The Effect of Overweight and Nutrition on Prognosis in Breast Cancer

Dagmar Hauner, Wolfgang Janni, Brigitte Rack, Hans Hauner

SUMMARY

Background: Breast cancer is the most common cancer in women. Body weight and nutrition are known to play an important role in its pathogenesis. The question thus arises whether lifestyle factors might influence the prognosis of breast cancer, potentially offering new approaches for secondary prevention.

Methods: We selectively searched the Medline database for all studies and meta-analyses on this topic that were published from 1966 to June 2010. We evaluated the cohort studies, interventional trials, and meta-analyses with respect to three target variables: tumor recurrence, tumor-specific mortality, and overall mortality.

Results: A high body-mass index (BMI) at the time of diagnosis of breast cancer is associated with higher overall mortality, as is weight gain at later times. A low-fat diet rich in fruit, vegetables, and fiber seems to be weakly associated with a better prognosis. On other hand, there is no evidence for any benefit from micronutrients, supplements, or antioxidant foods. Alcohol consumption does not affect the outcome in breast cancer. Two intervention trials of reduced fat intake showed no effect on survival, but the target of the intervention was not met in either trial.

Conclusion: The intervention trials yielded negative results. Nevertheless, in view of the methodological difficulties in this area of research and the overall life situation of women with breast cancer, the authors recommend a health-promoting lifestyle with avoidance of overweight and a low-fat diet rich in fruit, vegetables, and fiber.

information were found in the reference lists of the identified studies.

The defined end points were tumor recurrence, breast cancer specific mortality, and all-cause mortality. We evaluated the studies in the basis of the methods used by the World Cancer Research Fund (2). The evidence levels we used were “convincing”, “probable”, “possible”, and “limited”. We regarded recommendations for lifestyle changes as sufficiently sound only on the basis of convincing or probable evidence (2).

We did not conduct a systematic meta-analysis of comparable study data. Instead we adopted weighted hazard ratios (HR) from recently published meta-analyses (3, 4), in order to show effect sizes of individual factors. We used only HR and relative risk (RR) values after multivariate adjustment, in as far as this had been done in the publications we studied, since observational studies regarding diet/nutrition always have a complex association with people’s general health behaviors. It is easy to imagine that a healthy diet is associated with a generally healthy lifestyle, so that studies that investigate the effects of healthy nutrition may attribute successes to this factor when in actual fact the entire lifestyle is responsible.

**Results**

**Association of body weight and prognosis of breast cancer**

Even earlier meta-analyses found that obese women have a higher risk for tumor recurrence and a higher mortality compared with slender people (5). Our own research into this topic identified 17 cohort studies (e1–e17). In 13 out of 15 studies with the end point all-cause mortality, a significant positive association between body mass index (BMI) and mortality was found; in one study a trend in this direction was identified (eTable). Six out of 12 studies with the end point breast cancer specific mortality showed a significant positive association, three further studies showed a trend, and three studies (e3, e4, e13) did not find any association (eTable).

Premenopausal overweight is associated with a lower risk for developing breast cancer, according to the WCRF data (2), whereas the present study found a positive association between BMI at the time of diagnosis and mortality not only in women with postmenopausal breast cancer but also in those with premenopausal breast cancer. Seven out of nine studies that differentiated between premenopausal and postmenopausal breast cancer showed significant positive associations, one study merely a trend, and one study no association (e4) (eTable). This represents convincing evidence for an association between obesity and all-cause mortality and a probable evidence for an association between obesity and breast cancer specific mortality.

The results were less clear-cut for recurrence rates. Two (e6, e16) out of six studies with the end point breast cancer recurrence showed a significant association with BMI and two further studies (e10, e12) showed a trend; two further studies did not find any association (eTable). An unequivocal conclusion is therefore not possible.

**Association of weight gain and breast cancer prognosis**

The WCRF report stated that weight gain per se was a risk factor for developing postmenopausal breast cancer (2). Most observational studies found a weight gain in women after a breast cancer diagnosis. Seven cohort studies were identified to determine the importance of weight gain for breast cancer prognosis (e5, e8, e10, e14, e16, e18, e19). Five of six studies with the endpoint all-cause mortality and all four studies with the endpoint breast cancer specific mortality found a significant positive association with weight gain (Table 1). No clear result was found for the end point recurrence rate. Only two of five studies showed a significant positive association with weight gain; three studies showed no association. The results provide convincing evidence of an increase in all-cause mortality and breast cancer specific mortality after weight gain subsequent to a breast cancer diagnosis.

**The influence of diet/nutrition on the prognosis of breast cancer**

Only very few cohort studies have thus far investigated the influence of diet/nutrition on the prognosis of breast cancer (6–9, e9, e11, e13, e20–e26). In 11 of these studies, the importance of the composition of macronutrients for mortality was analyzed as an end point.

Only one of three studies providing data about carbohydrate consumption (6, 7, e23) showed a protective effect for a high consumption. Of the six studies including data on fat intake, four showed a trend for a risk increase (7, e20, e21, e23) for a high consumption, only one showed a significantly increased risk (7). Three out of four cohort studies showed a protective effect for dietary fiber (6, 7, e21, e23), in two of these the results reached significance, yielding a pooled hazard ratio of 0.63 (3). A diet rich in fruit, vegetables, wholegrain products, legumes, fowl, and fish also showed a beneficial effect on all-cause mortality (e24, e26). By contrast, a typical Western diet with a high intake of bleached flour products, red meat, full-fat dairy products, etc, was found to be non-beneficial and was associated with an increase in non-breast cancer specific mortality (e24, e26) and a significant increase in all-cause mortality (e26).

**Special food products, such as soy products or green tea**—An evaluation of the Shanghai Breast Cancer Survival Study (SBCSS) found an inverse relation between the intake of soy products and the risk of recurrence (hazard ratio [HR] 0.68; 95% confidence interval [CI] 0.54 to 0.87, highest versus lowest quartile) and all-cause mortality (HR 0.71; CI 0.54 to 0.92) (8). A recent meta-analysis identified three further studies into the topic but did not find this inverse correlation (9).

Only a small number of observational studies and case-control studies have investigated the effect of green tea on breast cancer. A study from Japan, which...
## TABLE 1

<table>
<thead>
<tr>
<th>Author</th>
<th>No of cases, tumor stages</th>
<th>Mean follow-up (years)</th>
<th>End points</th>
<th>Menopausal status and/or age</th>
<th>Timing of data collection</th>
<th>Results</th>
</tr>
</thead>
</table>
| Camoriano JK et al., 1990 (e18) | 646, LN positive          | 6.6                    | All-cause mortality, recurrence rate            | pre-post-menopausal          | After diagnosis            | Premenopausal women (n = 330): all-cause mortality: HR 1.62 (95% CI 1.01 to 2.62); p = 0.04; recurrence rate: HR 1.5; p = 0.17  
Postmenopausal women (n = 215): all-cause mortality: n.s.*, recurrence rate: n.s.* |
| Kroenke CH et al., 2005 (e5)    | 5204, invasive, no metastases | 9                     | Recurrence rate, breast cancer specific mortality, all-cause mortality | pre/post-menopausal          | After diagnosis            | In never-smokers: recurrence rate: weight gain (n = 984, 156 cases) vs. stable weight (n = 677, 75 cases), p for trend = 0.01; breast cancer specific mortality: weight gain (n = 984, 123 deaths) vs. stable weight (n = 677, 48 deaths), p for trend = 0.03; all-cause mortality: weight gain (n = 984, 167 deaths) vs. stable weight (n = 677, 78 deaths), p for trend = 0.04; In former and current smokers: n.s. |
| Caan BJ et al., 2006 (e19)      | 3215, stages I to IIIa    | 6.1                    | Recurrence rate                                 | 18–70 years                  | After diagnosis            | Moderate weight gain (5–10%) vs. stable weight: recurrence rate: HR 0.8 (95% CI 0.6 to 1.1), n.s.  
Notable weight gain (>10%) vs. stable weight recurrence rate: HR 0.9 (95% CI 0.7 to 1.2), n.s. |
| Cleveland RJ et al., 2007 (e8)  | 1508, invasive and in situ| 5.6                    | Breast cancer specific mortality, all-cause mortality | pre/post-menopausal          | Before diagnosis           | Breast cancer specific mortality: weight gain >16 kg (n = 123, 19 deaths) vs. stable weight (n = 78, 6 deaths) HR 2.09 (95% CI 0.80 to 5.48), p for trend = 0.08  
All-cause mortality: weight gain >16 kg (n = 123, 22 deaths) vs. stable weight (n = 78, 6 deaths) HR 2.45 (95% CI 0.96 to 6.27), p for trend = 0.062  
Postmenopausal: breast cancer specific mortality: weight gain >12.7 kg (n = 162, 15 deaths) vs. stable weight (n = 370, 12 deaths) HR 2.95 (95% CI 1.36 to 6.43), n.s.  
All-cause mortality: weight gain >12.7 kg (n = 162, 38 deaths vs. stable weight (n = 370, 28 deaths) HR 2.69 (95% CI 1.63 to 4.43), n.s. |
| Caan BJ et al., 2009 (e10)      | 1692, stages I to IIIa    | 7                      | Recurrence rate, all-cause mortality            | pre/post-menopausal          | After diagnosis            | Recurrence rate: weight gain (n = 604, 65 events) vs. stable weight (n = 799, 100 events), p for trend 0.99  
All-cause mortality: weight gain (n = 604, 52 deaths) vs. stable weight (n = 799, 100 deaths), p for trend 0.08 |
| Nichols HB et al., 2009 (e14)   | 3993, invasive, no metastases | 6.3                    | Breast cancer specific mortality, all-cause mortality | 20–79 years                  | After diagnosis            | Breast cancer specific mortality: per 5 kg weight gain (n = 2234, 77 deaths) vs. stable weight (n = 1037, 28 deaths), HR 1.13 (95% CI 1.03 to 1.25), p = 0.01  
All-cause mortality: per 5 kg weight gain (n = 2234, 197 deaths) vs. stable weight (n = 1037, 98 deaths), HR 1.12 (95% CI 1.04 to 1.22), p = 0.004 |
| Chen X et al., 2010 (e16)       | 5042, all stages          | 3.8                    | Recurrence rate, breast cancer specific mortality, all-cause mortality | 20–75 years                  | After diagnosis            | Recurrence rate: weight gain ≥ 5 kg (n = 1060, 72 events) vs. stable weight (n = 866, 32 events), HR 1.90 (95% CI 1.23 to 2.93)  
Breast cancer specific mortality: weight gain ≥ 5 kg (n = 1060, 72 deaths) vs. stable weight (n = 866, 32 deaths), HR 1.90 (95% CI 1.23 to 2.93)  
All-cause mortality: weight gain ≥ 5 kg (n = 1096, 69 deaths) vs. stable weight (n = 833, 35 deaths), HR 1.71 (95% CI 1.12 to 2.60) |

LN, lymph node; HR, hazard ratio; RR, relative risk; n.s., non-significant; CI, confidence interval; * no exact data available
<table>
<thead>
<tr>
<th>Author</th>
<th>No of cases, tumor stages</th>
<th>Mean follow-up (years)</th>
<th>End points</th>
<th>Menopausal status and/or age</th>
<th>Timing of data collection</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Holmes MD et al., 1999 (6)</td>
<td>1982, invasive</td>
<td>18</td>
<td>All-cause mortality</td>
<td>pre-/post-menopausal</td>
<td>N/A</td>
<td>Highest vs. lowest quartile RR 0.92 (95% CI 0.66 to 1.27), n.s.</td>
</tr>
<tr>
<td>Borugian MJ et al., 2004 (e23)</td>
<td>603, all stages</td>
<td>10</td>
<td>Breast cancer specific mortality</td>
<td>pre-/post-menopausal</td>
<td>At diagnosis</td>
<td>Alcohol consumers vs. those not drinking alcohol, n.s.</td>
</tr>
<tr>
<td>Barnett GC et al., 2008 (e9)</td>
<td>4560, invasive</td>
<td>6.8</td>
<td>All-cause mortality</td>
<td>&lt;55 years</td>
<td>After diagnosis</td>
<td>Risk per unit (= 8 g pure alcohol/week) (n = 4155, 564 deaths), HR 0.98 (95% CI 0.97 to 0.99), p = 0.0045</td>
</tr>
<tr>
<td>Reding KW et al., 2008 (e29)</td>
<td>1286, invasive</td>
<td>10 plus</td>
<td>All-cause mortality</td>
<td>≤ 45 years</td>
<td>Before diagnosis</td>
<td>Alcohol intake in the 5 years before diagnosis Consumer (n = 955, 254 deaths) vs non-consumer (n = 322, 106 deaths) HR 0.7 (95% CI 0.5 to 0.9)</td>
</tr>
<tr>
<td>Franceschi S et al., 2009 (e30)</td>
<td>1453, invasive</td>
<td>12.6</td>
<td>All-cause mortality</td>
<td>23–74 years</td>
<td>After diagnosis</td>
<td>Consumers of alcohol (n = 1127, 383 deaths) vs. never-drinkers (n = 326, 120 deaths), HR 0.95 (95% CI 0.79 to 1.22), n.s.</td>
</tr>
<tr>
<td>Flatt SW et al., 2010 (e31)</td>
<td>3088, stages I to Illa</td>
<td>7.3</td>
<td>Recurrence rate, all-cause mortality</td>
<td>pre-/post-menopausal</td>
<td>After diagnosis</td>
<td>Moderate alcohol consumption (&gt;300 mg/month) vs. alcohol &lt;10 g/month Recurrence rate: drinker (n = 634, 100 events) vs. non-drinker (n = 1133, 213 events), HR 0.91 (95% CI 0.71 to 1.18)* All-cause mortality: drinker (n = 634, 52 deaths) vs. non-drinker (n = 1133, 139 deaths), HR 0.69 (95% CI 0.49 to 0.97)</td>
</tr>
</tbody>
</table>

HR, hazard ratio; RR, relative risk; n. s., not significant; N/A, not available; 95% CI, 95% confidence interval; * no exact data available
Discussion
The incidence of breast cancer is increasing in Germany in the same way as in the rest of the world. In view of this increase, new concepts and strategies are desirable to prevent tumor recurrence and improve the quality of life and survival expectancy in those affected. The study results we presented imply that lifestyle choices can modify the prognosis for these patients, but our understanding of these associations is limited and incomplete.

What is currently known is derived almost entirely from cohort studies. Although the cohort sizes have notably increased in recent years and the quality of data collection has improved, intrinsic methodological limitations remain that restrict the validity of the results thus gained. Cohort studies can merely highlight associations; they cannot provide any information on cause and effect. Owing to the multitude of interactions between known and unknown factors—especially in the context of lifestyle—biases and incidental findings cannot be excluded. The result: reliable conclusions are possible only for effects that consistently occur in different cohorts or that have been confirmed in interventional studies.

According to the WCRF’s assessment criteria, the present analysis provides convincing evidence that a high BMI is associated with a worse prognosis for women with breast cancer. This association has a high biological plausibility, as has been shown repeatedly in the recent past (16, 17). A new meta-analysis found an increase in all-cause mortality and breast cancer specific mortality in association with obesity of 30%, respectively, which was more pronounced in premenopausal women than in postmenopausal women (4).

Weight gain after a diagnosis of breast cancer is common (18, 19). The reasons are complex and poorly understood (5, 18, 20, e33, e34). Such weight gain obviously increases the mortality risk, so that this aspect should be subject to great attention in the future.

A result in the present analysis that is particularly worth mentioning is the absence of evidence for the benefit of many products that women with breast cancer are often offered as support measures. This is particularly the case for the multitude of vitamin and mineral preparations on offer. According to a recent US study, more than 60% of women receiving adjuvant therapy for breast cancer take preparations containing beta carotene, vitamin C, vitamin E, or selenium (e35). For individual substances—for example, antioxidant preparations—if taken while undergoing chemotherapy or radiotherapy, a certain risk increase cannot be excluded (21).

An interesting finding of our literature search was the fact that the analysis of the prognostic factors for breast cancer deviates partly from the results reported by the WCFR (2). The WCRF reported convincing evidence for alcohol in the sense of a risk increase for
premenopausal and postmenopausal breast cancer, whereas our evaluation did not find a negative influence, however, this is probably masked by the beneficial effects of moderate alcohol consumption on cardiovascular risk. A convincing explanation for this discrepancy is so far lacking.

The two interventional studies in women with breast cancer that have been conducted so far (14, 15) addressed the question of the degree to which reducing fat intake to below 15% to 20% of the total energy intake improves the prognosis. The intervention programs did, however, not consider the quality of the fat and left body weight and exercise activity altogether out of the analysis. Since the desired fat reduction was only partly successful and had little effect on prognosis, the question is how future lifestyle intervention programs for women with breast cancer should be designed. Subgroup analyses of both studies showed that if the instructions were adhered to then a positive influence on individual end variables was noted (e32). However, nowadays the consensus is mostly that the focus is on weight management and exercise and that multimodal approaches should be studied (22).

On this background, new interventional studies are urgently needed. In view of the good prognosis for women with non-metastatic breast cancer (1), other intervention objectives should also be considered, such as the reduction of cardiovascular disorders that is to be expected from lifestyle adjustment, as well as type 2 diabetes or the women’s quality of life. Lifestyle programs should not be limited only to preventing tumor recurrence, as their benefits can be assumed to be rather more comprehensive. In Germany, the SUCCESS-C Study is currently investigating the benefit of a two-year lifestyle intervention with moderate weight reduction on the recurrence-free survival of women with non-metastatic breast cancer (23).

**Conflict of interest statement**

Professor Janni has received unrestricted educational grants from Sanofi-Aventis, Chugai, and Pfizer.

Dr Rack has been reimbursed for participation fees for continuing medical educational events and travel expenses by Sanofi-Aventis, Amgen, Pfizer, AstraZeneca, Chugai, Novartis, and cephalon. She has received honoraria for presenting from Sanofi-Aventis, Amgen, Pfizer, Novartis, Chugai, and Lilly.

Professor H Hauner has in the past received honoraria for presenting from Sanofi-Aventis, Lilly, Novartis, Novo Nordisk, Abbott, and BMS. Furthermore, he has received honoraria for acting as an adviser from Nycemed and Weight-Watchers, and is currently the principal investigator in a drug trial conducted by Riemser.

Dr D Hauner declares that no conflict of interest exists.

Manuscript received on 17 August 2010, revised version accepted on 9 May 2011.

Translated from the original German by Dr Birte Twisselmann.

**REFERENCES**


15. Pierce JP, Natarajan L, Caan BJ, et al.: Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following

---

**KEY MESSAGES**

- Overweight/obesity is associated with increased mortality in women with premenopausal and postmenopausal breast cancer.
- The widespread and common weight gain after a breast cancer diagnosis is also indicative of a poor prognosis.
- A healthy diet with a high proportion of fruit, vegetables, whole grain products, and low amounts of fat seems to be associated with better survival. However, interventional studies have thus far not confirmed this association. The typical Western diet is associated with a poorer prognosis.
- There is no indication that supplementation with vitamins, minerals, or trace elements improves the prognosis of women with breast cancer.
- Although the importance of alcohol is still not clear, only very moderate consumptions seems acceptable.
61: 301–16.
20. Irwin ML, Crumley D, McTiernan A, et al.: Physical activity levels be-
fore and after a diagnosis of breast carcinoma: the Health, Eating,
JB: Should supplemental antioxidant administration be avoided during chemotherapy and radiation therapy? J Natl Cancer Inst
ity, weight control, and breast cancer risk and survival: clinical trial
rationale and design considerations. J Natl Cancer Inst 2009; 101:
630–643.
CESS C Study—the first European lifestyle study on breast cancer.
Breast Care 2010 DOI: 10.1159/000322677
The Effect of Overweight and Nutrition on Prognosis in Breast Cancer

Dagmar Hauner, Wolfgang Janni, Brigitte Rack, Hans Hauner

eREFERENCES


### eTABLE

<table>
<thead>
<tr>
<th>Author</th>
<th>No of cases, tumor stages</th>
<th>Mean follow-up</th>
<th>End points</th>
<th>Menopausal status and/or age</th>
<th>Timing of BMI measurement</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daling JR et al., 2001 (e1)</td>
<td>1177, invasive, ductal</td>
<td>Not specified</td>
<td>All-cause mortality after 5 and 10 years</td>
<td>&lt;47 years</td>
<td>At diagnosis</td>
<td>All-cause mortality after 10 years: BMI highest quartile (n = 132, 44 deaths) vs. lowest quartile (n = 125, 27 deaths) HR 1.7 (95% CI 1.0 to 2.9); p&lt;0.05</td>
</tr>
<tr>
<td>Dignam et al., 2003 (e2)</td>
<td>3385, ER positive, early stages</td>
<td>13.8</td>
<td>Recurrence rate, breast cancer specific mortality, all-cause mortality</td>
<td>pre-/postmenopausal</td>
<td>After diagnosis</td>
<td>Recurrence rate (787 events in total): BMI ≥ 30 kg/m² vs. BMI &lt;25 kg/m², HR 0.98 (95% CI 0.80 to 1.18); n.s.</td>
</tr>
<tr>
<td>Berclaz G et al., 2004 (e3)</td>
<td>6792, early stages</td>
<td>14</td>
<td>Breast cancer-free survival, total survival</td>
<td>pre-/postmenopausal</td>
<td>After diagnosis</td>
<td>Breast cancer-free survival: BMI ≥ 30 kg/m² vs. BMI &lt; 25 kg/m², n.s. 10-year cancer-free survival: obese women (n = 1 024) 42 ± 2% “intermediate” women (n = 2038) 44 ± 1% women of normal weight (n = 3308) 45 ± 1 % Total survival: BMI ≥ 30 kg/m² vs. BMI &lt;25 kg/m², p = 0.03 10-year total survival: obese women (n = 1024) 55 ± 2% “intermediate” women (n = 2038): 57 ± 1% women of normal weight (n = 3308) 61 ± 1 %</td>
</tr>
<tr>
<td>Enger SM et al., 2004 (e4)</td>
<td>717, all stages</td>
<td>10.4</td>
<td>Breast cancer-specific mortality</td>
<td>premenopausal ≤ 40 years</td>
<td>Before diagnosis</td>
<td>Breast cancer specific mortality: highest BMI quartile (n = 118, 64 deaths) vs. lowest quartile (n = 110, 65 deaths), n.s.</td>
</tr>
<tr>
<td>Kroenke CH et al., 2005 (e5)</td>
<td>5204, invasive, no metastases</td>
<td>9</td>
<td>Recurrence rate, breast cancer specific mortality, all-cause mortality</td>
<td>pre-/postmenopausal</td>
<td>Before diagnosis</td>
<td>Recurrent tumors (n = 714): RR 1.00 (95% CI 0.76 to 1.31); n.s. Breast cancer specific mortality (n = 533): RR 1.09 (95% CI 0.80 to 1.48); p for trend = 0.045 All-cause mortality (n = 860): RR 1.20 (95% CI 0.95 to 1.52); p for trend &lt;0.001 Associations with BMI stronger in premenopausal than in postmenopausal women</td>
</tr>
<tr>
<td>Loi S et al., 2005 (e6)</td>
<td>1360, no metastases</td>
<td>5</td>
<td>Recurrence rate, all-cause mortality</td>
<td>&lt;60 years at diagnosis 74% premenopausal</td>
<td>Before diagnosis</td>
<td>Recurrence rate (not reported): obese vs. normal weight: HR 1.57 (95% CI 1.11 to 2.22); p= 0.02 All-cause mortality (184 deaths): obese vs. normal weight: HR 1.56 (95% CI 1.01 to 2.40); p= 0.06 Premenopausal women: Recurrence rate (not reported): obese vs. normal weight: HR 1.71 (95% CI 1.05 to 2.77), p = 0.04 All-cause mortality: obese vs. normal weight: HR 1.71 (95% CI 1.05 to 2.77), p = 0.04</td>
</tr>
<tr>
<td>Whitman MK et al., 2005 (e7)</td>
<td>3924, all stages</td>
<td>14.6</td>
<td>Breast cancer specific mortality</td>
<td>20–54 years</td>
<td>Before diagnosis</td>
<td>Breast cancer specific mortality: BMI ≥ 30 (n = 263, 109 deaths) vs. BMI ≤ 22.99 (n = 2331, 733 deaths) HR 1.34 (95% CI 1.09 to 1.65); p for trend 0.0001 Premenopausal women: Breast cancer specific mortality: BMI ≥ 30 (n = 161, 65 deaths) vs. BMI ≤ 22.99 (n = 1576, 501 deaths), HR 1.38 (95% CI 1.05 to 1.80), p for trend = 0.002</td>
</tr>
<tr>
<td>Cleveland RJ et al., 2007 (e8)</td>
<td>1508, invasive and in situ</td>
<td>5.5</td>
<td>Breast cancer specific mortality, all-cause mortality</td>
<td>pre-/postmenopausal</td>
<td>Before diagnosis</td>
<td>Breast cancer specific mortality (n = 127): obese vs. normal weight: HR 2.85 (95% CI 1.30 to 6.24) All-cause mortality (n = 196): HR 2.62 (95% CI 1.26 to 5.45)</td>
</tr>
<tr>
<td>Barnett GC et al., 2008 (e9)</td>
<td>4560, invasive</td>
<td>6.8</td>
<td>All-cause mortality</td>
<td>&lt;55 years</td>
<td>After diagnosis</td>
<td>All-cause mortality (620 deaths):</td>
</tr>
<tr>
<td>Dal Maso L et al., 2008 (e11)</td>
<td>1453, invasive</td>
<td>12.6</td>
<td>Breast cancer specific mortality, all-cause mortality</td>
<td>pre-/postmenopausal (58.3 years at diagnosis)</td>
<td>1 year before diagnosis</td>
<td>Breast cancer specific mortality (398 deaths): HR 1.3 (95% CI 1.02 to 1.66); p for trend 0.06</td>
</tr>
<tr>
<td>Majed B et al., 2008 (e12)</td>
<td>14 709, all stages</td>
<td>8</td>
<td>Recurrence rate, disease-free survival, total survival</td>
<td>pre-/postmenopausal</td>
<td>At diagnosis</td>
<td>Recurrence rate: HR 1.12 (95% CI 1.00 to 1.26); n.s.</td>
</tr>
<tr>
<td>Emaus A et al., 2009 (e13)</td>
<td>1364, all stages</td>
<td>8.2</td>
<td>All-cause mortality</td>
<td>27–79 years</td>
<td>Before diagnosis</td>
<td>All-cause mortality (429 deaths): p for trend = 0.04 for all BMI categories BMI ≥ 30 (n = 147, 60 deaths) vs. BMI 18.5 to 25 kg/m² (n = 808, 232 deaths)</td>
</tr>
<tr>
<td>Nichols HB et al., 2009 (e14)</td>
<td>3993, invasive, no metastases</td>
<td>6.3</td>
<td>Breast cancer specific mortality, all-cause mortality</td>
<td>20–79 years</td>
<td>Before and after diagnosis</td>
<td>Breast cancer specific mortality: BMI ≥ 30 kg/m² (n = 2058, 50 deaths) vs. BMI 18.5 to 25 kg/m² (n = 1479, 31 deaths)</td>
</tr>
<tr>
<td>West-Wright CN et al., 2009 (e15)</td>
<td>3539, invasive</td>
<td>At least 1 year</td>
<td>Breast cancer specific mortality, all-cause mortality</td>
<td>pre-/postmenopausal</td>
<td>After diagnosis</td>
<td>Breast cancer specific mortality: BMI ≥ 30 (n = 469, 39 deaths) vs. BMI &lt;25 kg/m² (n = 1945, 99 deaths); RR 1.71 (95% CI 1.16 to 2.53)</td>
</tr>
<tr>
<td>Chen X et al., 2010 (e16)</td>
<td>5042, all stages</td>
<td>3.8</td>
<td>Recurrence rate, breast cancer specific mortality, all-cause mortality</td>
<td>20–75 years</td>
<td>Before, at, and after diagnosis</td>
<td>At diagnosis: Recurrences/breast cancer specific mortality: BMI ≥ 30 kg/m² (n = 250, 41 deaths) vs. BMI &lt;25 kg/m² (n = 256, 44 deaths) vs. BMI 18.5 to 24.9 kg/m² (n = 3231, 284 deaths); HR 1.44 (95% CI 1.02 to 2.03)</td>
</tr>
<tr>
<td>Keegan TH et al., 2010 (e17)</td>
<td>4153, invasive</td>
<td>7.8</td>
<td>All-cause mortality</td>
<td>&lt;65 years</td>
<td>Before diagnosis</td>
<td>All-cause mortality: obese women (n = 712) vs. women of normal weight (n = 2220); HR 1.21 (95% CI 1.00 to 1.48); p for heterogeneity = 0.03 BMI and all-cause mortality p for trend = 0.01 for women ≥ 50 years (n = 1699)</td>
</tr>
</tbody>
</table>

ER, estrogen receptor; HR, hazard ratio; RR, relative risk; n.s., non-significant; CI, confidence interval; * no exact data available