

**Women's  
Health Study**

# Update

## Preventing common cancers after menopause: what you need to know

**B**reast, lung, and colorectal cancers account for half of new cancer cases (excluding nonmelanoma skin cancers) in U.S. women. Cancer risk rises as one grows older—the average ages at diagnosis of breast, lung, and colorectal cancer are 62, 70, and 72 years, respectively. It is true that several nonmodifiable factors affect risk. For breast cancer, a family history of breast or ovarian cancer increases risk. Reproductive factors also play a role. For example, the younger you were when you began menstruating and the older you were when you entered menopause, the greater your risk, presumably because the number of years of exposure to high levels of estrogen—which stimulates growth of breast tissue, including abnormal cells—is longer. Giving birth before age 24 and breastfeeding for at least one year each appear to protect against breast cancer after menopause. For lung cancer, although smoking is the greatest risk factor, a family history of the disease and exposure to environmental tobacco smoke and pollution also increase risk. For colorectal cancer, a personal history of precancerous polyps (colorectal adenomas) or inflammatory bowel disease raises risk, as does a family history of colorectal adenomas or cancer. However, it is also true that an estimated 40% of postmenopausal breast cancers, 90% of lung cancers, and 70% of colorectal cancers in U.S. women can be prevented by healthy behaviors, including these:

- **Avoid unnecessary use of hormone therapy.** Consider it only to relieve hot flashes and night sweats that disrupt your sleep or quality of life. (For vaginal dryness, consider topical estrogen, which has minimal absorption.) Take the lowest dose possible and try to limit use—particularly of estrogen plus progestin—to less than 5 years. Although estrogen plus progestin appears to cut the risk for colorectal cancer by 20%, these hormones boost risk for breast cancer and possibly lung cancer. Among postmenopausal participants in the WHS, women who took estrogen plus progestin for 5 or more years were 76% more likely to develop breast cancer than those who had never used hormone therapy. Although estrogen taken alone was not associated with an increased breast cancer risk in the WHS, longer-term studies suggest that the risk rises significantly after 10 to 15 years of estrogen use.
- **Maintain a healthy body weight.** After menopause, obesity doubles a woman's breast cancer risk, likely because fat cells overtake the ovaries as the body's main producer of estrogen. Obesity also boosts a woman's risk for colorectal cancer by 50%, perhaps because excess weight leads to high insulin levels, inflammation, and proliferation of the cells lining the gut. More than one fifth of postmenopausal breast and colorectal cancers in U.S. women are attributable to excess weight.

- **Be physically active for at least 30 minutes per day.** Physical activity lowers the risk for breast and colorectal cancer not only because it keeps obesity in check but also because it lowers insulin levels and favorably affects other hormones. It also speeds the passage of food, bile salts, and stool through the gut, shortening the exposure of the intestinal walls to potential carcinogens in these substances. In the WHS, postmenopausal women who regularly walked 2 miles per day (or expended equivalent energy in other physical activities) were 33% less likely than their sedentary counterparts to develop breast cancer over 4 years of follow-up. WHS investigators have yet to examine the relation between physical activity and colorectal cancer, but in another study of U.S. nurses, women who reported 5 or more hours per week of moderate activity experienced about half the risk for colon cancer as did inactive women.

- **Avoid cigarette smoke.** You know that smoking causes lung cancer, but were you aware that quitting or even just cutting back on a cigarette habit, even at older ages, significantly lowers lung cancer risk (although the risk never drops to that of a lifelong nonsmoker)? Or that exposure to secondhand smoke at home or work increases lung cancer risk among nonsmokers by at least 20%? Or that smoking is a probable risk factor for colorectal cancer? In one study of 469,000 U.S. women, current smokers

who had smoked for at least 20 years were 33 to 51% more likely than never smokers to die from colorectal cancer during a 14-year follow-up.

• **Limit alcohol intake.** Consuming more than one drink per day on a regular basis substantially boosts breast cancer risk. In the WHS, women who reported having two or more drinks per day were 43% more likely than teetotalers to develop breast cancer during 10 years of follow-up. Alcohol raises estrogen levels and may decrease the body's stores of folate, a vitamin essential for DNA replication and repair. Heavy alcohol use also raises colorectal cancer risk; in six large cohorts of women tracked from 6 to 16 years, consuming three or more drinks per day was associated with a 41% increase in colorectal cancer risk.

• **Eat folate-rich foods.** A high intake of folate—cruciferous or leafy dark-green vegetables; citrus fruits; peas; and garbanzo and other beans are good sources—may reduce breast cancer risk, especially in women who drink alcohol. The role of folate in colorectal cancer prevention is controversial. In the WHS, a high intake of folate from vegetable and other food sources was associated with reduced colorectal cancer risk among women not taking folate-containing supplements, but total folate intake—i.e., from food plus supplements—was unrelated to risk. And a recent clinical trial of folic acid supplements found a suggestion of *increased* risk for recurrence of precancerous polyps with such supplementation. More research is needed—it may be that folate works in concert with other B vitamins to prevent cancer, or that folate slows cancer initiation but accelerates its progression.

• **Eat a variety of fruits and vegetables.** Aim for 5 to 9 servings per day. While folate-rich green vegetables may be best for reducing breast and colorectal cancer risk, tomatoes, carrots, and

other orange/yellow vegetables may be more beneficial in preventing lung cancer. Although research has focused on the high carotenoid content of these vegetables, it is not yet clear which specific nutrient(s) are responsible for the apparent lung cancer protection seen in some studies. In the WHS, 2 years of beta-carotene supplementation did not affect the incidence of total or site-specific cancer. And findings from two other trials suggest that beta-carotene supplements may *increase* lung cancer risk in smokers. Fiber, a component of fruits and vegetables once believed to prevent colon cancer, actually does not: a pooled analysis of data from 13 large cohorts, including the WHS, found no link between fiber intake and colorectal cancer risk.

• **Cut dietary fat.** The Women's Health Initiative dietary trial assigned 49,000 postmenopausal women to a low-fat, fruit- and vegetable-rich diet or to their usual diet for 8 years. Although the intervention didn't significantly reduce breast cancer risk in the overall study population, it did do so in the women who had been eating a high-fat diet at study entry. The intervention also didn't reduce colorectal cancer risk, but it did decrease the occurrence of polyps, suggesting that longer-term dietary change might ultimately protect against colorectal cancer.

• **Limit consumption of red meat and processed meat.** A 4-ounce-per-day increase in intake of red or processed meat boosts colorectal cancer risk by an estimated 28% and 36%, respectively. The harmful effect of meat may result not from its high fat content but from its iron, which is a pro-oxidant and may damage DNA; growth-promoting hormones used in the animals; and compounds such as heterocyclic amines and polycyclic aromatic hydrocarbons created by high-temperature cooking (especially on a grill), curing, smoking, or other processing. Although high red meat consumption in adolescence and early adulthood has been linked

to premenopausal breast cancer, no relation between red meat intake and breast cancer after menopause has been observed to date. In a recent 8-year study of 500,000 U.S. middle-aged and older adults, higher consumption of red and processed meat was associated with a higher risk for lung cancer.

• **Get enough vitamin D.** Women with low blood levels of vitamin D are at increased risk for breast cancer and especially colorectal cancer. The sun's ultraviolet B rays trigger vitamin D synthesis in the skin. Sun exposure for 10 to 15 minutes twice per week usually provides an adequate dose, except in northern states during winter months. However, many women, especially those who burn easily or have a family history of skin cancer, may wish to get their vitamin D from food or supplements. Current guidelines call for daily intakes of 400 IU between age 51 and 70, and 600 IU after age 70, but many experts now recommend at least 1000 IU. Dietary sources include fatty fish (one serving, 250-360 IU), cod liver oil (1 tablespoon, 1,360 IU), eggs (1 yolk, 20 IU), and fortified milk (1 cup, 100 IU) and cereals; vitamin D is also available in multivitamins, some calcium tablets and osteoporosis medications, and as a stand-alone supplement.

• **Get enough calcium.** In observational studies, high calcium consumption is associated with a lower risk for colorectal cancer. Small trials of calcium supplementation also report reductions in risk for precancerous polyps. However, in the Women's Health Initiative calcium-plus-vitamin D trial among 36,000 women, supplementation did not lower colorectal cancer risk (a low dose of vitamin D was tested, so the trial didn't provide a definitive test of this vitamin). Research to clarify the relation is ongoing. The recommended daily intake after age 50 is 1200 mg. Dietary sources include dairy foods such as yogurt (1 cup, 415 mg) and milk

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(1 cup, 300 mg); canned oily fish with bones, such as salmon (3 ounces, 181 mg) or sardines (4 sardines, 184 mg); calcium-fortified orange juice (6 ounces, 200 mg) or cereals (3/4 cup, 250-1000 mg); figs (10 figs, 269 mg); blackstrap molasses (1 tablespoon, 172 mg); and collard greens (1/2 cup, 179 mg). Women with insufficient dietary calcium should take a calcium supplement.

• **Consider taking tamoxifen or raloxifene** if you're at high risk for breast cancer. These medications can reduce breast cancer risk. However, both increase the risk for blood clots, hot flashes, and possibly stroke, and tamoxifen also increases risk for endometrial cancer. Still, it's worth asking your doctor whether these medications are right for you.

• **Consider taking aspirin** if you're at high risk for colorectal cancer. Long-term use of aspirin—at higher daily doses than that tested in the WHS—may lower colorectal cancer risk. However, aspirin increases the risk for gastrointestinal bleeding, so check with your doctor before starting any aspirin regimen.

• **Be regularly screened for breast and colorectal cancer.** Although it doesn't technically prevent cancer, mammography detects tumors at earlier, more treatable stages, even among women aged 80 and older. Colonoscopy and sigmoidoscopy not only detect but also directly allow for removal of precancerous polyps or cancerous growths. Yet only 66% of U.S. women aged 40 and older have had a mammogram in the last 2 years, while just 41% of U.S. women aged 50 and older comply with colorectal screening guidelines. As for lung cancer screening, the ability of spiral computed tomography (*vs.* standard chest x-ray) to detect early-stage disease and reduce lung cancer mortality remains unclear but is now being tested in a large trial among current and former smokers.



 **Why are there items on recent WHS questionnaires about topics—for example, pet ownership, perceived fairness, and handedness—that seem unrelated to the study's main aims?**

The main aims of the WHS are to understand factors that influence risk for cardiovascular disease and cancer, but we are also interested in contributing to knowledge about other aspects of women's health. When new hypotheses based on solid scientific reasoning arise in the medical literature, we may include relevant questions on the WHS questionnaires. Although these hypotheses do not always turn out to be fruitful, we believe it is important for the WHS to contribute to their evaluation in a rigorous scientific way.

Some long-term studies have suggested that *pet ownership* has favorable effects on cardiovascular health and functional status. For example, a study utilizing health insurance records of elderly U.S. residents found that pet owners made fewer medical visits than non-owners. In another study, older adults' physical functioning declined less during a 1-year follow-up among dog and cat owners than among other individuals. In a study of patients with coronary heart disease, dog owners were 8½ times more likely to be alive one year later than those who did not own dogs, even after accounting for disease severity and social support, while cat ownership was not related to survival. We plan to use the WHS data to study the potential health benefits of owning a pet.

Questions about *perceptions of unfair treatment* seek to capture experiences that contribute to stress

in daily living. Many studies suggest that chronic stress may not only precipitate unhealthy habits such as overeating and smoking but also lead to high levels of stress hormones and perhaps other biochemical changes that unfavorably affect cardiovascular, metabolic, and immune systems, thus increasing disease risk. However, some studies have not found connections between stress and disease, particularly in women. We will examine whether and by what pathways stress influences women's health. Future questionnaires may ask about other sources of stress, including caregiving or retirement.

Although *handedness* commonly refers to the unequal distribution of fine motor skills between the right and the left hand, it actually reflects brain lateralization—i.e., the distribution of mental tasks between the right and left hemispheres of the brain. For example, 95% of right-handers use the left side of the brain for speaking, but only 27% of left-handers do. Our goal is to identify genetic determinants of handedness in order to better understand processes underlying brain lateralization. This research could ultimately lead to new treatments for patients with strokes, epilepsy, and other neurological diseases.



If you have questions regarding the WHS, please let us know. Julie Buring, ScD, the study's Principal Investigator, will answer them in future issues of *Update*.