

DEFEAT Cancer

EXERCISE & NUTRITION during/after CANCER

**CURRENT PEER-REVIEWED MEDICAL LITERATURE
and EXPERT COMMENTARY from RELIABLE MEDIA SOURCES and DR. BLEYER**

June 2008

Look for compilation of all prior newsletters next month

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Exercise and Nutrition

Cancer survivors' adherence to lifestyle behavior recommendations and associations with health-related quality of life: Results from the American Cancer Society's SCS-II

Christopher M. Blanchard, Kerry S. Courneya, Kevin Stein
 From Dalhousie University, Halifax, Nova Scotia; Faculty of Physical Education and Recreation, University of Alberta, Edmonton, Alberta, Canada; and the Department of Quality of Life Research, Behavioral Research Center, American Cancer Society, Atlanta, GA

[Physical activity and nutrition guidelines for cancer patients are being achieved in only one in 20 survivors; yet the quality of life is directly proportional to the number of guidelines met](#)

Purpose: To examine the prevalence and clustering of physical activity (PA), fruit and vegetable consumption (5-A-Day), and smoking across six major cancer survivor groups and to identify any associations with health-related quality of life (HRQoL).

Methods: A total of 9,105 survivors of six different cancers completed a national cross-sectional survey that included the lifestyle behavior questions and the RAND-36 Health Status Inventory.

Results: Only a minority of cancer survivors were meeting the 5-A-Day (14.8% to 19.1%) or PA (29.6% to 47.3%) recommendations, whereas most were meeting the smoking recommendation (82.6% to 91.6%). In terms of the lifestyle behavior clusters, only 5% of cancer survivors were meeting all three recommendations. Analyses of covariance generally showed higher HRQoL in survivors who were

meeting versus not meeting each lifestyle behavior recommendation with the strongest associations emerging for PA. Trend analyses showed a steep positive association between the number of lifestyle behavior recommendations being met and HRQoL for breast ($P < .001$), prostate ($P < .001$), colorectal ($P < .001$), bladder ($P < .001$), uterine ($P < .001$), and skin melanoma ($P < .001$) cancer survivors.

Conclusion: Few cancer survivors are meeting the PA or 5-A-Day recommendations, and even fewer are meeting all three lifestyle recommendations. The association between the current lifestyle recommendations and HRQoL in cancer survivors appears to be cumulative. Interventions to increase PA and fruit and vegetable consumption and reduce smoking are warranted and may have additive effects on the HRQoL of cancer survivors.

Presented at the 2008 Annual Meeting and Scientific Sessions of the Society of Behavioral Medicine, March 26-29, 2008, San Diego, CA.

Dr. Bleyer:

I charted the data for E&N (exercise and nutrition) from the report and average the result over the six types of cancer studied. One in every four survivors met the E guidelines (specified below table) and one in six achieved the N guidelines (ibid). Only one in 20 however met both E&N guidelines. It's as if there are exercise folks and there are the nutrition folks, and n'ere the twain shall meet (they ain't the same persons). Therein resides an explanation for nearly all reports on E&N in cancer survivors they address either E or N but not both (E&N). Its hard to get survivors to do both.

	Breast	Prostate	Colorectal	Bladder	Uterine	Melanoma	Average
No. Survivors	2,885	2,226	1,918	586	729	761	9,105
<i>Guidelines Achieved</i>							
E&N	5%	5%	5%	4%	4%	6%	5%
E*	24%	29%	21%	22%	19%	35%	25%
N**	18%	15%	15%	16%	19%	14%	16%

*Accumulate at least 150 minutes of moderate-to-strenuous or 60 minutes of strenuous PA per week

**5 vegetables or fruits a day

- E&N guidelines of DEFEAT Cancer are supported by this report
- So is our use of the SF-36 quality of life assessment tool
- It's DEFEAT's mission to make it more feasible to do both (E&N)
- Based on the E&N diary forms returned, DEFEAT Cancer participants are doing better than the average national results; just how much better are not yet able to determine since we would need more diaries completed and returned to us; the SF-36 survey will be conducted again in June.

Physical activity and obesity in Canadian cancer survivors: Population-based estimates from the 2005 Canadian Community Health Survey

Kerry S. Courneya KS, Katzmarzyk PT, Bacon E

University of Alberta, Edmonton, Alberta, CA; Pennington Biomedical Research Center, Baton Rouge, Louisiana; Queen's University, Kingston, Ontario, Canada

Interviews of 114,355 Canadians that included self reported cancer history, height and body weight to calculate body mass index (BMI) indicates that only about one in five cancer survivors are physically active and one in six are obese

Background. Physical inactivity and obesity are associated with poorer disease outcomes in several cancer survivor groups. Few studies, however, have provided population-based estimates of these risk factors in cancer survivors and compared them with individuals without a history of cancer. Here such estimates for the Canadian population are reported.

Methods. Data were obtained from the 2005 Canadian Community Health Survey consisting of computer-assisted interviews of 114,355 adults representing an estimated 23,285,548 Canadians. Participants self-reported their cancer history, height, and body weight to calculate body mass index and participation in various leisure-time activities.

Results. **Fewer than 22% of Canadian cancer survivors were physically active** and over 18% were obese. Few differences were observed between cancer survivors and those without a history of cancer

except that: 1) **prostate cancer survivors were more likely to be active** (adjusted odds ratio [OR] = 1.27; 95% confidence interval [CI] = 1.01-1.59) **and less likely to be obese** (adjusted OR = 0.71; 95% CI = 0.56-0.90); 2) skin cancer survivors (nonmelanoma and **melanoma**) **were more likely to be active** (adjusted OR = 1.33; 95% CI = 1.12-1.59); and 3) obese breast cancer survivors were less likely to be active compared with obese women without a history of cancer (adjusted OR = 0.51; 95% CI = 0.27-0.94).

Conclusions. Canadian cancer survivors have low levels of physical activity and a high prevalence of obesity that, although comparable to the general population, may place them at higher risk for poorer disease outcomes. Population-based interventions to increase physical activity and promote a healthy body weight in Canadian cancer survivors are warranted.

Dr. Bleyer:

- ☑ The authors conclude that cancer survivors are no different in their BMIs (measure of obesity) are no different than the general population
- ☑ They do not comment on the possibility that their average BMI was likely greater than the general population when diagnosed (since obesity increases the risk of cancer) and that after cancer they decreased their average BMI (with exercise and physical activity) to a level that was the same as in the general population.
- ☑ That more than 75% of the cancer survivors were sedentary counters this possibility
- ☑ The most sedentary survivors were females with breast cancer or melanoma, a worrisome observation since these survivors are younger than other survivors and capable of more physical activity and of nutrition improvement.
- ☑ Prostate cancer survivors had the highest level of physical activity; since they are the oldest group of survivors, age itself should not be a obstacle to physical exercise

Many cancer survivors are overweight and sedentary

By Serena Gordon

MONDAY, April 21 (HealthDay News) -- A healthy lifestyle may help cancer survivors prevent recurrence of the disease and live longer, yet cancer survivors have rates of obesity and physical inactivity similar to those of the general population, according to new research.

When the authors of the above study were contacted, they were expresses surprise that cancer survivors were so sedentary in view of the scientific evidence for benefit of physical activity

The study, published in the June 1 issue of *Cancer*, found that **less than one-quarter of cancer survivors were regularly physically active**, and more than 18 percent were obese.

"We thought this might be a time when people would be particularly motivated to exercise and control weight. But, a cancer diagnosis and treatment didn't seem to stimulate behavior change," said the study's lead author, **Kerry Courneya, a professor and Canada Research Chair at the University of Alberta** in Edmonton, Canada.

What's troubling is that maintaining a healthy weight and getting regular physical exercise may be even more crucial for cancer survivors than it is for the general public. Some studies have suggested that physical activity and losing weight may help prevent cancer recurrence and improve survival odds. Additionally, some research suggests that exercise can help reduce fatigue, improve physical functioning and improve quality of life for some cancer survivors.

For the study, Courneya and his colleagues gathered data from the Canadian Community Health Survey. This survey contains information based on interviews of more than **114,000 people** in Canada. Details of cancer history, weight, height and physical activity were all supplied by the respondents.

General population statistics for Canada find that 37 percent of people are overweight, and 22 percent are obese, according to background information in the study.

Fewer than 22 percent of cancer survivors reported being physically active. The lowest rates of physical activity were found among colorectal cancer survivors, breast cancer survivors and female survivors of melanoma.

Thirty-four percent of cancer survivors were overweight, and almost one in five was obese.

Obese breast cancer survivors were only about half as likely to be physically active as obese women who hadn't had cancer, a finding that's particularly worrisome, because poor outcomes in breast cancer have been associated with obesity and the often accompanying sedentary lifestyle.

"We really didn't know which way the research would go. Cancer survivors may be more motivated at the time of their diagnosis to make changes, but others point out that it's a very stressful time that can take a toll and lead to the opposite effect," Courneya said.

Kevin Stein, director of Quality of Life Research at the American Cancer Society, said, "This is an important finding to underscore the fact that cancer survivors need to pay attention to their health. You've dodged a bullet for the time being, but cancer survivors are actually at an increased risk for a number of health conditions, including cancer recurrence.

"There is a teachable moment when someone is diagnosed. It's the perfect opportunity to say, '**We all need to eat healthy and exercise, but it's even more important for you as a cancer survivor,**'" he said.

Courneya added: "This is something they can do for themselves to help beat cancer and improve quality of life. The cancer community needs to get more involved in the promotion of healthy lifestyles in cancer patients. Maybe a program something like cardiac rehabilitation. **The cancer community's been slower to realize the importance of lifestyle changes after cancer diagnosis.**"

SOURCES: Kerry Courneya, Ph.D., professor, and Canada Research Chair, University of Alberta, Edmonton, Canada; Kevin Stein, Ph.D., director, Quality of Life Research, Behavioral Research Center, American Cancer Society, Atlanta; June 1, 2008, Cancer

Dr. Bleyer:

- ☑ Cancer survivors should also be more motivated since it's even more important to avoid or reduce excessive BMI after a cancer diagnosis
- ☑ If heart disease survivors have been successful at exercise and nutrition improvement and in weight reduction, cancer survivors can too, albeit cancer survivors may find it harder to exercise during chemotherapy or radiation therapy
- ☑ On the other hand most exercise programs are started after chemotherapy and radiation and, DEFEAT Cancer argues, sedentary habits are reinforced during these treatments and more difficult to overcome thereafter.

Prognostic value of body mass index in locally advanced breast cancer

Dawood1 S, Broglio K, Gonzalez-Angulo AM, Kau1S-W, Islam R, Hortobagyi GN, Cristofanilli M
Clinical Cancer Research 14, 1718-1725, 2008

One of the worst types of breast cancer, inflammatory breast cancer, occurs more commonly in obese women and explains in part, but only in part, the shorter survival times in overweight and obese patients

Purpose: The purpose of this retrospective study was to determine the association and prognostic value of body mass index (BMI) at the time of initial diagnosis in patients with locally advanced breast cancer (LABC). The analysis includes the subsets of inflammatory (IBC) and noninflammatory (non-IBC LABC) breast cancer.

Experimental Design: We identified 602 patients who had LABC treated on prospective clinical trials. BMI was divided into three groups: (a) 24.9 (normal/underweight), (b) 25.0 to 29.9 (overweight), and (c) 30 (obese). Kaplan-Meier product limit method was used to estimate survival outcomes. Cox proportional hazards were used to determine associations between survival and BMI and to test for an interaction between BMI and breast cancer type.

Results: Eighty-two percent had non-IBC LABC and 18% had IBC. Obese patients tended to have a higher incidence of IBC compared with overweight and normal/underweight groups ($P = 0.01$). Median follow up was 6 years for all patients. Median overall survival (OS) and recurrence-free survival (RFS) were 8.8 and 5.9 years, respectively. Patients with LABC who were obese or overweight had a significantly worse OS and RFS ($P = 0.001$) and a higher incidence of visceral recurrence compared with normal/underweight patients. In a multivariable model, BMI remained significantly associated with both OS and RFS for the entire cohort. The interactions between BMI and LABC subsets and between BMI and menopausal status were not statistically significant.

Conclusion: Patients with LABC and high BMI have a worse prognosis. Evaluation of the biological factors associated with this observation can provide tools for additional therapeutic interventions.

Dr. Bleyer:

- ☑ My colleagues at MD Anderson add their data to the large body of evidence of shorter survival and high BMIs
- ☑ They have also found that obesity increases the risk of inflammatory breast cancer, the hardest type to treat and the type with the worst prognosis
- ☑ On the other hand they also found that obesity itself and not the type of cancer or menopausal status portends a worse prognosis

Weight gain following a breast cancer diagnosis increases likelihood of disease-specific mortality

Oncology Times May 2008, 30(9)10 p 54

Women who gain weight following a breast cancer diagnosis have an increased risk of death due to breast cancer compared with women who do not gain weight, researchers reported at the AACR Frontiers in Cancer Prevention Research meeting.

The risk of death due to breast cancer increases 14% for every 12 pounds gained after diagnosis, irrespective of a woman's weight at diagnosis

Numerous studies have looked at the impact of body mass index (BMI) at the time of diagnosis on clinical outcomes, and most have reported a positive association between increased weight and increased mortality risk. What our study can contribute, which has not so often been looked at, is the effect of weight gain after diagnosis, said Hazel B. Nichols, MS, a doctoral student at **Johns Hopkins** Bloomberg School of Public Health.

There was a significant trend between increasing weight gain and higher mortality risk from breast cancer and other causes.

Specifically, Ms. Nichols and colleagues found that in a group of 4,021 breast cancer patients, **the risk of death due to breast cancer increased 14% for every five kilograms gained after diagnosis, irrespective of a woman's weight at diagnosis.**

The risk of death due to any cause also increased 14%. Women who gained 10 kg after diagnosis had an increased risk of breast cancer death of 80%. (All mortality risk calculations were adjusted for BMI at baseline.)

There are a number of studies that have implicated weight as you go into a cancer diagnosis at predicting outcome, said **Craig Thompson, MD, Director of the Abramson Cancer Center at the University of Pennsylvania**, who moderated a press conference in which Ms. Nichols presented her study.

She has been able to show that it matters what your weight gain is after diagnosis, that it is still influencing outcome. That is something patients have control of.

To look at the potential impact of post-diagnosis weight gain on mortality, the researchers looked at breast cancer patients diagnosed between 1988 and 2001 in New Hampshire, Wisconsin, and Massachusetts. The women were part of a case-control study and were initially identified using state cancer registries.

Structured telephone interviews were used to collect information at the time of diagnosis on weight, height, diet, menstrual and reproductive history, family breast cancer history, and demographics. Between 1998 and 2001, survivors received a follow-up questionnaire which asked about post-diagnosis weight and weight gain, diet, physical activity, medication use, and quality of life. The investigators used the National Death Index through 2005 to obtain mortality data.

With a median follow-up of 5.8 years, there were 121 breast cancer deaths and 428 due to other causes in the study population. As expected from previous studies a higher BMI was associated with an increased risk of death, such that obese women had a 2.4-fold increased risk of breast cancer death and a 1.5-fold increased risk of death due to other causes.

The team has not yet looked at the impact of post-diagnosis weight loss on clinical outcome, but plan to do so using the data already collected. Additionally, **they want to examine the impact of physical activity and weight gain on mortality risk to see if active and inactive women who gain weight have the same increase in risk of death.**

These results generally support the recognized health benefits and potential mortality benefit of avoiding weight gain, Ms. Nichols concluded. And they add to a growing body of evidence that post-diagnosis lifestyle-things you can incorporate after breast cancer diagnosis-have the potential to improve survival. The study was funded by the Susan G. Komen Breast Cancer Foundation and the NCI.

Dr. Bleyer:

- ☑ It's good to know that the investigators can and plan to evaluate the combination of exercise and weight change, since DEFEAT Cancer considers exercise as having benefits beyond weight reduction.
- ☑ The importance of this study is that the increased risk of breast cancer recurrence and weight gain was quantified.

U.S. women worry more about weight than cancer: poll

Wed May 21, 2008

By Megan Davies

NEW YORK (Reuters Life!) - American women are more concerned about losing weight than they are about suffering from cancer, heart disease or diabetes, a survey showed.

[U.S. women's fear of weight gain more than cancer is prevalent despite knowledge that excessive weight gain increases cancer susceptibility](#)

More than half of the 3,000 women questioned in the poll by Meredith Corporation and NBC Universal were worried about diet and weight, compared to 23 percent who were concerned about cancer and 20 percent who were anxious about their cardiovascular health.

The women were asked to identify the health issues they were concerned about from a list of 20 problems.

The survey showed many women thought they should be slimmer, with more than 80 percent saying they were overweight.

But just 43 percent said they were exercising at least three times a week, and 11 percent played team and individual sports. And less than two-thirds of all women said they get an annual physical.

"These **findings should be a wake-up call to American women everywhere to make their yearly checkups without fail** and make their own personal health a top priority," said Diane Salvatore, editor in chief of Ladies' Home Journal, which is published by Meredith Corp.

While the majority of women said they were overweight, 68 percent said they were satisfied with their "identity and development as an individual".

But **40 percent said it was wrong for a man to tell a woman she was overweight.**

To improve their health, 26 percent of women said they took natural herbs and supplements, while 25 percent bought or adopted a pet, according to the survey.

Four percent visited a spiritual or religious leader and one percent went to a hypnotist.

Grant to support study of exercise program for women with cancer

Dr. Bleyer:

- ☑ Vanity must be greater than health concern since annual physical exams (with cancer prevention and early detection a major objective of annual exams) occur far less often than the anxiety of being overweight and since most women do not want to be informed about their weight status (at least not by the other sex)
- ☑ Less than one-fourth of U.S. women worry about cancer, yet 38% are expected to be develop cancer
- ☑ Cancer was of more concern than cardiovascular disease

Yale receives National Cancer Institute grant to study exercise for women with cancer

HemOncToday – May 10, 2008

[A Yale-developed exercise program designed to reduce bone loss and prevent weight gain in is being funded with a \\$2.2 million grant from the National Cancer Institute](#)

There are more than 10 million cancer survivors in the United States, and 22% are women diagnosed with breast cancer, notes the principal investigator, M. Tish Knobf, Ph.D., R.N., the American Cancer Society Professor at the School of Nursing and a member of the Yale Cancer Center.

“Cancer survivors face persistent physical symptoms as well as psychological distress when treatment ends,” Knobf says. “For long-term survivors, there are additional concerns related to late effects of cancer therapy, such as bone loss.”

Her team conducted a pilot study to look at the effects of exercise and found that 88% of the women adhered to the program, maintained their weight, had no changes in bone mass and improved psychologically.

“Weight gain, changes in body composition, decreased physical functioning, bone loss and menopause in women treated for cancer may increase risks for cardiovascular disease, diabetes, and osteoporosis,” Knobf says. “With an estimated 64% of cancer survivors now living longer than five years, interventions are needed to reduce the risk of cancer recurrence, secondary cancers, and health risks for other chronic illnesses.”

Co-investigators Dr. Lyndsay Harris and Dr. Karl Insogna will provide additional expertise to help monitor the women enrolled in the study. Harris, associate professor of medical oncology and director of the Yale Cancer Center Breast Cancer Program, studies the molecular classifications of breast cancer, particularly in minority women. Insogna, director of the Yale Bone Center and professor of internal medicine, has clinical expertise on the disease-related causes of bone loss.

Dr. Bleyer:

- ☑ If the NCI is willing to spend \$2,200,000 on studying the value of exercise in women with cancer, the Lance Armstrong Foundation is getting their money's worth in supporting DEFEAT cancer, where exercise and nutrition (E&N) in cancer patients and survivors is the focus.
- ☑ With pilot data indicating the 88% of women with breast cancer improved psychologically along with maintaining their weight – a dramatic result that we reviewed before and that was the basis for a large grant award and justifies test their exercise program in women with other kinds of cancer.

Exercise

Exercise combats cancer-related fatigue

NEW YORK (Reuters Health) - Exercise appears to be beneficial for patients suffering from cancer-related fatigue, both during and after treatment, a review of published studies indicates.

Exercise has been shown in 28 studies involving 2083 cancer patients and survivors to significantly diminish fatigue and related effects of pain, emotional distress, sleep disturbance, anemia and co-morbid illnesses

Nearly all cancer patients experience fatigue, Dr. Fiona Cramp and colleagues note in the latest issue of The Cochrane Library, a publication of **The Cochrane Collaboration**, an international organization that evaluates medical research.

According to guidelines from the National Comprehensive Cancer Network, treatable factors that may be related to cancer-related fatigue, such as pain, emotional distress, sleep disturbance, anemia, nutrition, activity level, and co-morbid illnesses, should be identified and treated.

However, there is no consensus regarding the effect of exercise on cancer-related fatigue once treatable causes have been addressed.

Cramp, of the University of the West of England in Bristol, UK, and colleagues searched the medical literature for controlled trials that evaluated the effect of exercise on cancer-related fatigue. They identified **28 studies involving 2083 participants**. More than half of the studies involved women with breast cancer.

"Statistically significant improvements in fatigue were identified following an exercise program carried out either during cancer therapy or following cancer therapy," the researchers report. Most programs involved **moderate-intensity exercise performed two or three times per week**.

Cramp's team recommends that exercise be considered as one of several components of the management strategy for cancer-related fatigue, which may also include other nonpharmacologic interventions, including psychological and social therapies, stress management, nutrition therapy and sleep therapy.

"Exercise shouldn't be used in isolation but should definitely be included as one of the components in the package of interventions used during and after treatment," Cramp said in a written statement.

SOURCE: The Cochrane Library 2008.

Dr. Bleyer:

- ☑ The Cochrane Study Group, based in England, is the world's most respected organization that researches published scientific literature; they only study important health issues and their results and conclusions are generally considered unassailable.
- ☑ That exercise was definitively shown to reduce cancer-related fatigue *per se* is a wonderful finding, that DEFEAT Cancer submits would be even more strongly demonstrated with excellence in nutrition.
- ☑ DEFEAT Cancer would also expect the benefit to be even more obvious if the exercise intervention were started during therapy rather than afterwards.

The potential link between physical activity and recurrence in breast cancer survivors

Hem Onc Today - April 10, 2008

Editor's note: The following is an excerpt of an interview with **Jennifer A. Ligibel, MD**, instructor of medicine at **Harvard Medical School**. She and her colleagues found a potential relation between exercise and a significant decrease in insulin levels and hip circumference in breast cancer survivors.

[Jennifer Ligibel, MD, principal investigator of a study at Harvard Medical School that a reduction in insulin levels may explain the benefit of exercise in prolonging survival after breast cancer, is interviewed regarding the significance of her study](#)

We performed this study because there is a growing amount of observational evidence that women who exercise after being diagnosed with breast cancer have a lower risk for recurrence. There was a report from another large study that came out recently that showed the same thing: **Women who are physically active after having breast cancer had about a 50% lower recurrence risk compared with women who were inactive, and this has been observed now in three large studies.**

Nobody understands what really happens during exercise that could be influencing recurrence rates. So the point of our study was to look at what happens, hormonally, when women become physically active. Specifically we looked at insulin, which is a hormone involved in diabetes and blood glucose regulation, but has also been shown to be a mitogen. Higher insulin levels have also been related with higher recurrence risks in patients with breast cancer.

There is probably a lot that happens when people begin to exercise that may influence cancer recurrence risks and we are at the cusp of figuring out how something like physical activity affects breast cancer recurrence risk. All the evidence so far that has shown recurrence is lower has been observational. Eventually we will need to not only figure out what happens when people begin to exercise, but really show through randomized trials that it is exercise that is making the difference and not something else that these women are doing.

We are a step away from an actual recommendation for patients with breast cancer. Data from many observational studies suggest that physical activity is a good thing for women who have had breast cancer. We all know that we should be exercising more for a variety of different reasons.

The results from another study recently showed that women with early stage breast cancer are more likely to die of other causes than die of breast cancer. There are many beneficial things that occur when women exercise, but **most oncologists do not spend time talking to their patients about physical activity.**

We are hoping that eventually as we can demonstrate that being physically active after having breast cancer can improve your odds for survival and exercise will become part of the treatment regimen for breast cancer patients. – Interview by Paul Burress

Dr. Bleyer:

- ☑ I believe that we are at the junction of recommending exercise, not *a step away*, for cancer patients
- ☑ DEFEAT Cancer is even more certain of this recommendation if excellence in nutrition is included with the advice

BMI linked to overall survival in locally advanced breast cancer

HemOnc Today - March 27, 2008

By Stacey L. Adams

In women with locally advanced breast cancer, prognosis is worse among those with high BMI, compared with patients who are normal or underweight.

Researchers from University of Texas M.D. Anderson Cancer Center in Houston and Dubai Hospital in United Arab Emirates analyzed data from 602 patients with locally advanced breast cancer who were treated in prospective clinical trials. Patients were divided into three groups based on BMI: ≤ 24.9 , normal/underweight; 25.0 to 29.9, overweight; ≥ 30 , obese.

Eighty-two percent of patients had non-inflammatory locally advanced breast cancer; 18% had inflammatory locally advanced breast cancer. Compared with overweight and normal/underweight groups, those in the obese category had a higher incidence of inflammatory breast cancer ($P=.01$). Compared with the normal/underweight population, overall survival and recurrence-free survival rates were worse for those in the obese or overweight categories who had locally advanced breast cancer ($P=.001$). The incidence of visceral recurrence was also higher among the overweight and obese groups. –
 Source: Clin Cancer Res. 2008;14:1718-1725.

[The type of breast cancer with the worst prognosis, inflammatory breast cancer, occurs more commonly in obese women than in any other subgroup; regardless of the subtype, overweight and obese women with locally -advanced breast cancer have a worse survival.](#)

Commentary from Donald W. Northfelt, MD

Associate Professor of Medicine, Mayo Clinic, Scottsdale, Ariz.

This article is important because we are hoping to use any and all information available to help us understand the risks that women with breast cancer face. In other words, we want to make sure that we recognize all of the information that might be valuable in helping to understand how to take care of women with breast cancer.

In this instance, we have been informed that **women who have a bad prognosis with breast cancer at the time of initial diagnosis will actually have a worse prognosis if they have a higher BMI.** This information, therefore, helps us begin to categorize women within a conventional high-risk group — to categorize these women into relatively higher and relatively lower-risk groups with respect to their prognosis.

This study does not offer us a means to treat those women differently, but what it can do is suggest to us that if we recognize that there is a particular group of women at higher risk — women with those types of cancer who also have higher BMI — then in the future, we might be able to study that group of women specifically and look for better ways to treat them as a ‘high, high’ risk subset. We do this often in cancer medicine; we try to distinguish, even within a bad disease, those people whose disease is worse because those people in particular would benefit from having better therapies devised for them. This study, in and of itself, is interesting intellectually, but it will not lead anywhere unless researchers now take these women who have been defined as ‘high, high’ risk based on high BMI and try to do something for them. That is why any study like this is done, really, it is not just the intellectual exercise but to help us understand who needs more help and then to begin to figure out ways to get them that help.

In medicine, we talk all the time to our patients about the value of maintaining a healthy weight. We know, for example, that the risk for diabetes is reduced if you maintain a healthy weight; we know that risk for cardiovascular disease, stroke, heart attack and high blood pressure will be reduced if you maintain a healthy weight. We believe that there are cancer risks that can be reduced by maintaining a healthy weight, and here is an example of that. There is a reasonably good foundation in this report to be able to say to women, ‘it is valuable to maintain a healthy weight because **if you ever are so unfortunate as to develop breast cancer, by having a healthy weight at that time, you are going to make your prognosis better.**’

So, I think this adds to the body of evidence that we need to make women aware that maintaining a healthy weight as a lifetime wellness strategy is a good thing to shoot for. I think the messages women get from medical professionals about maintaining a healthy weight are pretty widely disseminated in our culture and our medical care, but every opportunity we have to re-emphasize that and expand women’s understanding of that is worthwhile. So here is another instance in which it has been made clear that

maintaining healthy body weight will be advantageous. This **adds to the chorus calling** for maintaining healthy body weight and it has a particular focus because it is a very important women's health issue that a lot of women worry about.

Dr. Bleyer:

- ☑ We know of no subgroup of women who aren't at risk of breast cancer; it's safe to say that with our knowledge today, *no-one is spared*
- ☑ We do know however that the chance of getting breast cancer is increased in overweight women and that their chances of surviving the cancer are decreased
- ☑ From this study and Dr. Northfelt's perspective, we now know that the worst type of breast cancer is more likely to occur in obese women
- ☑ Thus obesity is a *triple whammy* for breast cancer, with an increased risk of breast cancer, and increased risk of the worst kind of breast cancer, and a decreased chance of survival regardless of the kind of breast cancer
- ☑ Dr. Northfelt is a colleague of Dr. Braich's, the two having worked together at the Mayo Clinic Scottsdale.

Recruiting and retaining breast cancer survivors into a randomized controlled exercise trial: the Yale Exercise and Survivorship Study

Cancer. 2008 Apr 21. [Epub ahead of print]

Irwin ML, Cadmus L, Alvarez-Reeves M, O'Neil M, Mierzejewski E, Latka R, Yu H, Dipietro L, Jones B, Knobf MT, Chung GG, Mayne ST.

[This study recruited breast cancer patients into a clinical trial that randomized exercise vs. usual care; less than 10% were enrolled, but when participating the compliance was excellent.](#)

BACKGROUND.: Given observational findings that physical activity reduces breast cancer risk, improves survival, and improves quality of life in breast cancer survivors, a need has been identified for randomized controlled trials that test the efficacy of exercise on biological mechanisms associated with breast cancer survival. The primary aims of the Yale Exercise and Survivorship Study were to 1) determine the feasibility of recruiting breast cancer survivors into a randomized controlled trial of the effects of exercise on biological markers and/or mechanisms associated with survival, 2) compare the effectiveness of various recruitment strategies on accrual rates and baseline characteristics, and 3) report adherence to the exercise trial. **METHODS.:** Seventy-five postmenopausal breast cancer survivors self-referred into the trial or were recruited through the Connecticut Tumor Registry and randomly assigned to an exercise (n = 37) or usual-care (n = 38) group. The exercise group participated in 150 min/wk of supervised gym-based and home-based aerobic exercise for 6 months. The usual-care group was instructed to maintain current physical activity level. **RESULTS.:** A total of 75 women (an accrual rate of 9.5%) were randomized to the trial. Rates of accrual were higher for women who self-referred into the study (19.8%) compared with women recruited via the cancer registry (7.6%); however, demographic, physiologic, and prognostic characteristics did not differ between the 2 recruitment strategies. On average, exercisers increased moderate- intensity to vigorous-intensity aerobic exercise by 129 minutes per week compared with 44 minutes per week among usual-care participants (P < .001). Women in the exercise-intervention group increased their average pedometer steps by 1621 steps per day compared with a decrease of 60 steps per day among women in the usual-care group (P < .01). **CONCLUSIONS.:** Findings from this study will provide useful information for investigators who are conducting exercise trials in cancer populations, clinicians who are treating women diagnosed with breast cancer, and exercise professionals who are developing community-based exercise programs for cancer survivors.

Dr. Bleyer:

- ☑ Self-referred patients remained in the program longer than those recruited via the Tumor Registry, indicating that self-motivation is a strong factor of compliance and emphasizing the need to educate cancer survivors of the importance and benefits of exercise
- ☑ DEFEAT Cancer takes advantage of self-commitment by offering four levels of exercise teams and a nutrition team that is designed to accommodate a variety of preferences.

Nutrition

Phytonutrients shown to inhibit cancer stem cells from regrowing tumors

Office of Cancer Complementary and Alternative Medicine Newsletter – 3(1), Spring 2008

Scientists in NCI's **Center for Cancer Research (CCR)** are finding early evidence that some phytonutrients – specifically EGCG, a green tea extract, and resveratrol, a compound isolated from grapes and red wine – can inhibit or eliminate cancer stem cells (CSCs) which are increasingly viewed as the driving force behind relapse and chemotherapy resistance in many cancers.

[The cancer stem cell—the current holy grail of targeting cancer therapy—is hard to find and yet has been found to be treatable with plant-derived compounds \(phytochemicals\)](#)

A growing body of evidence has identified CSCs as being the major cause of tumor progression, explained **William Farrar, Ph.D.**, CCR principal investigator for the phytonutrient/chemical study which is supported by OCCAM. CSCs are distinct from the cancer “progeny cells” which are created by CSCs and make up the bulk of most tumors. Current cancer treatments focus on destroying the progeny cells “but in many cases, even after the tumor is reduced or seemingly eliminated, it grows back and becomes resistant to further treatment,” he added. Many researchers now believe that the CSCs often survive initial treatment and act like “evil seeds” that regrow new, more treatment-resistant progeny cells.

Dr. Farrar is head of CCR's Cancer Stem Cell Section laboratory. One of the initial challenges faced was due to the miniscule numbers of CSCs found in tumors. “The very first time we extracted CSCs we came up with only 280 cells in the sample!” Dr. Farrar recalled. In contrast, high-throughput screening methods typically produce millions of progeny cells for study and analysis. Dr. Farrar and his colleagues focused first on developing tools for extracting and analyzing the small populations of CSCs from tumors.

“Phytochemicals (plant-derived compounds) have a long history demonstrating their cancer preventive properties,” he continued. However, the natural compounds had not been studied specifically for their effects on CSCs until now. Dr. Farrar's lab winnowed down 22 potential phytochemical compounds “into what I call our short list.” They ultimately decided to first study EGCG and resveratrol in lab cultures of CSCs from breast and prostate cancer tumors and in xenografts of human CSCs.

“The good news is our studies confirm that CSCs are not invulnerable to treatment as some have been concerned,” he reported. Both of the phytochemical compounds were shown to prevent proliferation and block tumor formation by CSCs. They were also effective against cancer progeny cells and did not trigger drug-resistance responses in the tumor cells.

In future studies, Dr. Farrar's lab will expand its library of phytonutrients and isolate CSCs to determine the effectiveness of phytonutrients for other cancers (i.e., pancreatic, lung, skin).

Dr. Bleyer:

- ☑ As we reported last month, E&N News will feature selected laboratory investigations; this one was chosen because it studied the elusive cancer stem cell, found chemicals that were effective (few are) in eliminating CSC.
- ☑ Moreover, the results support DEFEAT Cancer's emphasis on plant-based diets

Coffee and tea don't raise breast cancer risk - study [Prevention]

Reuters - New York, May 26, 2008 - Results from a decades-long study may enable women to drink coffee or tea without worry that doing so will increase their risk for breast cancer, study findings suggest.

[Caffeinated beverages and food \(chocolate\) do not increase the risk of breast cancer even long term exposure](#)

"In this large cohort of women, with 22 years of follow-up, we observed no association between coffee (caffeinated or decaffeinated) and tea consumption and the risk of breast cancer," Dr. Davaasambuu Ganmaa told Reuters Health.

"Coffee and tea are remarkably safe beverages when used in moderation," said Ganmaa, of the **Harvard School of Public Health** in Boston, Massachusetts.

Ganmaa and colleagues assessed coffee, tea, and caffeine consumption among **85,987 women** who participated in the Nurses' Health Study. The women were between 30 and 55 years old at the start of the study.

Over 22 years of follow up, **5,272 women developed breast cancer**.

After accounting for other factors potentially associated with breast cancer risk, such as age, smoking status, body mass, physical activity, alcohol intake, family history, menopausal status, history of hormone therapy, and number of children, the researchers found no elevated risk of breast cancer among women who reported drinking 4 or more cups of caffeinated or decaffeinated coffee or tea per day, compared with those who drank less than 1 cup daily.

They also found no apparent association between the occurrence of breast cancer and intakes of other caffeinated soft drinks and chocolate, which contribute to overall caffeine intake.

When the researchers further assessed breast cancer risk specifically among postmenopausal women, they found a modestly reduced risk associated with the highest versus the lowest caffeine intake. But, "this relation needs to be examined further," the investigators note.

Dr. Bleyer:

- ☑ Albeit prevention studies, which we don't include unless relevance to treatment studies (after cancer diagnosis) is obvious; in this case this and the previous study were included to illustrate how individual food substances are studied and how the results can be diametrically opposed
- ☑ The Nurses Study is the largest epidemiology study of late and long-term effects performed to date
- ☑ It takes more than 85,000 subjects to study and answer questions about items like the risk of coffee-induced breast cancer, since there are so many risk factors for breast cancer and these have to be controlled
- ☑ It's nice to know that chocolate is spared of increasing breast cancer risk.

Drinking may raise breast cancer risk [Prevention]

By Amanda Gardner

SUNDAY, April 13 (HealthDay News) -- Alcohol, consumed even in small amounts, increases the risk of breast cancer and particularly estrogen-receptor and progesterone-receptor positive breast cancer, a new study shows.

The increase in risk of breast cancer after menopause is proportional to the daily amount of alcohol consumed, increased with even small amounts and substantially increased with 3 or more drinks a day

The findings, expected to be presented Sunday at the annual meeting of the American Association for Cancer Research, in San Diego, are followed by a second study that found an association between breast cancer risk and two genes involved in alcohol metabolism.

Previous data has suggested that consuming alcohol ups the risk of breast cancer, although the precise mechanisms have not been clarified.

In some forms of breast cancer, malignant cells have receptors that render them sensitive to hormones such as estrogen. The first study aimed to see if the hormone receptor status of the tumor influenced the relationship between alcohol consumption and breast cancer risk.

In the study, a team led by **Dr. Jasmine Lew** of the U.S. **National Cancer Institute** followed more than **184,000 postmenopausal women** for an average of seven years.

Those who had less than one drink a day had a 7 percent increased risk of breast cancer compared to teetotalers, the team reported. Women who drank one to two drinks a day had a 32 percent increased risk, and those who had three or more glasses of alcohol a day had up to a 51 percent increased risk.

But the risk was seen mostly in those 70 percent of tumors classified as estrogen receptor- and progesterone receptor-positive. Researchers suspect that alcohol may have an effect on breast cancer via an effect on estrogen.

The risk was similar whether women consumed primarily beer, wine or spirits, the NCI team noted.

The second study dug deeper into other possible mechanism by which alcohol consumption increases breast cancer risk.

"For years, we've known that there's an association between alcohol drinking and breast cancer risk, but nobody knows yet what the underlying biological mechanisms are," said Dr. Catalin Marian, lead author of the study and a research instructor in oncology at the **Lombardi Comprehensive Cancer Center** at Georgetown University in Washington, D.C. "The logical step was to begin analyzing the alcohol metabolizing genes."

And indeed, two of these genes -- ADH1B and ADH1C -- were associated with a two-fold increase in breast cancer risk.

But the study does not prove a definite cause-and-effect link. "This is an association," Marian said. "This type of study is good for generating hypotheses. It's not a definite conclusion. It needs to be replicated by other studies to say for sure that what we found is there."

Another researcher urged caution in interpreting the results of both studies.

"These studies are too early for use in a clinical setting or to advance a public health message," said Dr. Peter Shields, co-author of the genetics study and deputy director of the Lombardi Comprehensive Cancer Center.

However, he added that the findings "really do advance science, and, with proper replication in other studies, then they may be highly clinically significant."

Dr. Bleyer:

- ☑ The dose-response is impressive, with even the smallest amounts raising the risk a small amount, and three drinks a day increasing the risk 50%, which is significant since the breast cancer has the highest incidence of cancer (in women)..
- ☑ That two alcohol-metabolizing genes were found to increase the risk of breast two-fold suggests that some women are vulnerable to the risk and others may not be.
- ☑ Identifying who has these genes may be helpful in the future; for now the evidence is too weak to use them and testing for them is not easy.
- ☑ It's not clear whether or how this applies to women who have had breast cancer, but it should be regarded as possibly applicable until we know of differences.

Related Articles

Lung cancer survival: Vitamin D could be just a marker of physical fitness

Dirk Van Renterghem

Algemeen Ziekenhuis Sint Jan, Brugge, Belgium

To the Editor:

[This original article, published a year ago, purported to show that higher vitamin D levels in patient with lung cancer was associated with a worse prognosis; this report attributes the higher levels to physical activity rather than to nutrition *per se*](#)

Zhou et al¹ report a positive correlation between circulating 25-hydroxyvitamin D levels and survival in early-stage non-small-cell lung cancer patients. They refer to epidemiologic data and in vitro and animal experiments suggesting that vitamin D has antiproliferative, antimetastasis, and antiangiogenesis activities. However, association does not mean causality, and vitamin D could be just a marker of physical fitness. Sunlight and time of exposure outdoors, determinants of vitamin D levels, are dependent on physical fitness. The correlations between outdoor walking and fitness,² between physical activity and vitamin D levels,³ and among physical fitness, strength, and vitamin D levels⁴⁻⁶ have been documented in the literature. Physical fitness (as indicated by maximum oxygen concentration (VO2 max), patient questionnaires, performance scores, or comorbidity scores) is a well-known prognostic variable throughout all stages of lung cancer.⁷⁻¹⁰ Physical fitness does not increase with oral vitamin D administration.¹¹ Fitness is also associated with a reduction in all-cause mortality and of cancer-related mortality, especially in men,^{12,13} and is associated with a better prognosis in head and neck cancer.¹⁴ The hazard ratios and P values indicated by Zhou et al¹ are more convincing for overall survival than for recurrence-free survival, and that could argue against an effect on tumor biology. Unfortunately, Zhou et al were not able to collect data on outdoor exposure; if they have data on VO2 max or other indicators of physical fitness, they could investigate whether patients with similar fitness still have a prognosis related

to vitamin D levels. They did not intend their article to be read as an incentive for prescribing vitamin D in cancer patients.

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In Reply

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Wei Zhou, Rebecca S. Heist, David C. Christiani

Harvard School of Public Health, Boston, MA

Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

Department of Epidemiology, Harvard School of Public Health, Boston, MA

We do agree that "association does not mean causality," "physical activity and fitness are associated with vitamin D levels," and the existing data are not powerful enough to draw any conclusion or make any recommendation regarding the use of vitamin D supplementation as adjuvant therapy for lung cancer. Therefore, results from this epidemiologic study need to be confirmed and validated by other observational studies as well as by randomized clinical trials. However, we **do not believe that "vitamin D should be considered just a marker of physical fitness,"** for a number of reasons. First, many studies have reported that dietary/supplemental vitamin D intake is associated with favorable prognosis of various types of cancers, and this association cannot be explained by physical fitness alone. Second, studies have also suggested that vitamin D receptor polymorphisms may be associated with prognosis of various types of cancers. Third, physical fitness/activity may explain only some of the effects of vitamin D in lung cancer prognosis. Other vitamin D determinants include season of diagnosis, residential region/latitude. These have been shown consistently to be associated with lung cancer prognosis, and are not necessarily associated with physical fitness. Fifth, the hazard ratios and P values for overall survival and disease-free survival are similar in our report, especially for the joint effects of circulation 25-

hydroxyvitamin D levels and vitamin D intake. Sixth, in vitro and animal assays support the biologic mechanism of vitamin D in the prognosis of lung cancer. Additional research is needed to define the clinical utility of vitamin D in lung cancer treatment.

Dr. Bleyer:

- ☑ With all due respect to the reply, the higher vitamin D levels may still be a “red herring” in that physical activity, being outdoors, and in general having an active leads to higher D levels. If so, it's the exercise rather than the D levels per se that explains the better QOL (quality of life)
 - ☑ Nonetheless, DEFEAT's premise that it's the E&N, and not either E or N alone, that is most beneficial. In this case, better nutrition (fruits and vegetables) and physical activity raise the D levels synergistically.
-