

Weight and Breast Cancer Risk



In a comprehensive approach to understanding the risks of cancer and the efficacy of preventive and therapeutic interventions, lifestyle factors, such as nutrition and physical activity, have been identified as important considerations.

In this issue brief we review current information on the impact of body weight on breast cancer incidence and mortality. Subsequent briefs will review interventions to address weight gain and weight loss in cancer patients.

Weight, weight gain, and obesity contribute to the incidence of 20-35% of all cancers, including esophageal, thyroid, colon, renal,

liver, melanoma, multiple myeloma, rectal, gallbladder, leukemia, and lymphoma; prostate cancer in men; and post-menopausal breast and endometrial cancer in women (1). In the United States, it has been estimated that 14% of cancer deaths in men and 20% in women are attributable to obesity and being overweight (2).

For women with cancer, pre-diagnosis weight gain appears to be the strongest predictor of an adverse breast cancer prognosis. Being obese before breast cancer diagnosis was associated with increased risk of recurrence and poorer survival (3). Circulating levels of inflammatory cytokines have been associated with the development of breast cancer (4). Several mechanisms have been suggested to explain an association of obesity with a chronic mild inflammatory state.

Among several contributing factors, including hormone levels, breast density, and adiposity, menopausal status plays a significant role in breast cancer incidence, recurrence and survival risk. Being overweight or obese during childhood and into early adulthood may be protective of breast cancer and, in fact, decrease risk for pre-menopausal breast cancer (5, 6). However, after menopause, obese women, compared to women of healthy weight, are at increased risk for dying from breast cancer. Highest risk for breast cancer appears to be in those women who are underweight or lean in early life (i.e., age 18 years) with positive weight gain both before and after menopause (16). Height may also incur additional risk for both pre- and post-menopausal breast cancer (7). Women at least 69 inches tall were found to be 20% more likely to develop breast cancer, compared to women 63 inches tall (15).

A number of mechanisms exist through which obesity may influence survival in obese or overweight survivors. Poor prognosis among overweight or obese post-menopausal women with breast cancer may be related to higher estrogen and androgen levels. There is also an association

between obesity and later stage at diagnosis and larger tumor size, as adiposity mediates carcinogenesis. Obesity and increased insulin and insulin-like growth factors also may play a large role in increasing risk for recurrence or contributing to poor prognosis (8).

Unfortunately, many women gain weight after breast cancer diagnosis. There is some indication that women gain weight and percent body fat within the first three years of diagnosis (9), and this period may be the most opportune time to provide intervention. Weight gain is associated with decreased quality of life, body dissatisfaction, increased risk of post-operative complications, and, of course, increased risk for recurrence (10).

Factors contributing to weight gain after breast cancer diagnosis include treatment regimen, tamoxifen use, fatigue, decreased physical activity, decreased lean body mass, decreased resting energy expenditure, increased consumption of foods to cope with nausea, or treatment-related increase in appetite. In a population-based cohort study of over 5,000 women with stage 0-III breast cancer, weight change patterns from diagnostic baseline to 36 months post-diagnosis were evaluated, and it was noted that more weight gain was observed in women with more advanced stage disease, of younger age, with lower body mass index at diagnosis, pre-menopausal, and/or receiving chemotherapy and radiation therapy within 6 months of diagnosis (11).

Weight gain during and after breast cancer diagnosis has an adverse effect on survival. Higher risk of relapse and death was noted in one study which found that, for each 5-kg gain in weight, there was an associated 12% increase in all-cause mortality, a 13% increase in breast cancer mortality, and a 19% increase in cardiovascular disease mortality (4). One of the largest studies to date of weight gain and survival found that greater than median weight gain led to higher risk for relapse and death compared to those with less than median weight gain (12).

What lies on the horizon to better understand weight, weight gain and breast cancer prognosis? How is survival influenced across the range of

weight gains? Time of lifestyle change needs further study as it appears important in determining risk of onset or survival. Weight gain and level of physical activity each contribute to risk. Counseling patients with breast cancer to increase physical activity, as well as diet interventions to avoid weight gain, may improve outcomes. Considerations related to exercise and cancer risk will be addressed in a subsequent issue brief.

In summary, weight, weight gain, and obesity represent important factors in post-menopausal breast cancer incidence and mortality risk. Although alternative explanations remain possible, studies have demonstrated weight gain during mid-to-late-adulthood appears most associated with increased post-menopausal breast cancer incidence risk. For breast cancer patients, weight gain during the first three post-diagnosis years most correlates with poor prognosis. Approaches to improved nutritional status and physical activity should be included in a comprehensive approach to cancer control.

Sources:

1. McTiernan A, Irwin M, Vongruenigen V. Weight, physical activity, diet, and prognosis in breast and gynecologic cancers. *J Clin Oncol.* 2010 Sep 10; 28(26):4074-80.
2. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ. Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. *New England Journal of Medicine* 2003; 348(17):1625-1638.
3. Caan BJ, Kwan ML, Hartzell G, Castillo A, Slattery ML, Sternfeld B, Weltzien E. Pre-diagnosis body mass index, post-diagnosis weight change, and prognosis among women with early stage breast cancer. *Cancer Causes Control.* 2008 Dec; 19(10):1319-28.
4. Pakiz B, Flatt SW, Bardwell WA, Rock CL, Mills PJ. Effects of Weight Loss Intervention on Body Mass, Fitness, and Inflammatory Biomarkers in Overweight or Obese Breast Cancer Survivors. *Int J Behav Med* 2011 Feb; published online.
5. Lahmann PH, Shulz M, Hoffmann K, Boeing H, Tjonneland A, Olsen A, Overvad K, Key TJ, Allen NE, Khaw KT, Bingham S, Berglund G, Wirfalt E, Berrino F, Krogh V, Trichopoulou A, Lagiou P, Tricopoulos D, Kaaks R, Riboli E. Long-term Weight change and Breast Cancer Risk: The European Prospective Investigation into Cancer and Nutrition (EPIC). *Br Journal of Ca.* 2005 Aug; 93: 582-589.
6. Van Den Brandt PA, Spiegelman D, Yaun SS, Adami H-O, Beeson L, Folsom AR, Fraser G, Goldbohm RA, Graham S, Kushi L, Marshall JR, Miller AB, Rohan T, Smith-Warner SA, Speizer FE, Willett W, Wolk A, Hunter DJ. Pooled Analysis of Prospective Cohort Studies on Height, Weight and Breast Cancer Risk. *American Journal of Epidemiology* 1999 June; 152(6): 514-527.
7. Nichols HB, Trentham-Dietz A, Egan KM, Titus-Ernstoff L, Holmes MD, Bersch AJ, Holick CN, Hampton JM, Stampfer MJ, Willett WC, Newcomb PA. Body mass index before and after breast cancer diagnosis: associations with all-cause, breast cancer, and cardiovascular disease mortality. *Cancer Epidemiol Biomarkers Prev.* 2009 May; 18(5):1403-9.
8. Kroenke CH, Chen WY, Rosner B, Holmes MD. Weight, weight gain, and survival after breast cancer diagnosis. *J Clin Oncol.* 2005 Mar 1; 23(7):1345-7.
9. Irwin ML, McTiernan A, Baumgartner RN, Baumgartner KB, Bernstein L, Gilliland FD, Ballard-Barbash R. Changes in body fat and weight after a breast cancer diagnosis: influence of demographic, prognostic, and lifestyle factors. *J Clin Oncol.* 2005 Feb 1; 23(4):774-82.
10. Ligibel JA, Partridge A, Giobbie-Hurder A, Campbell N, Shockro L, Salinadri T, Winer EP. Physical and psychological outcomes among women in a telephone-based exercise intervention during adjuvant therapy for early stage breast cancer. *J Womens Health (Larchmt).* 2010 Aug; 19(8):1553-9.
11. Gu K, Chen X, Zheng Y, Chen Z, Zheng W, Lu W, Shu XO. Weight change patterns among breast cancer survivors: results from the Shanghai breast cancer survival study. *Cancer Causes Control.* 2010 Apr; 21(4):621-9. Epub 2009 Dec 31.
12. Camoriano JK, Loprinzi CL, Ingle JN, and et: Weight change in women treated with adjuvant therapy or observed following mastectomy for node-positive breast cancer. *J Clin Oncol* 8:1327-1334. 1990
13. Makari-Judson G, Judson CH, Mertens WC. Longitudinal patterns of weight gain after breast cancer diagnosis: observations beyond the first year. *Breast J.* 2007 May-Jun; 13(3):258-65.
14. Cleveland RJ, Eng SM, Abrahamson PE, Britton JA, Teitelbaum SL, Neugut AI, Gammon MD. Weight gain prior to diagnosis and survival from breast cancer. *Cancer Epidemiol Biomarkers Prev.* 2007 Sep; 16(9):1803-11.
15. Van den Brandt PA, Spiegelman D, Yaun SS, Adami HO, Beeson L, Folsom AR, Fraser G, Goldbohm RA, Graham S, Kushi L, Marshall JR, Miller AB, Rohan T, Smith-Warner SA, Speizer FE, Willett WC, Wolk A, Hunter DJ. Pooled analysis of prospective cohort studies on height, weight, and breast cancer risk. *Am J Epidemiol.* 2000; 152(6):514.
16. Eliassen AH, Colditz GA, Rosner B, Willett WC, Hankinson SE. Adult weight change and risk of postmenopausal breast cancer. *JAMA.* 2006; 296:193-201.

