Overview

Scientific Details

Frequently Asked Questions



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Print

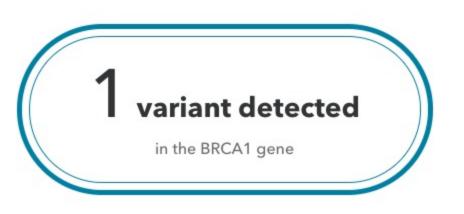
BRCA1/BRCA2 (Selected Variants)

Specific genetic variants in the BRCA1 and BRCA2 genes are associated with an increased risk of developing certain cancers, including breast cancer (in women and men) and ovarian cancer. These variants may also be associated with an increased risk for prostate cancer and certain other cancers. This test includes three genetic variants in the BRCA1 and BRCA2 genes that are most common in people of Ashkenazi Jewish descent.

play+5d4ef12c8b, you have a greatly increased risk of developing breast and ovarian cancer.

You have one of the three genetic variants we tested. Women with this variant have a much higher than average risk of developing breast and ovarian cancer. Risk for certain other cancers may also be increased.







Please share your result with a healthcare professional. It is important to confirm this result in a clinical setting before taking any medical action.

How To Use This Test

This test does not diagnose cancer or any other health conditions and should not be used to make medical decisions. Results should be confirmed in a clinical setting before taking any medical action.

Please talk to a healthcare professional about additional testing to confirm this result and to better understand your potential cancer risks.

Review the BRCA1/BRCA2 (Selected Variants)

tutorial

See Frequently Asked Questions

See Scientific Details for complete Indications for Use statement and full list of Warnings, Precautions, and Limitations

Intended Uses

- Tests for three specific genetic variants: the 185delAG and 5382insC variants in the BRCA1 gene and the 6174delT variant in the BRCA2 gene. These variants are associated with an increased risk of developing certain cancers.
- · Provides information on whether a person's genetic result is associated with an increased risk for breast and ovarian cancer and may be associated with an increased risk for prostate cancer and certain other cancers.

Limitations

- Does not test for all possible variants in the BRCA1 and BRCA2 genes. More than 1,000 variants in these genes are known to increase cancer risk. Only three of those variants are included in this test.
- Does not test for variants in other genes linked to hereditary cancers.

· The variants included in this test are most commonly found in people of

- . Does not account for non-genetic factors, like environment and lifestyle, that influence overall cancer risk.
- The interpretation of your genetic result depends on the sex you reported in your account settings.
- Important Ethnicities

Ashkenazi Jewish descent.

You have a greatly increased risk of developing breast and ovarian cancer based on your result.

It is important to talk with a healthcare professional about options for screening and prevention. It is also important to confirm this result in a clinical setting before taking any medical action.



We detected the 185delAG variant in the BRCA1 gene.

See Scientific Details

Estimates vary, but studies suggest that 45-85% of women with a BRCA1 variant develop breast cancer by age 70, and **39-46%** develop ovarian cancer.

This is much higher than the risk for women in the general population. Women with a BRCA1 variant who develop breast cancer also tend to do so at an earlier age, and they may develop ovarian cancer at an earlier age. They may also have an increased risk for certain other cancers. Exact risks depend on family history and other factors.

See Scientific Details





Since you share DNA with your family members, they may also wish to learn more about their cancer risk.

Your parents, siblings, and children each have a 50% chance of having the variant we detected. If you are thinking about sharing your results with family members, see this article for a discussion about things to consider before having the conversation. Genetic counselors can help your adult family members decide about genetic testing.

There are things you can do to reduce your risk for breast and ovarian cancer.

Women with a BRCA1 or BRCA2 variant have a greatly increased risk of developing breast and ovarian cancer. But there are options to consider to help manage your risk for these cancers, so it's important to talk with your doctor about your result. Genetic counseling can also help you understand your results and options. For more information about what to think about and possible next steps, see this help article.



Know your family history

Women with your genetic result who have a family history of breast or ovarian cancer have a higher risk of developing cancer than women without a family history. By knowing your family history, a healthcare professional can better assess your



Understand your options for screening and prevention

National guidelines recommend earlier and more frequent breast cancer screening for women with your genetic result, to help catch potential cancers at an early stage. However, there are currently no ovarian cancer screening tests that have been proven safe and effective. Your doctor can also explain options to reduce your risk for breast and ovarian cancer, which may include

surgery or medication.



Maintain a healthy lifestyle

In general, maintaining a healthy weight, engaging in physical activity, limiting alcohol consumption, and avoiding smoking can reduce the risk for breast and ovarian cancer. However, more research is needed to fully understand the impact of these and other lifestyle factors on cancer risk in women with your genetic result.

It is important to confirm your result in a clinical setting before taking any medical action.

See Scientific Details for more information

About BRCA1/BRCA2-Related Cancers

BRCA1 and BRCA2 variants are associated with an increased risk for several different cancers, including breast cancer (in women and men) and ovarian cancer. Variants in these genes may also be associated with an increased risk for prostate cancer, pancreatic cancer, and melanoma. The risk estimates below apply to BRCA1 and BRCA2 variants in general, including the three variants in this report.



Lifetime cancer risks

- Women with a BRCA1 variant have a 45-85% chance of developing breast cancer by age 70 and a 39-46% chance of developing ovarian cancer. They may also have an increased risk for pancreatic cancer.
- Women with a BRCA2 variant have a 45-85% chance of developing breast cancer by age 70 and a 10-27% chance of developing ovarian cancer. They may also have an increased risk for pancreatic cancer and melanoma.
- Men with a BRCA1 or BRCA2 variant have an increased risk for male breast cancer and may have an increased risk for prostate cancer, pancreatic cancer, and melanoma.
- See Scientific Details to learn more about these risks

When these cancers develop

In general, the chances of developing cancer increase as a person gets older. However, women with a BRCA1 or BRCA2 variant have an increased risk for early-onset breast cancer (before age 45) and multiple breast cancers. Women with a BRCA1 variant may also develop ovarian cancer at an earlier age. Men with a BRCA1 or BRCA2 variant may develop earlier and more aggressive prostate cancer.

Read more at: National Cancer Institute GeneReviews

How common are BRCA1 and BRCA2 variants?

About 1 in 400 people in the general population has a BRCA1 or BRCA2 variant linked to hereditary breast and ovarian cancer, although most of those variants are not included in this report. Among people of Ashkenazi Jewish descent, about 1 in 40 has a variant (usually one of the three variants in this report).



Screening and prevention

variant should be screened for breast cancer earlier and more often. However, there are currently no ovarian cancer screening tests that have been proven safe and effective. For women with a BRCA1 or BRCA2 variant, surgery and medication have been shown to be effective in reducing the risk of developing breast and ovarian cancer.

Guidelines recommend that women with a BRCA1 or BRCA2

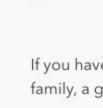
Men with a BRCA1 or BRCA2 variant should be screened for male breast cancer. Screening guidelines for prostate cancer vary.

Always consult with a healthcare professional before taking any medical action.

It is important to discuss this result with a healthcare professional.



It's important to consult with a healthcare professional to confirm your result and discuss options for cancer screening and prevention.



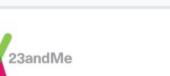
Print report

FAQs

If you have questions about your results or how they might affect you or your family, a genetic counselor may be able to help.



See our Frequently Asked Questions for more information.



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Help

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BRCA1/BRCA2 (Selected Variants) **Scientific Details**

Specific genetic variants in the BRCA1 and BRCA2 genes are associated with an increased risk of developing certain cancers, including breast cancer (in women and men) and ovarian cancer. These variants may also be associated with an increased risk for prostate cancer and certain other cancers. This test includes three genetic variants in the BRCA1 and BRCA2 genes that are most common in people of Ashkenazi Jewish descent.

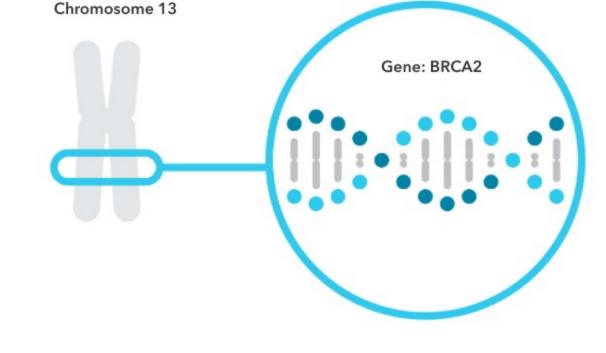
Genetic variants in the BRCA1 and BRCA2 genes are associated with an increased risk for certain hereditary cancers.

This report includes two variants in the BRCA1 gene and one variant in the BRCA2 gene. These three variants do not account for the majority of the BRCA1 and BRCA2 variants in the general population. More than 1,000 variants in these genes are known to increase cancer risk.

BRCA1 BRCA2

Like BRCA1, BRCA2 is a tumor suppressor gene. It contains instructions for making a protein that helps repair damaged DNA. Certain variants in the BRCA2 gene disrupt the protein's function. This can allow DNA errors to build up. These DNA errors can cause cells to grow and divide in an uncontrolled way, leading to cancer.

Read more at Genetics Home Reference



Print

You have one of the three genetic variants we tested.

<u>Variants</u> Detected			View All Tested Markers
Marker Tested	Genotype*		Additional Information
185delAG Gene: BRCA1 Marker: rs386833395	(-) <u>Variant copy from one</u> of your parents	Typical copy from your other parent	 Biological explanation Typical vs. variant DNA sequence(s) Percent of 23andMe customers with variant References [1, 12, 23, 36, 40, 42, 59, 60, 67, 97, 98, 103, 104, 116] ClinVar
This test cannot distinguish	customers with a <u>variant</u> may not which copy you received from w y impact how these variants are p	which parent. This test also can	ral population. not determine whether multiple <u>variants,</u> if detected, were inherited from only one parent or
23andMe always reports genotypes based on the 'positive' strand of the human genome reference sequence (build 37). Other sources sometimes report genotypes using the opposite strand.			

cases, these estimates represent a general risk for individuals with any BRCA1 or BRCA2 variant, not the specific risk estimates associated with the three variants in this report. This test does not take into account

This report provides risk estimates for several cancers associated with BRCA1 and BRCA2 variants. In most

Test Interpretation

non-genetic factors that influence a person's overall risk for these cancers. Lifetime risk

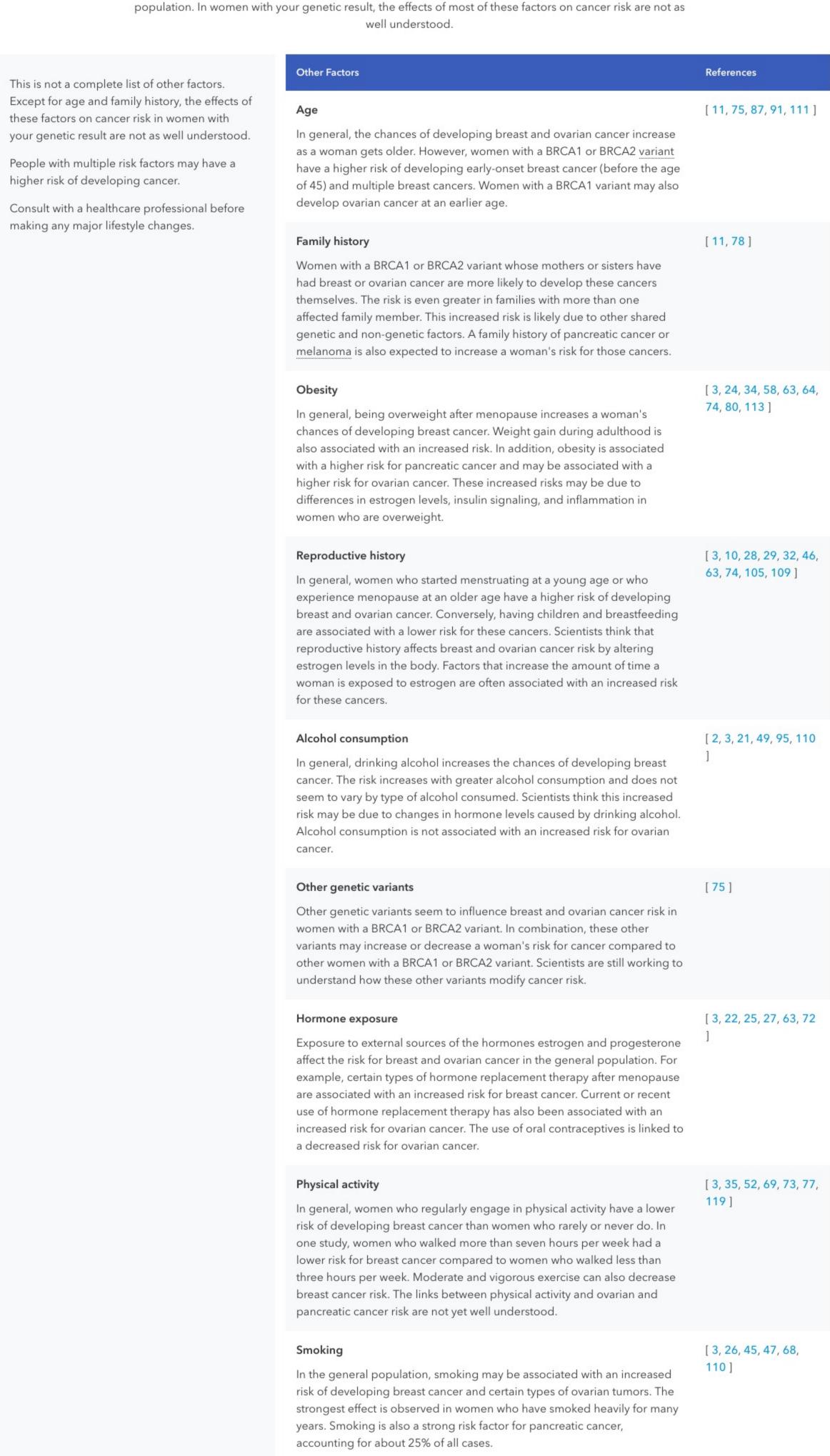
Risk by age Health Risk Estimates The risk estimates shown below represent the proportion of people expected to develop a given Risk estimates are based on clinical studies cancer during their lifetime. Estimates for the general population are based on observed cancers that identify an association between a among people in the United States. Estimates for men and women with a BRCA1 or BRCA2 variant are genotype and a health condition. based primarily on studies of people of European and Ashkenazi Jewish descent. Estimates for people with a BRCA1 or BRCA2 variant represent the risk of developing cancer by the age of 70 (for women) Numerical risk estimates are not available for or during their lifetime (for men). people who have both a BRCA1 and a BRCA2 variant. An interpretation of "increased risk" is provided to people with this result. It is likely **BRCA1** variant Cancer type General **BRCA2** variant that their risk is at least as high as the risk for population people with just one variant. More research is needed to understand the risk for people with 45-85% 12.4% 45-85% Breast (female) this result. 1.3% 39-46% 10-27% Ovarian For some cancers, numerical risk estimates are not available. 7-8% Breast (male) 0.12% 1-2% Consider talking to a healthcare professional if you have any concerns about your results. Prostate 11.6% May have an increased risk Increased risk 0 1.6% Pancreatic May have an increased risk May have an increased References [30, 54, 59, 61, 111, 112] 2.2% Melanoma Research ongoing May have an increased risk

well understood.

Other Factors

Many factors are known to influence the risk of developing breast and ovarian cancer in the general

See risk estimates by ethnicity for the general population

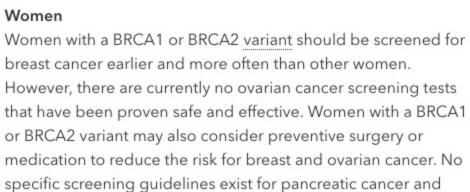


Cancer Screening and Prevention Guidelines

Cancer screening can help detect certain cancers at an earlier stage, when they may be more treatable. The guidelines below apply to people with a BRCA1 or BRCA2 variant. These guidelines may help you and your doctor decide on the best screening and prevention plan for you.

Men

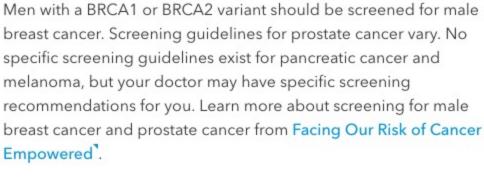
Empowered'.



melanoma, but your doctor may have specific screening

recommendations for you. Learn more about breast and ovarian

cancer screening and prevention options from Facing Our Risk of Cancer Empowered'. **Test Details** Indications for Use The 23andMe Personal Genome Service (PGS) uses qualitative genotyping to detect select clinically



relevant variants in genomic DNA isolated from human saliva collected from individuals ≥18 years with the Oragene Dx model OGD500.001 for the purpose of reporting and interpreting genetic health risks, including the 23andMe PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants). The 23andMe PGS Genetic Health Risk Report for BRCA1/BRCA2 (Selected Variants) is indicated for

[48, 50, 56, 57, 62, 71, 89, 93, 94, 108, 115, 116]

reporting of the 185delAG and 5382insC variants in the BRCA1 gene and the 6174delT variant in the BRCA2 gene. The report describes if a woman is at increased risk of developing breast and ovarian cancer, and if a man is at increased risk of developing breast cancer or may be at increased risk of developing prostate cancer. The three variants included in this report are most common in people of

Women

Ashkenazi Jewish descent and do not represent the majority of the BRCA1/BRCA2 variants in the general population. The test report does not describe a person's overall risk of developing any type of cancer, and the absence of a variant tested does not rule out the presence of other variants that may be cancer-related. This test is not a substitute for visits to a healthcare provider for recommended screenings or appropriate follow-up and should not be used to determine any treatments. **Special Considerations** Genetic testing for BRCA1 and BRCA2 variants in the general population is not currently recommended by any healthcare professional organizations. Cancer risk associated with a BRCA1 or BRCA2 variant varies from person to person. Exact risk depends on family history and other factors. **Test Performance Summary**

Clinical Performance

The variants included in this report represent a very small subset of all those associated with breast, ovarian, and prostate cancer. The three variants tested are associated with an increased risk of developing these cancers. However, some people who have these variants do not develop cancer. In addition, most cases of these cancers are not caused by inherited genetic variants.

This number is expected to be higher among individuals of Ashkenazi Jewish descent.

 The three variants in this report account for more than 90% of cancer-related BRCA1 and BRCA2 variants among people of Ashkenazi Jewish descent. These three variants account for a much smaller proportion of cancer-related BRCA1 and BRCA2 variants found in people of other ethnicities.

Approximately 5-10% of breast cancer cases, 10-15% of ovarian cancer cases, and 15-20% of male

breast cancer cases are known to be caused by inherited variants in the BRCA1 and BRCA2 genes.

this report. These three variants are much less common in people of other ethnicities. In 23andMe customers of other ethnicities, between 0% and 0.1% of individuals (up to 1 in 1,000) has one of the three variants in this report.

About 1 in 40 people of Ashkenazi Jewish descent is expected to have one of the three variants in

Analytical Performance

Accuracy was determined by comparing results from this test with results from sequencing. Greater than 99% of test results were correct. The 95% confidence interval was 83.9% to 100%. While unlikely, this test may provide false positive or false negative results. It is possible that the presence of certain mutations in your sample may interfere with the performance of this test. The effects of the interfering mutations on the performance of this test have not been studied. For more details on the analytical performance of this test, refer to the package insert.

confirmed in a clinical setting before taking any medical action. This test does not cover all variants that

Warnings, Precautions, and

This test does not diagnose cancer or any

determine your overall risk of developing

other health conditions and cannot

This test should not be used to make

medical decisions. Results should be

Limitations

cancer in the future.

hereditary cancers.

testing.

state of health.

could increase risk for cancer.* The absence of a variant tested does not rule out the presence of other genetic variants that may impact cancer risk.

· Other factors, such as environmental and

- lifestyle risk factors, may affect your risk of developing cancer. This test does not account for those factors, and does not test for variants in other genes linked to
- Your ethnicity may affect how relevant this test is for you. This test is intended to provide you with genetic information to inform conversations
- with your doctor or other healthcare professional. This device is not intended for prenatal
- presence of genetic variants that may impact response to medications. · This test is not intended to detect the presence of deterministic variants in

professional if you have any questions or concerns about your results or your current

· This test should not be used to assess the

- autosomal dominant diseases or conditions. This test is not a substitute for visits to a healthcare professional for recommended screenings. Consult with a healthcare
- Some people feel a little anxious after getting genetic health risk results. This is normal. If you feel very anxious, you should speak to your doctor or a genetic counselor.
- not be available on our genotyping platform, or may not pass our testing standards.

See the Package Insert for more details on use

* Variants not included in this test may be rare, may

and performance of this test.

References

early-onset breast cancer patients among Ashkenazi women." Am J Hum Genet. 60(3):505-14."

1. Abeliovich D et al. (1997). "The founder mutations 185delAG and 5382insC in BRCA1 and 6174delT in BRCA2 appear in 60% of ovarian cancer and 30% of

2. Allen NE et al. (2009). "Moderate alcohol intake and cancer incidence in women." J Natl Cancer Inst. 101(5):296-305."

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- 6. American Cancer Society. "Melanoma Skin Cancer." Retrieved March 5, 2018, from https://www.cancer.org/cancer/melanoma-skin-cancer.html." 7. American Cancer Society. "Ovarian Cancer." Retrieved March 5, 2018, from https://www.cancer.org/cancer/ovarian-cancer.html."

5. American Cancer Society. "Breast Cancer." Retrieved March 5, 2018, from https://www.cancer.org/cancer/breast-cancer.html."

10. Anderson KN et al. (2014). "Reproductive risk factors and breast cancer subtypes: a review of the literature." Breast Cancer Res Treat. 144(1):1-10." See all references V

8. American Cancer Society. "Pancreatic Cancer." Retrieved March 5, 2018, from https://www.cancer.org/cancer/pancreatic-cancer.html."

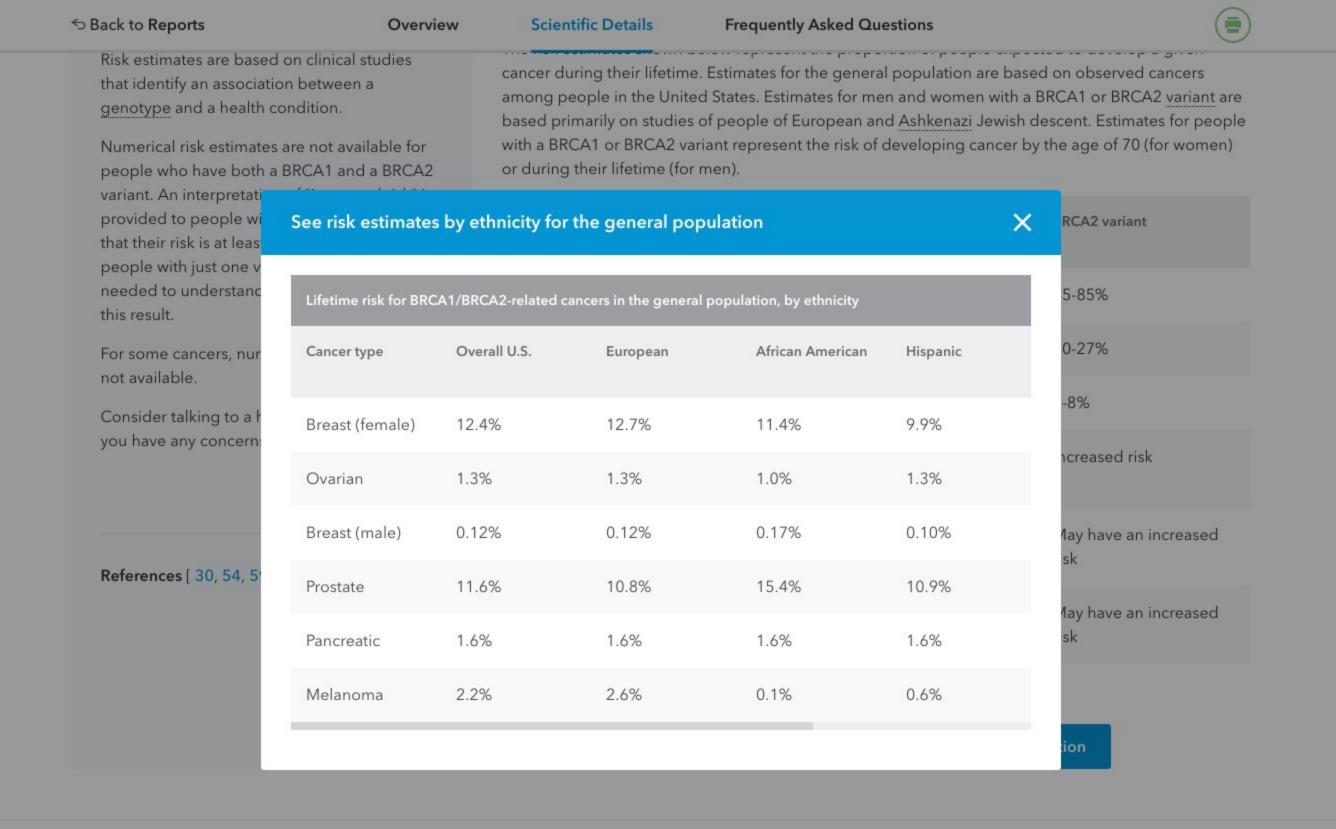
9. American Cancer Society. "Prostate Cancer." Retrieved March 5, 2018, from https://www.cancer.org/cancer/prostate-cancer.html."

Change Log

Your report may occasionally be updated based on new information. This Change Log describes updates and revisions to this report.

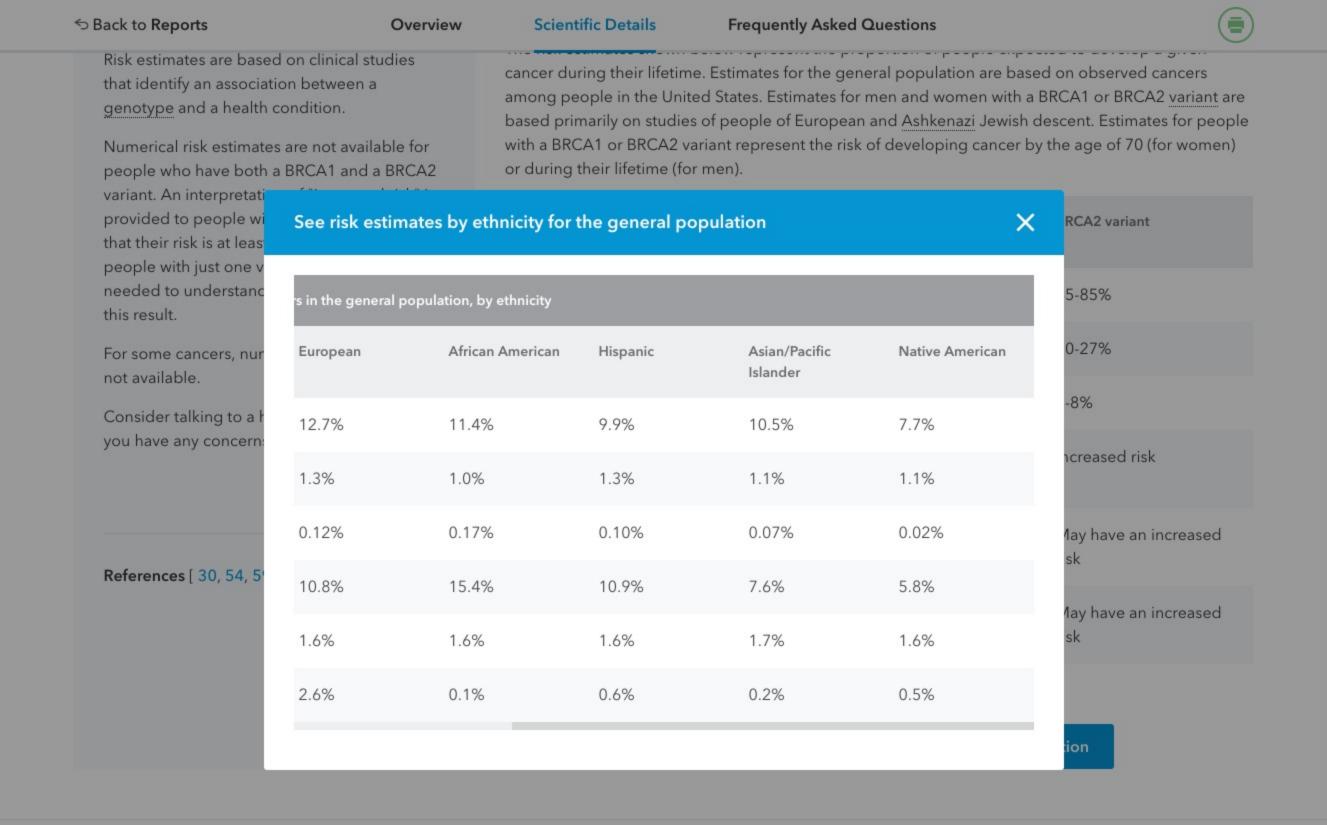
Date Change April 9, 2018

BRCA1/BRCA2 (Selected Variants) report created.



Other Factors

Many factors are known to influence the risk of developing breast and ovarian cancer in the general



Other Factors

Many factors are known to influence the risk of developing breast and ovarian cancer in the general

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BRCA1/BRCA2 (Selected Variants)

Frequently Asked Questions

Specific genetic variants in the BRCA1 and BRCA2 genes are associated with an increased risk of developing certain cancers, including breast cancer (in women and men) and ovarian cancer. These variants may also be associated with an increased risk for prostate cancer and certain other cancers. This test includes three genetic variants in the BRCA1 and BRCA2 genes that are most common in people of Ashkenazi Jewish descent.

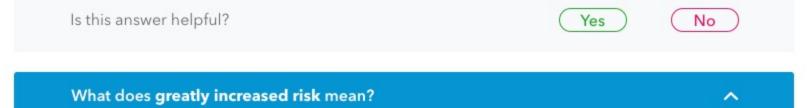
BRCA1/BRCA2 (Selected Variants) What does this test do? V What does this test not do? V The report says the variants included in this test are most common in people of V Ashkenazi Jewish descent. What if I'm not of Ashkenazi Jewish descent? Where can I learn more about cancer, support groups, and other resources? V My report says one variant called 185delAG was detected in the BRCA1 gene. What does this mean?

This means you have one of the three genetic variants we tested.

Women with a BRCA1 variant have a greatly increased risk of developing breast cancer and ovarian cancer. They also have an increased risk for early-onset breast cancer (before age 45) and multiple breast cancers, and may also develop ovarian cancer at an earlier age. In addition, they may have an increased risk for pancreatic cancer.

However, this result does not mean you have developed or definitely will develop any of these cancers.

It is important to discuss this result with a healthcare professional. Results should be confirmed in a clinical setting before taking any medical action.



A "greatly increased risk" means that, based on your genetic result for this test, your chances of developing breast and ovarian cancer are much higher than average. Studies have found that 45-85% of women with a BRCA1 variant develop breast cancer, compared to 12% for the general population. Similar studies have found that about 39-46% of women with a BRCA1 variant develop ovarian cancer, compared to 1-2% for the general population. See Scientific Details for more information.

Your risk for pancreatic cancer may also be higher than average. We cannot provide a numerical risk estimate because the risk for pancreatic cancer is not as well understood in people with your genetic result.

It is important to share this result with a healthcare professional.

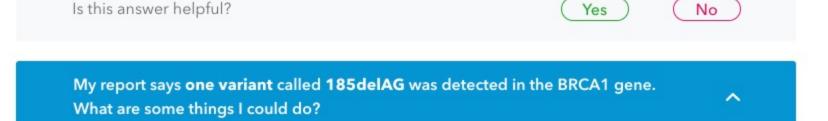


A 45-85% chance of developing breast cancer means that, out of 100 women with a BRCA1 variant, between 45 and 85 women will develop breast cancer by the age of 70.

A 39-46% chance of developing ovarian cancer means that, out of 100 women with a BRCA1 variant, between 39 and 46 women will develop ovarian cancer by the age of 70.

Many studies have looked at variants in the BRCA1 and BRCA2 genes, and these studies report somewhat different risk estimates. Some of these differences may be due to other factors besides the BRCA1 and BRCA2 variants. For example, women with a BRCA1 or BRCA2 variant who have a family history of breast or ovarian cancer have a higher chance of developing these cancers themselves. Because the group of women included in each study is different, the risk estimates may be different as well.

Your exact risk of developing breast and ovarian cancer depends on many factors, including family history, lifestyle, and genetic factors not included in this test. A healthcare professional can help you get a more precise estimate of your risk.



This result is associated with a greatly increased risk of developing breast and ovarian cancer. Women with your result may also have an increased risk for pancreatic cancer. It is important to share this result with a healthcare professional, such as a doctor or genetic counselor.

Professional guidelines recommend that women with your genetic result undergo more rigorous cancer screenings and consider certain medications and surgeries that can reduce the risk for cancer. Learn more about cancer screening and prevention.

For more information about what to think about and possible next steps, see this help article.

It is important to discuss your result with a healthcare professional. Results should be confirmed in a clinical setting before taking any medical action.

Is this answer helpful? Yes No

Since you share DNA with your family members, they may also be interested in your result. If you are thinking about talking to family members about your results, see this article for a discussion of things to consider before having the conversation.

Because you have one variant, it is expected that:

- Each of your children has a 50% chance of inheriting this variant from you.
- One of your parents has this variant.

How could my result affect my family?

Each of your siblings has a 50% chance of having this variant.

Because the variant we detected is associated with an increased cancer risk in both men and women, your adult family members may wish to learn more about their cancer risk. They can talk with a healthcare professional, such as a doctor or genetic counselor, to help them decide if genetic testing is right for them. Learn more about genetic counseling.

Is this answer helpful? Yes No I have questions about my results. Who should I talk to? It's normal to have questions or concerns after viewing this report. Some people feel anxious, upset, or worried about their risk or risk for their family members. Others simply

want to understand their results better or talk to someone about what they can do. Genetic counselors can help. Genetic counselors are healthcare professionals with special training in genetics and genetic testing. Learn more about genetic counseling.

article. Since you have a variant detected, it is also important to talk with a healthcare professional

For more information about what to think about and possible next steps, see this help

about your result and options.

Have more questions? Check out our Customer Care Help Center.



Receive up to \$20 when you refer family and friends to 23 and Me. Get started today.

No

Is this answer helpful?

Yes



