or adiponectin in the blood that are associated with fat mass, and measures of fat such as computed tomography. However, these more expensive technologies are not feasible for use in large population studies,” Ballard-Barbash said.

A Tangled Web
Besides discouraging tobacco use, recent American Cancer Society guidelines recommend maintaining a healthful weight, staying physically active, and eating a healthy diet—all of which are thought to reduce lifetime risk of developing or dying from cancer.

Over the last 20 years research and exploded on how physical activity influences cancer risk and prognosis, said Ballard-Barbash, to think that researchers can fully untangle the effects of healthy behaviors such as weight control, diet, and exercise is naïve. “Both diet and physical activity are key components of weight control; the two cannot be truly separated.”

Chronic diseases, including cancer, can take 20–50 years to develop through multiple insults over a lifetime. Body weight during adolescence or childhood may affect cancer later in life. But a large gap, which remains to be filled is how obesity and nutritional risk factors that have complex and changing pattern of exposure over the course of one’s life affect cancer risk, according to Parekh.

“If you are obese for a major portion of your adult life, does this stay with you, or is your risk of cancer reduced if you lose weight and keep it off?” said Gapstur. Little research on this question exists, and on the potential benefits of weight loss, she said, partly because of the difficulty of sustaining weight loss.

That's precisely the question Murphy now wants to study: how changes in fat tissue and fluctuations in weight affect cancer risk.

“This type of study would partly address how cumulative effects of lifelong obesity and changes in weight are linked with cancer risk,” Murphy said.

“Randomized, controlled trials suggest that there are some benefits of modest weight loss of about 10 pounds when it comes to heart disease, diabetes, and hypertension but how long the benefit lasts if weight is regained is not clear,” said Ballard-Barbash. “For cancer risk, we think it may be beneficial to maintain a healthy body weight, but whether a few episodes of small weight loss reduce risk is not known because there is no clinical trial evidence of whether weight loss will reduce risk or improve prognosis.”

Informally observing the interaction of clinicians and patients (both cancer survivors and noncancer patients) in clinics and offices, Parekh said that obesity and unhealthy food habits by healthcare professionals may prevent them from bringing up obesity and recommending changing diet and exercise habits to their patients.

“We need individual, targeted counseling for patients. Despite a lot of work to understand obesity trends and general policy and messaging efforts we haven't seen many changes—yet.”

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Nuts May Lower Cancer Risk
By Mike Fillon

During the last decade, studies have sporadically linked nut consumption with a decreased risk of, and as potential therapies for, many diseases. Several new studies, including one in the November 13, 2013 issue of The New England Journal of Medicine (NEJM), have found that people who ate a daily handful of nuts were significantly less likely to die from any cause than those who never ate nuts. The researchers found that of the 521,763 study subjects that reported they ate nuts, the 164,042 who ate nuts five of more times per week, that over a 30-year-period, there were 5,203 deaths among those who never at nuts versus 1746 deaths from those who ate nuts daily.

The biggest gain was for cardiovascular deaths; the study found 1,355 deaths for the non-nut eaters, versus 457 deaths from those who ate nuts daily. For cancer, the results were also pronounced; there were 1,883 reported deaths for the non-nut eaters versus 632 for those who ate nuts daily.

Lead author of the NEJM study, Ying Bao, MD, associate epidemiologist at Brigham and Women’s Hospital and Harvard Medical School, said that earlier observational and intervention studies of nut consumption uncovered reductions in many chronic disease triggers, including oxidative stress, inflammation, visceral adiposity, hyperglycemia, insulin resistance, and endothelial dysfunction. Also, prospective cohort studies associated increased nut intake with reduced risks of type 2 diabetes mellitus, metabolic syndrome, colon cancer, hypertension, gallstone disease, diverticulitis, and death from inflammatory diseases.

“Despite these inverse associations between nut intake and several major chronic diseases,” said Bao, “few studies have investigated nut consumption in relation to total mortality.”

She added that investigations have often been limited by small samples, single assessment of diet and other covariates, or inadequate adjustment for important confounding factors. To overcome these limitations, Bao and colleagues examined nut consumption in relation to total and cause-specific mortality in two large, independent cohort studies of nurses and other health professionals. The Nurses’ Health Study supplied data on 76,464 women between 1980 and 2010, and the Health Professionals’ Follow-up Study yielded data on 42,498 men from 1986 to 2010. Study participants filled out detailed food
questionnaires every 2–4 years. These studies offer repeated measures of diet, including several types of nuts, extensive data on known or suspected confounding variables, 30 years of follow-up, and data on more than 27,000 deaths for analysis. Bao said that theirs is the largest study of its kind.

Marco Falasca, PhD, professor of molecular pharmacology at the Blizard Institute Barts and the London School of Medicine and Dentistry, said of the study, “It makes a very strong case for the nut consumption–cancer link. I think it will be interesting to see if this leads to stronger correlations and evidence for particular forms of cancer—maybe, for example, prostate or colorectal cancer—based on clinical data.” Falasca cowrote a review on this topic, “Cancer Chemoprevention by Nuts: Evidence and Promises,” in the January 1, 2012, issue of *Frontiers in Bioscience*.

**Nuts May Thwart Disease—but How?**

Tree nuts consist of walnuts, almonds, hazelnuts, cashews, pistachios, macadamias, and pecans. Brazil nuts, which are seeds, and peanuts, which are legumes, are often grouped with tree nuts because they have similar nutritional properties. Chestnuts have more starch and are therefore nutritionally distinct.

The nutritional content of nuts is substantial enough for the US Food and Drug Administration to have approved a health claim that eating 1.5 ounces daily as part of a diet low in saturated fat may reduce risk of heart disease. Bao’s study, showing a significant decrease in the risk for a range of cardiovascular deaths, certainly supports this claim. Falasca said that one of the biggest unanswered questions is which nutritional component prevents cancer.

Keith Block, MD, medical and scientific director at the Block Center for Integrative Cancer Treatment in Skokie, IL, said that scientists have some solid ideas about how nuts may help reduce cancer mortality.

“The phytochemical content of nuts is notable, and many nuts contain phytochemicals directly relevant to cancer. These probably contribute to the antioxidant effects of nuts that have been observed in clinical trials.”

Block said that the mix of phytochemicals in nuts also serves as a valuable inhibitory cocktail that can counter the onset, dissemination, and recurrence of cancer.

“These inhibitors act by targeting not one, but a multiple of interconnected pathogenic drivers. Oxidation and insulin are two examples of such pathogenic drivers and are involved in the promotion of a variety of cancers. The reduction in cancer mortality that Bao reports may be due in large part to the effect of nuts in these areas.”

Block added that consensus is growing among cancer researchers that carefully chosen phytochemicals and natural products can diminish treatment-related toxicity, reduce treatment resistance, and synergistically enhance cancer-related treatment.

Other Factors Ruled Out

“This study was well done and is very strong,” said Barnett S. Kramer, MD, Director, Division of Cancer Prevention, National Cancer Institute, in Rockville, MD. “But, there’s a saying in epidemiology that observational studies are guilty until proven innocent, meaning, you always have to be concerned about confounders, or other factors that could have explained the association, other than the one that you are particularly interested in.”

Recognizing these potential pitfalls, the researchers in the *NEJM* study ruled out other factors that might have accounted for the mortality benefits. For example, individuals who ate more nuts were leaner; less likely to smoke; and more likely to exercise, use multivitamin supplements, consume more fruits and vegetables, and drink more alcohol. However, analysis isolated the association between nuts and mortality independently of these other factors.

When the *NEJM* study came out, an editorial in the November 2013 *Lancet Oncology*, “Nuts and Cancer: Where Are We Now?” also discussed this issue.

“Nuts is just one of those topics that the more I read, the less I know or understand about it,” said coauthor Justin Stebbing, professor of cancer medicine and oncology at Imperial College London. “The relationship between food and cancer is a very complex area, and, I think on the basis of the data regarding nuts, we’re not there yet, and it’s too soon to form any firm conclusions.”

Bao has no illusions that the study is the final word. She said that with their study’s observational nature, they cannot conclude that the observed inverse association between nut consumption and mortality reflects cause and effect.

“However, our data are consistent with a wealth of existing observational and clinical-trial data in supporting the health benefits of nut consumption for many chronic diseases,” she said.

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