



PREAMBLE

Although the first draft of the human genome was unveiled less than a decade ago, genetic information is fast becoming integrated into the everyday flow of data that impacts not only human health but also influences personal lifestyle choice. The ubiquity of the Internet as a tool to access and disseminate this information and the number of test providers directly offering consumers everything from sophisticated medical diagnostics to personal ancestry research to dietary supplement profiles has raised both a sense of opportunity and one of caution with many stakeholders.

Among its primary missions, the Personalized Medicine Coalition (PMC) seeks to bring timely, accurate and pertinent reports to the public about the issues impacting the development of personalized and predictive health care. This *Consumer Guide to DNA-based Health Information Testing* is an important part of fulfilling that mandate.

This guide seeks to demystify genetic testing. It provides an overview of the types of genetic tests available to consumers and describes how these tests are obtained, how the results are analyzed and what the implications might be for the various types of tests. The guide also discusses issues that are fundamental to all types of genetic testing such as protecting the privacy of individuals and restricting access to personal genetic data.

The PMC hopes that this guide informs and enables consumers to make thoughtful choices when considering genetic tests whether they be for health care-related or other reasons. We also welcome comments on this guide and suggestions for its evolution and improvement.

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Consumer Guide to DNA-based Health Information Testing

Our genome is made up of little units or “letters” of DNA, commonly called A, C, G and T. These letters can be grouped into genes, which are your own personal “blueprint.” They influence how tall you are, your hair color, the tenor of your voice, even aspects of your personality. How your genes interact with each other, the environment you live in, and the lifestyle choices you make affect your risk to develop diseases. We have known for some time that certain rare diseases are inherited – that is, they are passed down from parents to children. Today, scientists are making exciting discoveries about how variations in our DNA may also be linked to many common diseases, such as cancer and diabetes.

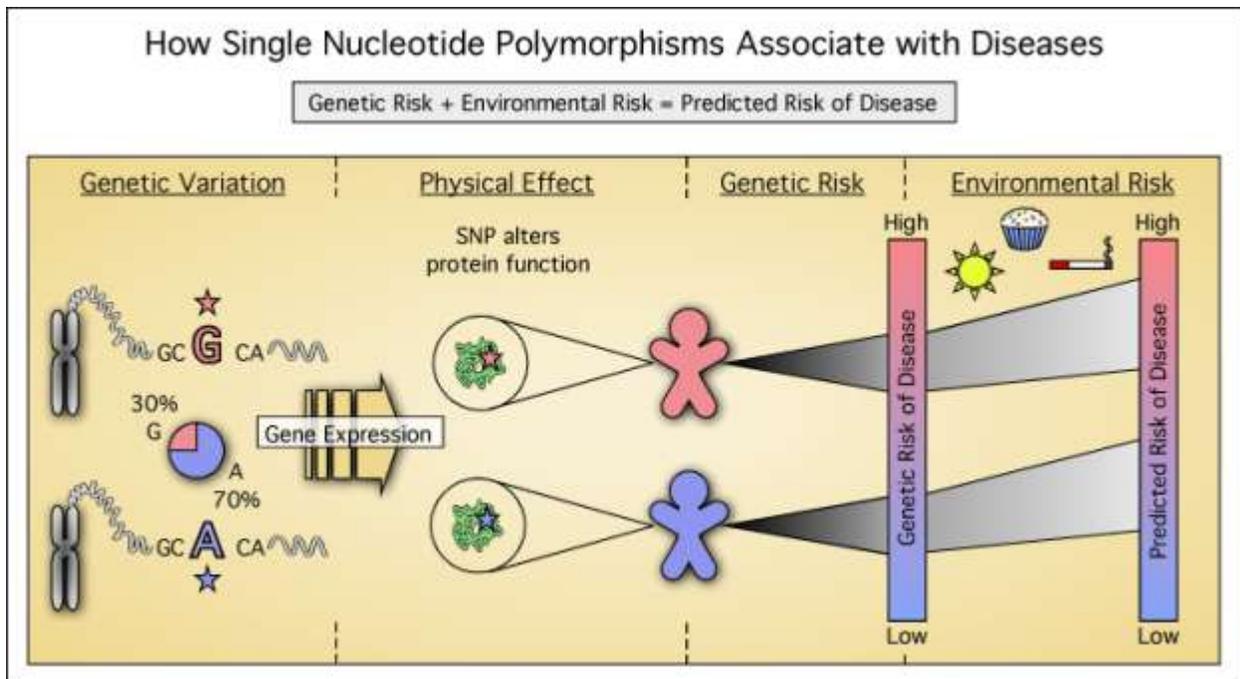
Advances in Genomic Medicine

The reason we differ from one another in appearance, likelihood of disease, and even personality is because we have inherited from our ancestors single-letter differences in our DNA – for instance, a G instead of a C. The single-letter differences are called **single nucleotide polymorphisms** or SNPs (pronounced "snips").

The Human Genome Project and other scientific advances have begun to uncover how variations in our DNA can affect our chance of developing certain diseases. There are some relatively rare genetic diseases that are caused by changes in a single gene (like cystic fibrosis or muscular dystrophy). But, most human diseases are called “**multifactorial**” because multiple factors are involved. Genetic and family history predispositions, environmental influences, and lifestyle behaviors (diet, exercise, smoking, etc.) contribute a **risk factor**, which healthcare providers use to inform medical decisions.

We are beginning to unravel the genetic component of such multifactorial diseases as breast cancer, Crohn’s Disease, diabetes, macular degeneration, prostate cancer, and many others. Since 2006, more than 100 genetic relationships have been discovered between SNPs and many common diseases¹ (see Table 1). Finding the relationship between a SNP and a disease is just the beginning. Much more research then has to be done before we understand how this information can be used for making medical decisions. The effect of a single SNP or gene may be small, but when combined with other genes, SNPs, or environmental factors, the overall effect may become significant (see box “How SNPs Associate with Diseases”). Although these relationships have been published in respected scientific journals, many of these new insights require additional research before they can be integrated into routine medical practice. The genetic and other risk factors that remain undiscovered may play a larger role than those currently known.

¹Topol, E.J., Murray, S.S., Frazer, K.A. The Genomics Gold Rush, *JAMA*, 2007, 298: 218-21



Types of Genetic Testing

Discoveries in “genomic medicine” have been translated into tests for more than 1,500 diseases and conditions.² These various tests may be classified by the type of information provided and how the person taking the test may use the results to make health and medical decisions. For the purpose of this guide, we separate genetic tests into either **medical** or **informational**, depending on how their test results can be used.

Medical Genetic Testing

A medical genetic test is usually ordered by a healthcare provider – like a doctor, nurse practitioner, or physician assistant. However, some medical genetic tests are available directly to consumers, through web- and phone-based companies. Most medical genetic test results will directly change your medical care and those changes are based on evidence gathered through clinical trials and other medical practice. Medical genetic tests may be used to:

- Diagnose a genetic disease.

Example: Finding changes, called mutations, in a single gene can diagnose such genetic disorders as familial hypercholesterolemia, muscular dystrophy, Huntington disease, and other single gene diseases.

- Assess the chance of having a child with certain genetic conditions.

Example: Some genetic conditions are particularly common in people whose ancestors come from specific areas of the world. People who carry these genetic conditions usually have no family history and no way to know that they carry a gene that could cause a

² www.genetests.org

genetic condition in their children – like cystic fibrosis, Tay-Sachs disease, or sickle cell anemia.

- Predict if a person may be more likely to have side effects or an abnormal response to a certain drug.

Example: Variations in some genes that direct drug metabolism can cause people to metabolize, or process, certain drugs faster or slower than usual. Knowing about these variations may help your doctor avoid drugs that may be problematic for you or choose the safest, most effective dose of a drug. Examples of drugs for which genetic testing is in the early stages of usage are blood thinners, psychiatric drugs, and certain types of cancer chemotherapies.

- Find an increased risk for a common disease.

Example: Some people have a very high risk of a common disease like breast, ovarian, or colon cancer – often at an earlier age than usual – because of a mutation in a single gene. The actual risk may depend on the disease and the gene mutation. Knowing about this very high risk increases the chance that the disease can either be prevented or caught early when the treatment options are best.

Informational Genetic Testing

More recently, researchers have explored how various SNPs are associated with the risk or likelihood that a person will develop a disease, have a specific trait, or react to medications. Most of these SNPs do not contribute very high risk factors, but instead predict smaller risk changes. A number of companies have emerged that offer consumers genetics tests (called genome-wide scans) of these SNPs, counseling services, and personalized interpretations of the results. Testing SNPs can provide information on **ancestry, lifestyle traits** (such as athletic ability, nutrition, eye color, or susceptibility to hair loss), and various **conditions with strong or suggested genetic components** (See Table 1). Because the relationships between the SNPs and a condition are recent discoveries, most healthcare providers may not be prepared to use the results of genome-wide scans to guide your health or medical care; thus, these tests are more informational than medical tests.

Currently, informational genetic testing tends to take place independent of the healthcare system and typically is ordered directly by the consumer over the telephone or through a website. As the results are returned to the consumer by a web-site, the testing is not incorporated into the consumer's medical record unless the consumer chooses to share this information with his/her healthcare provider.

Genetic Tests to provide ancestral information

In addition to studying the genetic basis for disease, scientists have compared the DNA from modern and ancient people in different areas of the world. Comparing our own DNA to those results provides information about where our ancestors originated and how they may have moved around the world. Some of these tests estimate how much of your genome was likely to come from ancient African, Asian, or European roots. Consumers can order these tests directly from the companies that offer them.

Table 1: Some Common Conditions Included in Informational Tests

abdominal aortic aneurysm	intracranial aneurysm
age-related macular degeneration	lactose intolerance
alcohol flush reaction	lung cancer
alpha-1 antitrypsin deficiency	lupus
Alzheimer's disease	malaria resistance
asthma	male pattern baldness
atrial fibrillation	multiple sclerosis
bitter taste perception	nicotine dependence
bladder cancer	obesity
blood-clotting disorders	osteoarthritis
breast cancer	peripheral arterial disease
celiac disease	prostate cancer
colorectal cancer	psoriasis
Crohn's disease	restless legs syndrome
exfoliation glaucoma	rheumatoid arthritis
glaucoma	sickle cell anemia
heart attack	type 1 diabetes
hemochromatosis	type 2 diabetes

The focus of this paper is to help you understand the implications of genetic testing, especially for informational testing. The following questions and answers will help inform your decision to initiate informational testing:

- How do I order a test?
- How do I submit a sample?
- Should I speak with a genetic counselor before ordering a test?
- How is DNA analyzed?
- How is the accuracy of DNA testing determined?
- How do I receive the results?
- What will the results look like?
- What actions are supported by the results?
- What privacy protections are in place?
- Can my results be used for additional research?
- Will my insurance pay for informational testing?

How do I order a test?

Typically, you can order the test you want from the company's website. To place your order online, you will need to give shipping and billing addresses and credit card information. With some companies, the ordering process requires a phone call, an email, or a genetic counseling session. In some cases, the test has to be ordered by a healthcare provider. If so, the company will most likely provide you with information and an order form to take to your healthcare provider.

Before sending off your DNA sample for testing, it is your responsibility to review all of the materials provided to you about the test. You should be required to sign a consent form or some type of agreement that states that you understand the benefits, limitations, and potential risks of undergoing testing. This consent or agreement might be in print, or it could be electronic via a website. If you have any questions, if feel that you need more information, or if you are not sure about the risks and benefits of the test, you should not send off your sample until your questions have been answered. It is your responsibility to feel comfortable with your level of understanding of the risks and potential benefits involved in the test.

How do I submit a sample?

Most DNA tests are done on DNA collected from a cheek swab or a saliva sample. Most companies will send you a sample collection kit. Some DNA tests need a larger amount of DNA than a cheek swab or saliva sample can collect, so they require a blood sample. Blood samples need to be drawn by a trained healthcare provider.

Should I speak with a genetic counselor before ordering a test?

Talking with a genetic counselor, either a company employee or a professional in your community, will help you understand the risks and benefits of proceeding with testing. Depending on the company, you may be able to talk with a genetic counselor before and/or after testing. Some companies require this genetic counseling before and/or after certain tests. Before you go ahead with any genetic testing, it is important that you have your questions

answered by a company employee or a qualified professional of your choice, such as your healthcare provider or a genetic counselor.

Genetic Counseling Before and After Testing

Genetic counselors are health professionals who have been specially trained to interpret genetic information and explain its significance to you and your family. Genetic counselors can work with you to identify genetic risks, discuss options in genetic testing, interpret test results, and review the options that are available for prevention, early detection, and diagnosis. These professionals follow a code of ethics that includes maintaining the highest levels of privacy and confidentiality. Genetic counselors can provide information and support both when you are deciding whether to have testing and when your results come back.

Genetic counselors work in a variety of healthcare settings. Some companies that provide genetic testing services include genetic counseling in their fees. Others help you locate a genetic counselor near you. If you would like to find a genetic counselor near where you live, you can search for one through the National Society of Genetic Counselors at www.nsgc.org.

How is DNA analyzed?

Advances in technology in the last 10 years have provided new techniques for analyzing DNA. There are two common techniques used in genetic testing: SNP-based analysis and full gene sequencing.

SNP-Based Analysis

SNPs are single letter changes in DNA. Scientists use SNPs as flags or markers for nearby genes that affect your health. One approach for genetic testing is to scan a person's genome to see if they have certain SNPs, and estimate that person's lifetime risk for medical conditions as compared to the general population. Most companies that offer testing services to consumers use SNP analysis tests. These companies do not test for the same SNPs, and they may not report the test results in the same way. However, there are efforts underway to make the test result information provided to consumers more comparable.

Full Gene Sequencing

Several companies analyze genes on a more detailed level. Instead of looking at SNPs, they will sequence the entire gene of interest letter-by-letter. These tests look for variations that can be linked to the development of a certain disease. An example of full gene sequencing is the BRCA1 and BRCA2 gene test, which looks for an inherited risk for breast and ovarian cancers.

How is the accuracy of DNA testing determined?

The accuracy of a test is determined by three things:

- **analytical validity:** does it detect what it is supposed to detect?
- **clinical validity:** does it detect information that is known to be associated with a specific disease?
- **clinical utility:** how useful is the information to improve health outcomes?

Analytical validity looks at the laboratory methods and makes sure that the lab is testing exactly what it claims to be testing. The Clinical Laboratory Improvement Amendments passed by the US Congress in 1988 (CLIA) require inspections of all clinical laboratories to ensure they meet quality standards. For example, if a DNA sequence is A-C-T-G, the genetic tests run by that lab correctly identify DNA sequences as A-C-T-G and not A-T-T-G. Not all genetic testing is conducted in CLIA-certified laboratories, so it is important to know whether the company you are considering uses such a laboratory.

Clinical validity is based on research studies that show the relationship between the genes or SNPs and specific diseases or traits. As more research is done and the studies are duplicated by other scientists in different groups of patients, the clinical validity improves. Because research is always taking place, the clinical validity of a gene or SNP can change over time. Some companies will only provide results on tests that have high clinical validity, while others will report all results with a disclaimer that clinical validity is low due to limited research.

The measure of *clinical utility* is more subjective, as each person may find different meaning depending on their current health status, desire for information, and values and beliefs. For medical test results, there often are guidelines for medical professionals on how to use this information. For informational testing, the usefulness of the information will mostly be determined by you.

How do I receive the results?

Your genetic test results can come in many forms. If your healthcare provider ordered the test, they will receive the results, interpret them, and communicate them to you. If you ordered the test, you will receive the results directly, by mail, phone, email, or an online account. Some companies give you with the opportunity to review your results with a genetic counselor at a time of your choosing, for example, when you first receive them or at some time after you have reviewed your results.

What will the results look like?

Many genetic test results do not provide yes or no answers. Most provide you with an estimated risk of developing a disease and thus, you will find some uncertainty with your results. You may receive information about:

- Your estimated lifetime risk for each condition being tested and whether you have an increased, average, or below average risk of developing a specific condition during your lifetime based on your genetic data (this risk can be calculated in several different ways), and
- How your genetic risk for each condition compares to other people in the general population.

For example, you might receive results stating that your risk of developing colon cancer is 3% greater than the average person, what is called the “general population risk” or “that your risk of developing Alzheimer’s disease is 6% lower than the general population risk.” Genetic risk factors are not guarantees that you will develop a condition, and in many cases, the presence of a particular SNP may only play a minor role in your risk for a disease, compared with environment and lifestyle factors.

If you have decided to be tested for the genetic risk for a particular condition (such as prostate cancer or type 2 diabetes), carefully consider the tests offered by different companies. Not all companies offer the same tests, and not all tests look for at the same SNPs or genes. You also should decide whether there are certain diseases for which you do not want to be tested. Some companies allow you to “opt out” of receiving those test results. For example, some people ask not to receive test results for a SNP that is associated with a risk for Alzheimer’s disease because there is not much you can do to prevent it.

Some companies provide ongoing updates, genetic counseling, or other professional services to keep you informed when future studies alter the significance of your test results. Testing companies will often provide information and tools to help you work with your primary healthcare provider, so that you can ask well-informed questions and make the most of the information you have. Some companies provide opportunities to participate in research studies (see below).

What actions are supported by the results?

Some people value any and all types of health information, even if there is no immediate action to be taken based on that information, and even if the information provides only probabilities rather than definitive diagnoses. Other people do not find risk information useful unless they can take concrete and immediate action to reduce their risk. Only you can determine whether such predictive information will be meaningful and useful to you.

One of the major reasons people select informational testing is to inform personal decisions to prevent disease. The following are examples of how informational genetic testing results may inform your interactions with a healthcare provider:

- If your test results show you are at an increased risk for developing colon cancer, you might ask your healthcare provider to recommend your first colonoscopy earlier than age 50, which is the general guideline.
- If you have an increased risk of developing type 2 diabetes, you might make changes in your diet and exercise habits, and ask your healthcare provider to help you develop a plan to watch for early symptoms of disease.
- If you have an increased risk for developing glaucoma, you might be more conscientious about scheduling an annual eye exam.

On the other hand, if you find that you are at equal or lower risk of developing a specific illness than the general population, this does not mean that you can forget the usual precautions. Remember that genetics, environmental, and other factors all work together to affect health. Regular checkups and a healthy lifestyle are very important regardless of your genetic risk factors. Everyone should eat a healthy diet, exercise, control high blood pressure, maintain a healthy weight, not smoke, and have routine checkups and screening (such as mammograms and colonoscopies).

The actions you take after receiving your results depend on the type of test you took and the information you learned. With medical tests, you may need to follow up with your healthcare provider to discuss preventative or other treatments. Unlike most medical tests, which tell you definitively whether you have a specific gene or disease, informational tests generally focus on what your risks are relative to the rest of the general public. With informational tests, the meaning of the results might change over time as more research is done on the relationship between the disease and SNPs. Thus, you may or may not choose to follow up with a healthcare provider right away. It is important to remember that the information and services provided by most companies do not constitute a “doctor-patient relationship” and are not intended as medical advice. You should be particularly cautious of companies that offer supplements tailored by your genome. As with any health-related decision, you should work with your healthcare provider to develop a personalized health management strategy for you, though your healthcare provider may have experience utilizing the risk factors derived from SNP testing.

What privacy protections are in place?

Your genetic information belongs to you. You should only disclose this information to people who have your best interests in mind. Most genetic testing companies have a privacy policy. Find out what it is. Typically these privacy policies will state that the testing company will not let any third party have access to any of your personal data, including your results, unless you specifically allow it. Third parties include insurance companies, health management organizations, hospitals, doctors, businesses, and government agencies.

You might decide to share your test results with your healthcare providers. Any genetic test results or other information you share with your healthcare provider may become part of your medical record.

Some companies might use your information for internal quality control procedures or for research. Make sure you understand what any other possible uses might be. Before testing,

make sure you agree to such uses and you are comfortable with the company's privacy protections.

Right now, most informational genetic testing happens outside of regular medical practice. So, these results are not protected by federal privacy protections for medical information, like the Health Insurance Portability and Accountability Act of 1996 (HIPAA). There currently is no unified or universally required set of regulations governing the genetic testing industry. As a result, you should find out if the company that you are considering provides information about its compliance with the following existing federal or state requirements and its adherence to professional best practices:

At the federal level:

- The Genetic Information Nondiscrimination Act of 2008 (GINA) protects consumers from discrimination by health insurers and employers on the basis of genetic information. However, it does not require that your insurer cover genetic tests and it does not stop insurers from adjusting your rates based on your current health status. In addition, GINA does not apply to life, disability, or long-term care insurance.
- The Federal Trade Commission (FTC) regulates the communications that genomic companies provide to consumers, such as guarding against false advertising or false claims. FTC issued a Consumer Alert in 2006 warning that "some of these tests lack scientific validity, and others provide medical results that are meaningful only in the context of a full medical evaluation."³

At the state level:

- Some states only allow a licensed physician to order tests. You will want to find out if that is the case in your state and if the testing service you are considering employs a licensed physician for that purpose.

At the professional level:

- Two professional organizations (the American Society of Human Genetics⁴ and the National Society of Genetic Counselors⁵) have issued guidelines about how to best provide direct-to-consumer genetic testing. While these guidelines are not binding, they are widely seen as critical standards to be followed by professionals.

Can my results be used for additional research?

The more information researchers gather about the relationships between DNA and disease, the more accurate and useful the test results can be. For this reason, some companies do their own research or work with other scientists to investigate the connections between genes and disease. If you test, you might be asked if you want to donate your DNA data to research. Before you do, find out if your identity will be protected and if there are any risks or potential benefits involved in participating.

³ <http://www.ftc.gov/bcp/edu/pubs/consumer/health/hea02.pdf>

⁴ http://www.ashg.org/pdf/dtc_statement.pdf

⁵ <http://www.nsgc.org/about/position.cfm#DTC>

In the United States, it is routine that research on humans is reviewed by an ethics board, called an Institutional Review Board (IRB). This review makes sure that your rights and welfare are protected. However, these reviews are not required for all research. Before participating in a research study, you may want to find out if it has been reviewed by an IRB. You should also be given a separate informed consent for research participation.

Will my insurance pay for informational testing?

In some cases, insurance will cover the cost of genetic tests, especially those that test for specific conditions and are ordered by your healthcare provider (medical tests). However, the majority of informational genetic tests are not currently covered by insurance. If you are interested in submitting the costs of your genetic test to your insurance provider, you should contact your provider beforehand to ask about coverage.

When considering genetic testing, you may consider these summary questions:

- ✓ What information do you hope to get and what would it mean at this point in your life?
 - ✓ Are the conditions being tested for important to you?
 - ✓ What is your motivation for testing - informational, recreational, or medical?
 - ✓ Will the test results increase stress and anxiety or peace of mind?
 - ✓ Will the test results help me make better health choices? Are there actions I can take to improve my health based on test results?
 - ✓ Does the company provide information about its test or laboratory methods and how it develops its test results?
 - ✓ Are the tests conducted in a CLIA-certified laboratory?
 - ✓ Does the company provide information I can use after testing? Will I have access to health information or updates on new information?
 - ✓ Does the company provide access to an appropriately trained health professional, such as a certified genetic counselor or a clinical geneticist?
 - ✓ Is the test covered by my insurance policy and if so, do I want my insurer to know the results of my test?
 - ✓ Will my results be kept private?
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