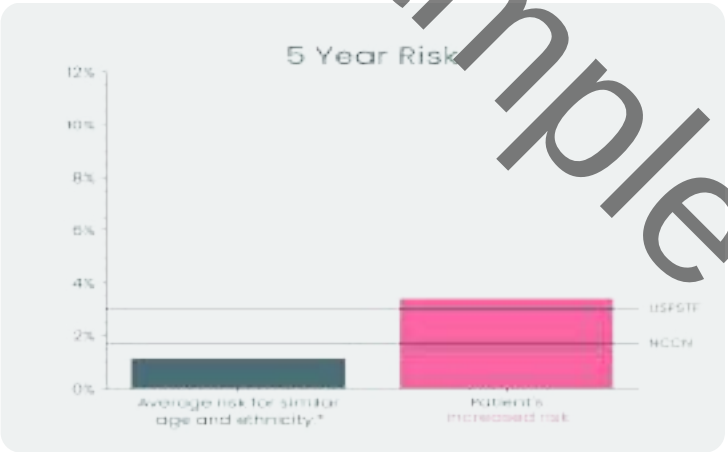
Breast Cancer Risk Assessment Final Test Report

GeneType for Breast Cancer

This patient is at an
INCREASED
risk of breast cancer

3.41%
Patient's
5 year risk

36.67%
Patient's
Lifetime risk



**The average risk is based on the same age, biological gender and race/ethnicity as the patient from the general population.*

Interpretation

This patient has a 36.67% chance of developing breast cancer within her remaining lifetime up to age 90 years. This is considered an increased risk because it is above the 20% threshold defined by the American Cancer Society and other medical associations.

This patient has a 3.41% chance of developing breast cancer over the next 5 years which is considered an increased risk. This is higher than the actionable threshold of 1.67% as defined by NCCN and higher than 3% as defined by USPSTF.

The patient should continue following general population breast screening protocols at a minimum, regardless of their estimated risk score. Also note that the risk scores are patient-specific and cannot be used to estimate risk in relatives. Furthermore, these results should be interpreted by a healthcare professional in the context of the patient's full clinical history, particularly for patients close to a threshold risk value.

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Clinical Responses

as provided on the requisition form

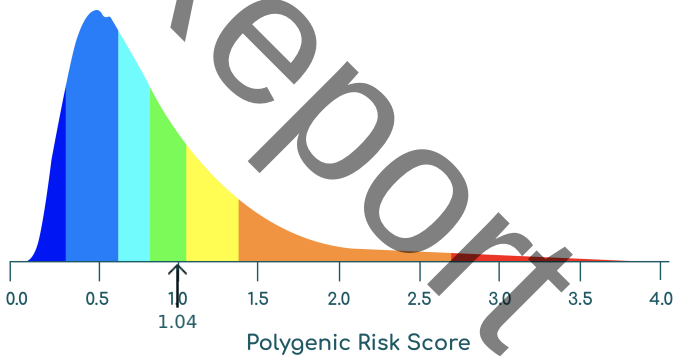
Does the patient have a medical history of any breast cancer or ductal carcinoma *in situ* (DCIS)?*	**No**
Does the patient have a mutation in either the *BRCA1* or *BRCA2* gene, or a diagnosis of a genetic syndrome that may be associated with elevated risk of breast cancer?*	**No**
What is the patient's age?	**48**
What is the patient's race/ethnicity?	**Black non-Hispanic**
What is the patient's height?	**4'10"**
What is the patient's weight?	**115 lbs**
How many first-degree relatives does the patient have who have had breast cancer? (mother, sister, daughter)	**1**
What was the age of the youngest first-degree relative when they were diagnosed with breast cancer?	**49**
How many second-degree relatives does this patient have who have had breast cancer? (aunts, nieces, grandparents, grandchildren, half-siblings, and double cousins)	**0**
What is the patient's menopausal status?	**pre-menopausal**
Has the patient ever had a breast mammogram?	**Yes**
What is the patient's reported mammographic breast density?	**Bi-Rads c**

**please note, this risk assessment does not test for any of the aforementioned genetic syndromes, or high penetrance variants in genes associated with hereditary breast cancer.*

Polygenic Risk Score

1.04

Patient's Polygenic Risk Score



The Polygenic Risk Score (PRS) is the genetic contribution to risk. It is a relative risk calculated as the multiplicative product of the patient's risk alleles weighted according to ethnicity-specific allele frequencies and odds ratios. This graph represents the breast cancer PRS range in the general population. The arrow represents where the patient falls compared to the general population. Note that PRS alone is not clinically actionable – it is just one of the factors integrated into the patient's breast cancer risk scores. Please refer to the 5 year and remaining lifetime for the absolute breast cancer risk scores.

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GeneType for Breast Cancer

The Test

GeneType for Breast Cancer incorporates clinical responses with an analysis of the genetic markers known to be associated with breast cancer. The test is intended to help patients and their healthcare professional make informed decisions regarding breast cancer screening and prevention options. The risk scores are patient-specific and cannot be used to estimate risk in relatives. These results should be interpreted by a healthcare professional in the context of the patient's full clinical history.

The patient's genetic information is used to generate a polygenic risk score. The polygenic risk score is calculated using a multiplicative model of breast cancer susceptibility. The risk model incorporates clinical risk factors (see Clinical Responses for a full list) and polygenic risk, combined with incidence and mortality data for breast cancer derived from the US Surveillance, Epidemiology, and End Results (SEER) database, in a proprietary algorithm to provide an absolute estimate of the 5 year and remaining lifetime risk of developing breast cancer.

Indication: GeneType for Breast Cancer is a breast cancer risk assessment test for women aged 30-85, but the recommended age to begin risk assessment for sporadic breast cancer is 35 years or older. The test is intended to better inform decision- making for breast cancer screening and risk-reduction. It is applicable to women who have not already been shown to carry a (likely) pathogenic variant in a hereditary breast and ovarian cancer (HBOC) associated genes, such as *BRCA1* or *BRCA2*.

Population Risk: The average lifetime risk of developing breast cancer is 1 in 8 for women (or 12%).

Validation: GeneType for Breast Cancer is currently validated in women 35 years or older of Non-Hispanic White descent and relies on the patient correctly reporting their ethnicity. The risk model incorporates ethnicity-specific population incidence data derived from the Surveillance, Epidemiology, and End Results (SEER) Program, For patients without ethnic-specific polygenic risk scores (PRS), the non-Hispanic white-derived PRS will be utilized until ethnic-specific PRS can be derived and cross-validated. Peer reviewed publications suggest the performance of the non-Hispanic white-derived-PRS in women of Asian and African descent is suitable for stratification in these ethnicities. The clinical risk factors are applicable across ethnicities, however the model has not been validated in these populations as yet.

Limitations: GeneType for Breast Cancer is a breast cancer risk prediction test only. An increased risk score does not mean that a patient will definitely develop breast cancer. Conversely, a low risk score does not mean that a patient will definitely not develop breast cancer.

GeneType for Breast Cancer provides an estimate of the likelihood that a woman will develop disease at some stage in the future. Cancer is a multifactorial disease and it is not possible to incorporate all potential risk factors into a risk prediction model. Test results should be interpreted by a healthcare professional in the context of the patient's full clinical and family history. Medical management and decision-making for breast cancer screening and prevention practices should not rely solely on a patient's geneType for Breast Cancer results.

The reliability of results for this test are dependent on the accuracy of the information provided in the clinical responses. If the responses to clinical questions change (e.g. number of first- degree relatives), the patient's risk percentages and risk category may also change.

Although the current test incorporates ethnic-specific incidence data, not all risk factors, such as PRS, have been optimized for ethnic-specific stratification improvements. While geneType improves risk stratification compared to current standards, ethnic-specific-improvements can still be made. Work is ongoing for ethnic-specific expansions that will further improve the calibration and discrimination of the assay across more genetic ancestries. This test is not applicable to women who have a personal history of breast cancer or who have already been shown to have an HBOC mutation, for example in the *BRCA1* or *BRCA2* gene, or a diagnosis of a genetic syndrome that may be associated with elevated risk of breast cancer. In this case, the patient should be referred to a specialist for genetic counselling.

Test Methodology: GeneType for Breast Cancer uses genotyping arrays to determine the genotype of 313 polymorphic breast cancer susceptibility loci; Genomic DNA is extracted from the Oragene Dx saliva kit using standard DNA extraction methods. SNPs are genotyped using a customized Infinium Global Screening Array from Illumina processed on an iScan system. Any SNPs which fail genotyping in the laboratory are imputed using a validated imputation algorithm to remove any measurement uncertainty. The polygenic risk score is calculated using a multiplicative model of breast cancer susceptibility combined with US Surveillance, Epidemiology, and End Results (SEER) incidence and mortality data for breast cancer in a proprietary algorithm to provide an absolute estimate of the 5-year and remaining lifetime risk of developing breast cancer.

This test has not been cleared or approved by the United States Food and Drug Administration (FDA). The FDA does not require this test to go through pre-market FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research.

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Breast Cancer Risk Assessment Final Test Report

GeneType for Breast Cancer

Your risk of developing breast cancer is considered INCREASED for a woman your age.

Many women in this risk category will never develop breast cancer, but some will.

Your risk of developing breast cancer over the rest of your life is 36.67% . This is greater than 20%, which puts you at increased risk.

The risk for an average woman your age developing breast cancer over their life is 14.39%.

Your risk of developing breast cancer over the next 5 years is 3.41%. This is greater than 1.67%, which puts you at increased risk.

The risk for an average woman your age developing breast cancer over the next 5 years is 1.17%.

**The average risk is based on the same age, biological gender and race/ethnicity as the patient from the general population.*

Understanding Breast Cancer Risk Factors

A risk factor is anything that may increase your chance of developing a disease. Some risk factors are strong and significantly increase your personal risk of the disease while others are weaker and only have a small impact on overall risk. Some risk factors can be modified by making changes to your lifestyle, while others are beyond your control.

Age: Increasing age is one of the strongest risk factors for breast cancer. Most breast cancers occur in women over the age of 50 years. This is why it is important to maintain regular wellness visits as you get older.

Weight: Being overweight, particularly post-menopause, has been shown to increase the risk of breast cancer.

Genetics: You are born with a set of genetic markers called Single Nucleotide Polymorphisms (SNPs). GeneType for Breast Cancer looks at your SNPs to help determine your risk of developing breast cancer.

Family History: If you have relatives who have been diagnosed with breast cancer, this will impact your risk of developing the disease. The more relatives with breast cancer you have, the more your risk increases.

Breast Density: Breast density often changes with age, hormonal fluctuation and weight. Women with dense breasts are at increased risk of developing breast cancer.

Oestrogen: Oestrogen is a female sex hormone that helps regulate a woman's reproductive system. Levels of oestrogen fluctuate from adolescence through adulthood as a woman goes through changes such as menarche, childbirth and menopause. Oestrogen is associated with the development of some types of breast cancer.

Hormone Replacement Therapy: Use of hormone replacement therapy (HRT), especially for long periods, has been associated with a modest increase in risk of breast cancer. However, it is important to note that the benefits of these medicines may outweigh the risks for many women. If you are taking combined HRT, review your needs every six to twelve months with your healthcare professional.

Smoking: Smoking increases your risk of breast cancer.

Alcohol: Alcohol consumption has been associated with an increased risk of breast cancer in both pre- and post-menopausal women.

Physical Activity: If you're not physically active, you have a greater chance of developing breast cancer. Being more active can help lower your risk.

What You Can Do

Together with your healthcare provider, you will discuss options for breast cancer risk reduction, including screening. Below we briefly outline some of the clinical recommendations that your healthcare provider may discuss with you in greater detail.

Risk Reduction

A woman can develop breast cancer at any age, regardless of her level of risk. As a result, it is important to know the normal look and feel of your breasts and to perform regular self- examinations. Make sure you visit your healthcare provider if you detect any change in your breasts.

Maintaining a healthy lifestyle is a simple way to reduce your risk of breast cancer. This includes maintaining a healthy weight, not smoking and limiting your alcohol intake. In order to reduce your risk of breast cancer, it is best not to drink alcohol or, if you drink, limit consumption to 1 standard drink or less per day. Moderate physical activity of between 1.5 to 4 hours per week has also been shown to reduce risk for breast cancer.

For women at potentially high risk of developing breast cancer or risk-reducing medications may also be discussed with a specialist.

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GeneType for Breast Cancer

Women with a 5 year risk of ≥1.67% should be offered risk reduction counselling. Furthermore, the United States Preventive Services Taskforce (USPSTF) guidelines state that women with an estimated 5 year risk of 3% or greater are more likely to benefit from tamoxifen or raloxifene to prevent invasive breast cancer. The American Society of Clinical Oncology (ASCO) also recommend the option of aromatase inhibitors for post- menopausal women, and suggest at risk above 3% the risk reducing benefits outweigh harms. Discuss your breast cancer prevention options, including the risks and benefits of risk-reducing medication, with your healthcare provider.

Screening

Regardless of risk score, we recommend that all women undergo routine mammography as recommended by her healthcare provider. Women at average risk of developing breast cancer have the option to begin annual mammogram screening between the ages of 40 and 50. Your screening may be tailored to your risk, within the context of your full medical history, following an informed decision-making discussion between you and your healthcare provider.

Women who have a lifetime risk of ≥20% as defined by models that are dependent on family history are recommended to consider an annual breast MRI. Discuss your screening options with your healthcare provider.

You may be referred to a high-risk center or a healthcare provider who specializes in breast cancer prevention to discuss your risk and the potential risk-reducing options that may be available to you.

End of report