



E & N News

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EXERCISE & NUTRITION during/after **CANCER**

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

Note: The entire year of 2008 *E&N News* is now available as a year summary for downloading, either in its entirety or just for exercise (including exercise and nutrition), on the DEFEAT Cancer website: www.defeatcancer.info.

Both versions include executive summaries and are fully indexed and bookmarked.

Note: This month's newsletter has a considerable number of *prevention* reports, especially in the nutrition category. As usual, they were included because of their direct potential applicability to prevention of cancer recurrence.

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DIET | EXERCISE | FAMILY | EDUCATION | ATTITUDE | THRIVING

Exercise and Nutrition

Adopting a healthy lifestyle 'helps cancer suffers after diagnosis'

Adopting a healthy lifestyle can help cancer patients even after they have been diagnosed with the disease, researchers believe.

[Of 110 men with aggressive prostate cancer who did not receive immediate therapy, a lifestyle change in exercise and nutrition was associated with PSA stabilization or decline in 40.](#)

Telegraph.co.uk - Nov. 7, 2008

By Kate Devlin, Medical Correspondent

A study found that almost four in ten patients with aggressive prostate cancer did not need planned surgery or radiotherapy after making simple lifestyle changes.

Doctors found that the adjustments slowed down or even halted the progression of their disease.

And they claim that there is no reason that the benefits could not be seen in other types of cancer.

Previous studies have shown that adopting a more healthy lifestyle can help to prevent different types of cancer. Rising obesity rates have been linked to at least six different types of cancer, including breast cancer, the most common form of the disease in women.

Researchers at **Addenbrooke's hospital in Cambridgeshire** decided to test the effects of adopting a healthy lifestyle in 110 men who had been diagnosed with the aggressive form of prostate cancer.

Changes made included **cutting down on salt and alcohol, eating more oily fish, losing weight and taking moderate amounts of regular exercise.**

Some of the patients were also given **vitamin and mineral supplements, which the findings show made no difference** to their cancer.

All the patients also took **small doses of aspirin, although the researchers say that there was no conclusive evidence that the drug helped patients.**

Doctors monitor the progression of prostate cancer using a test for Prostate Specific Antigens (PSA).

These rise as tumours grow, but doctors found that lifestyle changes caused levels to stabilise and even fall for some patients in the trial. The findings show that **40 of the patients, 36 per cent, did not need further treatment.**

Robert Thomas, a consultant oncologist, from Addenbrooke's, who led the study, said: "Because prostate cancer is very slow growing it is possible for us to monitor its progress.

"(The same thing) is hard to evaluate other cancers. It would not be correct to delay chemotherapy or surgery to see whether the effects of a healthy lifestyle would be the same in breast cancer, for example.

"The main benefit of lifestyle changes in other types of cancer would probably be in helping to ensure that the disease did not recur."

Paul Sinclair, from Bedford, who took part in the trial, started drinking more pomegranate juice as one of the adjustments to his lifestyle.

He said that he was surprised in the difference that the changes made to his condition.

He said: "We followed (the disease) with a series of blood tests to monitor the levels, and they started reducing.

"The results I had in April/March this year were nearly normal, really much to my surprise."

Prostate cancer affects more men in Britain than any other form of the disease.

About 35,000 men are diagnosed with the condition every year and a third go on to die from the disease.

Dr. Bleyer:

☑ Although this report has not (yet) appeared in the peer-reviewed medical literature yet (according to PubMed), the findings are consistent with the report **DEFEAT Cancer** covered in July 2008 in which a study of 30 men with low-grade prostate cancer who declined immediate therapy, an aggressive low fat diet and physical therapy regimen was associated with changes in the genes in their tumor that reduced its malignant potential (Ornish D, Magbanua MJM, Weidner G, et al. Proc Natl Acad Sciences 105(24) ePub June 16, 2008)

☑ In the current report, the patients had more advanced prostate cancer, allowing PSA to be measured instead of testing for active genes in the tumor itself - albeit the test on the tumor itself tell us more about the biology of the tumor and how exercise and nutrition can have favorable effects

☑ The study was uncontrolled and had relatively few patients (n = 110), which for prostate cancer is problematic since indolent and long-term disease is common and leads to relatively unpredictable outcomes

☑ Nonetheless, if 40% of the patients did not need further therapy over a long enough period of followup when ≥80% would have expected to progress and require therapy, the results are significant; not being able to read the study detail compromises evaluation of the study

Diet, exercise may modify breast cancer risks [includes Laboratory Study]

Combined, they produce more potent anti-disease effect in postmenopausal women, study says
HealthDay News - Nov. 18. 2008

[The combination of nutrition and exercise \(E&N\) may be synergistic because each affects different parts of a major biochemical pathway that leads to cancer and cancer recurrence, leading to a more complete effect.](#)

Scientists believe they have found out why diet and exercise affect a women's chance of breast cancer after she's past menopause, a new study says.

Researchers at the **University of Texas at Austin** found that **cutting calories and exercise affect pathways to mTOR**, a molecule that integrates energy balance with cell growth and can contribute to various human diseases when it is not functioning properly.

The research team, expected to present its findings Nov. 18 at the **American Association for Cancer Research's** annual conference on cancer prevention research, in National Harbor, MD., said these pathways are different, though. Calorie restriction affects more upstream pathways, which may explain why cutting calories delays tumor growth better than exercise when tested on animals.

"One of the few breast cancer modifiable risk factors is obesity," study lead author **Leticia M. Nogueira**, a research graduate assistant at the University of Texas, said in a news release issued by the conference organizers. "Our study may provide a good scientific basis for medical recommendations. If you're obese, and at high risk for breast cancer, diet and exercise could help prevent tumor growth."

Past research has suggested that consuming fewer calories or increasing exercise levels creates a "negative energy balance" where less energy is taken in than expended, and this lowers the risk of postmenopausal breast cancer associated with obesity. While scientists have thought hormones may play a part in this, it has never been proven. For the new study, researchers studied 45 obese mice that had their ovaries surgically removed to model the postmenopausal state. After eight weeks, mice fed a calorie-restricted diet had significantly lower blood levels of leptin, a hormone that plays a role in fat metabolism, than those mice only put on an exercise program or those allowed to eat at will with no forced exercise. The calorie-restricted mice also had increased levels of adiponectin, a hormone produced in fat tissue that regulates some metabolic processes, the researchers said.

Some of the cell signaling pathways these hormones manage converge at mTOR, and the researchers found that the key proteins found downstream of mTOR were less active in both the calorie-restricted and exercised mice compared to the controls.

"These data suggest that **although exercise can act on similar pathways as caloric restriction, caloric restriction possesses a more global effect on cell signaling and, therefore, may produce a more potent anti-cancer effect,**" Nogueira said.

Dr. Bleyer:

- ☑ This study invokes yet another biologic explanation for how exercise and nutrition (E&N) help prevent cancer from recurring or occurring in the first place
- ☑ The mTOR biochemical pathway is becoming a more important mechanism of carcinogenesis, with anticancer drugs now in clinical trials that were specifically designed to affect this mechanism
- ☑ The concept derived from the laboratory study in this report that nutrition may be more important than exercise in preventing cancer and cancer recurrence does not detract from the **DEFEAT Cancer** synergism hypothesis. If the nutrition effect is stronger and has, say, an arbitrary value of 2 vs. 1 for exercise, then 2+1 could still equal 10 (or another value that is more than the sum of the parts). And if exercise turns out to be more important than nutrition, then 1+2 could still equal 10. Either way, each makes the other more effective (synergism).

Body-mass index and progression of hepatitis B: A population-based cohort study in men

Ming-Whei Yu,* Wei-Liang Shih, Chih-Lin Lin, Chun-Jen Liu, Jhih-Wei Jian, Keh-Sung Tsai, and Chien-Jen Chen
From the National Taiwan University, National Taiwan University College of Medicine, and Genomics Research Center, Academia Sinica, Taipei, Taiwan
J Clin Oncol Dec 1 2008; 5576-5582.

[In men, excess body weight results in a more rapid transition from healthy hepatitis B virus carrier state to liver cancer and liver-related death](#)

Purpose: To determine prospectively whether body-mass index (BMI) is associated with liver-related morbidity and mortality among male hepatitis B virus (HBV) carriers.

Patients and Methods: We performed a prospective study of 2,903 male HBV surface antigen–positive government employees who were free of cancer at enrollment between 1989 and 1992. Main outcome measures included ultrasonography, biochemical tests, incident hepatocellular carcinoma (HCC), and liver-related death.

Results: During mean follow-up of 14.7 years, 134 developed HCC and 92 died as a result of liver-related causes. In Cox proportional hazards models adjusting for age, number of visits, diabetes, and use of alcohol and tobacco, the hazard ratios for incident HCC were 1.48 (95% CI, 1.04 to 2.12) in overweight men (BMI between 25.0 and 29.9 kg/m²) and 1.96 (95% CI, 0.72 to 5.38) in obese men (BMI 30.0 kg/m²), compared with normal-weight men (BMI between 18.5 and 24.9 kg/m²). Liver-related mortality had adjusted hazard ratios of 1.74 (95% CI, 1.15 to 2.65) in overweight men and 1.50 (95% CI, 0.36 to 6.19) in obese men. Excess BMI was also associated with the occurrence of fatty liver and cirrhosis detected by ultrasonography, as well as elevated ALT and -glutamyltransferase (GGT) activity during follow-up. The association of BMI with GGT was stronger than with ALT, and elevated GGT activity and cirrhosis were the strongest predictors for incident HCC and liver-related death.

Conclusion: This longitudinal cohort study indicates that excess body weight is involved in the transition from healthy HBV carrier state to HCC and liver-related death among men.

Dr. Bleyer:

- ☑ Cancer of the liver is an end-result of years of hepatitis and cirrhosis; the process of a premalignant lesion becoming fully malignant appears to be accelerated in patients with obesity
- ☑ How this occurs is not known; one explanation is that the chronic inflammation is worse in obese patients and it's the inflammation that increases cell turnover and an increased likelihood that a daughter cell will be cancerous

Excess body weight may be involved in course of hepatitis B

Reuters Health, New York
November, 2008

[Commentary on the preceding report](#)

A report in the Journal of Clinical Oncology suggests a role for excess body weight in the transition from healthy hepatitis B virus (HBV) carrier state to hepatoma and liver-related death.

In the issue published online on October 27 in the Journal of Clinical Oncology in advance of print, **Dr. Ming-Whei Yu**, of **National Taiwan University**, Taipei, and colleagues describe a prospective study in 2903 male HBV surface antigen (HBsAg)-positive government employees enrolled between August 1989 and June 1992.

Over a mean follow-up period of 14.7 years, 134 patients developed hepatocellular carcinoma (HCC). Of 218 deaths that occurred during follow-up, 92 (42.2% of total deaths) were attributable to liver-related disease, with deaths due to HCC in 71 patients and to cirrhosis in 21.

Hazard ratios for incident HCC were 1.48 in overweight men (those with body mass index of 25.0 to 29.9 kg/m²) and 1.96 in obese men (at least 30.0 kg/m²), compared with normal-weight men. Hazard ratios for liver-related mortality were 1.74 in overweight men and 1.50 in obese men.

Excess body weight was associated with elevated serum levels of ALT and gamma-glutamyltransferase (GGT) and reduced AST:ALT ratios.

In 257 subjects, cirrhosis was detected by ultrasonography during follow-up. According to the article, the risk of cirrhosis increased with increasing quartiles of BMI (p trend = 0.0005). The adjusted odds ratio for cirrhosis was 2.37 among obese HBsAg carriers compared with those of normal weight.

"The association of higher BMI with increased risk of HCC or death resulting from liver disease is independent of diabetes," the authors note. "The spectrum of liver diseases in relation to excess weight among HBsAg carriers extends from simple fatty liver at the most benign end to chronic hepatitis, cirrhosis and HCC at the opposite end."

Dr. Bleyer:

- ☑ Liver cancer is much more common in Asia than in the U.S., in part due to the higher incidence of hepatitis in Asia
- ☑ Since obesity is much more common in the U.S. than in Asia, the likelihood that Americans with hepatitis B are more likely to develop liver cancer

Breast cancer: Research lends biologic plausibility to link with alcohol; even minimal exercise may lower ... risk and recurrence [includes Prevention]

[Review of studies of alcohol intake and exercise lead to the conclusions that the risk of breast cancer is increased by daily intake of as little as a drink or two a day, individual susceptibility varies with ability to metabolize alcohol, and exercise as little as 30 minutes a week reduces risk](#)

Oncology Times, 30(12)25 June 2008. p 55-56

Reported by Charlene Laino

SAN DIEGO- The risk of hormone-receptor positive breast cancer is increased by as little as a drink or two a day, according to the largest study to look at the association between the two to date.

A second study shows that variations within two genes coding for the alcohol dehydrogenase enzyme (ADH) that is involved in metabolizing alcohol affect the risk of breast cancer in postmenopausal women.

The studies lend biologic plausibility to the fairly strong epidemiologic link between alcohol consumption and breast cancer, suggesting that drinking may affect risk through hormonal and genetic pathways, said **Chi-Chen Hong, PhD**, Assistant Professor of Oncology at the **Roswell Park Cancer Institute**.

Dr. Hong was not involved with the research, presented here at the **American Association for Cancer Research Annual Meeting**.

Also at the meeting, researchers reported that **as little as 30 minutes of recreational exercise a week appeared to lower breast cancer risk**. Those findings came from an analysis of data on some **6,000** women enrolled in the ethnically diverse **Global Epidemiology Study**.

Largest Study to Date

Experimental data suggest that alcohol intake increases the risk of breast cancer through its effect on estrogen, but only three major studies have looked at the association between alcohol use and breast cancer according to hormone-receptor status, noted **Jasmine Q. Lew**, a fourth-year **medical student at the University of Chicago**. Ms. Lew led the first study as a recipient of the Howard Hughes Medical Center-NIH Research Scholarship at the NCI's Division of Cancer Epidemiology and Genetics.

In that context, the researchers conducted the largest study to date to determine if the relation between alcohol and breast cancer differed by hormone-receptor status in postmenopausal women.

The evidence for exercise-breast cancer link is strong. It appears not only to protect against the development of breast cancer, but also appears to prolong the life of women who already have breast cancer.

Data were reviewed for **184,418** postmenopausal women, with a mean baseline age of 62, who were enrolled in the prospective **NIH-AARP Diet and Health Study**. At the study's outset, a food frequency questionnaire was given to determine alcohol and other nutrient intakes, and data on demographics, lifestyle, and medical history were collected.

The women were followed for an average of seven years, during which 5,461 cases of invasive breast cancer were identified. Information on receptor status was available in 2,391 cases: 1,641 tumors were estrogen-receptor and progesterone-receptor positive (ER+/PR+); 366 tumors were negative for both receptors (ER-/PR-); 336 were positive for ER and negative for PR (ER+/PR-); and 48 were negative for ER and positive for PR (ER-/PR+).

Thirty percent of the women reported that they did not drink alcohol, and in those who did, consumption averaged 8.2 g, or less than one drink, per day.

Alcohol Raises Risk

Results showed that the greater the self-reported consumption of alcohol, the greater the risk for any type of breast cancer.

Compared with women who abstained from alcohol, women who reported consuming less than 5 g a day had a nonsignificant 4% increase in breast cancer risk. Women who consumed 10 to 20 g per day had a significant 14% increase in risk, and women who consumed 45 g or more a day had a significant 38% increase in breast cancer risk.

A similar pattern was observed for ER+/PR+ tumor types, which Ms. Lew said account for 70% of breast cancers.

Compared with women who abstained from alcohol, women who reported consuming one to two drinks a day were 32% more likely to develop ER+/PR+ invasive breast cancer. Having **three or more drinks daily raised the risk of ER+/PR+ tumors by 51%**.

She added that drinking alcohol also appeared to raise the risk of ER+/PR- and ER-/PR- tumors, but that there were too few women in these categories to make definitive conclusions.

The relationship between alcohol and breast cancer was not significantly affected by body-mass index, use of hormone-replacement therapy, family history of breast cancer, or folate intake.

Alcohol-Estrogen Link

The findings support the hypothesis that alcohol interferes with estrogen metabolism, leading to changes in cell metabolism and growth, Ms. Lew said.

Dr. Hong agreed. Alcohol influences estrogen hormone, so there are increased levels of estrogen and increased production of estrogen. It can also decrease metabolism of androgens. And alcohol can increase the transcription activity of ER-alpha. Normal breast tissue expresses mostly ER-beta receptors; as it progresses to breast cancer, more ER-alpha receptors are expressed.

The findings support the hypothesis that alcohol interferes with estrogen metabolism, leading to changes in cell metabolism and growth.

She noted that a review article in *Nature Clinical Practice Oncology* last year (Chen W, Colditz G: 2007;4:415-423) showed that alcohol consumption, parity (having never given birth vs having three or more children), and age over 30 at first birth are all associated with an increased risk of ER-positive breast cancer.

Very few risk factors have been associated with ER-negative tumors, which are more difficult to treat, Dr. Hong said.

Gene Variants

To determine whether genes coding for ADH may help explain the apparent link between alcohol and breast cancer, Lombardi Comprehensive Cancer Center researchers analyzed DNA samples from 991 postmenopausal women with breast cancer and 1,698 controls matched by age, race, and county of residence.

Variations were found within the DNA sequences rs1042026 in the gene ADH1B and rs1614972 in the gene ADH1C that affected the risk of breast cancer.

Women who had a variant form of ADH1B and drank alcohol were 94% more likely to have breast cancer as those who didn't have the variant and abstained.

The higher their alcohol consumption, the higher their risk, said Catalin V. Marian, MD, PhD, a research instructor in the Division of Genetics and Epidemiology in the Oncology Department at Georgetown University.

The variant form of ADH1C appeared to protect against breast cancer, he said, but protection was lost with increased alcohol consumption.

Commenting on the study, Dr. Hong said that if confirmed, the findings may help to pinpoint women who may be genetically susceptible to alcohol's damaging effects—But they don't really help much on a public health level; unless you go in and test everybody, you're still dealing with trying to control exposure as opposed to telling people who can drink.

Still, genotypes are useful for developing targeted therapies and picking what type of therapy people should get, she said.

AACR Abstracts 4168, 5814, 3083

Talking to Patients

So what should oncologists tell patients, particularly those who bring up the fact that studies have suggested that a few glasses of wine may offer cardioprotection?

Clinicians should be aware that alcohol increases the relative risk of breast cancer. But it is too early to tell at this point if it is a definitive risk factor, Ms. Lew said.

Elizabeth A. Platz, ScD, MPH, Associate Professor and Director of the Training Program in Cancer Epidemiology, Prevention, and Control at Johns Hopkins Bloomberg School of Public Health and Stanley Kimmel Cancer Center, said the increased risk of breast cancer associated needs to be balanced against any protective effect against heart disease.

If the patient has breast cancer in the family, I would imagine you would have to think about cardiovascular risks. There are other ways to modify cardiovascular risk besides having a drink a day. But most risk factors for breast cancer, such as genetics or family history, are non-modifiable, Dr. Platz said.

For the **exercise study**, researchers analyzed data on 1,468 breast cancer cases and 4,865 non-cancer controls in the Global Epidemiology Study (GES), which assesses disease risk factors in people recruited from the United States, Tunisia, and Poland.

The GES is linked to a biobank at **BioServe Biotechnologies** in Beltsville, MD, that houses more than 600,000 human specimens from 160,000 individuals, allowing us to do all sorts of studies without ever picking up a pipette, said **Teresa A. Lehman, PhD, the company's Chief Technical Officer.**

Patients with newly diagnosed breast cancer filled out an extensive questionnaire that asked about their diet, smoking, and exercise habits.

Results showed that women who engaged in recreational exercise 30 to 150 minutes a week were 50% less likely to have breast cancer than women who exercised less than a half-hour per week. African-American women benefited the most: They were 69% less likely to have breast cancer if they exercised 30 to 150 minutes a week than if they exercised less. But exercise had a protective effect in Caucasian-American, Hispanic-American, Tunisian-Arab, and Polish-Caucasian women as well, Dr. Lehman said.

Exercising more than 150 minutes a week did not confer additional benefit, and subgroup analyses showed that the findings held true regardless of menopausal, lymph node, or hormone-receptor status. The odds ratios were adjusted for age, pack-years smoked, and body-mass index.

Dr. Hong said the evidence for an exercise-breast cancer link is strong. It appears not only to protect against the development of breast cancer, but also appears to prolong the life of women who already have breast cancer.

A recent study showed that **exercise appears to be more protective against ER+/PR- tumors**, which are **associated with a clinically more aggressive tumor phenotype**, than against ER+/PR+ tumors, she said.

Marji McCullough, ScD, RD, Strategic Director of Nutritional Epidemiology and Surveillance Research at the American Cancer Society, said that the findings are consistent with the group's recommendation to engage in regular physical activity as a means of lowering breast cancer risk.

But she said that patients should be advised to work out at least 30 minutes a day, five times a week, to lower their risk.

Studies have shown that being consistent over a lifetime is particularly beneficial. But it's never too late to start.

Dr. Bleyer:

☑ The benefit of a diet that includes moderate wine consumption has been clearly shown to reduce heart disease is compromised somewhat, but probably not entirely by an increased risk of breast cancer

☑ Men may be spared this adverse interaction but until other, non-female specific cancers that are associated with alcoholism, such as head, neck and liver cancers, are studied for this interaction in detail they should not assume they are not affected

☑ The bottom line is that wine consumption should *in moderation*, and that 2 or more glasses a day is *too much*, and that, as **DEFEAT Cancer** promulgates, the nutrition (of wine) should be combined with exercise for maximum benefit (and protection)

Excess weight seems to boost breast cancer risk [Prevention]

[Cancer experts summarize recent reports linking obesity and breast cancer, speculate on the mechanism, and conclude that 30 to 60 minutes of daily exercise reduces cancer risk](#)

By Dennis Thompson

HealthDay News - Nov. 2, 2008

Obesity can wreck a person's health for many reasons. But for women, too much weight tacks on an additional danger: Studies have linked obesity and breast cancer in a variety of ways.

Doctors aren't sure why this link exists and are trying to figure out what ties weight gain to breast cancer. But they are more and more convinced the link is there, and they are urging women to watch their weight and increase their exercise to help stave off what is the most common cancer among females, nonmelanoma skin cancer aside.

"There are a lot of factors we need to figure out," said **Dr. Jennifer A. Ligibel**, of the **Dana-Farber Cancer Institute** in Boston. "There are a lot of things we don't know."

An estimated 182,500 women in the United States will be found to have invasive breast cancer in 2008, according to the American Cancer Society, and about 40,480 women will die from the disease this year. Currently, there are about 2.5 million breast cancer survivors in the United States.

Studies have found that, in general, obesity is linked to cancer. **The higher a person's body-mass index (BMI, a ratio of weight to height), the more likely she or he will develop cancer**, according to recent research by scientists at the **University of Manchester in England**. Other studies have found similar links to increased body fat. Still other studies have found that women with breast cancer are more likely to live shorter lives and suffer a recurrence of their cancer if they are overweight.

For example, in a recent study conducted at the **University of Texas M.D. Anderson Cancer Center** in Houston, more than two-thirds of women with stage III locally advanced breast cancer were either overweight or obese. The study also found that a **greater proportion of obese patients** were likely to be diagnosed with a rare and more deadly form of breast cancer, known as **inflammatory breast cancer**.

Scientists vary in their opinions on why this link exists, and what it means. Some believe that obesity may make tumors harder to detect, so a woman's breast cancer will be further developed before it is discovered.

"It could be because there's more breast tissue, a lump would be less evident," Ligibel said.

Researchers also believe that the systemic effects of obesity might do something to spur cancer on. For example, obesity or overweight can lead to fluctuations in hormone levels in the body.

"When women are heavier, their **estrogen levels are higher**," Ligibel said. "That could be a pathway through which weight affects breast cancer. Other studies have shown that when **insulin levels are high**, there's more chance a cancer will come back."

Another link to obesity was found in a study from the **University of North Carolina** at Chapel Hill that showed that **obese women are more likely to skip screenings for breast and cervical cancer**. Without those screenings, women are less likely to catch breast cancer at a more treatable stage.

Debbie Saslow, director of breast and gynecologic cancer at the American Cancer Society, said it's not completely clear what role obesity plays in breast cancer risk.

"For obesity, which is independent of breast size, I would think two factors would come into play," Saslow said.

"One, a positive, is that the breasts may be fatter, which would make a mammogram easier to read. The second, a negative, is indirect: Obese women are less likely to go to a doctor."

Menopause appears to be a critical time, Ligibel said. Obesity creates a greater risk for breast cancer post-menopause, while pre-menopausal women actually have a reduced risk.

"Gaining weight around the time of menopause is a risk factor in developing breast cancer," Ligibel said.

The increased risk of developing breast cancer and dying of it after menopause is believed due to increased levels of estrogen in obese women, said **Colleen Doyle, director of nutrition and physical activity with the American Cancer Society**.

There is good news. Studies have shown that exercise -- 30 minutes to 60 minutes a day of moderate-to-high intensity physical activity -- decreases breast cancer risk, Doyle said.

"Physical activity reduces breast cancer risk both directly, by decreasing circulating estrogens, and also indirectly, by helping with weight control," she said. "Women are so concerned about breast cancer risk. Communicating that there are key things you can do to reduce risk -- watch your weight and be more active -- are valuable messages."

Ligibel agreed, noting that exercise might be valuable enough to counteract the strain on the body caused by obesity.

"You might not need to lose weight if you exercise," Ligibel said. "Exercise could affect the hormone levels and help keep cancer from occurring or recurring."

Dr. Bleyer:

☑ **DEFEAT Cancer** has reported on each of the studies mentioned in this review in prior *E&N News*, including those from the University of Texas M.D. Anderson Cancer Center, the University of North Carolina at Chapel Hill, the University of Manchester, and the Dana Farber Cancer Institute

☑ The statement that a critical factor for developing breast cancer is gaining weight during menopause is magnified by the fact that menopause is one of the most frequent times in life when weight gain occurs

☑ The statement that obesity prior to menopause reduce breast cancer incidence has also been reported by *E&N News*, with the caveat that other cancers such as ovarian, cervical, colon and stomach cancer, occur at increased frequency in women who become overweight before menopause

☑ The review focuses on exercise and includes a speculation that exercise alone, without weight loss, may be sufficient to reduce cancer risk

☑ **DEFEAT Cancer** asserts that the combination of exercise and nutrition (**E&N**) are more effective in reducing cancer risk and recurrence than either exercise or nutrition alone, and further all of the other benefits of maintaining a health BMI can accrue

Weight boosts older women's breast cancer risk [Prevention]

It's the added pounds, not impaired detection, that's to blame, study concludes

[A study reported in the Journal of the National Cancer Institutes finds that excess weight boosts breast cancer risk in postmenopausal women who do not receive hormone replacement therapy](#)

By Kathleen Doheny

HealthDay News - Nov. 25, 2008

Being overweight boosts the risk of getting advanced breast cancer for older women, according to a new study that looked at more than 287,000 women and took into account their mammogram habits.

The weight itself is to blame for the added risk, the researchers concluded.

"Women who are above their healthy weight have higher levels of circulating estrogens," noted study lead author

Dr. Karla Kerlikowske, director of the **Women Veterans' Comprehensive Health Center at the San Francisco Veterans Affairs Medical Center**. "The estrogen is promoting tumor growth," she said.

In previous studies, Kerlikowske and her colleagues looked at postmenopausal women who took hormone replacement therapy (HRT) and found an increased breast cancer risk. In the current study, to be published in the Dec. 3 issue of the Journal of the National Cancer Institute, they looked at postmenopausal women not using HRT.

In years past, some research has suggested that the increased risk for breast cancer for obese women may be due to their not getting screened adequately, or because their tumors are perhaps more difficult to detect on mammography.

But those risk factors were ruled out in the current study. "We took into account how often they were screened and how well you could detect [the cancer]," Kerlikowske said. "There was still an increased risk."

In her study, Kerlikowske and her colleagues collected ongoing data from mammograms performed on more than 287,000 women past menopause. The women got routine mammograms. The researchers did not find that the tumors were harder to detect in women who were overweight or obese.

Nevertheless, "the risk of an advanced stage cancer for an obese women is 56 percent to 82 percent higher than for a normal-weight woman," Kerlikowske said. And the findings also revealed the more obese a woman was, the higher her risk for breast cancer. Women who were overweight but not obese had a 10 percent to 35 percent increased risk of breast cancer compared to normal-weight women, the researcher said.

According to Kerlikowske, adding strength to the idea that the increased estrogen in heavy women is fueling the tumor is the fact that the rate of tumors called "estrogen receptor-positive" (which are spurred on by estrogen) increased across the various weight groups, while ER-negative tumors did not.

Kerlikowske's team used the standard definitions of healthy weight, overweight, and obesity. For instance, a 5-foot, four-inch woman who weighs from 107 to 145 was considered at a healthy weight. The same woman weighing 146 pounds or more was considered overweight, and a weight of 175 pounds or more was considered obese.

About two-thirds of American adults are now either overweight or obese, according to recent government statistics. Of the study, Kerlikowske said: "It's very representative. It's from mammography registries across the U.S."

The research provides valuable new information on basic biology and risk factors for breast cancer, said mammography researcher Dr. Joann Elmore, professor of medicine and adjunct professor of epidemiology at Harborview Medical Center in Seattle. "They basically found that there are biological effects of obesity, and this can influence breast cancer development or progression."

The study results, Elmore said, should inspire women who are above their healthy weight to shed some pounds.

While many risk factors -- such as increasing age, being female, or having genetic mutations that raise breast cancer risk -- are not changeable, losing weight remains under a woman's control, she said.

Kerlikowske agreed. "Here is a risk factor to modify," she said.

Dr. Bleyer:

- ☑ The article notes that previous studies we have reported suggested these women were at increased risk because their tumors may be more difficult to diagnose, but this study found that the excess weight itself increased risk, possibly because of elevated estrogen levels
- ☑ In retrospect some of the increased rate of breast cancer in the U.S. that was blamed on hormone replacement therapy (to prevent menopausal symptoms) can now be attributed to the increasing rate of obesity in our country

Exercise

Prospective study of physical activity and risk of postmenopausal breast cancer [Prevention]

[A 32% reduction in breast cancer in 11 years was observed in lean women who reported having regularly exercised](#)

Leitzmann MF, Moore SC, Peters TM, Lacey JV, Schatzkin A, Schairer C, Brinton LA, Albanes D
Breast Cancer Research 2008, 10:R92doi:10.1186/bcr2190 Published: 31 October 2008

Introduction. To prospectively examine the relation of total, vigorous and non-vigorous physical activity to postmenopausal breast cancer risk.

Method. We studied 32,269 women enrolled in the Breast Cancer Detection Demonstration Project Follow-up Study. Usual physical activity (including household, occupational and leisure activities) throughout the previous year was assessed at baseline using a self-administered questionnaire. Postmenopausal breast cancer cases were identified through self-reports, death certificates and linkage to state cancer registries. A Cox proportional hazards regression was used to estimate the relative risk and 95% confidence intervals of postmenopausal breast cancer associated with physical activity.

Results. During 269,792 person-years of follow-up from 1987 to 1998, 1506 new incident cases of postmenopausal breast cancer were ascertained. After adjusting for potential risk factors of breast cancer, a weak inverse association between total physical activity and postmenopausal breast cancer was suggested (relative risk comparing extreme quintiles = 0.87; 95% confidence interval = 0.74 to 1.02; p for trend = 0.21). That relation was almost entirely contributed by vigorous activity (relative risk comparing extreme categories = 0.87; 95% confidence interval = 0.74 to 1.02; p for trend = 0.08). **The inverse association with vigorous activity was limited to women who were lean (ie, body mass index <25.0 kg/m²: relative risk = 0.68; 95% confidence interval = 0.54 to 0.85).** In contrast, no association with vigorous activity was noted among women who were overweight or obese (ie, body mass index [greater than or equal to]25.0 kg/m²: relative risk = 1.18; 95% confidence interval = 0.93 to 1.49; **p for interaction = 0.008**). **Non-vigorous activity showed no relation to breast cancer** (relative risk comparing extreme quintiles = 1.02; 95% confidence interval = 0.87 to 1.19; p for trend = 0.86). The physical activity and breast cancer relation was not specific to a certain hormone receptor subtype.

Conclusion. In this cohort of postmenopausal women, breast cancer risk reduction appeared to be limited to vigorous forms of activity; it was apparent among normal weight women but not overweight women, and the

relation did not vary by hormone receptor status. Our findings suggest that physical activity acts through underlying biological mechanisms that are independent of body weight control.

Dr. Bleyer:

- ☑ The most remarkable finding was that the anticancer effect of exercise was observed in lean women, suggesting that the benefit of diet and exercise (together) is greater in overweight women (and men), probably since lean persons have already optimized their nutrition
- ☑ That overweight women did not have apparent benefit from exercise alone, even "strenuous" exercise, may support the need to combine nutrition with exercise (and weight loss), as advocated by **DEFEAT Cancer**
- ☑ The magnitude of the decrease in breast cancer (in lean women), 30%, or essentially one in every three women, due to exercise alone, if accurate, is a dramatic reduction

Vigorous exercise protects against breast cancer [Prevention]

[Expert commentary of above report, including potential explanations as to how exercise reduces breast cancer risk \(and recurrence\)](#)

LONDON (Reuters) – Oct 30, 2008



ET Reuters – Chinese women practice ballet at a university for senior citizens in Tianjin

Plenty of vigorous exercise can cut a healthy, older woman's breast cancer risk by 30 percent, researchers said on Friday.

A study of more than **30,000 post-menopausal women** showed that strenuous activity -- ranging from housework such as scrubbing floors to running -- protected against breast cancer even among those who do not have a higher risk. **The effect was clearest among lean women.**

"We know that being overweight puts women at increased risk of breast cancer," said **Michael Leitzmann**, who led the study while at the **National Cancer Institute** of the U.S. National Institutes of Health. **"What our study shows is that even among women without this increased risk, if they exercise they can get some benefit."**

Breast cancer is the leading cause of cancer deaths among women worldwide. The American Cancer Society estimates about 465,000 women died of breast cancer globally in 2007, and 1.3 million new cases were diagnosed. A number of studies have shown that regular strenuous exercise can help people avoid heart disease, cancer and a range of other conditions.

Leitzmann and colleagues used questionnaires to determine how often the women exercised vigorously. All were healthy when the study began. After 11 years the researchers found that overall the volunteers who exercised most were 13 percent less likely to have developed breast cancer.

The **reduced risk was even higher -- 30 percent -- when the researchers compared only women of normal weight**, Leitzmann, now working at **Germany's University Hospital in Regensburg**, said in a telephone interview. "The relationship was much stronger among leaner women," he added.

Interestingly, non-vigorous activity such as light housework, walking, hiking and easy jogging, did not seem to offer any protection against breast cancer, the team reported in BioMed Central's **Breast Cancer Research** journal.

The researchers did not look at why exercise may help but Leitzmann noted other studies have shown that **working out reduces estrogen levels** -- a known risk factor for the disease -- and protects the body's general immune system.

Dr. Bleyer:

- ☑ If housework such as scrubbing floors and running were considered as *vigorous* exercise in this study, then the exercise required for the magnitude in cancer reduction reported in this study is achievable by most
- ☑ Estrogen levels are known to decrease with exercise (e.g. long-distance runners hardly ever develop breast cancer) and may well be how exercise reduces breast cancer risk
- ☑ Since anti-estrogens (tamoxifen, fulvestrant, anastrozole, exemestane, letrozole) are core elements of breast cancer therapy, it stands to reason that exercise may reduce the need for these agents in women with hormone-responsive breast cancer, which represent the majority of cases.

Vigorous exercise can cut breast cancer risk [Prevention]

But benefits only apply to normal-weight women, study says

[More commentary of afore-cited report, including better description of what constitutes *vigorous* exercise and light exercise and additional mechanisms of exercise-mediated cancer protection](#)

FRIDAY, Oct. 31 (HealthDay News) -- Vigorous activity can reduce the risk of breast cancer by about 30 percent in normal-weight women, according to an 11-year U.S. study of 32,269 postmenopausal women.

For the study, vigorous activity was defined as **heavy housework (scrubbing floors, washing windows, demanding yard work, digging, chopping wood) and strenuous sports or exercise, such as running, fast jogging, competitive tennis, aerobics, bicycling on hills, and fast dancing.**

While vigorous activity reduced breast cancer risk in normal-weight women, it had no effect in women who were overweight or obese, according to study leader Michael F. Leitzmann and colleagues.

They also found that non-vigorous activity, such as **light housework (vacuuming, doing laundry, painting, general gardening) and light sports or exercise (walking, hiking, light jogging, recreational tennis, bowling) offered no protection against breast cancer.**

The findings were published in the journal *Breast Cancer Research*.

"Possible mechanisms through which physical activity may protect against breast cancer that are independent of body mass include reduced exposure to growth factors, enhanced immune function, and decreased chronic inflammation, variables that are related both to greater physical activity and to lower breast cancer risk," the study authors wrote. "**An alternative explanation for the stronger apparent effect of vigorous activity among lean over heavy women is that heavier women may misreport non-vigorous activities as vigorous activities,**" the researchers added.



Dr. Bleyer:

- ☑ The more expansive description of what constitutes vigorous vs. light exercise suggests that the level of exercise may be too difficult for some to achieve
- ☑ If so, improved nutrition may help make up for the inability of some to exercise vigorously (and routinely) ... i.e., the combination of exercise and nutrition (**E&N**) as advocated by **DEFEAT Cancer**
- ☑ The most revealing explanation for why exercise did not appear to benefit overweight women is the supposition that heavier women are inclined to misrepresent their relatively lighter exercise as vigorous
- ☑ If so, had only overweight women reported their level of exercise accurately, those with truly vigorous exercise may well have also benefited, as shown in other studies.

Exercise and rest reduce cancer risk [Prevention]

[The first study to demonstrate that the quality of sleep may augment the benefit of exercise on reduction of cancer risk and recurrence](#)

NewsRx.com - November 26, 2008

(from Cancer Compass <http://www.cancercompass.com/cancer-news/1,15041,00.htm?c=1003:5:1:2>)

Exercise is good for more than just your waistline. A recent study presented at the American Association for Cancer Research's Seventh Annual International Conference on Frontiers in Cancer Prevention Research suggests that regular physical activity can lower a woman's overall risk of cancer but only if she gets a good night's sleep. Otherwise, lack of sleep can undermine exercise's cancer prevention benefits.

"Greater participation in physical activity has consistently been associated with reduced risk of cancer incidence at several sites, including breast and colon cancers," said **James McClain, Ph.D.**, cancer prevention fellow at the **National Cancer Institute** and lead author of the study. "Short duration sleep appears to have opposing effects of physical activity on several key hormonal and metabolic parameters, which is why we looked at how it affected the exercise/cancer risk relationship."

Even though the exact mechanism of how exercise reduces cancer risk isn't known, **researchers believe that physical activity's effects on factors including hormone levels, immune function, and body weight** may play an important role. The study examined the link between exercise and cancer risk, paying special attention to whether or not getting adequate sleep further affected a women's cancer risk.

Researchers assessed the association between physical activity energy expenditure (PAEE), sleep duration and incidence of overall, breast, and colon cancer in **5,968 women** at least 18 years old with no previous cancer diagnoses. The women completed an initial survey in 1998 and were then tracked through the **Washington County Cancer Registry and Maryland State Cancer Registry for nearly 10 years.**

The results pointed to a sleep-exercise link. "Current findings suggest that sleep duration modifies the relationship between physical activity and all-site cancer risk among young and middle-aged women," he said.

Out of those 5,968 women, 604 experienced a first incidence of cancer, including 186 breast cancer cases. Women in the upper 50 percent of PAEE showed significantly reduced risk of overall cancer and breast cancer. Among

women 65 or younger when surveyed and in the upper half of PAEE, sleeping less than seven hours a day increased overall cancer risk, negating much of the protective effects of physical activity on cancer risk for this group. The next step, says McClain, would be to confirm current findings and investigate potential mechanisms underlying the interaction between sleep and exercise in order to better understand their roles in cancer prevention. Research is expanding rapidly on the effect of insufficient and prolonged sleep duration on many health outcomes although few studies have examined the association of sleep duration with cancer risk. This novel study of the interaction of sleep and physical activity suggests another future research focus on health behaviors and cancer

Dr. Bleyer:

- ☑ Since regular exercise reduces fatigue and promotes better sleep, this study's finding not only supports the role of exercise in reducing cancer risk, but offers another biological explanation for how exercise helps *defeat* cancer
- ☑ It may be that, at least in women, the effect of sleep on hormonal effects (estrogen, insulin, et al) may augment the benefit of exercise via the same mechanisms
- ☑ As **DEFEAT Cancer** routinely notes, the contribution of anti-cancer nutrition to the interaction between exercise and rest may well show, when ultimately studied, greater benefit of the interaction

Nutrition

Fish oils may help fight prostate cancer progression

NCI CAM News, Fall 2008, Vol. 3, Issue 2 Original Source: British Journal of Cancer (2006) 94, 842-853.

[Why American men have so much more prostate cancer than men in other countries may be related to their higher rate of obesity and the nature of their diet relative to those in other parts of the world, particularly Asia](#)

Prostate cancer kills more American men annually than any other type of cancer except for lung cancer. These high rates of mortality and morbidity do not occur in Japan and other Asian countries, although men in those cultures are found to have just as many small or latent prostate cancers when autopsied. Much more often, prostate cancer in men of Western Europe and America progress and metastasize, especially to the bone marrow. Many scientists believe that behavioral and dietary risk factors may hold the key to understanding these variations in the disease.

Cancer research examines benefits of fish oils

Noting the much higher intake of fish and seafood in Asian diets, **Yong Q. Chen, Ph.D.** director of Basic Science at **Wake Forest University's Prostate Center of Excellence**, believes that polyunsaturated fatty acids (PUFAs) found in fish oils could play an important role in cancer progression. This relationship is being investigated further. Just as there are "good" and "bad" forms of cholesterol, some evidence suggest this may also be true of the omega PUFAs, omega-3 and omega-6. Omega-6 PUFAs found in many vegetable oils—and dairy, meats, and some plants—may have a role in prostate and colon cancer progression; however, omega-3 PUFAs found in some fish and plant oils have shown evidence of suppressing prostate tumor metastasis, most recently in a 2006 study from the **British Journal of Cancer**. Nutritionists often focus on these two dietary components together and recommend they be consumed in equal amounts. However, current Western diets have omega-6/omega-3 ratios of 30 to 1, explained Dr. Chen, "and they can be as high as 50 to 1."

Supported by NCI*, Dr. Chen and his colleagues began by feeding various amounts of the two types of PUFA to mice bred with a propensity for prostate cancer. "The omega-3s slowed the growth of tumors, and many of the cancer cells we examined were progressing at a much slower pace," Dr. Chen reported. "The omega-6 fatty acids had the opposite effect."

The effect seen with omega-3 appears to work, in part, through a gene called *Bad*, which produces a protein that goes by the same name. Dr. Chen noted, "When we knocked down (inactivated) the *Bad* gene in the mice, the cancer cell death stopped, and then the cell death resumed when we added the *Bad* protein." This finding highlights the importance of gene-diet interactions in prostate cancer. "Our work reinforces the idea that the amount and content of dietary fat can have a drastic impact on the health of animals with identical genetic profiles," he added. Dr. Chen said their research also suggests the idea that omega-6 and omega-3 PUFAs "fight" each others' effects in the body, often producing opposite effects at the molecular level in the cells. "Thus, it is crucial that the Western diet move toward the one-to-one ratio for intake of both types of fats," he noted. "We realize that dietary change for an entire population is a major challenge, but for prostate cancer patients, this takeaway message is much more critical—omega-3 fatty acids in the diet may inhibit metastasis." As a next step, Dr. Chen is planning a phase I trial of PUFA diets in patients with locally advanced prostate cancer.

Dr. Bleyer:

- ☑ Omega-3 fatty acids may help keep early prostate cancer in check, since Asians consume much more of these types of lipids and have a much lower incidence of prostate cancer.
- ☑ There's also the benefit on cardiovascular health, and in combination with exercise—a **DEFEAT Cancer** principal—the benefit may be synergistically improved

A 22-year prospective study of fish intake relative to prostate cancer incidence and mortality

This long-term study by Harvard University nutritionists concludes that a diet of fish 5 or more times per week both helps prevent prostate cancer and may reduce the risk of dying from it

Chavarro JE, Stampfer MJ, et al, Am J Clin Nutr, 2008; 88(5): 1297-303

Department of Nutrition, Harvard School of Public Health, Boston, MA 02115, USA.

In a prospective cohort study involving data from **20,167 men** free of cancer at baseline, followed up with for 382,144 person-years, during which time 2,161 developed prostate cancer and 230 died of prostate cancer, intake of fish 5 or more times per week was associated with a 48% reduced risk of death from prostate cancer, as compared to consuming fish less than once/week (RR=0.52). Intake of seafood omega-3 fatty acids was also associated with a reduced risk of prostate cancer mortality (RR=0.64). No association was found between fish intake and incidence of prostate cancer. The authors conclude, "These results suggest that fish intake is unrelated to prostate cancer incidence but may improve prostate cancer survival."

Dr. Bleyer:

- ☑ The conclusion that a fish-enriched diet may improve prostate cancer survival is very tenuous since the incidence was much lower and thus the mortality rate would be correspondingly low
- ☑ Nonetheless, the survival conclusion is consistent with the report above from Asia

Effect of selenium and vitamin E on risk of prostate cancer and other cancers: The Selenium and Vitamin E Cancer Prevention Trial (SELECT)... [Prevention]

Lippman SM, Klein EA, Goodman PJ, et al

JAMA. 2009;301(1):(doi:10.1001/jama.2008.864)

The largest randomized placebo-controlled cancer prevention trial performed to date was closed early due to no evidence that vitamin C or selenium, or both, were of any benefit in reducing the risk of prostate cancer or of any other cancer in the men on the study

Context Secondary analyses of 2 randomized controlled trials and supportive epidemiologic and preclinical data indicated the potential of selenium and vitamin E for preventing prostate cancer.

Objective To determine whether selenium, vitamin E, or both could prevent prostate cancer and other diseases with little or no toxicity in relatively healthy men. Design, Setting, and Participants A randomized, placebo-controlled trial (Selenium and Vitamin E Cancer Prevention Trial [SELECT]) of **35,533** men from 427 participating sites in the United States, Canada, and Puerto Rico randomly assigned to 4 groups (selenium, vitamin E, selenium + vitamin E, and placebo) in a double-blind fashion between August 22, 2001, and June 24, 2004. Baseline eligibility included age 50 years or older (African American men) or 55 years or older (all other men), a serum prostate-specific antigen level of 4 ng/mL or less, and a digital rectal examination not suspicious for prostate cancer.

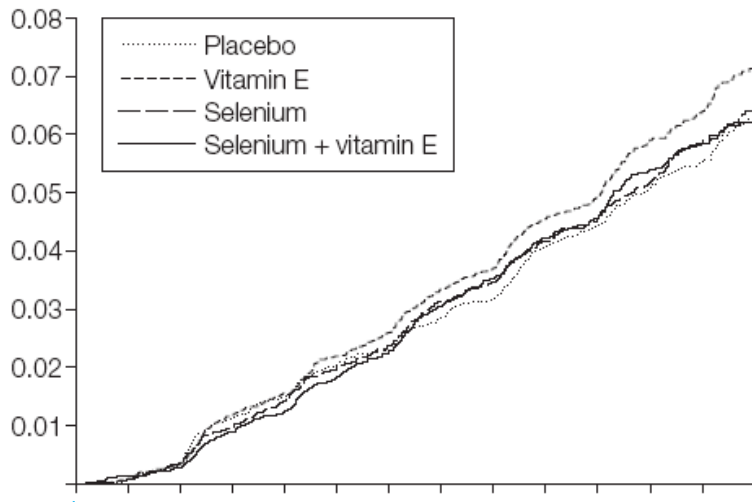
Interventions Oral selenium (200 µg/d from L-selenomethionine) and matched vitamin E placebo, vitamin E (400 IU/d of all rac- γ -tocopheryl acetate) and matched selenium placebo, selenium + vitamin E, or placebo + placebo for a planned follow-up of minimum of 7 years and a maximum of 12 years.

Main Outcome Measures Prostate cancer and prespecified secondary outcomes, including lung, colorectal, and overall primary cancer.

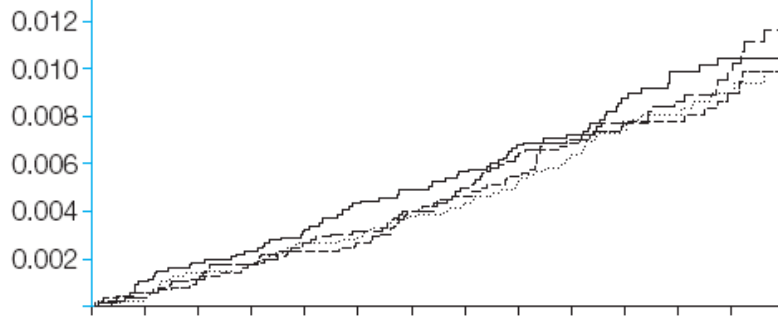
Results As of October 23, 2008, median overall follow-up was 5.46 years (range, 4.17-7.33 years). Hazard ratios (99% confidence intervals [CIs]) for prostate cancer were 1.13 (99% CI, 0.95-1.35; n=473) for vitamin E, 1.04 (99% CI, 0.87-1.24; n=432) for selenium, and 1.05 (99% CI, 0.88-1.25; n=437) for selenium + vitamin E vs 1.00 (n=416) for placebo. There were no significant differences (all $P > .15$) in any other prespecified cancer end points. There were statistically nonsignificant increased risks of prostate cancer in the vitamin E group ($P = .06$) and type 2 diabetes mellitus in the selenium group (relative risk, 1.07; 99% CI, 0.94-1.22; $P = .16$) but not in the selenium + vitamin E group.

Cumulative Incidence Rates of Prostate and Other Cancers by Randomized Vitamin E, Selenium, and Vitamin E + Selenium Assignment in the SELECT Study

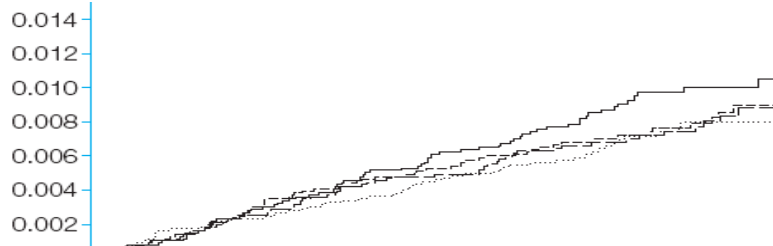
Prostate Cancer



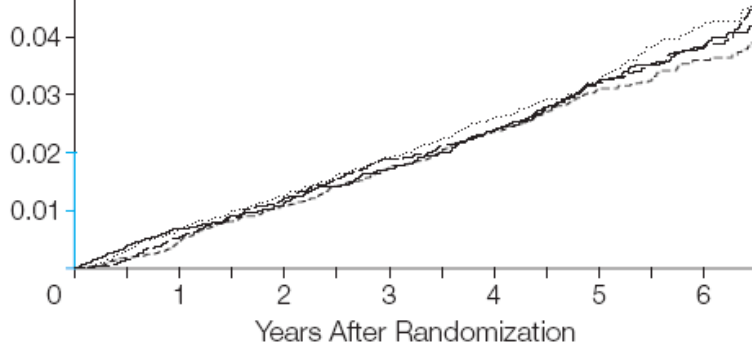
Lung Cancer



Colorectal Cancer



All Other Cancer



Conclusion Selenium or vitamin E, alone or in combination at the doses and formulations used, did not prevent prostate cancer in this population of relatively healthy men.

Dr. Bleyer:

☑As reported last month, Central Oregon has more than a professional interest in this trial, with 17 men on the study

- ☑ Not only did vitamin E and selenium, either alone or together, fail to prevent prostate cancer, there was a trend, as reported last month, in an increased rate of prostate cancer with vitamin E supplementation, and as shown in the charts of an increased risk of lung and colorectal cancer when vitamin E was combined with selenium
- ☑ These paradoxical results were not statistically significant however, as of the time of analysis, but they may become statistically significant with further follow-up
- ☑ The "opposite" trends are not surprising, however, in that prior randomized trials have show an increase in cancer occurrence with vitamin supplementation, such as the increased rate of lung cancer with both of two forms of vitamin A and of selenium vs. cancers other than prostate cancer
- ☑ Dr. Bleyer was involved with a study of another vitamin A derivative, fenretinide, in which no benefit in reducing bladder cancer was observed (Clin Cancer Res 14:224-9, 2008)
- ☑ This study also demonstrates an important point about **subset analysis**: the reason that vitamin E and selenium were studied is that prior trials that were not designed to prevent prostate cancer but randomized the dietary supplements to study other disease happened to show, in retrospect, in a subset analysis looking for other effects, less prostate cancer in the men on the study; the danger of subset analysis, which has been repeatedly demonstrated is that the subset finding can just a likely happen by chance and not be real, as shown, once again, in the SELECT trial
- ☑ Bottom line: vitamins and other antioxidants can do more harm than good and, as stated by one of the world's experts on definitive studies of this type (see next report) "anyone who argues that is ignoring the facts"

Vitamin E and selenium do not prevent prostate cancer; Use of the supplements stopped in large-scale study [Prevention]

[More on the SELECT study reported above and alerted last month, including comments from the Chair of the sponsoring research group, Southwest Oncology Group \(SWOG\)](#)

Nick Mulcahy

October 29, 2008 — The SELECT (Selenium and Vitamin E Cancer Prevention Trial) prostate cancer prevention study is instructing its 35,000-plus participants to stop taking the 2 nutritional supplements because of an apparent lack of benefit and a possibility of harm.

"The Data and Safety Monitoring Committee made the decision to stop use of the supplements, not to stop the trial. We will follow participants for 3 more years to determine if there is any benefit or any harm," said

Larry Baker, MD, chairman of the Southwest Oncology Group, which coordinated the trial, and professor of medicine at University of Michigan Medical School in Ann Arbor.

The Data and Safety Monitoring Committee said that "the data could not exclude a small chance that the study supplements might have effects later in the men's lives." However, the antioxidants selenium and vitamin E, taken alone or together for an average of 5 years, did not prevent prostate cancer, according to the committee.

The antioxidants selenium and vitamin E, taken alone or together for an average of 5 years, did not prevent prostate cancer.

"We went back to the biologists, and they said that 8 months was sufficient exposure to see benefit," Dr. Baker explained.

The data from SELECT also show 2 trends that were of concern but not statistically significant: in **men taking only vitamin E, there were slightly more cases of prostate cancer; and, in men taking only selenium, there were slightly more cases of diabetes**. Neither of these findings means an increased risk from the supplements, and they could be due to chance, according to the National Cancer Institute (NCI), which funded the trial.

The Data and Safety Monitoring Committee also determined that it was unlikely that selenium and vitamin E supplementation would ever produce a 25% reduction in prostate cancer, which was the study's goal.

Dr. Baker said that the results to date speak for themselves, and that SELECT is a much larger trial than previous trials that suggested benefit. **"This is the definitive study and anyone who argues that is ignoring the facts."**

SELECT Details

Participants were randomized to 1 of 4 groups (2 capsules a day): selenium (200 µg) and vitamin E (400 mg); selenium and placebo; vitamin E and placebo; or 2 placebos. The **35,000-plus participants** consisted of African-American men who were 50 years or older, and men of other races and ethnicities who were 55 years or older. The eligibility age was lower for African Americans because of the earlier average onset of the disease.

Selenium is a nonmetallic trace element found especially in plant foods, such as rice, wheat, seafood, meat, and Brazil nuts. Selenium is an antioxidant that may help control the cell damage that can lead to cancer, according to the NCI.

Vitamin E is found in a wide range of foods, especially vegetables, vegetable oils, nuts, and egg yolks. Like selenium, vitamin E is an antioxidant.

According to the NCI, **selenium was selected for study in part because of results from the Nutritional Prevention of Cancer Trial, which was a skin cancer trial of 1312 men and women that incidentally revealed prostate cancer data**; the results showed that men taking selenium for more than 7.5 years had about 52% fewer new cases of prostate cancer than men taking placebo.

Vitamin E was selected for the trial in part because of results from a 1998 study of 29,133 male smokers in Finland; men in the study who took vitamin E to prevent lung cancer had 32% fewer new cases of prostate cancer and 40% fewer deaths from prostate cancer than men taking placebo.

Other Objectives and Related Research

SELECT is not limited to an analysis of the impact of selenium and vitamin E on prostate cancer. The other objectives of SELECT include assessments of the impact of the 2 supplements on the incidence of lung cancer and colon cancer, and on total cancer incidence and survival. SELECT will also provide a basis for studying the molecular genetics of cancer risk and associations between diet and cancer, according to the NCI. A biorepository of blood samples obtained from SELECT participants at their entry into the trial and at 5 years was created for use in molecular and mechanistic studies of cancers in men and other diseases of male aging. Additionally, SELECT has been examining the impact of selenium and vitamin E supplementation on quality of life.

According to the NCI, the Institute is the primary funding agency for SELECT, awarding about **\$114 million** to Southwest Oncology Group from 1999 to 2008. An additional \$4.5 million was contributed by the National Center for Complementary and Alternative Medicine. NCI has also funded a substudy of SELECT to learn whether the supplements affect colon polyp growth.

Additionally, 3 ancillary studies related to SELECT are ongoing and are evaluating selenium and vitamin E for different conditions in the SELECT participant population. The **Prevention of Alzheimer's Disease with Vitamin E and Selenium (PREADVISE)** trial, cosponsored by the National Institute on Aging, is evaluating whether these supplements can help prevent memory loss and dementia, such as that found in Alzheimer's disease. The **SELECT Eye Endpoints Study (SEE)**, cosponsored by the National Eye Institute, is evaluating the dietary supplements in the prevention of age-related macular degeneration and cataract. The **Respiratory Ancillary Study (RAS)**, cosponsored by the National Heart, Lung and Blood Institute, is evaluating whether the supplements can affect the loss of lung function experienced with aging, which is higher in people who smoke cigarettes.

More than 400 sites in the United States, Puerto Rico, and Canada are involved in the SELECT study.

Dr. Bleyer:

- ☑ The key point in this media report is the comment by the Southwest Oncology Group chair: "This is the definitive study and anyone who argues that is ignoring the facts," which likely was stated because the antioxidant advocates are likely to attempt to dismiss this study's results
- ☑ **DEFEAT Cancer** questions whether it was worth \$114+ million to test a hypothesis generated from retrospective subset analysis of a prior trial on another topic, for which the answer is probable in the affirmative given how much Americans spend on vitamins and other antioxidants
- ☑ **DEFEAT Cancer** would prefer to study the combination of exercise and nutrition, with the latter a broad change in diet (as in plant-based) rather than an individual food substance or supplement

Vitamins E and C in the prevention of prostate and total cancer in men: The Physicians' Health Study II Randomized Controlled Trial [Prevention]

Gaziano JM, Glynn RJ, Christen, et al

JAMA. 2009;301(1):(doi:10.1001/jama.2008.862)

Neither vitamin C nor vitamin E, or both, had any effect of the incidence of any cancer, including prostate cancer, in more that 14,000 male physicians over 50 years of age who were followed for an average of 8 years

Context Many individuals take vitamins in the hopes of preventing chronic diseases such as cancer, and vitamins E and C are among the most common individual supplements. A large-scale randomized trial suggested that vitamin E may reduce risk of prostate cancer; however, few trials have been powered to address this relationship. No previous trial in men at usual risk has examined vitamin C alone in the prevention of cancer.

Objective To evaluate whether long-term vitamin E or C supplementation decreases risk of prostate and total cancer events among men.

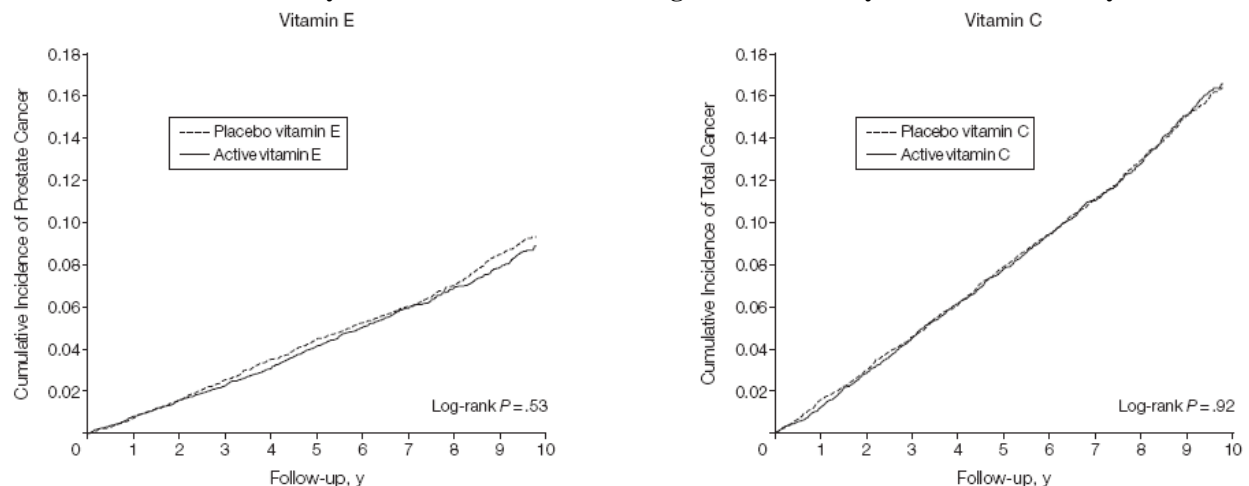
Design, Setting, and Participants The Physicians' Health Study II is a randomized, double-blind, placebo-controlled factorial trial of vitamins E and C that began in 1997 and continued until its scheduled completion on August 31, 2007. A total of **14,641 male physicians** in the United States initially aged 50 years or older, including 1307 men

with a history of prior cancer at randomization, were enrolled. Intervention Individual supplements of 400 IU of vitamin E every other day and 500 mg of vitamin C daily.

Main Outcome Measures Prostate and total cancer.

Results During a mean follow-up of 8.0 years, there were 1008 confirmed incident cases of prostate cancer and 1943 total cancers. Compared with placebo, vitamin E had no effect on the incidence of prostate cancer (active and placebo vitamin E groups, 9.1 and 9.5 events per 1000 person-years; hazard ratio [HR], 0.97; 95% confidence interval [CI], 0.85-1.09; P=.58) or total cancer (active and placebo vitamin E groups, 17.8 and 17.3 cases per 1000 person-years; HR, 1.04; 95% CI, 0.95-1.13; P=.41). There was also no significant effect of vitamin C on total cancer (active and placebo vitamin C groups, 17.6 and 17.5 events per 1000 person-years; HR, 1.01; 95% CI, 0.92-1.10; P=.86) or prostate cancer (active and placebo vitamin C groups, 9.4 and 9.2 cases per 1000 person-years; HR, 1.02; 95% CI, 0.90-1.15; P=.80). Neither vitamin E nor vitamin C had a significant effect on colorectal, lung, or other site-specific cancers. Adjustment for adherence and exclusion of the first 4 or 6 years of follow-up did not alter the results. Stratification by various cancer risk factors demonstrated no significant modification of the effect of vitamin E on prostate cancer risk or either agent on total cancer risk.

Cumulative Incidence Rates of Total Prostate Cancer by Randomized Vitamin E Assignment or Total Cancer by Randomized Vitamin C Assignment in the Physicians' Health Study II



Conclusions In this large, long-term trial of male physicians, neither vitamin E nor C supplementation reduced the risk of prostate or total cancer. These data provide no support for the use of these supplements for the prevention of cancer in middle-aged and older men.

Dr. Bleyer:

- ☑ This report substantiates the lack of benefit of vitamin E (and of selenium) on prostate and other cancers in the SELECT study described in the two prior reports
- ☑ The cumulative incidence curves in the Results section show absolutely no benefit of vitamin E or C on prostate cancer
- ☑ This was also not just a study of prostate cancer. As in the SELECT study, no other cancer was found to have been affected by either vitamin C or E or both
- ☑ Once again, the vitamin C claims made by many, including Linus Pauling, PhD, Nobel Laureate, has been convincingly disproven in randomized double blind trial

Vitamins don't cut heart attack and breast cancer risks, studies say [Prevention]

Almost half of all adults in the U.S. take supplements daily, but the studies should prompt some of them to reconsider their rationale for doing so, one expert says.

[The results of two large randomized trials, published in JAMA, show no benefit to standard doses of vitamin D and calcium in preventing breast cancer, or of vitamins E and C in preventing heart disease](#)

By Karen Kaplan

Los Angeles Times - November 12, 2008

Vitamin supplements -- taken by millions of Americans to boost or maintain their health -- don't reduce the risk of heart attacks, strokes or breast cancer, according to two large studies published today.

In one of the trials, **14,641** middle-aged male physicians took **vitamins E and C for an average of eight years** but did not see any benefit to their cardiovascular health. The other study tracked **36,282 postmenopausal women** for an **average of seven years** and found that a daily regimen of **vitamin D and calcium did not offer any protection against invasive breast cancer**.

Almost half of all adults in the U.S. take vitamins daily, but the results should prompt some of them to reconsider their rationale for doing so, said Howard Sesso, who led the cardiovascular disease study appearing in the Journal of the American Medical Assn.

The breast cancer study, reported in the Journal of the National Cancer Institute, was part of an effort to determine whether a combined pill of **1,000 milligrams of calcium and 400 IUs of vitamin D** could help prevent hip fractures.

Since some studies suggested vitamin D might reduce the risk of breast cancer, the researchers, led by **Dr. Rowan Chlebowski**, a medical oncologist at the **Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center**, decided to track that too.

Over the course of the study, 528 of the 18,176 women, or 2.9%, who got the combined pill developed invasive breast cancer compared with 546 of the 18,106 who got the placebo, or 3.0%.

In an editorial accompanying the study, **Corey Speers** and **Dr. Powel Brown** of the **Baylor College of Medicine** in Houston praised the research for its "scope and complexity" but said it did not rule out a benefit from vitamin D. Other studies suggest the daily dose should be between 1,000 and 2,000 IUs per day, well above the amount used in this trial.

The supplements might also prove valuable to premenopausal women, who were not part of this study, they said. Chlebowski, whose study was also funded by the NIH, cautioned that women shouldn't stop taking vitamin D based on his results.

"Take it anyway, for other reasons," he said.

"You don't know whether something is really true until you test it in one of these large-scale, long-term clinical trials," said Sesso, an epidemiologist at Brigham and Women's Hospital in Boston and a professor at Harvard Medical School.

But **Dr. David Heber**, director of the **UCLA Center for Human Nutrition**, said the studies didn't prove vitamins were useless, especially considering that observational studies and experiments with animals had produced mixed results.

"Absence of evidence is not evidence of absence," said Heber, who was not involved with the latest studies.

The heart study was prompted by basic research showing that antioxidants such as vitamins E and C kept the formation of atherosclerotic plaque in check and helped prevent tissue damage that causes cardiovascular disease. Sesso's team tested the effect of 400 international units, or IUs, of vitamin E every other day and 500 milligrams of vitamin C daily. Doctors who participated in the study received either both vitamins, one vitamin and one placebo, or two placebos.

Among the 7,315 people who took vitamin E, there were 620 cases of heart attacks, strokes and deaths from heart disease compared with 625 such cases among the 7,326 people who took the dummy pills, the study said.

The only difference the researchers found was a 74% increase in hemorrhagic strokes among those who took vitamin E, though Sesso said that the strokes were rare in both groups and that the finding could have been a fluke. The results for vitamin C were also underwhelming -- 619 major cardiovascular events among the 7,329 doctors who got the vitamin versus 626 events for the 7,312 who got the placebo, according to the study, which was funded by the National Institutes of Health and BASF Corp., a vitamin maker.

Dr. Bleyer:

- ☑ With all the interest in vitamin D from reports a couple of months ago, this large scale trial of vitamin D (with calcium) is sobering
- ☑ Goes to show, the saying goes, that it ain't over until the fat lady sings;... but isn't the idea to eliminate the fat?

Effect of combined folic acid, vitamin B6, and vitamin B12 on cancer risk in women: A randomized trial [Prevention]

[Combined folic acid, vitamin B6, and vitamin B12 treatment had no significant effect on overall risk of total invasive cancer or breast cancer among women](#)

Shumin M. Zhang, MD, ScD; Nancy R. Cook, ScD; Christine M. Albert, MD, MPH; J. Michael Gaziano, MD, MPH; Julie E. Buring, ScD; JoAnn E. Manson, MD, DrPH

JAMA. 2008;300(17):2012-21.

Context Folate, vitamin B6, and vitamin B12 are thought to play an important role in cancer prevention.

Objective To evaluate the effect of combined folic acid, vitamin B6, and vitamin B12 treatment on cancer risk in women at high risk for cardiovascular disease.

Design, Setting, and Participants In the **Women's Antioxidant and Folic Acid Cardiovascular Study**, 5442 US female health professionals aged 42 years or older, with preexisting cardiovascular disease or 3 or more coronary risk factors, were randomly assigned to receive either a daily combination of folic acid, vitamin B6, and vitamin B12 or a matching placebo. They were treated for 7.3 years from April 1998 through July 31, 2005.

Intervention Daily supplementation of a combination of 2.5 mg of folic acid, 50 mg of vitamin B6, and 1 mg of vitamin B12 (n = 2721) or placebo (n = 2721).

Main Outcome Measures Confirmed newly diagnosed total invasive cancer or breast cancer.

Results A total of 379 women developed invasive cancer (187 in the active treatment group and 192 in the placebo group). Compared with placebo, women receiving the active treatment had similar risk of developing total invasive cancer (101.1/10 000 person-years for the active treatment group vs 104.3/10 000 person-years for placebo group; hazard ratio [HR], 0.97; 95% confidence interval [CI], 0.79-1.18; P = .75), breast cancer (37.8/10 000 person-years vs 45.6/10 000 person-years, respectively; HR, 0.83; 95% CI, 0.60-1.14; P = .24), or any cancer death (24.6/10 000 person-years vs 30.1/10 000 person-years, respectively; HR, 0.82; 95% CI, 0.56-1.21; P = .32).

Conclusion Combined folic acid, vitamin B6, and vitamin B12 treatment had no significant effect on overall risk of total invasive cancer or breast cancer among women during the folic acid fortification era.

Dr. Bleyer:

- ☑ Another study demonstrating that vitamins alone are insufficient to prevent cancer, and by extrapolation, cancer recurrence
- ☑ And another study that shows how a randomized, placebo-controlled trial can reverse beliefs generated from preliminary and insufficient evidence
- ☑ The finding is consistent with **DEFEAT Cancer's** hypothesis that a broader dietary change (plant-based diet) is required to substantially reduce risk and recurrence, and especially if combined with exercise

Vitamin B supplements do not prevent cancer: study [Prevention]

Review of Studies Dashes Cancer-Fighting Hopes for Nutrient

[Commentary on the aforementioned study of vitamin B supplements that showed no protection against cancer as some previous research had suggested](#)

ABC New – November 4, 2008

By Will Dunham

Reuters - Washington

Vitamin B supplements do not appear to protect against cancer as some previous research had suggested, according to a U.S. study published on Tuesday.

Women who took a daily supplement that included vitamins **B6 and B12 and folic acid**, also known as vitamin B9, **for about 7-1/2 years** were no more or less likely to develop or die from cancer than women who took a placebo, the researchers said.

"This study shows that supplementation with the combined B vitamins provided no beneficial effect and no harmful effect. So in terms of cancer risk, this may not be an effective approach," **Dr. Shumin Zhang** of **Brigham and Women's Hospital and Harvard Medical School** in Boston, who led the study, said in a telephone interview.

Researchers have been exploring whether a number of different vitamins may protect against cancer.

The study, published in the **Journal of the American Medical Association**, involved **5,442 female health-care professionals** from around the United States. Their average age was 63.

The women had cardiovascular disease or risk factors for it such as high blood pressure or high cholesterol levels.

Some experts had been hopeful that B vitamins might protect against cancer after earlier studies indicated that people who get more of these vitamins may have a lower risk of developing cancer, especially colon cancer.

But in the new study, the number of women who developed cancer was nearly identical in the vitamin supplement group (187 women) and the placebo group (192 women). The two groups had similar risks for developing any type of cancer or dying from any type of cancer.

The study **did find that among women 65 and older, those getting the daily B vitamins were 25 percent less likely to develop any type of cancer and 38 percent less likely to get breast cancer.** But Zhang said it is not clear whether this is a genuine finding or simply a chance result.

HEALTH BENEFITS

People can get folic acid and other B vitamins in the diet through leafy green vegetables and fortified cereals or through vitamin supplements.

It is important that people get the proper amount of the various B vitamins, which are essential nutrients for growth, development and numerous other functions. For example, folic acid is important in the production of red blood cells and is important for women to prevent certain birth defects of a baby's brain and spine, known as neural tube defects.

Despite this study's findings, **other research suggests that people who eat foods high in folic acid may lower their cancer risk**, according to **Dr. JoAnn Manson** of **Brigham and Women's Hospital**, who also took part in the study.

Other studies have looked at whether B vitamins may provide additional health benefits. U.S. researchers reported on October 14 in the same journal that high doses of B vitamins failed to slow cognitive decline associated with Alzheimer's disease. Alzheimer's patients in that study took supplements of vitamins B6 and B12 and folic acid for 18 months.

Dr. Bleyer:

- ☑ Reduction in cancer risk is not only unaffected by long-term, increased vitamin B6, B12 or folic acid, another B vitamin, it is also not reduced with vitamin C; recent reports suggest that vitamin D may be prevented if, and perhaps, only if, a vitamin D deficiency exists
- ☑ The observation that the vitamins were helpful in a subset of persons who were over 65 years-of-age is worth testing further, but as in any retrospective subset analysis, this could be due to chance (see next report)
- ☑ **DEFEAT Cancer** submits, once again, that more comprehensive changes in diet and performed in combination with exercise, provided the best chance at cancer prevention and cancer progression or recurrence

Nostroms: Vitamins and cancer risk in women [Prevention]

[Additional coverage of the JAMA study reported above that folic acid, vitamin B6 and vitamin B12 supplements do not affect breast cancer risk or overall cancer risk in women. Researchers did note, however, that women over 65 experienced reductions in overall cancer risk compared to younger women.](#)

New York Times - December 2, 2008

By Nicholas Bakalar

There has been some evidence that vitamin B and folic acid can lower the risk for cancer, but a large randomized trial of the supplements suggests that they do not have that effect in women.

The seven-year study, published Nov. 5 in The Journal of the American Medical Association, assigned 2,721 women older than 40 to receive a daily combination of folic acid, vitamin B6 and vitamin B12, and compared them with a matched group of 2,721 who took a placebo. The vitamin doses were more than six times the recommended daily allowances.

In the placebo group, 192 women developed invasive cancer, compared with 187 in the vitamin group, a statistically insignificant difference. There were no differences in rates of breast or colorectal cancer, and no difference in rates of death from cancer or any other cause. It is well known that **vitamin B requirements increase with age, and the researchers did find a possible benefit among women over 65.**

“This doesn't preclude an important benefit from diets that are high in B vitamins and folates,” said

Dr. JoAnn E. Manson, the senior author, “and folate intake throughout pregnancy is very important.”

Dr. Manson, who is **chief of preventive medicine at Brigham and Women's Hospital** in Boston, said that the study found no evidence of increased risk from the supplements, and that taking an ordinary multivitamin is safe.

Dr. Bleyer:

- ☑ The inverse of the statement that older women may have some protection is that younger women clearly had no protection and they have in general worse outcomes and more years of life at stake, particularly productive ones, and a greater need to be a lower risk
- ☑ A problem with the over-65 observation is that it is a subset analysis that was not, before the study was started, considered to be an objective of the study; when subset analyses are done after the study is over, their findings are very preliminary, considered with great caution, and usually only thought to be of relevance for testing the observation (hypothesis generating) in a follow-up, definitive study
- ☑ Other benefits of folate and other B vitamins may offer reasons to take them as once-a-day multivitamins, not as higher-dose supplements, especially during and before pregnancy.

Is red meat's bad name justified? [Prevention]

Recent studies give red meat a bad name. But moderation, proper preparation -- and science -- can minimize the risks.

[Review of recent world literature on studies of red meat](#)

By Wendy Hansen

New York Times - November 10, 2008

The news for red meat seems to be getting worse and worse.

In December, a survey of more than **494,000 people** by the **National Institutes of Health** found that men who ate more than 5 ounces of red meat each day and women who ate more than 3 ounces had a 51% greater risk of esophageal cancer, 61% of liver cancer and 24% of colorectal cancer than those who ate less than an ounce of red meat daily.

In October 2007, the **World Cancer Research Fund** and the **American Institute for Cancer Research**, two charities that fund research on the effects of diet and activity on cancer risk, declared that the evidence linking red meat consumption and colorectal cancer was "convincing."

And though previous reports for breast cancer have been contradictory overall, findings published in July from a Harvard study of more than 39,000 young nurses suggested that the **risk of getting breast cancer before menopause goes up for every extra daily serving of red meat a woman ate as a teenager**, a time period that had not been studied before.

Add the numerous studies linking red meat to other cancers, cardiovascular disease, Type 2 diabetes and even Alzheimer's disease, and it sounds like the hamburger you had for lunch might as well have been laced with rat poison.

In fact, there is a place for red meat in a healthful diet, scientists say, but they recommend choosing smaller portions of lean cuts and cooking them well but not at high temperatures.

The question is which meat components are responsible for the observed health risks. Scientists have several theories, though none seems to tell the whole story.

Red meat can contain a lot of saturated fats and cholesterol, known contributors to cardiovascular disease. "We know that dementia is strongly related to vascular disease, so it's likely we'll find a relationship there as well," says **Dr. Walter Willett**, chair of the department of nutrition at the **Harvard School of Public Health**.

Contributing factors

Meat from commercially raised livestock also contains a high amount of **omega-6 fats**, which have been associated with poor cardiovascular health, but a low amount of omega-3 fats, which may be protective.

Another potential culprit is the **iron** in meat. Iron is essential for health, but iron from meat comes in a different form than that from vegetables and legumes, one that is absorbed whether the body needs it or not. "This type of iron can cause oxidative damage to all the components of the cell -- the protein, lipid, DNA, RNA," says **Al Tappel**, **professor emeritus of food science at UC Davis**.

Many of the studies that found an association between meat consumption and health risks did not differentiate between unprocessed meat, such as a steak, and processed or cured meats such as salami, bacon, pepperoni, bologna and hot dogs. Chemicals in processed meats may account for some of the cancer risk.

Finally, high-temperature cooking methods, such as grilling over charcoal, can cause the formation of known carcinogens such as **heterocyclic amines**, or HCAs, and **polycyclic aromatic hydrocarbons**, or PAHs.

Mary Young, a registered dietitian from the Centennial, Colo.-based National Cattlemen's Beef Assn., says that a study it commissioned on the science of red meat reached a very different conclusion (the study has not yet been published). "Red meat does not cause cancer," she says. "Beef is really one of the most underappreciated nutrient-rich foods out there" -- rich in protein and eight other nutrients, including B vitamins and zinc.

Some scientists, too, think that the risk of red meat has been overplayed. "The proof is not as strong as some people would like to think," says Iowa State University animal science professor Don Beitz. "Cancer is such a multifactorial [problem]. I don't see how one can just pin it on certain pollutants or nutrients."

Rock-hard conclusions require carefully controlled, long-term, well-defined studies of many people. Each one of these requirements can be difficult to meet, so scientists rely heavily on epidemiological studies in which the normal habits of large numbers of people are tracked, often pooling the results of multiple studies.

But unlike lab rats, humans don't live in a perfectly controlled environment, which makes it difficult to determine if it's meat or something else in the diet or environment that leads to an observed cancer risk. Also, some studies ask people to recall what they ate years ago, and many studies don't even define red meat the same way.

Even when a correlation between meat consumption and illness is found, the effect can be significant but small. In the December 2007 study, for example, high meat consumption resulted in only a 50% increased risk of developing esophageal cancer -- by way of comparison, smoking can increase a person's risk of developing lung cancer by 1,000% or more.

But to dismiss all risks because of inconsistencies in the research is unreasonable, Willett says. "That's exactly the same argument used by cigarette manufacturers to say that smoking is not harmful. . . . The perfect study will never be done. The next best thing will be epidemiology."

Keep it lean

Scientists generally agree that lean red meat has a place in a healthful diet -- in moderation. Studies showing increased cancer risks have mostly focused on high meat intake; the greatest risk increases are for those eating far more than the USDA-recommended limit of 18 ounces per week.

"One approach is to treat red and processed meat as a treat and not a regular staple," said **Dr. Michael J. Thun**, vice president of epidemiology and surveillance research at the American Cancer Society.

Moderation, it appears, is not the American way. According to the U.S. Department of Agriculture, in 2006 the average American consumed 95 pounds of beef and 64 pounds of pork -- about 7 ounces of red meat a day.

To sidestep some health concerns without giving up steak, some consumers have turned to grass-fed beef, which studies have shown to contain a heart-healthier ratio of omega-3 to omega-6 fatty acids.

Meanwhile, scientists are looking to make beef more healthful via selective breeding.

The amount of specific nutrients in steaks from two animals of the same breed can vary by a factor of two or three, Beitz says. He and others in a group of researchers known as the National Beef Cattle Evaluation Consortium hope to find genetic markers for a host of nutrients, including omega-3 and other beneficial fats, zinc and vitamins B6 and B12. The research, sponsored by Pfizer Animal Science, would help animal breeders look at animals' genetic profiles to select ones with the best nutritional composition.

"In a way, we're trying to allow people to indulge themselves to a greater extent than to moderate," said James Reecy, an Iowa State geneticist also involved in the project.

The same technique could be used to limit the unhealthy components of meat as well, such as specific saturated fats. Cattle breeders have already begun doing this, Reecy says.

Willett isn't convinced that these efforts will eradicate the health risks that come from consuming red meat. "You may make it healthier in one way, but you're unlikely to fix all the problems at the same time," he says.

Dr. Bleyer:

- ☑ On the topic of meat-based diet, **DEFEAT Cancer** recommends *The China Study* by T. Colin Campbell, which was reviewed at a DEFEAT Cancer meeting by cancer survivor and school teacher Rita Weich
- ☑ A study that "has not been published yet" should be taken with a grain of salt (note nutrition reference) and should not have been cited in a review of the literature, since it's not
- ☑ Relegating meat to a treat (taken occasionally in small portions), as recommended by the American Cancer Society is a reasonable strategy, if avoiding meat altogether is not feasible, the latter occurring in the vast majority of restaurants since menus have a plethora of meat entrees

Study: Vitamin C or E pills do not prevent cancer [Prevention]

[Vitamin C or E pills do not help prevent cancer in men, concludes the same big study that found these supplements ineffective for warding off heart disease.](#)

Marilynn Marchione, Medical Writer

Associated Press -- Nov 16, 2008

The public has been whipsawed by good and bad news about vitamins, much of it from test-tube or animal studies and hyped manufacturer claims. Even when researchers compare people's diets and find that a vitamin seems to help, the benefit may not translate when that nutrient is obtained a different way, such as a pill.

"Antioxidants, which include vitamin C and vitamin E, have been shown as a group to have potential benefit," but have not been tested individually for a long enough time to know, said **Howard Sesso** of **Harvard-affiliated Brigham and Women's Hospital** in Boston.

The **Physicians Health Study**, which he helped lead, was designed to do that. It involved **14,641 male doctors**, 50 or older, including 1,274 who had cancer when or before the study started in 1997. They were included so scientists could see whether the vitamins could prevent a second cancer.

Participants were put into four groups and given vitamin E, vitamin C, both, or dummy pills. The dose of E was 400 international units every other day; C was 500 milligrams daily.

After an average of eight years, there were 1,929 cases of cancer, including 1,013 cases of prostate cancer, which many had hoped vitamin E would prevent.

However, rates of prostate cancer and of total cancer were similar among all four groups.

The study was funded by the National Institutes of Health and several vitamin makers. Results were being reported Sunday at an **American Association for Cancer Research** conference in Washington.

"Well-conducted clinical trials such as this are rapidly closing the door on the hope that common vitamin supplements may protect against cancer," said **Marji McCullough, nutrition chief at the American Cancer Society**. "It's still possible that some benefit exists for subgroups that couldn't be measured, but the overall results are certainly discouraging.

"The American Cancer Society recommends getting these and other nutrients by eating a mostly plant-based diet with a variety of vegetables, fruits and whole grains. A bonus is that this type of diet helps to prevent obesity, which increases the risk of several cancers."

About 12 percent of Americans take supplements of C and E. The new study does not mean these vitamins have no value, just that they didn't prevent cancer in **this group of doctors, who may be healthier than the general population**, said **Dr. Peter Shields**, deputy director of **Georgetown University's Lombardi Comprehensive Cancer Center**.

The best bet, he said, is to do things that are known to prevent the disease — eat right, maintain a healthy weight, and exercise.

Dr. Bleyer:

- ☑ This report is coincident with the result of the SELECT (**Selenium and Vitamin E Cancer Trial**) that was reported a month earlier and showed no benefit in preventing prostate cancer and, at least for vitamin E, may have actually increased the incidence (*E&N News*, November 2008)
- ☑ Thus the speculation that the men in the study reported here may have been healthier (physicians) is not likely to be applicable
- ☑ And whether physicians are healthier seems debatable
- ☑ In any event, the bottom line is the bottom line in the report: *do things that are known to prevent cancer — eat right, maintain a healthy weight, and exercise*

Saturated fats in red meat and processed meats linked to cancer of small intestine [Prevention]

[Eating foods high in saturated fats -- such as red and processed meats -- may be a risk factor for cancer of the small intestine.](#)

Nov. 14, 2008 - HealthDay News

That's the conclusion of a **U.S. National Cancer Institute** study that included **half a million men and women** who provided information about their eating habits **over eight years**.

Previous research had identified a link between red and processed meats and cancer of the large intestine, but this is the first prospective study to examine the association between meat and fat intake and cancer of the small intestine. During the study, 60 adenocarcinomas and 80 carcinoid tumors of the small intestine were diagnosed among the participants, and an elevated risk for these cancers was associated with saturated fat intake, the NCI researchers reported in the current issue of the journal **Cancer Research**.

"Furthermore, there is some evidence to suggest that cancers of the small and large bowel both arise from adenomatous polyp precursor lesions, suggesting the adenoma-carcinoma sequence is relevant to both sites. For some unknown reason, the large intestine is much more susceptible to malignant transformation," the study's lead author, **Amanda Cross**, said in a news release.

"Identifying risk factors that are unique as well as those that are similar for the two sites may aid our understanding of the comparative resistance of the small intestine to carcinogenesis," she added.

Cancer of the small intestine is relatively rare, but rates of the disease have been increasing since the 1970s. People who develop this type of cancer are at increased risk for developing a second primary cancer, particularly colorectal cancer, the researchers said.

"Identifying modifiable risk factors for cancer of the small intestine is important not only because the incidence of this cancer is on the rise, but it may enable us to further understand other gastrointestinal malignancies," Cross said.

Dr. Bleyer:

- ☑ It probably took many years longer to identify meat as a causal factor in cancer of the small intestine than for the large intestine because of the much lower frequency of cancer of the small intestine
- ☑ The importance of plant-based nutrition is further emphasized by adding yet another cancer to the list associated with a meat-based (Western) diet

Broccoli helps prevent cancer in smokers - study [Prevention]

[Active and recent former smokers, especially those who smoke\(d\) a lot, had less lung cancer if their diet contained cruciferous vegetables like broccoli, cabbage, cauliflower and Brussel sprouts](#)

WASHINGTON (Reuters) – 11/18/08

Broccoli and similar vegetables appear to offer special protection from cancer for smokers, researchers reported on Tuesday.

They found that former smokers and, especially, people still smoking heavily got special benefits from eating the vegetables.

"The most significant effect was in heavy smokers," **Li Tang of Roswell Park Cancer Institute** in Buffalo, New York, who led the study, said in a telephone interview. People who smoked more than 20 cigarettes a day were considered heavy smokers.

Broccoli and other so-called cruciferous vegetables such as cabbage, cauliflower and Brussels sprouts have been known to lower the risk of cancer in general, perhaps through compounds called isothiocyanates.

Tang and colleagues studied **948 cancer patients** and 1,743 people being screened for cancer who turned out not to have it. All answered detailed questionnaires about habits, including their diet and smoking history.

People who ate cruciferous vegetables, especially raw, were between 20 percent and 55 percent less likely to have cancer than those who did not or only rarely ate these foods, Tang told a meeting of the **American Association for Cancer Research**.

The reduction in risk depended on the type of vegetable consumed and the duration and intensity of smoking.

"A significant effect was only observed among the former smokers and current smokers. We didn't see a significant association among never-smokers," Tang said.

"These findings are not strong enough to make a public health recommendation yet," she added.

And, she cautioned: "**If you smoke long enough, nothing can help.**"

Smoking raises the risk of many types of cancer, including lung cancer, head and neck cancer and bladder cancer.

Dr. Bleyer:

- ☑ **DEFEAT Cancer** includes this prevention study since it assessed a broad group of vegetables (cruciferous) that have a known anticancer agent (isothiocyanates) that has also been shown to reduce cancer recurrence
- ☑ Also, smokers are at such high risk of cancer that it is one of the most efficient groups in which to learn about the potential anticancer benefit of dietary components applicable to persons already diagnosed with cancer
- ☑ Studies in smokers have also taught us that dietary supplements may actually increase cancer risk (e.g. long-term exposure to vitamin A and related retinoids), as recently apparently observed in the SELECT study to prevent prostate cancer with vitamin E and/or selenium (reported in the October and November 2008 issues of *E&N News*)

Cranberries -- good for what ails

[In honor of Thanksgiving, and for their general health effects, cranberries potential health benefits, including anticancer effects, are reviewed](#)

By Elena Conis

Associated Press - November 24, 2008

Indians and settlers may have been on to something about the tart fruit's healing abilities.

European settlers first put cranberries on the Thanksgiving table because the local fruit lasted through winter and enhanced the flavor of gamy meat. The settlers had picked up on the berry's culinary potential from Native Americans, who survived cold winters by filling up on pemmican, a cake of cranberries, nuts and dried venison or bear meat.

Both groups also prescribed cranberries for fevers, gastrointestinal problems and dropsy -- a term used to describe any swelling or inflammation. Turns out, they were onto something. In the last few decades, scientists have begun to confirm and explain the **cranberry's ability to fight infections of the urinary tract and gut and its potential to fight gum disease, heart disease and cancer**.

"For over a hundred years, women have known that cranberry juice can prevent urinary tract infections," says Amy Howell, associate research scientist at the U.S. Department of Agriculture-supported Marucci Center for Blueberry and Cranberry Research at Rutgers University in Camden, N.J. "They thought it was due to acidity, but that's actually not the case."

Cranberry's antibacterial properties are due to a class of chemical compounds called proanthocyanidins. Ten years ago, Howell's research group isolated the compounds and demonstrated how they work: Proanthocyanidins bind to

harmful bacteria such as E. coli, forming a "Teflon-like" coating around them. The coating prevents the bacteria from sticking to gastrointestinal and urinary tract walls, impeding infections.

The nonstick properties of proanthocyanidins may explain the results of several clinical trials that showed that cranberry juice can reduce the frequency of urinary tract infections.

For example, a study published in the British Medical Journal in 2001 showed that women who drank a couple of ounces of cranberry juice daily for six months had a 20% lower risk of urinary tract infections, compared with women in a control group. A study published in the Canadian Journal of Urology in 2002 showed that just 20% of women who drank three glasses of cranberry juice daily for a year experienced urinary tract infection symptoms, compared with 32% of women who drank a placebo.

And last month, a study in the journal Urology found that two glasses of cranberry juice a day reduced the frequency of urinary tract infections by 41% among pregnant women.

Proanthocyanidins also appear to keep the bacterium H. pylori, which causes ulcers, from sticking to the linings of the stomach and intestines. A 2005 study of 189 adults with H. pylori infections in the journal Helicobacter, showed that two glasses of cranberry juice daily for three months reduced the degree of infections, compared with those who drank a placebo.

And a study in the journal Nutrition this year showed that a daily glass of cranberry juice eliminated H. pylori infections in 16% of infected children; a placebo eliminated only 1.5%.

Other research suggests that the compounds could keep plaque-forming bacteria at bay. In lab experiments, cranberry proanthocyanidins stopped oral streptococci and other bacteria from sticking to surfaces. But researchers warn against using the juice as a mouthwash because of its sugar content and acidity.

Cranberries are high in vitamins A, E and C, iron, calcium, potassium and antioxidants. The last may explain the fruit's possible **anti-cancer** and anti-heart-disease effects. **Cranberry impedes the growth of liver and breast cancer cells in lab dishes, says Jie Sun, a scientist at General Mills who previously researched the fruit's anti-cancer effects at Cornell University.**

And in 2006, Canadian researchers published suggestive findings in the British Journal of Nutrition showing that drinking a glass of cranberry juice a day increased concentrations of good HDL cholesterol by 8% in overweight men. (The study was funded by the Canadian Cranberry Growers Coalition.)

But the tart red berries may not be for everyone. Gorging on too many or guzzling too much juice can result in an upset stomach or diarrhea. A couple of reports indicate that cranberry juice may increase the risk of kidney stones in people prone to them. And there's conflicting evidence that cranberries may interfere with blood thinning drugs, such as warfarin.

The common cranberry's benefits still seem to outweigh its drawbacks, but despite this, most Americans limit their consumption to a single day of the year. The reason for this may have been best summed up by writer and naturalist Henry David Thoreau more than 150 years ago: Cranberries, he wrote, were easy to harvest, but their taste was "a little bitterish."

Given the amount of sugar in most cranberry sauce recipes, most Americans, it seems, would agree.

Dr. Bleyer:

☑ **DEFEAT Cancer** does not expect any one food item or supplement to have major anticancer effects, but cranberries seem potentially worth including in a **DEFEAT Cancer** recommended plant-based diet
