

National Action Plan on Breast Cancer Etiology Working Group: Workshop on Physical Activity and Breast Cancer

Supplement to Cancer

Summary of the Workshop

Workshop on Physical Activity and Breast Cancer, November 13–14, 1997

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The Workshop on Physical Activity and Breast Cancer, sponsored by the National Action Plan on Breast Cancer, the American Cancer Society, the Susan G. Komen Foundation, and the U.S. Public Health Service's Office on Women's Health, was held in Albuquerque, New Mexico, on November 13 and 14, 1997. It brought together more than 80 researchers and consumer advocates to review the current status of research on the possible relation between physical activity and breast cancer and to formulate recommendations for future research in this area. Participants and speakers represented diverse fields, including breast cancer epidemiology, measurement of physical activity, exercise physiology, endocrinology, immunology, energy balance, and physical activity prevalence and interventions.

CURRENT RESEARCH

There are at least 19 published studies and 18 current studies that include some measure of physical activity and its relation to breast cancer. Although the hypothesis that physical activity can reduce breast cancer risk is promising, the epidemiologic data collected to date show mixed results. Retrospective case-control studies have suggested a typical risk reduction of 25–30% for the most active women (larger reductions have been observed in some studies), but there have been inconsistent results in terms of the time of life when activity occurs and breast cancer risk. Furthermore, several large prospective studies have shown little or no association between physical activity and breast cancer risk. There are several likely reasons for these inconsistencies: most studies did not focus on an association between physical activity and breast cancer as a primary hypothesis, and the methods for evaluating and measuring physical activity were not standardized among studies and often were incomplete and imprecise.

The methodologic limitations of studies measuring physical activity were discussed. Recent studies employing more complete methods of measuring and evaluating physical activity have more consistently found a lower risk of breast cancer related to increased levels of physical activity. Although the studies completed to date have had numerous methodologic limitations, overall they have shown that increased physical activity has been associated with modest reductions in breast cancer risk. The advisability of measuring all physical activity—leisure, occupational, home-related, and child care-related—was emphasized. It is also important to determine the intensity, duration, and frequency of physical activity; some data suggest that high intensity physical activity may be uniquely important, but indi-

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vidual variations complicate the situation. What is strenuous or high intensity activity for one person may not be high intensity for another, depending on the individual's past athletic training. The significance of obtaining a lifetime history of physical activity was discussed, as well as the importance of examining study results by menopausal status.

There is evidence that weight gain affects breast cancer risk, and it was noted that weight change can be measured more easily than physical activity. Heavier women have poorer survival rates and an increased likelihood of disease recurrence. Among women who have gone through menopause, those who gained weight during adulthood were at increased risk of developing breast cancer.

Several mechanisms that may mediate an association between physical activity and breast cancer were reviewed: energy balance, hormonal mechanisms, and immunologic mechanisms. Energy balance is measured by the difference between energy intake and energy expenditure. If the energy intake exceeds the energy expended, a positive energy balance can occur, even when a person is on a low-fat diet. There is a hypothesis that low energy expenditure is a predictor of weight gain, but some studies are challenging that theory. For example, in one study it was difficult to distinguish between the energy expenditure levels of lean and obese research participants.

Also discussed were issues related to the value of resistance training, which can result in increased muscle mass, versus other types of physical training. Muscle mass relates to insulin resistance and possible increases in growth factors, but it is unclear whether this mechanism has a significant impact on breast cancer risk.

A number of risk factors for breast cancer are related to hormonal status, including early age at menarche. In a longitudinal study, it was observed that girls who began menstruating at a younger age had higher levels of follicle-stimulating hormones and estradiol than those who began at a later age. The difference in estradiol concentration in the two groups persisted 30 years later. This study concluded that delayed puberty and menarche are associated with a reduced risk of breast cancer. Another study showed that women who have a history of irregular menstrual cycles have half the risk of breast cancer. It is known that increasing physical activity or decreasing energy intake reduces the luteal hormone pulse and can cause an irregular menstrual cycle or delay puberty, but it was emphasized that overall health must always be taken into account and that delayed puberty has negative consequences related to osteoporosis. It is possible that

physical activity can reduce breast cancer risk by lowering endogenous estrogen levels, particularly in postmenopausal women; but the amount of physical activity needed to reduce the hormones that regulate the menstrual cycle is unknown. In addition to estrogenic hormones, possible roles might be played by hormones such as insulin, growth hormones, and glucocorticoids.

Physical activity has profound effects on the immune system. After periods of acute exercise, there is a marked increase in the level of natural killer cells that can destroy or suppress the growth of cancer tumor cells. It is possible that physical activity reduces breast cancer risk because it elevates the level of natural killer cells. More research is needed to explore these potential mechanisms further.

Research on the association of physical activity with osteoporosis, colon cancer, and cardiovascular disease was reviewed in order to glean lessons that could be transferred to research related to breast cancer risk. Evidence of the consistent relation between higher levels of activity and reduced risk of heart disease and colon cancer illustrated how a cohesive body of epidemiologic data is possible and highlighted the inconsistencies within the breast cancer field. Several of the cohort studies showing correlations with heart disease, diabetes, and colon cancer show no correlation with breast cancer. However, breast cancer has a particularly complex etiology, and activity levels may have to be higher, sustained for a longer period of time, or performed early in life to reduce the risk of this disease.

Osteoporosis researchers have learned that physical activity is a general term and is not synonymous with exercise, an experimental variable in research studies. The type of activity and its intensity, duration, and frequency are important considerations when using exercise as an experimental variable. The effects of exercise differ depending on when it is performed during the life span and what previous athletic training has been undertaken. It is now known that girls achieve about 90 percent of adult peak bone mass by age 18. Girls with abnormally low estrogen levels, which can be caused by excessive exercise or weight loss, do not reach their biologic potential for peak bone mass and are at risk of premature osteoporosis. Physiologic systems are interdependent, and researchers have recognized the importance of considering physical training principles when designing studies involving exercise. It also is important to use randomization in exercise studies, even if it requires extra effort to keep women in the study.

Research on colon cancer has found a consistent

association between the intensity of physical activity and colon cancer risk, but there is little information on the level of physical activity needed to provide a protective effect. Information is needed on a number of mechanisms related to physical activity, such as body size maintenance, energy balance maintenance, prostaglandin production, immune response, and insulin resistance, the last of which may be associated with both colon and breast cancer. Colon cancer researchers have discovered that it is important to observe as many dimensions of physical activity as possible when studying these mechanisms. Two areas of measurement are important to explore: the intensity of physical activity and long-term reporting. Because many people are reluctant to admit that they do not engage in moderate levels of physical activity, colon cancer researchers recommended that physical activity studies measure light levels of physical activity as well as moderate and intense levels of activity. It may be that, to determine physical activity patterns among women, it is necessary to determine activity levels at multiple points over the life span. Although there is no evidence of confounding between physical activity and colon cancer risk, it is important to examine effect modification. Researchers have found differences in associations by underlying population characteristics, and this could have an impact on breast cancer research.

Cardiovascular disease research suggests that studies should be designed to provide evidence of causality. Once again, it was emphasized that future studies need to analyze the relative importance of various components of physical activity and should use measurements that can define the intensity, duration, and frequency of that activity. It is important to examine changes in fitness and physical activity over time as well as to interpret analyses that control for potential confounders versus controlling for factors in the causal pathway.

The prevalence of regular physical activity varies according to age, gender, income, education, geographic region, race, and ethnicity. The data show that many young females in the United States do not engage regularly in vigorous physical activity. According to a 1992 national survey, 47% of female youth and 60% of male youth engaged in vigorous activity 3 or more times per week. At age 12 years, almost 66% of female youth reported regular vigorous activity of some type; but by age 21 years, the percentage decreased to 30%. According to a 1991 survey, 16% of women ages 18–29 years regularly engaged in vigorous physical activity and only 12% of women ages 45–64 years did so. About 23% of women age 75 years or older regularly engaged in vigorous activity (re-

searchers noted that adjustments were made to compensate for the decline in maximal capacity that occurs with age).

There can be personal, physical, interpersonal, and environmental barriers to becoming physically active. Research shows that many women are physically inactive during their leisure hours. Strategies to encourage women to change their behavior and become more physically active must consider health education, exercise prescription, behavior management, and environmental approaches. More efforts are needed to remove barriers to becoming physically active and to reward a physically active lifestyle. Social or environmental changes (e.g., constructing more bicycle paths) can help remove barriers to women's adopting a physically active lifestyle.

The role that physical activity can play among women who have been diagnosed with breast cancer and are undergoing treatment was reviewed. There is little research in this area, and more studies are needed with respect to quality of life and prognosis. Women undergoing treatment for breast cancer typically gain weight, but it is not clear why this happens. These gains cannot be explained simply by increased dietary intake. Women typically gain 5–14 pounds during the course of their cancer chemotherapy, but it is not unusual for them to gain more—1 of 4 premenopausal women gain more than 22 pounds during treatment. Weight gain has been shown to decrease quality of life, increase risk for other diseases, and increase cancer recurrence. Increases in physical activity have the potential to minimize these effects.

The workshop concluded with small group discussions of issues raised throughout the first day of the meeting, and each group reported back to the full workshop. The groups emphasized the need to communicate clearly the current state of the science, which suggests a possible link between physical activity and protection against breast cancer; but it should also be communicated that the body of evidence is not as strong as that for other conditions, particularly heart disease and colon cancer.

SUMMARY OF RECOMMENDATIONS

General Recommendations Regarding Physical Activity

The workshop participants strongly endorsed national public health recommendations that people increase their level of physical activity. It was recommended that physical activity be promoted as an aid in avoiding weight gain and stimulating weight loss in overweight women, leading to better health and better quality of life. By helping to prevent weight gain, increased physical activity may reduce the risk of post-

menopausal breast cancer. Physical activity should be considered more frequently as a central component of weight control strategies after breast cancer has been diagnosed and during treatment.

Personal, cultural, and social barriers make it difficult to incorporate physical activity into daily life. Schools, churches, government agencies, employers, and medical clinics need to participate in efforts to promote regular physical activity, such as encouraging physical activity programs, allotting time for physical activity, or constructing bicycle paths.

Children should be encouraged to engage in physical activity at an early age. Learning good physical activity habits at an early age increases the probability that children will continue these habits into adolescence and adulthood. Physical education should be required in public schools through the end of high school. School physical education programs should also distinguish between appropriately high and inappropriately high levels of physical activity and include suitable training to guard against medical problems associated with excessive exercise and resulting weight loss.

Research Priorities

Although there is no conclusive evidence to prove that physical activity has a protective effect against breast cancer, there is sufficient evidence to warrant more research on this topic. While breast cancer research continues, advocates stressed the urgency of monitoring its progress and informing the public as soon as possible if a related benefit from physical activity becomes clear. Recommendations for the direction of future research include the following:

1. Controlled, randomized, clinical metabolic studies are needed on the effects of physical activity on possible mechanisms for breast cancer, such as the following:
 - Body composition, weight gain, and fat distribution;
 - Mammographic patterns;
 - Ovulatory patterns;
 - Hormone production and metabolism;
 - Immune function;
 - Insulin production and/or sensitivity;
 - Blood lipids, especially high density lipoprotein cholesterol;
 - Bone density and other possible side effects.

Such studies would examine the potentially beneficial effects of physical activity on breast cancer risk mediated by mechanisms other than

weight loss and avoidance of weight gain, such as hormonal and immunologic mechanisms. Information on bone density in adolescent girls is particularly needed. Measurements are needed both before and after periods of physical activity to allow for comparisons.

2. Animal models and short-term interventions should be used to collect data on the mechanisms involved in physical activity. Issues associated with age, time of life (e.g., adolescence), and all of the parameters associated with exercise should be examined.
3. Ascertaining the mechanisms involved in physical activity should be considered a priority when new tools for assessing physical activity are designed and evaluated. The current instruments used to assess and measure physical activity need to be improved, and new instruments need to be developed and validated.
4. Epidemiologic studies are needed to measure physical activity and its various dimensions, such as intensity, duration, frequency, changes in activity levels over time, and types of physical activity (e.g., resistance training and aerobic activity). The importance of the time in life when physical activity is undertaken needs to be evaluated, and the full range of physical activities should be evaluated, including recreational, occupational, and household activities. Little research has been done on the relation between resistance training and breast cancer and should be examined in future studies.
5. Epidemiologic studies are needed to explore the interrelation among physical activity, life-style, and diet. It is possible that physical activity itself may be a marker of a healthful life-style. More integrated information is needed on the risks and benefits associated with a variety of life-style factors that affect health, disease risk, quality of life, and mortality.
6. More research is needed to determine whether physical activity can improve quality of life and/or prognosis for women who have been diagnosed with breast cancer.

Next Actions

Participants expressed interest in taking the following actions:

1. Reassess studies that have collected information on participants' physical activity at some time in the past, to determine the accuracy of the study participants' recall. This would involve locating

- study participants and reassessing their physical activity histories.
2. Assess quality of life in an existing series of breast cancer cases, and determine whether past or present physical activity patterns relate to quality of life, social support, or other variables.
 3. Retrieve information from existing research that may yield insight into the following:
 - The etiologic relation of physical activity to breast cancer;
 - The avoidance of weight gain or weight loss and subsequent breast cancer risk;
 - The effects of physical activity on breast cancer recurrence, survival, and quality of life.
 4. Develop R01s (traditional research grants) to coordinate research on specific issues. Interdisciplinary research strategies need to be developed for a comprehensive approach. Recommendations need to be made for funding groups to accomplish long-term research goals.
 5. Convene a follow-up meeting to facilitate collaboration among participants.