EXERCISE CAN IMPROVE BREAST CANCER SURVIVAL

A few hours of walking each week may help breast cancer survivors live longer, new research suggests. In the study of nearly 3,000 women participating in the Nurses’ Health Study, those who exercised this amount were significantly less likely to die of their breast cancer than women who got less than 1 hour of physical activity each week.

“Women with breast cancer have little to lose and much to gain from exercise,” said the study’s lead author, Michelle Holmes, MD, DrPH, of Harvard Medical School and Brigham and Women’s Hospital in Boston. “We already know that breast cancer patients who exercise have better mood, better body image, and better self-esteem. We know it fights other diseases that women with breast cancer can also get, like heart disease and diabetes. And it may also help these women avoid dying from breast cancer.” Holmes and her colleagues published their findings in *JAMA* (2005;293:2479–2486).

The women involved had all been treated for Stage 1, 2, or 3 invasive breast cancer with standard therapies. The researchers asked the women how often they exercised during their free time after they had finished treatment. Activities included walking, hiking, jogging, or running, as well as cycling, swimming laps, tennis, aerobics, squash, racquetball, or using a rowing machine.

They compared the intensity level of each form of exercise with breast cancer survival, taking into account factors such as stage, treatment (with chemotherapy, radiotherapy, and/or tamoxifen), body mass index, hormone use, menopausal status, age at first birth, and parity, which might have an effect on survival.

Women who exercised the equivalent of walking about 1 hour a week, at a 2 to 3 mile-per-hour pace, had a lower risk of dying from breast cancer than women who got less than an hour’s worth of physical activity each week (relative risk [RR] 0.80, 95% confidence interval [CI] 0.60–1.06). Women who did a little more than that—the equivalent of walking about 3 to 5 hours per week at that pace—had the lowest risk of dying (RR 0.50, 95% CI 0.31–0.82). Women who got more exercise than that had a similar risk of dying (RR 0.56, 95% CI 0.38–0.84 for 5 to 8 hours per week; RR 0.60, 95% CI 0.4–0.89 for more than 8 hours per week).

“The benefit seemed to level off,” Holmes said, “so the good news is women don’t have to run marathons to get the maximum benefit.”
The benefit was about the same for pre- and postmenopausal women. However, the benefit was statistically significant only in women with tumors expressing estrogen and progesterone receptors. That makes sense, Holmes said, because exercise reduces levels of estrogen in the body. She noted, though, that there were relatively few women with hormone receptor-negative tumors in the study, so it is not possible to draw firm conclusions about whether exercise can help them survive longer, too.

Exercise lowered the overall risk of death from all causes to a similar degree. For example, women who exercised for 3 to 5 hours per week had a relative risk of 0.59 (95% CI 0.41-0.84). Although this is not surprising, it is an important point because the majority of breast cancer survivors eventually die of a cause other than breast cancer.

After 10 years of follow up, 92% of the women who exercised 3 to 5 hours per week (or about half an hour per day) were still alive, compared with 86% of those who got less than 1 hour a week of physical activity. Holmes said it didn’t matter if the exercise was done all at once or spaced throughout the day.

The amount of exercise that was helpful is right in line with what the American Cancer Society (ACS) recommends for cancer survivors, said Debbie Saslow, PhD, director of breast and gynecologic cancers for the ACS.

Until there are more studies on lifestyle issues and cancer recurrence, the ACS advises survivors to follow its Nutrition and Physical Activity Guidelines for Cancer Prevention. Those guidelines recommend that adults get at least 30 minutes of moderate activity on 5 or more days of the week; for breast cancer risk reduction, 45 minutes or more may be even better.

“It’s great that we can tell women there’s something they can do that’s not going to have horrible side effects,” Saslow said. “To the contrary, the side effects of exercise on other aspects of health are very positive. Even though the effect on breast cancer-specific survival is not huge, a lot of new treatments don’t make a bigger difference than this, and some make a whole lot less.”

Holmes said women should not think of exercise as a replacement for standard breast cancer treatment. And Saslow noted it is not the only factor that could influence a woman’s survival.

“We need to make sure women understand that survival rates for breast cancer are high regardless of whether women exercise or not. Women who are unable to be physically active should not feel that they are harming themselves, and women who do follow the physical activity guidelines have no guarantee against a recurrence,” she said. “But that’s true of every drug or intervention.

“However, this study shows that in addition to the quality of life benefits, following ACS activity guidelines can make a significant difference for breast cancer survival,” Saslow added.

COST CONFUSION KEEPS WOMEN FROM MAMMOGRAMS

What does a woman on Medicare have to pay for her yearly mammogram? At most, about $25. But a portion of women on Medicare and in private health plans think it will cost them far more, according to health services researcher Ann Scheck McAlearney, ScD—and this knowledge gap may cause women to avoid this important cancer screening test.

McAlearney and colleagues found great confusion about mammogram costs and insurance coverage in a recent study of 897 mainly low-income North Carolina women, aged 40 and older, who were overdue for an annual mammogram to detect early signs of breast cancer.

“When breast cancer is diagnosed early, the odds of survival are very, very good,” explained McAlearney. Research shows that more women survive breast cancer every year, thanks to wider use of mammography and improving treatments.

American women’s use of mammograms is not, however, where it should be. The ACS recommends that women at average risk of breast cancer begin having annual mammograms at age
An estimated 25% of women who need the exam (aged 40 and older) have not had one in the past 2 years, and nearly 40% of poor women have never had a mammogram.

McAlearney’s study looked for barriers that may prevent women from getting the exams on time. The group’s racial composition was 32% African American, 41% Native American, and 25% White.

“Cost was far and above the biggest issue. It seemed to be more of a knee-jerk reaction, rather than knowing how much it would truly cost,” said McAlearney, Assistant Professor of Health Services Management and Policy at the Ohio State University School of Public Health in Columbus. Study findings were published in the journal Cancer (2005;103:2473–2480).

Interviewers asked about mammography in general and each woman’s specific reasons for not getting the exam on time, as part of a larger study in rural Robeson County, NC (the ROSE Project). Afterward, women’s beliefs about their coverage were compared with their actual insurance policies. Researchers found:

- More than half (53%) of the women identified cost as a barrier to getting a screening mammogram.
- Of that group, 40% did not fully understand how much their insurance companies would pay for the exam.
- Women aged 65 and older and those at the lowest incomes were more likely to misunderstand their insurance benefits.

A mammogram’s total cost was about $60 in Robeson County in 1998 when the interviews took place, yet a number of women with health insurance stated (wrongly) that their out-of-pocket cost would be $50—nearly the full price.

In reality, the women with any kind of health insurance were not likely to pay more than $12 out-of-pocket; most often there would be no copayment at all. Medicaid and private insurance plans typically paid 100% of the bill for a mammogram, according to the study authors. Medicare paid 80% without requiring women to pay any deductible—so their 20% copayment was no more than $12.

The average cost for a mammogram nationwide is now $125, according to a recent study.

Women who had Medicare alone, and especially those with private insurance, often underestimated how much their plans would pay for the exam. Women insured by Medicaid were better informed about their insurance, which covers the total cost of a mammogram.

The study findings suggest that doctors and insurance companies could play a critical role in increasing adherence to mammography guidelines, according to McAlearney, by making extra efforts to inform women of exactly what they’ll pay out-of-pocket for a mammogram.

“The physician community could provide this information,” said McAlearney. “Doctors could say, ‘Go get a mammogram. And, by the way, you have Medicaid; they pay 100% of the cost.’ Or: ‘Medicare pays for 80% and other groups can help you with the 20%.’”

Most study participants had one or more physician office visits in the year or two before they were interviewed—and McAlearney sees those visits as missed opportunities to clear up any confusion about the cost of a mammogram. Specifically, nearly 70% of the women reported having a medical checkup in the 12 months before the study.

“Doctors generally blame the insurance companies, but this was a group in which close to half of the women were on Medicare or Medicaid or some combination. It should not be that hard to figure out what a mammogram will cost,” she said.

“Most private insurers cover it at 100%,” added McAlearney. “With a little leg work, medical practices could find out which insurers don’t cover the cost of a [screening] mammogram. Unless you are uninsured, you should not be paying $100 today for a mammogram. At most, it should be $25.”

McAlearney also noted that women without insurance and at low incomes can turn to the National Breast and Cervical Cancer Early Detection Program for low-cost or free mammograms in most communities across the country.
Information on the program is available online at http://www.cdc.gov/cancer/nbccedp/index.htm.

RESEARCHERS WEIGHT RISKS DUE TO OVERWEIGHT

After several weeks of debate among researchers and confusion among the general public, it has become increasingly clear that being overweight is not good for your health.

In an article published in the April 20, 2005, issue of *JAMA* (2005; 293:1861–1867), scientists from the Centers for Disease Control and Prevention (CDC), led by Katherine Flegal, PhD, estimated the excess deaths associated with underweight (body mass index [BMI] less than 18.5), overweight (BMI 25 to less than 30), and obesity (BMI 30 or higher). As expected, substantial mortality—111,909 deaths during 2000—was attributed to obesity. The researchers attributed 33,746 deaths to being underweight but, surprisingly, being overweight appeared to have prevented 86,094 deaths during 2000.

The results were applauded in advertisements from organizations affiliated with the food and restaurant industry as evidence that concern about the health effects of overweight and obesity constitutes unsubstantiated hype spread by trial lawyers and the “food police.” Other researchers, however, questioned the new CDC findings.

The new figures were vastly different from those in an earlier CDC analysis which attributed some 365,000 deaths to poor diet, physical inactivity, and excess weight (JAMA 2004; 291:1238–1245 and 2005; 293:293–294), although this earlier article did not report the methods used to estimate the mortality attributed to obesity.

Over the subsequent weeks, epidemiologists from the ACS, American Heart Association, Harvard School of Public Health, and other organizations raised specific methodologic questions about the recent CDC study and presented analyses of other data sets.

The main concern regarding the newer CDC analysis is that it did not adequately account for weight loss from serious illnesses such as cancer and heart disease. Including such individuals in the analysis created the false appearance that being overweight protected against death during the follow up.

The newest CDC analysis also failed to account adequately for the effect of smoking on weight. Smokers tend to be a little lighter than nonsmokers, although the negative health impact of smoking far outweighs that of a few extra pounds. As a result, the Flegal study underestimated the risks from obesity and overestimated the risks of leanness.

“Measuring the effect of excess weight on survival is difficult precisely because of these issues,” says Michael Thun, MD, MS, ACS Vice President for Epidemiology and Surveillance. “Being sick and smoking tobacco cause people to be thinner and to die earlier. They distort the relationship between leanness and health.”

Analyses of the Society’s Cancer Prevention Study II cohort and Harvard University’s Nurses’ Health Study both concluded that people within the range of “healthy” body weight (BMI 18.5 to 24.9) are, in fact, the healthiest and least likely to die prematurely. Obese individuals have substantially higher mortality rates (RR of up to 2.6, for example, in the ACS study), and people who are overweight have intermediate risk (RR of death per year per 100,000 people of up to 1.28, according to the ACS).

Of course, the health effects of excess weight are not limited to mortality, but also include nonfatal cancers, nonfatal heart disease, type II diabetes, and other conditions that adversely impact quality of life but which are unlikely to be fatal—arthritis, for instance.

In a June 2, 2005, press conference, CDC Director Julie Gerberding, MD, MPH, emphasized that excess weight is harmful.

“We need to be absolutely, explicitly clear about one thing: Obesity and overweight are critically important health threats in this country,” she said.

On questioning by journalists, Gerberding also downplayed the suggestion derived from
the Flegal study that overweight people might have a lower risk of death.

“I think when you talk to the investigator, and I would encourage you to do that, there are some statistical aspects of the way the study was designed and the data sources used in that the author herself would not claim that overweight is protective of ill health,” Gerberding said.

“I know a lot of people were hoping that CDC was going to come out and say it was OK to be overweight,” she added, “but we’re not saying that. It is not OK to be overweight. People need to be fit, they need to have a healthy diet, and they need to exercise.” Despite the strong statements, Thun said some people may still be confused about the true health risks of excess weight.

“Some of the methodologic issues probably seem a little abstract,” Thun said, “and it’s easy to see how some overweight individuals may be more likely to believe a report suggesting there is no need for them to lose weight. However, the key message for clinicians to provide to their patients is the importance of maintaining a healthy body weight throughout life. It’s easier to avoid those excess pounds than to lose them, and so weight gain should be considered just as important a problem as high cholesterol or blood pressure.”

EVOLUTION AND RESOLUTION OF SIDE EFFECTS FOLLOWING TREATMENT OF LOCALIZED PROSTATE CANCER

A recent study of prostate cancer survivors’ long-term health-related quality-of-life (HRQOL) identified some important differences among men initially treated with radical prostatectomy, three-dimensional conformal radiotherapy, or brachytherapy, and a control group without prostate cancer. With all three treatments yielding excellent survival, HRQOL figures prominently in the preferences of men with localized prostate cancer.

Investigators from the University of Michigan and Beth Israel-Deaconess Medical Centers studied HRQOL among men who had been treated for localized prostate cancer, with a median time since treatment of 6.2 years. Analyses were done to identify any differences associated with initial treatment, and to compare long-term HRQOL with earlier evaluations done at a median time from treatment of 2.6 years. Several prostate-cancer-specific domains of HRQOL were considered—urinary irritative, urinary incontinence, bowel, sexual, and hormonal/vitality.

The key findings, reported in the Journal of Clinical Oncology (2005;23:2772–2780), relate to how the long-term side effects of various treatments develop and resolve over time.

“Perhaps our most novel and important finding is that disease-specific HRQOL continues to change and evolve among men treated with brachytherapy and 3-D conformal radiation, whereas postprostatectomy HRQOL remains relatively stable between 2 and 6 years of median follow up,” said first author David C. Miller, MD, Lecturer at the Michigan Urology Center, University of Michigan Medical Center.

At a median follow up of 6.2 years, men treated with radical prostatectomy had HRQOL summary scores significantly lower than those of controls in the urinary incontinence and sexual domains; conformal radiotherapy significantly diminished scores in the bowel and sexual domains; and brachytherapy had significant adverse impact on the urinary irritative, urinary incontinence, bowel, and sexual domains.

Compared with their responses 4 years earlier, men in the brachytherapy group reported a significant resolution in urinary irritative problems. During the same period, urinary continence became more problematic among men initially treated with conformal radiotherapy or brachytherapy. Bowel side effects improved in the brachytherapy group. Sexual function declined among controls and among men treated with conformal radiotherapy. None of the four groups reported any significant changes in the hormonal/vitality domain.
The item of “problem with pain or burning on urination” typifies trends in the urinary irritative domain. This problem was reported by 23% of survivors at 2.6 years after brachytherapy; 4 years later, this problem was reported by 10%. This problem was reported by no more than 3% of prostatectomy or conformal radiotherapy patients at both follow-up intervals.

During the same interval, “leakage of urine more than once a day” increased from 11% to 18% in the brachytherapy group. Corresponding values at 2.6 and 6.2 years were 17% and 16% for the prostatectomy patients, and 6% and 4% following conformal radiotherapy.

As an example of bowel concerns, “problem with urgency to have a bowel movement” declined from 19% to 10% during this period for brachytherapy patients. In each time period, 14% of men treated with conformal radiotherapy reported this problem; in the prostatectomy group, there was no substantial change in this side effect over time (3% and 5% at 2.6 and 6.2 years, respectively).

The percentage reporting “poor to no ability to have an erection” remained relatively unchanged over time following prostatectomy (62% and 65% at 2.6 and 6.2 years), but increased in the conformal radiotherapy group (from 65% at 2.6 years to 75% at 6.2 years) and in the brachytherapy group (from 71% to 82%). The control (no prostate cancer) group also reported an increase in this item, from 19% to 29%. In comparing the prevalence of this problem, however, it should be noted that the median ages differed among the control (69.1 years), prostatectomy (67.2 years), conformal radiotherapy (75.7 years), and brachytherapy (70.4 years) groups.

Although these results are generally consistent with those of previous studies, they provide a clearer view of likely outcomes than most earlier reports because the data are recent enough to reflect outcomes of modern technology for brachytherapy and conformal radiotherapy, yet mature enough to be relevant over a follow-up interval of interest to men facing these decisions.

“We believe that this study is useful because it is one of the first to use a validated instrument (EPIC) to measure long-term, patient-report HRQOL changes during the late survivorship phase following contemporary therapies for localized prostate cancer, including brachytherapy and 3-D conformal radiotherapy,” said Miller. “These observations highlight the need for corroborative multi-institutional, prospective studies that further characterize HRQOL evolution among long-term (>5 years) prostate cancer treatment survivors. Until such studies mature in coming years, the observed HRQOL changes described herein may provide clinicians and patients that choose a specific treatment with an estimation of their long-term HRQOL outcomes.”

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