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### THE ROLE OF NUTRITION IN BREAST CANCER RECURRENCE RISK AND SURVIVAL By Lawrence H. Kushi, ScD, and Isaac J. Ergas, PhD

Breast cancer continues to be the most common cancer among women in the U.S.<sup>1</sup> and worldwide,<sup>1, 2</sup> and it is the second most common cause of cancer-related death in the U.S., after lung cancer.<sup>1</sup> With breast cancer incidence gradually increasing and mortality rates from breast cancer decreasing,<sup>3</sup> the American Cancer Society (ACS) now estimates that there are more than four million breast cancer survivors in the U.S. today.<sup>4</sup>

In part because of the large number of breast cancer survivors, there is growing interest in whether lifestyle measures outside conventional medical therapy can improve quality of life and prognosis after a diagnosis of breast cancer. A 2006 ACS position paper on diet and physical activity in cancer survivors noted that people diagnosed with cancer often wonder whether lifestyle changes may lower recurrence risk or improve outcomes.<sup>5</sup> This organization's most recent position paper highlights increasing evidence of the important role of diet; especially in the case of breast cancer, but notes that the evidence to support definitive recommendations are still lacking.<sup>6</sup>

Several studies have evaluated the impact of diet on breast cancer recurrence and survival, with notable insights from both randomized controlled trials (RCTs) and observational studies. Two significant RCTs are the Women's Intervention Nutrition Study (WINS)<sup>7</sup> and the Women's Healthy Eating and Living (WHEL) study.<sup>8</sup> WINS assessed the impact of a low-fat diet (15-20% of total daily calories from fat) on breast cancer recurrence and overall survival, while the WHEL study focused on a low-fat diet rich in fruits, vegetables, and fiber. Although a meta-analysis of these studies suggested modest effects on overall survival,<sup>9</sup> the WINS study reported a 24% reduction in recurrence risk among those following the low-fat diet.

Observational studies have also provided valuable insights into the relationship between diet and breast cancer outcomes. The Nurses' Health Study (NHS), a longrunning prospective cohort study of female nurses, has examined numerous health outcomes in relation to diet and other factors. This study has the unique benefit of having dietary data both before and after occurrence of disease, including breast cancer, because periodic assessment of food intake has been a central part of the study. Analyses based on these data showed that intake of a prudent ("healthy") dietary pattern, which typically includes high consumption of fruits, vegetables, whole grains, poultry, and fish, was associated with reduced mortality from causes other than breast cancer. In contrast, a Western ("unhealthy") dietary pattern, characterized by high intake of red and processed meats, refined grains, sweets, high-fat dairy products, and high-calorie fast food, was associated with increased mortality from non-breast cancer causes.<sup>10</sup> Findings also showed increased survival among women eating more protein, but not red meat.<sup>11</sup> The Pathways Study is one of the first prospective cohort studies designed specifically to examine risk factors associated with outcomes after breast cancer diagnosis.<sup>12</sup> Among other areas, the cohort study of approximately 4,500 women is investigating various aspects of diet and lifestyle following diagnosis. Key findings among women indicate that diet quality aligned with healthy eating recommendations (such as the ACS nutrition guidelines, the alternate Mediterranean diet index (aMED), Dietary Approaches to Stop Hypertension (DASH), and the 2015 Healthy Eating Index (HEI)) around the time of diagnosis are associated with lower risks of non-breast cancerspecific and all-cause mortality.<sup>13</sup> Moreover, sustained concordance with healthful plant-based diets comprised of foods such as soy foods, legumes, nuts, and seeds, is associated with lower risks of all-cause and non-breast-cancer mortality, while unhealthful plant-based diets, which can include high intakes of refined grains, sugars, and processed foods, showed opposite associations.<sup>14</sup>

Furthermore, improvements in diet quality, coupled with increased physical activity and reduced smoking post-diagnosis, were estimated to substantially lower risks of allcause mortality over both short and long-term periods.<sup>15</sup> Also, a post-diagnosis lifestyle score, based on alignment with comprehensive lifestyle recommendations from the ACS (which encourages fruits, vegetables, legumes, and whole grains, and discourages saturated fats), demonstrated inverse associations with all-cause and breast cancerspecific mortality.<sup>16</sup> Finally, higher diet quality at diagnosis was associated with lower risk of cardiovascular disease events and related deaths among breast cancer patients, suggesting potential dual benefits of healthy dietary habits in this population.<sup>17</sup>

Findings from other recent publications generally align with those of the Pathways Study. The Shanghai Breast Cancer Survivors Study which included about 3,450 women who survived at least five years after a breast cancer diagnosis, found that healthy dietary patterns, including concordance with the DASH and 2015 HEI, were associated with lower risk of total mortality over the subsequent 10 years.<sup>18</sup> Consistency with a healthy dietary pattern based on Chinese dietary guidelines also was associated with lower mortality.<sup>18</sup> Similarly, an analysis from the Breast Cancer Family Registries that included over 6,100 women with breast cancer reported that greater alignment with healthy dietary patterns (DASH, HEI, and aMED), was associated with lower all-cause mortality, particularly among women with a body mass index less than 25kg/m2 or women with hormone-receptor positive tumors.<sup>19</sup> Analyses in over 13,000 women with breast cancer in the European Prospective Investigation into Cancer suggested that greater concordance with a healthy Mediterranean diet pattern was associated with a modest reduced risk of death over nearly nine years after diagnosis.<sup>20</sup>

In conclusion, evidence from the Pathways Study and other recent research supports the growing consensus that dietary choices before and after a diagnosis of breast cancer can significantly impact prognosis. In particular, women who consumed diets that were concordant with healthy dietary patterns had a lower risk of death. While these findings do not point to specific foods or biological mechanisms, they are directly relevant to informing dietary guidelines for women diagnosed with breast cancer. Current evidence suggests that emphasizing plant foods, including whole grains, soy foods, legumes, vegetables, and fruits, is beneficial not just for the general population, but also for women diagnosed with breast cancer.

#### ABOUT THE AUTHORS

**Lawrence Kushi, ScD,** is a research scientist at the Division of Research, Kaiser Permanente Northern California. Among other projects, he founded and co-leads the NCI-supported Pathways Study, a prospective cohort study of women with breast cancer that is examining diet and other factors in breast cancer prognosis and outcomes.

**Isaac J. Ergas earned his PhD** in Epidemiology from the University of California, Berkeley and is a staff scientist at Kaiser Permanente Northern California's Division of Research. His research focuses on diet, lifestyle, and behavioral risk factors and their impact on breast, bladder, and prostate cancer survivorship.

# DOES POSTDIAGNOSIS SOY INTAKE IMPACT BREAST CANCER OUTCOMES?

### By Mark Messina, PhD, MS

Despite 30 years' worth of research, the question of whether postdiagnosis soy intake impacts breast cancer outcomes cannot be definitively answered because the necessary clinical data to do so are not available. However, dietary advice based on imperfect data is routinely issued. In fact, most of the understanding about diet/ health relationships, especially as related to chronic disease risk, is based on the results of observational studies (which do not allow cause and effect relationships to be established).

As highlighted below, in the case of soy and women with breast cancer, there is an impressive body of evidence upon which intake recommendations can be based.

#### Origins of the Controversy

The classification of soybean isoflavones as phytoestrogens, despite being much different than the hormone estrogen;<sup>1</sup> and the lack of evidence that estrogen therapy worsens the prognosis of women with breast cancer<sup>2,3</sup> provided a conceptual basis for concern.

The stimulatory effect of isoflavones on the growth of existing estrogen-sensitive mammary tumors in athymic ovariectomized mice, first reported in the late 1990s, is generally seen as the genesis of the soy and breast cancer controversy.<sup>4,5</sup>

#### **Clinical Studies**

In healthy women, at-risk women, and women with breast cancer, isoflavones delivered in the form of supplements or soy protein -- even in amounts greatly exceeding typical Asian intake -- have no effects on markers of breast cancer risk including mammographic density<sup>6-19</sup> and breast cell proliferation.<sup>20-25</sup>

In contrast to isoflavones, combined hormone therapy (estrogen plus progestin) adversely impacts breast cancer risk markers<sup>26,27</sup> and increases breast cancer risk,<sup>2</sup> whereas drugs used to treat breast cancer favorably impact these markers and disease outcomes.<sup>28-30</sup>

#### **Prospective Studies**

Seven prospective observational studies have examined the impact of postdiagnosis soy intake on breast cancer recurrence and/or survival. One study was conducted in Hong Kong,<sup>31</sup> and two each in China,<sup>32,33</sup> the U.S.,<sup>34,35</sup> and Korea.<sup>36,37</sup> (Note: only studies involving sufficient isoflavone intake are being considered for reasons discussed in the reference.<sup>38</sup>) Postdiagnosis soy intake is associated with reduced recurrence and there is suggestive evidence that breast cancer-specific mortality is also reduced.<sup>39-41</sup>

#### **Results According to Breast Cancer Type**

In a combined analysis of the largest Chinese study<sup>32</sup> and the two U.S. studies,<sup>34,35</sup> soy intake was protective against both estrogen receptor-positive (ER+) and estrogen receptor-negative breast cancer but more so against the latter. However, in this same analysis, soy was more protective for women on tamoxifen who undoubtedly had ER+ breast cancer.<sup>39</sup>

## The Following are Scientifically Supported Responses to Frequently Asked Questions Regarding Postdiagnosis Soy Intake and Breast Cancer.

#### Q: Do results differ according to the type of soy consumed?

**A:** Clinical trials have intervened with either isoflavone supplements or isoflavone-rich soy protein. Observational studies have involved free-living populations, specifically from soy food-consuming countries or individuals of Asian ethnicity, so consumption came in the form of traditional Asian soy foods like tofu, edamame, and tempeh.

#### Q: Does soy impact the efficacy of endocrine therapy?

**A**: Very limited clinical data suggest isoflavones do not interfere with tamoxifen treatment.<sup>39</sup> Similarly, limited observational data indicate soy does not impact the efficacy of endocrine therapy for breast cancer, including both tamoxifen and aromatase inhibitors.<sup>39,42</sup>

## Q: How much soy or isoflavones were consumed in the relevant clinical and epidemiologic studies?

**A:** In the clinical studies, isoflavone intake was typically 40-100mg/d, the equivalent of about 2-4 servings of traditional Asian soy foods like tofu, edamame, and tempeh, but in a few cases, intake greatly exceed 100mg/d. In the observational studies, intake in the highest intake category ranged from about 25mg/d-100mg/d.

#### Conclusions

If human research alone was considered, recommendations would likely be for women with breast cancer to consume soy foods because the clinical data are supportive of safety and the observational data suggestive of benefit. As it stands, health and cancer organizations consistently conclude that women with breast cancer can safely consume soy foods and note the possibility that doing so may improve cancer outcomes. However, it is important to consider the limitations of the data, and a cautious interpretation of the literature is warranted.

Plant-based diets are recommended for women with breast cancer, specifically to improve outcomes as well as for overall health. Given that soy foods undoubtedly make adhering to such diets easier, there is ample reason for women with breast cancer to consider including soy foods in their diet.

#### ABOUT THE AUTHOR

**Mark Messina**, **PhD**, **MS**, is chairperson of the Soy Connection editorial board and director of nutrition science and research for Soy Nutrition Institute (SNI) Global. He is also the co-owner of Nutrition Matters, Inc., a nutrition consulting company, and is an adjunct professor at Loma Linda University. His research focuses on the health effects of soy foods and soybean components.

# LIFESTYLE CHOICES AFTER BREAST CANCER: PUTTING EVIDENCE INTO PRACTICE

### By Karen Collins, MS, RDN, CDN, FAND

After breast cancer treatment, many wonder, "What's next?" Conflicting information in the media can cause anxiety and food fears, or inaction. As a follow-up to primary cancer treatment, the American Institute for Cancer Research (AICR) and the American Cancer Society recommend the following cancer risk reduction steps.<sup>1,2</sup>

#### Make Physical Activity a Part of Everyday Life

Regular physical activity is associated with lower risk of breast cancer mortality and all-cause mortality in breast cancer survivors.<sup>3</sup> According to the 2023 WCRF/ AICR CUP Global report, each increase in physical activity, up to about five hours of moderate activity weekly, is linked with further reduction in these risks. Benefits apply regardless of age and are not dependent on weight loss.

Controlled intervention trials show that physical activity also improves health-related quality of life, reduces anxiety and depression, and enhances physical functioning.<sup>4</sup>

#### Tips to Share:

- Start small with even short blocks of time set aside for activities like walking or whatever you enjoy. Aim for feeling energized, not exhausted.
- Combine physical activity with established routines.
- Pay attention to immediate benefits like improved energy and sleep to reinforce the new habits you're establishing.

#### Adopt a Plant-Forward, Healthy Dietary Pattern

The recommended dietary pattern emphasizes plant foods and limits added sugars, refined grains, and red and processed meats.<sup>1,2</sup> Research does not identify any specific diet as best, so choices can be adapted to fit individual preferences.<sup>5</sup>

A healthy diet should support a healthy weight and body composition. Excess adiposity is strongly associated with greater risk of breast cancer mortality and all-cause mortality (and potentially with breast cancer recurrence).<sup>6</sup> A dietary pattern that helps to manage cardiovascular risk factors is also important, since cardiovascular disease risk can increase after breast cancer.<sup>7</sup>

#### Tips to Share:

- Adjust food proportions on your plate and within mixed dishes; offset smaller meat portions with increased vegetables, whole grains, pulses (like chickpeas and black beans), and soy foods.
- Swap all or some of the meat in a stir-fry, pasta dish, or chili with tofu, tempeh, canned pulses or soybeans, or plant-based sausage or soy-based crumbles.
- Make new foods feel more familiar by using them with favorite recipes and flavors.
- Shift snack choices. Include tree nuts, soy nuts, edamame, and soy- or dairybased yogurt for protein. Spread nut butter like peanut, soy, or almond on apple slices or whole grain pita or crispbread.
- Forego high-sugar commercial smoothies and whip up your own with soymilk or yogurt and some unsweetened frozen fruit.
- Save time by quick-cooking whole grains (like quinoa, bulgur, quick-cooking brown rice, and whole-grain pasta). Rely on choices like lentils, tofu, tempeh, and canned or frozen pulses and soybeans to pull a meal together in under 20 minutes.

People living with and beyond breast cancer are inundated with misinformation. Dietitians and other healthcare professionals play a vital role in helping them find reliable health information to make evidence-based lifestyle choices to support their health and well-being.

#### **ABOUT THE AUTHOR**

**Karen Collins, MS, RDN, CDN, FAND,** is known for translating nutrition research on cancer prevention and survivorship, heart health, and their intersection. Karen is Nutrition Advisor to the American Institute for Cancer Research (AICR). She's written multiple book chapters and research reviews for health professionals and over 2,000 articles for the public. You can find her posts on the AICR blog, and her cardiovascular and cancer nutrition research reviews on her own website, <u>KarenCollinsNutrition.com</u>.

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