This is not the first time we’ve seen medical dogma upended. Remember breast self-examination? It was proven to have no life-saving benefit and a high risk of unnecessary breast biopsies. Now it is calcium supplements and a low-fat diet that will not save your life.

February 2006 was a banner month for disproving medical dogma. First, the public learned that the low-fat diet does not prevent heart disease. The next week, another study found that calcium does not protect against fractures or colon cancer. And in between, yet another study provided the surprising news that estrogen might lower the risk of heart disease in some women. (This last one actually reconstituted a previously disproved medical belief. For over ten years, women had been told that estrogen will save them from heart disease, but a major clinical trial was stopped early several years ago when it found that this hormone caused heart-related problems.) In each case, the findings were strongly contested.

Women’s Health Initiative

All these newsworthy announcements came from the same landmark clinical trial called the Women’s Health Initiative (WHI), an $18 million government-funded project, which involves thousands of healthy women over age 50. It is designed to test the prevailing health advice about how to prevent the chief causes of death and disability in older women.

Medical research is constantly evolving and we should expect health advice to change as more studies are published. But how is it that so many recommendations based on uncertain evidence can become orthodoxy? Recall how women were made to feel negligent by their doctors for not doing breast self-exams. Similar guilts were laid on those who refused to take postmenopausal hormones or were doubtful about high-dose calcium.

Surrogate Endpoints

Physician acceptance of the preventive measures was nearly universal, though they were based on a less reliable type of study called population, or observational studies. In this type of study, for example, the women who chose to take estrogen (as opposed to being randomly assigned to take it in a clinical trial) tended to have lower rates of heart disease. A closer look at these less reliable studies showed that women in the higher income brackets were more likely to take estrogen, and a high income is known to be associated with better health and a longer life.

Often, health recommendations are based on what researchers call surrogate endpoints—plus a heavy dose of assumptions. Estrogen lowers cholesterol in women; therefore it must save them from heart disease. Calcium improves bone density; therefore it must cut the risk of hip...
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fracture. Long-term trials that follow participants until they have a heart attack or a hip fracture are expensive and take many years to produce answers, which is why so much health advice is based on surrogate endpoints.

The WHI is a massive research effort that involves multiple clinical trials. As researchers continue to sift through the data generated by the WHI, they will be publishing results for years to come. What follows is a summary of the evidence (or gaps in the research) that led the WHI to study the low-fat diet, high-dose calcium, and estrogen in younger women; the doubts that long surrounded each preventive measure; and the questions that remain unanswered.

LOW-FAT DIET AND HEART DISEASE

The supporting evidence:

No long-term trial had ever been conducted to support the idea that a low-fat diet (below 20% of total calories) reduces the risk of heart attack in healthy older people. While the WHI was still underway, a 2001 Cochrane review on this topic was published in the British medical journal, BMJ. Lee Hooper, PhD, and colleagues assessed all clinical trials in which healthy older men and women had been randomly assigned to continue on their normal diet or go on a low-fat or a reduced-fat diet.

This review exposed the difficulty in finding definitive answers as heart disease takes years to develop and few of the trials lasted more than six months. Results were predictably unimpressive: There was no reduction in heart attacks or cardiac deaths, but the few trials that lasted two years hinted at a lower risk of heart disease.

Flaws in the WHI:

The most valid criticism of the WHI/diet trial centers on the fact that it made no distinctions in the types of fat, as in: olive oil is good; trans-fatty acids (partially hydrogenated vegetable oils) are bad. Participants were simply instructed to keep their total fat intake below 20%. Because the WHI was designed 15 years ago, it reflects the general thinking among nutrition scientists at the time, said nutrition scientist Sharon Akabas, PhD, in a telephone interview. “As recently as 12 to 15 years ago, you still had people [in the nutrition field] who thought trans-fatty acids were OK and omega-3 fatty acids were seen as fringe—olive oil and other monosaturated oils were thought to be neutral.”

The Mediterranean-type diet is favored by many nutritionists today and that is a glaring omission of the WHI, according to Dr. Akabas, who is associate director of education at the Institute of Human Nutrition, Columbia University in New York City. “If I could design the WHI now, I would have had a group whose fat intake was 40% of calories with a significant contribution from olive oil. The Mediterranean diet also puts more emphasis on omega-3 fatty acids; it is high in plant food; low in animal foods; has more whole food; and less processed foods,” she said, adding that there is more to healthful living than dietary choices. Referring to the numerous population studies that showed the Mediterranean diet to be one of the most healthful in the world, Dr. Akabas continued, “People eating the Mediterranean diet at the time of these studies were taking a nap in the afternoon, they didn’t snack all day; they were physically active. And they are on the diet by choice, as opposed to have it imposed on them during a study.”

Doubters Have Reason to Remain Doubtful:

Even the highly motivated women who volunteered for the WHI could not get their fat intake under 20% of calories. (Many critics of the WHI saw this as a sign that a low-fat diet is impossible for Americans.) The best the WHI participants could do was 24% in the first year and 29% in the subsequent years. Since that narrowed the difference between them and the other women who had been assigned to remain on their usual diet, the WHI results were seen by some critics as not proving anything one way or another about the value of the low-fat diet.

The most steadfast proponent of the low-fat diet is Dean Ornish, MD, president of Preventive Medicine Research Institute and clinical professor of medicine at the University of California, San Francisco. The author of several books about reversing heart disease, Dr. Ornish has also
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coa-authored a study that showed regression of severe coronary atherosclerosis after only one year, without the use of cholesterol-lowering drugs. In addition to a low-fat vegetarian diet, the study participants took part in a program of comprehensive lifestyle changes that included smoking cessation, stress management training, and moderate exercise. As yet, Dr. Ornish has not published a clinical trial that proves his program results in lower rates of heart attack or cardiac death.

Other Potential Benefits to Low-Fat Diet

The WHI produced a hint that even small reductions in dietary fat might reduce the risk of developing breast cancer. There was a 9% reduced rate of breast cancer in the women who attempted a low-fat diet, but this was not regarded as statistically significant, though it came close. Dr. Jacques Rossouw, the project officer for the WHI has stated that this finding might have become statistically significant had the trial lasted longer.

CALCIUM AND HIP FRACTURES

Supporting Evidence:

The body needs calcium for strong teeth and bones. That’s a fact. A controversy, however, surrounds the question whether anyone (including children) has to get it from milk or other dairy foods. It was also unclear whether massive increases in calcium intake in middle age will make any difference in fracture reduction.

Many population or observational studies show an increase in calcium intake in middle age improves bone density, but others show that women with high intake of calcium from diet or supplements actually have higher rates of fractures. Until, the WHI published its results last month, no well-designed clinical trial followed women long enough to prove increased calcium intake in middle age will reduce the rate of hip fractures.

The WHI Findings:

The WHI/calcium plus vitamin D trial involved 36,282 women. The hip fracture rate in those taking calcium plus vitamin D was the same as that of the women taking inactive placebos. One benefit shown in the calcium/vitamin D group was a 1% increase in bone density at the hip. Another is a slightly lower risk of hip fracture in one subgroup—women over the age of 60 years at the start of the trial.

Only 70% of the women in the calcium/vitamin D group took their assigned supplements regularly. When the investigators looked solely at this group, they found that these women had 29% fewer hip fractures than those taking placebo. In other words, there were 10 compared to 14 hip fractures per 10,000 women each year.

Furthermore, the supplements did not prevent colon cancer as originally thought, but they slightly raised the risk of developing kidney stones. There were an additional five cases of kidney stones per 10,000 women per year among those on supplements.

Doubts That Remain:

Since the WHI was planned, researchers have begun to view the recommended dose of vitamin D3 (400 international units) as inadequate and the recommended dose of calcium (1200 milligrams) as excessive. The WHI chose to use a daily dose of 1,000 milligrams of calcium and 400 international units of vitamin D3 (cholecalciferol). Last year, an analysis of all clinical trials that looked at the relationship between fractures and vitamin D was published in the Journal of the American Medical Association. It concluded: “Oral vitamin D supplementation between 700 to 800 IU a day appears to reduce the risk of hip and any non-spinal fractures in ambulatory or institutionalized elderly persons. An oral vitamin D dose of 400 IU/day is not sufficient for fracture prevention.”

Doubters Proven Correct (so far):

The two high-profile doubters about the relevance of calcium intake to hip fracture are Walter Willett, MD, Harvard School of Public Health, and T. Colin Campbell, PhD, professor emeritus of nutritional biochemistry at Cornell, who have, respectively, conducted numerous studies on the topic. Both argue that there is too much...
follow the 10,739 participants who had undergone a hysterectomy. All had been randomly assigned to take daily doses of estrogen (0.625 milligrams) or a placebo. Their mean age at entry into the WHI was 63 years. In February 2003, this arm of the WHI was also stopped early due to a higher stroke rate among women on estrogen.

The WHI Findings:

A study that looked at the heart-related WHI findings for the hysterectomy group was published last month in the Archives of Internal Medicine. After about seven years, the rate of heart attack and cardiac death was exactly the same for both the estrogen and the placebo groups. But there was “a suggestion” of a lower heart disease risk only among the women who had started taking estrogen while in their fifties. There was no suggestion of benefit in women who were 60 years or older when they started taking estrogen. Stroke was not taken into account in this particular study.

Doubts that Remain:

Whenever researchers use the word suggestion to describe their results, as in “a suggestion of lower heart disease risk,” they are saying that the findings aren’t clearly established. Despite the breathless headlines that went out across the country heralding the results of this study (“Estrogen May Help Heart”), they could be due to chance, which is how the WHI Web site (see below) describes them. A co-author of this study, quoted frequently in the media, saw the lack of an increased risk of heart disease as reassuring to women who want to take hormones on a short-term basis to alleviate hot flashes.

For More Information:

The WHI is a 15-year project that includes 161,000 women. It is paid for by taxpayer money, and as such, the WHI has been entirely open—via its Web site (www.whi.org)—about its findings both good and bad. The WHI has two major components: a randomized clinical trial (RCT) and an observational study. The RCT section is divided into three additional components: hormones, dietary modification and calcium/vitamin D. ±
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