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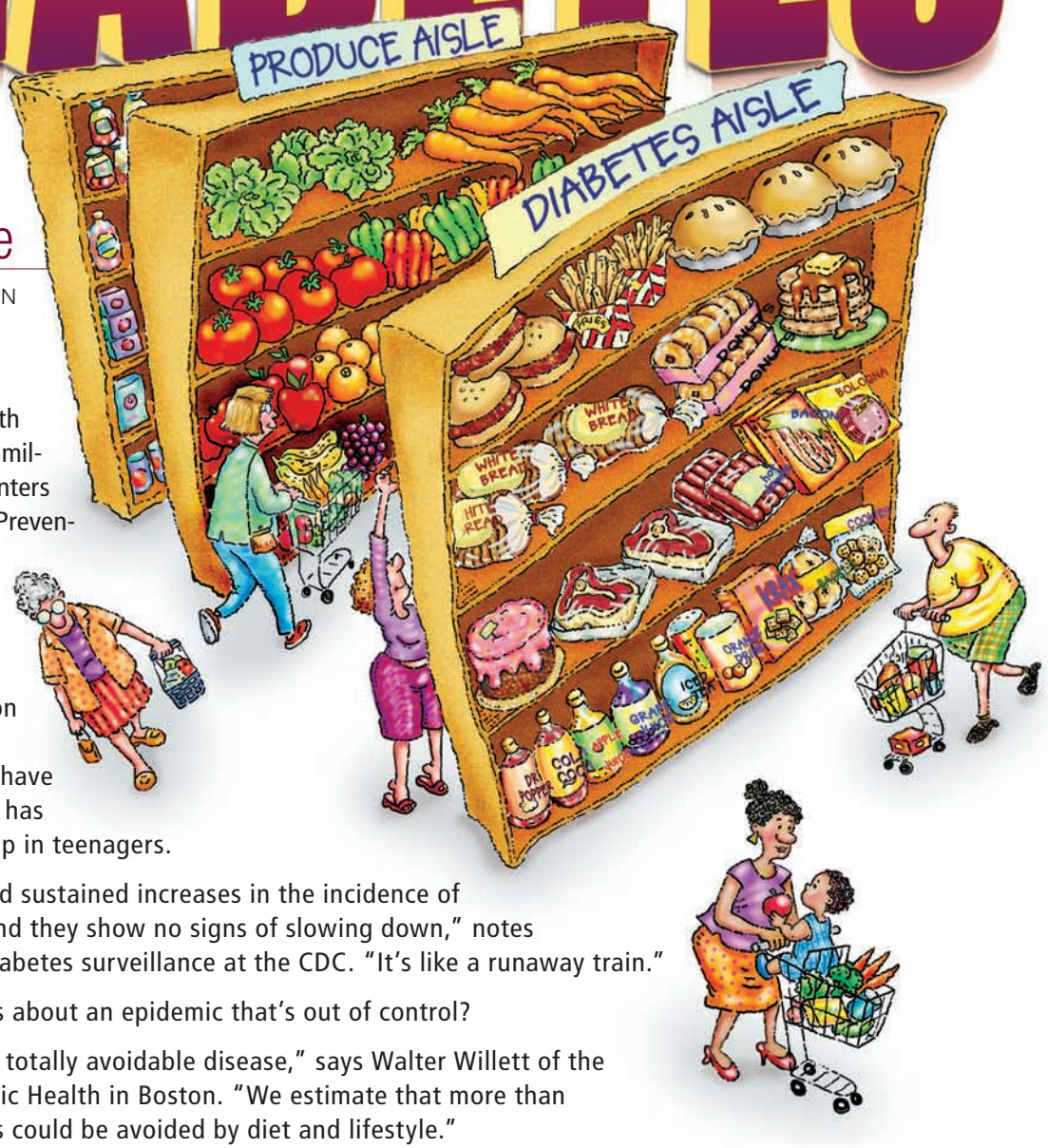
DIABETES



How to Play Defense

BY BONNIE LIEBMAN

"Number of people with diabetes increases to 24 million," announced the Centers for Disease Control and Prevention in June.

One out of four Americans aged 60 or older now has the disease. Another 57 million people—40 percent of those aged 40 to 70—have pre-diabetes. Diabetes has even started to show up in teenagers.

"We've seen strong and sustained increases in the incidence of diabetes since 1990, and they show no signs of slowing down," notes Linda Geiss, chief of diabetes surveillance at the CDC. "It's like a runaway train."

Is there any good news about an epidemic that's out of control?

"Diabetes is an almost totally avoidable disease," says Walter Willett of the Harvard School of Public Health in Boston. "We estimate that more than 92 percent of the cases could be avoided by diet and lifestyle."

And the answer isn't just on your bathroom scale.

Continued on page 3.

Illustration: Loel Barr.

DIABETES

HOW TO PLAY DEFENSE

Want to avoid diabetes? Keep your weight—and especially your waist—under control, and spend more time on your feet than on your seat.

"Weight is the strongest risk factor by far for diabetes," says Harvard's Walter Willett. But losing excess pounds isn't the only strategy. "Given that most people are not going to get down to an optimum weight," says Willett, "diet quality is almost as important as weight control."

Here's a recipe for an anti-diabetes diet.

DIABETES 101

Diabetes is no picnic.

In people with type 1 diabetes, the beta-cells in the pancreas no longer produce insulin, the hormone that works like a key to admit fuel (blood sugar) into muscle, fat, and other body cells. Scientists believe that type 1 diabetes is triggered by genes, viruses, or an autoimmune disorder, rather than by diet, inactivity, or obesity.

Roughly 90 to 95 percent of people with diabetes have type 2, which means that their insulin doesn't do its job well. It's as though the key (insulin) has trouble opening the door (insulin receptors on cell surfaces).

That "insulin resistance" leaves excess sugar in the bloodstream, which damages small blood vessels in the eyes, kidneys, and other organs (see "From Head to Toe," p. 6).

"Getting blood sugar levels reasonably well controlled can dramatically lower the risk of eye and kidney disease, which lead to blindness and dialysis," says Hertzel Gerstein, director of the division of endocrinology & metabolism at McMaster University in Hamilton, Canada.

What's more, diabetes makes larger blood vessels more susceptible to heart attacks and strokes. "Seventy percent of people with diabetes die of cardiovascular disease," notes Gerstein.

And it's not just the 24 million Americans who have diabetes that trouble doctors. Most of the 57 million who have pre-diabetes—their fasting blood sugar levels are between 100 and 125—don't even know they have a problem.

"These people have blood sugar levels that are not normal and not diabetic," endocrinologist Alan Garber told a press conference in July, when a task force for the American Association of Clinical Endocrinologists released a report on the diagnosis and management of pre-diabetes. Garber, who is a professor of medicine, biochemistry, and molecular biology at the Baylor College of Medicine in Houston, chaired the task force.

"But it's now increasingly clear that we can see the beginnings of complications that ultimately lead to kidney failure, blindness, and amputations in these people," Garber noted. "And they're already at excess risk for cardiovascular disease."

Clearly, the answer for everyone—those who have or want to avoid both diabetes and pre-diabetes—is to keep blood sugar levels in or near the normal range. The question is: how?

WEIGHT & EXERCISE

You can't miss the link between weight and diabetes. More than 80 percent of people with diabetes are overweight or obese. But researchers have only recently begun to understand why.

"It's been a puzzle for a long time," says JoAnn Manson, a professor of medicine at Harvard Medical School and chief of preventive medicine at Brigham and Women's Hospital in Boston. "We didn't know how local deposits of fat cells could cause insulin resistance at distant sites like the liver, muscle, and elsewhere in the body."

Now scientists know that fat cells, especially in the deeper visceral fat around the belly, are

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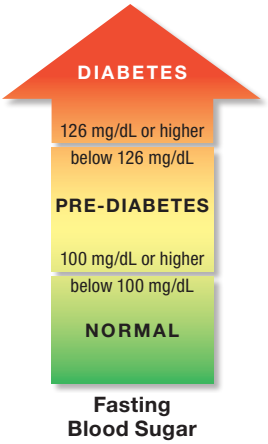
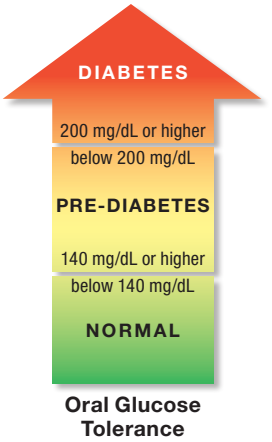
What's Your Blood Sugar?



Fasting Blood Sugar

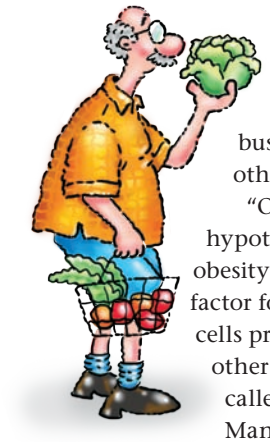
People with pre-diabetes have blood sugar levels that are higher than normal but not high enough to be diabetic. The cutoffs depend on whether your blood is tested after a 12-hour fast (fasting blood sugar) or two hours after you're given a glucose-laden liquid to drink (oral glucose tolerance).



Oral Glucose Tolerance

Source: American Diabetes Association (www.diabetes.org/pre-diabetes/pre-diabetes-symptoms.jsp).

Illustrations: Loel Barr.



busy sending signals to other cells.

"One of the leading hypotheses to explain why obesity is such a strong risk factor for diabetes is that fat cells produce hormones and other chemical messengers called adipokines," says Manson. "Some of them produce a state of inflammation, and that interferes with the insulin receptors on cells."

(Inflammation is the body's immune response to injury. Very low levels of chronic inflammation throughout the body—with no visible signs like redness, swelling, or pain—may raise the risk of diabetes, heart disease, and other illnesses.)

The good news: you don't have to lose all your extra fat cells to keep diabetes at bay.

In the Diabetes Prevention Program, researchers randomly assigned more than 3,000 people with blood sugar levels at or just below the pre-diabetes range to a placebo, to metformin (a drug that lowers blood sugar), or to "lifestyle" changes.

The goal was to have the "lifestyle" people lose weight by boosting exercise (to 2½ hours a week of brisk walking or a similar activity) and adopting a healthy, lower-fat diet. The results were so dramatic that the study had to be stopped early.[1]

After three years, "the lifestyle intervention cut the risk of diabetes in these high-risk individuals by more than half," says Rena Wing of Brown University in Providence, Rhode Island, who led the study at one of its 27 clinical centers. The key to prevention: weight loss.

"Weight loss was really driving the benefit," explains Wing. "Exercise contributed to weight loss, and in people who didn't lose weight, exercise was helpful in reducing risk, but weight loss trumped exercise."

The participants didn't have to lose that much weight. "The average was about 14 pounds initially, and it dropped to about 9 pounds after three years," says Wing. "That's only a 7 percent weight loss initially and a 4.5 percent weight loss after three years. People are surprised that preventing diabetes doesn't require a bigger weight loss."

The drug that lowered blood sugar also worked, but only about half as well as weight loss.

"The Diabetes Prevention Program was extremely strong proof that weight loss that's achievable can have tremendous bang for the buck, and that it's twice as effective as metformin," Wing notes. "Yet I often hear that the results get translated by physicians as 'let's put all these people on metformin.' I find that upsetting."

What cuts the risk of diabetes other than weight loss and exercise?

Clinical trials like the Diabetes Prevention Program are few and far between. Instead, researchers simply ask healthy people what they eat and wait to see who gets diagnosed with the disease. That evidence is less powerful than a clinical trial, but it can detect links for researchers to pursue. Here's what they've learned so far.

FATS

"Trans fats are adverse and polyunsaturates are beneficial for diabetes risk," says Harvard's Walter Willett. "It's virtually identical to what we see for cardiovascular disease."

The Nurses' Health Study, which tracked more than 84,000 women for 14 years, found a 30 percent higher risk of diabetes in those who reported eating the most trans fat than in those who reported eating the least.[2]

The study also found a 25 percent lower risk in those who reported eating the most polyunsaturated fats (found in foods like soybean oil, nuts, and fish) than in those who reported eating the least.

Why do fats matter? "We're not clear about the mechanism, but they probably alter the structure of cell membranes," explains Willett. "Polyunsaturates may make membranes more fluid, and that probably reduces insulin resistance."

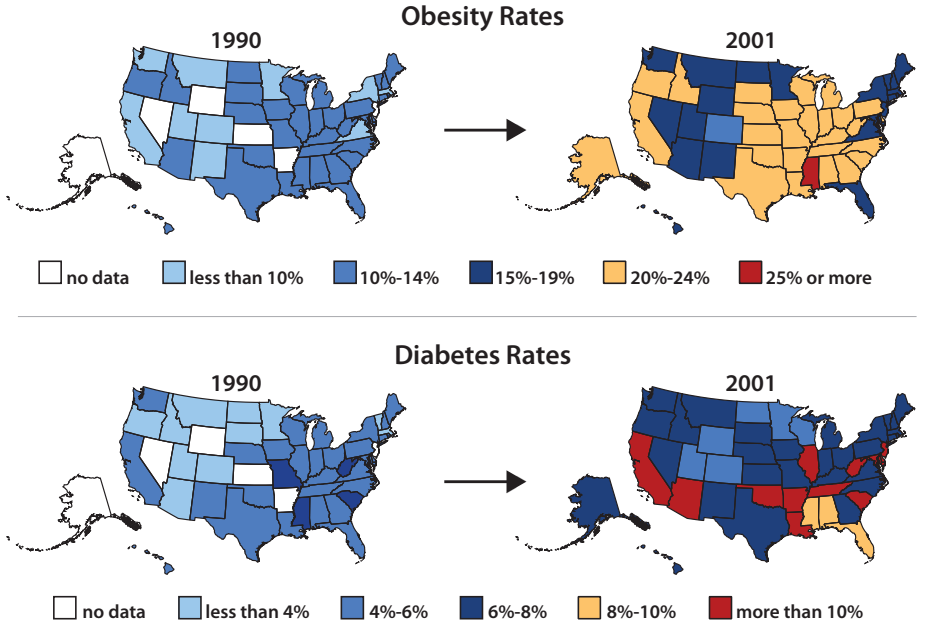
What's more, he adds, "trans fat increases inflammatory factors, while most polyunsaturates reduce them."

Polyunsaturated fats may help explain why women who reported eating nuts or peanut butter at least five times a week had a 20 to 30 percent lower risk of diabetes than those who almost never ate those foods.[3]

But "polys are only part of the explanation," says Willett. The fiber, magnesium, or other nutrients in nuts may also matter.

Trans fat may promote diabetes by boosting your belly fat. For six years,

TROUBLING TRENDS



The top two maps show the dramatic increase in the percentage of obese adults, which helps explain the rise in the percentage of adults with diabetes shown in the bottom two maps. Roughly 55% of U.S. adults with type 2 diabetes are obese. (Another 25% are overweight.)

Source: *MMWR 53*: 1066, 2004.

researchers fed monkeys diets rich in either oleic acid (the monounsaturated fat in olive oil) or an equal amount of trans fat (from partially hydrogenated soybean oil). The monkeys fed trans gained more weight, especially around the abdomen.[4]

"The researchers tried to keep the diets equal in calories, but they couldn't keep the trans fat monkeys from gaining weight," notes Willett. "And the monkeys who got the trans diet also developed a pre-diabetic state."

Fortunately, trans fat is rapidly disappearing from supermarkets, though it's still added to some pie crusts, cake frostings, frozen pizzas, microwave popcorns, and refrigerated biscuits, among other foods.

And you can get plenty from restaurant food like French fries, fried chicken, and pastries that are made with partially hydrogenated oils. (McDonald's and other large chains—but not Burger King—have largely gotten rid of trans.)

CARBS

"The evidence is moderately strong that refined carbohydrates and a high glycemic load increase the risk of diabetes, while a diet high in whole grains and fiber and a low glycemic load are associated with a lower risk," says Harvard's JoAnn Manson.

For example, in a study of more than 42,000 men and another study of 75,000 women, those who ate the most whole grains had a 40 percent lower risk of diabetes than those who ate the least.[5,6]

Could it be the fiber in whole grains that makes the difference?

In a meta-analysis that pooled the results of eight studies, people who got more fiber from breads, cereals, and other grains (but not from fruits or vegetables) had about a 30 percent lower risk of diabetes.[7]

"It's not just fiber," explains Willett. "It's also the nutrients, which get stripped away when grains are refined."

Among those nutrients are magnesium and chromium. The same meta-analysis found about a 20 percent lower risk of diabetes in people who ate the most magnesium-rich foods (like whole grains, nuts, leafy greens, and beans).

"There's a lot of evidence that magnesium improves insulin resistance," says Willett. That's also true for chromium, he adds, but it's more complicated. "Work on chromium has been hindered because it's hard to measure."

WHAT'S YOUR RISK?

Most people who have pre-diabetes—and many others who have diabetes—don't know it. The only way to find out is to get your blood sugar tested (at least every three years starting at age 45). Your risk is higher if you:

- are age 45 or older
- are overweight (see table)
- are African-American, Hispanic/Latino-American, Asian-American, Pacific Islander, or American Indian
- have a parent, brother, or sister with diabetes
- have high blood pressure (above 140 over 90)
- have low HDL ("good") cholesterol (less than 40 for men; less than 50 for women)
- have high triglycerides (250 or more)
- had diabetes when pregnant or gave birth to a large baby (over 9 pounds)
- are active fewer than three times a week

Overweight starts at:

Height (no shoes)	Weight (no clothes)	Height (no shoes)	Weight (no clothes)
4'10"	119	5'8"	164
4'11"	124	5'9"	169
5'0"	128	5'10"	174
5'1"	132	5'11"	179
5'2"	136	6'0"	184
5'3"	141	6'1"	189
5'4"	145	6'2"	194
5'5"	150	6'3"	200
5'6"	155	6'4"	205
5'7"	159		

Source: Adapted from National Diabetes Education Program (www.diabetes.org/risk-test/text-version.jsp).

Whole grains may also lower the risk of diabetes because some of them have a lower glycemic load—that is, they cause less of a jump in blood sugar levels—than refined grains.

"Whole grains are more likely to slow the absorption of food if they're intact and not finely milled," explains Willett. So you're better off with whole wheat bulgur than whole wheat bread.

As carbs go, potatoes deserve special mention. In one study, women who ate potatoes the most frequently (about four times a week) had a 14 percent higher risk of diabetes over 20 years than women who ate them the least frequently (about twice a month).[8]

"Potatoes are a problem because they contribute to the glycemic load," says Willett.

SWEET DRINKS

When it comes to diabetes, sweet beverages seem to be a double whammy.

"Their high-fructose corn syrup and other sugars increase the demand for insulin and have a high glycemic load," explains Manson.

What's more, the sugar you sip may add flab more than the sugar you chew.

"Liquid calories don't seem to lead to satiety and the reduction in subsequent food intake that you might have with solid calories," notes Manson.

That may explain why women who drank at least one sugar-sweetened soft drink or fruit punch a day had nearly twice the risk of diabetes over four years as women who drank less than one a month.[9]

Fruit juice may also promote diabetes.[10] "Fruit juice and fruit punch, but not fruit, are associated with an increased risk," says Manson.

Other sweets aren't harmless, adds Willett. "Any kinds of sugars are adverse. But consuming sugars as beverages does seem to be worse because you can take in such large amounts so easily."

MEAT & IRON

In a study of roughly 70,000 women, those who ate the most red meat (about one serving a day) had a 22 percent higher risk of diabetes than those who ate the least (about one serving a week).[11]

One possible culprit: iron, or, more precisely, the heme iron found in animal foods. "Heme iron is much more readily absorbed, even if you already have enough on board," explains Willett. "We're better at regulating the non-heme iron that we get from plants and supplements."

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In a study of more than 35,000 women in Iowa, those who consumed the most heme iron had a higher risk of diabetes than those who consumed the least.[12]

Scientists have a hunch why heme iron might cause harm.

"In extreme cases of iron overload, called hemochromatosis, we know that there's damage to the beta-cells in the pancreas that secrete insulin," explains Willett. "The iron seems to be directly toxic."

What's more, people with one version of the gene that makes a person more susceptible to hemochromatosis are more likely to get diabetes if they consume heme iron than people who have a different version of the gene.[13] "If you see that kind of genetic interaction, it strengthens the evidence quite a bit," notes Willett.

The sodium nitrite that's added to processed meats (like hot dogs, bacon, and lunch meats) for color and as a preservative could also play a role. In a study of 42,000 men, those who ate the most processed meats (five times a week) had a 46 percent higher risk of diabetes than those who ate the least (twice a month).[14]

"The nitrosated compounds could be directly toxic to beta-cells, or it could be that the mix of fatty acids in processed meats isn't good," says Willett.

COFFEE

"The evidence is becoming very consistent that both caffeinated and decaf coffees reduce the risk of diabetes," says Manson.

In one study of 88,000 nurses, the risk of diabetes was 13 percent lower for those who drank one cup a day, 42 percent lower for those who drank two to three cups a day, and 47 percent lower for those who drank at least four cups a day than for those who drank none.[15] Tea didn't raise or lower risk.

What's in coffee that protects the pancreas? "There's a long-standing hypothesis that oxidative stress is one of the pathways by which diabetes develops," notes Willett.

And coffee is a huge source of antioxidants. "When we look at total antioxidant capacity of the diet, coffee is way out ahead of fruits, vegetables, and everything else," says Willett.

That's good news for coffee lovers, who may have worried that their habit is harmful.

"It's pretty reassuring that there's no clear evidence that coffee increases the risk of cancer, and it doesn't increase the risk of cardiovascular disease, even though caffeine increases heart rate in some people," notes Manson. "And coffee may be protective for diabetes."

ALCOHOL

"It's counterintuitive, and we wondered if it was real, but it's amazing how consistent the findings are," says Manson. "Moderate, not heavy, alcohol consumption—one or two drinks a day for men and one drink for women—is linked to a lower risk of diabetes."

For example, among 20,000 male physicians, the risk of

From Head to Toe

Diabetes strikes nearly every part of the body. But studies show that treating the disease aggressively can curb the damage.

EYES

Diabetes is the leading cause of blindness among adults aged 20 to 74.

Every 1% reduction in hemoglobin A1C lowers the risk of eye, kidney, and nerve disease by 40%. (Hemoglobin A1C measures blood sugar over the long term.)

Treating eye disease with laser therapy can reduce severe vision loss by 50% to 60%.

BRAIN

People with diabetes are more likely to be diagnosed with dementia. Researchers don't know if the dementia is due to diabetes or to multiple mini-strokes (common in people with diabetes) that gradually impair mental function over time. If it's mini-strokes, lowering blood pressure might protect the brain.

KIDNEYS

Diabetes is the leading cause of end-stage kidney disease.

Detecting early diabetic kidney disease (by testing urine for protein each year) and treating it can curb the loss of kidney function by 30% to 70%.

HEART & BRAIN

The risk of heart attack or stroke is two to four times higher in people with diabetes.

Lowering high cholesterol can reduce heart attack and stroke by 20% to 50%.

Lowering high blood pressure can reduce the risk of heart attack and stroke by 33% to 50%.

NERVES

An estimated six out of ten people with diabetes have nerve damage that can cause problems like numbness or pain in the feet or hands, carpal tunnel syndrome (in the wrist), and delayed digestion of food.

Lowering high blood pressure can reduce the risk of nerve, eye, and kidney damage by 33%.

FEET

Diabetes causes more than 60% of foot and leg amputations that are not caused by accidents.

Proper foot care (trim nails, check feet daily for red spots, cuts, swelling, blisters, etc.) can reduce the risk of amputation by 45% to 85%.

Source: www.cdc.gov/diabetes/pubs/pdf/ndfs_2003.pdf.

diabetes was about 25 percent lower in those who had two to four drinks per week than in those who had none.[16] The risk was 33 percent lower in those who had five to six drinks per week and 43 percent lower in those who had at least one drink a day.

How might alcohol help? "It seems to reduce glucose production by the liver," says Manson. "And it may even have a direct effect on insulin resistance that may be due to reduced inflammation."

"Inflammation seems to muck up insulin signaling," she adds. "It's a major risk factor for diabetes."

But diabetes is no excuse to *start* drinking. "We certainly would not recommend that someone begin to drink to reduce their risk, because alcohol has other risks," says Manson. "But if you drink and you're doing well, you should be aware of the apparent benefit of a lower diabetes risk."

VITAMIN D

In numerous studies, people with higher blood levels of vitamin D—and, usually, higher dairy or calcium intakes—are less likely to have diabetes. But that's not proof that too little vitamin D causes diabetes.

"It's tricky because people with diabetes have lower vitamin D levels," says Anastassios Pittas, associate professor of medicine at Tufts Medical Center in Boston.

That's because people with diabetes tend to be older, to exercise less, to have less exposure to sunlight, to eat a less healthy diet, and to be overweight. And obesity itself means lower vitamin D levels.

"Vitamin D is stored in adipose tissue, so if you have more fat, more vitamin D is stored and less is available to circulate," explains Pittas. "We call it fat sequestration."

Researchers try to account for those confounders. Better yet, they give people vitamin D to see if it keeps blood sugar levels or diabetes rates from climbing. So far, two studies have done that.

In one, which was designed to look at osteoporosis, Pittas and colleagues gave roughly 300 people either a daily placebo or calcium citrate (500 mg) plus vitamin D (700 IU) for three years.[17]

"We found no effect in people who started with normal glucose tolerance," says Pittas. "But in people with pre-diabetes, we found a significant difference."

If you follow people with pre-diabetes for three years, their fasting blood sugar levels tend to rise, he explains. "That's the natural history of pre-diabetes."

Indeed, average blood sugar in the placebo group rose by 6 points during the three-year study. "But we found no rise in fasting blood glucose in people supplemented with vitamin D and calcium," reports Pittas.

In contrast, the huge Women's Health Initiative found no lower rate of diabetes in roughly 17,000 women who were assigned to take vitamin D (400 IU) and calcium (1,200 mg) every day than in the same number of women who took a placebo.[18]

"But the vitamin D dose was small, and a lot of the women taking the placebo were taking calcium and vitamin D on their own," notes Pittas.

Other evidence suggests that vitamin D may ward off diabetes. For example, "beta-cells in the pancreas convert vitamin D to its active form, so we know that the cells use vitamin D," explains Pittas. "And vitamin D ameliorates systemic inflammation, which is a cause of insulin resistance."

But he's less optimistic that vitamin D would help people who have advanced diabetes. "It's not going to do much if beta-cells are no longer working. You reach a point where there's little you can do to reverse the decline in the function of the beta-cell."

OTHER FACTORS

An hour a day of brisk walking trims the risk of diabetes by 34 percent. But you still shouldn't spend the rest of the day in a chair.

A study of 68,000 women found a 14 percent increase in diabetes risk for every two hours they spent watching TV and a 7 percent increase for every two hours they spent sitting at work.[19]

"It's definitely good to have a high activity level," says Harvard's Walter Willett. "But you need to pay attention to all 24 hours."

Smoking also raises the risk of diabetes.[20] And, of course, genetics plays a role.

"Diet and lifestyle factors become even more important if you have a close relative with diabetes," says Willett, "because with good diet and lifestyle, you can still have a low risk."

THE BOTTOM LINE

- Losing any excess weight—and keeping off unwanted pounds—is the best defense against diabetes.
- Take a brisk walk daily, and limit the time you spend sitting at work, at home, or in between.
- Avoid trans fats, which are in some French fries, pies, cake frostings, and other foods that are made with partially hydrogenated oils.
- Replace saturated fats (butter, cream, etc.) with polyunsaturated and monounsaturated fats (oils, nuts, etc.).
- Replace red meats, especially processed meats, with seafood, poultry, beans, and soy foods.
- Replace refined grains and sweets with whole grains.
- Drink water instead of soft drinks or even fruit juices.
- If you drink coffee (decaf or regular) or alcohol in moderation, don't stop.

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