

Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

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Options for Primary Prevention: Modifiable Lifestyle Factors

Prevention

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- **Version 2011:**
Gerber / Thomssen
- **Versions 2012–16:**
Dall / Diel / Gerber / Maass / Mundhenke
- **Version 2017:**
Mundhenke / von Minckwitz

Further
Information

References

Non-modifiable Risk Factors for Breast Cancer

- **Older age**
- **Genetic risk factors**
- **Family cancer history**
- **Personal history of breast lesions**
 - **Non-proliferative lesions**
 - **Proliferative lesions w/o atypia**
 - **High risk lesions (ADH, LIN)**
 - **Breast cancer (DCIS, InvBC)**
- **Breast density**
- **Chest irradiation**
- **Lifetime number of menstrual cycles**
 - **Early menarche, late menopause, mat. pregnancy factors (e.g. preeclampsia (risk reduction), gestational diabetes (risk increase))**

Reproductive risk factors

- **Lower number of births or no pregnancy**
- **Higher age at first full term delivery**

Modifiable

Risk Factors for Breast Cancer

- **Less breast feeding**
- **BMI < 18.5 and > 25 and especially > 40 (obesity)**
- **Diabetes mellitus Type II**
- **Food content**
- **Steroid hormone therapy**
 - Recent oral contraceptive use
 - Hormone therapy in postmenopausal women
- **Alcohol intake**
- **Smoking**
- **Light exposure at night (night shifts)**
- **Low physical activity**
- **Toxic agents in fetal and early childhood development (DES, polyfluoroalkyls)**
 - So far, there is no evidence for a correlation between aluminium containing antiperspirants and breast cancer
 - So far, there is no evidence for Glyphosate herbicide use and breast cancer



High Proportion of Postmenopausal Breast Cancer Attributable to Lifestyle Factors

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population attributable fractions (PAFs) of modifiable risk factors

Risk factors: obesity, physical inactivity, alcohol, low-fibre 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 are attributable to lifestyle factors

- 8.8% for obesity
- 6.6% for alcohol
- 5.5% for physical inactivity
- 3.2.% for low fibre intake
- 4.6% for smoking

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Further Information

References

**FORSCHEN
LEHREN
HEILEN**

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

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)

Prevention by Changing Pregnancy Related Factors



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- | | Oxford / AGO
LoE / GR |
|--|--------------------------|
| ➤ Any full term pregnancy | 2b B |
| ➤ Number of pregnancies | 2b B |
| ➤ First full term pregnancy
before age of 30 years | 2b B |
| ➤ Breast feeding
(protective if total breast feeding
time exceeds 1.5–2 years) | 3a B |

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Prevention by Changing Lifestyle Factors: Body Mass Index / Diet

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- | | |
|--|--|
| <ul style="list-style-type: none"> ➤ Maintaining normal weight
(BMI at 18,5 – 25 kg/m²) <ul style="list-style-type: none"> ➤ Premenopausal ➤ Postmenopausal
 ➤ Prevention/Screening and treatment
of diabetes mellitus type II
(reduction of breast cancer incidence
and mortality) | <p>2a B ++</p> <p>3a B ++</p> <p>2a B ++</p>
<p>2b B ++</p> |
|--|--|

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Prevention by Changing Lifestyle

Factors: Diet

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LoE / GR

	Oxford / AGO LoE / GR
➤ Preference of a balanced diet*	2b B +
➤ Dietary components	
➤ Fat reduced food (unsaturated > saturated fatty acids)	2a B +
➤ Reduced consumption of red meat	2a B +
➤ Supplementation of vitamins, minerals, tracer elements	2a B -
➤ Vitamin D substitution for prevention	3a B +/-
➤ Vegetables / fruits	2a B +/-**
➤ Phytoestrogens / soya	2a B +/-
➤ Fiber containing food	1b A +
➤ Vegetarian diet (no risk reduction)	1b B +/-
➤ Vegan diet (no significant risk reduction)	1b B +/-

* As recommended by German Society of Nutrition (DGE)

**Recommended as a part of healthy nutrition

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Prevention by Modifying Lifestyle Risk Factors: Alcohol

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- **Reduction of alcohol intake reduces risk of breast cancer**

2b B

Particularly for

- **ER+/PgR+ tumors**
- **Invasive lobular tumors**

2b B

2b B

Prevention by Modifying Lifestyle Risk Factors: Smoking

Oxford / AGO
LoE / GR

- **Never smoking reduces risk of breast cancer (~ 15-24% reduction of lifetime risk)**
- **Young women smoking have a 60% increased risk of bc, when smoking > 10 years before the first childbirth (vs. never smokers)**

2a B ++

Prevention by Modifying Lifestyle Risk Factors: Physical Activity

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➤ **Physical exercise**

2a⁽⁻⁾ B ++

(Metabolic equivalents to 3–5 hrs moderate pace walking per week)

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

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- **Avoiding hormonal therapy in postmenopausal women**
 - **Avoiding estrogen / progestin combinations**
 - **Avoiding estrogens only**
(no increasing risk for breast cancer by using estrogens alone, but increasing risk for endometrial cancer)

1b A +

1b A +/-

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Hormones in Postmenopausal Patients

	N	MC-RR(95%CI)	Further information
WHI WHI: JAMA 2002	~ 27 000	1.3 (1,0-1,6)	1,3 (1,1-1,6) coronaric 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 ⁷
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 Studien	1.21-1.40	side effects as compared to WHI +

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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
Case- Control- Study, retrospect. Australia		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

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Prevention by Modifying Lifestyle Risk Factors: Oral Contraception (OC)

Oxford

LoE

1a

- Overall, OC does not significantly increase risk of cancer
- Risk of breast cancer may be slightly increased, risk of ovarian, endometrial cancer is decreased

1a⁽⁻⁾

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Options for Primary Prevention: Modifiable Lifestyle Factors (2/17)

Further information and references:

Screened data bases:

Pubmed 2005 - 2016, ASCO 2012 – 2016, SABCS 2012 – 2016, Cochrane data base (2014)

Screened guidelines:

NCI (National Cancer Institute , 2015): <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 , 2015):

http://www.nccn.org/professionals/physician_gls/PDF/breast.pdf (download 13. JAN. 2015)

Non Modifiable Risk Factors for Breast Cancer (3/17)

No further information

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Modifiable Risk Factors for Breast Cancer Risk (4/17)

No further information

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High Proportion of Postmenopausal Breast Cancer Attributable to Lifestyle Factors (5/17)

No further information

No references

Secondary Prevention, Lifestyle and TNBC Subgroup (6/17)

No further information

No references

Secondary Prevention, Lifestyle and ER-positive Subgroup (7/17)

No further information

No references

Prevention by Changing Pregnancy Related Factors (8/17)

No further information

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Prevention by Changing Life Style Factors: Body Mass Index / Diet (9/17)

No further information

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Prevention by Changing Life Style Factors: Diet (10/17)

No further information

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Prevention by Modifying Life Style Risk Factors: Alcohol (11/17)

No further information

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Prevention by Modifying Life Style Risk Factors: Smoking (12/17)

No further information

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Prevention by Modifying Life Style Risk Factors: Physical Activity (13/17)

No further information

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Prevention by Modifying Life Style Risk Factors: Hormone Therapy in Postmenopausal Women (14/17)

No further information

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Prevention - Hormones in Postmenopausal Patients (15/17)

No further information

No references

Prevention - Hormones (EGC) in Postmenopausal Patients (16/17)

No further information

No references

Prevention by Modifying Life Style Risk Factors: Oral contraception (17/17)

No further information

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