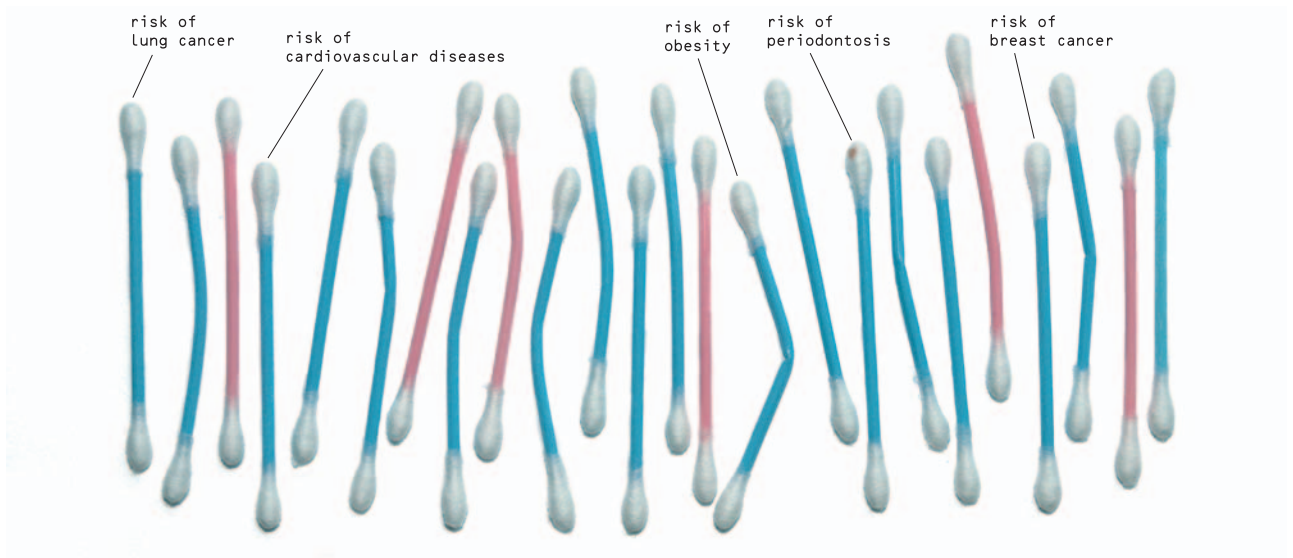


Do-it-yourself diagnosis

Despite apprehension and controversy, direct-to-consumer genetic tests are becoming more popular



Sandra Thomas is a trailblazer in the brave new world of genetic testing. Less than 5% of Americans have undergone a single genetic test, but the 56-year-old Florida woman has taken a dozen tests of the sort now available over the internet. Thomas is unmarried and has no children, but wanted to know if she has the mutation for haemochromatosis, the disease that killed her mother. Tests for two genes uncovered that she is a carrier of the potentially deadly but treatable iron-overload disease. The tests also gave Thomas a passion for genetic testing in general. She found she has genes that put her at an above-average risk for periodontal disease, which prompted her to improve her oral hygiene. The results of further tests, which she declined to name, have put her mind at ease about developing other serious conditions.

Some might consider Thomas a genetic-testing hypochondriac, but she maintained, "I'm just ahead of my time." Annette Taylor,

a molecular geneticist and founder of Kimball Genetics (Denver, CO, USA), which runs genetics tests for major reference labs and now offers direct-to-consumer (DTC) testing, said, "Sandra is passionate about gathering information."

Testing for genetic disorders is becoming almost as easy as taking a home pregnancy test. People can use their credit card to order a kit on the internet, use a brush to remove a few cheek cells, return the kit and receive a report via e-mail, often without involving their personal physicians. DTC tests cost from a few hundred to a few thousand US dollars, and are available for more than 800 conditions including breast and ovarian cancer, cystic fibrosis, coeliac disease, blood-clotting disorders, dyslipidaemia, fragile X syndrome, Tay-Sachs disease and narcolepsy.

Although apprehension over the ease of DTC genetic testing in the USA is only

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just developing, a major controversy erupted in the UK three years ago over 'home-brew' genetic tests. In 2002, the Human Genetics Commission, an advisory body to the UK Government, and the public interest group GeneWatch UK (Buxton, UK), expressed concerns about Sciona (Boulder, CO, USA), a company that offered DNA testing in well-known high-street shops. After consumers provided cheek cells and filled in a questionnaire, the company used the data to look for gene variants that affected an individual's response to food, medications and the environment. They then provided advice on what consumers should do to improve their health with diet and skincare, based on their genetic makeup.

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GeneWatch UK charged that Sciona's tests were misleading because most people need only to combine a balanced diet with exercise and no smoking to remain healthy. They also expressed concerns over the potential abuse of genetic information by insurers and employers, and worried that there were no laws to prevent the sale of genetic information or to prevent the patenting of genes without the customer's knowledge. Sciona subsequently changed some of its practices and pledged to destroy its database but retailers distanced themselves from the tests.

The Human Genetics Commission investigated further and although it stopped short of recommending a ban on genetic testing without the involvement of a physician, it did call for stricter regulation. The Commission was especially critical of genetic tests at home or tests that involve home sampling (Human Genetics Commission, 2003). Their report criticized that "...most genetic tests that provide predictive health information should not be offered as direct genetic tests." It suggested that testing be offered in the same way as medications: some dispensed through pharmacists, with low-risk tests dispensed through any shop. According to GeneWatch UK, the commission did not go far enough.

Although the controversy died down in the UK, the USA is now becoming a fertile ground for DTC genetic testing, as start-up companies such as DNA Direct (San Francisco, CA, USA), and established companies such as HealthCheckUSA (San Antonio, TX, USA) and Kimball Genetics, enter this new market. Sciona moved its headquarters to the USA in 2005 to be closer to its investors. The US population may be particularly ripe for DTC testing because it has a do-it-yourself ethic and is accustomed to marketed medicine and paying out of pocket for healthcare services.

Glenn McGee, Director of the New York Bioethics Institute at the Albany

Medical Center (NY, USA) and Editor-in-Chief of the *American Journal of Bioethics*, characterized the DTC genetic testing scene in the United States as "really the wild west." McGee, who also serves on the European Union's Genetic Testing Panel, said, "In the EU, they understand what it is to regulate testing. They've always regulated it, both on the research side and the clinical side. Of course, most [EU member states] have national healthcare so it's not so difficult for the same government who regulates one to use the rules on the other side. Here, it's catch as catch can. It's anarchy on genetic testing." He particularly criticized that regulation in the USA is so limited that "you could open up a genetic testing facility in a high-school lab as long as you satisfy the criteria for keeping it clean. The one federal rule is literally a 'washing your hands' rule; it doesn't pertain to accuracy." The US Food and Drug Administration (FDA; Rockville, MD, USA) only regulates four DTC genetic tests. All four are considered 'devices' and subject to regulation because they are manufactured by companies. The rest are considered 'home brews' because they are offered by individual academic or biotechnology laboratories rather than by a company.

Companies that offer genetic tests are enthusiastic about the prospects of widespread DTC testing. Holt Vaughan, President of HealthCheckUSA, argues that genetic testing is no different from non-DNA tests, such as those for C-reactive protein, homocysteine or sexually transmitted diseases. Vaughan, whose company offers 100 tests, including about a half dozen genetic tests, said, "What critics don't seem to grasp is, if it wasn't for a service like ours, people wouldn't get this testing done. In a perfect world, everybody could get an hour with their physician and the physician could run every test known to man. But that's just not the way our healthcare system is evolving right now."

Taylor contends there is an unwarranted fear of genetic tests owing to media reports about possible discrimination in

jobs or for insurance, as legislation in many states has prevented such prejudice. Kimball's customers receive detailed reports and the results are faxed to their personal physicians—for security reasons, results are not available online. Taylor estimates that 30%–50% of her customers call for genetic counselling after receiving a positive result. She maintained that when consumers decide to take a test on their own, it is "a great empowerment. If they want the test, we feel they should be able to get it."

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According to Ryan Phelan, founder and chief executive officer of DNA Direct, many people have been unable to avail themselves of the benefits of DTC genetic testing. This is due to a shortage of genetic counsellors and the fact that they are often concentrated in urban medical centres that specialize in prenatal care and paediatrics. The worldwide web has changed that: DNA Direct takes a family history and delivers results online, but also provides counselling when needed, meeting all state and federal regulations. Phelan added, "We have no interest in selling somebody a test if it's going to be of no use to them. And in fact, the truth is that a very high percentage of our customers, when they test, are carrying significant mutations. What it tells you is that the right people are testing."

Phelan cited a study showing that "in terms of imparting factual information, the Web was far superior. It's not surprising. Online, people can digest [the results] on their own. They can go back and look at it. They can review it over time and they're not being distracted by the personal one-on-one encounter of who's delivering the knowledge. The computer isn't responding to your anxiety." But she stressed that DNA Direct provides access to a human counsellor over the phone if needed.

Not everyone is thrilled about the ease with which consumers can take genetic tests. Ronald Bachman, Chief of Genetics for Kaiser Permanente Medical Group, which serves a 3.2 million member non-profit prepaid health plan in Oakland (CA, USA), said

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DTC genetic testing poses dangers to the public. "It's bad for medicine. You're letting individuals take into their own hands decisions that they're not really capable of. Patients may experience psychological harm in that they might not understand what the results mean to them." Bachman argues that a family pedigree prepared by a medical geneticist may prove to be more useful than undergoing testing.

Paul Billings, Senior Geneticist and Vice President for Biotechnology and Healthcare Strategy at Laboratory Corp. of America Holdings (Research Triangle Park, NC, USA), the second largest provider of genetic services in the world, also worries about the accuracy of some labs and their ability to provide consumers with good information. He cited an incident in which a university lab provided disconcerting results based on a test for BRCA, a gene involved in breast cancer. The woman tested underwent a prophylactic mastectomy, only to discover later that the test results were wrong. While some labs are ethical and provide adequate counselling, other labs are more motivated by profits and may offer only superficial counselling over the phone or the internet. Marketers must therefore make it clear that just because the patient has a gene does not mean they have the condition. Billing maintains that the impact of other factors, such as environment or other genes, in determining whether an individual develops a disease, should also be explained.

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Still, Billings is not closed to the idea of genetic testing: "Consumers aren't idiots. In fact, [DTC marketing] is an untapped resource in improving the quality of medicine." He said firms such as DNA Direct "allow [consumers] to act in a more educated manner with their physicians as advisors. I think that's a benefit to the healthcare system." Billings notes, however, that many physicians are ill-prepared to interpret genetic information: "There are a lot of doctors who are involved in this decision making who don't know what they're talking about and are less knowledgeable than some of the lay public."

The lack of regulation, especially in the internet era, has also opened the door to fraud. "People who are selling tests on the Web could be offering completely bogus tests and giving you information that could be very misleading and potentially harmful to you," commented Kathy Hudson, founding director of the Genetics and Public Policy Center at Johns Hopkins University (Washington, DC, USA). She referred to a site that offers genetic testing for "reward deficiency syndrome, which of course is not found in medical textbooks, nor is it taught routinely as a part of medical school curriculum because as far as I know it's made up. And reward deficiency syndrome includes being able to detect whether or not people have genetic predispositions to addictions including nicotine, alcohol, gambling and sex." However, Hudson agrees that many people are comfortable with the lack of regulation as long as a physician acts as a gatekeeper.

David Magnus, Director of the Center for Biomedical Ethics at Stanford University's School of Medicine (CA, USA), said, "On the whole, it's a scary time in medical genetics because of consumer advertising. One of the worries that a lot of us have is that we wouldn't want to see genetic testing go the way of full-body scans, where a lot of fly-by-night operations were set up. It really is one of those caveat emptor, 'let the buyer beware', situations." Magnus therefore argues for more governmental oversight: "Leaving it up to marketplace is not the optimal way to do medicine. It didn't work for whole-body scans. It's not going to work for genetic testing over the Web." He said clear standards are needed to define what testing is appropriate and cost-effective, which tests are good for certain populations, and which are reliable.

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Within this vacuum of regulation, professional groups, such as the American College of Medical Genetics (ACMG; Bethesda, MD, USA) and the American College of Obstetricians and Gynecologists (Washington, DC, USA), have stepped in to define voluntary standards. In 2004, ACMG's Board of Directors declared that

genetic tests are medical tests and "should be provided to the public only through the services of an appropriately qualified health care professional [who] should be responsible for both ordering and interpreting the genetic tests, as well as for pre-test and post-test counseling of individuals and families..." (ACMG, 2004). They noted that consumers ordering 'home testing' kits over the phone or the internet face potential harms, including the inappropriate use of tests, misinterpretation of results and lack of necessary follow-up.

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So what does the future hold for DTC genetic testing? In the USA, the lack of a national healthcare system, a strong consumer interest in health matters and the present lack of regulation provides an interesting basis for future development. Taylor does not expect widespread do-it-yourself screening for genetic disease in the years ahead, unless usable markers become available for common conditions, especially heart disease. But she predicts a growth in DTC genetic testing for pharmacogenetics, or personalized medicine to determine genes indicating whether certain medicines are best for patients based on their genotypes. "It's definitely coming. I'm definitely going in that direction," she said.

Futurist Andrew Zolli, founder of Z+ Partners, a think-tank in Brooklyn (NY, USA), believes genetic testing will develop into a robust market in ten years. "We have a huge ageing demographic in both Europe and the USA—'baby boomer' folks—and they're going to take a very active role in healthcare management," he said. "They will be turning to [DTC] genetic testing. It will catch on. No question about it. I fully expect that this kind of technology is going to be with us."

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