DEFEAT Cancer

Synergistic Benefit of
EXERCISE & NUTRITION
in Improving the Quality and Quantity of Survival during / after Cancer

The Evidence for Exercise

January-December 2008 ♫ 80 Articles

Compiled, Critiqued and Summarized
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St. Charles CANCER CENTER
Bend, Oregon

ADVANCED SPECIALTY CARE

VALUE of EXERCISE during/after CANCER

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

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The **Lance Armstrong Foundation** supports ***DEFEAT Cancer*** via a Community Grant

Advanced Specialty Care of Central Oregon is a sponsor of the ***DEFEAT Cancer*** Nutrition Program. ASC has a focus on obesity and diabetes management and is the only certified bariatric program in Oregon outside of Portland

Increasingly, the reports on cancer prevention via exercise and nutrition have relevance for ***DEFEAT*** participants, particularly for family members concerned about their cancer risk. Hence, selected *prevention* reports appear in this resource, with the identifier '[Prevention]' in the title, including the Table of Contents. In addition, a few laboratory studies are included in response to questions about them from ***DEFEAT*** participants.

DIET | EXERCISE | FAMILY | EDUCATION | ATTITUDE | THRIVING

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Obesity with depleted muscle mass affects mortality in cancer patients **80**
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Active lifestyle may prevent cancer: Japan study [Prevention] **81**
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Obesity and risk of cancer in postmenopausal Korean women [Prevention] **81**
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Piling on the pounds increases men's colon-cancer risk, research reveals [Prevention] **84**
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Adopting a healthy lifestyle 'helps cancer suffers after diagnosis' **85**
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Breast cancer: Research lends biologic plausibility to link with alcohol;
Even minimal exercise may lower … risk and recurrence [includes Prevention] **86**
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Excess weight seems to boost breast cancer risk [Prevention] **88**
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

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Executive Summary

► Exercise (pp. 13-46)

Studies in this section evaluated exercise but not nutrition

The year 2008 set a record in the number of randomized controlled trials that demonstrated significant benefits in the quality or quantity of survival after a diagnosis of cancer and in prevention of cancer. Studies at the Dana-Farber Cancer Institute found that non-metastatic colon cancer patients who routinely exercised had a 50 percent lower mortality rate during the study period than their inactive peers, regardless of how active they were before the diagnoses (pp. 38-40). In men with colorectal, liver, esophageal, stomach and lung cancer who also had pre-diabetes, death from cancer was correlated with their degree of physical fitness (p. 24). Among 40- to 65-year-old females, walking just an hour a week significantly reduced the occurrence of colon cancer; walking more than an hour week reduced it further. (p. 34). Exercising 15 minutes a day for less than 3 times a week helps prevents breast cancer in persons of all races and ethnicities (p. 34). A 32% reduction in breast cancer in 11 years was observed in lean women who reported having regularly exercised (pp 44-46).

Investigators at Harvard Medical School found that a reduction in insulin levels may explain the benefit of exercise in prolonging survival after breast cancer (p. 20). This finding appears to supplement the beneficial effect of exercise and nutrition on tumor gene expression study (p. 60)

A review of pedometer studies included 8 randomized controlled trials, five of which showed a statistically significant benefit for pedometers, within a mean of 4-5 months and including BMI reduction. Overall (meta) analysis resulted in a highly statistically significant advantage. (p. 13).

A variety of studies in patients with different types of cancer demonstrated improvement in the quality of life during and after cancer therapy. Exercise has been shown in 28 studies involving more than 2000 cancer patients and survivors to significantly diminish fatigue and related effects of pain, emotional distress, sleep disturbance, anemia and co-morbid illnesses (p. 20). For patients being treated with surgery, chemotherapy, radiation or medication regimens, cardiovascular and strength training can help counter side effects such as extreme fatigue and muscle wasting, and bolster healing, propelling them back into normal life faster (p. 41). Five times weekly, half-hour, stationary bicycle and muscle exercises during high-dose chemotherapy increased physical performance, reduced fatigue, and decreased nausea and vomiting (p. 24). In cancer patients, 20-30 minute sessions of mixed exercise 4 times per week together with an educational, supportive care program significantly improved fatigue, depression and overall quality of life (p. 30). With just four months of exercise, overweight breast cancer patients significantly reduced their hip circumference and blood insulin level; patients randomized to routine care did not (p. 14). A 90-minute, three-times-weekly, strength training session for 12 weeks prevented loss of muscle strength and functional capacity in prostate cancer patient on androgen ablation therapy (p. 25). Benefits of strength-training programs and cardiovascular workouts for cancer survivors include increased energy, improved flexibility and cardiovascular function, stronger muscles and bones (p. 11).

A stationary bicycle session three times weekly for 14 weeks was not only feasible after surgery in patients with early lung cancer, it improved lung function, quality of life, and amount of fatigue (p. 26). Six weeks of biweekly yoga sessions during radiation were associated with a better quality of life, including less fatigue, sleeplessness, and depression and with a sense of more meaning of life when measured one and three months after radiation (p. 28). Daily 1-hour sessions of yoga dramatically reduced depression during radiation therapy and during chemotherapy in breast cancer patients (p. 28). Ten weeks of gentle exercise and meditation/breathing relaxation based on the Chinese Medicine theory of energy channels

improved quality of life, including sexual activity, for cancer patients (p. 31). An athletic form of yoga is shown to improve quality of life but also is associated with a biological mechanism than may mediate the sense of well being (p. 14). Eight weeks of twice-weekly 90-minute exercise sessions in patients with advanced lung cancer reduced lung cancer symptoms (p. 27).

A dedicated medical oncologist has stimulated breast cancer patients to undertake triathlon training (p. 15). Experience with dragon boat racing suggests that exercise in groups, with the associated camaraderie and goal setting, is more beneficial than individual programs (p, 17). Aerobic classes are recommended (p. 38).

Health clubs have shown to have effective programs to combat fatigue, elevate mood and energy levels, and control weight (p. 41). Personal exercise trainers are becoming part of the cancer therapy program as more and more evidence documents the benefits and research is uncovering the mechanisms of benefit (p. 32). A study recruited breast cancer patients into a clinical trial that randomized exercise vs. usual care; less than 10% were enrolled, but when participating the compliance was excellent. (p. 21). Those who stand to gain the most with exercise to improve their quality of life are those with the greatest need in mental and psychosocial intervention (pp. 38, 40).

Regular exercisers should realize that even if they don't see big changes on the scales or in their measurements, they are still getting health benefits (p. 18). As the evidence for the benefits of exercise in cancer patients grows, national, international standards to assess physical fitness of cancer patients should now be implemented and followed (p. 38).

High levels of exercise did not increase the frequency or severity of lymphedema associated with axillary dissection and lymph node removal (p. 28).

In mice, voluntary exercise (having a running wheel in the cage) was associated with an increase in the rate of growth of prostate cancer cells injected into the mice (p. 31), whereas in other experiments a decrease in the rate of growth of pancreas cancer cells injected into the mice was noted, and the benefit of exercise was further improved with a simultaneous cancer treatment (p. 32). In adult mice, daily exercise maintained testicular function whereas sedentary behaviors led to testis cell damage, sperm reduction, and lower testosterone levels (p. 33).

As the evidence for the benefits of exercise in cancer patients grows, national, international standards to assess physical fitness of cancer patients should now be implemented and followed (pp. 37-38). The decreased risk was more clearly observed in women than in men, especially among the elderly and those who regularly engaged in leisure-time sports or physical exercise (pp. 37. By site, decreased risks were observed for cancers of the colon, liver, and pancreas in men and for cancer of the stomach in women. Increased daily physical activity may be beneficial in preventing cancer in a relatively lean population (ibid).

► **Exercise and Nutrition** (pp. 47-89)

Studies in this section are those that combined exercise and nutrition or measured outcomes that are a measure of both, such as body weight or body mass index (BMI)

> ***DEFEAT Cancer** promotes the combination of exercise and nutrition (E&N) with the underlying hypothesis that the two interact synergistically to eliminate the suffering from cancer. Increasingly, as manifest in this compilation, scientific evidence is accumulating to convert the E&N hypothesis to fact.*

There is a wealth of data on the deleterious effects of overweight and obesity, with emphasis on the utility of body mass index (BMI) as a measure of risk (p. 47-57, 62, 63, 68, 69, 73, 75). An analysis of the world literature extends the association between BMI and cancer to include more than 10, as many as 12 different types (pp. 68-69). The Million Women Study of 1.2 million women in

the United Kingdom indicates that 1 in every 20 cases of cancer in females are related to an overweight or obese status (p. 67).

Among nearly 4,000 women with breast cancer evaluated at Johns Hopkins University, each 11 pounds of increase in body weight after diagnosis translated into a 14% decrease in survival, irrespective of a woman's weight at diagnosis (pp. 47-50). From the prestigious Massachusetts General Hospital, a study quantifies the increased risk of prostate cancer as a function of body mass index (p. 53).

Physical activity *and* nutrition guidelines for cancer patients are being achieved in only one in 20 survivors; yet the quality of life is directly proportional to the number of guidelines met (p. 54). Interviews of more than 100,000 Canadians indicates that only about one in five cancer survivors are physically active and one in six are obese (p. 55). When the authors of this study were contacted, they expressed surprise that cancer survivors were so sedentary in view of the scientific evidence for benefit of physical activity (p. 55). U.S. women's fear of weight gain more than cancer is prevalent despite knowledge that excessive weight gain increases cancer susceptibility (p. 58).

Drs. Weinberg and Komaroff of MIT and the Whitehead Institute and Harvard, respectively, in a superb review summarized the recent data that links exercise and nutrition to cancer prevention and eradication, how cancer causing genes are involved, and what can be done to reduce risk of occurrence and recurrence (p. 70). In 30 men with low-grade prostate cancer who declined immediate surgery, radiation therapy and/or hormonal therapy, an aggressive low fat diet and physical therapy regimen was associated with changes in the genes of their tumor that reduced its malignant potential (p. 60). Reducing body mass index (BMI) in obese patients with bariatric surgery had an 80% reduction in developing cancer within 5 years (pp. 73, 74). The reduction in cancer after bariatric (weight reducing) surgery appears to be a more broad effect than just reducing those cancers most known to occur in obese persons (p. 50).

Many studies of specific types of cancer documented the increased treatment required, higher rate of recurrence, shorter survival, and more co-morbidities in patients with an elevated BMI. Patients with early breast cancer who are overweight have increased co-morbidities, more negative prognostic factors, and require more extensive surgery. (p. 60). One of the worst types of breast cancer, inflammatory breast cancer, occurs more commonly in obese women than in any other subgroup; regardless of the subtype, overweight and obese women with locally -advanced breast cancer have a worse survival. (pp. 56, 57). The aggressiveness (grade) of prostate cancer was increased in patients with a high BMI (p. 62). Patients with liver cancer and an elevated BMI had more evidence for invasion of their cancer into the blood stream (and potential for spread throughout the body) than those with a normal BMI (p. 62). Obese patients with stomach cancer required longer operations and had more postoperative complications than non-obese patients (p. 61). Severely obese patients with uterus cancer did not have a worse survival; they may even have had a better survival (p. 63). Obese patients with ovarian cancer received less therapy than non-obese patients (p. 64). Lung cancer patients at the MD Anderson Cancer Center and health matched controls from the community, the risk of lung cancer was correlated with salad consumption and with gardening in both former and active smokers and in non-smokers (p. 66).

Some benefits of overweight status were reported. A prestigious health news reporter interprets the national Centers for Disease Control and Prevention report that indicates overweight (but not obese) persons have a lower death rate from some non-cancer diseases (p. 64).

In any event, the evidence that regular physical activity both prevents cancer and cancer recurrence is substantial and increasing at record rates.

► Exercise

Using pedometers to increase physical activity and improve health: A systematic review

Dena Bravata, MD, MS; Crystal Smith-Spangler, MD; Vandana Sundaram, MPH; Allison Gienger, BA; Nancy Lin, ScD; Robyn Lewis, MA; Christopher Stave, MLS; Ingram Olkin, PhD; John Sirard, PhD
Stanford University
JAMA. 2007;298 (19):2296-2304.

This review of pedometer studies includes 8 randomized controlled trials, five of which showed a statistically significant benefit for pedometers, within a mean of 4-5 months and including BMI reduction. Overall (meta) analysis resulted in a highly statistically significant advantage.

Context. Without detailed evidence of their effectiveness, pedometers have recently become popular as a tool for motivating physical activity.
Objective. To evaluate the association of pedometer use with physical activity and health outcomes among outpatient adults.
Data Sources. English-language articles from MEDLINE, EMBASE, Sport Discus, PsychINFO, Cochrane Library, Thompson Scientific (formerly known as Thompson ISI), and ERIC (1966-2007); bibliographies of retrieved articles; and conference proceedings.
Study Selection. Studies were eligible for inclusion if they reported an assessment of pedometer use among adult outpatients, reported a change in steps per day, and included more than 5 participants.
Data Extraction and Synthesis. Two investigators independently abstracted data about the intervention;n participants; number of steps per day; and presence or absence of obesity, diabetes, hypertension, or hyperlipidemia. Data were pooled using random-effects calculations, and meta-regression was performed.
Results. Our searches identified 2246 citations; 26 studies with a total of 2767 participants met inclusion criteria (8 randomized controlled trials [RCTs] and 18 observational studies). The participants' mean (SD) age was 49 (9) years and 85% were women. The **mean intervention duration was 18 weeks**. In the RCTs, pedometer users **significantly increased their physical activity by 2491 steps per day** more than control participants (95% confidence interval [CI], 1098-3885 steps per day, P < .001). Among the observational studies, pedometer users significantly increased their physical activity by 2183 steps per day over baseline (95% CI, 1571-2796 steps per day, P < .0001). Overall, pedometer users increased their physical activity by 26.9% over baseline. An **important predictor of increased physical activity was having a step goal such as 10,000 steps per day** (P = .001). When data from all studies were combined, pedometer users significantly **decreased their body mass index by 0.38** (95% CI, 0.05-0.72; P = .03). This decrease was associated with older age (P = .001) and having a step goal (P = .04). Intervention participants **significantly decreased their systolic blood pressure** by 3.8 mm Hg (95% CI, 1.7-5.9 mm Hg, P < .001). This decrease was associated with greater baseline systolic blood pressure (P = .009) and change in steps per day (P = .08).
Conclusions. The results suggest that the use of a pedometer is associated with significant increases in physical activity and significant decreases in body mass index and blood pressure. Whether these changes are durable over the long term is undetermined.

Dr. Bleyer:
- ☑ When interviewed, Dr. Bravata, the senior author, said "Much to my surprise, these little devices were shown to increase physical activity by about one mile of walking per day. *Nothing is simpler than getting a pedometer*."
- ☑ After 8 randomized controlled trials, each of which demonstrated benefit in the pedometer group, there is no need for more controlled trials; the answer is: *pedometers are effective*, period.
- ☑ I'm impressed, but not surprised, with the statistically and clinically significant reduction in BMI
- ☑ My son has a device from Nike that he puts in his running shoes and communicates by blue tooth (wireless) to his iPod and tells him how many steps he's run every 1000 strides and encourages to keep going, including a message from Lance Armstrong
- ☑ The question is how to sustain the benefit; pedometers, like any other device with the possible exception of the cell phone, tend to be used less and less; the answer may be to add pedometers to cell phones and have them auto-call when insufficient walking (or running) is detected by the cell phone

Impact of a mixed strength and endurance exercise intervention on insulin levels in breast cancer survivors

Jennifer A. Ligibel, Nancy Campbell, Ann Partridge, Wendy Y. Chen, Taylor Salinardi, Haiyan Chen, Kristie Adloff, Aparna Keshaviah, Eric P. Winer
Dana-Farber Cancer Institute, Brigham and Women's Hospital, Harvard Medical School, Channing Laboratory, Boston, MA
Journal of Clinical Oncology, Vol 26, No 6 (February 20), 2008: pp. 907-912

With just four months of exercise, overweight breast cancer patients significantly reduced their hip circumference and blood insulin level; patients randomized to routine care did not

Purpose: Accumulating data suggest that exercise may affect breast cancer risk and outcomes. Studies have demonstrated that high levels of insulin, often seen in sedentary individuals, are associated with increased risk of breast cancer recurrence and death. We sought to analyze whether exercise lowered insulin concentrations in breast cancer survivors.
Methods: One hundred one sedentary, overweight breast cancer survivors were randomly assigned either to a 16-week cardiovascular and strength training exercise intervention or to a usual care control group. Fasting insulin and glucose levels, weight, body composition, and circumference at the waist and hip were collected at baseline and 16 weeks.
Results: Baseline and 16-week measurements were available for 82 patients. Fasting insulin concentrations decreased by an average of 2.86 μU/mL in the exercise group (P = .03), with no significant change in the control group (decrease of 0.27 μU/mL, P = .65). The change in insulin levels in the exercise group seemed greater than the change in controls, but the comparison did not reach statistical significance (P = .07). There was a trend toward improvement in insulin resistance in the exercise group (P = .09) but no change in fasting glucose levels. The exercise group also experienced a significant decrease in hip measurements, with no change in weight or body composition.
Conclusion: Participation in an exercise intervention was associated with a significant decrease in insulin levels and hip circumference in breast cancer survivors. The relationship between physical activity and breast cancer prognosis may be mediated, in part, through changes in insulin levels and/or changes in body fat or fat deposition.
Supported by the American Society of Clinical Oncology and Lance Armstrong Foundation.

Dr. Bleyer:
- ☑ No only may the insulin level be a factor in explaining how weight gain increases cancer recurrence (cf. 1st report above in Exercise & Nutrition section), it can be reduced by exercise
- ☑ And within just 4 months of moderate exercise, along with decreased hip circumference
- ☑ Weight (and BMI) did not decrease significantly but could have if nutrition was also addressed in this study

Yoga gives immune boost to breast cancer survivors

By Megan Rauscher

An athletic form of yoga is shown to improve quality of life but also is associated with a biological mechanism than may mediate the sense of well being

NEW YORK (Reuters Health) - In breast cancer survivors, the Iyengar method of yoga not only promotes psychological well-being, but seems to offer immune system benefits as well, according to research reported Monday.
The research was reported at the American Physiological Society meeting in Washington, DC.
The Iyengar method, created by B. K. S. Iyengar, "is considered to be one of the more active forms of yoga," lead researcher and presenter **Pamela E. Schultz** from **Washington State University**, Spokane, told Reuters Health.
"It still has the meditative component, but it's been shown to have a **physical output equivalent to a moderate-intensity exercise**," she explained.

Schultz and colleagues randomly assigned 10 breast cancer survivors to **8 weeks of Iyengar yoga (2 classes and 1 solo session at home per week)** and 9 to a wait-list control group. The women had an average age of 61 years, were about 4 years out from initial cancer diagnosis and were being treated with hormone therapy. None of the women had any prior experience with Iyengar yoga.
Psychosocial tests showed that the "demands of illness," which reflects the burden of hardship of being a breast cancer survivor, fell in the yoga participants.
"Psychosocial variables indicated improved quality of life with Iyengar yoga," Schultz said.
Importantly, these improvements correlated with **decreased activation of** an important immune system protein called **NF-kB**, which is a marker of stress in the body.
"So it's possible," Schultz said, "that decreased activation of NF-kB indicates decreased stress in the body, which would be a positive thing. NF-kB can be activated by any type of stress in the body, like physical stress and mental stress."
Schultz plans to continue her research by looking at different immune system proteins to see if they too show changes for the better, "which would confirm immune and psychosocial benefits of Iyengar yoga."

Dr. Bleyer:
☑ Small but randomized trial for which no statistical significances in the observed differences are reported.
☑ The very short interval (2 months) required to show a benefit is impressive.
☑ Also, NF-kB is only one of many markers of the immune system; the observed difference could be insignificant in the greater composition of stress-related markers and cytokines.
☑ Nonetheless the data are a sufficient body of pilot data to warrant further investigation of this more athletic form of yoga
☑ Again, if nutrition were combined with the physical activity intervention, the results may have shown an even greater, statistically-significant difference

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Changing lives through fun and physical fitness

Fran Mason, MD, is an oncologist on a mission to shape the way survivors cope.
HemOnc Today - March 10, 2008
By Stacey L. Adams

For ten years, a dedicated medical oncologist in Boulder, Colorado has stimulated breast cancer patients to undertake triathlon training

"Empowerment through fitness and fun," is what Fran Mason, MD, and the group at Rocky Mountain Team Survivor in Boulder, Colo., strive to provide for the 500 women cancer survivors in their program. For over a decade, Rocky Mountain Team Survivor, an affiliate of the National Association of Team Survivor, has given these women a sense of control in an otherwise powerless struggle by offering physical fitness programs and activities at any stage of cancer, cancer recovery or survivorship. "Team Survivor promotes participation in physical fitness and

2007 Rocky Mountain Team Survivor at the Denver Danskin Women's Triathlon.
Source: Rocky Mountain Team Survivor

fun activities. Our signature event, and the signature event for many of the Team Survivor groups, is the Danskin Triathlon," Mason, medical director of Cancer Exercise Programs for Healthlinks Clinic at the

University of Colorado, Boulder, and Rocky Mountain Team Survivor Board Member, told HemOnc Today.

Participants are assisted in the training process and during the triathlon; 'swim angels' are available in the water to help.

"We have about 175 survivors who all swim, bike, run and cross that finish line," she said. "If you put your foot on the starting line, you're going to make it to the finish line."

Oncologist, fitness advocate

Mason, a board certified medical oncologist, began her physical fitness advocacy in Colorado in the 1990s when she realized how beneficial exercise programs were to her patients. While working part-time in a cancer center, Mason spent the rest of her time lecturing to physicians, nurses, physical therapists, patients and advocacy groups about cancer and fitness.

"I began doing some physical fitness for myself, and then I started applying it among my patients by encouraging them to be more active, to gain the benefits of training, to learn to use a heart rate monitor and to monitor their training progress. I became increasingly dedicated to promoting fitness in a hands-on way as a doctor," she said.

Despite medically practiced beliefs about the detriments of physical fitness on the health of patients diagnosed with or recovering from cancer, Mason continued to work to change that paradigm in the professional arena. Working with a physiologist and a physical therapist, Mason developed and instructed a class at the University of Colorado called The Clinical Exercise where students were taught the therapeutic benefits of fitness in a clinical setting. Using their hands-on knowledge and experience, the group moved to a clinic to help patients recovering from cancer therapy become strong and regain energy.

Mason and her group performed original research and presented two papers at the American College of Sports Medicine, one that confirmed the benefit of resistance training in patients recovering from chemotherapy and a second that reported a suitable exercise program for patients with advanced cancers.

At their clinic, Mason and her group work with patients recovering from cancer therapies to design individualized exercise programs to suit their needs, whether that included resistance training, flexibility or balance training.

"I try to do things that are fun for patients and that make them feel better. My clinic is full of laughter. It is not full of tragic stories, but instead full of people really working hard but having a good time," she said. "There is really good data and evidence that show that for patients recovering from cancer therapy, a supervised exercise program can lead to improved self esteem, which is really important because it is their body that has let them down in the first place."

Improving quality of life

Rocky Mountain Team Survivor coincides with the efforts Mason works toward every day in her clinic, but according to her, they go beyond her team's work.

"Team Survivor is an extension of my work; what I do in my practice is really much more for people acutely going through their treatments or getting better. The Team Survivor group goes beyond that for people who are, essentially, anywhere with their cancer survivorship; they've done some incredible things."

The survivors participate in weekly hikes, snowshoeing outings, yoga classes and weekly gym nights at a local clinic with a volunteer physical therapist. The organization has also teamed up with local survivorship organizations such as Casting for a Cure, a lottery-drawn fly fishing program for women survivors, and the Colorado Therapeutic Riding Center, an equestrian program where three-quarters of the volunteers are survivors themselves.

"These are activities that seem to be suitable for almost everyone, and the women in the horse class told me, 'I've gotten more out of working with these other cancer survivors and horseback riding than I could've ever gotten out of sitting in a support group,'" Mason said. "So that is the concept behind Team Survivor — to really encourage participation and healing through physical fitness."

A perfect example of how much survivors can achieve is Rocky Mountain Team Survivor board member, Diane Groff. Groff is a two-time cancer survivor who has competed in every Danskin Triathlon in one

season. She will receive the 2007 Inspiration Award at the 34th Annual Sports Women of Colorado award ceremony in March.
"This is statewide recognition for cancer survivorship and how far you can take that," Mason said. "We're not Lance Armstrong here, but by golly, we can do things and inspire other women, and men too, to reach the highest heights."
For more information: www.rockymtn-teamsurvivor.org. 2007 Rocky Mountain Team Survivor at the Denver Danskin Women's Triathlon.

Dr. Bleyer:
☑ A great program that needs to include other cancers and males, and nutrition!
☑ We have three athletic teams for this year; maybe we enter Pole Pedal Paddle teams next year.
☑ We should consider equestrian and flyfishing, too, since our environment even more conducive to these activities than the Boulder, Colorado region

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The contribution of dragon boat racing to women's health and breast cancer survivorship

Parry DC.
Department of Recreation and Leisure Studies, University of Waterloo, Waterloo, Ontario, Canada.
Qual Health Res. 2008 Feb;18(2):222-33

This study and the next one suggest that exercise in groups, with the associated camaraderie and goal setting, may be more beneficial than individual programs

Survivorship is one of the least studied and thus least understood aspects of a breast cancer experience. Defined as a life-long, dynamic process, survivorship begins when people have completed medical treatment for breast cancer, yet live with the memories of their treatment and the possibility of a cancer reoccurrence. The numbers of women surviving breast cancer are growing, which means research on survivorship is imperative. In this article, dragon boat racing for breast cancer survivors is examined. Dragon boat racing has been adapted to a woman-centered, community-based leisure pursuit focused on life after medical treatment for breast cancer. Active interviews with 11 participants revealed that DBR contributes to women's social, emotional, physical, spiritual, and mental health. In turn, feeling healthy in these five dimensions enhanced the women's survivorship of breast cancer. The findings demonstrate the roles of leisure in the health and well-being of women who are breast cancer survivors.

Dr. Bleyer:
☑ Somehow *dragon boat racing* and *Canada* seem incongruous.
☑ DEFEAT is also based on the benefits derived from peer-pressure and leisure physical activities

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Psychosocial experiences of breast cancer survivors involved in a dragon boat program

Sabiston CM, McDonough MH, Crocker PR
University of British Columbia, Vancouver, BC.
J Sport Exerc Psychol. 2007 Aug;29(4):419-38.Links

Dragon boat racing in teams is another way of exercising to gain control collectively

This study explored psychosocial experiences of breast cancer survivors involved in dragon boat programs. Twenty women (mean age = 58.7, SD = 6.9) were interviewed for 45-60 min about their experiences as members of survivor dragon boat teams. Interviews were analyzed using constructivist grounded theory methods. The dragon boat program facilitated social support from women with common challenges and a shared understanding of survivorship. It also provided opportunities to (re)gain a sense of personal control, develop new identities as athletes, and overcome physical challenges. Together these elements contributed to positive psychological growth and linked to the literature on posttraumatic growth. Future physical activity interventions targeting breast cancer survivors may benefit from developing strategies that share key characteristics of dragon boating.

Dr. Bleyer:
☑ The personification in a dragon of DEFEATing cancer should not go unnoticed

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Physical activity may lower breast cancer risk [Prevention]

New York, MAR 18, 2008 (Reuters Health)

This study, from Poland, focuses the benefit of exercise in preventing breast cancer to the age range of the 50s, when it is becomes most likely to occur and be diagnosed.

A new study in the journal Epidemiology adds to evidence that women can cut their breast cancer risk by being physically active.

Dr. Beata Peplonska of the Nofer Institute of Occupational Medicine in Lodz, **Poland**, and her colleagues also found that the benefits appeared to be particularly strong for women who boosted their recreational activity levels in their 50s.

There is a growing body of research showing that very active women are significantly less likely to develop breast cancer than their sedentary peers, Peplonska and her team note, but there is less information on whether the timing of exercise during a woman's life also influences the risk, and whether moderate physical activity is also beneficial.

To investigate, the researchers compared 2,**176 women with breast cancer** and **2,346 healthy controls**. All were asked about their level of recreational and occupational physical activity throughout their adult lives.

The women with the **highest total adult lifetime activity were 20 percent less likely** to have developed breast cancer than the least active women, the researchers report in the medical journal Epidemiology.

Being in the top fourth of the group based on moderate-to-vigorous recreational physical activity conferred a 26 percent lower risk of the disease compared to being in the bottom fourth.

Furthermore, exercise was beneficial no matter whether a woman was slim, normal weight, or overweight; whether or not she had a family history of breast cancer; and whether or not she had reached menopause.

In fact, women who spent **more time in moderate-to-vigorous recreational activities in their 50s than they had in their 20s, 30s and 40s were 34 percent less likely to develop breast cancer**, while those who increased their activity the most were at 41 percent lower risk, Peplonska's team found.

They conclude: "Although the beneficial role of engaging in physical activity was observed for all age periods, our study suggests that increases in activity levels when a woman is in her 50s might be particularly relevant."

SOURCE: Epidemiology, March 2008

Dr. Bleyer:

☑ Just how many more countries need to demonstrate the value of physical activity in preventing breast cancer?

☑ The benefit would likely have been demonstrated to be even greater if good nutrition were combined with exercise.

☑ It's never too late to begin a regular regimen of physical activity, and it may be particularly important when typically, at the age of 50, many tend to reduce or stop exercising

Action speaks of health louder than weight

By Nanci Hellmich, USA TODAY- April 15, 2008

Regular exercisers should realize that even if they don't see big changes on the scales or in their measurements, they are still getting health benefits

"You can lose a lot of waist without losing a lot of weight," says Timothy Church, director of preventive medicine research at the Pennington Biomedical Research Center in Baton Rouge and former medical director of the Cooper Institute in Dallas. That is the conclusion reached by exercise expert Church and colleagues in a new book, Move Yourself: The Cooper Clinic Medical Director's Guide to All the Healing Benefits of Exercise (Even a Little).

That's important because belly fat, also called visceral or intra-abdominal fat, is considered particularly dangerous, he says. Research has indicated that people with too much fat in their midsection are at greater risk of developing dementia, including Alzheimer's disease.

Walking the weight off

Church and his co-authors — Tedd Mitchell, medical director at the **Cooper Clinic**, and health writer Martin Zucker — reviewed research conducted at the Cooper Institute. The institute focuses on research into physical activity and health, and the clinic offers consultation and treatment.

In one study, 464 postmenopausal women were directed to do different amounts of exercise, most of it walking. The four subgroups were sedentary or exercised about 73, 135 or 193 minutes a week. The women who were active lost 1 to 2 inches around their middles, even if they didn't lose much weight. They noticed that their pants fit better, Church says.

Other research has yielded similar findings. Scientists at the **Fred Hutchinson Cancer Research Center in Seattle** found that men and women who adhere to an exercise program for a year — about 45 to 60 minutes a day of walking, five to six days a week — had significant decreases in total body and belly fat. The exercisers who did the most — 60 minutes, six days a week — decreased their intra-abdominal fat by 10%, says Anne McTiernan, an internist and director of the Prevention Center at Fred Hutchinson.

Regular exercisers should realize that even "if they don't see big changes on the scales or in their measurements, they are still getting big health benefits," McTiernan says. "We saw **a decrease in hormones and other factors that contribute to cancer**."

Fat cells in the abdomen secrete chemicals that play a role in a number of diseases, Church says. "This deep visceral fat in the belly produces six times more bad chemicals than subcutaneous fat, the stuff you can pinch right under your skin. "Plus, the plumbing of visceral fat drains directly to the liver, where these chemicals interfere with the liver's ability to metabolize blood sugar and cholesterol."

Danger at 35 or 40 inches

Men have too much fat around their middle if their waist is 40 inches or more. For women, it's 35 inches or more, Church says.

Besides reducing belly fat, physical activity lowers blood pressure, cholesterol and the risk of diabetes and cancer. It reduces depression and anxiety, and it improves bone and joint health, sex drive, sleep and memory, he says.

But Church notes that fewer than 25% of Americans meet the minimum guidelines of being moderately active for 30 minutes five or more days a week, estimates show.

"The average American doesn't understand that other than not smoking, **exercise is the most important thing you can do for your health**," Church says. "They think exercising is a health suggestion on par with leaving mayonnaise off their sandwich."

He highly recommends wearing a step counter and keeping a physical activity log, especially at the beginning of an exercise program, because these tools help quantify current exercise levels and identify opportunities for activity throughout the day.

Church is always looking for ways to do more. He used to train for Ironman triathlons, but now that he has children, 3 and 5 years old, he jogs for 30 to 35 minutes two to three days during the week. On weekends, he and his wife put their kids in a jogger and go out for fast walk/jog for an hour or more. And they plan active weekends, such as walking around the zoo for an afternoon.

"The bottom line is that most people do not appreciate that exercising, even a little, is the quick fix that they are looking for to improve their health and quality of life."

Dr. Bleyer:

- ☑ Losing a *lot of waist without losing weight* appears to have real benefits that at least for improving quality of life applies to cancer patients/survivors
- ☑ Comparing exercise to *leaving mayonnaise off the sandwich* is, as implied, an inadequate analogy. Exercise is more like leaving out *most* of the detrimental foods.
- ☑ The described change on the ability to exercise after getting married and having to take care of a family with children is appropriate. It is also key in that sharing an exercise schedule with someone else, including one's own children, as a source of motivation can actually make it easier.
- ☑ The statement about reducing depression and anxiety and improving sex drive, sleep and memory should be appreciated; DEFEAT Cancer advocates exercise and nutrition (**E&N**) for its beneficial effect on quality of life

Exercise combats cancer-related fatigue

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

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

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

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

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

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

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

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

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

SOURCE: The Cochrane Library 2008.

Dr. Bleyer:

☑ The Cochrane Study Group, based in England, is the world's most respected organization that researches published scientific literature; they only study important health issues and their results and conclusions are generally considered unassailable.

☑ That exercise was definitively shown to reduce cancer-related fatigue *per se* is a wonderful finding, that DEFEAT Cancer submits would be even more strongly demonstrated with excellence in nutrition.

☑ DEFEAT Cancer would also expect the benefit to be even more obvious if the exercise intervention were started during therapy rather than afterwards.

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

Hem Onc Today - April 10, 2008

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

Jennifer Ligibel, MD, the Principal Investigator at Harvard Medical School is interviewed regarding her findings that showed a reduction in insulin levels may explain the benefit of exercise in prolonging survival after breast cancer

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

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

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

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

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

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

Dr. Bleyer:

☑ I believe that we are at the junction of recommending exercise, not *a step away*, for cancer patients

☑ DEFEAT Cancer is even more certain of this recommendation if excellence in nutrition is included with the advice

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

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

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

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

Background.: Given observational findings that physical activity reduces breast cancer risk, improves survival, and improves quality of life in breast cancer survivors, a need has been identified for randomized controlled trials that test the efficacy of exercise on biological mechanisms associated with breast cancer survival. The primary aims of the **Yale Exercise and Survivorship Study** were to 1) determine the feasibility of recruiting breast cancer survivors into a randomized controlled trial of the effects of exercise on biological markers and/or mechanisms associated with survival, 2) compare the effectiveness of various recruitment strategies on accrual rates and baseline characteristics, and 3) report adherence to the exercise trial.

Methods.: Seventy-five postmenopausal breast cancer survivors self-referred into the trial or were recruited through the Connecticut Tumor Registry and randomly assigned to an exercise (n = 37) or usual-care (n = 38) group. The exercise group participated in 150 min/wk of supervised gym-based and home-based aerobic exercise for 6 months. The usual-care group was instructed to maintain current physical activity level.

Results.: A total of 75 women (an accrual rate of 9.5%) were randomized to the trial. Rates of accrual were higher for women who self-referred into the study (19.8%) compared with women recruited via the cancer registry (7.6%); however, demographic, physiologic, and prognostic characteristics did not differ between the 2 recruitment strategies. On average, exercisers increased moderate- intensity to **vigorous-intensity aerobic exercise by 129 minutes per week** compared with 44 minutes per week among usual-care participants ($P < .001$). Women in the exercise-intervention group increased their average pedometer

steps by 1621 steps per day compared with a decrease of 60 steps per day among women in the usual-care group (P < .01).
Conclusions.: Findings from this study will provide useful information for investigators who are conducting exercise trials in cancer populations, clinicians who are treating women diagnosed with breast cancer, and exercise professionals who are developing community-based exercise programs for cancer survivors.

Dr. Bleyer:

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

Cancer Rx: Move?

Exercise May Have Role in Treatment
Washington Post - June 17, 2008
By Lindy Washburn
The standard weapons in the fight against cancer -- surgery, chemotherapy and radiation -- may soon be joined by something far simpler: exercise.
New research shows that regular physical activity helps reduce the risk of recurrence of breast cancer and slows the advance of prostate cancer.

Personal exercise trainers are becoming part of the cancer therapy program as more and more evidence documents the benefits and research is uncovering the mechanisms of benefit

In a few years, exercise will probably be prescribed regularly for cancer rehabilitation, said **Melinda Irwin**, an expert on cancer and exercise at **Yale University School of Medicine**. Personal trainers may join oncologists, surgeons and radiologists as members of the cancer-treatment team.
Exercise will become a "targeted therapy, similar to chemotherapy or hormonal therapy," Irwin said.
Any regular physical activity -- the equivalent of a 30-minute walk, five times a week -- will do.
Exercise offers many other advantages: It fights the fatigue caused by cancer treatment, calms anxiety and helps survivors feel better about themselves and their bodies.
Some **personal trainers** now specialize in working with cancer patients, and more will soon be **certified through a program of the American College of Sports Medicine**.
There are 10 million cancer survivors in the United States, 22 percent of them women who have had breast cancer, 17 percent of them men who've had prostate cancer. Exercise makes sense for most of them -- to live longer, avoid other health problems and just feel better.
Heart attack patients are now routinely put on exercise plans. But workouts for cancer patients are neither prescribed by doctors nor covered by health insurance.
"We're where cardiac rehab was 20 years ago," Irwin said. Once exercise was shown through research to prevent fatal heart attacks, 12 weeks of rehabilitation became the standard of care for most heart patients. In fact, many hospitals opened cardiac rehab centers.
Even with a low level of exercise, people **benefit psychologically**, said **Rita Musanti**, an oncology nurse practitioner at the **Cancer Institute of New Jersey**. With so many cancer survivors in the community, she'd like to see informal networks created to encourage recovering cancer patients.
Beth Wajts of Hillsdale, N.J., joined a YMCA's free "Living Healthy, Living Strong" class in January after her second surgery for breast cancer, followed by chemotherapy and radiation.
"I cannot believe the way I walked in and the way I walked out," she said.
"I never believed I would get out of that slump," Wajts said. "Now I feel incredible."
One of her classmates, Joyce Murray of Hawthorne, N.J., had three surgeries in an eight-week period last summer, then chemotherapy with many complications. No amount of sleep could cure her fatigue, she said.

After she started the twice-weekly program of resistance training and cardiac fitness, "I was surprised at the quick rebound," she said. "I really feel better."

Angelo Chiusano, 81, joined the Y's program after 43 radiation treatments for prostate cancer and surgery for an aortic aneurysm. Thanks to the camaraderie in the weight room, "I've gained a new family," he said. "It's made such a difference in my feelings."

After doing the weight-resistance circuit in the gym each session, he swam. "Then, when I go home, I walk a mile," he said. He has continued his workouts even though the program has ended.

Researchers are working to understand how physical activity helps fight cancer. Their findings so far suggest that exercise:

- **Reduces blood levels of insulin**, a substance that causes cells to divide and grow more quickly. Women with high levels of insulin have a slightly higher risk of breast cancer and a much higher rate of recurrence.
- **Helps repair infection-fighting T-cells**, restoring the immune system after it has been damaged by chemotherapy.
- **Reduces levels of circulating estrogen and testosterone**, two hormones linked to breast, endometrial and prostate cancers. Even with medication to suppress estrogen production, some estrogen is stored in fat cells. Exercise may help by converting fat to muscle.
- **Prevents weight gain and promotes weight loss**, important because obesity is associated with lower rates of survival for many forms of cancer. For women with breast cancer, obesity at the time of diagnosis and weight gain afterwards are associated with worse outcomes. The heavier and less active a person is, the more likely her cancer will return.

Most of the scientific work so far has focused on women with breast cancer. But studies have shown exercise also has positive effects for survivors of colorectal and prostate cancers. Among men older than 65, three hours of vigorous activity a week was associated with a decline in death from prostate cancer.

Exercise is now considered so beneficial that cancer experts are even encouraging patients to begin or resume exercise while treatment is underway.

Workouts might need to be scaled back in intensity and pace, but "evidence strongly suggests that exercise is not only safe and feasible during cancer treatment, but that it can also improve physical functioning and some aspects of quality of life," according to the American Cancer Society.

Lockey Maissoneuve, a 41-year-old personal trainer, went through two mastectomies and chemotherapy two years ago. She is now training for a triathlon.

"If you're in treatment, the first week or two you try to do anything, you need to take a nap," she said. "If there's a day you want to exercise, do it."

Wearing a wig was uncomfortably hot, so she switched to a kerchief. With her immunity reduced by chemo, she wiped down the equipment before she used it. She is now certified to work with cancer patients.

"The trainer is almost like your bodyguard," said Julie Percy of Parisi Sports Club in Midland Park, N.J., who also specializes in work with cancer patients. "We maneuver you to the right equipment, give you a sense of security."

When scar tissue forms after surgery, it limits flexibility. Percy helps women who have had mastectomies and underarm incisions restore their range of motion.

Trainers have to be particularly attentive when someone has had surgery to remove lymph nodes.

If the tiny valves in the vessels that transport lymph around the body fail, that can lead to lymphedema, a dreaded side effect of cancer surgery. The arm, for breast patients, or the leg, for prostate patients, becomes permanently swollen.

"We watch the amount of weights they use," Percy said.

She starts light and increases gradually. Women who have lymphedema, or a heightened risk of it, wear a compression sleeve.

Dr. Bleyer:

☑ The Washington Post, with help from Yale University and the Cancer Institute of New Jersey, has superbly summarized the state-of-art and state-of-science of exercise and cancer recurrence reduction

☑ I've heard that Medicare and other insurance organizations are planning to cove physical trainers (a Pilates instructor told me they already have); that would be wonderful.
☑ Meanwhile DEFEAT Cancer patients have access to physical trainers at Therapeutic Associates in Bend (thank you, Chuck Brockman) and Redmond (thank you, Karen Walsh) without charge!

Fitness related to lower cancer mortality in men with pre-diabetes, diabetes

HemOnc Today - April 24, 2008
Review of *Diabetes Care. 2008;31:764-769* by Stacey L. Adams
Compared with pre-diabetic men with low levels of fitness, those with higher levels of cardiorespiratory fitness may have a lower risk for cancer mortality, especially mortality from gastrointestinal tract cancers.

In men with colorectal, liver, esophageal, stomach and lung cancer who also had pre-diabetes, death from cancer was correlated with their degree of physical fitness

Researchers from the United States and Canada assessed 18,858 men with pre-diabetes and 2,805 men with diabetes to determine the relationship between fitness and mortality for all-cause and site-specific cancer mortality. The researchers followed the patients for about 16.4 years.
In an adjusted model, the researchers found a correlation between moderate and high fitness and a lower risk of cancer mortality in men with pre-diabetes, compared with those in the low-fitness group. Hazard ratios were 0.71 for moderate fitness and 0.76 for high fitness. A similar correlation was found in those with diabetes (HR 0.53 for moderate fitness and HR 0.44 for high).
Fitness was also related to a lower risk of mortality from gastrointestinal (HR 0.55), colorectal (HR 0.53), liver (HR 0.22) and lung cancer (HR 0.43) in all men, according to the researchers.

Perspective by Robert Blank, MD, PhD, Associate Professor of Medicine, University of Wisconsin: This is an interesting finding from a large cohort observational study. The main finding is that better aerobic fitness in men with impaired glucose tolerance or diabetes is associated with decreased cancer mortality, relative to those with poorer fitness. Since this is an epidemiological investigation, it should be interpreted as hypothesis-generating rather than hypothesis-confirming. The authors speculate that individuals with better fitness may experience lower levels of insulin, insulin-like growth factor-1 or pro-inflammatory cytokines, and that these changes, if verified, might underlie the observed mortality difference. Much work needs to be done to demonstrate that the reported observations reflect something more than a preexisting stratification of the cohort.

Dr. Bleyer:
☑ I agree with Dr. Blank that the authors' explanation as how fitness may have helped men liver longer with their cancer is speculative, especially because levels of insulin and insulin growth factor 1 (IGF-1) were not measured
☑ On the other hand, other studies (some reviewed in E&N News) have shown that cancer patients in whom physical activity lowered IGF-1 had longer survival; also, increasingly cancer cells are being found to have IGF-1 mechanisms as the basis of their malignant behavior and to be inhibited from growing by with IGF-1 inhibitors
☑ That the more fit patients lived longer is not speculative, however, since other studies in men have shown similar benefit, independent of the presence of diabetes or pre-diabetes
☑ The reduction in the mortality rate is impressive: 45% for gastrointestinal cancers, 47% for colorectal cancer, 78% for liver cancer and 57% for lung cancer
☑ And of course, DEFEAT Cancer would question how much greater these reductions would have been if nutrition had also been analyzed

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Effects of aerobic exercise on physical performance during myeloablative chemotherapy

J Clin Oncol 26: 2008 (May 20 suppl; abstr 9502)
M. de Wit, Z. Seyfi, Y. Süsse, K. Oechsle, C. Bokemeyer

Five times weekly, half-hour, stationary bicycle and muscle exercises during high-dose chemo-therapy increased physical performance, reduced fatigue, and decreased nausea and vomiting

Background: Cancer disease and treatment-related effects during long or recurrent hospitalization induce loss of physical performance of patients. The aim of this study were to evaluate the effects of aerobic exercise training on physical performance in patients with hematological malignancies or solid tumors

during **myeloablative anti-leukemic therapy or high dose chemotherapy followed by autologous peripheral blood stem cell transplantation**.
Methods: In this prospective controlled study **58 patients with were randomly assigned** to a training (TG, n= 29) or control (CG, n=29) group. The TG performed an individual **supervised exercise program with ergometer training for 10 min and three exercises using the main muscle groups for 20 min, five times per week during hospitalization**. Patients in the CG did not train, but they received physiotherapy as usually indicated. At the beginning and the end of each cycle of chemotherapy physical performance was evaluated with spiroergometry including lactate controls, immune system function with flow cytometry and blood samples. Treatment related side effects were documented by daily patients-interviews and quality of life by EORTC-QLQ-30 questionnaire.
Results: There was a significant **increase in physical performance** of the TG 8,96±24 W and a decrease in the CG -7,24±20 W, p=0,02, thus the study met the primary endpoint. At 2mmol/ml blood lactate concentration the TG achieved significant increased oxygen consumption VO2 (p=0,03) and minute ventilation VE (p=0,04) compared to the CG. Furthermore the TG achieved an increase in physical functioning score (p=0,04) and **complained significantly less days of fatigue** compared to the CG (p=0,05). The TG also consumed **less antiemetics** (p=0,01). The other variables showed no significant changes between both groups.
Conclusions: These results demonstrate positive effects of aerobic exercise on the physical performance and treatment-related symptoms **during myeloablative chemotherapy**. We suggest an enhanced physical activity intervention **during hospitalization** of cancer patients

Dr. Bleyer:
☑ This study tested the value of exercise in difficult group—bone marrow transplant and equivalent high-dose chemotherapy patients—in sufficient numbers to demonstrate meaningful and important results
☑ The primary (physical performance) and most secondary objectives were achieved; albeit quality-of-life *per se* as not improved
☑ That fatigue was reduced—despite the daily (weekday) exercise sessions—is not surprising; an extensive review from the Cochrane Collection that was in last month's ***E&N*** *News* (June 2008) clearly documents the correlation between exercise and fatigue reduction
☑ That the need for anti-nausea and anti-vomiting medication was also reduced is somewhat surprising since the effect of exercise on nausea and vomiting *per se* has rarely been included in studies of this type

Can a rehabilitative strength training program reverse muscle atrophy/weakness associated with androgen ablation therapy in prostate cancer patients?

J Clin Oncol 26: 2008 (May 20 suppl; abstr 9642)
C. L. Van Patten, A. W. Sheel, J. M. LaBreche, D. C. McKenzie

A 90-minute, three-times-weekly, strength training session for 12 weeks prevented loss of muscle strength and functional capacity in prostate cancer patients on androgen ablation therapy

Background: Men treated with hormone therapy for prostate cancer often experience fatigue, muscle loss,bone loss and weight gain, among other side effects. To determine the effects of a rehabilitative strength training program on muscle mass and functional capacity in prostate cancer patients receiving androgen ablation therapy 20 patients were randomly assigned to exercise or control groups.
Methods: Upper and lower extremity strength measurements were made using an algorithm that considers resistance and the number of repetitions. Muscle and fat mass were measured using DXA and functional capacity and lower extremity power were determined with a Wingate Cycle ergometer test. The baseline pre-test was completed prior to commencing hormone therapy and the post-test following a 12-week supervised strength training exercise program consisting of three 90-minute sessions per week.
Results: Eight patients acted as control (age= 71.6 yrs, ht=177 cm, wt=86.3 kg, BMI=27.6) and 10 completed the exercise trial (**age= 65.8 years**, ht=178 cm, wt=85.5 kg, BMI=27.0). Strength measurements in controls decreased (mean change=-3%) over the 12-week period. Strength increased significantly ($p<0.05$) with the chest press (15%), seated row (14%) and hamstring curl (22%) in exercisers and nonsignificant increases were observed in lat pull (12%) and leg press (4%). Mean change

in all exercises, E=+11%. Lean mass and fat mass did not change significantly (p>0.05). Peak power (PP) and total work (TW) decreased in controls (PP=-11%; TW=-10%) and increased in exercisers (PP=+7%; TW=+9%) (p<0.05).
Conclusions: This pilot data suggest that a 12-week supervised strength training program helps prostate cancer patients maintain or increase muscle strength and functional capacity while undergoing androgen ablation therapy.

Dr. Bleyer:
- ☑ That a comparison of only10 subjects who completed the exercise trial with 8 control subjects led to statistically significant benefits in muscle strength and work capability is impressive
- ☑ Equally impressive is that 10 of 12 patients completed the ambitious exercise schedule
- ☑ When a larger trial is undertaken to determine, the results will have to be evaluated according to *intent to treat* (whether or not the exercise schedule was completed) in order to evaluate the full potential (or lack thereof) of the exercise regimen
- ☑ Also, ideally, nutrition and exercise should be combined in a definitive comparison, as *DEFEAT Cancer* emphasizes

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Effect of aerobic exercise training on cardiorespiratory fitness and quality of life in postsurgical non-small cell lung cancer patients

L. Jones, J. Garst, N. Eves, M. West, S. Mabe, J. Crawford
J Clin Oncol 26: 2008 (May 20 suppl; abstr 7577)

A stationary bicycle session three times weekly for 14 weeks was not only feasible after surgery in patients with early lung cancer, it improved lung function, quality of life, and amount of fatigue

Background: The effects of standard NSCLC adjuvant therapy (i.e., pulmonary resection, adjuvant chemotherapy) together with deconditioning secondary to treatment has a profound negative impact on patients functional capacity leading to increased susceptibility to other common age-related diseases, poor quality of life, and likely premature death. Accordingly, we conducted a feasibility study examining the effects of an aerobic exercise training program on cardiorespiratory fitness and QOL among newly diagnosed postsurgical NSCLC patients.
Methods: Using a single-group design, 20 patients with newly diagnosed, histologically confirmed stage I-IIIA NSCLC who had undergone complete surgical resection were recruited. Exercise training consisted of three endurance cycle ergometry sessions per week at 60% to 100% of baseline peak oxygen consumption (VO2peak) for 14 weeks. VO2peak was assessed using a maximal, incremental, cardiopulmonary exercise test with expired gas analysis. Overall QOL and fatigue was assessed by the Functional Assessment of Cancer Therapy-Lung (FACT-L) scale.
Results: Nineteen patients completed the study and overall adherence rate was 82% (range: 28% - 100%). Intention-to-treat analysis indicated that VO2peak increased 1.1 mL.kg.min-1 (95% CI, -0.2 to 2.5; p=0.095) whereas FACT-L increased 10.6 points (95% CI, -1.0 to 22.2; p=0.071) and fatigue decreased 6.9 points (95% CI, 1.0 to 12.8; p=0.026) from baseline to postintervention. Per protocol analysis indicated that patients who attended >80% exercise sessions (n=13) increased 1.7 mL.kg.min-1 (95% CI, 0.2 to 3.1; p=0.028) whereas FACT-L increased 13 points (95% CI, -1.9 to 28.2; p=0.081) and fatigue decreased 7.7 points (95% CI, 0.3 to 15.1; p=0.042). Linear regression analysis indicated that change in VO2peak was associated with total exercise volume (r=0.54, p=0.016) but not exercise adherence (r=0.38, p=0.105).
Conclusions: Postoperative aerobic exercise training is feasible and associated with significant improvements in VO2peak, QOL, and fatigue in NSCLC patients, particularly if acceptable adherence is achieved. This benefit may have important implications for post-operative recovery and survivorship in operable NSCLC patients.

Dr. Bleyer:
- ☑ That 19 of 20 patients completed a 14-week, three-times-per-week, in-hospital exercise schedule is extraordinary
- ☑ If lung cancer patients can do this after chest operations, most cancer patients should be able to do also

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A pilot study of an exercise program for patients with advanced non-small cell lung cancer

J. S. Temel, J. Greer, S. B. Goldberg, P. Ostler, P. D. Vogel, W. F. Pirl, T. J. Lynch, D. C. Christiani, M. R. Smith

J Clin Oncol 26: 2008 (May 20 suppl; abstr 9593)

Eight weeks of twice-weekly 90-minute exercise sessions in patients with advanced lung cancer reduced lung cancer symptoms

Background: The benefit of exercise for lung cancer patients is unknown. Although physical activity improves quality of life and fatigue for certain cancer populations, co-morbid lung disease and impairment may make exercise impractical in advanced lung cancer patients. In this study, we examined the feasibility of an exercise program for patients with advanced NSCLC.

Methods: Patients with newly diagnosed advanced NSCLC and good performance status were eligible to participate. For the intervention, a senior physical therapist facilitated 90-minute, twice-weekly exercise sessions of weight training and aerobic exercise at **Massachusetts General Hospital** over an eight- week period. The primary endpoint was the feasibility of the program as defined by compliance with the exercise sessions. Secondary endpoints included functional capacity, measured by the 6-minute walk test (6-MWT), as well as quality of life, lung cancer symptoms, and fatigue, measured by the FACT-lung and FACT-fatigue scales.

Results: Between 10/04 and 8/07, 25 patients (median age=68 years; 74% female) were enrolled, the majority of whom had stage IV disease (84%). Twenty patients (80%) underwent the baseline physical therapy evaluation. Twelve patients (48%) completed the program, with 11 patients attending all 16 sessions, and 1 patient completing 15 sessions prior to death. An additional 5 patients attended at least 6 sessions before declining in health status or being admitted to the hospital or hospice. Overall, 18/25 (72%) participated in the program as long as physically able. For the participants who completed baseline and post study assessments, there was a significant reduction in lung cancer symptoms.

Conclusions: While the majority of participants attempted the exercise program (72%), just under half were able to complete the intervention. Those who completed the program experienced an improvement in their lung cancer symptoms. However, home-based or briefer exercise interventions may be more feasible in this population.

Variable (N=11)	Base Mean (SD)	Post Mean (SD)	p-value
6- MWT (meters)	410.55 (83.28)	435.73 (72.66)	.11
FACT-L Total Score	103.44 (14.19)	104.66 (14.51)	.72
Lung Cancer **Symptom** Scale	20.23 (4.70)	22.77 (3.01)	**.04**
FACT-Fatigue Scale	35.35 (12.64)	38.77 (11.42)	.35

Dr. Bleyer:

☑ Attempting two 90 minute, hospital-based exercise sessions twice weekly for 8-weeks was ambitious, especially for lung cancer patients with advanced disease

☑ That the plan was feasible in only half the patients is not surprising

☑ The table indicates that fatigue was not improved with the exercise schedule

☑ On the other hand, there was no control group of patients who did not participate in an exercise program and who, if it were available for comparison, may have a significantly worsening of fatigue that was prevented by exercise

☑ *DEFEAT Cancer* maintains that the combination of nutrition and exercise would have had greater beneficial effects.

Physical activity does not promote lymphedema after axillary clearance

Elsevier Global Medical News. 2008 Jun 1, K Wachter

CHICAGO (EGMN) - Women with breast cancer don't need to limit their physical activity following axillary clearance for fear of developing arm lymphedema, according to a prospective study presented in a poster Friday, June 30, at the American Society of Clinical Oncology.

High levels of exercise did not increase the frequency or severity of lymphedema associated with axillary dissection and lymph node removal

Ms. Åse Sagen and her colleagues at **Ullevål University Hospital, Oslo**, randomized 204 women between the ages of 32 and 72 years to high or low levels of activity after axillary clearance. She reported there were no significant differences between the two cohorts in average arm volume; in the volume of a woman's affected arm, compared with her unaffected arm; or in occurrence of lymphedema.

Women with breast cancer are generally restricted from any physical activity involving the affected limb following axillary clearance because of concern that it might initiate or aggravate lymphedema. According to the researchers, there is little data to support this precaution.

They placed no such restrictions on 104 women randomized to the high level of activity, whereas 100 women in the low-level group were limited in the physical activity they were allowed to perform with the affected limb.

The women were assessed at baseline, at 3 and 6 months, and at the 2-year follow-up. The primary outcomes were arm volume - the difference (mL) in volume between a woman's affected and unaffected arms - and arm lymphedema. Arm lymphedema was defined as a 10% increase in the volume of the affected arm, compared with the volume of the control arm.

These new findings confirm recent data that indicate that exercise may not be a trigger for lymphedema, **Dr. Barbara A. Murphy of the Vanderbilt-Ingram Cancer Center** in Nashville, Tenn., said during a formal discussion of the poster. "We can advocate that our patients maintain a good activity level, so they can maintain a good level of health," she said.

The researchers also found that a **body mass index greater than 25** kg/m², surgery on the dominant side, and baseline volume differences between the affected and control arm greater than 1 mL were **significant predictors of arm lymphedema**.

Dr. Bleyer:

☑ Together with another report *DEFEAT Cancer* previously reviewed, the results of this study should put to rest the concept that exercise with is a cause of, or contributes to, lymphedema in breast cancer patients

☑ This study also found that lymphedema is more common in overweight (BMI >25) patients

Randomized trial of yoga in women with breast cancer undergoing radiation treatment: Long-term effects

J Clin Oncol 26: 2008 (May 20 suppl; abstr 9639)

L. Cohen, K. D. Chandwani, G. Perkins, B. Thornton, B. Arun, N. V. Raghuram, H. R. Nagendra

University of Texax M.D. Anderson Cancer Center

Six weeks of biweekly yoga sessions during radiation were associated with a better quality of life, including less fatigue, sleeplessness, and depression and with a sense of more meaning of life when measured one and three months after radiation

Background: A yoga program was developed that included postures, a breathing exercise, a relaxation technique, and meditation for patients with breast cancer who were undergoing radiotherapy. We previously reported on the short-term benefits of yoga at improving physical functioning and general health perceptions at the end of radiotherapy.

Methods: Women participated in bi-weekly classes during their 6 weeks of radiation treatment. Sixty-one women with breast cancer were randomly assigned to either the yoga program or to a waitlist control group. Patients completed measures of intrusive thoughts (Impact of Events Scale: IES), depressive symptoms (CES-D), sleep disturbances (Pittsburgh Sleep Quality Index), fatigue (BFI), quality of life

(SF-36), and Finding Meaning in Cancer (FM) at baseline, 1 week, and 1 and 3 months after the last radiation therapy. We report on the outcomes 1 and 3 months after the end of radiotherapy.
Results: The average age was 52, 3% stage 0, 28% stage I, 43% stage II, and 26% stage III, 48% had undergone breast-conserving surgery, and 75% had received chemotherapy. Analysis of covariance, controlling for baseline, age, stage of cancer, time since diagnosis, type of surgery, and prior chemotherapy (yes/no) revealed that the yoga group had significantly higher IES scores 1 month after radiotherapy (adjusted means: yoga 7.1 vs. control 4.1, P=0.01) and significantly higher FM scores 3 months after radiotherapy (adjusted means: yoga 52.8 vs. control 47.3, P=0.01). There were no other group differences on any scales. Interestingly, there was a positive correlation between IES scores at 1 month and FM scores at 3 months (P=0.02) suggesting that the more intrusive thoughts at 1 month the greater the finding meaning at 3 months. Regression analyses including group and IES scores at 1 month in predicting FM scores at 3 months revealed that IES scores remained a significant predictor in the model and group was no longer significant, suggesting that intrusive thoughts mediated the effects of group on FM scores.
Conclusions: The results indicated that the yoga program was associated with increased finding meaning in the cancer experience 3 months after the end of radiotherapy and that this was mediated through increases in intrusive thoughts at 1 month.

Dr. Bleyer:
- ☑ Despite a relatively small group of randomized patients and relatively light exercise and exercise schedule, a statistically significant better quality and meaning of life was reported by patients in the exercise group
- ☑ That the benefits lasted for at least 3 weeks after radiation therapy was completed is impressive
- ☑ Again, *DEFEAT Cancer* would expect that if nutrition were combined with the exercise program the benefit would have been even greater and broader in scope

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Antidepressant effects of a yoga program in breast cancer patients undergoing conventional treatment: A randomized controlled trial

J Clin Oncol 26: 2008 (May 20 suppl; abstr 9556)
B. S. Ajaikumar, R. M. Raghavendra, S. Patil, D. B. Ravi, S. B. Srinath, K. S. Gopinath, R. Nagarathna

Daily sessions of yoga (1 hour) dramatically reduced depression during radiation therapy and during chemotherapy in breast cancer patients

Background: Depression is common among breast cancer patients and warrant clinical attention because of their adverse effects on quality of life in cancer patients. We compared the effects of a yoga program with supportive therapy on self-reported symptoms of depression in breast cancer patients undergoing conventional treatment.
Methods: Thirty-eight stage II and III breast cancer outpatients were randomly assigned to receive yoga (n = 18) or brief supportive therapy (n = 20) over a 24-week period during which they underwent surgery followed by adjuvant radiotherapy and chemotherapy. Intervention consisted of yoga sessions lasting 60 minutes daily while the control group was imparted supportive therapy during their hospital visits as a part of routine care. Primary outcome measure was self reported Beck's Depression Inventory and secondary outcomes were symptom checklist quality of life assessed using modified version of Memorial symptom assessment scale and Functional living index of cancer respectively. Assessments were done at baseline, after surgery, before, during, and after radiotherapy and chemotherapy.
Results: A GLM repeated measures ANOVA showed overall decrease in depression ($p < 0.001$) in yoga group as compared to controls. However, there was no significant group by time interaction effects. Post hoc tests using Bonferroni correction showed significant decreases in depression following surgery ($p = 0.01$), during radiotherapy ($p = 0.005$) and during chemotherapy ($p < 0.001$) in yoga group as compared to controls. There was a positive correlation between depression score with symptom severity and distress during conventional treatment intervals and negative correlation with quality of life.
Conclusions: The results suggest that yoga can be used for managing self reported depressive symptoms in breast cancer patients undergoing conventional treatments.

Dr. Bleyer:

☑ The remarkably high statistical significance with a small number of randomized patients underscores the potency of yoga in reducing depression during radiation therapy and during chemotherapy.

☑ *DEFEAT Cancer* points out again that combining nutrition with yoga (and with other forms of exercise) would likely have led to even greater benefits

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Exercise helps improve cancer-related fatigue

33rd Annual Congress of the Oncology Nursing Society
Ruth van Gerpen, RN, MS, OCN, as reported by HemOnc Today, June 10, 2008, p. 16

In cancer patients, 20-30 minute sessions of mixed exercise 4 times per week together with an educational, supportive care program significantly improved fatigue, depression and overall quality of life

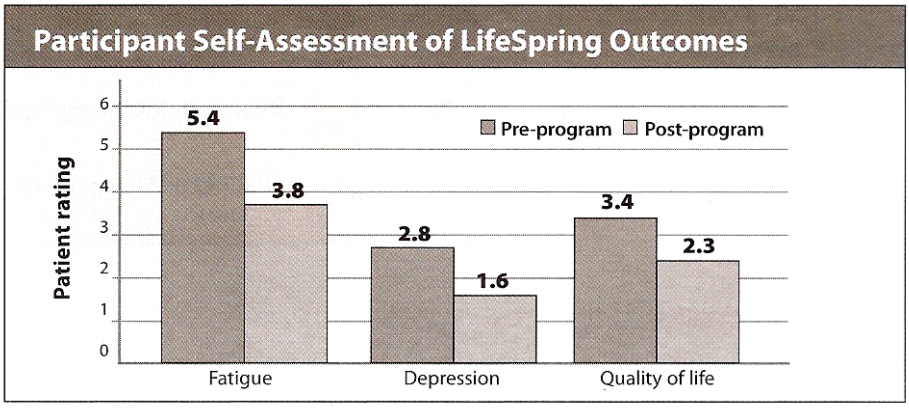
Exercise eases the burden of cancer-related fatigue, depression and decreased quality of life, according to Ruth van Gerpen, RN, MS, OCN, a clinical nurse specialist at "The prevalence of fatigue is between 60% and 96% among patients sill on treatment," van Gerpen said. "Fatigue can persist in patients with cancer for months or years following completion of treatment."

Results from prior research have supported the use of exercise as an intervention to reduce fatigue, according to van Gerpen. To test this intervention, she and colleagues initiated the LifeSpring Program, a **12-week exercise and education program** for people with cancer diagnosed in the past two years or who are still on active treatment. It was designed to impact fatigue associated with cancer and cancer treatment. To date 47 participants aged between 32 and 77 have participated.

The patients had to rate their level of fatigue, depression, pain, sleep quality and quality of life prior to beginning the program. They repeated the self-assessment mid- and post-program.

Exercise was required at least two times per week with 20 to 30 minutes of cardiovascular exercise and 20 to 30 minutes of additional exercise through a method such as yoga, pilates, strength training or stretching. Education classes included information about a wide variety of topics such as energy conservation, relationships, sleep, and spirituality. There was a statistically significant improvement seen between pre-program and post-program outcomes (see chart).

Patients enrolled in the program also benefited from the supportive environment, sharing and discussion, and a sense of belonging and being understood, van Gerpen said.



Dr. Bleyer:

☑ This study is noteworthy because it was accomplished by oncology nurses, produced statistically significant results within a 3-month program, included patients on treatment, and tackled the most common side effect of cancer and cancer treatment: fatigue

☑ What it doesn't rule out is that the improvement may have occurred regardless of the LifeSpring program since there was no control group of matched patients who were followed over the same time interval and environment

☑ The contribution of the support group aspect of the program should not be underemphasized and is appropriately recognized by the principal investigator

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The Impact of Medical Qigong (traditional Chinese medicine) on fatigue, quality of life, side effects, mood status and inflammation of cancer patients: Randomized clinical trial

J Clin Oncol 26: 2008 (May 20 suppl; abstr 9565)
B. Oh, P. Butow, B. Mullan, S. J. Clarke, P. Beale, D. Rosenthal

Ten weeks of gentle exercise and meditation/breathing relaxation based on the Chinese Medicine theory of energy channels improved quality of life, including sexual activity, for cancer patients

Background: The quality of life (QOL) of cancer patients is often diminished due to the side effects of treatment and symptoms of the disease itself. Medical Qigong (MQ), coordination of **gentle exercise** and relaxation through meditation and breathing exercise based on the Chinese Medicine theory of energy channels, may improve health and mental wellbeing and reduce the symptoms of cancer patients. However, there have been few studies of MQ in the cancer setting, and none exploring its impact in a randomized clinical trial (RCT) on QOL, side effects (including fatigue), mood status and inflammation. This was a pilot study preceding a full RCT of this intervention.
Methods: Forty-three patients diagnosed with a range of cancers, were randomly assigned to two groups: a control group (n=21) that received usual health care and an intervention group (n=22) who participated in a MQ program for 10 weeks in addition to receiving usual health care at the hospital. Randomization was stratified by completion of cancer treatment (n=20) or under active cancer treatment (n=23). Patients completed measures before and after the program. Cancer related fatigue was measured by FACT-F, quality of life and symptoms were measured by the FACT-G, mood status by POMS. The inflammatory marker serum C-reactive protein (CRP) was also monitored serially.
Results: The Medical Qigong intervention group reported clinically significantly improved fatigue (t30 =2.67, p=0.012, mean difference=5.9) and overall QOL (t30 =1.22, p=0.017, mean difference =10.2) compared to the control group. Analysis of the FACT- G subscales revealed that satisfaction with sex life (t12 =2.38, p=0.035) was significantly higher in the MQ group. The MQ intervention also reduced side effects (nausea, pain and insomnia), mood and inflammation biomarker (CRP) but these differences were not statistically significant compared to the control group.
Conclusions: Data from the study suggests that MQ with usual health care can improve fatigue, satisfaction with sex life and QOL in cancer patients. This pilot study supports the use of MQ as an intervention for cancer patients. However, further research with a larger sample size is needed.

Dr. Bleyer:
☑ Despite the relatively few patients randomized (in this phase II study), statistically significantly differences were nonetheless achieved with 10 weeks of gentle exercise and medication in improving the quality of life, enhancing sex life, and reducing fatigue
☑ *DEFEAT Cancer* suggests that combining nutrition with exercise/meditation would have an even greater effect

Effects of voluntary wheel running on prostate cancer growth and progression in LAPC-4 xenografts [Laboratory Study]

Michael Potter, Stephen J. Freedland, Susan Poulton, Mark Dewhirst, Lee W. Jones, **Duke University**
2008 American Association for Cancer Research Annual Meeting, April 12-16, 2008, San Diego, CA

In mice, voluntary exercise (having a running wheel in the cage) was associated with an increase in the rate of growth of prostate cancer cells injected into the mice

Background: Preliminary evidence suggests that exercise training may be an effective supportive intervention to enhance quality of life and to reduce treatment related symptoms in prostate cancer patients. No study to date has examined the effects of exercise on prostate cancer tumorgenesis using in vivo models. The purpose of this study is to evaluate whether exercise training can modulate tumor growth in vivo using an LAPC-4 xenograft model. Methods: Fifty aythmic male mice consuming an ad libitum Western diet (40% fat, 44% carbs, and 16% protein) were subcutaneously implanted with LAPC-4 prostate cancer (106 cells per mouse) and randomly assigned to voluntary wheel running (n=25) or a non-intervention control group (n=25). Voluntary wheel running was recorded continuously for the entire

duration of the study. Tumors were measured twice weekly and mice were sacrificed when tumor volumes reached 1000 mm3. Results: The primary endpoint will be tumor growth delay, calculated as the number of days for each tumor reach 1000 mm3. Tumor growth survival growth curves will be compared between groups using Cox model for pairwise comparisons. Serum and tumor samples will be collected at the time of sacrifice and analyzed for postulated biologic mechanisms underlying the association between exercise and prostate tumorgenesis. We anticipate data collection will be completed by February 2007, and final results will be presented at the time of the meeting. Conclusions: This study is essential to understand the efficacy of exercise as a potential intervention to inhibit prostate cancer growth and the biologic mechanisms underlying this relationship.

Dr. Bleyer:

- ☑ Extrapolations from mice to men (and women) are fraught with all kinds of difficulties
- ☑ Of 1000s of chemicals that are effective in treating mice with cancer work in people; the same can be expected of factors that promote cancer growth in mice
- ☑ In this study, the mice were not treated for their cancer (which we try to avoid in people) and the cancer did not arise in them (it was injected), making the extrapolation to people all the more tenuous
- ☑ Also, no study of exercise in people with cancer has shown increased cancer growth; they either have demonstrated no benefit or, more frequently, a reduction in cancer occurrence (e.g., above article) or cancer recurrence
- ☑ Please read the next study, which was presented at the same meeting and shows that mice allowed to exercise in the same can also have less cancer growth after pancreas tumor cells are injected with or without additional therapy of the cancer

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Exercise, alone and in combination with an anti-CEA vaccine, reduces pancreatic tumor cell growth and enhances survival in mice [Laboratory Study]

Connie J. Rogers, Kenneth W. Hance, David A. Zaharoff, Susan N. Perkins, Stephen D. Hursting, Jeffrey Schlom, John W. Greiner. National Cancer Inst., Bethesda, MD, University of Texas, Austin, TX, Univ, of Texas, Dept. Carcinogenesis UT-MD Anderson Cancer Center, Austin, TX

In mice, voluntary exercise (having a running wheel in the cage) was associated with a decrease in the rate of growth of pancreas cancer cells injected into the mice, and the benefit of exercise was further improved with a simultaneous cancer treatment

Regular exercise is strongly associated with reduced risk of colon, breast, and endometrial cancer, and possibly pancreatic and lung cancer. Furthermore, regular exercise is associated with a reduced risk of recurrence and death from colorectal and breast cancer. One mechanism that may mediate the protective effect of exercise on tumor incidence and/or recurrence is an enhancement of anti-tumor immunity. We have previously demonstrated that **exercise significantly enhances NK cell function and vaccine responses** in normal mice. Our laboratory has also demonstrated in both preclinical and clinical studies that therapeutic cancer vaccines targeted against the tumor antigen, carcinoembryonic antigen (CEA), enhance anti-tumor immunity and increase survival. The goal of this study was to explore the effects of exercise, alone and combined with a therapeutic cancer vaccine, on in vivo tumor growth and survival. The murine Panc02.CEA pancreatic tumor cell line was chosen because it shares many characteristics with human pancreatic tumors and because in vivo anti-tumor immunity against the parental cell line is mediated by NK and CD8+ T cells. CEA.Tg mice were randomized to 1 of 4 treatment groups (n=16/group): vehicle (HBSS), vaccine (V), exercise (EX), or vaccine + exercise (V+EX). Mice in the EX and V+EX groups had access to voluntary running wheels for 8 weeks prior to tumor implantation (10^6 cells) and throughout the vaccination protocol (17 wks) and ran 3.5 ± 0.4 and 3.0 ± 0.3 mi/day, respectively. Mice in the V and V + EX groups received a primary vaccination with 10^8 pfu recombinant vaccinia (rV)-CEA/TRICOM + 10^7 pfu recombinant fowlpox (rF)-GMCSF when mean tumor volume reached 30 mm3, followed by booster vaccinations with 10^8 pfu rF-CEA/TRICOM + 10^7 pfu rF-GMCSF at 2-wk intervals for 15 wks. At day 41 post tumor implantation, the mean tumor volumes in the HBSS, V, EX and V+EX groups were significantly different, 655 ± 138, 381 ± 105, 156 ± 61, 100 ± 46, respectively ($P<0.001$), and all treatment groups had enhanced survival ($P<0.001$). Furthermore, the V+EX group had significantly greater survival than the V group ($P<0.05$). These results

demonstrate that **exercise alone (in a prevention model, 8 wks prior to tumor implantation) is highly effective in reducing the growth of an immunogenic tumor and significantly increases survival**, suggesting that **exercise may augment in vivo immunosurveillence mechanisms**. Furthermore, these results demonstrate that exercise is a viable intervention that may yield significant clinical benefit when used in combination with therapeutic cancer vaccines.

Dr. Bleyer:

- ☑ Typical of the mice experiments, opposite results can be demonstrated.
- ☑ With the ability to do 1000s of experiments in mice in comparison to what can be done in people, there should be little surprise to have experiments reported in mice with paradoxical results
- ☑ One feature of this study that is better than the above report is that the mice were also treated for their cancer (as people would be treated) and the two together (exercise and cancer treatment) were more effective than either alone
- ☑ Remarkably, this study showed a greater reduction in the cancer with exercise alone than with the cancer treatment (a vaccine) alone
- ☑ Mice are one of men's best friends, but just like human friends, they can teach us different lessons

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Lifelong running reduces oxidative stress and degenerative changes in the testes of mice
[Laboratory Study]

J Clin Oncol 26: 2008 (May 20 suppl; abstr 14693)
S. Chigurupati, T. G. Son, D. H. Hyun, J. D. Lathia, T. V. Arumugam, M. P. Mattson

In adult mice, daily exercise maintained testicular function whereas sedentary behaviors led to testis cell damage, sperm reduction, and lower testosterone levels

Background: One plausible effective link between lifestyle (diet and exercise) and cancer risk is oxidative stress. Regular exercise can counteract the adverse effects of aging on the musculoskeletal, cardiovascular systems and cancer risk. In males the normal aging process is associated with reductions in testosterone production and impaired spermatogenesis, but the underlying mechanisms and their potential epigenetic modification by exercise are unknown.
Methods: Here we report that lifelong regular exercise (running) in mice protects the testes against age-related cellular alterations, and that this effect of running is associated with decreased amounts of oxidative damage to proteins, lipids and DNA in spermatogenic and Leydig cells.
Results: Six month-old male mice were divided into a sedentary group and a group which ran an average of 1.75 km/day, until the mice reached the age of 20 months. Seminiferous tubules of runners exhibited a full complement of cells at different stages of the spermatogenic process and a clear central lumen with large numbers of spermatozoa, in contrast to sedentary mice which exhibited disorganized spermatogenic cells and lacked spermatocytes in a central lumen. Levels of protein carbonyls, nitrotyrosine, lipid peroxidation products and oxidatively modified DNA were significantly greater in spermatogenic and Leydig cells of sedentary mice compared to runners. Serum testosterone levels are significantly lower in sedentary aged mice compared to runners. These findings suggest that lifelong regular exercise suppresses aging of the testes by a mechanism that involves reduced oxidative damage to spermatogenic and Leydig cells.
Conclusions: These findings suggest that lifelong regular exercise suppresses aging of the testes by a mechanism that involves reduced oxidative damage to spermatogenic and Leydig cells and plausible cancer risk.

Dr. Bleyer:

- ☑ The benefits of regular and long-term exercise may now, according to these laboratory studies, include maintenance of fertility and virility in men
- ☑ I don't know if testicular cancer is more common in sedentary men, but I would suspect that testicular cancer is more likely to recur in men who do not exercise, based on the biochemical effects measured in this experiment

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Walking an hour a week cuts colon cancer risk *[Prevention]*

Jan 21, 2008

NEW YORK (Reuters Health) - A large new study confirms that physical activity reduces colon cancer risk.

Among 40- to 65-year-old females, walking just an hour a week significantly reduced the occurrence of colon cancer; walking more than an hour week reduced it further.

While just an hour of walking a week seemed to protect against the disease, the more strenuously women exercised, the lower their risk, **Dr. Kathleen Y. Wolin** of **Washington University** School of Medicine in St. Louis and colleagues found.

"Our findings suggest that participation in lower intensity activities may be sufficient to reduce risk though more vigorous activity provides comparable or perhaps additional risk reduction," they write in the International Journal of Cancer.

Research showing that exercise reduces colon cancer risk has been "consistent and convincing," Wolin and her team say, but questions remain about the intensity of exercise necessary to reduce risk.

To investigate, they followed at **79,295 women, aged 40 to 65 years old,** for 16 years, during which time 547 developed colon cancer. All were participating in the **Nurse's Health Study**.

Women who walked for 1 to 1.9 hours each week were 31 percent less likely to develop colon cancer than those who didn't walk at all, the researchers found. And women who exercised at moderate or vigorous intensity for more than 4 hours weekly were at 44 percent lower risk of colon cancer than those who exercised for less than an hour a week.

There was no link between exercising over the long term and colon cancer risk, but the researchers note that the number of long-term exercisers may have been too small to detect a relationship.

They conclude: "Leisure-time physical activity should be encouraged for all adults for health benefits, including colon cancer prevention."

SOURCE: International Journal of Cancer, December 15, 2007.

Dr. Bleyer:

☑ This study appears to demonstrate that minimal exercise (walking 1 hour weekly) protects against colon cancer

☑ This study only addressed colon cancer (since many prior studies have associated physical activity with a reduced risk of colon cancer); it should have at least indicated whether other cancers were (or will be) investigated

☑ If moderate walking is also true for cancer recurrence, adding cancer-reducing nutrition to the equation should amplify the benefit.

Exercise and reduced breast cancer risk: A multinational study [Prevention]

Luke Ratnasinghe, Michael Seddon, Rama Modali, Teresa Lehman. Genomic Nanosystems, Beltsville, MD, BioServe Biotechnologies, Ltd., Beltsville, MD

Exercising 15 minutes a day for less than 3 times a week helps prevents breast cancer in persons of all races and ethnicities

Exercise and physical activity are modifiable risk factors for cancer. There is little data evaluating the relationship between exercise and breast cancer risk comparing different ethnic groups. We evaluated the association between exercise and breast cancer risk among 1468 breast cancer cases and 4865 non-cancer controls in the Global Epidemiology Study (GES). The GES is a multinational study to assess disease risk factors with subjects recruited from countries including the United States, Tunisia and Poland. The GES is linked to the Global Repository® that houses biomaterial including blood, serum, DNA, RNA, frozen tissue, formalin-fixed paraffin embedded tissues, and pathology slides. For breast cancer, newly diagnosed subjects provided informed consent and were asked about exercise activity during in-person interviews. The same survey instrument was used for all subjects in this study, following translation to the local language. For all subjects combined, the multivariate-adjusted adds ratio (OR) was 0.5 (95% confidence interval (95% CI): 0.4-0.7) for women who exercised once per week or more after adjusting for age, race, BMI and packyears of smoking. **All ethnic groups in the study population, Caucasian-**

Americans, African-Americans, Hispanic-Americans, Tunisian-Arabs, and Polish-Caucasians, were at 50% or greater reduced risk for breast cancer if they exercised once or more per week. **Women who exercised 4 times per week or more did not gain any additional reduced breast cancer risk**. The amount of time spent exercising per session was also significantly associated with reduced breast cancer risk. **Women who exercised 15 minutes per session or more were at 40% or greater reduced risk for breast cancer** (OR 15-30 mins: 0.5 (95% CI: 0.4-0.7, OR greater than 30 Mins: 0.6 (95% CI 0.5-0.7) in the multivariate model compared to women who exercised less than 15 minutes. This study shows that regular exercise has the potential to reduce breast cancer risk among all women regardless of race.

Dr. Bleyer:

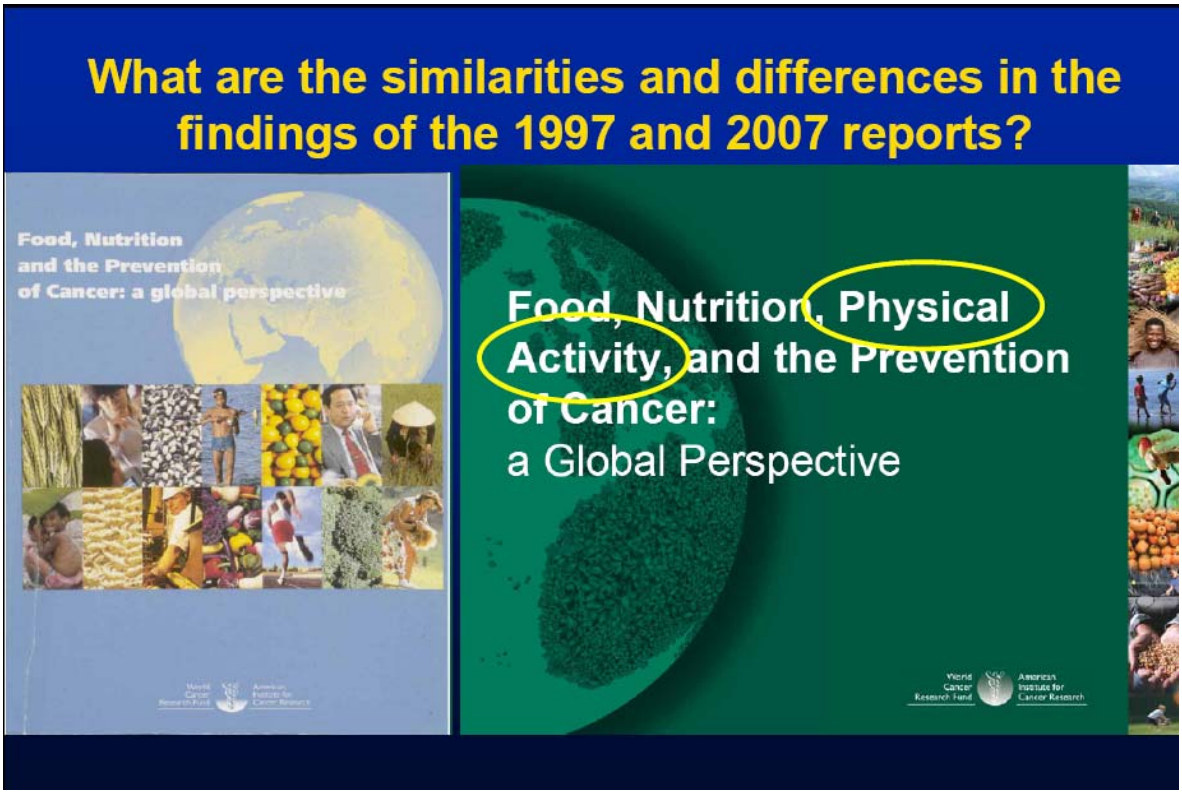
- ☑ Whenever a primary prevention article such a this one is included in *E&N News*, remember to be careful in applying the result to preventing **re**currence of cancer
- ☑ It could well be that more exercise may be necessary to prevent **re**currence of cancer in one who has already been diagnosed to have it than to prevent it in the first place
- ☑ We really don't need any more evidence that physical activity substantially reduces the risk of cancer
- ☑ It is reassuring however that every race and ethnicity that has been studied thus far have shown similar benefits
- ☑ What we need to learn is how much exercise is necessary and how it works, biochemically and cellularly, in order to improve the benefit
- ☑ It is helpful to know that exercising less than 15 minutes at a time does not seem to be sufficient to prevent breast cancer; a relatively safe extrapolation is that is it probably not adequate for prevention of cancer recurrence.

Comparison of the 1st and 2nd Expert Report on Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective

The Latest Scoop on Diet and Cancer Risk: An Update on the WCRF/AICR 2007 Report on Food, Nutrition, Physical Activity, and the Prevention of Cancer

Johanna Lampe, PhD, RD
Public Health Sciences Division, Fred Hutchinson Cancer Research Center, Seattle, WA

One of the major differences between the 1st (1997) and 2nd (2007) *Expert Report on Food, Nutrition, Physical Activity and the Prevention of Cancer* was the addition of physical activity



Dr. Bleyer:
☑ Whereas the First Expert Report only covered nutrition, the Second Expert Report added physical exercise, indirectly emphasizing the importance of combining **E&N**
☑ This too supports DEFEAT Cancer's stance that the two are synergistic (make each other more effective and leading to a result that is greater than the sum of the parts)

Daily total physical activity level and total cancer risk in men and women: Results from a large-scale population-based cohort study in Japan [Prevention]

Manami Inoue1, Seiichiro Yamamoto2, Norie Kurahashi1, Motoki Iwasaki1, Shizuka Sasazuki1, Shoichiro Tsugane1 for the Japan Public Health Center-based Prospective Study Group
American Journal of Epidemiology published online on July 2, 2008, doi:10.1093/aje/kwn146

More than 4000 cases of cancer that were prospectively studied in nearly 80,000 Japanese indicate that physical activity was associated with a 7-16% reduction of cancer risk in women and a 4-13% reduction in males, the magnitude depending on the amount of exercise

The impact of total physical activity level on cancer risk has not been fully clarified, particularly in non-Western, relatively lean populations. The authors prospectively examined the association between daily total physical activity (using a metabolic equivalents/day score) and subsequent cancer risk in the Japan Public Health Center-based Prospective Study. A total **of 79,771 general-population Japanese men and women aged 45–74 years** who responded to a questionnaire in 1995–1999 were followed for total cancer incidence (4,334 cases) through 2004. Compared with subjects in the lowest quartile, increased daily physical activity was associated with a significantly decreased risk of cancer in both sexes. In men, hazard ratios for the second, third, and highest quartiles were 1.00 (95% confidence interval (CI): 0.90, 1.11), 0.96 (95% CI: 0.86, 1.07), and 0.87 (95% CI: 0.78, 0.96), respectively (p for trend = 0.005); in women, hazard ratios were 0.93 (95% CI: 0.82, 1.05), 0.84 (95% CI: 0.73, 0.96), and 0.84 (95% CI: 0.73, 0.97), respectively (p for trend = 0.007). The decreased risk was **more clearly observed in women** than in men, **especially among the elderly and those who regularly engaged in leisure-time sports or physical exercise**. By site, decreased risks were observed for **cancers of the colon, liver, and pancreas in men** and for **cancer of the stomach** in women. Increased daily physical activity may be beneficial in preventing cancer in a relatively lean population.

Dr. Bleyer:
☑ As shown in Korea (p. 81) and other Asian countries, each of which is characterized by a much more lean population than in the U.S., physical activity still can be demonstrated to significantly reduce cancer risk
☑ Even when nutrition appears optimal—lifespans in Asia are considerably longer than in the U.S.—physical activity has an anticancer effect
☑ Once again, DEFEAT Cancer finds evidence in this report that exercise *in combination with* nutrition is more anticancer than either alone

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Active lifestyle may prevent cancer: Japan study [Prevention]

July 10, 2008
TOKYO (Reuters) - Physically active people are less likely than sedentary types to develop cancer, a research group led by the Japanese health ministry announced on Thursday.

Report on the preceding article with commentary from experts

Men in the most active group of people surveyed had 13 percent less risk of developing cancer compared with the least active group, and women in the most active group had a 16 percent lower risk than their sedentary counterparts.
"There has been a lot of research done in the past on the relationship between leisure and development of cancer in the West," said **Dr. Manami Inoue**, section chief of the **National Cancer Centre**.
"However, our research is the first in Japan of its size and scope -- we looked at overall exercise and labor, which is not only related to leisure."
According to the study, published in the American Journal of Epidemiology, researchers surveyed around 80,000 men and women between the ages 45 to 74 living in nine Japanese prefectures.
The surveyed population was divided into four groups according to their ratio of individual working metabolic rate, or MET (metabolic equivalent), which was determined by the amount of time respondents spent sitting, walking, standing, sleeping and exercising.

"Our research looked at overall physical activity that people take part in daily, and not just exercise that people take part in for leisure or fitness," said Inoue.
The trend was **most noticeable among Japanese women**, who were less likely to develop cancer if they were engaging in regular exercise and led an active lifestyle.
The results of the study also showed the trend to be prevalent for colon, liver and pancreas cancer risks for men and the development of stomach cancer among women.
The study, conducted by the Japan Public Heath Centre was first of its kind to survey a non-Western population for clues on the causes of cancer.
Inoue said: "There are a lot of physical differences between Asians and our Western counterparts. Asians are usually leaner, with a lower BMI (Body Mass Index). Many contributing factors for cancer have been suggested ... our research showed that **lack of general physical activity** is one of such reasons."

Dr. Bleyer:
☑ This is one of the first studies to include physical activity on the job (employment) in evaluating exercise and cancer
☑ Of particular interest is the philosophic difference in reporting the results: in Asia (at least Japan) physical activity is the baseline (the norm) and lack of exercise is the point of study whereas in the West sedentary behavior is the norm and exercise is the novel variable
☑ But then again, our society is among the most obese in the world and our children are the most obese

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Exercise testing for cancer fails to follow guidelines

Study urges national, international standards to ensure safety, reliable results

As the evidence for the benefits of exercise in cancer patients grows, national, international standards to assess physical fitness of cancer patients should now be implemented and followed

TUESDAY, July 29 (HealthDay News) -- Exercise testing has become a common part of cancer care and research, but most tests aren't administered according to American Thoracic Society guidelines, say Duke University Medical Center researchers.
In cancer care, exercise tests are used to determine the pre-surgical fitness of lung cancer patients. In cancer research, exercise tests are most often used to evaluate patients' cardiorespiratory fitness after a cancer diagnosis.
"We reviewed studies that performed exercise testing among adults with cancer and found most studies did not follow the guidelines recommended for clinical settings," lead author Lee W. Jones, an assistant professor of surgery, said in a Duke news release.
"We also found that studies typically do not report key physiological outcomes that provide immediate information on the fitness level in a particular cancer population or whether the test was valid," Jones said.
The findings were expected to be published in the August issue of the journal The Lancet Oncology.
A number of studies have concluded that exercise can benefit cancer patients before and after treatment. "Several recent studies reported a strong association between increased levels of exercise and significant reductions in cancer recurrence and cancer mortality among patients with colon and breast cancer," Jones said. "As the level of evidence continues to grow, the need for exercise testing will grow in parallel."
Such tests need to be standardized to ensure safety and reliable results.
"We need to develop a plan for nationally and internationally mandated recommendations specific to the clinical and research applications of exercise testing for oncology patients," Jones said.

Dr. Bleyer:
☑ The need to assess and improve physical fitness in cancer patients before and during cancer treatment is now being promoted by Duke University and national societies … bravo!

Said the doctor to the cancer patient: Hit the gym

The bandwagon of exercise programs for cancer patients and survivors is rolling

New York Times - August 14, 2008
By ANAHAD O'CONNOR
AS the group of women trickled into the aerobics studio at the Bendheim Integrative Medicine Center in Manhattan on a recent Thursday morning, there were subtle signs that this was no ordinary fitness class.

One woman told the instructor that she had missed a string of previous classes because she was grappling with fatigue, a side effect of her new cancer medication. Others wore colorful wraps on their arms, containment sleeves meant to protect against lymphedema, a painful swelling of the arm stemming from breast cancer surgery.

Sponsored by **Memorial Sloan-Kettering Cancer Center**, this class for cancer patients has been around for some time, mostly in a league by itself. But in recent years, following studies that found exercise to be beneficial in combating the effects of cancer, the class has gained some company.

Gyms and fitness centers have begun stepping in to meet a small but growing demand for programs designed to not only hasten recovery but to address the fatigue of chemotherapy, the swelling of lymphedema and the loss of muscle tone.

There have always been athletically inclined patients who stayed active, even competitive, in the wake of a diagnosis.

A recent high-profile example is **Eric Shanteau, an American Olympic swimmer** who decided to put off testicular-cancer surgery until he had competed in Beijing.

But most of the roughly 10 million cancer survivors in the United States are not amateur Lance Armstrongs. Many, though, are inspired by celebrities like Mr. Armstrong, seeing them as models for how to come out on the other side of often-debilitating treatment regimens.

A new program from the **Y.M.C.A., in partnership with the Lance Armstrong Foundation**, offers cancer fitness classes at more than a dozen Y's in 10 states. At the women's gym **Curves International, researchers from Fox Chase Cancer Center in Philadelphia** are looking at whether overweight breast-cancer patients can keep to a five-day-a-week Curves routine for six months. And survivors are organizing their own classes.

"There used to be this understanding that if you're getting treatment you're supposed to be in your bed," said Pam Whitehead, an architect and survivor of uterine cancer who started the Triumph Fitness Program at gyms in Modesto and West Sacramento, Calif.

In some cases, oncologists are prescribing exercise, gently prodding patients to tackle whatever activity they can manage: light walking, simple stretches, exercise with resistance bands.

"I started in 1992 and that was really a time when not as many patients were exercising," said Dr. Alexandra Heerdt, a breast surgeon at Sloan-Kettering who is conducting a pilot program involving exercise. "If a patient came to me back then and asked about exercise, I would have said there wasn't really any information."

But now, she added, "they have a lot of options."

Wendy Rahn, 46, an associate professor of political science at the University of Minnesota, knows this well. After a double mastectomy, her shoulders hurt so much that she was often hunched in pain. Then, while researching her illness, she discovered a 2005 study on cancer and exercise.

"The effects — what we call effect sizes in statistical research — were enormous," she said, "and I was like 'How come no one is talking about this?' " She had given up exercise a decade earlier, but the study inspired her to go back to the gym.

"I started feeling so much better," she said. "And it struck me that if I'm feeling this good, then every cancer survivor should."

So she founded a nonprofit group called Survivors' Training, and in January opened a fitness studio in White Bear Lake, Minn., offering yoga, strength training, Pilates and Nia, which combines dance and martial arts. "I like to think of it as a support group that moves," she said.

Cancer experts say the shift in thinking began in the mid-1980s, coinciding with a greater awareness of health and fitness. Oncologists were faced with questions about exercise that they had never heard before: how much was allowable and when?

Scientists also took notice of studies showing that those who were physically active and eating well were less likely to develop cancer. They then asked what impact exercise and diet would have on those with the disease, said **Dr. Charles Fuchs**, an oncologist at the **Dana-Farber Cancer Institute** in Boston who studies cancer and exercise.

In the last eight years, a dearth of research has become a flood of studies. Among them is one sponsored by the National Cancer Institute in 2006 that looked at the effects of moderate exercise on groups of breast and prostate cancer patients undergoing radiation therapy for six weeks.
Those assigned to a daily program — taking walks of increasing distance and doing exercises with a resistance band — had less fatigue, greater strength and better aerobic capacity than those who were not instructed to exercise. This finding, and similar ones, has been replicated many times.

Other studies indicate that moderate exercise has additional benefits like strengthened immune function and lower rates of recurrence. **Studies at Dana-Farber found that non-metastatic colon cancer patients who routinely exercised had a 50 percent lower mortality rate during the study period than their inactive peers, regardless of how active they were before the diagnoses**.
Dr. Fuchs, a study author, said it influenced his advice. "I am counseling all of my patients to increase their activity," he said, "or if they were regularly exercising before their diagnosis, to continue."
But every recommendation has its caveats. There will be days during treatment when meaningful activity is not possible, oncologists say, and that's fine. The American Cancer Society promotes moderate exercise but encourages patients to discuss their exercise plans with their oncologists, and lists on its Web site 13 precautions (cancer .org/docroot/MIT/MIT_0.asp).
In the biweekly Focused Fitness class at the Bendheim Integrative Medicine Center in New York, the instructor, Donna Wilson, seeks to ease her charges back into exercise after, and often during, physically draining treatments. Arm extensions and other range-of-motion exercises that can help relieve lymphedema were first on the agenda on a recent morning, followed by heart-pumping lunges and core exercises. A woman who had breast cancer slogged through a set of isometric exercises. "It looks easy," she said, "but try keeping your arms up all the time when your nerves have been cut."
Ms. Wilson, a registered nurse, encouraged the woman to keep pushing. Then she looked at the class and turned to a visitor. "They're amazingly strong," she said.

Dr. Bleyer:
☑ **Therapeutic Associates** have been offering personal fitness training programs for ***DEFEAT Cancer*** participants at both their Bend and Redmond facilities since the beginning of the ***DEFEAT Cancer*** program, at no charge
☑ The LAF Program at YMCA is very similar to ***DEFEAT Cancer***'s program.
☑ ***DEFEAT Cancer*** been a pace setter!

Moderator analyses of participants in the Active for Life after cancer trial: implications for physical activity group intervention studies.

Whereas an overall comparison of exercise versus educational support versus standard care showed no benefit on quality of life in prostate cancer patients, a subset analysis showed that patients in greater need of mental and psychosocial intervention did benefit and for at least a year

Ann Behav Med. 2007;33(1):99-104
Carmack Taylor CL, de Moor C, Basen-Engquist K, Smith MA, Dunn AL, Badr H, Pettaway C, Gritz ER.
Department of Behavioral Science, The **University of Texas M. D. Anderson Cancer Center**, Houston, TX
BACKGROUND: Prostate cancer patients on hormonal therapy experience significant treatment-related physical and psychological sequelae.
PURPOSE: We examined moderator variables to determine whether certain participants demonstrated quality of life (QOL) benefits from a group-based lifestyle physical activity program compared to a group-based educational support program and standard care.
METHODS: Participants were 134 prostate cancer patients on continuous androgen ablation in a controlled trial that used adaptive allocation.
RESULTS: As reported elsewhere, no significant differences were found between study conditions on primary QOL outcomes following the 6-month interventions. However, in a secondary analysis, several significant interactions indicated that both group programs benefited patients with lower psychosocial functioning at baseline; patients with lower mental health and social support scores had significant improvements in these measures compared with standard care. For those with higher pain, the educational support program resulted in significant improvements compared with the other two conditions. Twelve-month findings indicated lasting effects.
CONCLUSIONS: Consistent with existing research, results indicate that group interventions benefit cancer patients with limitations in psychosocial functioning. Findings underscore the importance of physical activity/exercise studies to employ control conditions that consider the attention and support provided by health educators and group members, particularly when examining psychosocial outcomes and pain.

Dr. Bleyer:

☑ This study was reported last year but missed in our monthly survey of the peer-reviewed literature
☑ An earlier report of the study (Psychooncology. 2006 Oct;15(10):847-62) reported no overall benefits and concluded that the "results suggest a lifestyle program focusing on cognitive-behavioral skills training alone is insufficient for promoting routine physical activity in these patients."
☑ This follow-up report indicates that survivors in greatest need have the greatest benefit of exercise, a not unexpected result
☑ Once again, the result may have been more obvious and apparent overall, if nutrition was included in the study

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Health clubs gear programs for those with ailments (especially cancer)

Health clubs are providing programs specifically for cancer patients as the evidence for benefit of exercise continues to accumulate

By JAMIE STENGLE - The Associated Press
Sept. 28, 2008

DALLAS — When Patti Kiernan found out she had osteoporosis, she decided it was time to find a more focused workout.

The 61-year-old signed up for a fitness program at her Dallas gym that's geared specifically for women with health problems. Kiernan liked the four-week Female Focus program so much she's still in after two years.

"I just felt that this was the right way to go," said Keirnan, who also began taking medication and saw her bone density improve after a year. "Plus, there were other women in the program who had the same problem."

More and more clubs are offering exercise programs fine-tuned for people coping with a variety of ailments, said **Joe Moore**, head of the **International Health, Racquet and Sportsclub Association**. He said the number of programs has grown along with the number of studies showing the health benefits of exercise.

Medical and fitness experts say that exercise not only elevates the mood and energy levels, but helps control weight — a contributing factor for many diseases.

For breast cancer patients, "being overweight or gaining weight post diagnosis is a huge risk factor" for recurrence, said Colleen Doyle, director of nutrition and physical activity for the American Cancer Society.

Her group and the American College of Sports Medicine are devising a special certification for people who work with cancer patients on exercise programs.

Julie Main developed such a program after she was diagnosed with breast cancer at the age of 36 in 1993. She was inspired after her doctor mentioned that she seemed to be going through treatment better than other patients.

She told him one thing she was doing was continuing to exercise.

"He said, 'Most of my other patients don't do that.' I said, 'Well, maybe they should,'" Main said.

Now president of West Coast Athletic Clubs with five gyms in California, Main teaches other health clubs how to set up programs similar to her twice-a-week, 10-week program. Her free programs are done in collaboration with the Cancer Center of Santa Barbara and focus on strength-training.

"With cancer, people feel too tired to exercise, but if they exercise the fatigue is less," said Christine Brown, the Cancer Center's wellness manager.

In suburban Boston, patients are referred to the Dedham Health and Athletic Complex after they've been diagnosed with anything from heart disease to arthritis to diabetes, said Lloyd Gainsboro, co-owner and director of business development.

Sixty-day programs that cost $60 emphasize strength and cardiovascular training and are taught in an area of the gym with more carpet and sofas and fewer "spandex and beautiful bodies," Gainsboro said.

Participants in the Female Focus program at Dallas' Cooper Fitness Center pay **$580 for an evaluation, eight training sessions, two lectures — one on exercise and another on nutrition — and a workout booklet to help them continue their routine**.

Program founder Colette Cole said the evaluation helps her tailor the workouts to each participant and their capabilities.

The program appealed to 47-year-old Gretchen Montgomery, who was feeling some trepidation about resuming exercise after a bout with food poisoning and an emergency hysterectomy in the spring.

"I loved that it wasn't a room of workout babes," Montgomery said.

Ellen Orzel did two sessions of the program last spring, about a year after a double mastectomy. After the surgery and treatment, the 49-year-old said she was weaker and carrying 20 extra pounds.

"I was comfortable going in there, knowing I could tell her I had a mastectomy," she said.

Orzel said she's less sore, stronger and has lost about half of the extra weight.

"My whole upper body just really felt so much better," she said.

Experts say such programs can also serve as a support group.
"There's no substitute for the camaraderie that forms among those that know what the other is going through," said Brown of the Santa Barbara center.
Dr. John Pippen, a cancer specialist at **Baylor University Medical Center, said that he tells his breast cancer patients to try to walk three to five hours a week.**
"To me, it's killing several birds with one stone — preventing osteoporosis, reducing cancer risk, perhaps most important of all, reducing cardiovascular risk," Pippen said.
And while joining a fitness club might help keeping up with an exercise routine, he said it's not necessary.
"You can just start at your own front door with your comfortable walking shoes and away you go," he said.

Dr. Bleyer:
☑ Obviously the health clubs are identifying a niche for cancer survivors that will not only help their business but also the clients
☑ As promulgated by DEFEAT Cancer, increased physical activity decreases fatigue rather than increasing it.
☑ If combined with a nutrition program, these programs are well worth the cost (e.g. $580 for an evaluation, eight training sessions, two lectures — one on exercise and another on nutrition)

Cancer patients are making their bodies strong again

For those weathering, or about to weather, surgery, chemotherapy, radiation or medication regimens, cardiovascular and strength training can help counter side effects such as extreme fatigue and muscle wasting, and bolster healing, propelling them back into normal life faster.

By Jeannine Stein
Los Angeles Times - October 20, 2008

Stephen Osman / Los Angeles Times
Kate Schmidt, foreground, leads an exercise class for cancer patients at the Wellness Community in Santa Monica.

Despite the challenges, they're turning to exercise to help counter the side effects of treatment and to bolster healing.
The strength-training class doesn't look that different from any other -- men and women are lying on mats, stretching hamstrings before beginning work with elastic bands, stability balls and dumbbells. Then you notice a few uncommon things.
One woman has doffed her long, blond wig to reveal a low pile of fuzz on her head. The instructor mentions that a particular upper body exercise is especially good for people with brain tumors. And some participants are out of breath after a few ab crunches.The people in this bare room in a Santa Monica office building are undergoing cancer treatment or recovering from it. Despite fatigue, neuropathy, surgical scars and nausea, they have decided to push their bodies toward physical fitness, whether they feel ready or not.
Over the next hour, they follow Wellness Community instructor Kate Schmidt through stretching, balance and strength-training, some modifying the drills to accommodate low lung capacity, stiffness from surgery or weak muscles.
For cancer-traumatized bodies, the experience can be challenging -- but it is becoming increasingly common. As studies mount up showing the benefits of regular, moderate physical activity before, during and after treatment, cancer rehabilitation facilities, wellness centers and YMCAs are offering exercise programs to help people through the disease.
For those weathering, or about to weather, surgery, chemotherapy, radiation or medication regimens, cardiovascular and strength training can help counter side effects such as extreme fatigue and muscle wasting. For those recovering from treatment or who are in remission, exercise can bolster healing, propelling them back into normal life faster.
"This is a population that is not unlike people who have cardiac disease -- they have a damaged body system that can be helped by exercise," says **Kathryn Schmitz**, assistant professor of epidemiology at the Center for Clinical Epidemiology and Biostatistics at the **University of Pennsylvania**.
That's not to say that launching an exercise routine under such circumstances is easy.

To begin with, Schmitz says, people may feel a bit betrayed by their bodies: "Like, you're not sure if you're best friends with your body right now."
Then there are the effects of treatment. Surgery can cause muscle imbalances, weakness, pain and scarring. Steroid drugs can cause muscle breakdown; interferon often leads to intense fatigue; and some medications, such as sunitinib (used to treat some kidney and gastrointestinal cancers) and the breast cancer drug trastuzumab, may cause heart damage.

Good for everyone

But what exercise does for healthy people -- increasing energy, improving flexibility and cardiovascular function, strengthening muscles and bones -- it also does for those with cancer, oftentimes more profoundly.
"I knew it was really good for me to do it," says Los Angeles resident Barbara Converse, who was diagnosed with rectal cancer in 2005. She's been coming to Schmidt's strength training workshop at a Santa Monica branch of at the Wellness Community, a cancer support and education center, for 2 1/2 years. "I knew it would make me feel like a whole person again, not just a poor little tree that dropped its leaves at the wrong time of the year."
She started the class not believing she could even do the exercises. Her shoulder was immobile from a fall while on chemo. (She whips her arm around in a complete circle to demonstrate her improvement.) Exercise has helped her with balance and fatigue so strong she used to head for the bed after climbing a flight of stairs.
"The class gave me more confidence to get out of the house," she adds, "and I had the endurance to be able to do things for hours at a time."

Where trend began

The **Rocky Mountain Cancer Rehabilitation Institute** at the University of Northern Colorado in Greeley was one of the earliest facilities to use exercise and nutrition as rehabilitation for cancer patients. Like many such programs, it was started by someone who had first-hand experience with cancer.
Carole Schneider, a professor of exercise physiology at the university, was diagnosed with cervical cancer in 1995. After going through extensive radiation treatment, she says, "I was so fatigued, and felt awful and so weak. I asked my physician what to do, and he didn't really know."
When she started to look into the side effects of chemo and radiation -- muscle loss, heart damage, fatigue -- she realized that exercise was a viable antidote. A few early nurses' studies on the positive effects of exercise for cancer patients bolstered her beliefs.
After starting the institute, she did the program first: three days of aerobic training, two of strength training. When the intense regimen failed to ease her fatigue, she came up with a more moderate full-body workout that included aerobic, strength and flexibility components. "I felt so much better in no time," she says. "I felt more energized, my treadmill time was better, my strength was better -- my whole physical functioning and quality of life was better. And we're seeing that with all our patients."

Then there's exercise as pre-hab.

At **City of Hope** in Duarte, **Dr. Brian Tiep**, director of pulmonary rehabilitation, gets lung cancer patients in shape before their surgery or other treatments. Simple walking and muscle endurance regimens can improve cardio function and enhance oxygen transportation into blood and muscles, creating a body better equipped to handle the rigors of an operation.
"For the most part," Tiep says, "people with lung cancer have been inactive and get short of breath when they try to walk. Walking is most important, so we start with that."

Trainers are on board

The traditional fitness world has gotten the message about the importance of exercise for people with cancer. A growing niche of trainers are being schooled to understand the nature of the disease and its various treatments -- and learning how to work with patients in devising individualized workouts. Some are taking their skills to gyms and wellness centers.
This fall, the American College of Sports Medicine began offering a specialty certification in working with cancer patients from diagnosis through treatment. And the Lance Armstrong Foundation and the YMCA have teamed up to offer wellness and exercise programs for cancer survivors. The program is being piloted in 10 cities across the country.
Some trainers have also taken workshops at the West Linn, **Oregon-based Cancer Exercise Training Institute**, which offers instruction for fitness and health professionals. Andrea Leonard, a thyroid cancer survivor and trainer, founded the institute. She says what patients get from educated trainers is more than a workout. "It's a recovery program. It gets them back to doing functional day-to-day activities, as well as feeling stronger and looking better."

Some doctors lag

Not all healthcare professionals are so informed, despite the growing mountain of research. "One of the biggest pushes we need to make is to educate [them]," says **Anna Schwartz**, research professor at the **University of Washington** who has done numerous studies on cancer and exercise. "**Physicians need to tell their patients to exercise**."

One doctor who is convinced is **Dr. Henry Farkas**, a **hospice physician in Elkton, MD**., who had surgery for lung cancer two years ago (but was never a smoker). He tried Schmidt's class at the Wellness Community because he knew of the research on the benefits of exercise for cancer patients.

"I'm getting strong again," he says, a few perspiration marks visible on his T-shirt. "I measure my progress by how far I can walk without having to stop and rest, and whether I can cross the street as fast as other normal pedestrians. At least I can keep up now with people who aren't in a hurry. I do see improvement."

Dr. Bleyer:

☑ The point about the difficulty for a cancer patient/survivor of starting and maintaining an exercise routine is well taken

☑ And, as stated by Dr. Schwartz of the University of Washington, physicians have reneged on their responsibility to inform patients about the need to exercise; an educational program for physicians is warranted.

The benefits of exercise for cancer patients

This article discusses several studies on the benefits of strength-training programs and cardiovascular workouts for cancer survivors

Jeannine Stein

Los Angeles Times - October 20, 2008

Strength-training programs and cardiovascular workouts may lessen fatigue, improve muscle function and quality of life for current or former cancer patients, studies show

* A regular weight-training program can improve quality of life among breast cancer survivors. In a study published in the journal **Cancer** in **2006**, 86 **breast cancer** survivors were put into a weight-training program or a control group; at the end of the program, those women with increased upper body strength and lean mass were generally found to have higher quality-of-life scores.

* Aerobic training can boost physical performance in **cancer patients** who have just finished a high-dose chemotherapy program. In a study published in the journal **Cancer** in **1997**, 16 patients completed a seven-week treadmill rehab program and 16 served as a control group. By the end of the study, the exercise group showed improvements in maximum physical performance and hemoglobin concentration. Also, none of them reported fatigue or limitations in their daily activities due to low physical performance; one quarter of the patients in the control group did.

* Men with **prostate cancer** appear to have less fatigue after participating in a resistance training program. In a study published in the **Journal of Clinical Oncology** in **2003** (abstract provided in next review), 155 men who were scheduled to receive androgen deprivation therapy for at least three months were assigned to a thrice-weekly, 12-week exercise program or a control group. Those in the exercise group suffered less fatigue during daily activities and had a higher quality of life than the men in the control group. The exercise group also showed higher levels of upper- and lower-body fitness than the control group.

* **Head and neck cancer** survivors can reduce pain and disability with a progressive, resistance-exercise training program. A **2008** study in the journal **Cancer** found that 27 cancer survivors assigned to a resistance program for 12 weeks showed significant improvement in shoulder pain and disability, compared with 25 people assigned to a standardized therapeutic exercise protocol. The resistance training group also had improved upper extremity muscle strength and endurance compared with the other group.

Dr. Bleyer:

☑ Ms Stein, reporter of the prior article, summarized four reports on the value of exercise for cancer patients/survivors, three of which have previously appeared in ***E&N*** *News* [the fourth is provided below).

☑ In each case, however, nutrition was not assessed and would, had it been included in the study, have likely shown additional, if not synergistic, benefit

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Resistance exercise in men receiving androgen deprivation therapy for prostate cancer

A 2003 study, cited above, demonstrated that men with prostate cancer who undergo hormone therapy and participate in a regular exercise program experience less fatigue than men who do not exercise regularly

Roanne J. Segal, Robert D. Reid, Kerry S. Courneya, Shawn C. Malone, Matthew B. Parliament, Chris G. Scott, Peter M. Venner, H. Arthur Quinney, Lee W. Jones, Monika E. Slovinec D'Angelo, George A. Wells
From the Department of Medical Oncology, Ottawa Regional Cancer Centre; University of Ottawa Heart Institute; Department of Epidemiology and Community Medicine, Faculty of Medicine, University of Ottawa, Ottawa, Ontario; Faculty of Physical Education, University of Alberta; Division of Radiation Oncology, Department of Medicine, Cross Cancer Institute, Edmonton, Alberta, Canada.
Purpose: Androgen deprivation therapy is a common treatment in men with prostate cancer that may cause fatigue, functional decline, increased body fatness, and loss of lean body tissue. These physical changes can negatively affect health-related quality of life. Resistance exercise may help to counter some of these side effects by reducing fatigue, elevating mood, building muscle mass, and reducing body fat.
Methods: In a two-site study, 155 men with prostate cancer who were scheduled to receive androgen deprivation therapy for at least 3 months after recruitment were randomly assigned to an intervention group that participated in a resistance exercise program three times per week for 12 weeks (82 men) or to a waiting list control group (73 men). The primary outcomes were fatigue and disease-specific quality of life as assessed by self-reported questionnaires after 12 weeks. Secondary outcomes were muscular fitness and body composition.
Results: Men assigned to resistance exercise had **less interference from fatigue** on activities of daily living ($P = .002$) and **higher quality of life** ($P = .001$) than men in the control group. Men in the intervention group demonstrated higher levels of upper body ($P = .009$) and lower body ($P < .001$) muscular fitness than men in the control group. The 12-week resistance exercise intervention did not improve body composition as measured by changes in body weight, body mass index, waist circumference, or subcutaneous skinfolds.
Conclusion: Resistance exercise reduces fatigue and improves quality of life and muscular fitness in men with prostate cancer receiving androgen deprivation therapy. This form of exercise can be an important component of supportive care for these patients.

Dr. Bleyer:
- ☑ Reducing fatigue with exercise, instead causing it, may seem to be a paradox, but this inverse relationship of increased physical activity and decreased fatigue has been well documented and may be summed up as "To prevent fatigue, make yourself tired with exercise".
- ☑ That just three months of relatively light physical activity (resistance exercise) three times a week resulted in a highly significant reduction in fatigue and improvement in quality of life.
- ☑ ***DEFEAT Cancer*** suggests that if high quality nutrition were combined with the exercise program, the results would have been even more impressive

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

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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 researchers said.

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, according to the American Cancer Society. The group 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, anastrazole, 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

Photo from HealthDay News report

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 Nutrition

Weight gain hurts breast cancer survival

By Marilynn Marchione
Associated Press

Breast cancer patients might have a powerful incentive to avoid gaining weight: better odds of surviving the disease.

New research suggests that for every 11 pounds a woman gains after being diagnosed with breast cancer, the chances of it proving fatal go up 14 percent.

> Among more than 4000 women with breast cancer evaluated at Johns Hopkins University, each 11 pounds of increase in body weight after diagnosis translated into a 14% decrease in survival

The study is by no means definitive, but gives the strongest evidence yet that controlling weight — a good idea anytime in life — may be especially important after breast cancer.

"There was a significant trend between increasing levels of weight gain and higher mortality," said Hazel Nichols, a doctoral student at Johns Hopkins Bloomberg School of Public Health. "Lifestyle factors, the things you incorporate after a breast cancer diagnosis such as diet and exercise, do show potential to influence survival."

Nichols led the study and reported results Friday at an American Association for Cancer Research conference in Philadelphia.

Researchers started with 4,021 women in Wisconsin, Massachusetts and New Hampshire who had been diagnosed with breast cancer from 1988 to 2001. They gave information on their height, weight, family history and breast cancer risk factors during telephone interviews.

From 1998 to 2001, all survivors were mailed surveys asking for updated information on these factors and lifestyle habits like exercise and diet.

After an average of six years of followup since their diagnoses, 121 breast cancer deaths and 428 non-breast cancer deaths had occurred. **For every 11 pounds of weight gain after diagnosis, the risk of death from breast cancer or other causes increased by 14 percent**.

The link remained even after researchers took into account differences in age, menopausal status, smoking and the stage of disease when the women were diagnosed.

For women classified as obese by body mass index — a measure of weight and height — the death risk was more than twice that of women with a normal body weight.

The study was paid for by the Susan G. Komen for the Cure Breast Cancer Foundation.

"It's a large study, it was a very well-conducted study at several centers in the United States" by well-known researchers on this topic, said **Joanne Dorgan**, a breast cancer scientist at **Fox Chase Cancer Center** in Philadelphia.

Doctors have long known that women who are overweight when they are diagnosed with breast cancer have poorer prospects.

"They're more likely to relapse and to die of their cancer than women who are thinner," Dorgan said.

Previous research found that women who exercised after being diagnosed with breast cancer cut their chance of dying by as much as one-half, depending on how much exercise they did.

However, it is common for women to gain weight after being diagnosed with breast cancer. One reason may be that chemotherapy can leave them tired and ill so they don't feel like exercising, Dorgan said.

The new work shows how important it is to get back on track and keep from gaining pounds.

"It still matters what your weight gain is after diagnosis," said **Dr. Craig Thompson**, director of the Abramson Cancer Center at the University of Pennsylvania.

Dr. Bleyer:
☑ Dr. Thompson and I were on the faculty together at the University of Washington. He is a wise man.
☑ Look for this report to appear in an important peer-review journal during 2008

Weight gain after breast cancer diagnosis reduces survival

Lisa M. Cockrell

Sixth Annual International Conference on Frontiers in Cancer Prevention Research: Abstract B95.
Presented December 7, 2007.
Medscape Medical News

Interviews of the experts and commentary on the prior report by a discerning reporter

December 10, 2007 (Philadelphia, Pennsylvania) — Gaining weight after a breast cancer diagnosis increases the risk for mortality, according to a study presented at the American Association for Cancer Research 6th Annual International Conference on Frontiers in Cancer Prevention Research.

Dr. Craig Thompson, MD, director of the Abramson Cancer Center at the **University of Pennsylvania**, in Philadelphia, who was not involved in the study, said that this work emphasized a "growing appreciation of the problem we have with obesity and metabolic diseases in this country over the past 25 to 30 years," and "an increased understanding of the impact these diseases have on the progression of cancer."

More than 2 million women in the United States have a diagnosis of breast cancer, and more than 30% of US women are obese. This study, designed to investigate the relationship between mortality and weight gained after a breast cancer diagnosis, was presented by **Hazel Nichols**, from the **Johns Hopkins** Bloomberg School of Public Health, in Baltimore, Maryland.

The 4021 women enrolled in the study received a diagnosis of invasive breast cancer between the ages of 20 to 79 years from 1988 to 2001. These individuals had previously participated in a parent study, and therefore information on their body weight and height had been obtained during a previous telephone interview. After an average of 5.8 years postdiagnosis, further details were gained from a questionnaire sent to breast cancer survivors. This questionnaire was designed to obtain information on treatment, diet, physical activity, and weight after their breast cancer diagnosis. Body-mass index (BMI) was used to classify the participants as underweight (< 18.5 kg/m2), normal (18.5 – 24.9 kg/m2), overweight (25.0 – 29.9 kg/m2), or obese (> 30 kg/m2).

Using statistics from the National Death Index through 2005, the investigators determined that 121 women had died from a breast-cancer-related mortality, and 421 had died as a result of any cause.

According to Ms. Nichols, the finding that an increase in BMI and weight gain was associated with an increased risk for death from both breast cancer and all causes was "not surprising." A significant trend occurred between increasing weight gain after diagnosis and higher mortality risk. For every 5 kg (approximately 11 lbs) of weight gained, the risk for death increased approximately 14%. This was true for both breast-cancer-related and all-cause mortality.

In women who reported gaining more than 10 kg (approximately 22 lbs) after their breast cancer diagnosis, an 83% increased breast-cancer–related mortality risk was shown. Women who were classified as obese after their diagnosis had more than twice the risk for breast-cancer–related death than women with a normal BMI (hazard ratio, 2.39). The risk for death from any cause for obese women also increased, although not as dramatically (hazard ratio, 1.46, compared with women with a normal BMI). Obesity was associated with increased mortality even after other factors, such as age, menopausal status, and smoking, were accounted for.

Additional analysis of the patients in this data set are planned for the future, according to Ms. Nichols. The role of physical activity will be addressed to see whether the relationship between weight gain and breast cancer mortality differs in groups that are more or less physically active. Also, cardiovascular-disease–related mortality will be investigated.

According to Ms. Nichols, 1 of the limitations of this study was the scarcity of information on other age-related medical diseases, and she hopes future studies from other groups will include a complete medical history.

Previously, several epidemiologic studies have shown a correlation between increased weight at the time of diagnosis and decreased breast cancer survival. "What our study is able to contribute that has not as often been looked at is changes in body weight after diagnosis," stated Ms. Nichols.

"These results generally support the recognized health benefits and potential in mortality reduction that is associated with avoiding weight gain." They also add to a "growing body of evidence that postdiagnosis lifestyle factors, the things that you incorporate after a breast cancer diagnosis, such as diet and exercise, do have a potential to improve survival."

Dr. Thompson echoed this, stating that what is clear from this study is that "it still matters what your weight gain is after your diagnosis, and that's something patients can help contribute to and control." Future studies might help to confirm whether weight loss after diagnosis can lead to increased breast cancer survival.

Dr. Bleyer:

☑ More reaction to the report cited above from an objective reporter

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After breast cancer diagnosis: Weight gain increases mortality

Clinical Oncology - 2/2008, Vol: 02:08
Barbara Boughton

Further comment on the Hopkins study, and additional interview of expers

PHILADELPHIA—A recent study highlights the dangers of weight gain for women living with a breast cancer diagnosis.

The study of 3,993 breast cancer survivors, presented at the **American Association for Cancer Research** Frontiers in Cancer Prevention meeting, showed that for every 5 kg (11 lb) gained in the five years following a breast cancer diagnosis, women experienced a 14% increased risk for mortality. Women who reported even more weight gain—10 kg (22 lb) of weight gain—after their breast cancer diagnosis had an 80% increased risk for mortality from their disease, according to the study. Women who were obese after diagnosis also doubled their risk for mortality compared with those who were normal weight.

“Our study shows that weight gain after diagnosis matters—that it influences outcomes,” said lead author **Hazel Nichols, MS**, of the **Johns Hopkins** Bloomberg School of Public Health, Baltimore. While other studies have looked at the influence of weight on prognosis after a breast cancer diagnosis, the new study by Nichols and colleagues is one of the first to analyze the influence of weight gain following breast cancer diagnosis and treatment.

“The message we can take home from this study is that for **all women with a breast cancer diagnosis, trying to avoid additional weight gain may have benefit in terms of mortality risk**,” said **Craig Thompson, MD**, director of the Abramson Cancer Center at the **University of Pennsylvania**, Philadelphia.

“It has grown increasingly apparent that as obesity and metabolic syndrome have become increasingly severe, we are seeing linkage with cancer incidence and prognosis,” Dr. Thompson said. “No common malignancy has escaped the link to obesity.”

For the analysis, data on body weight before and after a breast cancer diagnosis, as well as on diet and physical activity, were obtained from women aged 20 to 79 who had previously participated in a population-based, multicenter case–control study. The study was conducted in Wisconsin, Massachusetts and New Hampshire. A total of 18,273 women with incident invasive breast cancer were enrolled from a parent study into the Collaborative Women’s Longevity Study (CWLS).

Current body weight was obtained in the CWLS questionnaire mailed to approximately 14,500 breast cancer survivors from 1998 to 2001. Almost 6,000 women returned the questionnaire—a response rate of about 40%. Women were excluded from the study if they had distant metastases, recurrence of breast cancer before follow-up, unintentional weight loss of greater than 5% of body weight or if their disease or treatment interfered with their diet.

After six years, there were 121 breast cancer deaths and 421 total deaths. In addition to increasing the risk for death from breast cancer, weight gain also predicted all-cause mortality. For every 5 kg (11 lb) gained, risk for dying from other causes increased by 14%. Women who were obese after diagnosis had a 1.46 increased risk for dying from all causes compared with normal-weight women.

Ms. Nichols noted that one of the limitations of the study was that the researchers had scarce information on medical conditions related to weight gain that could influence mortality. The low response rate to their questionnaire as well as a potential selection bias for a healthier cohort may have influenced their results, the researchers also noted.

The researchers now hope to analyze the ways that diet and exercise impact mortality from breast cancer and other causes. "We'd like to study these questions because **we know that diet and exercise do have the potential to improve survival**," Ms. Nichols said. "We have the data to address these questions, and **it would be interesting to see if physical activity influences breast cancer mortality, as did weight**."

Dr. Bleyer:

☑ This is a *tour de force* study, with 14,000 questionnaires sent to breast cancer survivors and 6,000 returned
☑ When this study is published (it was presented at a meeting of a very reputable group – AACR), it will be helpful to see the charts that correlate cancer recurrence risk with weight gain after diagnosis of breast cancer
☑ The comment by Craig Thompson, MD, a reliable (friend, colleague and) expert, is important
☑ The investigators got it right, in DEFEAT terms, by concluding that they need to analyze physical activity, not just weight (and nutrition)

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

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

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

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

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

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

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

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

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

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

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

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

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

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

These results generally support the recognized health benefits and potential mortality benefit of avoiding weight gain, Ms. Nichols concluded. And they add to a growing body of evidence that post-diagnosis lifestyle-things you can incorporate after breast cancer diagnosis-have the potential to improve survival.

The study was funded by the Susan G. Komen Breast Cancer Foundation and the NCI.

Dr. Bleyer:

☑ It's good to know that the investigators can and plan to evaluate the combination of exercise and weight change, since DEFEAT Cancer considers exercise as having benefits beyond weight reduction.

☑ The importance of this study is that the increased risk of breast cancer recurrence and weight gain was quantified.

Too fat? No more excuses: Research is revealing how very damaging extra baggage is

U.S. News & World Report - December 31, 2007

By Sarah Baldauf with Katherine Hobson

This report summarizes the wealth of data on the deleterious effects of overweight and obesity, with emphasis on the dimensions and significance of body mass index (BMI) and waistline

You may think your jiggling spare tire is just along for the ride, an inert mass that slows you down and forces a slackened belt. But far from just sitting there quietly, your body fat is talking. And what it's saying—in a constant stream of messages to your brain, liver, muscles, and points in between—amounts to an urgent reason to finally follow through on that New Year's resolution. Researchers worried about the obesity epidemic are furiously studying body fat in an effort to decode its effect on health. And they have discovered that fat is as active and important an endocrine organ as the thyroid or reproductive glands. In healthy amounts, it tightly regulates the amount of energy burned or stored by releasing a cadre of hormones. In excess, the fat cells swell and multiply, and their functioning overwhelms the system: Nasty inflammatory factors spew into the bloodstream, and the delicate balance of hormones becomes skewed, altering the brain's normal response to fat's signals. The result: a much-elevated risk of diabetes, cardiovascular disease, cancer, and liver disease. Plus metabolic changes that make losing weight—and keeping it off—seem impossibly tough.

"People think obesity is two behaviors: gluttony and sloth," says **Robert Lustig**, director of the Weight Assessment for Teen and Child Health Clinic at the **University of California-San Francisco** Children's Hospital. "That's not what it is. Obesity is a manifestation of a biochemical problem." Excessive fat strengthens the dysfunction, too, trapping the body in a vicious cycle. Even slightly overweight people can be on the path to a disturbed physiology—no matter that their clothes can still disguise a paunch. For evidence, look no further than the recent surge in type 2 diabetes, which correlates in near lockstep with Americans' expanding waistlines. As fat stores go up, so does the pancreas's production of insulin, the hormone that helps usher glucose out of the bloodstream and into cells where it's used for fuel. So people with too many extra pounds end up with a glut of the stuff, typically leading to "insulin resistance"—and too much glucose in the blood. Meantime, the excess insulin sends energy into the fat cells, causing them to plump up and multiply ad infinitum—and end up in places fat shouldn't be, like muscles, the liver, and deep in the gut, wrapped around vital organs.

Discipline

Insulin resistance has been Jesse Manek's nemesis. Now 15, Manek was told three years ago that—seriously overweight at 283 pounds and prediabetic—he would very likely have full-blown diabetes or a heart attack by the time he reached his 20s. Manek, who lives in Novato, Calif., sought help from Lustig

and the watch clinic and has managed to drop more than 75 pounds and bring his body-mass index, a number that relates weight to height, from 41.6 to a closer-to-normal 29.9. His regimen has been ultradisciplined: at least four classes per week at Marin Mixed Martial Arts, weekly sessions of strength training with a personal trainer, and a diet nearly devoid of fructose (found in table sugar and high-fructose corn syrup) and chock-full of fruits, vegetables, and whole grains. Lustig also has treated Manek with metformin, a diabetes drug, to rein in his insulin-gone-haywire. "It really comes down to a mental battle," Manek says of his struggle. "Do you want to be healthy?" He's now safely out of the prediabetic zone.

Besides upsetting the insulin balance, too much fat seems to unleash a flood of molecules called cytokines that trigger systemwide inflammation. "Obesity is a pro-inflammatory state," says **Michael Charlton**, medical director of liver transplantation at the **Mayo Clinic** in Rochester, Minn. Normally, inflammation is a healthy immune response, critical to fighting off infection. But chronic inflammation causes widespread tissue damage. The plumper and more abundant a person's fat cells, the greater the number of cytokine-releasing macrophage cells in the fat tissue. "It's these macrophages that are causing a lot of the trouble," says **Rudolph Leibel**, a **Columbia University** geneticist and noted obesity researcher. "They make mischief related to how fat you are."

The cardiovascular system appears to be one victim. Macrophages play an important role in the development of the fatty plaques that lead to atherosclerosis. And cytokines can make tissues resistant to the effects of insulin and cause inflammation in the blood vessels. Meantime, too much insulin can promote salt retention—and soaring blood pressure. "If I hadn't lost the weight when I did, they say [I'd have had] a heart attack or stroke," says Sheri Fanning, 41, a geriatric care manager and now weight-loss coach in Sparta, Wis., who has heart disease in her family and recently experienced a dangerous blood pressure spike.

Five years ago, Fanning tipped the scale at 192 pounds, and her doctor delivered an ultimatum: Go on hypertension meds for life. Instead, Fanning credits a physician-directed program that offered thrice-weekly weigh-ins, counseling, and a calorie-restricted diet for helping her to get down to a healthy 130 pounds. Taking up marathoning, triathlon, and competitive road biking certainly did its part, too. Though she's been on blood pressure medication since her recent crisis, she was able to keep her numbers down for years without drugs; her doctors say that shedding those pounds and keeping them off probably saved her life.

Cancer experts, too, now strongly advise burning excess fat. In fact, the top recommendation in the new cancer prevention guidelines issued by the American Institute for Cancer Prevention and the World Cancer Research Fund puts it this way: "Be as lean as possible within the normal range of body weight." That means keeping your body-mass index between 21 and 23—or, for someone who is 5 foot 4, staying between 122 and 134 pounds. "A BMI of 25 increases the risk of postmenopausal breast cancer more than [a BMI] of 21," says **Meir Stampfer**, who researches nutrition and epidemiology at the **Harvard School of Public Health. Extra fat is strongly believed to raise the risk of six types of cancer—esophageal, pancreatic, colorectal, breast** (in postmenopausal women), **endometrial** [uterus]**,** and **kidney—**and **possibly gallbladder cancer**, too.

The mechanisms that link obesity and cancer are not known, but the usual suspects—insulin resistance and inflammation—are likely players. Research released at December's **American Association for Cancer Research** conference on cancer prevention found that women with diabetes are 1.5 times more likely to develop colorectal cancer than those who aren't diabetic. "It's possible that fairly high levels of insulin—higher than seen in the prediabetics—are necessary to encourage cancer growth," says **Andrew Flood**, an epidemiologist at the **University of Minnesota**. And cytokines released from fat tissue are known to promote tumor growth and cell death. …

The one trick that researchers can agree upon so far is both simple and painfully familiar: **Eat less and move more**.

For Jesse Manek, that meant ditching what he craved most: fast food, ice cream, and sugary foods. In his doctor's mind, the ever present sweetener fructose, which shows up in everything from pasta to sports

drinks to soda to breads, is the refined carbohydrate most culpable in the rise of obesity. Its breakdown in the liver, says Lustig, promotes inflammation, hypertension, and insulin resistance. The extra fiber Manek gets by stocking up on fruits, vegetables, and whole grains helps control his insulin levels and makes him feel fuller, longer. Thanks to his vigorous exercise regimen, he says, an irony has unfolded: "I actually eat more now."

Dr. Bleyer:

☑ The "baggage" of overweight and obesity is, once again, mainly quality-of-life deficit

☑ The increased risk of developing cancer or shortening survival after a cancer diagnosis are key, too, but not as obvious (see report on "Causes of death are linked to a person's weight" below)

☑ Diabetes and the pre-diabetic state not only increase the risk of obesity-related cancer, they also adversely affects the delivery of cancer therapy (surgery and chemotherapy in particular)

Extra weight increases prostate cancer patients' risk of dying

By Nicole Ostrow

Nov. 12 (Bloomberg) -- Overweight men are more likely to die of prostate cancer within five years of diagnosis than those who are thinner, according to a study in the U.S.

Extra fat raised the risk of dying from the disease by 52 percent and obesity increased it to 64 percent, after researchers adjusted for some other medical reasons, scientists reported in the Dec. 15 issue of the journal Cancer.

This report from the prestigious Massachusetts General Hospital quantitates the increased risk of prostate cancer as a function of body mass index (BMI)

More than 218,000 American men are expected to be diagnosed with prostate cancer this year, according to the researchers. More studies are needed to determine whether weight loss will lower the chances of dying from prostate cancer, said senior author **Matthew Smith**.

"There's lots of reasons to try to maintain an ideal body weight: lesser risk of cardiovascular disease and diabetes," said Smith, a director of research at **Massachusetts General Hospital** Cancer Center in Boston, in a telephone interview on Nov. 9. "It may be that those same lifestyle approaches would reduce the risk of adverse outcomes from prostate cancer."

The researchers examined the records of 788 patients who were diagnosed with advanced prostate cancer. Of those, 241 were considered of normal weight, 402 were overweight and 145 were obese, according to a measure called body mass index. BMI is weight in kilograms divided by height in meters squared. A figure of less than 25 is deemed normal, while a BMI over 30 is considered obese.

The five-year rate of mortality ascribed specifically to the disease was 13.1 percent for ``overweight'' men in the study and 12.2 percent for ``obese'' men, compared with 6.5 percent for other men, according to the study. The relative risk suggested by those rates is before adjustment for tumor size at the time of diagnosis and other circumstances.

More Work Urged

It may be that prostate cancer treatments are less effective in men who have higher weights, Smith said, or that other illnesses these men may have, such as diabetes, play a role in the increased risk of prostate cancer death.

"More work needs to be done to understand the mechanisms," Smith said.

Prostate cancer occurs in the tissue of the prostate, a walnut-sized gland in the male reproductive system that is found below the bladder. More than 27,000 Americans are expected to die of the disease this year.

Dr. Bleyer:

☑ Since many of our DEFEAT participants have prostate cancer, this report has special relevance

☑ There is evidence that treatment is less effective in overweight and obese patients. We still don't know, for example, how to optimally calculate the dose of chemotherapy and hormonal therapy in obese patients and radiation therapy is more difficult. In prostate cancer, PSA levels are different and less accurate in obese patients, making it more difficult to know when and for how long to treat. These *treatment* factors affect survival benefit

☑ Compare this article with the next report, in which benefits of overweight, and even obesity, are suggested

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

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

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

Purpose: To examine the prevalence and clustering of physical activity (PA), fruit and vegetable consumption (5-A-Day), and smoking across six major cancer survivor groups and to identify any associations with health-related quality of life (HRQoL).
Methods: A total of 9,105 survivors of six different cancers completed a national cross-sectional survey that included the lifestyle behavior questions and the RAND-36 Health Status Inventory.
Results: Only a minority of cancer survivors were meeting the 5-A-Day (14.8% to 19.1%) or PA (29.6% to 47.3%) recommendations, whereas most were meeting the smoking recommendation (82.6% to 91.6%). In terms of the lifestyle behavior clusters, only 5% of cancer survivors were meeting all three recommendations. Analyses of covariance generally showed higher HRQoL in survivors who were meeting versus not meeting each lifestyle behavior recommendation with the strongest associations emerging for PA. Trend analyses showed a steep positive association between the number of lifestyle behavior recommendations being met and HRQoL for breast ($P < .001$), prostate ($P < .001$), colorectal ($P < .001$), bladder ($P < .001$), uterine ($P < .001$), and skin melanoma ($P < .001$) cancer survivors.
Conclusion: Few cancer survivors are meeting the PA or 5-A-Day recommendations, and even fewer are meeting all three lifestyle recommendations. The association between the current lifestyle recommendations and HRQoL in cancer survivors appears to be cumulative. Interventions to increase PA and fruit and vegetable consumption and reduce smoking are warranted and may have additive effects on the HRQoL of cancer survivors.

Dr. Bleyer:

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

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

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

**5 vegetables or fruits a day

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

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

Kerry S. Courneya KS, Katzmarzyk PT, Bacon E
University of Alberta, Edmonton, Alberta, CA; Pennington Biomedical Research Center, Baton Rouge, Louisiana; Queen's University, Kingston, Ontario, Canada

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

Background. Physical inactivity and obesity are associated with poorer disease outcomes in several cancer survivor groups. Few studies, however, have provided population-based estimates of these risk factors in cancer survivors and compared them with individuals without a history of cancer. Here such estimates for the Canadian population are reported.
Methods. Data were obtained from the 2005 Canadian Community Health Survey consisting of computer-assisted interviews of 114,355 adults representing an estimated 23,285,548 Canadians. Participants self-reported their cancer history, height, and body weight to calculate body mass index and participation in various leisure-time activities.
Results. **Fewer than 22% of Canadian cancer survivors were physically active** and over 18% were obese. Few differences were observed between cancer survivors and those without a history of cancer except that: 1) **prostate cancer survivors were more likely to be active** (adjusted odds ratio [OR] = 1.27; 95% confidence interval [CI] = 1.01-1.59) **and less likely to be obese** (adjusted OR = 0.71; 95% CI = 0.56-0.90); 2) skin cancer survivors (nonmelanoma and **melanoma) were more likely to be active** (adjusted OR = 1.33; 95% CI = 1.12-1.59); and 3) obese breast cancer survivors were less likely to be active compared with obese women without a history of cancer (adjusted OR = 0.51; 95% CI = 0.27-0.94).
Conclusions. Canadian cancer survivors have low levels of physical activity and a high prevalence of obesity that, although comparable to the general population, may place them at higher risk for poorer disease outcomes. Population-based interventions to increase physical activity and promote a healthy body weight in Canadian cancer survivors are warranted.

Dr. Bleyer:

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

Many cancer survivors are overweight and sedentary

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Dr. Bleyer:

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

Prognostic value of body mass index in locally advanced breast cancer

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

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

Purpose: The purpose of this retrospective study was to determine the association and prognostic value of body mass index (BMI) at the time of initial diagnosis in patients with locally advanced breast cancer

(LABC). The analysis includes the subsets of inflammatory (IBC) and noninflammatory (non-IBC LABC) breast cancer.
Experimental Design: We identified 602 patients who had LABC treated on prospective clinical trials. BMI was divided into three groups: (a) 24.9 (normal/underweight), (b) 25.0 to 29.9 (overweight), and (c) 30 (obese). Kaplan-Meier product limit method was used to estimate survival outcomes. Cox proportional hazards were used to determine associations between survival and BMI and to test for an interaction between BMI and breast cancer type.
Results: Eighty-two percent had non-IBC LABC and 18% had IBC. Obese patients tended to have a higher incidence of IBC compared with overweight and normal/underweight groups (P = 0.01). Median follow up was 6 years for all patients. Median overall survival (OS) and recurrence-free survival (RFS) were 8.8 and 5.9 years, respectively. Patients with LABC who were obese or overweight had a significantly worse OS and RFS (P = 0.001) and a higher incidence of visceral recurrence compared with normal/underweight patients. In a multivariable model, BMI remained significantly associated with both OS and RFS for the entire cohort. The interactions between BMI and LABC subsets and between BMI and menopausal status were not statistically significant.
Conclusion: Patients with LABC and high BMI have a worse prognosis. Evaluation of the biological factors associated with this observation can provide tools for additional therapeutic interventions.

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

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BMI linked to overall survival in locally advanced breast cancer

HemOnc Today - March 27, 2008
By Stacey L. Adams
In women with locally advanced breast cancer, prognosis is worse among those with high BMI, compared with patients who are normal or underweight.
Researchers from University of Texas M.D. Anderson Cancer Center in Houston and Dubai Hospital in United Arab Emirates analyzed data from 602 patients with locally advanced breast cancer who were treated in prospective clinical trials. Patients were divided into three groups based on BMI: ≤24.9, normal/underweight; 25.0 to 29.9, overweight; ≥30, obese.
Eighty-two percent of patients had non-inflammatory locally advanced breast cancer; 18% had inflammatory locally advanced breast cancer. Compared with overweight and normal/underweight groups, those in the obese category had a higher incidence of inflammatory breast cancer (P=.01).
Compared with the normal/underweight population, overall survival and recurrence-free survival rates were worse for those in the obese or overweight categories who had locally advanced breast cancer (P=.001). The incidence of visceral recurrence was also higher among the overweight and obese groups. –
Source: Clin Cancer Res. 2008;14:1718-1725.

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

Commentary from Donald W. Northfelt, MD
Associate Professor of Medicine, Mayo Clinic, Scottsdale, Ariz.
This article is important because we are hoping to use any and all information available to help us understand the risks that women with breast cancer face. In other words, we want to make sure that we recognize all of the information that might be valuable in helping to understand how to take care of women with breast cancer.
In this instance, we have been informed that **women who have a bad prognosis with breast cancer at the time of initial diagnosis will actually have a worse prognosis if they have a higher BMI**. This

information, therefore, helps us begin to categorize women within a conventional high-risk group — to categorize these women into relatively higher and lower-risk groups with respect to their prognosis.
This study does not offer us a means to treat those women differently, but what it can do is suggest to us that if we recognize that there is a particular group of women at higher risk — women with those types of cancer who also have higher BMI — then in the future, we might be able to study that group of women specifically and look for better ways to treat them as a 'high, high' risk subset. We do this often in cancer medicine; we try to distinguish, even within a bad disease, those people whose disease is worse because those people in particular would benefit from having better therapies devised for them. This study, in and of itself, is interesting intellectually, but it will not lead anywhere unless researchers now take these women who have been defined as 'high, high' risk based on high BMI and try to do something for them. That is why any study like this is done, really, it is not just the intellectual exercise but to help us understand who needs more help and then to begin to figure out ways to get them that help.
In medicine, we talk all the time to our patients about the value of maintaining a healthy weight. We know, for example, that the risk for diabetes is reduced if you maintain a healthy weight; we know that risk for cardiovascular disease, stroke, heart attack and high blood pressure will be reduced if you maintain a healthy weight. We believe that there are cancer risks that can be reduced by maintaining a healthy weight, and here is an example of that. There is a reasonably good foundation in this report to be able to say to women, 'it is valuable to maintain a healthy weight because **if you ever are so unfortunate as to develop breast cancer, by having a healthy weight at that time**, **you are going to make your prognosis better**.'
So, I think this adds to the body of evidence that we need to make women aware that maintaining a healthy weight as a lifetime wellness strategy is a good thing to shoot for. I think the messages women get from medical professionals about maintaining a healthy weight are pretty widely disseminated in our culture and our medical care, but every opportunity we have to re-emphasize that and expand women's understanding of that is worthwhile. So here is another instance in which it has been made clear that maintaining healthy body weight will be advantageous. This **adds to the chorus calling** for maintaining healthy body weight and it has a particular focus because it is a very important women's health issue that a lot of women worry about.

Dr. Bleyer:

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

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

Wed May 21, 2008
By Megan Davies
NEW YORK (Reuters Life!) - American women are more concerned about losing weight than they are about suffering from cancer, heart disease or diabetes, a survey showed.

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

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

The survey showed many women thought they should be slimmer, with more than 80 percent saying they were overweight.
But just 43 percent said they were exercising at least three times a week, and 11 percent played team and individual sports. And less than two-thirds of all women said they get an annual physical.
"These **findings should be a wake-up call to American women everywhere to make their yearly checkups without fail** and make their own personal health a top priority," said Diane Salvatore, editor in chief of Ladies' Home Journal, which is published by Meredith Corp.
While the majority of women said they were overweight, 68 percent said they were satisfied with their "identity and development as an individual".
But **40 percent said it was wrong for a man to tell a woman she was overweight**.
To improve their health, 26 percent of women said they took natural herbs and supplements, while 25 percent bought or adopted a pet, according to the survey.
Four percent visited a spiritual or religious leader and one percent went to a hypnotist.

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

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

HemOncToday – May 10, 2008

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

There are more than 10 million cancer survivors in the United States, and 22% are women diagnosed with breast cancer, notes the principal investigator, M. Tish Knobf, Ph.D., R.N., the American Cancer Society Professor at the School of Nursing and a member of the Yale Cancer Center.
“Cancer survivors face persistent physical symptoms as well as psychological distress when treatment ends,” Knobf says. “For long-term survivors, there are additional concerns related to late effects of cancer therapy, such as bone loss.”
Her team conducted a pilot study to look at the effects of exercise and found that 88% of the women adhered to the program, maintained their weight, had no changes in bone mass and improved psychologically.
“Weight gain, changes in body composition, decreased physical functioning, bone loss and menopause in women treated for cancer may increase risks for cardiovascular disease, diabetes, and osteoporosis,” Knobf says. “With an estimated 64% of cancer survivors now living longer than five years, interventions are needed to reduce the risk of cancer recurrence, secondary cancers, and health risks for other chronic illnesses.”
Co-investigators Dr. Lyndsay Harris and Dr. Karl Insogna will provide additional expertise to help monitor the women enrolled in the study. Harris, associate professor of medical oncology and director of the Yale Cancer Center Breast Cancer Program, studies the molecular classifications of breast cancer, particularly in minority women. Insogna, director of the Yale Bone Center and professor of internal medicine, has clinical expertise on the disease-related causes of bone loss.

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

Changes in prostate gene expression in men undergoing an intensive nutrition and lifestyle intervention

Ornish D, Magbanua MJM, Weidner G, Weinberg V, Kemp C, Green C, Mattie MD, Marlin R, Simko M, Shinohara K, Haqq CM, Carroll PR
Proceedings of the National Academy of Sciences | vol. 105 | no. 24 | Published online June 16, 2008
University of California at San Francisco

In 30 men with low-grade prostate cancer who declined immediate surgery, radiation therapy and/or hormonal therapy, an aggressive low fat diet and physical therapy regimen was associated with changes in the genes of their tumor that reduced its malignant potential

Epidemiological and prospective studies indicate that comprehensive lifestyle changes may modify the progression of prostate cancer. However, the molecular mechanisms by which improvements in diet and lifestyle might affect the prostate microenvironment are poorly understood. We conducted a pilot study to examine changes in prostate gene expression in a unique population of men with low-risk prostate cancer who declined immediate surgery, hormonal therapy, or radiation and participated in an **intensive nutrition and lifestyle intervention** while undergoing careful surveillance for tumor progression. Consistent with previous studies, **significant improvements in weight, abdominal obesity, blood pressure, and lipid profile** were observed (all $P < 0.05$), and surveillance of low-risk patients was safe. Gene expression profiles were obtained from 30 participants, pairing RNA samples from control prostate needle biopsy taken before intervention to RNA from the same patient's 3-month postintervention biopsy. Quantitative real-time PCR was used to validate array observations for selected transcripts. Two-class paired analysis of global gene expression using significance analysis of microarrays detected 48 up-regulated and 453 down-regulated transcripts after the intervention. Pathway analysis identified **significant modulation of biological processes that have critical roles in tumorigenesis**, including protein metabolism and modification, intracellular protein traffic, and protein phosphorylation (all $P < 0.05$). Intensive nutrition and lifestyle changes may modulate gene expression in the prostate. Understanding the prostate molecular response to comprehensive lifestyle changes may strengthen efforts to develop effective prevention and treatment.

Dr. Bleyer:
☑ Dr. Ornish, the principal investigator of this study, is well known for his advocacy of exercise and nutrition (**E&N**) for cancer patients
☑ The journal in which this article appears is also well known for publishing studies of the highest quality
☑ If the results can be confirmed, this will be the first study to shown that the very genes that cause cancer can be turned off by **E&N** alone

The relation between body mass index, comorbidity, choice of surgery, and prognostic factors in early breast cancer: Data from a nation-wide Danish cohort

A. R. Jensen, S. Christensen, R. Zachariae, S. Moller, A. B. Jensen
J Clin Oncol 26: 2008 (May 20 suppl; abstr 11110)

Patient with early breast cancer who are overweight have increased co-morbidities, more negative prognostic factors, and require more extensive surgery.

Background: Overweight females have a higher incidence and wirse prognosis of breast cancer. We explore the associations between body mass index (BMI), prognostic factors and choice of surgery. Methods: The study included 4917 women aged 18-70 yrs. diagnosed with primary loco-regional breast cancer from October 2001 to March 2004. Sixty-eight percent (3343) returned a questionnaire including data on height and weight. Co-morbidity was assessed using Charlson Co-morbidity Index (CCI). The Danish Breast Cancer Cooperative Group provided data on surgery and prognostic factors. Differences in treatment associated with (BMI) and CCI- score were analyzed with ψ2-tests. Correlations between BMI, CCI, age, tobacco, alcohol, and prognostic factors were analyzed using Spearman's ρ.
Results: Twenty-six percent had BMI >25 and 8% had BMI >30. Twelve percent had CCI-score>0, the majority (80%) having one co-morbid condition. Prevalence of co-morbidity increased significantly with

both BMI and age (p<0.001). There was a positive association between CCI-score and mastectomy (p<0.001), whereas sentinel lymph node procedures decreased with increasing CCI-score (p<0.001). No associations were found between CCI-score and tumor size, grade, estrogen-receptor status, number of removed or metastatic lymph nodes. Increasing BMI was positively correlated with age and use of alcohol or tobacco. The incidence of sentinel lymph node procedures decreased with BMI above 25, whereas the number of lymph nodes removed increased with higher BMI. BMI was not associated with the chance of mastectomy. Higher BMI was significantly correlated to 1)increasing tumor size, from median 14 mm in patients with BMI<18.5 to 22 mm for BMI>30, 2)increasing number of positive lymph nodes, 3)stage and 4)grade, but not estrogen-receptor status.
Conclusions: The study suggeststhat higher BMI is associated with increased co-morbidity and negative prognostic factors. Patients with overweight had more extensive axillary surgery and more positive lymph nodes. Co-morbidity did not influence prognostic factors. A correlation between surgery and co-morbidity was found. However, these differences are not expected to affect outcome.

Dr. Bleyer:
☑ The overweight breast cancer not only has a greater likelihood that the cancer will recur but also from the start requires more surgery to evaluate and treat the cancer
☑ The much lower rate of obesity in Denmark compared to the U.S. is apparent in this study

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Impact of body mass index on lymph node dissection and surgical outcomes of patients with gastric cancer.

J Clin Oncol 26: 2008 (May 20 suppl; abstr 15655)
S. Noh, S. Oh, S. Kim, J. Song, W. Hyung, S. Rha, Y. Lee, S. Choi, H. Chung

Obese patients with stomach cancer required longer operations and had more postoperative complications than non-obese patients

Background: There has been a general consensus that increased body mass index (BMI) is correlated with poor surgical outcome. The purpose of this study was to clarify the effects of BMI on surgical outcomes of gastric cancer patients.
Methods: A total of 517 patients who underwent curative total gastrectomy with D2 dissection from January 2000 to December 2003 were studied retrospectively from a prospectively designed computer database. The patients were assigned to three groups according to their BMI: group A, BMI < 23 kg/m2 (normal and underweight); group B, BMI 23-24.9 kg/m2 (overweight); group C, BMI > 25 kg/m2 (obesity). The parameters such as operation time, blood loss, packed RBC transfusion, number of retrieved lymph nodes, first time of flatus, start of soft diet, postoperative hospital stay, postoperative morbidity, mortality, recurrence, and prognosis were analyzed.
Results: Group C patients had significant longer operation time and higher postoperative complications in comparison to group A and B. However, there were no significant differences regarding blood loss, packed RBC transfusion, number of retrieved lymph nodes, first time of flatus, start of soft diet, postoperative stay, mortality, recurrence, and survival rates among three groups. Logistic regression analysis revealed that tumor size, histological type, serosal invasion, and nodal metastasis were independent risk factors for recurrence while obesity was not. Multivariate analysis showed that age, tumor size, histological type, serosal invasion, and nodal metastasis were independent prognostic factors whereas obesity was not.
Conclusions: Although BMI affect somewhat operation time and postoperative morbidity, it does not affect long-term outcomes of patients with gastric cancer.

Dr. Bleyer:
☑ The primary finding that obesity was associated with longer operations and more post-operative complications is well known from other reports
☑ The investigators did not find that increased BMI *per se* was associated with a worse survival from the cancer

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Obesity and microvascular invasion in hepatocellular carcinoma

Siegel AB, Yu JC, Moss J, et al
J Clin Oncol 26: 2008 (May 20 suppl; abstr 4520)

Patients with liver cancer and an elevated BMI had more evidence for invasion of their cancer into the blood stream (and potential for spread throughout the body) than those with a normal BMI

Background: Obesity is a risk factor for worsened outcomes in hepatocellular carcinoma (HCC). Adipokines such as leptin are known to be angiogenic, and are increased in those with obesity. We hypothesized that tumor specimens from obese patients would be more likely than those from non-obese patients to show microvascular invasion, a known predictor of poor survival in HCC.
Methods: 164 consecutive patients who underwent surgery (resection or transplantation) at Columbia University Medical Center from 1/1/2002-12/31/2006 with available pathology were evaluated retrospectively for clinical and pathological characteristics and overall survival.
Results: The median age of our patients was 58 years. 49%, 27% and 24% were Child-Pugh class A, B, and C respectively. At surgery, 34% had a BMI >30 kg/m2, 42% had a BMI of 25-30 kg/m2, and 24% had a BMI <25 mg/m2. 33% had microvascular invasion on pathology. Table 1 shows the positive association between BMI and presence of microvascular invasion in our cohort. A Cochran- Armitage test for trend showed a significant association between microvascular invasion and BMI ($p = 0.002$). The presence of microvascular invasion was associated with significantly worsened overall survival, as expected. BMI tertile was not associated with overall survival in univariate and multivariable analyses.
Conclusions: We showed a significant association between obesity and increased microvascular invasion in a cohort of patients who received surgery for HCC. The association remained when we adjusted for Child- Pugh score to control for potential confounding with ascites. This analysis suggests that increased body mass may have a dose-response relationship with microvascular invasion, perhaps mediated by adipokines such as leptin. A larger prospective study is planned.

Association between BMI and Microvascular Invasion

BMI ($kg/m^{2)}$	Crude OR (95% CI)	Adjusted for Child-Pugh OR (95% CI)
<25	1.0 Referent	1.0 Referent
25-30	3.2 (0.8-19.1)	3.3 (0.6-17.9)
>30	6.8 (1.6-39.9)*	6.7 (1.2-36.9)*

= $p < 0.05$

Dr. Bleyer:
☑ The importance of this study is that it may provide an explanation for how obesity can make cancer worse; obesity increases the amount of fat in the liver and a molecule elaborated by fat cells (adipokine) such a leptin may enable cancer cells to enter the blood
☑ The investigators did not find that increased BMI *per se* was associated with a worse survival from the cancer

Association between serum adiponectin and prostate cancer risk

J Clin Oncol 26: 2008 (May 20 suppl; abstr 5147)
S. Jacobus, D. J. Sher, M. M. Regan, J. Chamberland, W. K. Oh, C. Mantzoros

The aggressiveness (grade) of prostate cancer was increased in patients with a high BMI

Background: Adiponectin is a fat adipokine that has been linked with several hormonally-active adenocarcinomas. Recent studies have suggested a relationship between serum adiponectin and hormone-dependent prostate cancer (PCA), supported in part by an association between BMI and prostate cancer grade. We evaluated this potential relationship.
Methods: PCA patients evaluated at Dana-Farber Cancer Institute (DFCI) between 2001 and 2006 who enrolled in a prospective serum banking protocol and were without prior hormonal therapy and/or metastatic disease were eligible. Serum adiponectin levels were ascertained and clinical data were

contributed by the DFCI prostate cancer Clinical Research Information System (CRIS) database. Associations between adiponectin quartiles and categorical patient characteristics were assessed using the chi-square test (ψ2). Spearman correlation coefficients were used to quantify associations between continuous variables. High-grade disease was defined as biopsy or radical prostatectomy (RP) Gleason score (GS) of > 7. Logistic regression models were used to assess the relationship between high-grade disease and adiponectin levels while adjusting for other potential prognostic variables.
Results: There were 539 pts included in this study, 199 of whom underwent RP. Median age was 60 yrs with 94% of pts white. Median PSA was 5.1 ng/dL (IQR 4.2-7.3). 21% of cancers were clinical T2 or higher. GS >7 was seen in 47% of pts at diagnosis and 51% of RP pts. Spearman correlation coefficients showed weak associations of adiponectin with PSA and age, but a stronger and significant inverse association between BMI and adiponectin was observed. Higher PSA, higher age, and higher BMI were significantly associated with increased odds of biopsy GS at diagnosis >7, but adiponectin was not. There was a significant inverse relationship (p=0.014) between RP GS and adiponectin dichotomized at the median. Although, adiponectin analyzed in quartiles showed a non-monotonic pattern. Dichotomized adiponectin remained significant after adjusting for BMI, PSA and age. No significant interaction between BMI and adiponectin was observed.
Conclusions: In a subset of RP patients, lower adiponectin was inversely associated with prostate cancer grade, independent of BMI, age and PSA.

Dr. Bleyer:
☑ The worse outcome after a diagnosis of prostate cancer in obese patients may be explained by a higher grade of prostate cancer
☑ Why obese patients have a more aggressive prostate cancer is unknown but may be due to lower levels of adiponectin that are associated with obesity

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The impact of body mass index on the surgical staging and outcome in women with intermediate risk endometrial cancer

J Clin Oncol 26: 2008 (May 20 suppl; abstr 16517)
A. Olawaiye, A. Rauh-Hain, M. Del Carmen, A. Goodman

Severely obese patients with uterus cancer did not have a worse survival; they may even have had a better survival

Background: To test the null hypothesis that morbid obesity has no influence on the surgical staging and outcome in women with intermediate risk endometrioid adenocarcinoma.
Methods: We reviewed the charts of all women diagnosed with intermediate risk endometrioid adenocarcinoma in our institution between January 1, 1995 and January 1, 2005. There were 200 eligible women out of whom 9 were excluded because of incomplete medical records. Statistical analysis was performed by SPSS. Median follow up was 50.8 months (range 2 - 152 months).
Results: Patients were divided into 3 groups according to their BMI, normal or overweight (<30), obese (>30<40) and morbidly obese (>40). Morbid obese patients accounted for 26 % of the study group. The morbidly obese patients were younger than patients with BMI of < 30 (61.53 vs. 68.81, p<0.001). Other medical co-morbidities (hypertension, lung disease, hypothyroidism and diabetes) were more common among the morbidly obese patients (P<0.01). There was no difference in the number of patients with grade III histology between morbidly obese and patients with BMI of <30 (18% vs. 29% p = 0.14). The proportion of patients who had adjuvant radiotherapy was similar across groups). Surgical staging was less complete among morbidly obese patients as suggested by a lower lymph node count compared to all other groups combined (11 vs. 16, p < .05). However, compared to patients with BMI < 30, morbidly obese patients did not show any difference in disease free survival (p = 0.83) and their overall survival was superior (124 vs. 111 months, p = 0.036).
Conclusions: Morbidly obese women with intermediate risk endometrioid adenocarcinoma may have a better outcome even though their BMI precludes thorough surgical staging. Factors other than tumor grade may account for the better outcome in this group.

Dr. Bleyer:
☑ A limitation of this study is that the severely obese patients could not be staged as well (their operations were more difficult) and hence they may have had a better stage and thereby a better survival independent of their obesity
☑ Another possibility is that their obesity prevented as an intensive a therapy as received by non-obese patients such that when their tumor progressed it was less resistant to subsequent therapy and they thereby stay alive longer; the combination of a similar disease-free survival and better overall survival supports this explanation

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Reduced chemotherapy dose intensity in patients with ovarian cancer: Results from a prospective nationwide study.

J Clin Oncol 26: 2008 (May 20 suppl; abstr 16508)
M. S. Poniewierski, J. Crawford, D. C. Dale, E. Culakova, N. M. Kuderer, D. A. Wolff, G. H. Lyman

Obese patients with ovarian cancer received less therapy than non-obese patients

Background: Chemotherapy represents a central component of effective multidisciplinary management of women with ovarian cancer. The study reported here was conducted to evaluate the delivery of ovarian cancer chemotherapy and the risk of treatment- associated toxicity.
Methods: A prospective observational study of adult cancer patients initiating a new chemotherapy regimen was conducted at randomly selected US practice sites. Unselected patients with ovarian cancer were consented and followed over the first 4 cycles of chemotherapy. Demographic, clinical and treatment-related measures were captured at baseline and during treatment
Results: Between 2002 and 2005, 312 patients with ovarian cancer were registered with mean age of 62.3 years (range: 18-89 years). 80% of patients were stages 3 or 4 with 46% reporting one or more comorbidities. Mean body mass index (BMI) was 27.5 with 30.4% classified as obese with BMI > 30. Combination chemotherapy was administered to 228 (73%) patients with carboplatin-paclitaxel (47%) and carboplatin-docetaxel (10%) most frequently utilized. One-fourth of patients experienced severe or febrile neutropenia (FN) over 4 cycles of treatment. While FN was reported in only 6.6% of patients, two-thirds occurred in cycle 1. A nonstandard regimen was identified in 38 (12.2%) patients with such patients experiencing greater risk of FN (22%) than other patients (5%) (P=.001). Among the remaining 274 patients, the average relative dose intensity (RDI) over 4 cycles was 76% with 60% of patients receiving RDI <85% half of which was planned from the start of treatment. **The strongest predictors of reduced RDI in multivariate analysis was the presence of obesity (P=.001)**, poor ECOG performance status and use of nonplatinum chemotherapy regimens. In addition, geographic residence and type of oncology practice were significant predictors of reduced RDI.
Conclusions: Most patients with ovarian cancer received combination chemotherapy for locally advanced or metastatic disease. Hematologic toxicity occurred early and nearly 75% of patients received chemotherapy RDI <85% or a nonstandard regimen potentially compromising long term outcomes.

Dr. Bleyer:
☑ Treating obese patients with chemotherapy is more difficult than treating non-obese patients, in part because it is not clear how to calculate or adjust dosage in obese persons
☑ That obese patients may be under-doses and under-treated—I have certainly observed this pattern in children, adolescents and young adults—may be another reason for their know worse outcome

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Causes of death are linked to a person's weight [Prevention]

By GINA KOLATA
New York Times - November 7, 2007; Source: **JAMA**, November 7, 2007
About two years ago, a group of federal researchers reported that overweight people have a lower death rate than people who are normal weight, underweight or obese. Now, investigating further, they found out which diseases are more likely to lead to death in each weight group.

A prestigious health news reporter interprets the national Centers for Disease Control and Prevention report that indicates overweight (but not obese) persons have a lower death rate from some diseases

Linking, for the first time, causes of death to specific weights, they report that overweight people have a lower death rate because they are much less likely to die from a grab bag of diseases that includes

Alzheimer's and Parkinson's, infections and lung disease. And that lower risk is not counteracted by increased risks of dying from any other disease, including cancer, diabetes or heart disease.

As a consequence, the group from the Centers for Disease Control and Prevention and the National Cancer Institute reports, there were more than 100,000 fewer deaths among the overweight in 2004, the most recent year for which data were available, than would have expected if those people had been of normal weight.

The researchers also confirmed that obese people and people whose weights are below normal have higher death rates than people of normal weight. But, when they asked why, they found that the reasons were different for the different weight categories.

Some who studied the relation between weight and health said the nation might want to reconsider what are ideal weights.

"If we use the criteria of mortality, then the term 'overweight' is a misnomer," said Daniel McGee, professor of statistics at Florida State University.

"I believe the data," said **Dr. Elizabeth Barrett-Connor,** a professor of family and preventive medicine at the University of California, San Diego. **A body mass index of 25 to 30, the so-called overweight range, "may be optimal,"** she said.

Others said there were **plenty of reasons that being overweight was not desirable**.

"Health extends far beyond mortality rates," said **Dr. JoAnn Manson**, chief of preventive medicine at Brigham and Women's Hospital in Boston.

Dr. Manson added that other studies, including ones at **Harvard**, found that being obese or overweight increased a person's risk for a number of diseases, including diabetes, heart disease and several cancers. And, she added, excess weight makes it more difficult to move about and impairs the quality of life.

"That's the big picture in terms of health outcomes," Dr. Manson said. "What the public needs to look at."

Researchers generally divide weight into four categories — normal, underweight, overweight and obese — based on the body mass index, which is a measure of body fat based on height and weight. A woman who is 5 foot 4, for instance, would be considered at normal weight at 130, underweight at 107 pounds, overweight at 150 pounds and obese at 180.

In this study, those with normal weight were considered the baseline and others were compared to them.

The federal researchers, led by **Katherine Flegal**, of the Centers for Disease Control and Prevention, said the big picture they found was surprisingly complex. The higher death rate in obese people, as might be expected, was almost entirely driven by a higher death rate from heart disease.

But, contrary to expectations, the obese did not have an increased risk of dying from cancer. They were **slightly more likely than people of normal weights to die of a handful of cancers that are thought to be related to excess weight — cancers of the colon, breast, esophagus, uterus, ovary, kidney and pancreas.** Yet they had a **lower risk of dying from other cancers**, including lung cancer. In the end, the increases and decreases in cancer risks balanced out.

As for diabetes, it showed up in the death rates only when the researchers grouped diabetes and kidney disease as one category. Diabetes can cause kidney disease, they note. But, the researchers point out, the number of diabetes deaths may be too low because many people with diabetes die from heart disease, and often the cause of death is listed as a heart attack.

The diverse collection of diseases other than cancer, heart disease and diabetes, which show up in the analyses of the underweight and the overweight, have gone relatively unscrutinized among epidemiologists, noted **Dr. Mitchell Gail**, a cancer institute scientist and an author of the paper. But, Dr. Gail added, "these are not a negligible source of mortality."

The new study began several years ago when the investigators used national data to look at death risks according to body weight. They concluded that, compared with people of normal weight, the overweight had a decreased death risk and the underweight and obese had increased risk.

That led them to ask if being fat or thin affects a person's life span, what diseases, exactly, are those individuals at risk for, or protected from?

The research involved analyzing data from three large national surveys, the National Health and Nutrition surveys, which are administered by the National Center for Health Statistics. Their participants are a

nationally representative group of Americans who are weighed and measured, assuring that heights and weights are accurate, and followed until death. The investigators determined the causes of death by asking what was recorded on death certificates.

The researchers caution that a study like theirs cannot speak to cause and effect. They do not yet know, precisely, what it is about being underweight, for instance, that increases the death rate from everything except heart disease and cancer. Researchers tried to rule out those who were thin, because they might have been already sick. They also ruled out smokers, and the results did not change.

Dr. Gail, though, had some advice, which, he said, is his personal opinion as a physician and researcher: **"If you are in the pink and feeling well and getting a good amount of exercise and if your doctor is very happy with your lab values and other test results, then I am not sure there is any urgency to change your weight."**

Dr. Bleyer:

- ☑ Gina Kolata is one of the best healthcare reporters in the business [Margaret Kolata, a relative, is an administrator at St. Charles-Bend]; I nearly always pay attention to Gina [and I definitely always pay attention to Margaret]
- ☑ Be careful in reading this report to distinguish two issues: overweight vs. obese and length of life vs. quality of life
- ☑ The overweight data suggest that one may be able to live longer by being modestly overweight but that the tradeoff is having a higher risk of cancer, living with a lower quality of life (with or without cancer)
- ☑ Bottom line: being overweight (but not obese) may lengthen life in some persons, but quality of life more than compromises this longevity effect; weight alone does not tell the whole story
- ☑ Living longer but now enjoying it doesn't seem worthwhile
- ☑ Also, once cancer is diagnosed, the weight of the evidence clearly indicates that being overweight is not beneficial

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Diet and exercise are key factors in determining lung cancer risk [Prevention]

Lisa M. Cockrell - Medscape Medical News

Sixth Annual International Conference on Frontiers in Cancer Prevention Research: Abstract B143. Presented December 7, 2007.

> In this comparison of lung cancer patients at the MD Anderson Cancer Center and health matched controls from the community, the risk of lung cancer was correlated with salad consumption and with gardening in both former and active smokers and in non-smokers

December 10, 2007 (Philadelphia, Pennsylvania) — Smoking is not the only factor to be considered in the determination of a person's risk of developing lung cancer, according to a recent study presented at the American Association for Cancer Research (AACR) 6th Annual International Conference on Frontiers in Cancer Prevention Research. This study, highlighted at an AACR press conference on the effects of lifestyle on cancer prevention, suggested that, in addition to smoking, diet and physical activity are key in determining a person's overall risk of developing lung cancer. This is important, especially when considering that although smoking is the leading cause of lung cancer, approximately 15% of all lung cancers are diagnosed in people who have never smoked.

"The way we live our lives does influence our risk of getting cancer," said **Tim Byers, MD**, professor of preventative medicine at the **University of Colorado**, in Aurora, who was not involved in the study. "Choices we make in tobacco use, sun exposure, food, and physical activity all seem to add up to explain half or more of cancer risk in the population."

Recently, a model to predict lung cancer development in never, former, and current smokers was developed. Although this Spitz model showed clear associations with lung cancer development and smoking history, family history of respiratory disease, and exposure to second-hand smoke or dust, the model did not take into account the relative contributions of several other factors. In the current study, presented by **Michele Forman, PhD**, from the **University of Texas MD Anderson Cancer Center**, in Houston, fruit and vegetable intake, as well as physical activity, were examined as potential risk factors. According to Dr. Forman, this study was the first risk-prediction model for lung cancer that took into account, in addition to smoking, both diet and physical activity.

Data were obtained from the same people used in the generation of the Spitz model. Participants included lung cancer patients enrolled from the University of Texas MD Anderson Cancer Center and healthy

matched controls recruited from a local private-physician clinic group. The controls were matched on age, sex, and smoking status. All study participants were categorized as either never, former, or current smokers.

A 135-point questionnaire modified from the National Cancer Institute was used to gather dietary data for all participants. For lung cancer patients, dietary data were gathered for the 1 year prior to diagnosis; for the healthy controls, data were gathered for the 1 year prior to recruitment. The questionnaire responses were standardized by converting to 2006 USDA food-pyramid guidelines. In additional, level of physical activity was established for the study participants.

Interestingly, the participants who ate fewer than 3 salads per week (or vegetables that were associated with salads, such as carrots) had more than twice the risk of developing lung cancer than those who consumed more than 4 salads per week. Importantly, this was shown to be true regardless of smoking status, although the effect was more dramatic in former and current smokers.

Impact of Salad Consumption on Developing Lung Cancer
Odds Ratio (95% Confidence Interval)

	Never Smokers	Former Smokers	Current Smokers
≥ 4/wk	1.00	1.00	1.00
3/wk	2.09 (1.03 – 4.21)	2.16 (1.39 – 3.37)	1.62 (1.02 – 2.59)
< 3/wk	2.15 (1.17 – 3.95)	2.52 (1.69 – 3.77)	2.72 (1.77 – 4.18)

However, fruit consumption was not found to affect the risk for lung cancer. In addition, Dr. Forman emphasized that "all of the vegetables that we did find [that were associated with a decreased risk] were in the raw form, and this is very important because the raw form of vegetables may have higher levels of nutrients than the processed form."

Dr. Forman stated that another factor, physical activity, also reduced the risk for lung cancer across all smoking groups. For this study, the **physical activity assessed was gardening, because current smokers rarely engaged in any other type of exercise**. Participants who gardened on a weekly basis experienced a 33% to 46% decreased risk for lung cancer development, with those who never smoked showing the most dramatic decrease.

When the newer risk-prediction model, which incorporated both diet and exercise, was compared with the original Spitz prediction model, Dr. Forman said it was found to have "a significant increased improvement." However, she cautioned that this study was preliminary in that it did not take into account the effects of many other food groups, alcohol, or vitamin use. In addition, she suggested that 1 possible explanation for the decreased risk associated with salad consumption and gardening is that these individuals inherently have a preventive lifestyle overall. Future analyses to look closely at other preventive and lifestyle factors might add to this prediction model.

Dr. Bleyer:

☑ I included this *prevention* report since it shows how **E&N** as a factor of cancer protection is powerful enough to be effective in a cancer for which smoking is an overwhelmingly potent factor

☑ That gardening was used as the measure of physical activity (active smokers generally undertake little exercise) and yet even this modest level of exercise showed a beneficial effect in preventing lung cancer in smokers and nonsmokers is impressive

☑ That **E&N** were minimally evaluated—gardening for exercise and salad for nutrition—and yet each showed a protective effect implies that had more E&N been undertaken the benefits may well have been more apparent.

Obesity causes cancer in 6,000 British women a year [Prevention]

LONDON (Reuters) - Nov 7, 2007

Reporting by Ben Hirschler, editing by Giles Elgood

The Million Women Study of 1.2 million women in the United Kingdom indicates that 1 in every 20 cases of cancer in females are related to an overweight or obese status

Findings from the Million Women Study -- an investigation of disease incidence in 1.2 million British women aged 50 to 64 -- suggest that being overweight or obese accounts for 5 percent of new cancer cases among middle-aged and older women.
Scientists from **Cancer Research UK** and **Oxford University**, writing in the British Medical Journal, said body weight was particularly important in cancer of the womb and the esophagus, where about half of all cases were attributable to being too fat.
The cancer risk of being overweight or obese was highlighted in a sentinel report released jointly by the World Cancer Research Fund and the American Institute for Cancer Research.

Dr. Bleyer:
☑ That half of all the cases of any cancer (esophagus and uterus cancers in this report) is associated with obesity is striking; the correlation is second only to tobacco as a cause of lung cancer
☑ See Nutrition below for more on World Cancer Research Fund and American Institute for Cancer Research

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Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies [Prevention]

Renehan AG, Tyson M, Egger M, Heller RF,' Zwahlen M
The Lancet 2008; 371:569-578

This retrospective analysis of the world literature extend the association between overweight, as measured by the body mass index (BMI), and cancer to include more than 10 different types

Background Excess bodyweight, expressed as increased body-mass index (BMI), is associated with the risk of some common adult cancers. We did a systematic review and meta-analysis to assess the strength of associations between BMI and different sites of cancer and to investigate differences in these associations between sex and ethnic groups.
Methods We did electronic searches on Medline and Embase (1966 to November 2007), and searched reports to identify prospective studies of incident cases of 20 cancer types. We did random-effects meta-analyses and meta-regressions of study-specific incremental estimates to determine the risk of cancer associated with a 5 kg/m2 increase in BMI.
Findings We analysed 221 datasets (141 articles), including 282,137 incident cases. In men, a 5 kg/m2 increase in BMI was strongly associated with oesophageal adenocarcinoma (RR 1·52, p<0·0001) and with thyroid (1·33, p=0·02), colon (1·24, p<0·0001), and renal (1·24, p <0·0001) cancers. In women, we recorded strong associations between a 5 kg/m2 increase in BMI and endometrial (1·59, p<0·0001), gallbladder (1·59, p=0.04), oesophageal adenocarcinoma (1·51, p<0·0001), and renal (1·34, p<0·0001) cancers. We noted weaker positive associations (RR <1·20) between increased BMI and rectal cancer and malignant melanoma in men; postmenopausal breast, pancreatic, thyroid, and colon cancers in women; and leukemia, multiple myeloma, and non-Hodgkin lymphoma in both sexes. Associations were stronger in men than in women for colon (p<0·0001) cancer. Associations were generally similar in studies from North America, Europe and Australia, and the Asia–Pacific region, but we recorded stronger associations in Asia–Pacific populations between increased BMI and premenopausal (p=0·009) and postmenopausal (p=0·06) breast cancers.
Interpretation Increased BMI is associated with increased risk of common and less common malignancies. For some cancer types, associations differ between sexes and populations of different ethnic origins. These epidemiological observations should inform the exploration of biological mechanisms that link obesity with cancer.

Dr. Bleyer:
☑ With now more than 10 cancers having a link with high BMI, the association of body weight and cancer continues to get stronger, albeit the mechanism of cancer development in overweight persons remains elusive
☑ The report below includes a critique of limitations of the findings of this study
☑ For conversion of the kilogram values to pounds, see the next article

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Being overweight may increase risk of developing up to dozen types of cancer [Prevention]

By Maria Cheung, Associated Press
February 15, 2008

This report reviews the above study and presents the data in pounds instead of kilograms

LONDON - Being obese or even overweight may increase a person's risk of developing up to a dozen different types of cancer, European researchers report in a new study.

Doctors have long suspected a link between weight gain and certain cancers, including colon and breast cancers. But the new study, published Friday in the journal Lancet, suggests it could also increase chances for cancer of the esophagus, thyroid, kidney, uterus and gall bladder, among others.

While the study suggests a link, there is no definitive proof that being fat in itself causes cancer.

"To make the link between cause and effect, we need to tick several boxes," said **Dr. Andrew Renehan**, the study's lead author and senior lecturer at the University of Manchester. "This study begins to tick the first two or three boxes, but more research is needed to confirm it."

The researchers compiled data from 141 studies and considered more types of cancers and more diverse populations than had been done previously. The research covered more than **280,000** cases from North America, Europe, Australia and Asia.

The subjects, both overweight and normal weight, were followed for about nine to 15 years, with researchers tracking their body mass index, or **BMI** — a calculation based on weight and height — and correlating it with incidents of cancer.

In men, an average weight gain of 33 pounds increased the risk of esophageal cancer by 52 percent, thyroid cancer by 33 percent, and colon and kidney cancers each by 24 percent, the research found. In women, a weight gain of 29 pounds increased the risk of cancer in the uterus and gall bladder by nearly 60 percent, esophagus by 51 percent and kidney by 34 percent, the study said.

The link was weaker for bone and blood cancers, for both men and women.

In Asian populations, there appeared to be a stronger link between increased BMI and breast cancer.

"This study provides a lot of circumstantial evidence about the dangers of obesity," said **Dr. David Robbins**, a gastroenterologist at **Beth Israel Medical Center in New York**, who was not involved in the study. "It also highlights the cancer crisis we face as obesity rates increase worldwide."

Scientists are unsure how being overweight could make people more susceptible to cancer.

"One of the hypotheses is that the presence of excess fat cells could affect the levels of hormones in your body," Renehan said. "At a cellular level, that may favor the development of tumors in humans."

Because many studies have found that fatter people are more likely to get cancer, experts often recommend losing weight to reduce cancer risk.

"The simple message is that, if you manage to keep a healthy body weight, you will have a lower risk of developing cancer," said **Ed Yong**, of Cancer Research United Kingdom.

Dr. Bleyer:

- ☑ This is the largest metanalysis (method of combining the results of multiple studies into one) conducted to date on the relationship between BMI and the incidence of cancer
- ☑ The evidence may be circumstantial, and the scientific explanation wanting, but the increasing strength of the association can not be denied
- ☑ I don't expect hormone differences in overweight persons to be the reason, if there is a single one
- ☑ Much more likely, there will be multiple factors, including the insulin mechanism described below in the Exercise report from the Dana Farber Cancer Institute and in the June 2007 E&N News

Your lifestyle, your genes and cancer [Prevention]

Robert A. Weinberg, Ph.D., and Anthony L. Komaroff, M.D.
NEWSWEEK - June 14, 2008
New research explores the complex interactions that cause our most dreaded disease. A look into some of the steps you can take to reduce your risk

Drs. Weinberg and Komaroff of MIT and Harvard summarize the recent data that links exercise and nutrition to cancer prevention and eradication, how cancer causing genes are involved, and what all of us can do to reduce risk of occurrence and recurrence

We've known for a long time that a high-fat diet, obesity and lack of exercise can increase the risk of developing heart disease and type 2 diabetes, two conditions that affect millions of Americans. What we are finding out now is that those same lifestyle factors also play an important role in cancer. That's the bad news. The good news is that you can do something about your lifestyle. If we **grew thinner, exercised regularly, avoided diets rich in red meat (substituting poultry, fish or vegetable sources of protein) and ate diets rich in fruits and vegetables**, and stopped using tobacco, we would **prevent 70 percent of all cancers**.

The strongest evidence of the importance of lifestyle in cancer is that most common cancers arise at dramatically different rates in different parts of the globe. Several cancers that are extremely common in the United States—colon, prostate and breast cancer—are relatively rare in other parts of the world, occurring only 1/10th or 1/20th as often. Equally striking, when people migrate from other parts of the world to the United States, within a generation their cancer rates approach those of us whose families have lived in this country for a long time. Even if people in other parts of the world stay put, but adopt a U.S. lifestyle, their risk of cancer rises; as Japanese have embraced Western habits, their rates of colon, breast and prostate cancer have skyrocketed.

What is it about our lifestyle that raises the risk of many types of cancer? The **main culprits seem to be the Western diet, obesity and physical inactivity**. While we've known about the importance of tobacco and cancer for more than 50 years, we are just beginning to understand how diet, a healthy body weight and regular exercise can protect us against cancer.

A striking example of the profound influence of diet was reported last summer in The Journal of the American Medical Association. Doctors determined the eating habits of patients with colon cancer in the years following surgical removal of the cancer. Over the next five years, those who ate a traditional Western diet had a threefold greater likelihood of developing a recurrence of the disease than did those who ate a "prudent" diet rich in fruits and vegetables and including only small amounts of red meat. How had diet affected these patients? The surgery clearly had not removed all their colon-cancer cells: prior to the surgery, some cells had already spread from the primary tumor. The Western diet had somehow stimulated the growth of these small deposits of residual cancer cells.

Obesity is the second most important factor in causing cancer in Western populations after tobacco, and there is evidence that maintaining a healthy weight is protective against the disease. A study by the American Cancer Society in 2003 found that the **heaviest people**, in comparison with the leanest, had a significantly **increased risk of death from 10 different kinds of cancer in men, and from 12 different kinds in women**. The most extreme examples were liver cancer in men (nearly fivefold increased risk) and uterine cancer in women (more than sixfold increased risk).

Exercise has also been shown to play an important role in protecting against some cancers. For example, the Nurses' Health Study reported that women who had one or more hours per day of moderate exercise had a 30 percent lower risk of colon cancer than women who exercised less. Exercise protects against breast cancer, as well.

Lifestyle influences a person's risk for cancer by generating growth-promoting signals that affect cells primed to become cancerous, or that already are cancerous. What primes those cells to become cancerous in the first place are changes in their genes.

All tumors begin with one renegade cell. Initially the cell is just one of about 30 trillion or so in the body. It looks no different from the cells around it, and, like those cells, it divides only if the organ it's part of needs it to divide. Then, even though the organ around it has enough cells, the renegade cell begins to multiply uncontrollably: one cell becomes two, two become four, four become eight, until the descendants are beyond counting.

Cancer is ultimately a disease of malfunctioning genes. Perhaps 10 percent of all cancers occur in people who have inherited genes that make them vulnerable. In some cases, those genes are so influential the risk of cancer is very high. However, most of us are born with good genes that succeed in flawlessly organizing our growth and development. After all, our genes have been optimized by more than 600 million years of evolution; they ought to work well. During the course of our lifetimes, though, genes are damaged in various cells throughout the body. It is these mutated genes that drive most cancers.

Every cell contains growth-promoting genes called "proto-oncogenes" and growth-stopping genes called "tumor suppressor" genes. Mutations that activate a proto-oncogene can cause the gene to release an unceasing stream of growth-stimulating molecular signals that cause the cell to multiply. Conversely, mutations that inactivate tumor-suppressor genes cause their growth-stopping messages to be silenced. In most human-cancer cells, there are multiple mutations—some that activate oncogenes and some that silence tumor-suppressor genes. In other words, cancer cells have stuck accelerator pedals and faulty brakes. During our lifetime, the cells in our bodies will divide 10^{16} times—that's 10,000 trillion times—creating 10,000 trillion opportunities for our "start" and "stop" signals to malfunction, and for a tumor to start.

Another important gene, called telomerase, is turned off in healthy cells, causing the cells to die after they have doubled about 50 times. Telomerase is turned on, however, in many cancer cells, which allows them to multiply indefinitely. There are other genes that cause a cell to "commit suicide" when the cell senses that it has been damaged; if such a cell suicide gene becomes disabled, a cancer cell will be allowed to multiply.

Genes also affect a cancerous cell's ability to metastasize—to detach itself from the primary tumor, crawl through the walls of nearby small blood or lymph vessels and spread through the circulation to other parts of the body. Research published in the past year has identified sets of genes that normally are active only when cells in an embryo need to migrate from one part of the embryo to another. In cancer cells that metastasize, these long-silent genes have somehow been activated. The genes make it easy for a cell to detach itself from the tissue around it and they improve the cell's ability to move toward and through the walls of blood and lymph vessels. Recently, a small molecule called microRNA-10b was discovered to powerfully affect the ability of breast-cancer cells to metastasize. This is exciting because, at least theoretically, such small molecules are attractive targets for treatments.

But what causes the various genetic changes that lead to cancer? Mutation-inducing chemicals—mutagens—in our environment can do so. Exhibit A, of course, is tobacco smoke. However, other environmental chemicals that many people suspect of causing cancer—food preservatives, contaminants in our drinking water, pollutants pouring out of smokestacks—rarely do so. In fact, in the developed nations, only 1 to 2 percent of cancers are attributable to such environmental pollutants.

Instead, most cancer-inducing mutations occur when cells damage their own genes accidentally. Each of our cells continuously produces mutation-inducing chemicals as byproducts of its normal metabolism. When our cells generate energy by converting oxygen into water, modified oxygen molecules called "oxygen radicals" are produced. These radicals strike wildly at all the molecules in our cells, including the DNA of our genes. Although our cells have the ability to repair this damage, the protection is not perfect, and so mutations and mutant genes accumulate as we grow older.

Mutations, while necessary, are not sufficient. Something else—something from outside the cancer cell—needs to fan the flames. A cell with several mutations may be primed to become cancerous, or may even be in the sluggish early stages of cancer, but that cell usually needs to be stimulated by additional growth-promoting signals to become a full-blown tumor. In fact, development of the great majority of human cancers is likely to be driven by these non-mutagenic "cancer promoting" molecular signals.

We don't know precisely how the Western diet increases our risk of cancer. The foods we eat contain chemicals that can mutate genes and that therefore could cause cancer. For example, red meat cooked at high temperatures generates potent mutagens called heterocyclic amines. Foods contain many different chemicals, and those chemicals are transformed in our body into many other chemicals, making it very difficult to pinpoint just what it is about the Western diet that raises our risk of cancer. But there is no doubt that it does.

While we don't really understand yet why obesity fosters cancer, cancer promoters could play a role. Obesity leads to high levels of insulin-like growth factor (IGF-1) in the circulation: theoretically, this could protect early-stage cancer cells scattered throughout the body from dying, since insulin-like growth factor inhibits the action of cell suicide genes. Inflammation also may explain the link between obesity and cancer. Inflammation is a normal body process designed to rid a tissue of infection and to heal it following injury. Cells of the immune system orchestrate inflammation, and some of the weapons they deploy are chemical signals called cytokines. Often, inflammation is brief. If your skin is cut, or develops a bacterial infection, inflammation aids in repairing the wound or eliminating the bacteria. Having done its job, inflammation then subsides.

However, if you have a condition that inflammation cannot rapidly heal, then the inflammation becomes protracted, chronic. The injured tissue is constantly bathed in growth-promoting cytokines that tell stem cells in the tissue to begin multiplying, in order to replace the cells that have been injured and destroyed. If any of these stem cells already have acquired mutations that make them precancerous, cytokines that encourage those cells to multiply can increase the risk that a tumor will start. For example, stomach tissue that can turn cancerous when it is chronically inflamed in response to the bacteria that cause many stomach ulcers. The same thing happens to the lining of gallbladders after years of irritation from gallstones, or to the liver after years of infection with hepatitis viruses.

What does inflammation have to do with obesity? Fat cells release inflammatory chemicals into the circulation that can stimulate the growth of cancer cells. The more overweight we are, the greater the level of inflammatory signals. It is possible that these cytokines act as cancer promoters, but much more research is needed to determine whether that is true.

Regular moderate exercise lowers the levels of both IGF-1 and cytokines in our blood, and it does so even if the exercise does not lead to a healthy weight. It is possible that the lowered levels of these cancer promoters are one explanation for the protective effect of regular exercise. Blood-estrogen levels are lowered by regular exercise in women, and this may be another way that regular exercise protects against getting breast cancer.

Our growing understanding of cancer genes, and how they are influenced by cancer-promoting chemical signals, already has led to important new diagnostic tests and powerful new treatments, and will likely lead to even more important advances in the future. But epidemiological studies of lifestyle and cancer have given us the power, today, to reduce our risk of cancer. While it isn't easy to make changes in lifestyle, it can happen. There are many fewer people using tobacco in the United States today than two generations ago, when the risks of tobacco were first revealed. It may take another two generations to further reduce tobacco use, and to improve our diets, weight and exercise patterns, but it can happen. If it does, our grandchildren are likely to look back at our generation, scratch their heads and wonder why it took so long for us to escape the disease that many of us feared the most, by simple changes in the way we led our lives.

Weinberg is Daniel K. Ludwig Professor for Cancer Research and American Cancer Society Research Professor at MIT, and a Member of the Whitehead Institute. His laboratory discovered the first human oncogene and the first tumor-suppressor gene. He is the author of "One Renegade Cell: The Quest for the Origin of Cancer," published by Basic Books, 1999. **Komaroff** is professor of medicine at Harvard Medical School and editor in chief of the Harvard Health Letter.

Dr. Bleyer:

☑ I included this report on cancer prevention for four reasons: 1) it emphasized the role of exercise and nutrition (**E&N**) together; 2) Dr. Weinberg is a pre-eminent cancer research (with whom I have worked) and discovered the first oncogene (genes that cause cancer; 3) he and his colleague at Harvard cite the study (bolded) that showed how Western diets increase cancer recurrence; 4) the mechanisms they cite in explaining how obesity can cause

cancer (insulin growth factor and chronic inflammation) are the same that *E&N News* has been reporting as the reason for earlier recurrence of cancer; 5) it is superbly written.
☑ For more information from Harvard on lifestyle and cancer, go to health.harvard.edu/newsweek

Study finds weight-loss surgery cuts cancer risk [Prevention]

Reuters - June 19, 2008
By Will Dunham
WASHINGTON (Reuters) - Morbidly obese patients who undergo weight-loss surgery greatly reduce their risk of cancer, according to a study providing fresh evidence of health benefits from these increasingly common operations.

Reducing body mass index (BMI) in obese patients with bariatric surgery had an 80% reduction in developing cancer within 5 years

Researchers from **McGill University** in Montreal found that the people who underwent bariatric surgery saw reductions in particular in the risk for breast and colon cancer. Many people see dramatic weight loss after such surgery.
People who are deemed morbidly obese typically are at least 100 pounds (45 kg) overweight. The researchers tracked 1,035 such patients who had bariatric surgery for five years. They also monitored 5,746 patients who matched the surgery group in age, sex and weight but did not have this surgery.
Those who underwent bariatric surgery had about an 80 percent lower risk of developing cancer, the study showed.
"The evidence is mounting that weight loss through weight-loss surgery, if you are extremely obese, is extremely beneficial both to your health as well as to your quality of life," **Dr. Nicolas Christou,** McGill's head of bariatric surgery who led the study, said in a telephone interview on Thursday.
In addition to **cutting the incidence of breast cancer by about 85 percent and colon cancer by about 70 percent**, those who underwent bariatric surgery **also saw reductions in the risk for pancreatic cancer, skin cancer, uterine cancer and non-Hodgkin's lymphoma**, the researchers said.
Obesity raises the risk for several types of cancer, including cancers of the breast, colon, esophagus and kidney, as well as numerous other diseases.
The study buttresses findings published last year in the New England Journal of Medicine that obese people who have bariatric surgery have a lower risk of death from heart disease, diabetes as well as cancer compared to obese people who do not have such surgery.
Bariatric surgery alters the digestive system's anatomy to cut the volume of food that can be eaten and digested.
In Christou's study, presented at a meeting of the American Society for Metabolic & Bariatric Surgery, most of the patients had gastric bypass surgery, which leaves the stomach smaller and permits food to bypass part of the small intestine.
"There's an old misconception that this is cosmetic surgery. But actually, people who are overweight don't live as long because a lot of them develop weight-related health problems that shorten their lives. What we see in all these studies is that when people lose the weight, their health gets better," said **Dr. Daniel Gagne** of the Western Pennsylvania Hospital in Pittsburgh, who presented another study at the meeting.
An estimated 205,000 people underwent bariatric surgery in the United States last year.

Dr. Bleyer:
☑ This study confirms another study, previously reviewed in E&N News, that suggested similar benefits
☑ The number of types of cancers (breast, colon, pancreas, skin, and uterine cancer and lymphoma) that were reduced and the speed (within 5 years) that were avoided are remarkable

Gastric bypass surgery cuts cancer risk, researchers say [Prevention]

The study builds on the belief that weight and disease are connected.
By Thomas H. Maugh II and Denise Gellene
Los Angeles Times - June 19, 2008
Gastric bypass surgery -- a treatment for obesity that is already known to reduce heart disease and diabetes -- decreases the incidence of cancer by 80% over the five years following the procedure, Canadian researchers reported Wednesday.

The Los Angeles Times interviews physicians with expertise in bariatric surgery to obtain their opinions regarding the reduction in cancer incidence within 5 years after bariatric surgery reported by investigators at McGIll University [report reviewed above]

The incidence of two of the most common tumors, breast and colon, was reduced by 85% and 70%, respectively, Dr. Nicolas Christou of McGill University in Montreal said.
The study confirms the findings of two papers issued in August that showed the surgery reduced overall deaths from cancer. The new study goes a step further by showing reductions in the incidence of several specific types of cancer, said **Dr. Philip Schauer** of the **Cleveland Clinic Lerner College of Medicine**, who was not involved in the study.
"This is really powerful information," said Schauer, immediate past president of the American Society for Metabolic and Bariatric Surgery. "It reaffirms that obesity is a profound risk factor for cancer" and shows that "weight loss does seem to affect the development of new cancers."
But **Dr. Edward H. Phillips**, a bariatric surgeon at **Cedars-Sinai Medical Center**, was skeptical about the findings because cancer takes a long time to develop and the patients were studied for only five years. He noted that it was now common for weight-loss surgery candidates to undergo mammograms, colonoscopies and endoscopies to screen for cancer before the procedure.
"It could be that we are selecting people out of the population who don't have cancer," biasing the results, Phillips said. He believes that losing weight will reduce the incidence of cancer but that it will take longer than five years for the effects to surface.
Christou countered that such screening "is not the standard of care" in Canada, where the subjects lived. Furthermore, many of the patients had undergone surgery as long as 15 years before the start of the study, he said, leaving plenty of time for cancer to develop.
There are two main types of bariatric surgery. The simpler is banding, in which an inflatable silicone band is placed around the stomach to reduce its capacity, allowing the patient to feel full after eating less food. In a gastric bypass, the stomach is sewn shut to reduce its capacity to 3 or 4 ounces, and the intestines are connected directly to the newly created pouch, bypassing part of the area where food absorption occurs. This is generally a more invasive surgery but produces greater weight loss.
About 205,000 Americans underwent bariatric surgery last year, according to the American Society for Metabolic and Bariatric Surgery, and the number is expected to rise by 5% this year. Only about 1% of those eligible for the surgery opt to undergo it, the society said.
Christou and his colleagues compared 1,035 patients who had had bariatric surgery between 1986 and 2002 with 5,746 carefully matched obese patients who had not had the surgery; 81% of the surgery patients had undergone a gastric bypass.
Neither the patients nor the controls had previously been diagnosed with cancer.
Those who underwent the surgery lost an average of 67% of their excess body weight.
In the five years of follow-up, the team observed 21 cancer cases in the surgery group (2%), compared with 487 cases (8.5%) in the control group, Christou told a Washington meeting of the American Society for Metabolic and Bariatric Surgery.
The most dramatic decreases were for breast and colon cancer. The researchers also observed a 70% reduction in pancreatic cancer, a 60% reduction in skin cancer, a 15% reduction in uterine cancer and a 50% reduction in non-Hodgkin's lymphoma, but there were not enough cases of any of these for the results to be statistically significant.

Combined with earlier evidence, Christou said, "the data is pretty convincing" that weight loss reduces the incidence of cancer. "We looked at extreme weight loss, where we were more likely to pick it up. But any weight loss, if it can be maintained, is likely to improve the risk of cancer."

Nobody knows how weight reduction reduces the incidence of cancer, said **Dr. Peter LePort**, director of the **Memorial Care Center for Obesity** in Fountain Valley, who was not involved in the study. But fat is known to secrete estrogen, which plays a crucial role in breast and some other cancers, he said.

The surgery may alter the production of other hormones as well. "What's really needed here are a couple of studies to confirm the results and explore the mechanisms," LePort said.

Despite evidence for the efficacy of the surgery, insurance companies have been "throwing subtle roadblocks" in front of patients seeking it, said **Dr. Jeremy Korman**, director of the **Los Angeles Bariatric Center** in Marina del Rey.

The surgery typically costs about $10,000 for banding and up to $25,000 for gastric bypass, according to **Dr. Neil Hutcher** of **Commonwealth Surgeons** Ltd. in Richmond, Va., past president of the society.

Some insurers require patients to try a medically supervised diet for six to 12 months before the surgery will be covered, although a recent survey found that most patients have been on an average of 24 diets before seeking surgical help.

"The hoops and hurdles are so onerous that patients give up before surgery," Hutcher said.

Dr. Lisa Latts, a vice president at **Anthem Blue Cross**, cautioned that "the reality is that it is very important to pick the right patients. The wrong patients can out-eat bariatric surgery and undergo a very costly and dangerous procedure for nothing."

Data from the Michigan Bariatric Surgery Collaborative presented earlier this month showed that the rate of life-threatening events during the surgery was 0.5%, down from 2% in 2000.

Recently, Maryland and Indiana passed legislation requiring insurers to cover the surgery, and other states are considering it, Hutcher said.

Dr. Bleyer:

- ☑ One of the experts questioned the authors' interpretation since the follow-up interval was too short (5 years) to expect a reduction; on the other hand, if the reported results are true they are all the more impressive
- ☑ The concern that patients selected for bariatric surgery are screened for cancer before they are accepted for surgery and thereby less likely to have (and subsequently develop) cancer is a weakness of the three reports on bariatric surgery published to date
- ☑ I would minimize this concern, however, since it is unlikely that the screening methods utilized would have found as many and as different cases of cancer that occurred after surgery

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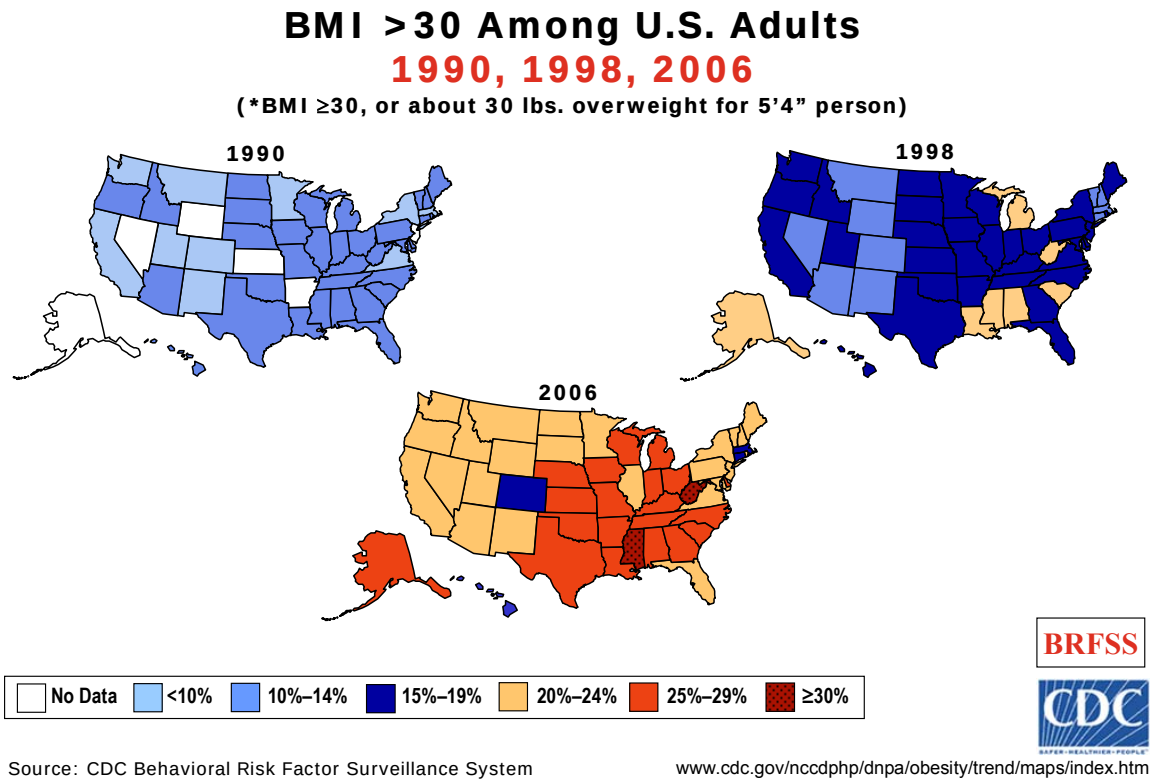
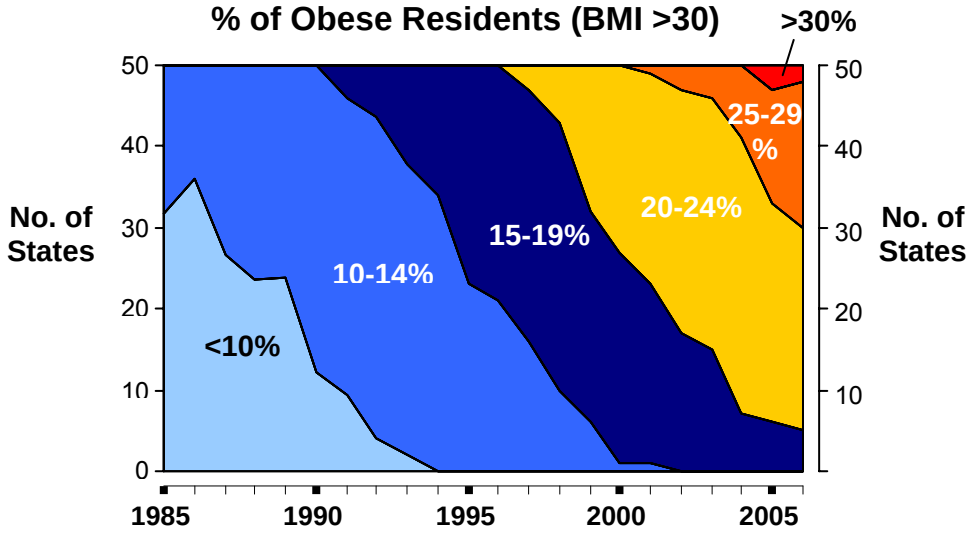
Body Mass Index (BMI) escalates dramatically in the U.S. [DEFEAT Cancer Analysis]

The U.S. obesity epidemic has been dramatic and relentless,
with current and potential dire consequences in cancer incidence

The Center for Disease Control (CDC) data regarding the obesity epidemic in the U.S. was restudied.



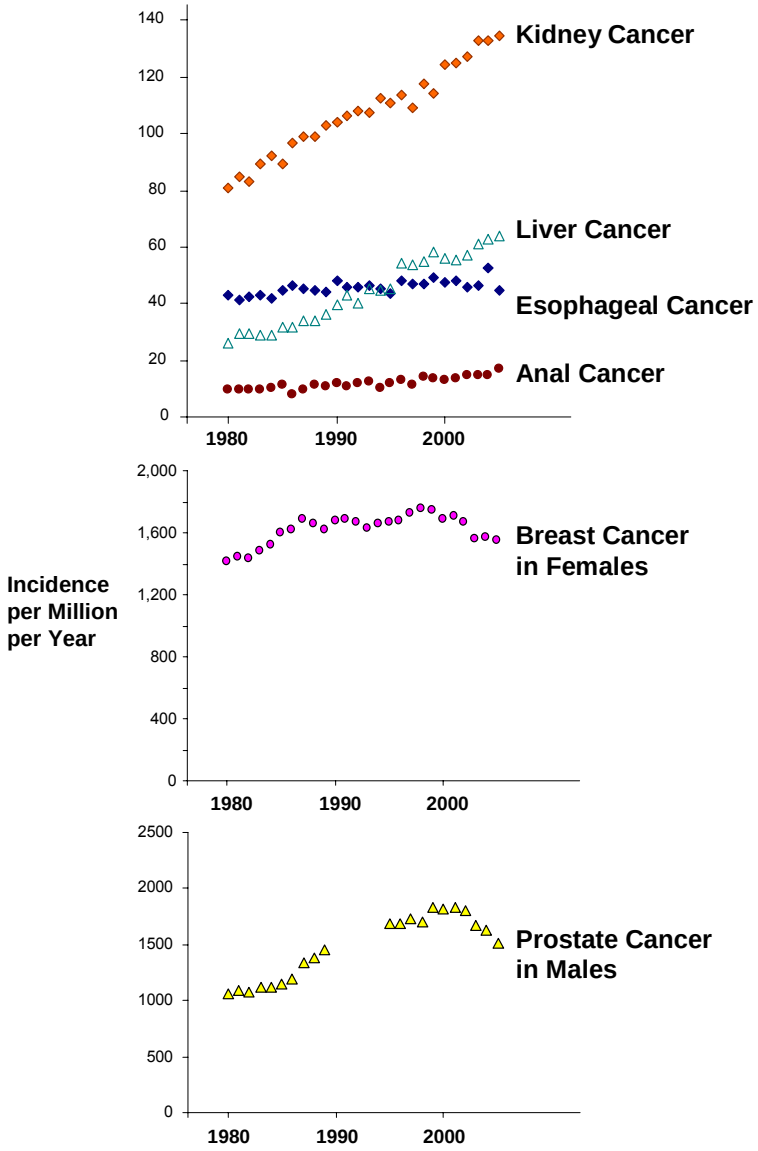
DEFEAT Cancer converted the CDC year-by-year data since 1985 to a chart that shows how the proportion of residents who are obese (defined by a BMI >30) has increased sharply, steadily and relentlessly. From 1991 to 2002, statewide obesity rates in excess of 15% went from none to all states.



If obesity increases the incidence of cancer, this should be apparent in the U.S. cancer incidence data for at least some of the 10 different kinds of cancer in men and 12 different kinds in women that are known to be associated with obesity: cancer of the colon, pancreas, esophagus, stomach, liver, and kidney, as well as leukemia (see next report), and cancer of the breast, uterus, and cervix in women; and prostate cancer in men. Hence DEFEAT Cancer analyzed the incidence of these cancers in the U.S. between 1980 and

2005, according to the National Cancer Institute Surveillance, Epidemiology and End Results (SEER) program.

Five of the cancers have had an increase incidence (Figure), whereas the others have not. The reduction in breast cancer during the last few years is attributable to the reduction in hormone replacement therapy for post-menopausal symptoms. The recent "reduction" in prostate cancer is probably due to overdiagnosis with the advent of the PSA blood test. Several of the cancers that have not had an increase have also been attributed to screening, best exemplified by colonoscopy and stool blood tests to prevent colon and rectal cancer. Since the obesity epidemic should precede the cancer increase by years, if not decades, the other cancers may yet suffer an obesity-related increment.



Dr. Bleyer:

- ☑ Although this is not a report *per se*, DEFEAT Cancer was prompted to evaluate the national incidence trends of cancers known to be associated with obesity by studies that were reported last month and are covered in this edition of ***E&N*** *News*
- ☑ It is remarkable that half of the obesity-related cancers have an incidence pattern that is temporally related to the obesity epidemic in the U.S.; among cancers not declining due to known prevention interventions, only gastric cancer, pancreas cancer and leukemia do not (yet) demonstrate a correlation

Obesity and positive surgical margins by anatomic location after radical prostatectomy: Results from the Shared Equal Access Regional Cancer Hospital database

The SEARCH Database Study Group
BJU International, published online August 8, 2008

Surgery in obese men is more difficult, their tumors are less likely to be completely removed, and their survival is significantly shorter

ABSTRACT To determine if there is predilection for any specific anatomical location of positive surgical margins (PSMs) after radical prostatectomy (RP) for prostate cancer in obese men, as previous studies found that obesity was associated with an increased risk of PSMs.

PATIENTS AND METHODS We analysed retrospectively 1434 men treated with RP between 1989 and 2007 within the Shared Equal Access Regional Cancer Hospital database. The association between

increased body mass index (BMI) and overall and site-specific PSMs was assessed using multivariate logistic regression.
RESULTS After adjusting for several preoperative clinical and pathological characteristics, a **higher BMI was associated with an increased risk of PSMs both overall and at all specific anatomical locations (all P ≤ 0.007)**. For mildly obese men, this risk was very similar across all anatomical sites (44–78% increased risk relative to men of normal weight). When BMI was coded as a continuous variable, the odds ratio for the risk of overall PSMs or at any specific locations was nearly identical at 1.05–1.06. Among men with a BMI of ≥35 kg/m2, there was more variation, with the highest excess risk of PSMs at the bladder neck and apex.
CONCLUSIONS Obesity was associated with an increased risk of overall PSMs and at all anatomical locations. Although the excess risk of PSMs was similar across all anatomical locations, there was a suggestion of a higher risk of apical margins among the most obese men, which if validated, further supports the importance of the apical dissection in all men and suggests added difficulty in obese patients.

Dr. Bleyer:
☑ A worse outcome in obese men with prostate cancer has been known for several years; a new is this study is that obese men are more likely to have tumor left behind after their surgery.
☑ The technically more difficult surgery in obese men (see surgeon's quote in the HeatlhDay News article below), together with the finding of this study, adds to the reasons for a shorter survival associated with obesity.

Obesity and oncological outcome after radical prostatectomy: Impact of prostate-specific antigen-based prostate cancer screening: Results from the Shared Equal Access Regional Cancer Hospital and Duke Prostate Center Databases [Prevention]

Stephen J. Freedland, Leon Sun, Christopher J. Kane, Joseph C. Presti Jr, Martha K. Terris, Christopher L. Amling, Judd W. Moul and William J. Aronson
BJU International, published online August 8, 2008

PSA levels are less reliable, and often lower, in obese men than in men of normal weight, such that lower PSAs in obese men may explained their tendency to have more advanced disease at diagnosis

ABSTRACT To indirectly test the hypothesis that prostate-specific antigen (PSA)-based screening is biased against obese men due to haemodilution of PSA, and thus results in delayed diagnosis and poorer outcome beyond the biological link between obesity and aggressive prostate cancer.
PATIENTS AND METHODS We sought to examine the association between body mass index (BMI) and the outcome of radical prostatectomy (RP) separately for men with PSA-detected cancers (cT1c) or with abnormal digital rectal examination (DRE) findings (cT2/T3), and stratified by year of treatment, using two large databases. We conducted a retrospective cohort study of 1375 and 2014 men treated by RP between 1988 and 2007 using the Shared Equal Access Regional Cancer Hospital (SEARCH) and Duke Prostate Center (DPC) databases. We evaluated the association between BMI and adverse pathological features and biochemical progression, using logistic regression and Cox proportional hazards models, adjusting for several clinical characteristics, respectively. Data were examined as a whole and as stratified by clinical stage (cT1c vs cT2/T3) and year of surgery (≥2000 vs <2000).
RESULTS In both cohorts a higher BMI was associated with high-grade disease (P ≤ 0.02) and positive surgical margins (P < 0.001) and these results did not vary by clinical stage. A higher BMI was significantly associated with biochemical progression (P ≤ 0.03) in both cohorts. When stratified by clinical stage, obesity was significantly related to progression in both cohorts among men with T1c cancers (P ≤ 0.004) but not in men with cT2/T3 cancers (P > 0.3). Among men with T1c disease, the \association between BMI and biochemical progression was limited to men treated in 2000 or later (P ≤ 0.002) and was not apparent in men treated before 2000 (P > 0.4).
CONCLUSIONS Obese men with PSA-detected cancers and treated with RP since 2000 were at significantly greater risk of biochemical progression, while obese men treated before 2000 or diagnosed with an abnormal DRE were not at significantly greater risk of progression. These findings support the hypothesis that current PSA-based screening is less effective at finding cancers in obese men, leading to

more aggressive tumours at diagnosis. Lowering the PSA threshold for biopsy among obese men might help to improve outcomes among this high-risk group.

Dr. Bleyer:

- ☑ What's new in this report is the finding that changes in PSA interpretation appear to under-estimate the amount of cancer in obese men
- ☑ Not reported in this study is how the difficulty of using PSA levels to screen for prostate cancer also applied to using PSA to determine therapeutic benefit and early detection of progressive disease in men diagnosed with prostate cancer
- ☑ The suggestion to lower the threshold for suspicion of prostate cancer in obese men may not work because more false positives will occur with a lower cut-off and negate the value of a lower threshold
- ☑ A better recommendation, of course, is to reduce obesity which has the added potential of prolonging survival and the demonstrated benefit of an improved quality of life

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Obese men face twin threat from prostate cancer

Delayed diagnosis, less successful surgery, pair of studies finds
HealthDay News – August 12, 2008
By Ed Edelson

Coverage of prior two reports with commentary from participating investigators

The standard screening test for prostate cancer may not be accurate for obese men, leaving them more vulnerable to the disease, and surgery is less likely to be effective for them, a new pair of studies found.
"Obese men are more likely to be diagnosed with an aggressive form of the disease," said Dr. Stephen Freedland, an associate professor of urology and pathology at the Duke University Prostate Center, and an author of one of the studies.
The reason: The blood test that looks for elevated levels of the protein prostate-specific antigen (PSA), indicating a heightened cancer risk, doesn't seem as reliable for obese men, Freedland said.
"Our assumption is that these men have more blood volume, so PSA gets diluted, he said. "By the time obese men get to elevated levels, the cancer is more advanced."
The study, published online Friday in the journal BJU International included nearly 3,400 men who had PSA tests. The researchers found that the risk of an aggressive cancer was doubled in obese men diagnosed because of high PSA levels. No such association was found for obese men diagnosed by a digital rectal examination, in which the physician feels for an abnormally large prostate gland.
Prostate cancer is suspected when the PSA reading is 4 or higher. The current recommendation is for men aged 50 and older to be offered an annual PSA test, with explanations of its possible risks and benefits. A federal preventive medicine committee this week said that PSA screening should not be done for men aged 75 and older because the risks outweigh the benefits.
"I'm not sure that we should check obese men more often," Freedland said. "But we should have a higher [PSA] index of suspicion of what is not normal -- 3.4 rather than 4; for really obese men, 3.2."
The Duke study measured obesity using body-mass index, which is a ratio of weight to height. Obesity is defined as a BMI of 30 or more.
A **second report** from **Duke** in the same issue of the journal found that excess weight influenced the outcome of surgery for prostate cancer. Men with a **BMI of 35 or higher were nearly 60 percent more likely to have a recurrence of the cancer than thinner men**, the study of 1,434 men found.
One reason is "the **difficulty of operating on obese men in general**," said study author **Dr. Jayakrishnan Jayachandran**, a urology oncology fellow at the **Duke** Prostate Cancer Center. "The **prostate is a narrow thing to operate on, and when there is a big wad of fat in your way, if the abdominal wall is thick, it becomes a technical issue**."
The result is that not all the cancer may be removed, which means a recurrence after time, Jayachandran said. "**The only thing we can think of is that when you operate on obese people, you have to be more careful**," he said.

The studies results apply to men who might not regard themselves as obese, Freedland said. "We can't forget that when we use the term, we are not just talking about very large men," he said. "A man who is 5 foot 9 and weighs 203 pounds would be considered obese."
Jayachandran added, "We are not screening these obese men effectively and are not doing as good a job surgically as could be done."

Dr. Bleyer:
☑ When surgeons express exasperation, the problem is usually more worse than that to which they admit
☑ Duke is one of the premier centers for prostate surgery; when one of their surgeon complains about a "big wad of fat", the problem must be overwhelming

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Obesity with depleted muscle mass affects mortality in cancer patients

Obesity with Depleted Muscle Mass Affects Mortality in Cancer Patients
By CancerConsultants.com – July 22, 2008
Review of Prado C, Lieffers J, McCargar L, et al. Prevalence and Clinical Implications of Sarcopenic Obesity in Patients with Solid Tumours of the Respiratory and Gastrointestinal Tracts: a Population-Based Study. Lancet Oncology. 2008;9:629-635.
Sarcopenic obesity, or obesity with depleted muscle mass, affects distribution of chemotherapy and ultimately may significantly affect mortality among obese patients with cancer. These results were recently published in the Lancet Oncology.

In this Lancet report. obese patients with depleted muscle mass were found to have pharmacologic differences that interfere with chemotherapy benefit and/or increase toxicity

Body composition, or the ratio of muscle to fat, varies widely in patients who are obese, and the metabolism of different types of tissue can greatly affect the way medications—including chemotherapy—are distributed and broken down throughout the body. Researchers are discovering that physical activity, diet and obesity affect the overall risk and potential outcomes of cancer among patients. Therefore, researchers from Canada recently conducted a clinical trial to explore the potential effects of sarcopenic obesity and the corresponding outcomes of patients with cancer.
This trial included 250 patients with cancer who were classified as obese. Thirty –eight percent of these patients were considered to have sarcopenic obesity.
· Patients with sarcopenic obesity had a **four-fold increase in death** compared to those without sarcopenic obesity
· Patients with sarcopenic obesity had **worse functional status** (the ability to perform daily activities and self-care) than their counterparts.
· Due to the different distribution of chemotherapy within the body, researchers believe that sarcopenic obesity could also **significantly affect side effects caused by chemotherapy**.
The researchers concluded that "This study provides evidence of the great variability of body composition in patients with cancer and links body composition, especially sarcopenic obesity, to clinical implications such as functional status, survival, and potentially, chemotherapy toxicity." As well, the authors stated that "we estimated that individual variation in [different body compositions] could account for **up to three-times variation in effective volume of distribution for chemotherapy** administered per unit body-surface area, in this population."
These results provide data that could potentially affect chemotherapy dosing in the future. Further testing that explores outcomes associated with sarcopenic obesity is warranted.

Dr. Bleyer:
☑ *Sarcopenia* (from the Greek meaning "poverty of flesh") is the loss of skeletal muscle in the elderly
☑ It is an important independent predictor of disability, linked to poor balance, gait speed, falls, and fractures, similar. to osteoporosis, which is the age-related loss of bone
☑ This type of obesity is especially predictive of poor survival after a cancer diagnosis, not only in quality of survival but length of survival (the death rate was quadrupled, in this study)
☑ The novel contribution by these investigators is in explaining how chemotherapy can be less effective and/or more toxic in patients with sarcopenic obesity

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Active lifestyle may prevent cancer: Japan study [Prevention]

TOKYO (Reuters) - Physically active people are less likely than sedentary types to develop cancer, a research group led by the Japanese health ministry announced on July 10, 2008

In a study of 80,000 middle-aged Japanese, daily exercise—not just exercise for fitness or leisure activity—was associated with a distinct reduction in cancer incidence in both males and females

Men in the most active group of people surveyed had **13 percent less risk of developing cancer compared with the least active group**, and women in the most active group had a **16 percent lower risk** than their sedentary counterparts.

"There has been a lot of research done in the past on the relationship between leisure and development of cancer in the West," said Dr. Manami Inoue, section chief of the National Cancer Centre.

"However, our research is the first in Japan of its size and scope -- we looked at overall exercise and labor, which is not only related to leisure."

According to the study, published in the American Journal of Epidemiology, researchers surveyed around 80,000 men and women between the ages 45 to 74 living in nine Japanese prefectures.

The surveyed population was divided into four groups according to their ratio of individual working metabolic rate, or MET (metabolic equivalent), which was determined by the amount of time respondents spent sitting, walking, standing, sleeping and exercising.

"Our research looked at overall **physical activity that people take part in daily**, and not just exercise that people take part in for leisure or fitness," said Inoue

The trend was most noticeable among Japanese women, who were less likely to develop cancer if they were engaging in regular exercise and led an active lifestyle.

The results of the study also showed the trend to be prevalent for **colon, liver and pancreas cancer risks for men** and the development of **stomach cancer among women**.

The study, conducted by the Japan Public Heath Centre was first of its kind to survey a non-Western population for clues on the causes of cancer.

Inoue said: "There are a lot of physical differences between Asians and our Western counterparts. Asians are usually leaner, with a lower BMI (Body Mass Index). Many contributing factors for cancer have been suggested ... our research showed that lack of general physical activity is one of such reasons."

Dr. Bleyer:

☑ The article covered by this report was previously reviewed in ***E&N** News*. This report includes comments from the senior author who point out that even among lean person, with a low BMI, the benefits of physical activity (on a daily basis) in preventing cancer are still demonstrable

☑ That the senior author emphasizes that the benefit of physical activity was dependent on daily exercise and not the casual use of fitness centers, etc.

Obesity and risk of cancer in postmenopausal Korean women [Prevention]

Yun-Mi Song, Joohon Sung, Mina Ha
Journal of Clinical Oncology, Vol 26, No 20 (July 10), 2008: pp. 3395-3402

Korean women with BMIs that are higher than the country's normal range have a higher rate of cancer of the uterus, breast, colon, and kidney, and also, in non-smokers, a higher rate of leukemia

Purpose: To evaluate an association between obesity, measured by body mass index (BMI; kg/m2), and risk of cancer at individual and all sites in postmenopausal women.

Methods: A cohort of **170,481 postmenopausal Korean women** who were age 40 to 64 years at baseline measurement of BMI was observed prospectively from 1994 to 2003 for cancer incidence. Multivariable adjusted proportional hazard models were used for evaluating the association.

Results: Women with a BMI of 30 kg/m2 or higher had a 23% higher risk of cancer than women with a BMI between 21.0 and 22.9 kg/m2 (hazard ratio = 1.23; 95% CI, 1.08 to 1.41). According to the increase in BMI level, significant positive trends existed in cancers of colon, breast, corpus uteri, and kidney with hazard ratios of 1.05 (95% CI, 1.02 to 1.08), 1.07 (95% CI, 1.05 to 1.10), 1.13 (95% CI, 1.07 to 1.20), and 1.08 (95% CI, 1.02 to 1.15), respectively, for the increase of BMI by 1 kg/m2. **When the analysis was limited to never-smokers, women with a BMI of 25 kg/m2 or higher showed a significantly increased risk of cancers of the colon, breast, corpus uteri, and kidney and leukemia** compared with the normal BMI (18.5 to 22.9 kg/m2) group.

Conclusion: Although variations exist between the individual cancer sites, obesity was associated with an overall increased risk of cancer in postmenopausal Korean women. To reduce the risk of cancer, active strategies to prevent obesity should be implemented in postmenopausal women.

Dr. Bleyer:

- ☑ This prevention article is included because 1) it comes from Korea (cf. last bullet below), 2) the size of the study (170,000+ women), 3) that is was prospective, 4) that is started (baseline) relatively recently (1994) and hence is more current than many of the famous U.S. studies), and 5) it is BMI focused
- ☑ Of note, and as well-known but nonetheless impressive, is the lower normal range of BMI in Asian women: their 40-64 year-old normal BMI ranges is **18.5-22.9** vs. the U.S. range of **24-27**
- ☑ Another perspective on this BMI comparison is that women in the Korea who had a higher incidence of cancer were in the 'normal' range of BMI for women in the U.S.; this observation suggests that the optimal range of BMI for cancer prevention is lower than the current "ideal" U.S. range
- ☑ That now Korea has to be concerned about their obesity problems speaks against the Westernization of lifestyle and diet
- ☑ One thing new in this report is the addition of **leukemia** to the types of cancers that have been documented to be increased persons with excess fat
- ☑ Most impressive is that obesity among Asians, who are at much less risk of cancer in general, due to large part to their diet, is still a strong risk factor for cancer, despite a lifelong Asian plant-based diet

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Relationship between obesity and pathologic response to neoadjuvant chemotherapy among women with operable breast cancer

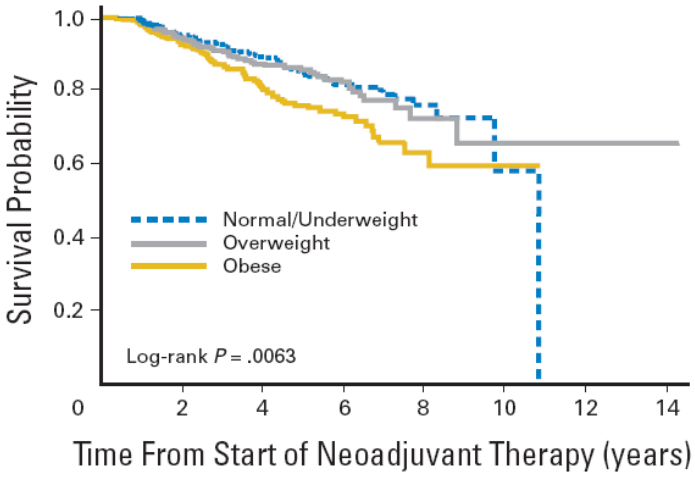
Overweight women with operable breast cancer are less likely to achieve a complete pathologic response to preoperative chemotherapy compared to women of normal weight, and had a worse overall survival during a median follow-up period of 4.1 years

Journal of Clinical Oncology, Vol 26, No 25 (September 1), 2008: pp. 4072-4077
Jennifer K. Litton, Ana M. Gonzalez-Angulo, Carla L. Warneke, Aman U. Buzdar, Shu-Wan Kau, Melissa Bondy, Somdat Mahabir, Gabriel N. Hortobagyi, Abenaa M. Brewster

Purpose: To understand the mechanism through which obesity in breast cancer patients is associated with poorer outcome, we evaluated body mass index (BMI) and response to neoadjuvant chemotherapy (NC) in women with operable breast cancer.

Patients and Methods: From May 1990 to July 2004, **1,169 patients** were diagnosed with invasive breast cancer at **M. D. Anderson Cancer Center** and received NC before surgery. Patients were categorized as obese (BMI ≥30 kg/m2), overweight (BMI of 25 to <30 kg/m2), or normal/underweight (BMI <25 kg/m2). Logistic regression was used to examine associations between BMI and pathologic complete response (pCR). Breast cancer–specific, progression-free, and overall survival times were examined using the Kaplan-Meier method and Cox proportional hazards regression analysis. All statistical tests were two-sided.

Results: Median age was 50 years; 30% of patients were obese, 32% were overweight, and 38% were normal or underweight. In multivariate analysis, there was no significant difference in pCR for obese compared with normal weight patients (odds ratio [OR] = 0.78; 95% CI, 0.49 to 1.26). **Overweight and the combination of overweight and obese patients were significantly less likely to have a pCR** (OR = 0.59; 95% CI, 0.37 to 0.95; and OR = 0.67; 95% CI, 0.45 to 0.99, respectively). **Obese patients were more likely to have hormone-negative tumors** (P < .01), **stage III tumors** (P < .01), and **worse overall survival** (P = .006) at a median follow-up time of 4.1 years.



Conclusion: Higher BMI was associated with worse pCR to NC. In addition, its association with worse overall survival suggests that greater attention should be focused on this risk factor to optimize the care of breast cancer patients.

Dr. Bleyer:

☑ Obesity is not only associated with a higher risk of breast cancer, the cancer is often more advanced, more difficult to treat, and has a worse survival rate when it does occur in overweight women

☑ That overweight patients has less benefit of chemotherapy on their tumor suggests either cancer arising in overweight persons is more drug resistant, or more likely, chemotherapy dosing in overweight patients leads to under-treatment; the latter indicates that overweight patients should be treated more intensively than with current dosing methods (cf. next report)

☑ This should be a powerful study in convincing persons to avoid excessive weight

☑ DEFEAT Cancer strongly recommends the combination of exercise and nutrition (**E&N**) in combating both obesity and cancer

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Higher BMI may reduce chemotherapy response in breast cancer patients

Comment on prior report, with speculation that obese women are undertreated, including noting that obese patients were also at greater risk for hormone-negative and stage III tumors

NEW YORK (Reuters Health) – Sep 12, 2008

New research indicates that overweight patients with operable breast cancer are less likely than their normal-weight peers to achieve a complete response with chemotherapy.

Prior research has linked obesity with worse breast cancer outcomes, but the mechanisms involved were unclear, note Dr. Abenaa M. Brewster and colleagues from the University of Texas M. D. Anderson Cancer Center in Houston.

The current investigation, reported in the Journal of Clinical Oncology, involved 1169 patients who were treated at the researchers' center from May 1990 to July 2004. Standard body mass criteria were used to divide patients into obese, overweight, and normal/underweight groups. This included body mass index (BMI) - the ratio of height to weight, often used to classify people into weight categories.

Compared to normal-weight patients, those in the overweight and the combination of overweight and obesity categories had a reduced likelihood of a complete response with chemotherapy response.

Although obese patients were as likely as normal-weight patients to have a complete chemotherapy response, they were at greater risk for hormone-negative, stage III tumors and had worse overall survival over a follow-up period of 4.1 years.

The link between a higher body mass index BMI and a reduced chemotherapy response, the authors note, "may be attributed to the influence of body mass index on the clinical effectiveness of chemotherapy or the underdosing of overweight and obese patients by clinicians because of fears of toxicity, despite randomized studies that have demonstrated that this practice contributes to worse disease-free survival."

SOURCE: Journal of Oncology, September 20008.

Dr. Bleyer:

☑ There is increasing evidence that overweight patients receive less chemotherapy that they could (or should)

☑ In addition to the fear of increased toxicity mentioned by the authors, the increased fat compartment of such patients may lead to deposition of lipid soluble chemotherapy drugs (of which there are many) in fat rather than in the tumor

☑ Also dosage calculation modifications may underestimate the need for equally effective dose administration

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Obesity, insulin level impact prostate cancer survival

Heavy men with prostate cancer who have a high output of insulin have quadruple the death risk

By Amanda Gardner

HealthDay News - Oct. 5, 2008)

Men who are overweight and who have high insulin levels when they are diagnosed with prostate cancer may be more likely to die from the disease, research shows.

This striking finding, published early online and expected to be in the November issue of **The Lancet Oncology**, is yet more reason to continue fighting the battle of the bulge, experts say.

"I don't want to be sensationalist, but obesity effects and the insulin effects are so big that I think if you had to choose between being thin and having a low insulin level or having access to the best chemotherapy, you would be more likely to survive without chemotherapy," said study senior author **Dr. Michael Pollak**, professor of oncology at **McGill University** in Montreal, Quebec, Canada.

"Tens of thousands of men are taking chemotherapy for prostate cancer -- as they should, because it is a good treatment. Doing so is actually helping," he said. "But **potentially, dealing with insulin, obesity may one day be of more benefit**."
The findings also have scientific import, giving researchers a clue that could lead to new prevention and treatment strategies.
Experts have long known that androgens, or male hormones, play a critical role in spurring prostate cancer.
In fact, these cancers are often treated with approaches that deprive the tumors of testosterone.
Smaller reports have suggested that obese patients with prostate cancer have a worse prognosis than patients ofregular weight, though weight hasn't been related to actually developing a malignancy.
"We found in a large sample that obesity has a very important influence on prostate cancer outcome," Pollak said. "Then the question becomes, why would obesity make the outcome worse?"
Pollak and his colleagues looked at information on more than **2,500 men** who had been **followed for 24 years** as part of the **Physicians' Health Study**. Information on body mass index (BMI) was available for all of these men, while information on C-peptide concentration (a marker of insulin levels in the blood) was available for 827 men.
Overweight men (those with a BMI of 25 to 29) had a 47 percent higher risk of dying from prostate cancer, while obese men (BMI of 30 or over) were more than two-and-a-half times more likely to die of the disease, compared with men of healthy weight (BMI under 25).
Men with the highest C-peptide concentrations also had more than double the risk of dying from their cancer compared with men with the lowest levels, the study found.
Finally, men who had a BMI of more than 25 and high C-peptide concentrations had quadruple the risk of dying from their cancer compared with men who had lower BMIs and lower C-peptide levels, the researchers reported.
"This suggests that there may be a whole new story to tell, whereby not just androgens have something to do with cancer behavior, but also insulin," Pollak said.
The insulin hormone may be latching onto insulin receptors located on prostate cancer cells, he speculated.
Some pharmaceutical companies are already testing drug candidates that target insulin signaling, Pollak added.
And the findings could have broader implications for other cancers, said study lead author **Dr. Jing Ma, of Harvard University**'s Channing Laboratory.
"The simple things are still the important things. Don't drink, don't smoke, exercise, and eat well," said **Dr. Ganesh Palapattu**, assistant professor of urology, pathology and oncology at the **University of Rochester School of Medicine**. "This is yet another piece of evidence suggesting that obesity is not a good thing for many reasons."
"**Obesity is the second leading cause of cancer death in this country next to tobacco**," emphasized **Dr. Jay Brooks**, chief of hematology/oncology at **Ochsner Health System** in Baton Rouge, La. "Two years ago, I would never have told my patients that obesity is increasing their risk of death from cancer. Today, I do."

Dr. Bleyer:
- ☑ Being overweight (BMI >25) and having a high plasma insulin levels is associated with a risk of magnitude (4 times) of premature death from cancer that exceeds most other reported increase risks of cancer associated with obesity
- ☑ Dr. Brooks' comment is worth repeating: "Obesity is the second leading cause of cancer death in this country next to tobacco"
- ☑ "Don't drink, don't smoke, exercise, and eat well" (Dr. Palaputtu) is also worth quoting, especially since this advice combines exercise and nutrition

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Piling on the pounds increases men's colon-cancer risk, research reveals [Prevention]

The correlation between the incidence of colon cancer and weight gain continues to accrue, with quantification of the risk in men at 33% for every 10 pounds gained since age 21

Reuters © The Gazette (Montreal) September 10, 2008
Men who gain weight as they age have an increased risk of suffering from colon cancer, according to new research.
In a study of more than 46,000 men between the ages of 40 and 75 years old, researchers said nearly one third of all colon cancer diagnosed over an 18-year period were in men who had a body mass index (BMI) - a weight-to-height ratio widely used as a measure of being overweight or obese - greater than 22.5.
BMI is a method of determining overweight and obesity. The normal range for men is a BMI of 18.5 -24.9.
The findings, "support public health interventions to avoid weight gain for prevention of colon cancer," **Dr. Lau Caspar Thygesen** and researchers from the **National Institute of Public Health in Copenhagen** said in a report in the **International Journal of Cancer**.

None of the men had cancer at the start of the study in 1986. Information on the men's medical history, weight and diet was updated every two to four years until 2004.
Men with an average BMI above 22.5 had a significant increased risk of colon cancer compared with those with an average BMI between 20 and 22.5, Thygesen said.
The risk was more than doubled among those with a BMI greater than 30, which is considered obese.
The researchers estimate that for every 10 pounds gained in the prior two to four years, the risk increased by 14 per cent. Similarly, for every 10 pounds of weight gained per 10 years since age 21, the risk increased by 33 per cent. By contrast, weight at age 21 was not associated with risk.

Dr. Bleyer:
☑ The link between excessive weight gain and colon cancer is undeniable, in both men (this report) and women
☑ The bariatric surgery experience closes the loop in that it shows that colon cancer risk is reduced in association with weight loss

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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, iIf 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

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***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.
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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

SUNDAY, Nov. 2 (HealthDay News) -- 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 fattier, 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

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