Help Me Understand Genetics

Direct-to-Consumer Genetic Testing

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Direct-to-Consumer Genetic Testing

1 What is direct-to-consumer genetic testing?

Most of the time, genetic testing is done through healthcare providers such as physicians, nurse practitioners, or genetic counselors. Healthcare providers determine which test is needed, order the test from a laboratory, collect the DNA sample, send the DNA sample to the lab for testing and interpretation, and share the results with the patient. Often, a health insurance company covers part or all of the cost of testing. This type of testing is known as clinical genetic testing.

Direct-to-consumer genetic testing is different: these genetic tests are marketed directly to customers via television, radio, print advertisements, or the Internet, and the tests can be bought online or in stores. After purchasing a test kit, customers send the company a DNA sample and receive their results directly from a secure website or app or in a written report. Direct-to-consumer genetic testing provides people access to their genetic information without necessarily involving a healthcare provider or health insurance company in the process.

Many companies currently offer direct-to-consumer genetic tests for a variety of purposes. The most popular tests use a limited set of genetic variations to make predictions about a certain aspects of health, provide information about common traits, and offer clues about a person's ancestry. The number of companies providing direct-to-consumer genetic testing is growing, along with the range of health information provided by these tests. Because there is currently little regulation of direct-to-consumer genetic testing services, it is important to assess the quality of available services before pursuing any testing.

Other names for direct-to-consumer genetic testing include DTC genetic testing, direct-access genetic testing, at-home genetic testing, and home DNA testing. Ancestry testing (also called genealogy testing) is also considered a form of direct-to-consumer genetic testing.

For more information about direct-to-consumer genetic testing:

Centers for Disease Control and Prevention (CDC) Genomics and Health Impact Blog: Direct to Consumer Genetic Testing: Think Before You Spit, 2017 Edition! (https://blogs.cdc.gov/genomics/2017/04/18/direct-to-consumer-2/)

National Human Genome Research Institute: Direct-to-Consumer Genomic Testing (https://www.genome.gov/dna-day/15-ways/direct-to-consumer-genomic-testing)

National Society of Genetic Counselors: What is At-Home Genetic Testing? (https://www.aboutgeneticcounselors.org/Reasons-to-See-a-Genetic-Counselor/At-Home-Genetic-Testing)

American Medical Association: Direct-to-Consumer Genetic Testing (https://www.ama-a

ssn.org/delivering-care/precision-medicine/direct-consumer-genetic-testing)

The Federal Trade Commission: Direct to Consumer Genetic Tests (https://www.consumer.ftc.gov/articles/0166-direct-consumer-genetic-tests)

Genes in Life: Direct-to-Consumer Genetic Testing (http://www.genesinlife.org/testing-services/testing-genetic-conditions/direct-consumer-genetic-testing)

Johns Hopkins Medicine: Five Things to Know about Direct-to-Consumer Genetic Tests (https://www.hopkinsmedicine.org/news/articles/five-things-to-know-about-direct-to-consumer-genetic-tests)

2 What kinds of direct-to-consumer genetic tests are available?

With direct-to-consumer genetic testing companies offering a variety of tests, it can be challenging to determine which tests will be most informative and helpful to you. When considering testing, think about what you hope to get out of the test. Some direct-to-consumer genetic tests are very specific (such as paternity tests), while other services provide a broad range of health, ancestry, and lifestyle information.

Major types of direct-to-consumer genetic tests include:

Disease risk and health

The results of these tests estimate your genetic risk of developing several common diseases that are caused by environmental factors and multiple variants in several genes. These common diseases include such as celiac disease, Parkinson's disease, and Alzheimer's disease. Some companies also include a person’s carrier status for less common conditions, including cystic fibrosis and sickle cell disease. A carrier is someone who has a gene variant in one copy of the gene that, when present in both copies of the gene, causes a genetic disorder. The tests may also look for certain genetic variations that could be related to other health-related traits, such as weight and metabolism (how a person’s body converts the nutrients from food into energy). These tests may also provide information about how a person may respond to certain drugs (pharmacogenomics).

Ancestry or genealogy

The results of these tests provide clues about where a person's ancestors might have come from, their ethnicity, and genetic connections between families. For more information, see What is genetic ancestry testing?

Kinship

The results of these tests can indicate whether tested individuals are biologically related to one another. For example, kinship testing can establish whether one person is the biological father of another (paternity testing).

Lifestyle

The results of these tests claim to provide information about lifestyle factors, such as nutrition, fitness, weight loss, skincare, sleep, and even your wine preferences, based on variations in your DNA. Many of the companies that offer this kind of testing also sell services, products, or programs that they customize on the basis of your test results.

Before choosing a direct-to-consumer genetic test, find out what kinds of health, ancestry, or other information will be reported to you. Most direct-to-consumer genetic tests do not sequence whole genes, but look at only a subset of variants within the

genes associated with the conditions or traits they report on. For more comprehensive genetic testing, see a genetics professional. Think about whether there is any information you would rather not know. In some cases, you can decline to find out specific information if you tell the company before it delivers your results.

Learn more about the available types of direct-to-consumer genetic testing:

National Society of Genetic Counselors: What is At-Home Genetic Testing? (https://www.aboutgeneticcounselors.org/Reasons-to-See-a-Genetic-Counselor/At-Home-Genetic-Testing)

GeneReviews: Resources for Genetics Professionals--Direct-to-Consumer Genetic Testing (https://www.ncbi.nlm.nih.gov/books/NBK542335/)

Applied & Translational Genomics (free full-text via PubMed Central): Only a click away — DTC genetics for ancestry, health, love…and more: A view of the business and regulatory landscape (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4796702/)

Stanford at the Tech: Kinship Testing (https://genetics.thetech.org/ask-a-geneticist/best-half-sibling-dna-test)

3 What is genetic ancestry testing?

Genetic ancestry testing, or genetic genealogy, is a way for people interested in family history (genealogy) to go beyond what they can learn from relatives or from historical documentation. Examination of DNA variations can provide clues about where a person's ancestors might have come from and about relationships between families. Certain patterns of genetic variation are often shared among people of particular backgrounds. The more closely related two individuals, families, or populations are, the more patterns of variation they typically share.

Three types of genetic ancestry testing are commonly used for genealogy:

Y chromosome testing

Variations in the Y chromosome can be used to explore ancestry in the direct male line. Only individuals with a Y chromosome (typically males) can have this type of testing done. However, people interested in this type of genetic testing sometimes recruit a relative to have the test done. Because the Y chromosome is passed on in the same pattern as are family names (surnames) in many cultures, Y chromosome testing is often used to investigate questions such as whether two families with the same surname are related.

Mitochondrial DNA testing

This type of testing identifies genetic variations in mitochondrial DNA. Although most DNA is packaged in chromosomes within the cell nucleus, cell structures called mitochondria also have a small amount of their own DNA (known as mitochondrial DNA). Both males and females have mitochondrial DNA so this type of testing can be used by either sex. Mitochondria DNA is passed on solely from egg cells so it provides information about the direct female ancestral line. Mitochondrial DNA testing can be useful for genealogy because it preserves information about female ancestors that may be lost from the historical record because of the way surnames are often passed down.

Single nucleotide polymorphism testing

These tests evaluate large numbers of individual variations (single nucleotide polymorphisms or SNPs) across a person’s entire genome. The results are compared to similar SNPs in a testing database to provide an estimate of a person's ethnic background. For example, the pattern of SNPs might indicate that a person's ancestry is approximately 50 percent African, 25 percent European, 20 percent Asian, and 5 percent unknown. (Sometimes, more regional specificity can be provided.) Genealogists use this type of test because Y chromosome and mitochondrial DNA test results, which represent only single ancestral lines, do not capture the overall ancestral background of an individual.

Genetic ancestry testing has a number of limitations. Test providers compare individuals' test results to different databases of SNPs, so ethnicity estimates may not be

consistent from one provider to another. Additionally, these databases do not have equal coverage of SNPs for all ethnic populations; so results for minority populations may be nonspecific or inaccurate. Also, because most human populations have migrated many times throughout their history and mixed with nearby groups, ethnicity estimates based on genetic testing may differ from an individual's expectations. In ethnic groups with a smaller range of genetic variation due to the group's size and history, most members share many SNPs, and it may be difficult to distinguish people who have a relatively recent common ancestor, such as fourth cousins, from the group as a whole.

Genetic ancestry testing is offered by several companies and organizations. Most companies provide online forums and other services to allow people who have been tested to share and discuss their results with others, which may allow them to discover previously unknown relationships. On a larger scale, combined genetic ancestry test results from many people can be used by scientists to explore the history of populations as they arose, migrated, and mixed with other groups.

For more information about genetic ancestry testing:

The University of Utah provides video tutorials (https://learn.genetics.utah.edu/content/basics/molgen/) on molecular genealogy.

The International Society of Genetic Genealogy (https://isogg.org/) promotes the use of DNA testing in genealogy.

The National Human Genome Research Institute discusses human origins and ancestry (https://www.genome.gov/dna-day/15-ways/human-origins-ancestry).

The Tech Museum of Innovation provides information about how ancestry testing works (https://genetics.thetech.org/ask-a-geneticist/how-ancestry-tests-work).

The Smithsonian National Museum of Natural History's exhibit 'Genome: Unlocking Life's Code' discusses the difference between ancestry and race (https://www.unlockinglifescode.org/genomics-insights/ancestry-vs-race-implications-society). The exhibit also discusses the Great Human Migration (https://www.unlockinglifescode.org/genomics-insights/hominid-development-great-human-migration-and-concept-race) and its influence on heredity and genealogy.

4 What are the benefits and risks of direct-to-consumer genetic testing?

Direct-to-consumer genetic testing has both benefits and limitations, as they are somewhat different than those of genetic testing ordered by a healthcare provider.

Benefits

- Direct-to-consumer genetic testing promotes awareness of genetic diseases.
- It provides personalized information about your health, disease risk, and other traits.
- It may help you be more proactive about your health.
- It does not require approval from a healthcare provider or health insurance company.
- As results are provided directly to the individual, they are not in your insurance or medical record (unless you share results with your healthcare professional).
- It is often less expensive than genetic testing obtained through a healthcare provider, which can make testing more accessible to people with no or limited health insurance.
- DNA sample collection is usually simple and noninvasive, and results are available quickly.
- Your anonymous data is added to a large database that can be used to further medical research. Depending on the company, the database may represent up to several million participants.

Risks and limitations

- Tests may not be available for the health conditions or traits that interest you.
- This type of testing cannot tell definitively whether you will or will not get a particular disease. Results often need to be confirmed with genetic tests administered by a healthcare professional.
- The tests look only at a subset of variants within genes, so disease-causing variants can be missed.
- Unexpected information that you receive about your health, family relationships, or ancestry may be stressful or upsetting.
- As testing is done outside of a healthcare clinic, individuals often are not provided with genetic counseling or thorough informed consent.
- People may make important decisions about disease treatment or prevention based on inaccurate, incomplete, or misunderstood information from their test results.
- There is currently little oversight or regulation of testing companies.
- Unproven or invalid tests can be misleading. There may not be enough scientific evidence to link a particular genetic variation with a given disease or trait.
- Genetic privacy may be compromised if testing companies use your genetic

information in an unauthorized way or if your data is stolen.

- The results of genetic testing may impact your ability to obtain life, disability, or long-term care insurance.

Direct-to-consumer genetic testing provides only partial information about your health. Other genetic and environmental factors, lifestyle choices, and family medical history also affect the likelihood of developing many disorders. These factors would be discussed during a consultation with a doctor or genetic counselor, but in many cases they are not addressed when using at-home genetic tests.

Learn more about the pros and cons of direct-to-consumer genetic testing:

National Human Genome Research Institute: Direct-to-Consumer Genetic Testing FAQ (https://www.genome.gov/For-Health-Professionals/Provider-Genomics-Education-Resources/Healthcare-Provider-Direct-to-Consumer-Genetic-Testing-FAQ)

Washington State Department of Health: Purchasing Genetic Testing- Buyers Beware! (https://www.doh.wa.gov/YouandYourFamily/InfantsandChildren/HealthandSafety/GeneticServices/PurchasingGeneticTestingBuyersBeware)

GeneReviews: Resources for Genetics Professionals--Direct-to-Consumer Genetic Testing (https://www.ncbi.nlm.nih.gov/books/NBK542335/#dtc_testing.Advantages)

Yale Medicine: Is an At-Home DNA Test an Ideal Gift, Really? (https://www.yalemedicine.org/stories/at-home-genetic-test-kit-holiday-gift/)

American College of Medical Genetics and Genomics (ACMG): Position statement on direct-to-consumer genetic testing (https://www.acmg.net/docs/ACMG%20Revised%20DTC%20Statement%20AOP%20Dec%202015.pdf)

5 How do I choose a direct-to-consumer genetic testing company?

If you are interested in direct-to-consumer genetic testing, do some research into the companies that offer these services. Questions that can help you assess the quality and credibility of a testing company include:

- Does the company's website appear professional? Do they have an app? Are both secure? Does the company provide adequate information about the services it offers, including sample reports, pricing, and methodology?
- Does the company have experienced genetics professionals, such as medical geneticists and genetic counselors, on its staff? Does the company offer consultation with a genetics professional if you have questions about your test results?
- Does the company explain which genetic variations it is testing for? Does it include the scientific evidence linking those variations with a particular disease or trait? Are the limitations of the test and the interpretation of results made clear?
- What kind of laboratory does the genetic testing, and is the laboratory inside or outside the United States? Is the laboratory certified or accredited? For example, does the laboratory meet U.S. federal regulatory standards called the Clinical Laboratory Improvement Amendments (CLIA)? Is the test approved by the U.S. Food and Drug Administration (FDA)?
- Does the company indicate how it will protect your privacy and keep your genetic data safe? Does that information include both current privacy practices and what may happen to your genetic data in the future?
- Does the company indicate who will have access to your data and how it may be shared? Does it share or sell their customers' genetic data for research or other purposes? For some companies, much of their profit comes from selling large amounts of participant data for research and drug development, not from selling individual test kits.

Be sure to read and understand the "fine print" on the company's website before purchasing a direct-to-consumer genetic test. This detailed information, which is often called the "terms of use" or "terms of service," is a legally binding agreement between you and the company providing the testing. It spells out what is included and excluded in the service and details your rights and the company's responsibilities. If you still have questions, contact the company to get more information before you make a decision about testing.

More information about factors to consider when choosing a direct-to-consumer genetic testing company:

Harvard Law Bill of Health Blog: Considering Direct-to-Consumer Genetic Testing? Spit with Caution. (https://blog.petrieflom.law.harvard.edu/2017/12/21/considering-direct-to-consumer-genetic-testing-spit-with-caution/)

National Human Genome Research Institute: Regulation of Genetic Tests (https://www.

genome.gov/about-genomics/policy-issues/Regulation-of-Genetic-Tests)

Personal Genetics Education Project: What is Consumer Genetics? (https://pged.org/direct-to-consumer-genetic-testing/)

6 How is direct-to-consumer genetic testing done?

For most types of direct-to-consumer genetic testing, the process involves:

1. Purchasing a test

Test kits can be purchased online (and are shipped to your home) or at a store. The price of some test kits includes the analysis and interpretation, while in other cases this information is purchased separately.

2. Collecting the sample

Collection of the DNA sample usually involves spitting saliva into a tube or swabbing the inside of your cheek and putting that swab into a tube. You then mail the sample as directed by the company. In some cases, you will need to visit a health clinic to have blood drawn.

3. Analyzing the sample

A laboratory will analyze the sample to look for particular genetic variations. The variations included in the test depend on the purpose of the test.

4. Receiving results

In most cases, you will be able to access your results on a secure website or app. (You will likely need to create an account on the testing company website to access results.) Other test companies share results in the mail or over the phone. The results usually include interpretation of what specific genetic variations may mean for your health or ancestry. At some companies, you can request additional explanation from a genetic counselor or other healthcare provider. This additional service may or may not involve an extra cost. Some testing companies may update your results over time based on new scientific information, such as a new genetic variant associated with a trait on their test.

The test kit will include step-by-step instructions, so be sure you understand them before you begin. If you have questions, contact the company before collecting your sample.

Learn more about the direct-to-consumer genetic testing process:

National Society of Genetic Counselors: At-Home Genetic Testing (https://www.aboutgeneticcounselors.org/Reasons-to-See-a-Genetic-Counselor/At-Home-Genetic-Testing)

National Human Genome Research Institute: Direct-to-Consumer Genetic Testing FAQ (https://www.genome.gov/For-Health-Professionals/Provider-Genomics-Education-Resources/Healthcare-Provider-Direct-to-Consumer-Genetic-Testing-FAQ)

7 How much does direct-to-consumer genetic testing cost, and is it covered by health insurance?

The price of direct-to-consumer genetic testing ranges from under a hundred dollars to thousands dollars. The cost depends on how many genetic variations are analyzed (and it will cost more if whole genome or whole exome sequencing is used), how extensive the interpretation of results is, and whether other products, programs, or services are included. Some companies charge separately for the sample collection kit and the analysis, while others offer the sample collection and analysis as part of a package. In some cases, consultation with a healthcare professional (such as a genetic counselor) is included in the cost of testing; in others, it can be added for an additional fee. Before you proceed with testing, make sure you know the total cost for all of the results, support, and other services you expect to receive.

Direct-to-consumer genetic tests, even tests that provide information about health and disease risk, are not covered by most health insurance plans. Because this testing is done without a referral from a healthcare provider and is not considered “diagnostic” (that is, it cannot be used to diagnose any disease or condition), health insurance companies generally will not pay for it. However, the tests may be eligible for reimbursement through flexible spending accounts (FSA) or health spending accounts (HSA) if the testing included health information. If you decide to share your results with your healthcare provider and he or she recommends additional testing or management, that follow-up care may be covered by insurance.

Direct-to-consumer genetic tests that are unrelated (or indirectly related) to health, such as ancestry testing and paternity testing, are typically not covered by FSAs, HSAs, or health insurance plans.

Learn more about the costs of direct-to-consumer genetic testing:

MedlinePlus Genetics provides information about:

- What is the cost of genetic testing and how long does it take to get the results? (https://medlineplus.gov/genetics/understanding/testing/costresults/)
- Will health insurance cover the costs of genetic testing? (https://medlineplus.gov/genetics/understanding/testing/insurancecoverage/)

8 What do the results of direct-to-consumer genetic testing mean?

Direct-to-consumer genetic testing can provide interesting information about your health, traits, and ancestry. However, the results may not be clear-cut. Companies that provide these tests often tell their customers that the results are for information, education, and research purposes only—they are not meant to diagnose, prevent, or treat any disease or health condition. It is useful to keep this distinction in mind when interpreting your own test results.

Health and disease risk

The results of these genetic tests provide information about your chance of developing certain diseases (such as celiac disease or Parkinson's disease) and the likelihood that you have particular traits (such as dimples or lactose intolerance). These tests may also provide information about how a person may respond to certain drugs (pharmacogenomics). Test results are usually based on an analysis of one or more genetic variations that are known or suspected to be associated with the disease or trait. Direct-to-consumer genetic tests do not look at all genetic variants associated with diseases or traits.

The results of tests to predict disease risk do not provide a “yes or no” answer about whether a person will develop a given disease. Other factors, including genetic variations that were not tested, environmental factors, and lifestyle choices (such as diet and exercise) also contribute to disease risk in ways that may not be fully understood. Therefore, a result showing an increased risk does not mean you will definitely develop the disease, and a result showing a reduced risk does not mean you will never develop the disease.

Ancestry or genealogy

The results of these tests give clues about major geographic areas that are your family’s origins. These results are calculated on the basis of genetic variations that are more common in people from certain areas of the world than in others.

Sometimes the results of ancestry testing are unexpected or inconsistent with what a person understands about his or her family history. People who are closely related, such as siblings, may receive slightly different information about their ancestry because results are limited by the number and diversity of people who have submitted DNA samples to a given direct-to-consumer genetic testing company. It is important to be aware that receiving unexpected or ambiguous information about your background is a potential risk with this type of testing.

Kinship

The results of these tests give information about individuals who are likely related to you. (These individuals have also undergone testing, and the predictions are based on

similarities among DNA sequences.) These tests can uncover previously unknown information about biological relationships among people (such as paternity). It is important to be aware that receiving unexpected or ambiguous information about your background or family is a potential risk with this type of testing.

Lifestyle

In most cases, direct-to-consumer lifestyle tests assess genetic variations related to very specific traits, such as how your body converts the nutrients from food into energy (metabolism), day/night (circadian) rhythm, or the senses of taste and smell. The company may recommend specific diet or fitness programs, dietary supplements, skincare products, or other products and services on the basis of your results. However, in most cases the link between a given genetic variation and a complex trait like weight, athletic performance, or sleep is indirect or unknown. Therefore, the results of these tests can be challenging to interpret, and it can be difficult to predict whether a recommended product or service will be helpful to you.

If you have questions about the meaning of your test results, professional support (such as guidance from a genetic counselor) may be available from the company that provided the test. You can also share questions about your results with your own healthcare provider. Talk to your doctor before making any major changes in managing your health, diet, or fitness after you receive results of a direct-to-consumer genetic test.

Read more about the issues raised by direct-to-consumer genetic test results:

Kaiser Health News: My Grandmother Was Italian. Why Aren't My Genes Italian? (https://khn.org/news/my-grandmother-was-italian-why-arent-my-genes-italian/)

PLOS DNA Science Blog: DNA Testing Kits as Holiday Gifts Can Bring Surprises (https://dnascience.plos.org/2017/12/14/dna-testing-kits-as-holiday-gifts-can-bring-surprises/)

British Journal of Sports Medicine (free full text from PubMed Central): Direct-to-Consumer Genetic Testing for Predicting Sports Performance and Talent Identification: Consensus Statement (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4680136/)

Stanford at the Tech: Going From DNA to Health Risk (https://genetics.thetech.org/ask-a-geneticist/how-gwas-works)

Stanford at the Tech: Why Can't a Genetic Test Predict Whether I Will Get Type 2 Diabetes? (https://genetics.thetech.org/ask-a-geneticist/genetic-tests-imprecise-complex-disease)

9 What can raw data from a direct-to-consumer genetic test tell me?

In addition to providing various reports and analyses based on your genetics, some direct-to-consumer genetic testing companies make your raw data available to download. The raw data are your genotype—the particular A's, C's, T's, and G's of your DNA—extracted from the sample you provided. These data are unique to you. Most companies caution that the raw data are only for research or education and are not suitable for medical purposes, such as diagnosing a disease.

It is challenging to interpret raw genotype data on your own. To help with this, several online "third-party interpretation" services offer analysis and interpretation of the raw data collected by another company. Third-party interpretation services can potentially use your genetic data to provide you with more information about your disease risk, traits, and ancestry. However, these services also have some risks and limitations:

- Relatively often, test results indicate an increased risk of disease when your risk is not actually higher than that of the general population. These errors can cause stress and anxiety.
- The results may include unexpected or upsetting information about your disease risk or family relationships without any context or guidance.
- The raw data, once you download it and send it by e-mail or store it on your computer, is no longer protected by the original service's privacy measures.
- There is little regulation of third-party interpretation services.

As with any kind of genetic testing, it is important to assess the credibility of any company you are considering and find out how it protects your privacy before submitting your genetic information. Your healthcare provider can help you understand your results and determine whether any follow-up testing would be useful.

Learn more about the interpretation of raw genetic data:

KQED/NPR: You Can Transform Your Genetic Ancestry Data Into Health Info, But Your Results May Vary (https://www.kqed.org/science/18728/you-can-transform-your-genetic-ancestry-data-into-health-info-but-your-results-may-vary)

Futurity: Home DNA Tests Put Gene Experts in an Awkward Spot (https://www.futurity.org/home-dna-tests-1695142/)

Stanford at the Tech: Dangers of Converting Ancestry Data Into Health Data (https://genetics.thetech.org/ask-a-geneticist/dangers-converting-ancestry-data-health-data)

10 Can a direct-to-consumer genetic test tell me whether I will develop cancer?

While a direct-to-consumer genetic test can estimate your risk, it cannot tell you for certain whether you will or will not develop certain forms of cancer. Many other factors, including sex, age, diet and exercise, ethnic background, a history of previous cancer, hormonal and reproductive factors, and family history also contribute to a person's overall cancer risk.

The U.S. Food and Drug Administration (FDA) has allowed at least one direct-to-consumer genetic testing company, 23andMe, to offer a test for cancer risk. The test identifies specific genetic changes that are associated with particular cancers. For example, it looks for three specific genetic variants (also known as mutations) in two genes: *BRCA1* and *BRCA2*. These variants are associated with an increased risk of breast cancer, ovarian cancer, and potentially other forms of cancer in people of Ashkenazi (eastern European) Jewish ancestry.

Researchers estimate that 5 to 10 percent of all cancers run in families. Some of these cancers are associated with inherited mutations in particular genes, such as *BRCA1* or *BRCA2*. More than 1,000 variants in each of these genes have been associated with an increased risk of cancer. However, the FDA-approved direct-to-consumer genetic test analyzes only three of these genetic changes. The variants included in the test are much more common in people of Ashkenazi Jewish background than in people of other ethnicities, so if you are not of Ashkenazi Jewish heritage, the results may not be useful to you.

The test offered by 23andMe also looks for two variants in the *MUTYH* gene. These variants can cause a condition called MUTYH-associated polyposis (MAP; also known as autosomal recessive familial adenomatous polyposis). MAP greatly increases a person's risk of developing colorectal cancer, but it accounts for less than 1 percent of colorectal cancer cases. The two variants included in the test are the most common MAP-associated changes in people of European descent; however there are more than 100 variants in the *MUTYH* gene known to be associated with an increased risk of developing cancer.

Because the variants included in these tests are uncommon, most people will have a negative result. A negative result does not mean that you will never get cancer. Similarly, a positive result (one that indicates a cancer-related genetic variation) does not mean that you will definitely develop cancer.

Direct-to-consumer genetic testing for cancer risk can be stressful and anxiety-producing. Health professional organizations and patient advocacy groups strongly recommend that people considering genetic testing for cancer-associated gene variants, including those included in direct-to-consumer genetic tests, talk with a genetic counselor about the reasons they want to undergo testing and what the results could mean for their health.

Learn more about direct-to-consumer genetic testing for cancer risk:

U.S. Food and Drug Administration: FDA Authorizes, with Special Controls, Direct-to-Consumer Test that Reports Three Mutations in the BRCA Breast Cancer Genes (https://www.fda.gov/news-events/press-announcements/fda-authorizes-special-controls-direct-consumer-test-reports-three-mutations-brca-breast-cancer)

American Cancer Society: What to Know Before Buying a Home DNA Test (https://www.cancer.org/latest-news/what-to-know-before-buying-a-home-dna-test.html)

American Cancer Society: Should I Get Genetic Testing for Cancer Risk? (https://www.cancer.org/cancer/cancer-causes/genetics/should-i-get-genetic-testing-for-cancer-risk.html)

11 Can a direct-to-consumer genetic test tell me whether I will develop Alzheimer's disease?

While a direct-to-consumer genetic test can estimate your risk, it cannot tell you for certain whether you will or will not develop Alzheimer's disease. Variations in multiple genes, together with lifestyle factors such as diet and exercise, all play a role in determining a person’s risk.

The U.S. Food and Drug Administration (FDA) has allowed at least one direct-to-consumer genetic testing company, 23andMe, to offer a test for Alzheimer's disease risk. The test analyzes a gene called *APOE*. Certain variations in this gene are associated with the likelihood of developing late-onset Alzheimer's disease (the most common form of the condition, which begins after age 65). Specifically, the test allows you to find out how many copies (zero, one, or two) you have of a version of the gene called the e4 allele. People who have zero copies of the e4 allele have the same risk of late-onset Alzheimer's disease as the general population. The risk increases with the number of copies of the e4 allele, so people with one copy have an increased chance of developing the disease, and people with two copies have an even greater risk. However, many people who have one or two copies of the e4 allele never develop Alzheimer's disease, and many people with no copies of this allele ultimately get the disease.

Variations in the *APOE* gene are among many factors that influence a person’s overall risk of developing Alzheimer's disease. Variations in many other genes, which are not reported in the FDA-approved direct-to-consumer genetic test, also contribute to disease risk. Additionally, there are risk factors for Alzheimer's disease that have yet to be discovered. Therefore the *APOE* e4 allele represents only one piece of your overall Alzheimer's disease risk.

Currently, there are no effective approaches for preventing Alzheimer's disease, and while the disease can be treated, it has no cure. For these reasons, the National Institute on Aging and patient advocacy groups strongly recommend that people considering genetic testing for Alzheimer's disease, including direct-to-consumer genetic testing, talk with a doctor or genetic counselor about the reasons they want to undergo testing and how they would cope with the results.

Learn more about direct-to-consumer genetic testing for Alzheimer's disease:

U.S. Food and Drug Administration: FDA Allows Marketing of First Direct-to-Consumer Tests that Provide Genetic Risk Information for Certain Conditions (https://www.fda.gov/news-events/press-announcements/fda-allows-marketing-first-direct-consumer-tests-provide-genetic-risk-information-certain-conditions)

National Institute on Aging: Alzheimer’s Disease Genetics Fact Sheet (https://www.nia.nih.gov/health/alzheimers-disease-genetics-fact-sheet#testing)

Alzheimer’s Association: Genetic Testing (https://www.alz.org/media/Documents/alzheimers-dementia-genetic-testing-ts.pdf)

Alzheimer’s Society (UK): Genetics of Dementia: Genetic Testing (https://www.alzheimers.org.uk/about-dementia/risk-factors-and-prevention/types-genetic-testing)

12 What does it mean to have Neanderthal or Denisovan DNA?

Several direct-to-consumer genetic testing companies report how much DNA a person has inherited from prehistoric humans, such as Neanderthals and Denisovans. This information is generally reported as a percentage that suggests how much DNA an individual has inherited from these ancestors. The percentage of Neanderthal DNA in modern humans is zero or close to zero in people from African populations, and is about 1 to 2 percent in people of European or Asian background. The percentage of Denisovan DNA is highest in the Melanesian population (4 to 6 percent), lower in other Southeast Asian and Pacific Islander populations, and very low or undetectable elsewhere in the world.

Neanderthals were very early (archaic) humans who lived in Europe and Western Asia from about 400,000 years ago until they became extinct about 40,000 years ago. Denisovans are another population of early humans who lived in Asia and were distantly related to Neanderthals. (Much less is known about the Denisovans because scientists have uncovered fewer fossils of these ancient people.) The precise way that modern humans, Neanderthals, and Denisovans are related is still under study. However, research has shown that modern humans overlapped with Neanderthal and Denisovan populations for a period, and that they had children together (interbred). As a result, many people living today have a small amount of genetic material from these distant ancestors.

Scientists have sequenced Neanderthal and Denisovan genomes from fossils discovered in Europe and Asia. This genetic information is helping researchers learn more about these early humans. Determining which areas of the genome are shared with archaic humans, and which areas are different, will also help researchers find out what differentiates modern humans from our closest extinct relatives.

In addition to the percentage of Neanderthal or Denisovan DNA, direct to-consumer testing reports may include information about a few genetic variants inherited from these ancestors that influence specific traits. Some studies have suggested that certain genetic variations inherited from archaic humans may play roles in hair texture, height, sensitivity of the sense of smell, immune responses, adaptations to high altitude, and other characteristics in modern humans. These variations may also influence the risk of developing certain diseases. However, other studies have not found the same associations. The significance of Neanderthal or Denisovan genetic variants on disease risk is still an area of active study, and most direct-to-consumer test results currently do not include them.

While knowing how much DNA a person has in common with his or her Neanderthal or Denisovan ancestors may be interesting, these data do not provide practical information about a person’s current health or chances of developing particular diseases. Having more or less DNA in common with archaic humans says nothing about how “evolved” a person is, nor does it give any indication of strength or intelligence. For now, knowing which specific genetic variants a person inherited from Neanderthal or Denisovan

ancestors provides only limited information about a few physical traits.

Scientific journal articles for further reading

Meyer M, Kircher M, Gansauge MT, Li H, Racimo F, Mallick S, Schraiber JG, Jay F, Prüfer K, de Filippo C, Sudmant PH, Alkan C, Fu Q, Do R, Rohland N, Tandon A, Siebauer M, Green RE, Bryc K, Briggs AW, Stenzel U, Dabney J, Shendure J, Kitzman J, Hammer MF, Shunkov MV, Derevianko AP, Patterson N, Andrés AM, Eichler EE, Slatkin M, Reich D, Kelso J, Pääbo S. A high-coverage genome sequence from an archaic Denisovan individual. Science. 2012 Oct 12;338(6104):222-6. doi: 10.1126/science.1224344. Epub 2012 Aug 30. PubMed: 22936568; Free full-text article from PubMed Central: PMC3617501.

Pääbo S. The diverse origins of the human gene pool. Nat Rev Genet. 2015 Jun;16(6):313-4. doi: 10.1038/nrg3954. PubMed: 25982166.

Sankararaman S, Mallick S, Dannemann M, Prüfer K, Kelso J, Pääbo S, Patterson N, Reich D. The genomic landscape of Neanderthal ancestry in present-day humans. Nature. 2014 Mar 20;507(7492):354-7. doi: 10.1038/nature12961. Epub 2014 Jan 29. PubMed: 24476815. Free full-text article from PubMed Central: PMC4072735.

Skov L, Coll Macià M, Sveinbjörnsson G, Mafessoni F, Lucotte EA, Einarsdóttir MS, Jonsson H, Halldorsson B, Gudbjartsson DF, Helgason A, Schierup MH, Stefansson K. The nature of Neanderthal introgression revealed by 27,566 Icelandic genomes. Nature. 2020 Jun;582(7810):78-83. doi: 10.1038/s41586-020-2225-9. Epub 2020 Apr 22. PubMed: 32494067.

Learn more about the genetics of Neanderthals and Denisovans:

The Smithsonian's Human Origins Program provides information about the genetics of archaic humans and its relevance to modern humans:

- Homo neanderthalensis (https://humanorigins.si.edu/evidence/human-fossils/species/homo-neanderthalensis)
- Ancient DNA and Neanderthals (https://humanorigins.si.edu/evidence/genetics/ancient-dna-and-neanderthals)

A news release about the complete sequencing of the Neanderthal genome (https://www.genome.gov/27539119/2010-release-complete-neanderthal-genome-sequenced) is available from the National Human Genome Research Institute.

The Max Planck Institute for Evolutionary Anthropology provides information and data about the Denisovan genome (https://www.eva.mpg.de/genetics/genome-projects/denisova/index.html).

13 How do direct-to-consumer genetic testing companies protect their customers' privacy?

A person's genetic data represent personal, private health information. If you are considering direct-to-consumer genetic testing, it is important to know how the testing company will protect your information. In particular, you should know how the company will handle your sample (for example, saliva), how it plans to safeguard your data, and whether and how your data will be used for secondary purposes (such as research or advertising).

Most direct-to-consumer genetic testing companies provide detailed information on their websites about their privacy and security practices. This information may be included in a "privacy policy," "privacy statement," or "privacy center." Be sure to read, understand, and agree with this information before you start the testing process. If you have questions, contact the company to get more information.

Questions that can help you assess a company's privacy practices include:

- What does the company do with your sample once it has completed the analysis? Will the sample be stored, shared, sold, or destroyed?
- Once you take the test, who owns your genetic data?
- How does the company safeguard your genetic data and other personal information that you provide? Is it stored in a database that is protected from unauthorized access? What happens if the database is hacked or otherwise compromised?
- Can you delete your results from the company's database if you wish?
- Does the company use your information for internal research, advertising, or other secondary purposes?
- Will the company share your genetic data or sell it to pharmaceutical or biotechnology companies, academic institutions, or nonprofit organizations? If so, will the shared data include other information that could identify you (such as your name or date of birth)? For what purposes will your data be used? Will you be informed when your data are shared or sold?
- If you do not want your genetic data shared, sold, or used for research, can you opt out? What happens if you agree to share your information but want to opt out later?
- Will you be notified in the future if the company changes its privacy policies?
- What would happen to your sample and your genetic information if the company is sold or goes out of business?

In some cases, even if a testing service promises not to share your genetic information with others, they may be required by law to disclose the information to authorities in response to a warrant, court order, or other legal requirement. Many companies now provide explicit information about whether and how your genetic data may be accessed by law enforcement officials. If you upload your data to public databases, such as those administered by some third-party interpretation services, that information will be available to law enforcement. Be sure to read and understand how your data may be

accessed by authorities before you submit your sample. Because everyone shares genetic similarities with their relatives, it may have implications not only for your own privacy but for that of people who are related to you.

Scientific journal articles for further reading

Berkman BE, Miller WK, Grady C. Is It Ethical to Use Genealogy Data to Solve Crimes? Ann Intern Med. 2018 May 29. doi: 10.7326/M18-1348. [Epub ahead of print] PubMed: 29809242.

Ram N, Guerrini CJ, McGuire AL. Genealogy databases and the future of criminal investigation. Science. 2018 Jun 8;360(6393):1078-1079. doi:10.1126/science.aau1083. PubMed: 29880677.

Shen H, Ma J. Privacy Challenges of Genomic Big Data. Adv Exp Med Biol. 2017;1028: 139-148. doi: 10.1007/978-981-10-6041-0_8. Review. PubMed: 29058220.

Learn more about privacy issues related to direct-to-consumer genetic testing:

Coalition for Genetic Data Protection: Privacy Best Practices for Consumer Genetic Testing Services (https://fpf.org/wp-content/uploads/2018/07/Privacy-Best-Practices-for-Consumer-Genetic-Testing-Services-FINAL.pdf)

Moffitt Cancer Center: Do DNA Test Kits Put Your Privacy on the Line? (https://moffitt.org/endeavor/archive/do-dna-test-kits-put-your-privacy-on-the-line/)

Harvard Law Bill of Health Blog: Transparency and Direct-to-Consumer Genetic Testing Companies (https://blog.petrieflom.law.harvard.edu/2016/11/22/transparency-and-direct-to-consumer-genetic-testing-companies/)

The Hastings Center: Addressing Questions About DTC Genetic Tests and Privacy (https://www.thehastingscenter.org/addressing-questions-dtc-genetic-tests-privacy/)

Proceedings of the National Academy of Sciences: Study uncovers new privacy worries for direct-to-consumer DNA testing (https://www.pnas.org/post/journal-club/study-uncovers-new-privacy-worries-for-direct-to-consumer-dna-testing)

Personal Genetics Education Project: Genetics, Law Enforcement, and Crime (https://pged.org/genetics-and-crime/)

14 Can the results of direct-to-consumer genetic testing affect my ability to get insurance?

Passed in 2008, a federal law called the Genetic Information Nondiscrimination Act (GINA) made it illegal for health insurance providers in the United States to use genetic information in decisions about a person's health insurance eligibility or coverage. This means that health insurance companies cannot use the results of a direct-to-consumer genetic test (or any other genetic test) to deny coverage or require you to pay higher premiums. However, GINA does not apply when an employer has fewer than 15 employees.

GINA does not apply to other forms of insurance, such as disability insurance, long-term care insurance, or life insurance. However, some states have laws that cover these forms of insurance. Unless prohibited by state laws, companies that offer these policies have the right to request medical information, including the results of any genetic testing, when making decisions about coverage and rates. Some of these companies request information about genetic testing as part of their application process, but others do not. It is unclear whether genetic information, including the results of direct-to-consumer genetic testing, will become a standard part of the risk assessment that insurance companies undertake when making coverage decisions.

You should weigh the possible benefits and risks of direct-to-consumer genetic testing, including potential impacts on insurance eligibility and coverage, before you start the testing process.

Learn more about the implications of direct-to-consumer genetic testing in insurance coverage:

National Human Genome Research Institute: Genetic Discrimination (https://www.genome.gov/about-genomics/policy-issues/Genetic-Discrimination)

Genome Statute and Legislation Database (https://www.genome.gov/about-genomics/policy-issues/Genome-Statute-Legislation-Database)

Genetic Alliance: Genetic Discrimination (http://www.geneticalliance.org/advocacy/policyissues/geneticdiscrimination)

Wharton Public Policy Podcast: Why Genetic Testing Is a ‘Perfect Storm’ for Insurers (https://knowledge.wharton.upenn.edu/article/why-genetic-testing-is-a-perfect-storm-for-insurers/)

15 Where can I read more about the diseases and traits covered in my direct-to-consumer genetic testing report?

Learn more from MedlinePlus Genetics about some of the health conditions and traits that may be included in your report. Each plain-language summary provides information about the condition's major features, frequency, causes, and inheritance. You will also find links to other reputable sources of online health information.

Health conditions

BRCA1- or *BRCA2*-related breast cancer and ovarian cancer

Familial adenomatous polyposis, including MUTYH-associated polyposis

Age-related macular degeneration

Alpha-1 antitrypsin deficiency

Celiac disease

Familial hypercholesterolemia

Glucose-6-phosphate dehydrogenase deficiency, also called *G6PD* deficiency

Hereditary hemochromatosis

Transthyretin amyloidosis

Hereditary thrombophilia: prothrombin thrombophilia and factor V Leiden thrombophilia

Alzheimer's disease

Parkinson's disease

Wellness

Lactose intolerance

Traits

Cheek dimples

Eye color

Hair texture

Hair color (light or dark hair)

Carrier status

Autosomal recessive spastic ataxia of Charlevoix-Saguenay, also called ARSACS

Andermann syndrome, also called agenesis of the corpus callosum with peripheral neuropathy

Polycystic kidney disease

Beta thalassemia

Bloom syndrome

Canavan disease

PMM2-congenital disorder of glycosylation, also called *PMM2*-CDG

Cystic fibrosis

D-bifunctional protein deficiency

Dihydrolipoamide dehydrogenase deficiency

Familial dysautonomia

Congenital hyperinsulinism, also called familial hyperinsulinism

Familial Mediterranean fever

Fanconi anemia

GRACILE syndrome

Gaucher disease

Glycogen storage disease type I

Hereditary fructose intolerance

Junctional epidermolysis bullosa

Leigh syndrome

Limb-girdle muscular dystrophy

Medium-chain acyl-CoA dehydrogenase deficiency, also called MCAD deficiency

Maple syrup urine disease

Mucolipidosis type IV

CLN5 disease, also called neuronal ceroid lipofuscinosis (*CLN5*-related)

CLN1 disease, also called neuronal ceroid lipofuscinosis (*PPT1*-related)

Niemann-Pick disease

Nijmegen breakage syndrome

Nonsyndromic hearing loss

Pendred syndrome

Phenylketonuria

Primary hyperoxaluria

Pyruvate kinase deficiency

Rhizomelic chondrodysplasia punctata

Sialic acid storage disease, including Salla disease

Sickle cell disease, also called sickle cell anemia

Sjögren-Larsson syndrome

Tay-Sachs disease

Tyrosinemia

Usher syndrome

Zellweger spectrum disorder, also called Zellweger syndrome spectrum

Pharmacogenetics

CYP2C19 drug metabolism

For more help understanding your test results:

MedlinePlus Genetics provides information about:

- How can I find a genetics professional in my area? (https://medlineplus.gov/genetics/understanding/consult/findingprofessional/)
- What happens during a genetic consultation? (https://medlineplus.gov/genetics/understanding/consult/expectations/)