Breast Cancer Risk Modification: 
The Importance of a Healthy Lifestyle 
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Webinar Objectives

• Explore the evidence supporting modifiable risk factors for breast cancer including physical activity, weight, diet /nutrition and alcohol consumption

• Review American Cancer Society nutrition and physical activity guidelines.

• Provide information on available resources for physicians and patients.
194,509,688

CDC, US Census
Risk Factors/ Causes of Cancer in U.S.

Prescription Drugs
UV and Ionizing Radiation
Alcohol
Family History/Genetics
Viruses
Occupational Exposure
Unknown
Obesity/Poor Nutrition/Inactivity
Smoking

Percent Attributable

Conclusion: Adherence to cancer prevention guidelines for obesity, diet, physical activity and alcohol consumption is associated with a lower risk of death from cancer, CVD and all causes in non-smokers.
2015 AICR Cancer Risk Awareness Survey

Percentages of Americans who answered ‘yes’ when asked if each of the following factors has a significant effect on whether or not the average person develops cancer:

<table>
<thead>
<tr>
<th>Factor</th>
<th>Percentage</th>
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</thead>
<tbody>
<tr>
<td>Overweight/obesity</td>
<td>52%</td>
</tr>
<tr>
<td>Alcohol</td>
<td>43%</td>
</tr>
<tr>
<td>Insufficient physical activity</td>
<td>42%</td>
</tr>
<tr>
<td>Diets low in fruits and vegetables</td>
<td>42%</td>
</tr>
<tr>
<td>Processed meats</td>
<td>38%</td>
</tr>
<tr>
<td>Diets high in red meats</td>
<td>35%</td>
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</table>
Breast Cancer and Physical Activity

Nearly all of the evidence shows the addition of physical activity decreases breast cancer specific mortality and all cause mortality and is safe and effective.
Physical Activity and Breast Specific and All Cause Mortality

Effects of Physical Activity during Cancer Treatment

Exercise makes a difference.

Fasting glucose decreases with intensity.

Insulin sensitivity increases with intensity.

Immune response best with moderate intensity.

Sex hormone levels decrease with exercise.

Chan, Annals of Onc, 2014
Recreational physical activity benefits Pre and Postmenopausal women

Physical activity effects are not the same for all.

- Asian and Black populations have the largest risk reduction when physical activity is added
- Asian 41% risk reduction
- Black 41% risk reduction
- Hispanic 38% risk reduction
- Indian 28% risk reduction
- Caucasian 20% risk reduction

Physical activity-breast cancer connection

The mechanism is not clearly understood, but several theories exist.

Physical Activity ➔ Cancer Prevention

Sex hormones
Metabolic hormones
Inflammation
Immune Modulation

ACS Physical Activity Recommendations

Be physically active.
✓ Adults: at least 150 minutes of moderate intensity or 75 minutes of vigorous intensity, or a combination each week.

✓ Children and teens: at least 60 minutes a day of moderate intensity or vigorous intensity 3 days per week.

✓ Limit sedentary behavior: sitting, lying down, TV, screen time.
Obesity and being underweight are established risk factors for breast cancer.

Obesity is linked to breast cancer recurrence and poor survival.
Body Mass Index (BMI)

BMI Categories

Underweight = <18.5
Normal weight = 18.5–24.9
Overweight = 25–29.9
Obesity = BMI of 30-39.9
Severely Obese= 40 or greater

\[
\text{BMI} = \left( \frac{\text{Weight in pounds}}{(\text{Height in inches}) \times (\text{Height in inches})} \right) \times 703
\]
This is a global crisis.

Top 5 Countries with Obese Adults, 2013

- US 86.9
- China 62.0
- India 40.4
- Russia 29.2
- Brazil 26.2

Reported in Millions
BMI affects mortality.


<table>
<thead>
<tr>
<th>Study</th>
<th>Per 5 kg/m² BMI RR (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-diagnosis BMI</td>
<td>1.14 (0.88, 1.47)</td>
<td>1.62</td>
</tr>
<tr>
<td>Kamlineni 2013</td>
<td>1.28 (1.14, 1.46)</td>
<td>6.95</td>
</tr>
<tr>
<td>Conroy 2011</td>
<td>1.09 (1.00, 1.19)</td>
<td>13.36</td>
</tr>
<tr>
<td>Lu 2011</td>
<td>1.15 (1.01, 1.32)</td>
<td>5.79</td>
</tr>
<tr>
<td>Chen 2010</td>
<td>1.14 (1.00, 1.30)</td>
<td>6.15</td>
</tr>
<tr>
<td>Emaus 2010</td>
<td>1.26 (1.05, 1.52)</td>
<td>3.21</td>
</tr>
<tr>
<td>Hallmann 2010</td>
<td>1.20 (1.06, 1.36)</td>
<td>7.26</td>
</tr>
<tr>
<td>Nichols 2009</td>
<td>1.15 (1.01, 1.31)</td>
<td>5.89</td>
</tr>
<tr>
<td>West-Wright 2009</td>
<td>1.26 (1.05, 1.52)</td>
<td>3.12</td>
</tr>
<tr>
<td>Caan 2008</td>
<td>1.11 (0.98, 1.26)</td>
<td>6.61</td>
</tr>
<tr>
<td>Dal Maso 2008</td>
<td>1.17 (1.10, 1.23)</td>
<td>25.25</td>
</tr>
<tr>
<td>Reding 2008</td>
<td>1.52 (1.16, 1.99)</td>
<td>1.49</td>
</tr>
<tr>
<td>Abrahamson 2006</td>
<td>1.13 (1.02, 1.25)</td>
<td>9.06</td>
</tr>
<tr>
<td>Kroenke 2005</td>
<td>1.14 (0.93, 1.39)</td>
<td>2.59</td>
</tr>
<tr>
<td>Zhang 1995</td>
<td>1.47 (1.14, 1.89)</td>
<td>1.67</td>
</tr>
<tr>
<td>Holmberg 1994</td>
<td>1.17 (1.13, 1.21)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

BMI <12 months after diagnosis

Ewertz 2012              | 1.08 (0.99, 1.19)             | 10.72    |
Goodwin 2012             | 1.12 (0.94, 1.34)             | 4.97     |
Kewei 2012               | 1.52 (0.89, 2.60)             | 0.71     |
Baumgartner 2011         | 0.94 (0.83, 1.06)             | 7.91     |
Azambuja 2010            | 1.17 (1.06, 1.29)             | 10.00    |
Chen 2010                | 1.13 (0.99, 1.29)             | 7.31     |
Dawood 2008              | 1.12 (0.96, 1.30)             | 6.30     |
Majed 2008               | 1.05 (1.01, 1.10)             | 16.49    |
Vitolins 2008            | 1.22 (1.10, 1.34)             | 10.03    |
Abrahamson 2006          | 1.27 (1.11, 1.45)             | 7.20     |
Tao 2008                 | 1.30 (1.01, 1.68)             | 2.78     |
Borlatz 2004             | 1.07 (1.02, 1.12)             | 15.58    |
Subtotal (I² squared = 54.8%, P = 0.011) | 1.11 (1.06, 1.16) | 100.00 |

BMI >=12 months after diagnosis

Elatt 2010               | 1.11 (0.98, 1.27)             | 28.42    |
Nichols 2009             | 1.10 (0.98, 1.24)             | 35.22    |
Caan 2006                | 1.14 (0.92, 1.42)             | 10.34    |
Ewertz 1991              | 0.99 (0.86, 1.13)             | 26.01    |
Subtotal (I² squared = 0.0%, P = 0.517) | 1.08 (1.01, 1.15) | 100.00 |

Figure 4. Linear dose–response meta-analysis of BMI and total mortality.
Weight Change After Diagnosis & Association with Recurrence & Mortality

Data from Cohort of 5204 Breast Cancer Survivors in Nurse’s Health Study
BMI affects breast specific and all cause mortality.

What happens with weight loss?


- Intentional weight loss is more complicated.
  
  WINS trial: 24% reduction with weight loss (BMI down 1.1 points), decreased fat intake, calorie reduction 10%. Pierce, JAMA, 2007.

  WHEL: No risk reduction with maintain/moderate increase in weight with increased fiber. Chlebowski, JNCI, 2006
Obesity-cancer connection.

The mechanism is not clearly understood.

### FREE RADICAL STRESS
- Oxidative Stress with increased levels and decreased elimination
- DNA mutations accumulate over time

### METABOLIC HORMONES
- Insulin and Insulin like Growth Factor-1 increased
- Cancers with insulin receptor now grow
- Less apoptosis and tumors form

### SEX HORMONES
- Increased Sex hormones by AROMATAZATION in extra fat tissue
- Inflammation intertwined with obesity
- TNF alpha and IL6 activate promoter to increase AROMATIZATION

### INFLAMMATION
- Chronic state inflammation with elevated cytokines
- Oxidative stress mediators are sensors and create a self reinforcing loop
- Short range cytokines promote expansion immune cells
- Long range cytokines promote insulin resistance and increase circulating insulin

Mazzarella, eCancer, 2015
On the HORIZON

- CURRENT ONGOING trials testing lifestyle change programs
  - Italian DIANA5
  - German SUCCESS
  - North American LISA and ENERGY trials
  - Canadian AMBER trial
Severely obese patients have decreased overall and disease free survival.
Achieve and maintain a healthy weight throughout life.
Stay as lean as possible
Avoid excess weight gain
Limit intake of high calorie foods and drinks
Breast Cancer and Diet/Nutrition

40% of cancers may be linked to dietary factors in industrialized countries.

Plant foods (vegetables, fruits, whole grains, and beans) help lower the risk of many cancers, including breast cancer.
Recent study in breast cancer survivors with high intake of fruits, vegetables, and fiber.

Results showed NO reduction in risk of recurrence and NO change in weight.

Chlebowski, JNCI, 2006
Women’s Healthy Eating and Living Trial (WHEL)

- High amounts of fruits vegetables, fiber AND physical activity improved survival.

- Not shown here, obese women, IN THIS GROUP, improved their survival 50% especially in hormone receptor positive cancers.

Chlebowski, JNCI, 2006
Women’s Intervention Nutrition Study (WINS)

- **Control** - 51 gm fat per day
- **Intervention**
  - 33 gm fat per day;
  - 6 lb. loss mean body weight
- **Recurrence/new breast cancer**
  - 12.4% control group
  - 9.8% intervention group
- Possibly more effect in subgroup of ER- cancers.

Red and processed meat is associated with the risk of colorectal cancer. It is a linear relationship. EPIC trial, Norat, JNCI, 2005

Mixed results with red/processed meat and breast cancer risk, but recent meta analysis showed a small increased risk of breast cancer with 120g/day increase red meat and 50g/day increase of processed meat. Guo, et al Breast Cancer Res and Treatment, 2015

Racial differences may exist. Chandran, Cancer Causes Control, 2013
Processed foods have hidden dangers.

Refining grains lower the amount of fiber.

Processing may cause cancer, especially nitrites.

Cooking or heat-treating may lower the content of some heat-sensitive vitamins, such as vitamin C and some B vitamins.
Not all foods are the same.

High Calories
Often low nutrient value

- Soft drinks
- Fried foods
- Milk chocolate
- Oil
- Butter
- Fat

Pork
Chicken
Beef
Fish
Eggs

Bread
Milk
Cheese

Flaxseed
Avocado
Nuts

Low calories
Often high nutrient value

- Fiber & water
- Leaf salad
- Vegetables
- Mushrooms
- Fruits
- Grains
- Beans
- Potatoes

Bread
Milk
Cheese

Pork
Chicken
Beef
Fish
Eggs
Multiple bioactive compounds in foods can protect and at the same time promote cancer.

Bioactive compounds work through the metabolic, inflammatory and immune pathways. Some compounds are direct toxins.

Each individual processes a food item uniquely.
The connections are complex.

• Bioactive compounds, especially phenols like **Resveratrol**, found in grapes, can inhibit cancer cell growth, BUT may also modulate initiation, promotion and progression of cancer.

• The beneficial effect of bioactive compounds may be more prevalent in tumors that do not depend on hormones.
  • ER negative tumors overexpress Cyclin E, epidermal growth factor and factor kappa B.
  • Bioactive compounds in vegetables reduce levels of all three.
  • High vegetable diet may be associated with less ER negative cancer.

• Obese women may have a survival benefit if they eat a high vegetable diet regardless the obesity.
Eat a healthy diet, with an emphasis on plant foods.
ACS Diet Recommendations

✓ Choose foods that help get to and maintain a healthy weight.
✓ Limit processed meat and red meat.
✓ Eat at least 2.5 cups (5 servings) of vegetables and fruit each day.
✓ Choose whole grains instead of refined grain.
What does a healthy food plate look like?

- Whole grain brown rice: ¼ plate whole grain
- Grilled salmon: ¼ plate protein
- Fruits and Vegetables: ½ plate

Myplate.gov
Alcohol has been a known carcinogen since 1988.

It is associated with several cancers including breast cancer.
How much you drink matters.

Alcohol and Risk of Breast Cancer

This is a linear relationship.

Number of drinks/day

% Risk Increase

Million Woman Study, Allen et al. JNCI, 2009
What is a standard drink?

Percent Alcohol

13%  5%  13%  20%  40%
Less is more when drinking.

• Light drinking is less clear
  -BMJ- one drink per day increases breast cancer risk. 13% Cao, et al. BMJ, 2015
  -Multiple studies- one drink per day may lower cardiovascular risk.


• Binge drinking (more than 60g on at least one occasion in the past 7 days). Chen, et al. JAMA, 2011


Alcohol-breast cancer connection


Exact mechanism unknown

- Alcohol Dehydrogenase
- Increase circulating estrogens
- DNA damage
- Tumor cell growth and proliferation
- DNA instability and lack of methylation
- Folate deficiency from alcohol use
- Alcohol breakdown products like acetaldehyde and acetate
- DNA damage

Tumor formation
ACS Alcohol Recommendations

Drink no more than 1 drink per day for women and 2 drinks per day for men.
Resources for Providers and Patients

CA Journal:
ACS Guidelines on Nutrition and Physical Activity for Cancer Prevention

ACS Guidelines on Nutrition and Physical Activity for Cancer Survivors

Healthcare Professional Resources
Fact sheets, presentations, guidelines, patient pages
http://www.cancer.org/healthy/informationforhealthcareprofessionals/index

Cancer Survivorship E-Learning Series for Primary Care Providers
The Importance of Prevention in Cancer Survivorship: Empowering Survivors to Live Well
https://cancersurvivorshipcentereducation.org/Module_4_Landing_Page.html
Resources for Providers and Patients

ACSM/ACS Cancer Exercise Trainer certification program
http://members.acsm.org/source/custom/Online_locator/OnlineLocator.cfm?ga=1.5369715.1921856623.1441367145

American Institute for Cancer Research
http://www.aicr.org

Livestrong
http://www.livestrong.org

USDA
http://www.choosemyplate.gov
2012 Recommendations for

Individuals:
1) Maintain a healthy weight throughout life.
2) Adopt a physically active lifestyle.
3) Consume a healthy diet, with an emphasis on plant sources.
4) If you drink alcoholic beverages, limit consumption.

Communities:
Work together to make it easier for people to eat better and be more active.
Recommendation for Community Action

Public, private and community organizations should work collaboratively at national, state and local levels to implement policy and environmental changes that:

- Increase access to affordable, healthy foods in communities, worksites and schools, and decrease access to and marketing of foods and beverages of low nutritional value, particularly to youth.

- Provide safe, enjoyable and accessible environments for physical activity in schools and worksites, and for transportation and recreation in communities.
Promote Fruits, Vegetables, Whole Grains
Primary Care Physicians

Be A Good Role Model
Support Weight Management Efforts
Encourage Regular Physical Activity
Be An Advocate For Change In Your Community
Promote Fruits, Vegetables, Whole Grains
Thank you for Participating

This webinar recording and presentation will be available for on-demand viewing on the American Cancer Society YouTube Channel and the NAPBC website.

www.cancer.org    www.napbc-breast.org