# Food and Vitamins and Supplements! Oh My!

Demystifying nutrition: the value of food, vitamins and supplements



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The Joseph B. Martin Conference Center Harvard Medical School 77 Avenue Louis Pasteur Boston, MA 02115





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Demystifying nutrition: the value of food, vitamins and supplements

# **Moderator**



Walter Willett, DrPH, MD Chair, Department of Nutrition, Harvard School of Public Health Fredrick Stare Professor of Epidemiology and Nutrition, Harvard School of Public Health Professor of Medicine, Harvard Medical School

Speakers



Howard Sesso, ScD, MPH, FAHA Associate Professor of Medicine, Harvard Medical School Associate Epidemiologist, Brigham and Women's Hospital



Eric Rimm, ScD Associate Professor of Medicine, Harvard Medical School Brigham and Women's Hospital Associate Professor of Epidemiology and Nutrition and Director, Program in Cardiovascular Epidemiology Harvard School of Public Health

# **About the Speakers**

# Walter Willett, DrPH, MD

Dr. Walter Willett is Professor of Epidemiology and Nutrition and Chairman of the Department of Nutrition at Harvard School of Public Health and Professor of Medicine at Harvard Medical School. Dr. Willett, an American, was born in Hart, Michigan and grew up in Madison, Wisconsin, studied food science at Michigan State University, and graduated from the University of Michigan Medical School before obtaining a Doctorate in Public Health from Harvard School of Public Health. Dr. Willett has focused much of his work over the last 30 years on the development of methods, using both questionnaire and biochemical approaches, to study the effects of diet on the occurrence of major diseases. He has applied these methods starting in 1980 in the Nurses' Health Studies I and II and the Health Professionals Follow-up Study. Together, these cohorts that include nearly 300,000 men and women with repeated dietary assessments are providing the most detailed information on the long-term health consequences of food choices.

Dr. Willett has published over 1,500 articles, primarily on lifestyle risk factors for heart disease and cancer, and has written the textbook, *Nutritional Epidemiology*, published by Oxford University Press. He also has three books book for the general public, *Eat*, *Drink and Be Healthy: The Harvard Medical School Guide to Healthy Eating*, which has appeared on most major bestseller lists, *Eat*, *Drink, and Weigh Less*, co-authored with *Mollie Katzen*, and most recently, *The Fertility Diet*, co-authored *with Jorge Chavarro and Pat Skerrett*. Dr. Willett is the most cited nutritionist internationally, and is among the five most cited persons in all fields of clinical science. He is a member of the Institute of Medicine of the National Academy of Sciences and the recipient of many national and international awards for his research.

### Howard Sesso, ScD, MPH, FAHA

Dr. Howard D. Sesso is an Associate Epidemiologist at the Divisions of Preventive Medicine and Aging at Brigham and Women's Hospital (BWH), and an Associate Professor of Medicine at Harvard Medical School. He received his BA in Human Biology from Stanford University, an MPH in Epidemiology from The George Washington University, and a ScD in Epidemiology from the Harvard School of Public Health. Dr. Sesso specializes in the epidemiology and prevention of cardiovascular disease (CVD), focusing on the roles of hypertension, physical activity, obesity, and dietary factors such as antioxidant vitamins, lycopene, flavonoids, and alcohol, as well as the role of novel biomarkers that underlie these associations. He is also interested in the role of diet and lifestyle factors in the prevention of cancer. Dr. Sesso is Director of Nutrition Research and Co-Director of Hypertension Research at the Division of Preventive Medicine. Dr. Sesso is also interested in the design, methodology, and conduct of epidemiologic studies and randomized clinical trials. He leads the Physicians' Health Study II, a recently completed randomized trial that tested whether common supplemental doses of vitamin E, vitamin C, and a multivitamin have any effect on cardiovascular disease, cancer, and other chronic diseases in 14,641 men initially aged  $\geq$ 50 years. Dr. Sesso is also currently testing the effects of vitamin D and fish oil supplements on ambulatory blood pressure and the risk of developing hypertension in an ancillary study from the large-scale *VIT*amin D and OmegA-3 TriaL (VITAL) trial.

# Eric Rimm, ScD

Eric Rimm is an Associate Professor of Epidemiology and Nutrition at the Harvard School of Public Health and Harvard Medical School and is the Director of the Program in Cardiovascular Epidemiology. He has an active research program in the study of diet, lifestyle characteristics, and cardiovascular disease and has published more than 400 peer reviewed publications during his 18 years on the faculty at Harvard. He has previously served on the Institute of Medicine's Dietary Reference Intakes for macronutrients and recently served as one of 13 members on the scientific advisory committee for the 2010 U.S. Dietary Guidelines for Americans. This year he was awarded the 2012 American Society for Nutrition General Mills Institute of Health and Nutrition Innovation Award.

Dr. Rimm is an international speaker on diet and health and has given talks to academic groups, industry, and public health organizations across the globe. For the last decade he has spoken at the Culinary Institute of America's Worlds of Healthy flavors to industry groups and also at the Healthy Kitchens, Healthy Lives to medical health professionals

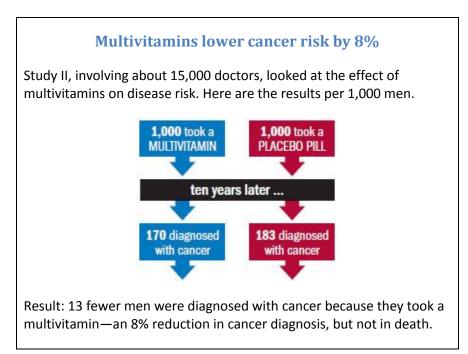
Dr. Rimm is an associate editor for the American Journal of Clinical Nutrition and the American Journal of Epidemiology.

# Do multivitamins protect you from disease?

Multivitamins may slightly reduce the risk of cancer but don't prevent heart disease. Keep the focus on diet, not supplements.

Up to half of all adults in the United States may already take a multivitamin. Most probably expect it to make them feel better and prevent common illnesses, even though the evidence has always been a little sketchy. Is the daily multivitamin habit truly healthful—or just wishful thinking?

The Harvard-led Physicians Health Study II (PHS II) recently found that taking a multivitamin slightly lowers the risk of being diagnosed with cancer. But if you take a multivitamin already or plan to, don't let it distract you from eating a varied and nutritious diet. "The studies of taking vitamins to prevent disease have been largely disappointing," says Dr. William Kormos, editor in chief of *Harvard Men's Health Watch and a primary care physician at Harvard-affiliated Massachusetts General Hospital*. "It does not appear that a multivitamin can replace a healthy diet high in fruits and vegetables."



# Putting multivitamins to the test

Many studies have looked at the effect of vitamin and mineral supplements on disease, but the evidence has never been convincing. So most experts have hedged on whether to recommend multivitamins for everyone.

The PHS II study involved nearly 15,000 physicians. Half were chosen at random to take a daily multivitamin; the others received a placebo pill containing no vitamins or minerals. The men took their pills for an average of just over 11 years. At the end of the study, researchers determined who developed cancer or heart disease and how many died from those diseases, which account for roughly half of all U.S. deaths annually.

The PHS II was the first study to test a standard multivitamin for the prevention of chronic disease. "All the other studies were done with a single supplement, or combinations of two or three, usually at higher levels than you could get from your diet," explains Dr. J. Michael Gaziano, a cardiologist at Harvard-affiliated Brigham and Women's Hospital and VA Boston Healthcare, and one of the leaders of the PHS II study.

The cardiovascular disease portion of the study focused on whether taking a multivitamin reduced the risk of heart attacks, strokes, and death from cardiovascular disease. There was no effect, weakening the case for taking a multivitamin "just in case" to prevent heart disease.

## **Cancer prevention**

However, PHS II did find that taking a supplement reduced the risk of being diagnosed with a new cancer by 8%. The trial found indications that the multivitamin might reduce death from cancer, too, but the effect was weak and could have been due to chance.

If you don't take a multivitamin now, should you do so based on the PHS II -findings? Dr. Gaziano thinks it's a reasonable choice. The cost of multivitamins is negligible for most people—less than a dime a day if you buy no-name brands in bulk at a large discount chain. And PHS II found no reason to believe that taking a multivitamin is dangerous. Moreover, "taking a multivitamin to prevent deficiency is not a bad idea," Dr. Gaziano says. "Many Americans don't get what they need."

As for cancer prevention, he argues, the supplement offers a new option to an aging population at high risk of developing cancer at some point in their lives. "Until now, the only things proven to prevent cancer were stopping smoking and never starting," Dr. Gaziano says. "Now we know that multivitamins provide a modest benefit."

# **Benefits for all?**

But it is difficult to know from the PHS II study what ultimate benefit a multivitamin would provide for the general population. Compared with most people, the doctors in the study ate better diets, were more physically active, and engaged in fewer unhealthy activities. Less than 4% were smokers, and 60% exercised at least once a week. In contrast, American men on average are overweight, don't exercise as much as they should, and take in too much fat and sodium. Would a multivitamin help them, too?

One could argue that if something helps healthy people a little, it should help less healthy people more. But it's also possible that the modest anti-cancer benefit of taking multivitamins wouldn't make much of a dent, compared with the effect of less healthy lifestyles in the general population. Don't expect to see a massive new clinical trial to answer that question anytime soon.

Dr. Gaziano takes the optimistic view: "If you consider even a modest reduction in risk for a disease as common as cancer in the population at large, it's not trivial numbers that you're talking about."

#### Vitamin and mineral supplements: Too much of a good thing can make you sick

When it comes to vitamins and minerals, some people subscribe to the notion that if a little is good, then more is better. But nutrients can be harmful when taken in amounts above what's considered beneficial.

Determining the right amount is tricky, however. Each nutrient has a range that starts with the minimum daily intake level necessary to meet the needs of most healthy people, called the Recommended Dietary Allowance (RDA). The top of the range is given as the tolerable upper intake level (UL) of the nutrient. The amount right for you must be based on your needs, so talk to your doctor before you start taking new vitamin and mineral supplements.

"Exceeding the RDA is not a medical problem essentially until the UL is reached, and then it can become harmful," explains Dr. Bruce Bistrian, chief of clinical nutrition at Beth Israel Deaconess Medical Center and professor of medicine at Harvard Medical School.

# A multivitamin for you?

Still, it's important not to overplay the benefit that PHS II found for preventing cancer. "The effect in this study is relatively small," Dr. Kormos says. Rather than relying on supplements, it's a better to obtain nutrients from food, which contains a variety of healthful ingredients.

Fruits and vegetables contain many biologically active ingredients that may help to prevent cancer in ways that vitamins and minerals alone do not. "A healthy diet still seems superior to taking a multivitamin, and if you already eat a healthy diet, there may be less overall benefit from taking the extra vitamins," Dr. Kormos says. You'll hear similar advice from the American Cancer Society and the American Heart Association.

In considering the pros and cons of multivitamins, stop for a moment and ask what you expect to gain and why you think you need a supplement to begin with. "If people ask me if they should take a multivitamin, I usually ask, Why do you think you need one?" Dr. Kormos says. "They say, well, I don't eat this, I don't eat that. But a multivitamin is not going to replace the things missing from your diet. Whatever money you are spending on your multivitamin, it's probably better to spend it at the farmer's market or the grocery store on healthy foods."

#### To learn more...

This information is prepared by the editors of the Harvard Health Publications division of Harvard Medical School. It originally appeared in the February 2012 issue of the *Harvard Men's Health Watch* available from <a href="http://health.harvard.edu/mens">http://health.harvard.edu/mens</a>.

# 12 Tips for healthier eating

#### It's not about individual nutrients anymore.

For much of the 20th century, nutrition research focused largely on the health risks and benefits of single nutrients. The findings translated into public health messages telling us to reduce fat; limit cholesterol; increase fiber; get more calcium; take vitamins E, C, and D; and so on. But as scientists learn more, they're finding that the health effects of food likely derive from the synergistic interactions of nutrients and other compounds within and among the foods we eat. This has led to a shift from nutrient-based recommendations toward guidelines based on foods and eating patterns.

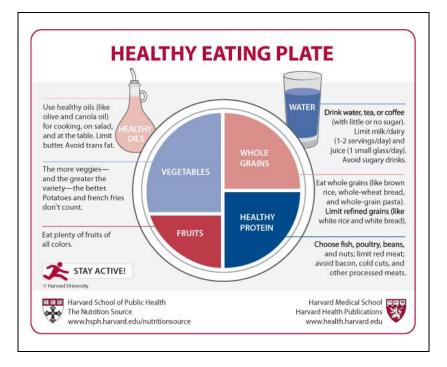
There's no single healthy diet. Many eating patterns sustain good health. What they have in common is lots of fruits, vegetables, and whole grains, along with healthy sources of protein and fats. Consistently eating foods like these will help lower your risk for conditions such as heart disease, stroke, diabetes, and certain forms of cancer. If you'd like to make this largely plant-based approach to eating one of your good-health goals for 2012, here's how to get started.

**1.** Build a better plate. In the fall of 2011, nutrition experts at the Harvard School of Public Health and colleagues at Harvard Health Publications unveiled the Healthy Eating Plate (see below), a visual guide to healthful eating that improves on the government's "MyPlate."

Both guides are meant to simplify the task of planning healthy meals. The Healthy Eating Plate is made up of one-half vegetables and fruits, one-quarter whole grains, and one-quarter healthy protein. "Whole" and "healthy" are important words here. Refined grains (think white breads, pastas, and rice) have less fiber and fewer nutrients than whole grains, such as whole-wheat bread and brown rice (see No. 4). Healthy proteins include fish, poultry, beans, and nuts — but not red meats or processed meats. Many studies have shown that red meats and especially processed meats are linked with colorectal cancer — and that you can lower your risk for heart disease by replacing either type of meat with healthier protein sources. So eat red meats sparingly (selecting the leanest cuts), and avoid processed meats altogether. *Hint:* To learn more about the Healthy Eating Plate, go to www.health.harvard.edu/plate.

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**2.** *Pile on the vegetables and fruit.* Vegetables and fruits are high in fiber and contain many vitamins and minerals as well as hundreds of beneficial plant chemicals (phytochemicals) that you can't get in supplements (see No. 8). Diets rich in vegetables and fruit can benefit the heart by lowering blood pressure, cholesterol levels, and inflammation and improving insulin resistance and blood vessel function. In long-term observational studies, people who eat more fruits and vegetables have a lower risk of heart disease, diabetes, and weight gain, and those who eat more fruit also have a lower risk of stroke. Hint: Fresh fruits and vegetables are great, but don't avoid the frozen kind (or dried fruit or canned fruits and vegetables minus the heavy syrup or salt) when they're more convenient.

**3.** Go for the good fats. At one time, we were told to eat less fat, but now we know that it's mainly the type of fat that counts. The most beneficial sources are plants and fish. You can help lower "bad" LDL cholesterol by eating mostly polyunsaturated fats (including vegetable oils and omega-3 fatty acids, found in fish, seeds and nuts, and canola oil) and monounsaturated fats (in avocados and many plant-based oils, such as olive oil and canola oil). Saturated fats (found mostly in dairy and meat products) and trans fats (hydrogenated fat found in many fried and baked goods) boost LDL cholesterol and triglycerides, increasing your risk of heart disease. Worse still, trans fats reduce your "good" HDL cholesterol. *Hint:* As long as you replace bad fats with good ones, you can get up to 35% of your calories from fat.

**4. Replace refined grains and potatoes with whole grains.** Whole grains retain the bran and germ of the natural grain, providing healthful fiber, vitamins and minerals, antioxidants, and phytochemicals. Many of these substances are removed from refined grains, such as white bread and white rice, and are barely present in starches such as potatoes. Starches and refined carbohydrates are digested quickly, causing surges in insulin and blood sugar, boosting triglycerides, and lowering HDL cholesterol. These changes increase the risk of heart disease and diabetes. The rapid rise and fall of blood sugar and insulin can also make you

hungry, raising the risk of weight gain. Potatoes aren't all bad; they're a good source of vitamin C, potassium, and fiber. But eat them only occasionally, in small amounts, and with the skins on (that's where the fiber is). *Hint:* Be adventurous. In addition to whole wheat and brown rice, try quinoa, millet, farro, and amaranth. Some of these whole grains can be cooked like hot cereal or rice, and some are ground into flour for baking.

#### "Carb-check" your breads and cereals

Some carbohydrates are good for health and others aren't. The worst carbohydrate sources use highly refined grains and sugars. The best have whole or minimally processed grains. One way to identify a good carb source is to divide the number of grams of carbohydrate per serving by the number of grams of fiber. Aim for less than 10 for breads and under five for cereals.

**5.** Eliminate liquid sugars. Sugar-sweetened beverages — non-diet sodas, sugary fruit drinks, iced teas with added sugar, and sports drinks — provide calories and little else. There's good evidence that these drinks can raise the threshold for satiety (feeling full), thereby increasing the amount you eat and promoting weight gain. A 2011 Harvard study found that sugar-sweetened beverages were one of the dietary components most strongly linked to long-term weight gain among healthy women and men. What about 100% fruit juice with no added sugar? Even all-natural fruit juice has a lot of calories. The Healthy Eating Plate guidelines suggest you drink no more than one small glass a day (say, 4 to 6 ounces). Hint: Add carbonated water to your "one small glass" for full-glass satisfaction.

**6. Drink enough water.** Many foods contain water, so you may get enough every day without making a special effort. But it can be helpful to drink water (or another no-calorie liquid, such as black tea, coffee, or carbonated water) with meals or as an alternative to snacking. A reasonable goal is 4 to 6 cups of water a day. *Hint:* As you add whole grains to your diet, water helps move the fiber smoothly through your digestive tract, reducing the chances of constipation.

**7.** Learn to like less sodium. The body needs sodium for proper muscle and nerve function and fluid balance, but excessive amounts can increase blood pressure and the risk of heart disease and stroke. The dangers of a salty diet (salt is 40% sodium) are greatest in people over age 50, African Americans, and women. You'll do yourself a favor if you wean your taste buds from a yen for salt. Limit your daily sodium intake to 2,300 milligrams (mg) — the amount in one teaspoonful of salt. If you have high blood pressure or are at risk for it, get no more than 1,500 mg per day. *Hint:* Most of the sodium Americans consume comes from processed and restaurant foods. Instead, choose fresh, unprocessed foods, and prepare them yourself. Read the nutrition content on labels and make sure that the per-serving sodium content is less than the calories per serving.

**8.** Rethink supplements. It's best to get your vitamins and minerals from food rather than supplements, but this can be hard, especially if you're cutting calories or your energy needs are low. We showed how to meet almost all your nutrient needs through food alone, even if you're consuming 1,500 calories or less per day (see <a href="http://www.health.harvard.edu/vits">www.health.harvard.edu/vits</a>). The key is choosing nutrient-dense foods, such as leafy greens, low-fat yogurt, dried beans, whole grains, and salmon. The only problem is vitamin D. Here a supplement is probably a good idea, because it's difficult to get the recommended daily intake (600 to 800 IU) through foods. Hint:

You can get enough calcium on a 1,500-calorie-a-day diet by eating low-fat dairy products and nondairy foods such as canned salmon, tofu, sesame seeds, dark leafy greens like collards and kale, and legumes such as pinto and kidney beans.

**9.** Dine mindfully. Taking time to savor your food not only makes eating more enjoyable, it can also help control your appetite. Your sense of fullness and satisfaction depends on hormonal signals from your digestive tract. If you eat too quickly, your brain may not receive the signals that say you're full. Try putting down your fork between bites and chewing more slowly. Tune in to your food's aroma, taste, and texture, and stop eating when you feel full. Some small studies suggest that this approach may help some people make healthier food choices. *Hint:* To start, try taking one mindful bite at the beginning of each meal — a sort of eating speed bump.

**10.** *Keep alcohol under control.* Many studies link moderate alcohol consumption (for women, no more than one drink per day) to heart benefits, including a reduced risk of heart attack, increases in "good" HDL cholesterol, and reduced risk for type 2 diabetes, gallstones, and dementia. One drink per day also slightly increases your risk for breast cancer, and the risk increases steadily the more alcohol you consume. There are plenty of other ways to get heart benefits, so if you don't like alcohol, don't have it. But if you enjoy an occasional cocktail or a glass of wine with dinner, you need to weigh the risks and benefits in light of your own situation. *Hint:* If you find that one drink often turns into two or more, consider quitting or getting help to cut back. For help, go to <a href="http://rethinkingdrinking.niaaa.nih.gov">http://rethinkingdrinking.niaaa.nih.gov</a>.)

**11.** Eat breakfast. It's easy to skip breakfast when you're in a rush, aren't hungry, or want to cut calories. But a healthy morning meal makes for smaller rises in blood sugar and insulin throughout the day, which can lower your risk of overeating and impulse snacking. (Eating breakfast every day is one characteristic common to participants in the National Weight Control Registry, who've lost at least 30 pounds and kept the weight off longer than a year.) *Hint:* A healthy, balanced breakfast is moderate in size and includes healthy protein, whole-grain carbohydrates, and fruit — for example, an egg, whole-wheat toast, and strawberries. If you like cereal, have whole-grain cereal with fruit and low-fat yogurt or milk.

**12.** *Plan for a snack attack.* Snacking isn't an essential part of a healthy eating plan, but try telling that to a rumbling stomach at midafternoon. A healthy snack can boost energy levels by stabilizing blood sugar while giving you an added dose of healthful nutrients. But unplanned, impulsive snacking often takes the form of cookies, chips, or candy bars. So prepare healthy snacks ahead of time, and keep them handy at home or in your office. Limit calories to about 100 to 150 per snack. Good choices include a small bunch of grapes, a banana, or other fruit; a handful of unsalted nuts or sunflower seeds; and plain nonfat yogurt with a few raspberries or strawberries tossed in. *Hint:* Before giving in to a snack attack, drink an 8-ounce glass of water and wait 10 to 15 minutes to see if you're still hungry.

#### To learn more...

This information is prepared by the editors of the Harvard Health Publications division of Harvard Medical School. It originally appeared in the January 2012 issue of the *Harvard Women's Health Watch* available from <a href="http://www.health.harvard.edu/newsletters/womens">http://www.health.harvard.edu/newsletters/womens</a>.

# Vitamin D and calcium supplements: take them or leave them

#### How to follow the changing recommendations without making yourself dizzy.

First we were advised to take calcium and vitamin D supplements to strengthen our bones and protect against fractures. Then in June, the U.S. Preventive Services Task Force recommended against low-dose calcium and vitamin D supplements, citing little evidence that they actually prevent fractures and noting that they can increase the risk of kidney stones.

A European study added another dose of bad news, linking calcium supplements with a greater risk for heart attacks. Then the tides shifted again, when another analysis suggested calcium and vitamin D supplements might help older adults live longer.

So which is it? Do calcium and vitamin D supplements help-or hurt?

#### Why you need calcium

There's no question that your body needs calcium. It's involved in everything from nerve signal transmission to blood vessel health. Calcium builds and strengthens bones—a function that's especially critical after menopause, when bones become more fragile and prone to fractures. Vitamin D helps the body absorb calcium, which is why the two nutrients are often paired up in supplements.

According to the Institute of Medicine (IOM), women over age 50 need 1,200 milligrams (mg) of calcium a day, and 600 to 800 international units (IU) of vitamin D a day. The issue isn't whether you need calcium—it's how you should get it. And most, if not all, of your calcium should come from your kitchen—not your medicine chest.

"I think calcium and vitamin D are important for bone health, but I recommend that patients get calcium from their diet," explains Dr. Meryl LeBoff, director of the Skeletal Health and Osteoporosis Center and Bone Density Unit at Brigham and Women's Hospital and professor of medicine at Harvard Medical School.

If you're not getting enough calcium from diet alone, add a supplement—but only take as much in pill form as you need.

"I tell patients to estimate the amount of calcium they are getting from their diet and then supplement it. I don't want them to take excess calcium," says Dr. David Slovik, associate professor of medicine at Harvard Medical School, chief of the Endocrine and Diabetes Unit at Newton-Wellesley Hospital, and endocrinologist at Massachusetts General Hospital.

#### Getting enough nutrients

Good food sources of calcium include

- low-fat yogurt, 8 ounces (415 mg)
- calcium-fortified orange juice, 6 ounces (375 mg)
- sardines, canned in oil, with bones, 3 ounces (325 mg)
- cheddar cheese, 1.5 ounces (307 mg)
- nonfat milk, 8 ounces (299 mg)
- canned salmon with bones, 3 ounces (181 mg)
- tofu, soft, made with calcium sulfate, 1/2 cup (138 mg)
- fresh cooked kale, 1 cup (94 mg).

Vitamin D is activated in sun-exposed skin, but that source can be hard to come by in the winter months, especially if you live in a northern climate. Too much unprotected sun exposure also increases your risk for skin cancers.

Good food sources of vitamin D include

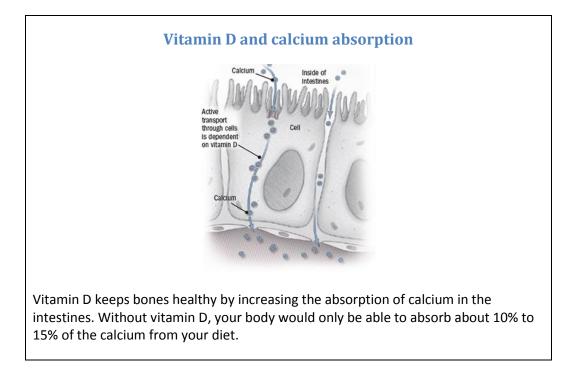
- cod liver oil, 1 tablespoon (1,360 IU)
- swordfish, cooked, 3 ounces (566 IU)
- salmon, cooked, 3 ounces (447 IU)
- tuna fish, 3 ounces (154 IU)
- vitamin D-fortified orange juice, 1 cup (137 IU)
- vitamin D-fortified milk, 1 cup (115-124 IU)
- vitamin D-fortified yogurt, 6 ounces (80 IU).

Get more calcium and vitamin D from your diet, but don't drop your supplement solely based on the latest news story. Your bones could suffer for it. The decision to take supplements should be individualized based on your diet, and your unique risks. "Review the specific recommendations with your doctor, because these are important health decisions," Dr. LeBoff advises.

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#### To learn more...

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# A primer on vitamin value abbreviations

Most people have heard of Recommended Dietary Allowances, the nutrition labeling guidelines established and used by the Food and Nutrition Board of the National Academy of Sciences for 70 years. But how do they differ from DRIs and DVs? And what are ULs and AIs? Reading nutrition labels and recommendations today involves interpreting an alphabet soup of abbreviations. Here's some help.

**Recommended Dietary Allowance (RDA):** This value refers to the average minimum amount of a specific nutrient needed to prevent clinical nutrient deficiency in almost all healthy people in a particular life stage and gender group. Because RDAs only apply to a selected set of nutrients and nutrient deficiency diseases, today RDAs are a subset of the broader dietary reference intake values (see below).

**Dietary reference intake (DRI):** Introduced in 1997, DRI values were created to allow guidelines for a broader range of nutrients and minerals, not to only prevent nutrient deficiencies, but also to enhance health and reduce the risk of chronic diseases such as osteoporosis, cancer, and cardiovascular diseases. DRIs include RDAs, AIs, ULs, and EARs. DRIs are what drive the U.S. Dietary Guidelines and food labeling regulations.

Adequate intake (AI): This value is determined as a range of recommended intake (rather than just a minimum), and is used for nutrients for which there is not a specific clinical deficiency disease, such as the recommended amounts of vitamin K, manganese, or potassium.

**Tolerable upper intake level (UL):** This is the recommended maximum amount of a nutrient that is considered safe to consume for an extended period by the population, including sensitive subgroups. Exceeding the UL does not mean that harmful effects will always occur; rather, the more a person exceeds the UL, the greater the potential risk of adverse effects.

**Estimated average requirement (EAR):** This is the amount of a nutrient that is estimated to meet the requirement of half of all healthy people in a particular life stage and gender group to prevent clinical nutrient deficiency. EARs are used as the basis for the RDA, and as such, apply to a relatively limited set of nutrients and their corresponding nutrient deficiency disease.

**Daily Value (DV):** This reference number, developed by the FDA, is designed to help consumers determine if a food contains a lot or a little of a specific nutrient, based on the DRI for that nutrient. DVs don't take your age, sex, or various other factors into account. They're based on the highest average daily allowance value and are presented as percentages of total daily intake, calculated for a person eating 2,000 calories a day.

#### To learn more...

This information is prepared by the editors of the Harvard Health Publications division of Harvard Medical School, and excerpted from the special report, *The Truth about Vitamins and Minerals: Choosing the nutrients you need to stay healthy.* You can learn more about this publication at www.health.harvard.edu/VM.

# Should you take supplements?

Many people who take supplements subscribe to the idea that "more is better" without carefully considering the arguments for or against their choices. At best, they may be wasting their money. At worst, they may be endangering their health.

In the 1980s, many nutritionists and some physicians began to recommend (and take) vitamin supplements. However, as described in "Cast of Characters: Vitamin A to zinc", the evidence for the health benefits of most supplements is not strong. Notable exceptions are fish oil for cardiovascular disease and vitamin D for bone health. Although foods that contain vitamin A and beta carotene, as well as vitamins B, C, and E, are clearly good for health, taking supplements of these vitamins has no proven health benefits.

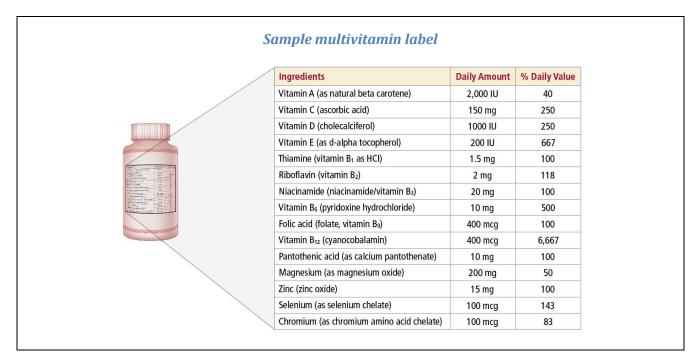
What about a simple multivitamin? These pills (which usually also contain multiple minerals) are the most popular among all dietary supplements—50% of Americans take them on a regular basis, shelling out more than \$20 billion annually on these products. On an individual basis, a daily multivitamin won't set you back that much: a year's supply of many popular brands costs about \$30.

However, despite widespread belief that multivitamins will prevent chronic diseases such as cancer and heart disease, there's no evidence to support such claims. The National Institutes of Health convened a meeting on multivitamin and mineral supplements in May 2006. The "state of the science" statement it issued was extremely cautious: present evidence is "insufficient to recommend either for or against the use of multivitamin/multi-mineral supplements by the American public to prevent chronic disease." The experts noted that the heaviest users of vitamin and mineral supplements are Americans who probably need them the least: people who are well educated, have higher incomes, exercise, and already have healthy diets. A 2008 study in Archives of Internal Medicine that tracked nearly 162,000 participants in the Women's Health Initiative found that multivitamins have no effect whatsoever in 10 health-related categories, including cancer, heart attack, and stroke. Supplement takers didn't live any longer, either.

Still, old habits die hard, and many nutrition experts still recommend taking a multivitamin daily as a form of nutritional insurance. Multivitamins are already part of some official recommendations. The federal government's 2005 Dietary Guidelines for Americans suggests that people older than 50 take them as a way to ensure adequate vitamin B12 intake. And the Centers for Disease Control and Prevention advises all women of childbearing age to take folic acid—and a multivitamin is also a good way to do that—because doing so lowers the risk of birth defects. That leaves men ages 50 and under as the only adult group not covered by this advice.

When choosing a multivitamin, look for an inexpensive preparation that contains 100% of the DV for vitamin D, vitamin B6, vitamin B12, and folic acid. Extra vitamin D is harmless—as noted earlier, many experts recommend 1,000 IU, which is roughly twice the DV. But extra amounts of other vitamins may do more harm than good. That's particularly true of vitamin A, since studies show that doses above 3,000 IU a day, which were previously considered safe, can increase the risk of hip fractures.

Don't waste your money on high potency, all-natural, or designer vitamins. Above all, remember that your daily multivitamin is just an insurance policy—a supplement, not a substitute, for a healthful diet.



# Potential pitfalls

Shopping for any kind of supplement can be confusing. A staggering array of multivitamins and other supplements crowd the shelves of pharmacies, grocery stores, and specialty stores, and many more are now available over the Internet. Before you buy, it's wise to realize that some of these products may offer much more—or possibly less—than you really need to enhance your health.

Dietary supplements may legally contain vitamins, minerals, herbs, amino acids, enzymes, organ tissues, and a few other substances—in short, practically any ingredient promoted as a way to bolster your diet and, presumably, your health. The FDA does not certify supplements for safety or effectiveness the way it monitors drugs. Under the Dietary Supplement Health and Education Act of 1994, the FDA cannot approve supplements or demand that manufacturers undertake rigorous studies to prove their worth. The FDA doesn't set potency or dosage standards, either. Manufacturers are left to police themselves. And before a worrisome supplement can be pulled off the market, the FDA has to prove that it creates a significant health risk.

This can be a problem, as is made clear by a January 2009 ConsumerLab report. The consumer watchdog organization tested the quality and contents of 29 of the leading multivitamin and multi-mineral products for adults and children sold in the United States and Canada. Eight products did not meet claims stated on their labels or had other quality issues, while another 12 provided levels that may be too high for healthy people. For example, one men's multivitamin supplement contained just over 2,000 mcg of folic acid, which is twice the safe upper limit for that vitamin.

While supplement manufacturers can't legally claim to prevent, treat, or cure specific diseases, they can come pretty close. They are allowed to make "structure-function" claims that sound impressive to most consumers. A product may "build strong teeth" or "improve memory" or "boost the immune system." Manufacturers can make these assertions without supplying a stitch of proof to any agency. Your cue for healthy skepticism should be the words printed alongside: "This statement has not been evaluated by the Food and Drug Administration."

Certain health claims backed by substantial scientific agreement and not limited to particular brands can appear on supplement bottles. For example, supplement manufacturers can advertise that "Calcium helps protect against osteoporosis" and "Folic acid may prevent neural tube defects in fetuses," because these statements are borne out by science and have been carefully evaluated.

## More isn't always better

Many people who take supplements subscribe to the idea that "more is better" without carefully considering the arguments for or against their choices. They may take a handful of other supplements along with their multivitamin. At best, they may be wasting their money. At worst, they may be endangering their health.

Take vitamins C and A, for example. Once your blood level of vitamin C reaches the saturation point—which occurs if you take about 200 mg per day—your body usually excretes the excess. That's why vitamin C toxicity rarely occurs. However, people who consistently take too much vitamin A won't be as fortunate. Because fat-soluble vitamins remain in the body, they can more easily build to toxic levels. A pregnant woman who takes too much vitamin A risks birth defects to her fetus. Excess vitamin A also compromises bone health and blood clotting, and it can overstimulate your immune system.

Many consumers are spurred to take excessive doses by overenthusiastic news stories on the potential benefits of certain vitamins and minerals. Remember, though, that the good news from the latest study may eventually prove true, or it may be refuted by other studies. Often, promising test-tube and animal studies don't pan out in people. And certain types of human studies offer more definitive information than others. Sometimes, exciting results from initial observational studies aren't confirmed by randomized controlled trials, which are considered the gold standard of research. And even these studies often have their limitations.

It's generally safest to wait for evidence to accumulate before jumping on the supplement bandwagon. Consider the potential risks, possible benefits, and costs.

### Specialized supplements for women, men, and older adults

What about supplements aimed at women, men, and seniors? While some of these supplements may be helpful in certain cases, others are merely marketing gimmicks designed to enhance profits rather than your health. Products vary widely; read the labels to make sure you get what you need while staying within safe limits.

Although a June 2002 report in The Journal of the American Medical Association concluded that there is limited evidence for tailored supplements, a mild argument can be made in favor of some products designed for women and men.

#### Formulas for women

If you're a woman, which vitamins and minerals are most helpful to you? That depends partly on your age and on childbearing concerns.

All women. Osteoporosis affects more women than men: about 80% of the 10 million Americans with osteoporosis are women. That's why it's especially important for women to get enough bone-building calcium and vitamin D. Some multivitamins supply relatively little calcium—typically only 40 mg to 160 mg, which is far below the daily requirement of 1,000 mg to 1,200 mg. And depending on your age, standard multivitamins may or may not meet your vitamin D needs, which increase as you get older. Vitamin and mineral supplements formulated for women usually supply more, although not all, of your daily calcium requirements and may have additional vitamin D, too. Although dietary sources of calcium and vitamin D are best, supplements can help make up the difference. You need 1,000 mg of calcium daily if you're between 19 and 50 years old, and 1,200 mg of calcium after that. As for vitamin D, some experts advise getting 1,000 IU from supplements.

**Women of childbearing age.** Folic acid supplements are necessary if there is a chance you could become pregnant, and iron is important for you if you are still menstruating. It's essential that you get enough folic acid to prevent birth defects called neural tube defects, which develop in the earliest days and weeks of pregnancy. Because not every pregnancy is planned, most experts suggest that all women capable of becoming pregnant take a daily multivitamin that has at least 400 mcg of folic acid. (Your doctor may suggest taking more than that amount if you plan to get pregnant and have previously had a child with a neural tube defect.)

To replace iron lost during monthly periods, you need a multivitamin or women's supplement with iron. Iron deficiency saps your energy, eventually leaving you weak and tired. In the United States, one in 10 women and girls who menstruate is deficient in iron. The recommended daily amount of iron for adult women ages 19 to 50 is 18 mg.

**Pregnant women.** If you're pregnant, you need larger amounts of certain vitamins and minerals, particularly iron and folic acid. Prenatal vitamins, which can be purchased by prescription or over the counter, meet these needs. It is important not to take other supplements unless specifically advised by a qualified health care provider. The earliest weeks of pregnancy are crucial in the fetus' development, so the sooner in pregnancy you start taking a prenatal vitamin, the better.

If you plan to get pregnant or learn that you are, talk with your doctor right away to find out which prenatal supplement would be best for you to take. During pregnancy, your iron requirement increases to 27 mg and your folic acid requirement to 600 mcg. The calcium RDA remains at 1,000 mg for women ages 19 and over, although some clinicians suggest adding calcium during pregnancy for extra insurance.

Guidelines from the World Health Organization also recommend that pregnant and nursing women consume an average of 300 mg per day or more of DHA either by eating fish or taking fish oil supplements.

Women who have reached menopause or have had a hysterectomy. In these cases, unless your doctor advises otherwise, you can switch to a supplement that reduces or eliminates iron. Diet alone should supply enough iron and prevent a possible iron overload. Iron overload can damage the liver and other body tissues, making diabetes, heart disease, arthritis, and liver cancer more likely. Supplements designed for older women typically have little or no iron and more calcium and vitamin D. After menopause or hysterectomy, you need only 8 mg of iron daily.

#### Multivitamins for men

Many experts shy away from any iron supplementation for men. That's because men—like women who no longer menstruate—aren't typically losing much iron. For that reason, supplements aimed specifically at men generally reduce iron or drop it from the formula. This can help prevent iron overload, which can stem from taking more iron than necessary through supplements. Iron overload may also occur because of a common genetic defect that occurs more often in men than women. Iron overload can damage the liver and other body tissues, raising the risks for diabetes, heart disease, arthritis, and liver cancer.

Men's multivitamin and mineral formulations typically add or increase selenium and lycopene, too, which may protect against prostate cancer and other types of cancer. Some drop calcium entirely. Formulas with low or no calcium are fine for men, as long as they get adequate amounts of calcium in their diets to prevent osteoporosis. Exercise, coupled with vitamin D and vitamin K, is more important for bone health in men.

#### Products for older adults

Products aimed at older people tend to boost the amounts of certain B vitamins, partly because many elderly men and women have trouble absorbing vitamin B12. These products also tend to add antioxidants and, often, vitamin D and selenium.

There is little evidence to support the value of antioxidant supplements. Some experts recommend getting at least 2,000 IU of vitamin D daily after age 70. As you age, your skin loses some of its ability to produce vitamin D from sunlight, and many older people do not spend much time in the sun. As for selenium, evidence suggests no benefit to this mineral. Until more information is available—or unless your doctor gives you other advice—a daily multivitamin should offer enough B vitamins. However, if you are over 70 and get little sun exposure, you may need to add a separate vitamin D supplement.

# Do your homework

Tailored formulas often add herbal boosters that are reputed to benefit certain populations—for example, soy for women and saw palmetto for men. Research suggests that saw palmetto can reduce benign enlargement of the prostate gland, called benign prostatic hyperplasia. While the estrogen boost of soy products may be helpful to some women, particularly those with symptoms of menopause, it may actually be harmful to other women. And evidence in favor of using many of the other substances—such as green tea or ginseng—is slim or controversial.

#### To learn more...

This information is prepared by the editors of the Harvard Health Publications division of Harvard Medical School, and excerpted from the special report, *The Truth about Vitamins and Minerals: Choosing the nutrients you need to stay healthy*. You can learn more about this publication at <a href="https://www.health.harvard.edu/VM">www.health.harvard.edu/VM</a>.

# HarvardMedicine

The following articles are selections from *Harvard Medicine* magazine's winter 2012 edition: Appetite for Life. Additional content can be found online, please visit: <u>http://harvardmedicine.hms.harvard.edu/</u>

Plate Shifts When choosing what to eat, it's best to go green by Jessica Cerretani



Kate feels like she's tried everything: Weight Watchers, Jenny Craig, grueling workouts at the gym. Yet she could swear those extra 50 pounds remain, stubbornly stuck to her hips. When she confesses her exasperation during her annual physical, her physician makes an intriguing suggestion: Allow him to take a blood sample.

Although she's pretty sure that obesity is obvious without a test, she goes along with her doctor's request.

Healthy foods vending machine

The results are stunning. Kate's blood reveals a genetic sensitivity to carbohydrates, explaining in part why she doesn't respond well to low-fat diets, which tend to be abundant in such refined carbs as pasta and rice. With this knowledge, her physician tailors a diet to work with her individual biochemistry, greatly increasing the odds that she'll shed those pounds—and keep them off.

Mom always told us to eat our broccoli, and her advice has been backed up by the U.S. Department of Agriculture's recommendations to fill our plates with five to nine daily servings of produce.

"There's a lot of excitement in research circles about the concept of dietary phenotypes, or the way our genes interact with food," says David Ludwig, an HMS professor of pediatrics and director of the New Balance Foundation Obesity Prevention Center at Children's Hospital Boston. In a study published in 2007 in the *Journal of the American Medical Association* and reported heavily in the media, Ludwig and his colleagues tested insulin response in a group of 73 obese young adults before giving them either a high-carb, low-fat meal or a low-glycemic meal rich in non-starchy vegetables and legumes. Glycemic measures, often expressed along an index as low, medium, and high, refer to how quickly foods break down and release glucose during digestion. The researchers found that people who tended to secrete high levels of insulin after ingesting glucose, compared with levels secreted by their peers, were more likely to lose weight when they followed a low-glycemic diet than when they adhered to a low-fat diet, probably because they were more sensitive to refined carbohydrates.

These results, says Ludwig, could explain individual differences in the ability to lose weight. "When it comes to food," he adds, "one size doesn't necessarily fit all." Eventually, this knowledge could help physicians learn which patients will respond best to which types of diets all determined by a simple blood test measuring insulin secretion.

# Food for Thought

Patients like our fictional Kate aren't alone in their struggles with the scale. Recent findings by researchers at the Harvard School of Public Health and elsewhere suggest that billions of people are fighting—and losing—the battle of the bulge. Worldwide, an estimated 1 in 3 adults is overweight and 1 in 9 is obese, according to a study published in February 2011 in *The Lancet.* The number of obese people now tops half a billion—a doubling of prevalence in less than three decades. And extra pounds don't just present a threat to our self-esteem. The World Health Organization estimates that obesity-related illnesses, including cardiovascular disease and stroke, type 2 diabetes, and cancers of the breast, endometrium, gallbladder, kidney, colon, and esophagus, claim some 3 million lives each year. Statistics like these are helping to spur investigations into the potential causes of obesity and related diseases—starting with what we put on our plates.



Photo courtesy of Cooking Light" Research in the 1950s and '60s first suggested a connection between food and the development of chronic conditions such as heart disease," says Walter Willett, an HMS professor of medicine and chair of the Harvard School of Public Health's Department of Nutrition. "Today, we're continuing to discover that many illnesses may be linked to modifiable risk factors like diet."

SECRETS OF THE PYRAMID: Using data from large epidemiological studies, Walter Willett teases out the links between diet and disease.

The key to establishing clear and accurate dietary advice may lie in the type of studies investigators conduct. Willett has been a driving force behind some of the largest epidemiological studies on nutrition, including the Nurses' Health Study, the Nurses' Health Study II, and the Health Professionals Follow-

up Study. These three studies have identified strong relationships between nutrition and disease, including links between the consumption of red meat and an increased risk of colorectal cancer; consumption of alcohol and an increased risk of breast cancer; and consumption of partially hydrogenated fats (also known as trans fats) and an increased risk of cardiovascular disease—data that have helped form much of our current dietary advice and guidelines.

Systematic reviews, in which investigators analyze studies to tease out and compare the similarities and differences in their results, and meta-analyses can provide even more insight into food and disease risk. "One study is never enough to make or break a key finding," says Eric Ding, an HMS instructor in medicine at Brigham and Women's Hospital. Ding also is affiliated with the Department of Nutrition at the Harvard School of Public Health. "Research has to be replicated time and again to show a solid relationship between nutrition and health."

"Different studies may look at the effects of nutrition in varied populations with a range of backgrounds and risk factors," explains Ding. "Systematic reviews can help account for variations in findings among studies." Such reviews can also aid investigators in pinpointing specific relationships between food and disease so that umbrella statements about benefit and risk gain precision.

# Lean Cuisine

Nutrition research can also overturn misconceptions about diet and health. "There are a lot of strong beliefs in the area of nutrition—it's not unlike religion," says Willett. "The trouble is that the strength of these beliefs often seems to be inversely related to the strength of the data." He points to long-held convictions that eggs are major culprits in cardiovascular disease and that margarine is a healthy alternative to butter. We now know that egg consumption has no real association with heart attacks and that the trans fats found in processed foods, and earlier formulations of margarine, are far worse for cardiovascular health than the saturated fat in butter. Yet this sea change in dietary guidance came only after several decades of research by Willett and scientists at other institutions.

Today, as studies continue to shed light on the most promising foods for good health, one significant theme has emerged: While caloric intake still governs weight gain and loss, what we eat may matter just as much as how much we eat. Ludwig and his colleagues share some responsibility for this shift in thinking. In 1999, curious to better determine how dietary composition affected body-weight regulation, Ludwig's research team gave 12 obese teenage boys a meal that ranked low, medium, or high on the glycemic index. Each of the meals had the same number of calories, only the foods varied. The meal that registered high on the glycemic-index scale consisted of instant oatmeal, a refined carbohydrate; the medium-indexed meal featured steel-cut oatmeal, a more complex carbohydrate, and the meal low on the glycemic-index scale included an omelet, rich in protein and fat.



Photo by Justin Sullivan/Getty

The result: blood sugar spiked after instant oatmeal, only to crash a few hours later, leaving the

boys much hungrier—and leading them to consume about 700 more calories—than their peers who dined on steel-cut oatmeal or an omelet. "The findings suggested that meals with a high glycemic index provoke hormonal and metabolic changes that trigger overeating," says Ludwig. "We've spent the past 12 years or so refining our research of this concept."

Studies by Eleftheria Maratos-Flier, an HMS professor of medicine at Beth Israel Deaconess Medical Center, suggest that diet composition has an impact on weight gain and weight loss. Diets high in carbohydrates and fats can pack on the pounds, while those low in sugar and in total carbohydrate may help spur weight loss. In a study published in the June 2007 issue of the *American Journal of Physiology, Endocrinology, and Metabolism*, Maratos-Flier and colleagues fed mice one of four diets: high-sugar, high-fat; restricted calorie; very-low-carbohydrate, high-fat; or regular chow. While the mice on the high-sugar, high-fat diet became obese, those on the very-low-carbohydrate, high-fat diet lost as much weight as those whose calories were restricted—even though they consumed as many calories as the mice fed the high-sugar, high-fat diet.

Looking more closely, her team identified biochemical processes behind such findings. They found that the very-low-carbohydrate, high-fat diet appeared to stimulate the production of fibroblast growth factor 21, a liver-derived protein that triggers the body to burn fat. Although the effect of low-carbohydrate diets on FGF21 in humans is less clear, Maratos-Flier remains optimistic—and believes such an eating plan may be the key to weight loss for some people. "A successful diet is a successful diet," she says. "If someone is having trouble losing weight, it's worth a shot to restrict carbohydrates."



SCALABLE OPTIONS: Eleftheria Maratos-Flier (left), David Ludwig, and C. Ronald Kahn all investigate how macro- and micronutrients affect waistlines and well-being. Photos: John Soares (Maratos-Flier and Ludwig); Courtesy of Joslin Diabetes Center (Kahn) Photos by John Soares (Maratos-Flier and Ludwig); Photo courtesy of Joslin Diabetes Center (Kahn)

# Fare Trade

Before you switch your cereal for steak, though, consider this: "The quality of macronutrients that we eat is tremendously important for good health," says Willett. Take fat, for instance. On the whole, it isn't always bad—the monounsaturated fat in such foods as olive oil and nuts, the polyunsaturated fats in vegetable oils, and the omega-3 fats found in fish like salmon and sardines have all been shown to have cardiovascular benefits.

Likewise, all carbohydrates are not created equal. "Some carbs may be just as problematic for cardiovascular health as saturated fat," says Ding. Those that rank high on the glycemic index can cause blood sugar levels, and then insulin production, to skyrocket, which can lead to decreases in HDL ("good") cholesterol and higher levels of triglycerides—both of which can raise cardiovascular risk. Carbohydrates near the top of the glycemic index have also been linked to a greater risk of type 2 diabetes. Over time, the spikes in insulin production that these foods trigger can fatigue the pancreas, so that it stops producing sufficient quantities of the hormone. The inevitable crash in blood sugar levels that follows consumption of these carbohydrates can result in weight gain, too, as the drop tends to spark a feeling of hunger, increasing the likelihood of overeating and, perhaps, increasing the odds of developing heart disease and diabetes.

Although it may seem clear that we should all try to avoid white bread, candy bars, and other carbohydrate culprits that top the glycemic index, troublesome carbohydrates can lurk in less-expected places. Potatoes, especially their baked and mashed forms, Ding notes, rate quite high on the glycemic index—they've been shown to raise blood sugar levels as quickly as pure table sugar does—yet their inclusion in the produce food group can cause people to think of French fries as a vegetable rather than a starch.

High amounts of sugar and high-glycemic index carbohydrates work in more insidious ways. "Over the past several years," says Willett, "we've come to see that sugar-sweetened beverages are a very troubling part of the food supply." Observational studies have linked soft drinks and other sugary beverages to excess weight gain, an association that Willett attributes partly to the drinks' carbohydrate content but also to their form: It's easier, he says, to consume more calories when they're delivered in a liquid. Ding agrees. "If you eat a handful of jellybeans, you know you're having a snack that's high in sugar and calories," he explains. "But you could drink several sweetened beverages and not realize just how much you're taking in—plus, they're not filling, so you may find yourself snacking in addition to drinking."

Although more randomized, controlled trials are needed to firmly establish this relationship, some research suggests that cutting back on sugary drinks may encourage weight loss. Ludwig's pilot study of 103 adolescents, published in 2006 in *Pediatrics*, found that reducing intake of sugary drinks among adolescents who were overweight—that is, having a body-mass index (BMI) greater than 25 kg/m<sup>2</sup>—led to a 0.75 kg/m<sup>2</sup> decrease in BMI over a 25-week period,

when compared with a control group. For a 160-pound, 5'6" adolescent, this roughly translates to an 11-pound weight loss over the study period.

# Vegging Out

If there's one area of nutrition research where findings seem clear cut, it's fruits and vegetables. Mom always told us to eat our broccoli, and her advice has been backed up by the U.S. Department of Agriculture's recommendations to fill our plates with five to nine daily servings of produce. Whether you meet this requirement or not, you likely have heard that fruits and vegetables have powerful anticancer properties.

There's just one problem. "The benefits of produce for cancer prevention have been greatly overstated," says Willett. Although early case–control studies suggested that fruits and vegetables might protect against cancer, those studies relied on research participants' recollection of their diet, a methodology notorious for recall bias. More recently, large prospective studies have examined the role of produce in overall cancer risk, with disappointing results. (To highlight the complexity of such research, Willett points out that these same studies have shown produce's benefits for cardiovascular disease.) Summing up these findings in a report in the April 21, 2010, issue of the *Journal of the National Cancer Institute*, Willett wrote that evidence to date suggests that "a broad effort to increase consumption of fruits and vegetables will not have a major effect on cancer incidence."

So should you toss that salad? Not so fast, say researchers. First, cancer itself can pose a challenge to investigators. "There are so many different types and sub-types," explains Ding. Some research has identified specific compounds within foods that may indeed help reduce the risk of certain cancers. "Additionally, most cancers have their roots in young adulthood or even earlier, yet the majority of studies have focused on middle-aged and older people," he adds. "We need to start tracking cancer throughout life to get a clearer picture of risk."

Even if produce doesn't protect against cancer, it does appear to promote cardiovascular health: Consumption of at least five daily servings of fruits and vegetables is associated with a 30percent lower risk of coronary heart disease and stroke. Research also hints at a relationship between fruits and vegetables and a reduced risk of diabetes. And produce can displace lesshealthy fare in your diet. When you fill your plate with a rainbow of fruits and vegetables, for example, there's less room for red meat—consumption of which has been linked to cardiovascular disease.

# Life Support

At its most basic, food keeps us alive. And while your main concern about nutrition may be what to make for dinner tonight, nourishment takes center stage for someone who is critically ill or injured. Until about 50 years ago, patients with severe intestinal damage that prevented normal digestion found themselves in a fear-filled race against time: Would their organs heal before they starved to death?

Fortunately, parenteral nutrition has made that fear a thing of the past. In this feeding technique, a catheter delivers a liquid blend of glucose, amino acids, and lipids directly into a patient's bloodstream, completely bypassing the gastrointestinal system. It is "one of the great medical inventions of the past century," says Bruce Bistrian, chief of clinical nutrition at Beth Israel Deaconess Medical Center and an HMS professor of medicine. "It allows us to nourish sick people as long as necessary."

Parenteral nutrition is not without controversy: its use can increase the risk of infection. This drawback has led some physicians to prescribe enteral nutrition, which introduces nutrients directly into the stomach through a tube, for critically ill patients whose intestines still function. Yet a meta-analysis published in *Intensive Care Medicine* in 2005 found that the mode of feeding patients in intensive care units—whether enterally or parenterally—may matter less in terms of mortality and morbidity than in the timing and amount of nourishment. Providing critically ill patients too much glucose, for instance, can be problematic. "We're discovering," says Bistrian, "that starting enteral and parenteral nutrition as soon as necessary and limiting caloric intake to 50 to 70 percent of the daily recommendation decreases the patient's chances of becoming hyperglycemic, which in turn may lower the risk of infections."

Some research suggests that this caloric calibration approach may even reduce the inflammatory response of the underlying illness or injury—a dampening action that could potentially speed healing.

Now a regular tool for physicians, parenteral nutrition continues to be fine-tuned. "It's a wellestablished therapy," says Bistrian. "But we still have much to learn."

# Details, Details

As studies continue to shed light on the most promising foods for good health, one significant theme has emerged: While caloric intake still governs weight gain and loss, what we eat may matter as much as how much we eat.

It may turn out that the real benefits of such foods as fruits, vegetables, and whole grains are found in the individual compounds they contain.

"We should be looking not just at macronutrients like fat, carbohydrates, and protein, but at micronutrients as well," says C. Ronald Kahn, the Mary K. Iacocca Professor of Medicine at HMS and head of the Integrative Physiology and Metabolism section at Joslin Diabetes Center. To that end, he investigated the effects of leucine, an amino acid found in dietary protein that appears to play a role in insulin signaling. For the study, published in 2011 in*PloSOne*, he and his team gave rats twice the normal amount of leucine in their chow, then fed them either a regular or a high-fat diet. They found that the rats receiving extra leucine showed reductions in blood sugar levels and less fat in their livers. High blood sugar and fat harbored in the liver can contribute to what is known as metabolic syndrome, an array of medical disorders that, taken together, can increase a person's risk for cardiovascular disease and diabetes. The rats were also better able to respond to insulin production and to handle glucose, even though leucine didn't help them lose weight. "Adding just this one amino acid to the diet changed the metabolism in a lot of different pathways," says Kahn. "It's evidence that even a small dietary change can make a big difference."

Folate, a B vitamin found in such foods as leafy greens, legumes, sunflower seeds, and orange juice, also shows promise for good health—but only in some people. Once touted for its potential to reduce the risk of heart disease, folate has had disappointing effects in many studies. "This is another case where we need to look at the specific populations being studied," says Ding. He points out that studies of U.S. men and women show little cardiovascular benefit from this vitamin, but adds that very few Americans are deficient in folate. "But meta-analyses," Ding notes, "actually suggest that folate may indeed help prevent stroke in people who have low blood levels of it."

A similar careful approach to nutrition research may someday shed light on the health effects of vitamin D, says Ding. Found in seafood, dairy products, and fortified cereals, this vitamin is being heavily studied for its role in diseases as diverse as osteoporosis, multiple sclerosis, diabetes, and prostate, breast, and colorectal cancers. Yet researchers still need to tease out many of the particulars, including refining what blood levels of the vitamin are optimal and whether the vitamin prevents the onset or worsening of these diseases.

# Food Fight

For many nutrition researchers, the work doesn't end in the lab. Instead, they are using their findings to help educate consumers; overhaul the food available in schools, hospitals, and

workplaces; and in some cases, even change public policy. Willett and colleagues have created research-based versions of the USDA's food pyramid and healthy plate icons, aimed at helping people make healthier meal choices without the influence of lobbyists, an influence that sparked criticism of the government's guidelines. He hopes that hospitals and schools will begin applying these dietary recommendations to their cafeterias. Although Willett was instrumental in improving the culinary choices offered at the Harvard School of Public Health, he finds that the fare at some Boston-area hospitals remains dismal and that many academic institutions are still failing nutritionally. "These places," he says, "are literally feeding the obesity epidemic."

Ludwig also advocates for dietary changes that encourage both children and adults to achieve and maintain a healthy weight. "Highly processed foods and sugary drinks have become the basis of the American diet," he says. "We need to start implementing intelligent public health actions, including increasing educational programs, overhauling school cafeterias, and placing sensible taxation on junk foods and beverages."

Ding, in fact, is currently involved in a movement in Slovenia to begin taxing sugar-sweetened beverages, and he hopes to see the same happen here someday. Yet he knows that such a victory would be just one small step in the journey to better nutrition. "Access to inexpensive, nutritious food is a huge roadblock in many communities," he says. "The price of fruits and vegetables has outpaced the rate of inflation, and the poor in this country have become poorer. It's a double whammy."

Change comes slowly in the worlds of both nutrition and government, and the major structural shifts needed for public policy progress may still be decades away. Meanwhile, investigators hope that their work will help inform what ends up on consumers' plates—and how it affects their health. "Nutrition," says Ding, "is about much more than just what to eat."

—Jessica Cerretani

Jessica Cerretani is a Boston-based health and medical writer.

### Stone Soup A pinch of food and a dash of stress may lead to a long life by Jake Miller



SURVIVOR: Bristlecone pines can thrive for thousands of years in arid, high-altitude landscapes by following what some might consider a botanical version of calorie restriction. Photo by Scott T. Smith/Corbis

Imagine a plate filled with vegetables, vibrant with color. They're sprinkled with nuts, drizzled with extra-virgin olive oil, and topped with a tidy serving of grilled salmon or, perhaps, tofu. Sliced strawberries decorate the plate's edge. Now imagine scraping away a sizable wedge—as much as a third—of that meal. Even worse, imagine this subtraction occurring day in and day out, whisking away food and nearly half the calories of each meal.

Such spare servings aren't simply a formula for weight loss. They're part of a considered lifestyle based on the idea that a lean life might lead to a longer life marked by fewer age-related diseases and slowed senescence. On the edge of starvation, deep in the heart of hunger, some believe they have found the fountain of youth.

# A Slim Edge

The roots of this belief can be traced to evolutionary changes incorporated billions of years ago into the genes of living organisms. When severely stressed, as when an organism is hungry

almost to the point of starvation, running repeatedly from unrelenting predators, or chasing everelusive prey, cells within the body open chemical pathways that increase the efficiency of energy processing and speed up the repair and recycling of damaged proteins, allowing the organism to survive. In humans, these responses improved our chances for survival throughout the millennia. But scientists think stress responses may have another role: they may help prevent cancer, diabetes, and other diseases associated with aging.

"Since the ancient Greeks, we've known that exercising and eating less or fasting is good for you, but we've never really known why," says David Sinclair, an HMS professor of genetics and a codirector of the Paul F. Glenn Laboratories for the Biological Mechanisms of Aging at Harvard Medical School.

Sinclair studies sirtuins, a family of genes found in most living things. He thinks these genes may play key roles in the stress-related responses that protect us against disease and increase our chances for living longer and remaining healthy. In addition, Sinclair and other scientists think that therapeutics based on sirtuins or their activity may help trigger the genes and biochemical pathways that control the effectiveness of our disease defenses, which may become less active as we age.

# Less Is More

Currently, the best understood means of triggering a cascade of anti-aging defenses is calorie restriction. Research has shown it plays a crucial role in preventing obesity, fighting diabetes, preventing tumor growth, and metabolizing fat. There's also evidence that, while calorically restricted animals become infertile while they are hungry, once they start to eat again they can delay menopause and extend fertility much later into life than normal.

The first experiments on calorie restriction, which took place during the Great Depression, were conducted on rats. Researchers cut back the amount of food they gave to the animals and expected to see the animals' health deteriorate. Instead, the rats' health improved and they lived longer. In just about every creature in which calorie restriction has been tested—brewer's yeast, bacteria, roundworms, and mice—it has lengthened the life span of the species, sometimes nearly doubling it. What's more, vitality remained high even as age increased.



SLOW BURN: Some tortoise species live 150 years or more. Photo by stock.xchng Humans already have a long life span. In fact, only a few species of animals outlive us: Some tortoises live to be 150 or so, and bowhead whales may reach 200. Certain plant species, like the bristlecone pine, live thousands of years in the austere environments of the arid southwestern United States. Interestingly, the bristlecone and similar long-lived plants might be said to practice a botanical version of calorie restriction.

Our long life span makes it difficult to measure the outcomes of calorie restriction. But one attempt, a short-term test, is found in research undertaken during World War II. A group of conscientious objectors volunteered to adhere to a diet that approximated the levels of deprivation found in the war-devastated regions of Europe. Scientists found that the participants not only experienced ravenous hunger, but that they were also constantly irritable. More troubling were the instances of participants suffering severe psychological troubles, including self-mutilation. One participant attempted suicide.

A contemporary, nonscientific look at the long-term effects of calorie restriction can be found among the thousands of members of the Calorie Restriction Society, based in New York. Society members voluntarily restrict their calorie intake by at least 25 percent of what might be considered normal for a healthy adult. They do this out of a conviction that by radically lowering their caloric intake, they will prolong their lives and stay healthy into their old age. Many adherents have steadfastly practiced their lean eating regimen for more than a decade.

Unfortunately, many people find it almost unimaginably hard to maintain this sort of diet. To achieve it, a moderately active 155-pound male would need to cut his intake from around 2,500 calories a day to around 1,800 calories, the caloric intake recommended for a low-activity male weighing less than 130 pounds. And cutting back to such spartan amounts is not the only challenge; in order to maintain healthy levels of key nutrients, the calories must be well chosen. That leaves precious little room for French fries or even low-fat French vanilla yogurt.

# Round Round Get Around



T. Keith Blackwell Photo by courtesy of Joslin Diabetes Center

For those who despair that they haven't the will power to follow such a lean diet, yet still would like to enjoy a long, healthy life, there is good news. According to ongoing longitudinal studies of centenarians, most people who live extraordinarily long lives don't follow calorie restriction. They also often don't work out, or do anything else intended to prolong their lives. Some early theories of aging posited that we grew old as we consumed our lifetime allotments of physiological actions—a quantum of calories to metabolize, a quantity of breaths, or a quota of heartbeats, for example. It was initially thought that calorie restriction worked because it slowed the body's clock and its inevitable ticking toward the end of life. It turns out that it's not the act of eating or processing fewer calories that matters. People who eat what they like, skip exercise, enjoy life, and still remain active for more than 100 years may simply have more robust repair processes than most of their peers.

These carefree super-centenarians give T. Keith Blackwell, an HMS professor of genetics at the Joslin Diabetes Center, hope for the field of aging research. "People who live past about 104 tend to be surprisingly healthy. Until they get a serious infection or the body just stops working, most of these super-centenarians are up and around and energetic," he says.

One goal for researchers who study aging, Blackwell says, would be to find a much simpler way to achieve a vital, disease-free old age than by calorie restriction—perhaps a drug, a particular pattern of exercise, or tweaking certain nutrients in the diet.



To find that simpler way, Blackwell has been researching skn-1, a gene-regulating protein found in the much-studied roundworm Caenorhabditis elegans. This regulator is analogous to regulatory proteins coded for in the human genome. Skn-1 plays multiple roles in the life of a roundworm: It helps build its digestive system; it manages the recycling of wastes and toxins that contribute to its aging, and it triggers several of the roundworm's longevity pathways.

STRESS TESTERS: Researchers such as investigate how calorie restriction and other physiological pressures might prevent diseases that are associated with aging. In just about every creature in which calorie restriction has been tested-brewer's yeast, bacteria, roundworms, and mice-it has lengthened the life span of the species, sometimes nearly doubling it. Photo by Kris Snibbe/Harvard University News Office

Blackwell has found that *skn-1* is important to *C*. T. Keith Blackwell and David Sinclair (above) elegans in a variety of stress situations, not only when the organism undergoes calorie restriction. "Stress defenders talk to other stress defenders and help each other out," he says. It seems that there are many different stress-response processes and that they work together, back each other up, trigger, and reinforce one another in rather complicated ways.

But how do we get these processes talking to one another when we need them most? How do we make it so that we all can benefit from these life-prolonging powers?

"The complexity of this process at the nano scale is mind-blowing," Sinclair says. "And the challenge is to try to find a medicine that can directly tweak that system without causing any side effects at the nano level. It is going to take the careers of many people to get there."

#### —Jake Miller

Jake Miller is a writer and editor in the HMS Office of Communications and External Relations.

### Place Setting An orchard can be a labor of love—and a testament to biodiversity by Angela Alberti



An orchard can be a labor of love and a testament to biodiversity Photo by Steven Vote

A glint of turquoise passes in front of him as he stands quietly, one hand wrapping a yellow coffee mug. The dragonfly lightly touches Eric Chivian's shoulder. Once. Twice. Then, it zooms away, its color blurring, its whisperless flight threading through the buzzes, chirps, and song that fill the morning air. The hum of daily life on his 42-acre farm and orchard in central Massachusetts pleases Chivian '68. So does the knowledge that history is rooted all around him. And he savors the names that go with that history: Newtown Pippen. Esopus Spitzenberg. Ashmead's Kernel. Roxbury Russet.

These are just a few of the seventeenth- and eighteenth-century heirloom apples that Chivian, an HMS assistant clinical professor of psychiatry, has nurtured in his orchard for nearly two decades. And although he is connected to the past through his orchard, it's Chivian's hope that the sustainable methods he uses to cultivate his trees—together with his dedication to fostering biodiversity in agriculture—will help protect the health of Earth and its people for years and generations to come.

# Johnny Appleseed

When not enjoying the ambience of his acreage, Chivian works to interest and enlist his fellow physicians in efforts to protect the environment and to increase public understanding of the potential health consequences of global environmental change. His dedication to these goals led him, in 1996, to found the Center for Health and the Global Environment at Harvard Medical School. But this was not Chivian's first effort to spur physicians to social action. In 1980, he cofounded the International Physicians for the Prevention of Nuclear War. The efforts of this group brought its founders, all members of Harvard's faculty, the 1985 Nobel Peace Prize.

"Physicians can greatly influence public opinion and policy that relates to health issues. Alterations to the environment ultimately affect human health on every level," he says. "Food is definitely a health issue. I'm interested in how changes to the environment affect food, the food supply, and biological diversity."

Biological diversity, or biodiversity, is simply the variety of life in an ecosystem. In an agricultural ecosystem, this includes the microbes that live in the soil and make it fertile, the above-ground insects that pollinate and protect crops against pests, and the range of plant species that grow within a self-sustaining area.

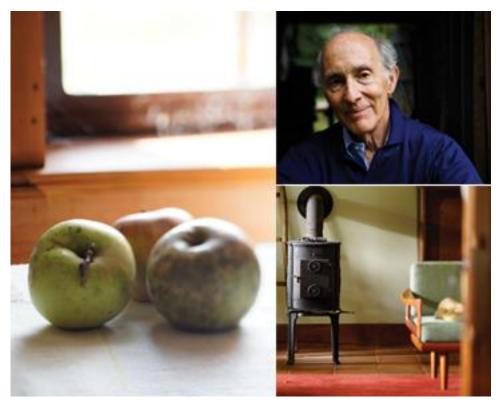
# Seed Catalog

Chivian's interest in food and food production started when he was young. His family planted a backyard garden during World War II, part of a national effort to help alleviate food shortages. But it was family trips to a local cider mill that sparked his lifelong interest in apples. "The cider would just pour out of the press," he says. "And the smell! It was magic to me."

Since the days of those backyard Victory Gardens, agriculture in the United States has undergone a revolution. According to the U.S. Department of Agriculture, in 1940, there were more than six million farms in this country; by 1997, that number had decreased 70 percent, dropping to just shy of two million. By contrast, during that same period, the average farm size increased nearly threefold, from an average of 174 acres to 487. Agribusinesses, as the larger industry-affiliated farms came to be known, drastically reduced the variety of food grown, by focusing on a handful of crops, such as corn, wheat, and soy. Today, just 12 plant species, primarily starch-rich commodities such as grains and beans, provide nearly 75 percent of the world's food supply. "The vast plant monocultures that large-scale farming produces not only strips us of the diversity of plant life, but it also jeopardizes the world's food supply," says Chivian. "Monoculture agriculture is extremely vulnerable to such environmental variations as climate change."

Loss of plant species—and the seeds that they grow from—is not without consequence. Between 1900 and 2000, 75 percent of crop diversity was lost owing to disuse or the disappearance of particular plant varieties, according to a recent report from the U.N.'s Food and Agriculture Organization. In the U.S., as elsewhere, this drop in diversity has meant the disappearance of species: More than 80 percent of corn, cabbage, apple, and pea varieties known at the start of the twentieth century are now extinct.

According to Chivian, most varieties of fruits and vegetables available today aren't necessarily the healthiest or even the best tasting. "When food began to be shipped long distances, rather than being grown and sold locally," he says, "there was a movement toward producing food that shipped well and looked beautiful. Unfortunately, sturdiness and beauty often came at the expense of flavor."



THE DEPTHS OF **BEAUTY: Just as** the understated grace of stove and chair in Eric Chivian's home quietly attest to purpose and function (bottom right), the natural splendor of heirloom apples speak to a genetic lineage that preserves flavor and stamina. Heirloom fruits are often compared to wine because of their complex flavor profiles. And like wine, such fruits are beginning to be appreciated and savored. Photos by Steven Vote

# Soul Food

Like Chivian, Katherine McManus believes the produce in today's grocery aisles is of lesser character than its heirloom counterparts. And, as director of the Department of Nutrition at Brigham and Women's Hospital, she spreads this gospel to her patients. "I do recommend heirloom because I think they taste better," says McManus. "Taste trumps nutrition every time, so when taste and nutrition go hand in hand, so much the better."

In recent years there have been some studies that suggest a general decline in nutrient levels in fruits and vegetables, but there is no consensus on the issue among experts. According to McManus, comparing nutritional values across varieties, also known as cultivars, is difficult because several factors can influence the micronutrient value of a particular food: the soil composition, temperature during growth, fertilization methods, ripeness at the time of harvest, and how far the food was shipped before being eaten.

A 2001 review of more than 400 research reports by the United Kingdom–based Soil Association found that vitamin C and mineral content may be higher in organically grown crops. More recent studies report higher levels of disease-fighting phytochemicals in organic varieties compared with their conventionally grown relatives. In addition to a possible improvement in nutritional profile, organically grown foods do not depend on the use of chemical insecticides and petroleum-based fertilizers. In the years 2000 and 2001, according to the U.S. Environmental Protection Agency, more than five billion pounds of pesticides were applied to crops grown conventionally throughout the world.

"We lack a real food culture," says McManus. "Buying whole foods, supporting our farmers, and doing more of our own cooking are key to improving that culture. If we had a better appreciation for food, we might be better able to address some of our nation's nutritional issues, such as overconsumption."

According to the Centers for Disease Control and Prevention, obesity rates have spiked throughout the past two decades, with nearly 34 percent of U.S. adults and 17 percent of children and adolescents categorized as obese. McManus thinks a dysfunctional relationship with food may be one cause, a link that may result in type 2 diabetes, cardiovascular disease, and certain cancers.



GARDEN OF EARTHLY **DELIGHTS:** Apple varieties that date to the eighteenth and nineteenth centuries share ground in a biodiverse community of birds, insects, and plants such as garlic (bottom left) and coleus (top left). Agribusinesses, as the larger industryaffiliated farms

came to be known, drastically reduced the variety of food grown. Today, just 12 plant species provide nearly 75 percent of the world's food supply. Photos by Steven Vote

# **Palate Pleasers**

McManus follows her own advice, and she and her husband organically cultivate a garden of heirloom tomatoes, preferring the Brandywine and Brandywine Pink varieties. Heirloom fruits are often compared to wine because of their complex flavor profiles. And like wine, such fruits are beginning to be appreciated and savored.

"There's a resurgence of interest in heirloom apples," says Chivian. "Farmers' markets are beginning to carry Roxbury Russets and Baldwins and other incredible apples that had fallen out of favor. And that's all to the good because the flavor of these fruits is magnificent."



Eric Chivian Photo by Steven Vote Popular culture reflects this renewed interest in the locavore and snout-to-tail food movements, specialty cooking magazines, websites, and food-centric cable television networks like the Cooking Channel and the Food Network.

"It's a really interesting sort of movement in our culture," says Kathleen Frith, managing director of the Center for Health and the Global Environment, "one we wanted to involve Harvard students in."

In April 2010, the students got that chance with the advent of the Harvard Community Garden in Harvard Square. A large plot that includes about 1,200 square feet of raised beds, the organic garden produces 50 varieties of vegetables, including heirlooms with such evocative names as Purple Haze carrots, lemon cucumbers, and fairy tale eggplants.

The Association for the Advancement of Sustainability in Higher Education reports a surge in the number of such campus gardens sprouting on more than 100 U.S. colleges during the past two years. From its most recent poll, the Vermont-based National Gardening Association says that 37 percent, or an estimated 43 million, U.S. households planned gardens in 2009, an increase of 7 million households over 2008 estimates. And the number of farmers' markets is also burgeoning, up 17 percent in 2011 from the previous year and 36 percent from 2009, according to the USDA.

Bringing food production out of the dark and into the limelight is beneficial on many levels: It can lessen the use of fossil fuels to transport food long distances, cutting contributions to climate change; it also helps local farmers build community, which, in turn, can benefit local economies. And then there are the benefits of the food itself, for locally sourced food can be picked at the height of its nutrient content and flavor.

# **Gentlemen Farmers**

Back in his orchard, Chivian picks an apple from an Esopus Spitzenburg tree, a variety that was Thomas Jefferson's favorite. "I'm a biologist and naturalist," he says, "so for me, being a farmer is field biology at its best." He polishes the apple on his shirt and takes a bite.

"The only way to get an Esopus Spitzenburg tree is to cut a branch and graft it onto a root; the genetics is in the branch, not in the seed," he explains. "I love that connection. I love the fact that I have the same tree as Jefferson's, and thus a connection to him."

"This orchard is magical to me," he adds. "There's a power that comes from being connected to the earth. When Jefferson was in his late 70s he said, 'I may be an old man, but I'm still a young farmer.' I agree with him completely."

—Angela Alberti

Angela Alberti is an editorial specialist in the HMS Office of Communications and External Relations.

# **For More Information**

\*If clicking on a link below does not take you to the website, please copy and paste the URL into your browser\*

Harvard Medical School Division of Nutrition <a href="http://nutrition.med.harvard.edu/">http://nutrition.med.harvard.edu/</a>

The Nutrition Source Harvard School of Public Health http://www.hsph.harvard.edu/nutritionsource/

Healthy Eating Plate vs. USDA's My Plate The Nutrition Source Harvard School of Public Health <u>http://www.hsph.harvard.edu/nutritionsource/healthy-eating-plate-vs-usda-myplate/</u>

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