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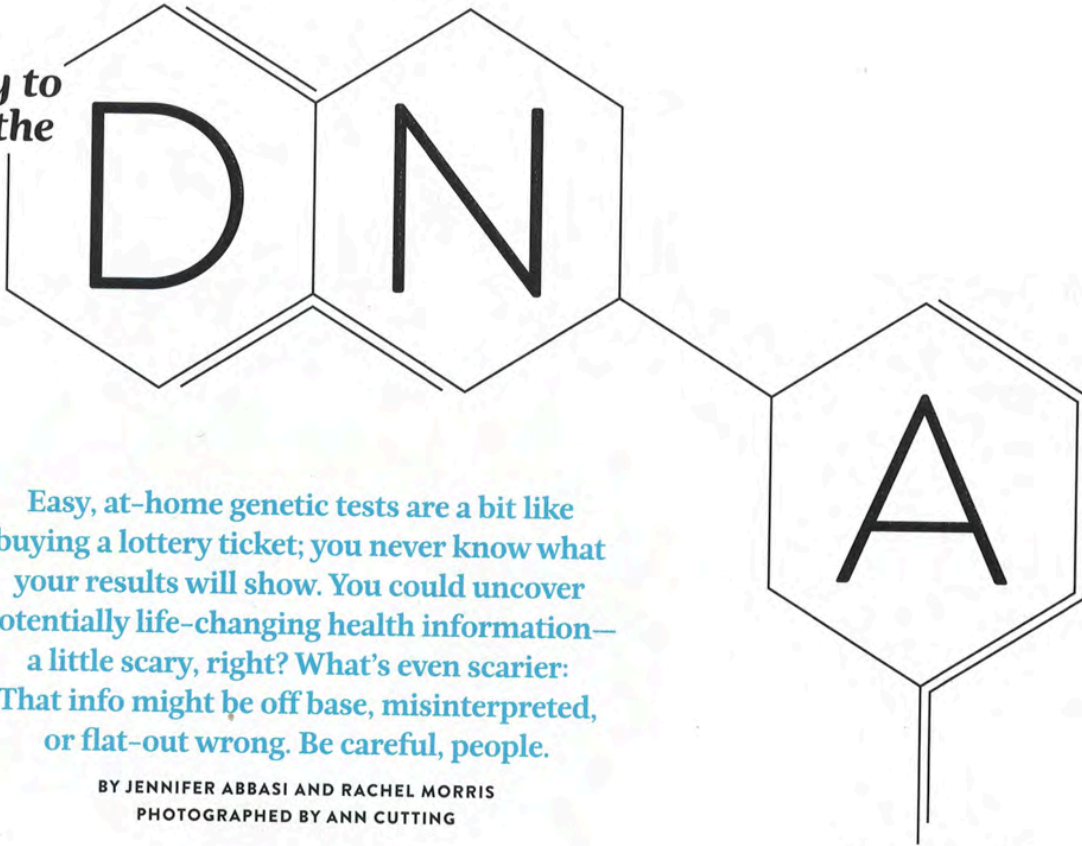
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Easy, at-home genetic tests are a bit like buying a lottery ticket; you never know what your results will show. You could uncover potentially life-changing health information—a little scary, right? What's even scarier: That info might be off base, misinterpreted, or flat-out wrong. Be careful, people.

BY JENNIFER ABBASI AND RACHEL MORRIS
PHOTOGRAPHED BY ANN CUTTING

Game?

What could pop up in
your DNA test?

AN INCREASED RISK
OF EYE DISEASE...



A BETTER RESPONSE
TO CERTAIN MEDS...



A SLIGHT CHANCE
OF HEART DISEASE...



Last November, Ann, a 47-year-old event coordinator and mom of two, got curious about her background. She shopped around online and quickly found a genetic test that promised to illuminate her ancestry. When the kit arrived, she spit into the plastic test tube, boxed it up, and mailed off the DNA-rich sample for analysis. Her results arrived via email, with a colorful map showing where her relatives originated—primarily England and Ireland. Initially, the biggest surprise was a slight but traceable connection to sub-Saharan Africa. But things started to get more interesting when Ann (whose name has been changed) scrolled down and came across details on how her genes influence her health.

The feedback was limited to trivia—how well her body breaks down alcohol and whether she’s likely to toss and turn during sleep, for example—but it made Ann wonder what else she could learn about her well-being from her genes. “My father and I have a strained relationship—we haven’t talked in a decade—which means I don’t know much about that side of my family’s medical history,” she says. A message board discussion linked her to an online service that uses data from genetic tests (like the one she had taken) to provide a more detailed personal assessment. *Click*. She made an impulse buy. “At that point, I didn’t even know how it worked, but I had this momentum and it didn’t cost much, so I thought, *Why not try it out?*”

With a few keystrokes, Ann uploaded the data from her genetic test. Just minutes later, a lengthy report popped up in her inbox. “Good news” was highlighted in green and “bad news” in red. One crimson box in particular jumped out with a risk assessment that made her stomach churn: Based on her DNA, the report said, Ann was at risk for early-onset Alzheimer’s, a potentially devastating disease that tends to strike

people between the ages of 30 and 60. The rest of the report might as well have been blank. “I was so hyperfocused on the Alzheimer’s feedback that I didn’t notice if there was anything positive in the findings. I felt completely panicked, overwhelmed, and alone.” If she had looked at the green boxes, she would have seen that the report also tagged her with a lower heart attack risk and—file this under “Stuff You Can’t Make Up”—the ability to handle stress well.

Ann initially kept the test results to herself. “I didn’t want to scare my husband or anyone else around me, because I didn’t really understand what the report meant. That’s when I went nuts on the Internet trying to find someone to talk to.” Her search led to an appointment with Brianne Kirkpatrick, a genetic counselor in Crozet, VA, who inspected Ann’s report and looked into why she’d been flagged for early-onset Alzheimer’s. Ann waited two weeks for her feedback. “It was a dark time. I was angry that I had put myself in this position,” she says. “Just forgetting someone’s name made me think I was already showing signs.”

To Ann’s relief, Kirkpatrick determined that her risk had been misinterpreted. Early-onset Alzheimer’s had been red flagged because Ann doesn’t carry a few tweaks in her DNA that

THE POSSIBILITY
OF ALZHEIMER’S...



A LOWER RISK FOR
OSTEOPOROSIS...



AND SO MUCH MORE.
BUT CAN YOU TRUST
THE RESULTS? AND ARE
YOU SURE YOU WANT
TO FIND OUT?





“Even we geneticists agonize over test interpretations.”

—James Evans, M.D., genetics professor

may provide some protection against the disease. But as Kirkpatrick explained to her, this doesn't actually raise her risk. Ann's true chance for developing the uncommon form of dementia? No higher than that of the average person's.

We've come a long way since genetic testing got its start in the '60s during neonatal exams. Today, it can be a lifesaving tool for the screening and diagnosis of a variety of rare genetic diseases. And with the rise of at-home, direct-to-consumer (DTC) tests like the one Ann used, it no longer takes a doctor's appointment to learn what's lurking in your DNA—just a credit card. Genetic testing kits are as simple to order online as your latest Amazon purchase (and yes, Amazon sells them). “It's easy to see the appeal,” says James Evans, M.D., a professor of genetics and medicine at the University of North Carolina at Chapel Hill. A simple spit sample or cheek swab can seemingly shine a bright light on your well-being. The problem, according to most experts, is that from a medical standpoint the results are about as useful as your horoscope when it comes to determining the future of your health.

GENES VS. CHOICES

Unlike pregnancy tests, which provide easy-to-understand feedback in a matter of minutes, genetic tests produce results that are tricky to unscramble, even for experts with decades of work in the

Look Who Wants Your Testing Business

Up until a few years ago, direct-to-consumer (DTC) tests claimed to provide detailed reports that included information on how a person's genes influence the risk for Alzheimer's, breast cancer, and other frightening conditions. But in 2013, the FDA ordered one popular company, 23andMe, to stop marketing its kit, questioning its accuracy and worrying about how users would react to test results. The company modified its product and now provides feedback such as ancestry reports, information on whether you carry genetic mutations that could be passed on to offspring, and wellness data—how your genes influence lactose tolerance, for example.

Competing companies took notice. Some scaled back on what they tested for, while others opted out of the DTC business altogether or started requiring a doctor's approval before a consumer could place an order. (No doctor? No problem. Certain companies provide their own M.D. who can sign off.) A few, however, still offer tests that claim to report your genetic risk for conditions—say, heart disease, diabetes, or osteoporosis—while others give personalized nutrition and exercise plans based on your genetic makeup.

There are also online programs like the one Ann used. They work like this: Companies such as 23andMe and Ancestry provide raw data—DNA digital files—with their reports. People can then send that raw data to third-party sites such as Promethease, Interpretome, and LiveWello and get back an extensive analysis of how their genes may affect hundreds of diseases and conditions. Results are fast and affordable, but Ann's experience highlights how these (and all genetic tests) can be misinterpreted.

field, says Evans. For some rare variants, the science is clear. (See “How Genetic Tests Work,” opposite page.) Take Huntington's, a disease that is 100% determined by genes. If you have a defect in the gene associated with the disease, you'll get Huntington's. But for the majority of variants, the impact on your well-being isn't black-and-white. For example, carrying a variant in the APOE gene is linked to a higher chance of developing Alzheimer's, but having the defect doesn't mean you'll definitely get the disease, and not having it doesn't mean you won't. And for most health issues, whether diabetes, cardiovascular disease, or cancer, experts can't say how much variants actually affect your risk of becoming sick. Why? Because other factors, such as weight, stress levels, vices—like smoking or drinking—and exercise habits play starring roles in the story of our health. In fact, and this is a critical point, *most genetic variants have a very small effect, or none at all.*

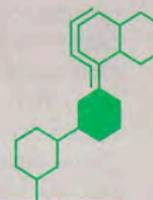


IS IT A WINNING TICKET? GOOD LUCK FIGURING THAT OUT.

It's not possible to say exactly what percentage of our total risk for a disease or condition is based on lifestyle and what percentage is genetic. But in most cases, your DNA doesn't determine your destiny. "If you looked at just my genes, you'd think I was at an increased risk of heart disease," says Cecile Janssens, Ph.D., a professor of epidemiology at Emory University. "But I work out a lot and eat well, so my chance of developing the disease is actually much lower than the average risk. And this is the problem with these tests: You could give the wrong information to people."

GRAY ZONE

To make things even murkier, you can send the same DNA sample to multiple companies and receive different risk assessments, because there are no agreed-upon standards for interpreting the genetic risk of complex diseases. Companies use published research to create their own algorithms to determine risk, and experts say that some of these algorithms are more reasonable than others. One company, for example, may have used a study that linked a cer-



How Genetic Tests Work

Here's a quick bio class brushup: Your DNA contains about 10 million genetic variants called single nucleotide polymorphisms (SNPs)—think of them as typos in your DNA—that are inherited from Mom and Dad. Ongoing research shows that most SNPs don't affect your health. Of those that do, the majority have just a small influence on your risk of various diseases and conditions—whether that's cancer or hair loss. Other variants may also have protective effects (say, a reduced risk of heart disease).

Combing through all 10 million SNPs is time-consuming and expensive and would pick up too many typos that we know little or nothing about. That's why most direct-to-consumer kits use a genotyping test, which seeks out a limited number of specific, known variants—typically the ones we understand the best. But because each test may search for a different combination of variants, you get a look at only a sliver of what's going on. For example, a test may report back on a certain variant linked to an increased chance of type 2 diabetes. But since a limited part of your DNA was analyzed, it's possible that the test missed other typos associated with the disease that could also influence, and possibly decrease, your risk.

tain variant to a doubled increase of diabetes, while another used a different study that said the variant caused *triple* the risk. And tomorrow, new research could show a higher risk. The problem isn't that the test results are wrong—we just don't yet know when they're right.

Things become plain misleading when tests prescribe diet or exercise plans—say, recommending a low-carb diet or high-intensity cardio based on genes, says Janssens. “There’s no validity to what they’re inferring from the results,” she says. It’s one thing to have a variant that’s associated with increased benefits from eating monounsaturated fats, but to say that you’ll be a healthier person if you chow down on more avocados? “We don’t have the science to make that second leap,” says Lawrence Brody, Ph.D., a geneticist at the National Human Genome Research Institute. “Eating extra avocados probably won’t hurt you, but there’s no evidence that it’s especially beneficial to a person with that variant.”

The cherry on top of all this confusion and uncertainty? People typically aren’t pros at putting risk into perspective. (We may worry about our chance of dying in a plane crash, for example, yet the most dangerous part of flying is the drive to the airport.) Consider a test indicating that you have double the risk for a disease that affects one person out of every thousand. Sounds scary on pa-

per, sure, but here’s the breakdown: Instead of a one in 1,000 chance, now your risk is one in 500. In other words, you’re still very unlikely to get the disease. “Think of it like this,” says Brody. “I could easily increase my odds of winning the Powerball tenfold by buying 10 tickets, but am I actually going to win the Powerball? No.”

MIND GAMES

Despite these limitations, some experts believe that at-home genetic tests have their place, and that it’s our right to know what’s lurking in our DNA. “All your health information—what’s in your medical chart, on your X-rays, or in your genes—should be available to you if you want it and are properly prepared to receive it,” says Robert Green, M.D., a medical geneticist at Brigham and Women’s Hospital and Harvard Medical School. That last bit poses a challenge, however, when the emotional weight of test results turns out to be heavier than expected. Despite weeks of anxiety while waiting to learn about her results, Ann was lucky to have her mind put at ease by a genetic counselor. For those who don’t have an expert to clarify a test’s findings—or in the case where a test may actually reveal a true, heightened risk—the angst of knowing what health trouble lies ahead can leave people baffled and anxious. Geneticists are also quick to point out that the seemingly personal decision to learn more about your own genetics can have an impact on your relatives, since variants run in families. A woman who discovers that she has a variation in a BRCA breast cancer gene may feel compelled to relay her results to her siblings—who are also at risk of carrying it. They never sought this information, and now it’s on them to decide whether to get tested.

HEALTHY HABITS
TRUMP GENES WHEN
IT COMES TO YOUR
FUTURE WELL-BEING.



“For predicting who gets type 2 diabetes, BMI is probably more useful than any genetic test.”

—Lawrence Brody, Ph.D., geneticist

DR. OZ ILLUSTRATION BY KATHRYN RATHKE



The Privacy Problem

Employers and health insurance providers cannot discriminate against you based on your genetic test results and family history, thanks to the Genetic Information Nondiscrimination Act, passed in 2008. However, it doesn't protect against life, disability, or long-term care insurance discrimination. Let's say you take a DTC genetic test that shows you're at an increased risk for Alzheimer's. It's possible that later, you could be denied life insurance or long-term-care coverage based on your results. (It's also a reason why Ann's name was changed for this story.) "I advise people to think about setting up these insurance plans before they decide to pursue DNA testing," says Kirkpatrick.

Let's say you're still curious about diving into your DNA. If you want to analyze your genes because you find it interesting, go for it, keeping the limitations and faults of the test in mind. Should your test reveal something you're concerned about, consider a consultation with a genetic counselor. (Visit nsgc.org to find one near you.) This kind of specialist has the training to communicate genetic information in an understandable way—something physicians aren't always prepared to do. And if you're on the fence about taking a test, a genetic counselor can walk you through the potential consequences before you take the plunge. This is especially important when your results could turn up indicators for diseases like Alzheimer's; the news could be profound, and there are a limited number of steps you can take to prevent the problem.

Truly concerned that you may carry a dire disease-causing defect? Skip the DIY option and go through a genetic counselor or physician to take a clinical test. These can turn up false positives too, but there's a key difference in what happens next, says Evans. As opposed to direct-to-consumer tests, if a clinical lab finds something serious in your genetic test, they will usually confirm it with backup technology rather than just trusting it at face value.

TOO SOON TO SAY

The bottom line: Even if DTC test results were accurate, the medical payoff would be questionable. "If I could determine that a patient indeed has an increased risk of diabetes, there's nothing I would do differently," says Evans. "I'd recommend that she eat right, stay active, and check sugar levels when she's older—but I'd do the same thing for a patient who didn't carry that added risk." In the future, our analysis and understanding of genetic results may reach a point where at-home tests reveal actual health revelations, Evans says—but it will likely be decades until the science is ready for that.

For now, experts say that if you honestly want to make a difference in your well-being, your money would be better spent in the produce aisle or on a great pair of walking shoes. And truthfully, gaining insight into your health doesn't need to cost a dime: "When it comes to something like type 2 diabetes, looking in the mirror is a stronger way to determine your risk than all your genes put together," says Janssens. If the reflection is a woman who is active and at a healthy weight, you're already on the right track. And—hello—you don't need a test to tell you that. ■



DR. OZ SAYS...
Genetic testing may be confusing for consumers, but it's a great tool for doctors. I'm excited about the potential for tapping our genes to help determine which medications individuals may respond to best, since our genetic makeup can influence the effectiveness of certain drugs, such as some used to fight depression or cancer. If you're interested in learning more, go through your physician rather than using a direct-to-consumer test.