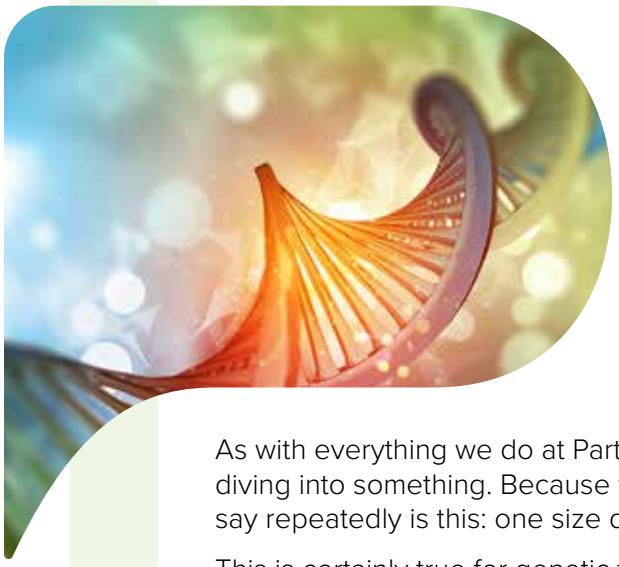
Genetic Testing

Understanding the Basics So You Can Make an Informed Decision

partnerMD



Genetic testing—it's a hot topic these days, showing up in headlines, late-night commercials, and your Facebook feed. At first blush, it sounds great. After all, why shouldn't we have our genes tested if we can?

As with everything we do at PartnerMD, we always research, reflect, and review before diving into something. Because when it comes to personal medicine, the one thing we say repeatedly is this: one size does not fit all.

This is certainly true for genetic testing.

So let's practice what we preach. Let's discuss the ins and outs of genetic testing, including what it is, the pros and cons, and the PartnerMD approach.

Genetics 101

First, a quick biology refresher. Please note that we're keeping this simple.

- Your body is made up of cells.
- Cells contain chromosomes.
- Chromosomes contain genes.
- Genes contain DNA.
- DNA provides specific instructions regarding the proteins your cells make.
- Proteins are the building blocks of life. Every part of your body—blood, bones, organs, hair, and so forth—has proteins.

You receive one set of genes from your mother. You receive another set from your father. In total, you could have anywhere from 20,000 to 30,000+ different genes. All of your genes combined are known as a "genome."

Sometimes genes have changes in the DNA known as "variants." What happens if genetic variants are present? Genetic variants might have:

- Little to no effect
- An unknown effect ("variants of uncertain significance" or VUS)
- Potentially adverse effects, meaning an increased risk for a certain disease or diseases

This is why doctors ask about your family's medical history. It all comes down to genes. So if your parents or grandparents have heart disease, for example, this could suggest you are at greater risk since you might have inherited a gene putting you at greater risk.

The key word here is "could."

> "Genetic testing is voluntary. Because testing has benefits as well as limitations and risks, the decision about whether to be tested is a personal and complex one."
>
> — NIH | Genetics Home Reference

Because you might not have inherited the gene putting you at greater risk. In fact, there might not even be a gene at play in this particular case, since other factors, like the environment (think toxins) or behavior (think diet) could be the culprits behind your family members' heart disease.

But what if you *could* see whether a gene had a variant? Wouldn't you want to get a test that tells you?

Which brings us to genetic testing.

What is genetic testing?

Genetic testing, also known as DNA testing, looks for variants in genes, chromosomes, and proteins.

As the National Institute of Health reports on its Genetics Home Reference page, "The results of a genetic test can confirm or rule out a suspected genetic condition or help determine a person's chance of developing or passing on a genetic disorder. More than 1,000 genetic tests are currently in use, and more are being developed."

In addition, some genetic tests can inform treatment protocols. For example, women with breast cancer often struggle with whether they should undergo chemotherapy. A 2018 study published in the New England Journal of Medicine "finds that many women with early-stage invasive breast cancer could safely forgo chemotherapy, if they score in the midrange or lower for risk that their cancer will recur, as measured by a commonly used genomic test."

Are there different types of tests?

Tests can look at one gene, a bunch of genes, or even a person's entire genome. All tests require DNA. How a test accesses the DNA often depends on the test itself and/or what is being tested. Blood tests and saliva tests are common (we've all seen cheek swabs done on episodes of Law & Order). Other fluids might be tested, such as amniotic fluid.

In addition, different types of tests exist, depending on the purpose. The Human Genome Project lists the following:

- **Diagnostic** – diagnoses the disease that's making a person sick;
- **Predictive** – determines whether a person is at increased risk for developing a certain disease;
- **Carrier** – helps determine whether a person carries a genetic variant; this is especially helpful for family planning purposes since "some diseases require a gene change to be inherited from both parents for the disease to occur";
- **Pre-natal** – screens the fetus during pregnancy;
- **Newborn** – screens infants for certain diseases affecting development;
- **Pharmacogenomic** – provides "information about how certain medicines are processed by an individual's body";
- **Research** – involves participants whose results can help further understanding, additional research, and treatments.

Where is genetic testing available?

Your medical doctor can order genetic testing, when appropriate. In fact, the American Medical Association's Code of Medical Ethics states, "Physicians should not encourage testing unless there is effective therapy available to prevent or ameliorate the condition tested for."

At PartnerMD, we agree with the AMA's directive. We recommend seeking actionable insights. Because of the complexity of issues surrounding this topic, this needs to be a thoughtful process in order to make sure it provides useful information.

In addition, physician-directed testing should include a referral to a certified genetic counselor (more on genetic counseling below) and come from high quality laboratories that produce reliable results.

"Direct-to-consumer" (DTC) tests are another type of genetic testing you've likely heard about, since they are widely available online. A recent study reports that the genetic testing market will be worth $22 billion by 2024. But DTC testing has many limitations and risks, so as with anything you purchase: buyer beware.

DTC companies often cite empowerment as a driving force behind its products—in other words, knowledge is power, and people have a right to know the information contained within their genes. While proponents point out other benefits of DTC tests, such as lower costs and wider availability, critics are rightly concerned about things like privacy issues, psychological ramifications, and the challenges that come from interpreting results, not to mention the accuracy of different tests—a seemingly impossible thing to measure, since there's little regulation.

As the Genetics Home Reference reports, "The most popular DTC genetic tests use genetic variations to make predictions about health, provide information about common traits, and offer clues about a person's ancestry. The number of companies providing DTC test kits is growing, along with the range of health conditions and traits covered by these tests."

About the Human Genome Project

The Human Genome Project (HGP) "was the international, collaborative research program whose goal was the complete mapping and understanding of all the genes of human beings."

Completed in April 2003, the HGP gave us the ability, for the first time, to read nature's complete genetic blueprint for building a human being.

The opportunity to use genomic information to improve health—genomic medicine—is a direct result of the Human Genome Project. The use of this information is called personalized medicine as it uses an individual's genetic information or profile to guide decisions about the prevention, diagnosis, and treatment of disease.

Advocates for genomic medicine cite the potential for significant health and economic benefit for patients and society by improving medical decision-making, delivery of appropriate therapies based on a patient's genotype rather than the general population, optimized disease prevention strategies, and reduced exposure to medications that have lower efficacy or the potential for greater toxicities.

Genetic experts caution, however, that while there are now over a 1,000 genetic tests available, the testing labs only need to prove that the test measures what it says it is measuring. There is no requirement that a test show clinical validity or clinical utility. While there are selective examples where specific biomarkers or genetic tests can help guide decision making, the issue remains that there is a lack of reliable biomarkers for most conditions and a lack of clear therapeutic alternatives based on genetic differences for many conditions.

Many of these DTC companies now provide health-testing ranging from cancer risks to Alzheimer's risk. They also offer testing for lifestyle genes that reportedly guide you in diet and exercise.

Here's the problem: The quality of current evidence to support the significance of these lifestyle genes is marginal, at best. At this time, there is currently little regulation of direct-to-consumer genetic testing services.

Can anyone interpret results?

Understanding the results of the test is essential, yet the results can be challenging to understand, even for medical doctors. In fact, the field of genetic counseling exists for this very reason, and this is precisely why PartnerMD recommends genetic counseling for anyone considering genetic testing.

The National Society of Genetic Counselors says, "Genetic counselors are healthcare professionals with unique specialized graduate degrees and experience in the areas of both medical genetics and counseling. Genetic counselors work as members of a healthcare team, providing risk assessment, education, and support to individuals and families at risk for, or diagnosed with, a variety of inherited conditions. Genetic counselors also interpret genetic testing, provide supportive counseling, and serve as patient advocates."

In addition, genetic counselors often specialize in specific areas. Cancer genetics and cardiovascular genetics are two examples.

Pros and Cons

What are the pros and cons of genetic testing?

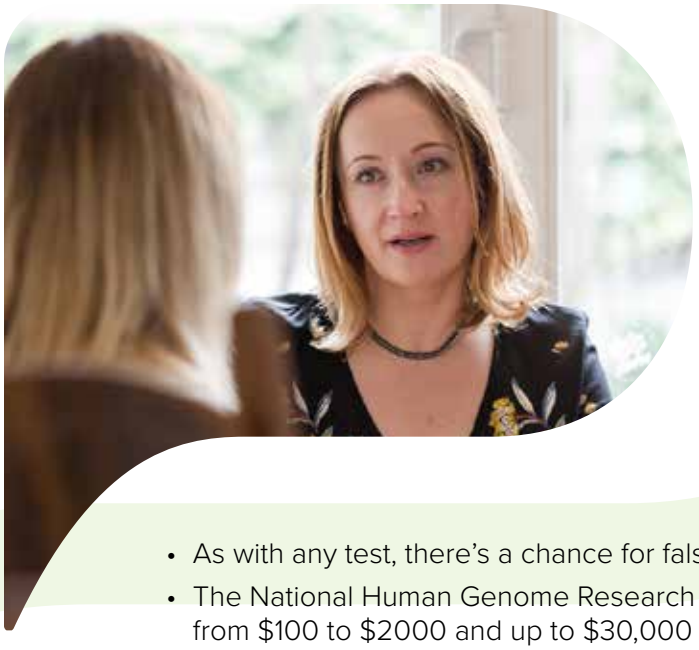
As noted earlier, while genetic testing does offer benefits, it also has risks and limitations. Let's consider the pros and cons.

Pros:

- If you already have a disease, understanding whether you have a genetic variant could inform treatment protocols.
- If you don't already have a disease, knowing you have a genetic variant for a particular disease could lead you to make positive lifestyle/behavioral changes to help lower the risk of getting that disease.
- Learning you do or don't have a genetic variant can often provide relief to the patient (the whole "fear of the unknown" concept).

Cons:

- A false test doesn't mean you won't get a certain disease; it simply means you don't have the genetic variant for that particular disease. Diseases have other causes, such as environmental and lifestyle, as previously mentioned.
- Knowing you're at greater risk for a disease doesn't automatically mean you will get the disease, but the knowledge can increase stress/anxiety in some people.
- There's also the risk of "genetic purgatory." You have a gene that's tested as "variant of unknown significance" or VUS, resulting in the mind game of "maybe it's bad, maybe it isn't." This can lead to mental anguish or worse—unnecessary medical interventions.



"Genetic testing can provide valuable information to support informed decision making about personal health risks and care options as well as reproductive choices. The fact that genetic information carries implications for others to whom the individual is biologically related raises ethical challenges of balancing confidentiality against the well-being of others."

— AMA Code of Medical Ethics Opinion 4.1.1

- As with any test, there's a chance for false-positives and false-negatives.
- The National Human Genome Research Institute notes that the cost of tests can range from $100 to $2000 and up to $30,000 for full genome mapping. As for health insurance coverage, that can vary as well, including partial coverage or complete coverage, depending on the test.
- Privacy concerns plague all of us in this Digital Age, and the same is true for genetic testing. Who controls the info? Who has access? According to the National Center for Biotechnology Information, the Health Insurance Portability and Accountability Act (HIPAA) "does not extend to DTC genetic testing companies."
- Ethical considerations are also at play. How will this info be used? Could it be used against you? The good news is that Congress enacted the Genetic Information Nondiscrimination Act (GINA) in 2008. This act prohibits employers and health insurance companies from using the results of your genetic tests to discriminate against you. But questions remain regarding other types of insurance, such as long-term care, life, and disability.
- Limitations exist with the tests themselves. They provide possibilities and insights, but not 100% percent certainty. A positive test doesn't mean you'll develop a disease, nor does it indicate how severe symptoms will be if you do.
- Qualified interpretation of results is essential. Direct-to-consumer kits can prove especially problematic for this reason.

Additional points to consider: Genetic testing can affect family dynamics in both potentially positive and negative ways. If family members are comfortable and/or open about sharing results from genetic tests, this information might help your physicians and your family members' physicians with treatment plans and overall health coaching. This would most definitely be a positive.

However, genetic testing can also create riffs—for example, if one person wants to know if they have a particular variant, but another family member doesn't. Or if one person discovers they have a genetic variant, but another family member discovers that they don't have the genetic variant. The family member without the genetic variant might experience survivor guilt.

And, finally, your genes have less influence on longevity than you might think. In fact, research shows "During the first 75 years of life, genes have a relatively small influence on longevity, accounting for only 20% to 25% of the reasons that you make it to that age. Not smoking, eating healthfully, getting plenty of exercise, and limiting alcohol matter the most."

Genetic Testing:
The PartnerMD Approach

PartnerMD believes that the highest level of care is individualized, personal, and based on our knowledge of you as a person.

Our first job is to listen and to understand you and then help guide you on your health journey. We believe in the delivery of evidenced-based, high quality medical care and treasure the trust our patients share with us. These same core principles guide us as we look to expand genetic testing at PartnerMD.

Types of genetic testing we recommend

We currently do genetic testing looking for specific conditions, such as hemochromatosis, which is a disease that causes iron deposition in tissues or in people whom we feel may have a hereditary clotting disorder. Your health insurance usually covers the cost of this type of genetic testing.

We also screen for hereditary diseases, including heart disease and cancers. In fact, we believe that the field of oncology has the best clinical evidence for the use of genetic testing currently. Genetic testing can identify high-risk individuals for hereditary cancers (BRCA genes are an example of this type of testing).

Genetic testing guides therapeutic options in many cancers. The oncology team usually manages this testing. There are broad panels of genetic tests that may include risks for cancers and heart disease, potential for drug metabolism issues, and other medical conditions. Insurance typically does not cover the cost of these tests.

Note: we recommend only clinically sound tests from reputable laboratories and pre- and post-testing counseling sessions with a certified genetic counselor.

Why we recommend genetic counseling before and after tests

In addition, we recommend genetic counseling pre-testing and post-testing. Before a test, you and your counselor will discuss motivations, possible outcomes, familial consequences, and so forth. After a test, your genetic counselor can help you make sense of the results—as well as your emotions surrounding the results.

At this time, we don't recommend genetic testing for everyone

We believe that a "one size fits all" mentality to genetic testing is ill advised. We feel the uniqueness and potential significance of genetic testing requires a thoughtful and individualized approach to testing. We see little value in genetic tests that do not allow you to take action to reduce or change your risk for a particular disease.

We welcome the opportunity to listen and understand your concerns and help guide you in determining if genetic testing may provide useful information to your care. We will continue to follow the recommendations of the leading experts in this rapidly changing genomic landscape to offer you the best in thoughtful and personal PartnerMD care.

Deciding If Genetic Testing Is Right For You: Questions to Ask

Q: What's my motivation for getting the genetic testing? General knowledge (about ancestry, for example)? To learn about potential risks for disease? To inform lifestyle? Something else?

Considerations: Many motivations can exist, and there's no one right or wrong answer here. But make sure you can answer this question, while also understanding genetic testing's limitations. For example, researching ancestry is a fun and popular pastime. So getting a test to help determine lineage can assist with this endeavor. If there's a history of a certain disease in your family, genetic testing could potentially provide insights. Again, the key word is "could." Genetic testing is one tool in a physician's toolbox. It's not a magic wand.

Q: Is there anything I would do differently with regard to treatment if I had this genetic information?

Considerations: While there are selective examples where specific biomarkers or genetic tests can help guide decision making, the issue remains that there is a lack of reliable biomarkers for most conditions and a lack of clear therapeutic alternatives based on genetic differences for many conditions. The test often cannot determine if a person will show symptoms of a disorder, how severe the symptoms will be, or whether the disorder will progress over time. Genetic testing will often report findings as "variations of unknown significance" (VUS), which means that we do not know if that particular genetic variation means anything important from a health standpoint to that individual or family members.

Q: Will I work with my doctor or buy my own kit?

Considerations: Keep in mind that direct-to-consumer (DTC) kits have very little regulations. Also, keep in mind that understanding test results can be challenging even among doctors, which is why the field of genetic counseling exists.

At PartnerMD, we help you determine if genetic testing is right for you, and, if it is, we introduce you to appropriate genetic counseling and use only the best testing and laboratories for that particular test.

Q: What are the chances for a false positive with this particular test?

Considerations: The National Institute of Health states the following on its Genetics Home Reference page: "Before undergoing genetic testing, it is important to be sure that the test is valid and useful. A genetic test is valid if it provides an accurate result. Two main measures of accuracy apply to genetic tests: analytical validity and clinical validity. Another measure of the quality of a genetic test is its usefulness, or clinical utility."

Q: How might I feel if I get a positive result on a certain test?

Considerations: While you can't know for sure how you're going to feel until you actually get the test results, it's worthwhile to reflect on how you might feel should a particular test come back as positive. For some, the knowledge might increase anxiety or stress. Even false tests can result in ambivalent feelings. Talking through the possibilities with a physician or genetic counselor can help prepare you for various outcomes.

Q: If testing is directly related to a problem my doctor and I are trying to solve, will insurance cover the genetic testing?

Considerations: Health insurance coverage varies. You might be responsible for some out-of-pocket expenses. Always check with your health insurance company prior to having a test so that there aren't any surprises.

Here's a roundup of helpful resources for further information:

National Institute of Health | Genetics Home Reference
National Society of Genetic Counselors
National Human Genome Research Institute
Genetic Information Nondiscrimination Act
Genetic Testing & Counseling: Code of Medical Ethics Opinion 4.1.1.

About PartnerMD

PartnerMD, a subsidiary of Markel Ventures Inc, is a concierge medical practice specializing in primary care and executive health. Founded in 2003, PartnerMD has offices in Virginia, Maryland, South Carolina, North Carolina, and Georgia. Learn more at PartnerMD.com.