

### Program on Breast Cancer C Environmental Risk Factors

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### TOPICS

Studies of physical activity

Physical activity and breast cancer risk

Relationship of physical activity and the level of risk

Amount of physical activity and breast cancer risk

Recommended amount of physical activity

Is age important?

Is body size important?

How might this occur?

Breast cancer survival and physical activity

# *Physical Activity and Breast Cancer Risk*

#### **Summary**

A panel of expert scientists assembled by the World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR) recently reviewed existing studies on the association of physical activity and breast cancer risk. The WCRF/AICR panel concluded that physical activity probably has a preventive effect on postmenopausal breast cancer. However, panel members found less evidence for a relationship between physical activity and premenopausal breast cancer, and they rated this association as being limited but suggestive. Studies examining physical activity and breast cancer risk have, on average, reported a 20 to 40 percent lower risk of breast cancer among women who are most physically active. Similar values have been reported for both pre- and postmenopausal breast cancer risk. These values are considered to represent a weak to moderate decrease in breast cancer risk. This finding is important because physical activity levels, unlike most breast cancer risk factors, can be changed. Over a lifetime each additional hour of physical activity per week, on average, has been linked with a six percent decrease in breast cancer risk.

Decreased breast cancer risk has been associated with increased physical activity in women of all but extremely high body sizes. This finding suggests that physical activity has benefits for breast cancer risk reduction beyond those associated with weight loss. There is also evidence that physical activity holds considerable promise for improving survival after a diagnosis of breast cancer. Other health benefits of physical activity include decreased risk of cardiovascular disease, stroke, diabetes, arthritis and other cancers.

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#### What is physical activity?

Physical activity can be defined as movement of the body by its muscles resulting in an increase in energy use. Several categories of physical activity have been used in studies of the relationship of physical activity and breast cancer risk. These include physical activity connected with recreational, occupational and household activities.

Historically people have led very physically active lives in order to acquire and maintain the food and shelter necessary for survival. However, in recent times, technological advances and urbanization have progressed to the point that people in wealthier countries can be considered largely physically inactive.

#### How has physical activity been studied to understand breast cancer risk?

Measurement of physical activity is challenging. Many of the techniques used to measure physical activity very precisely are not suitable for use with the large groups of people needed for studies of breast cancer risk. In addition, physical activity behavior is complex and differs widely from person to person. The ideal measure of physical activity, in this context, would be one that could be easily and reproducibly measured in large groups of people to accurately assess breast cancer risk. Such an ideal measure of physical activity does not exist; thus many different approaches have been used. As a result, studies of the relationship between physical activity and breast cancer risk are difficult to summarize because they often study different types of physical activity using different measures that are not readily comparable.

One approach to address this difficulty has been to measure the aspects of physical activity that are generally considered important to health. This approach measures how often, how long or how hard people engage in an activity such as running or walking. Another method has been to look at physical activity at different stages of a person's life, for example youth, middle age, recent times (relative to the data collection) or over a total lifetime. Both of these approaches are interrelated and an ideal study would address them both simultaneously.

Gathering this type of information from large groups of people is not simple. Various methods have been used including diaries that ask people to keep track of current activity, surveys that ask people to remember past activity, classification of people based on the level of physical activity involved in their jobs, and study of biologically

2

relevant markers in people's bodies.

Combining and comparing the results of all these different approaches is complicated. Nonetheless, the resulting variability of research results has greater impact on the practical details, such as how much physical activity is needed to affect breast cancer risk, than on the important overall question of whether or not physical activity is related to breast cancer risk.

#### Is physical activity related to breast cancer risk?

An expert panel assembled by the World Cancer Research Fund and the American Institute for Cancer Research (WCRF/AICR) examined the possible association of physical activity with both pre- and postmenopausal breast cancer. In 2007, the WCRF/AICR panel ruled that there is limited but suggestive evidence that greater physical activity is associated with a decrease in premenopausal breast cancer risk. This judgment was made because of a lack of consistency in the results of existing studies. In contrast, for postmenopausal breast cancer this expert panel ruled that there was ample evidence indicating that there was a probable association of greater physical activity with a decrease in the risk of postmenopausal breast cancer.

An earlier evaluation was in agreement with this conclusion. In 2002, an expert panel of the International Agency for Research on Cancer (IARC) issued a report stating that there was sufficient evidence that greater physical activity has a preventive effect on breast cancer in humans. However, they did not differentiate risk for pre- and post-menopausal breast cancer.

The studies of physical activity and breast cancer risk in women of all ages report, on average, a 20 to 40 percent lower risk of breast cancer among women who are most physically active. The studies examining premenopausal women separately have found an average 40 percent decrease in risk. The studies examining postmenopausal women reported an average 33 percent decrease in breast cancer risk. Risk reductions of these sizes are considered weak to moderate. Some studies reported an even stronger reduction, as much as an 80 percent lower risk of breast cancer among women who were the most active. It is important to recognize that this amount is an overall value and it does not take into account possible effects at different ages and other factors that might increase or decrease the effect of physical activity on risk. We should also keep in mind that the impact of these results can be considerable since physical activity, unlike most breast cancer risk factors, is a risk factor over which women have control.

#### Is there a dose-response relationship between physical activity and breast cancer risk?

A dose-response relationship between physical activity and breast cancer risk reduction was confirmed by most of the studies that investigated this connection. A doseresponse relationship means that the more active women were, the greater the reduction in breast cancer risk. This type of relationship is considered an important piece of supportive evidence. It not only provides evidence for a potential cause and effect association between physical activity and decreased breast cancer risk, but it also helps define the amount of physical activity necessary for a substantial risk reduction.

A task force of the Dutch Cancer Society recently evaluated the relationship between hours of physical activity per week and breast cancer risk. Using the results from seventeen case-control studies they found a statistically reliable six percent decrease in breast cancer risk for each additional hour of physical activity per week. The analysis assumed that the activity was continued throughout a woman's life. This result is good news as it predicts the potential for a sizeable effect of physical activity time on risk. For example, if we consider two groups of women whose weekly physical activity time differs by four hours or about 35 min per day. The group of women with high physical activity would be expected to have a level of breast cancer risk that is 21 percent lower than the group of women with low activity.

#### What percentage of breast cancer cases can be attributed to lack of physical activity?

A recent study of white women in California determined that 4.6 to 11 percent of all cases of breast cancer in this group of women could be attributed to a lack of physical activity. Similar studies in both England and Italy arrived at a value of 11 percent. The IARC review panel also examined this issue and stated that in industrial countries the value would be expected to be at least 11%. These values represent the population attributable fraction for physical inactivity in these groups of women. This epidemiological measure is best understood as the percentage of breast cancer cases that would be avoided if physical inactivity could be eliminated. This result is notable since physical inactivity has the second largest population attributable fraction of all modifiable breast cancer risk factors. Obesity has the largest value, 30 to 50 percent in the U.S. (For more detail see BCERF Fact Sheet # 56, Obesity and Breast Cancer Risk)

### Do various types of physical activity affect breast cancer risk differently?

It appears that the total amount of physical activity is more important than the type of activity for breast cancer risk reduction. Studies have examined physical activity at work, leisure physical activity, and total physical activity. Lower breast cancer risk has been reported for all these types of physical activity. Nonetheless, studies of total physical activity have been most consistent in demonstrating an association with lower breast cancer risk. This consistency of the results strongly suggests that that total activity is most important.

### Is the frequency of the physical activity important for reduced breast cancer risk?

Many studies have shown a dose-response relationship between the frequency (i.e. how many times per week physical activity was performed) of physical activity and decreased breast cancer risk. In other words, the more frequently women were physically active, the greater was the decrease in their breast cancer risk. It supports the concept that how often women are active plays an important role in the relationship of physical activity and decreasing breast cancer risk.

#### Is the duration or length of the physical activity important for reduced breast cancer risk?

The duration (i.e. amount of time physical activity was performed) of physical activity also shows a doseresponse relationship with breast cancer risk. Like the frequency of physical activity, this indicates that duration of physical activity is systematically related to decreased breast risk and plays an important role in this effect.

#### Is the intensity of the physical activity important for reduced breast cancer risk?

In the studies conducted to date, a decreased breast cancer risk has been found with both moderate and vigorous intensity activity. A slightly stronger risk reduction exists for women who do vigorous activity; however there is a benefit with even moderate activity. Moderate intensity activity is defined as activity that increases the heart rate and may cause moderate sweating. Examples of moderate intensity activity are brisk walking and general cycling.

#### Is there a recommended frequency, length of time or intensity of physical activity that will best reduce breast cancer risk?

The WCRF/AICR panel that reviewed physical activity and breast cancer risk recommended that women aim for 60 or more minutes of moderate or 30 minutes of vigorous activity every day. The IARC panel recommendation was similar 30 to 60 minutes a day of moderate to vigorous physical activity. These recommendations are comparable to that made by the U.S. Centers for Disease Control and Prevention and the American College of Sports Medicine as beneficial to health in general.

### Is there a specific age at which physical activity is most beneficial?

Currently it is not clear whether there is a specific age or life period when physical activity is most beneficial for reduced breast cancer risk. Several studies have suggested that total lifetime activity has the largest effect, but other studies have found benefits for specific ages and the years after menopause. A benefit exists for physical activity done at all ages in life with the greatest risk reduction occurring among women who remain physically activity throughout their lives. Some studies have also found a greater effect for activity done after menopause indicating that even if women have been inactive before menopause, they can still benefit from a breast cancer risk reduction if they become active after menopause.

#### Is physical activity beneficial for women of different body size?

Women with both a high or low body mass index (BMI: a measure of body fat) benefit from increased physical activity. Several lines of evidence support this concept. There have been 11 cohort studies and 5 case control studies that have studied the effect of physical activity on breast cancer risk based on women grouped by their BMI's. In a number of studies, a different and more detailed analysis looking for an interaction between BMI and physical activity on breast cancer risk was conducted. None of these studies found such an interaction

4

supporting the concept that women's body size does not affect the benefits of physical activity.

Also in support of these results, one study has directly examined the effect of physical activity on estrogen levels in postmenopausal women with high and low BMI values. As described in the next section, estrogen levels have been clearly linked to breast cancer risk. This study found that the women with higher physical activity levels generally had lower levels of estrogens than women with similar BMIs and low levels of physical activity. Thus physical activity was linked to a decrease in a well established breast cancer risk factor in women of all BMI values.

However it should be also kept in mind that some analyses have found that women with extremely high BMI values did not display a breast cancer risk benefit from physical activity. Nonetheless, these results are, overall, very good news as they indicate that women of almost all body sizes can benefit from physical activity. They also support the idea that physical activity affects breast cancer risk by doing more than just changing body fat content.

### How might physical activity affect breast cancer risk?

It is currently unclear exactly how physical activity affects breast cancer risk. There are a number of ways this effect might occur. First, physical activity may affect the production of estrogens and other hormones that increase breast cancer risk. Exposure of the breast to higher levels of ovarian hormones such as estrogen and progesterone is well established as a pathway to increased breast cancer risk.

Studies of hormones and physical activity in premenopausal women have been inconsistent. Several studies of young women athletes, participating in sports involving high levels of moderate to vigorous activity, reported that these athletes had symptoms of decreased hormone production. This included delayed menarche (beginning of menstrual cycling), irregular menstrual periods and menstrual periods without ovulation. While these effects likely reflect changes in hormone levels, direct examination of hormone level yielded different results. A recent 12-week- long randomized controlled trial directly examined hormone levels in 32 premenopausal women undergoing aerobic exercise training. This study saw no effect on the levels of active and inactive estrogen metabolites. Four other studies, of lesser design strength, have also examined aspects of physical activity on hormone levels. While two of these studies did not find an effect in premenopausal women, two others did. Since hormonal levels change throughout the menstrual cycle in premenopausal women, studies of this type are difficult to conduct. More study will be required to resolve this issue.

Postmenopausal women, whose ovaries are no longer producing estrogen, can produce estrogens from the conversion of other hormones in fat tissue. Physical activity among postmenopausal women may lead to reductions in estrogens by this route but this has not been established. Six studies have examined estrogen concentrations in postmenopausal women with different physical activity levels. Four of these reported a reduction in estrogen concentrations related to physical activity, one reported the opposite effect and another reported no effect.

Physical activity may also lower breast cancer risk in postmenopausal women by limiting the availability of estrogens. This effect may occur through a physical activity-associated increase in the levels of a protein that binds strongly to and carries estrogen in the blood. High levels of this protein, the sex hormone binding globulin have been linked to decreased breast cancer risk. The strong binding of estrogen to this protein makes estrogen less available and decreases its effects on the breast and other tissues in women who are physically active.

Physical activity also allows for better blood sugar control and less secretion of insulin. This response may be related to breast cancer risk as insulin secretion has been linked to levels of a related hormone called insulinlike growth factor levels (IGF). IGF has been associated with premenopausal, but not postmenopausal, breast cancer risk.

Physical activity has a number of effects on the immune system. As the immune system has a role in surveillance and elimination of cancer cells, the potential effects of physical activity may involve the immune system.

Finally, physical activity can generate free radicals and place the body under increased oxidative stress from these highly reactive molecules. The body can respond to this stress by increasing its levels of free radical defense and repair systems. Obesity is also thought to be associated with increased free radicals and oxidative

5

stress. This effect may be involved in increases in the risk of some cancers that have been linked to obesity. Some investigators have proposed that the free radical defense and repair systems potentially stimulated by exercise may also defend against cancer. Verification of this theory will require much more study.

## Does physical activity affect the risk of other types of cancer?

Both the WCRF/AICR and IARC panel have evaluated the epidemiologic evidence on physical activity and cancer prevention. Both panels ruled that there was convincing or sufficient evidence to indicate that physical activity had a preventive effect on colon cancer. They also both ruled that there was probable or limited evidence to support a preventive effect of physical activity on cancer of the uterus (Endometrium). The AICR/WCRF panel decided that there was limited but suggestive evidence for an association with decreased risk of lung and pancreatic cancer. The IARC panel added prostate cancer as having limited evidence for a preventive effect by physical activity. For all other cancer sites these panels ruled that the evidence was inadequate to make judgments at this time.

## What are the other health benefits of physical activity?

Physical activity has been shown to have many health benefits. Physical activity is associated with decreases in the risk of cardiovascular disease, type II diabetes, hip fracture, gall bladder disease and other types of cancer.

### Is physical activity beneficial for breast cancer survivors?

Almost all studies of physical activity among breast cancer survivors have measured physical activity levels before breast cancer diagnosis. This approach is largely aimed at understanding the effect of physical activity on the occurrence of breast cancer. The exception to this approach was a large cohort study of breast cancer survivors that examined levels of leisure time physical activity after completion of the active breast cancer treatment period. In this study the survival of almost 3,000 nurses who had been diagnosed with stage I, II, or III breast cancer was assessed. The results of this study were dramatic and have been described as having "rocked" the cancer survivorship research community. Women who expended the energy equivalent of 3 to 5 hours per week of walking at an average pace (2 to 2.9 mph) had half (50 percent) the risk of death from breast cancer of women who expended the energy equivalent of less than one hour of walking per week. This level of activity appeared to produce the maximum benefit as women who expended greater amounts of energy each week had a similar level of risk reduction. Nonetheless, risk was also decreased, albeit to a lesser extent, for women who were less active. A 20 percent decrease in relative risk for breast cancer death was seen for women whose energy expenditure was equivalent to 1 to 3 hours of average pace walking per week.

The women in this study were also examined based on the stage of their cancer diagnosis. The effect of physical activity was about the same, close to a 35 percent decrease in risk, for women with stage I and stage II levels of breast cancer. The effect was even greater for women with more advanced disease. Women with stage III disease whose weekly energy use was greater than the equivalent of 3 hours per week of average-paced walking had a 64 percent reduction in risk of death from breast cancer compared to women with less energy use. But these results are more tentative, since the number of women with more advanced disease was small.

Obesity (BMI value greater than 30) has been shown in many studies to have a negative impact on breast cancer survival (see BCERF Fact Sheet #56, *Diet and Lifestyle and Survival from Breast Cancer*). This study also

6

provided considerable hope for obese breast cancer survivors. When women with high BMI values were examined separately, the benefit of physical activity for obese women with breast cancer appeared to be greater than that for all women with breast cancer. The risk of death from breast cancer for obese women, who expended the equivalent of walking equivalent of 5 or more hours per week, was 70 percent lower than obese women whose activity was the equivalent of less than 1 hour walking per week. This level of risk reduction is considered a strong decrease in risk. While these results are also tentative values, they are, nonetheless, very encouraging.

#### What can women do now?

Physical activity has been called the real fountain of youth as it has been shown to have so many beneficial health effects. We can see that this adage is true about breast cancer as studies have shown that regular physical activity may decrease breast cancer risk an average of 20 percent to 40 percent. In addition, physical activity has benefits for the cardiovascular system, bone health, prevention of diabetes, and prevention of other types of cancer. Many studies have also shown how physical activity is linked to an increased quality of life. Because of all these benefits it makes good sense to try to meet the recommendation made by the U.S. Centers for Disease Control to engage in moderate-intensity physical activity for 30 minutes or more on 5 or more days of the week.

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