch JM, Coeytaux RR, Urrutia RP et al. Oral contraceptive use and risk of breast, cervical, colorectal, and endometrial cancers: a systematic review. Cancer Epidemiol Biomarkers Prev. 2013 Nov;22(11):1931-43.
3. Moorman PG, Havrilesky LJ, Gierisch JM et al.. Oral contraceptives and risk of ovarian cancer and breast cancer among high-risk women: a systematic review and meta-analysis. J Clin Oncol. 2013 Nov 20;31(33):4188-98.
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.