

### **Report Contents**

- 1. Coriell Personalized Medicine Collaborative Research Study Report. This report includes all data included in the clinical report as well as supplemental interpretations and educational material. This research report is based on Questionnaires Finalized on 08/01/2010**
- 2. Clinical Report. This report was generated and approved by Coriell's CLIA certified genotyping laboratory.**



## Sample Results

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### CPMC Research Study Report

<b>Name:</b>	NATALIE DEMO	<b>Gender:</b>	Female
<b>Date of Birth:</b>		<b>Date Collected:</b>	11-30-2016
<b>Coriell ID:</b>	DEMONAT	<b>Date Received:</b>	11-30-2016
<b>Lab Accessioning Number:</b>	DEMONAT	<b>Date of Report:</b>	05-07-2013
<b>Ordering Physician:</b>	Dr. Edward Viner		

#### Risk of Developing Breast Cancer Based on:

- CPMC Breast Cancer Variant 1 (rs2981582)
- Family History
- Body Mass Index
- Alcohol Consumption
- Hormone Replacement Therapy
- Age at First Menstrual Period
- Childbearing History

The CPMC is a research study investigating the utility of personalized genomic information on health and health behavior. At this time, the CPMC is reporting only one genetic variant per health condition. Since most common health conditions are caused by an interaction between more than one genetic factor and non-genetic factors such as lifestyle, the genetic variant risk in this report does not represent your complete genetic risk for breast cancer. The breast cancer risk factors that the CPMC reports on have only been studied in women; therefore men will not receive risk estimates for breast cancer. However, genetic variant results are provided to men because the result may be informative for their female relatives (mother, sisters, and daughters).

In some cases, a change in a single gene (like **BRCA1** or **BRCA2**), can cause significantly increased risk for breast cancer. These genetic variants are rare, associated with a strong family history cancer, and **are not tested as part of the CPMC research study**. If you have a family history of early onset breast cancer (before age 50), multiple family members with breast and/or ovarian cancer diagnosed at any age, or any male relatives with breast cancer, please contact a CPMC genetic counselor to determine if you are at risk for a hereditary form of cancer.

These results were generated as part of this research study in a CLIA-approved laboratory.

More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website <http://cpmc.coriell.org> or by contacting our genetic counselors. Participants may schedule an appointment with one of our board-certified genetic counselors through the web portal by clicking on "request an appointment". Our genetic counselors also can be reached by email at [cpmcgc@coriell.org](mailto:cpmcgc@coriell.org) or by phone at 888-580-8028.

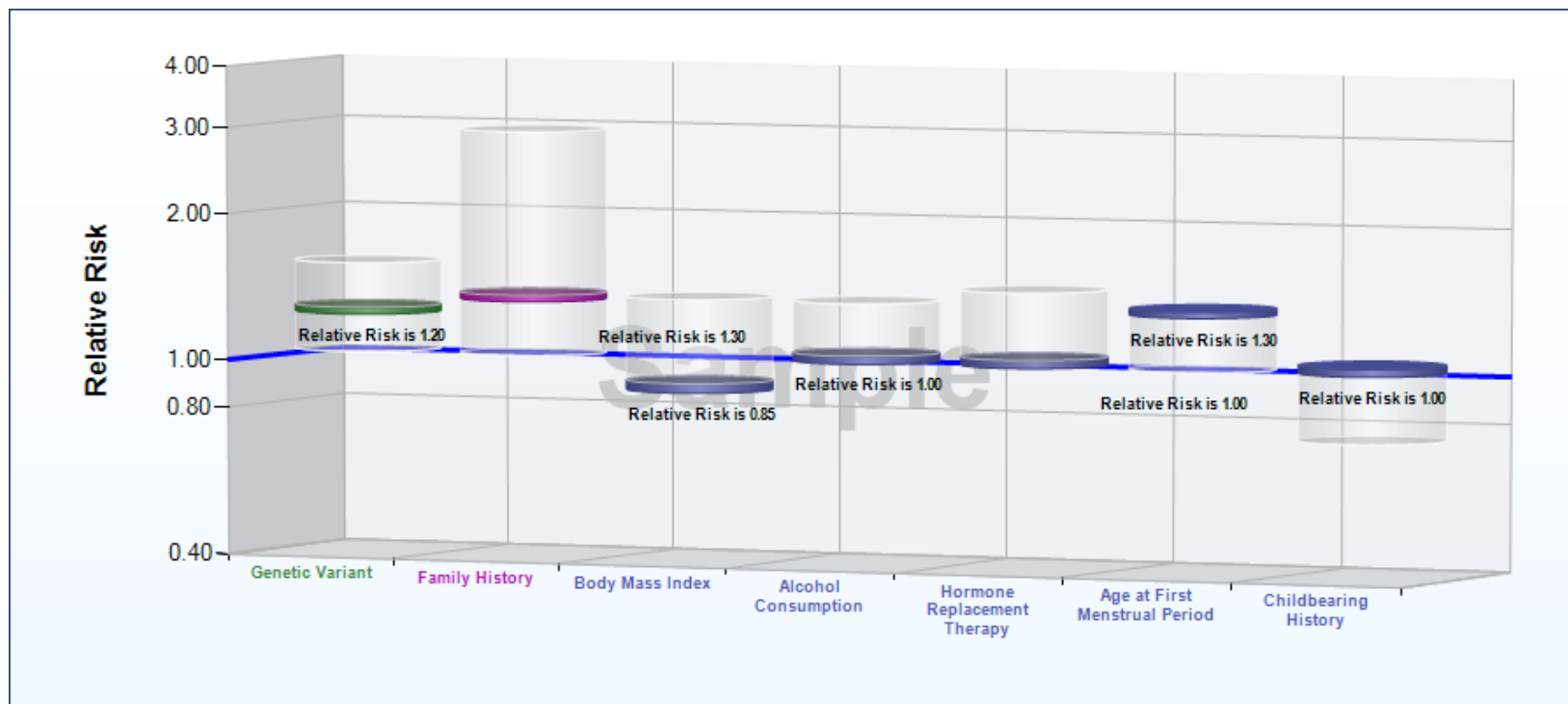
This research report includes all data included in the clinical report as well as supplemental interpretations and educational material. Please see the report that follows for the official clinical report.

## Genetic Variant Result, Details and Population Data

### Breast Cancer

Risk factors may be related to each other and risk estimates cannot be combined.

This graph provides a summary of the relative risks for genetic variant, family history, BMI, alcohol consumption, hormone replacement therapy, age at first menstrual period, and childbearing history.



You reported you are an African American woman, between 30 and 39 years old; 2 in 1,000 African American women in your age group have breast cancer.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	1.20	1.00	1.50	<b>You have 1 copy of the non-risk variant and 1 copy of the risk variant. Based on this result, you are 20% more likely (or 1.2 times as likely) to develop breast cancer as a woman with no copies of this variant.</b> <i>Having this risk variant contributes to your risk of breast cancer.</i>
	Family History	1.30	1.00	2.90	<b>Based on your family history, you are 30% more likely (or 1.3 times as likely) to develop breast cancer compared to a woman who does not have a family history of breast cancer.</b> <i>Having a grandmother with breast cancer contributes to your risk of breast cancer.</i>
	Body Mass Index	0.85	0.85	1.30	<b>Based on your BMI you have a lower risk of developing breast cancer compared to women who have a BMI of 22.5 or higher.</b>
	Alcohol Consumption	1.00	1.00	1.30	<b>Based on the amount of alcohol you reported drinking, you are not at increased risk to develop breast cancer compared to women who do not drink alcohol.</b>

<b>Chart Color</b>	<b>Relative Risk Due To:</b>	<b>Your Risk</b>	<b>Minimum Risk</b>	<b>Maximum Risk</b>	<b>Interpretation</b>
	<b>Hormone Replacement Therapy</b>	<b>1.00</b>	1.00	1.40	<b>Because you reported that you have never used hormone replacement therapy, you are at a lower risk of breast cancer compared to women who have used hormone replacement therapy.</b>
	<b>Age at First Menstrual Period</b>	<b>1.30</b>	1.00	1.30	<b>Because you reported that you were 13 years old or younger when you had your first menstrual period, you are 30% more likely (or 1.3 times as likely) to develop breast cancer as women who were 14 years of age or older when they had their first menstrual period.</b>
	<b>Childbearing History</b>	<b>1.00</b>	0.72	1.00	<b>Because you reported that you have never given birth to a child, you are at a greater risk of breast cancer compared to women who have given birth to at least one child.</b>

# Breast Cancer

## Risk Due To Genetic Variant #1 (rs2981582)

Your Result: 1 copy of the non-risk variant and 1 copy of the risk variant (GA)

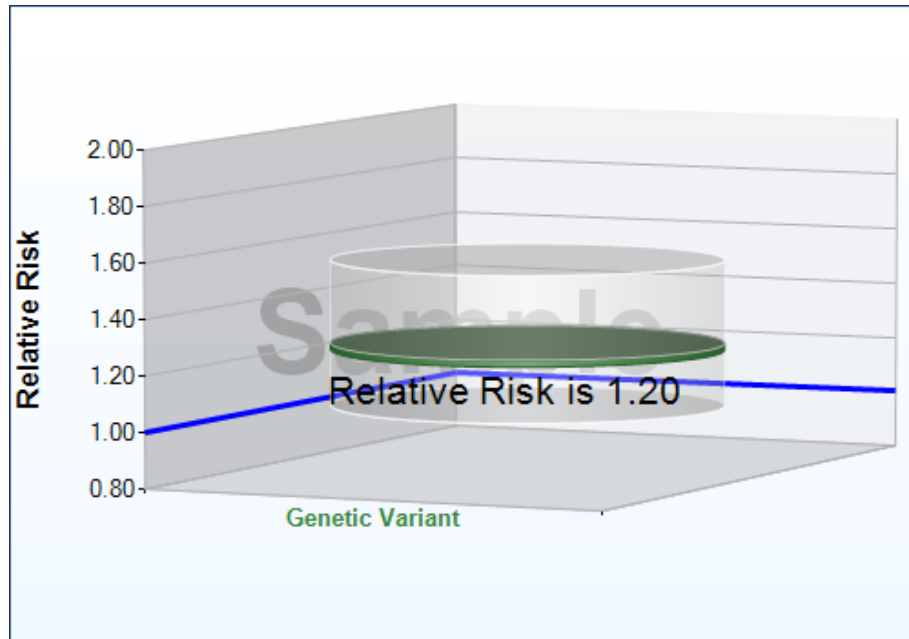
Non-Risk Variant = G Risk Variant = A

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.20	1.00	1.50	<p>You have 1 copy of the non-risk variant and 1 copy of the risk variant. Based on this result, you are 20% more likely (or 1.2 times as likely) to develop breast cancer as a woman with no copies of this variant.</p> <p><i>Having this risk variant contributes to your risk of breast cancer.</i></p>

Genetic Variant Risk is based on the number of copies of this genetic risk variant.

Women with one or two copies of the risk variant are compared to women with no copies of the risk variant to determine relative risk.

A relative risk greater than 1.0 indicates an increased risk.

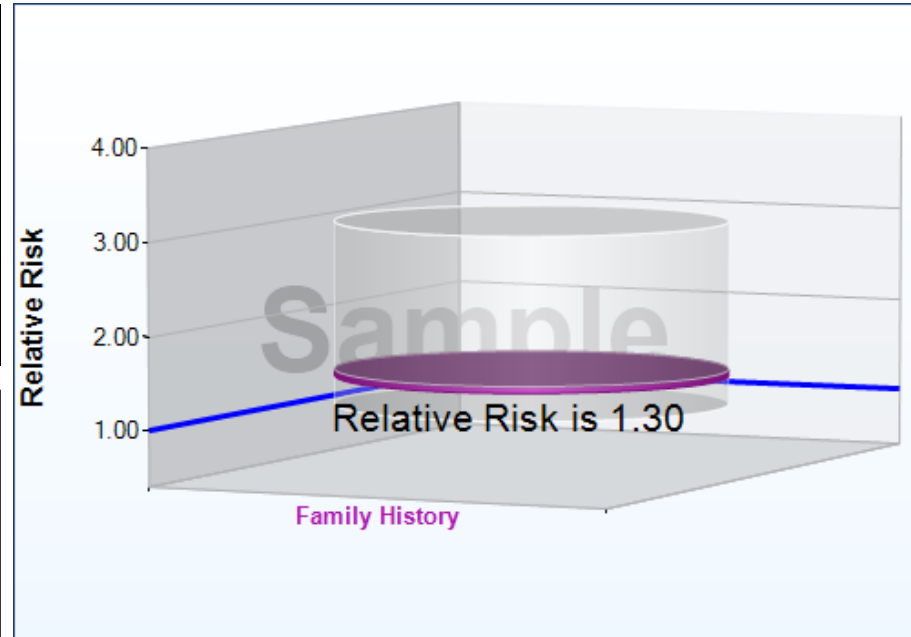


These risk estimates are based on a study including both pre and post-menopausal Caucasian women.

## Breast Cancer Risk Due To Family History

You reported that one grandmother has been diagnosed with breast cancer.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.30	1.00	2.90	<p>Based on your family history, you are <b>30% more likely (or 1.3 times as likely)</b> to develop breast cancer compared to a woman who does not have a family history of breast cancer.</p> <p><i>Having a grandmother with breast cancer contributes to your risk of breast cancer.</i></p>



Risk is compared based on family history.

Women with a family history of breast cancer are compared to women with no family history of breast cancer to determine relative risk of developing breast cancer.

A relative risk greater than 1.0 indicates an increased risk.

If you have a family history of early onset breast cancer (before age 50), 2 or more family members with either breast cancer or ovarian cancer diagnosed at any age, or any male relatives with breast cancer please [contact a CPMC genetic counselor](#) to determine if you are at risk for a hereditary form of cancer.

These risk estimates are based on a study including both pre and post-menopausal Caucasian women.

## Breast Cancer Risk Due To Body Mass Index

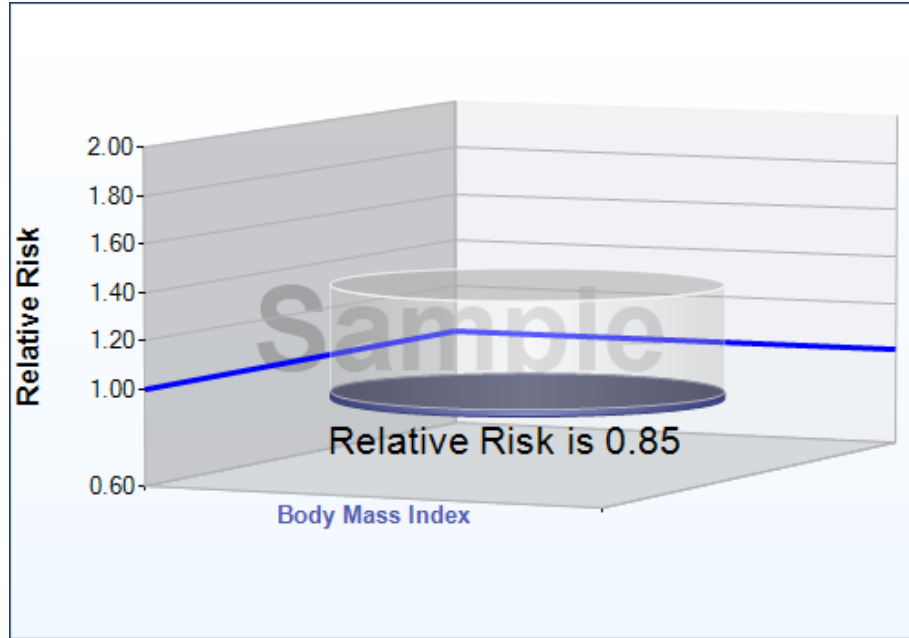
According to the height and weight you reported, you are not overweight or obese (BMI <25.0).

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	0.85	0.85	1.30	Based on your BMI you have a lower risk of developing breast cancer compared to women who have a BMI of 22.5 or higher.

Risk is compared based on **Body Mass Index (BMI)**  
 BMI is used to determine if someone is overweight or obese.

Women who are overweight (BMI 25-29.9) or obese (BMI ≥ 30) are compared to women who are not overweight (BMI < 25) to determine relative risk.

A relative risk less than 1.0 indicates a decreased risk. A relative risk greater than 1.0 indicates an increased risk.



These results are based on a study of postmenopausal women of different racial and ethnic backgrounds.



## Breast Cancer

### Risk Due To Alcohol Consumption

You reported that you drink less than 3 alcoholic beverages per week.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	1.30	Based on the amount of alcohol you reported drinking, you are not at increased risk to develop breast cancer compared to women who do not drink alcohol.

Risk is compared based on the amount of alcohol consumption.

Women who drink alcohol are compared to women who do not drink alcohol to determine relative risk.

A relative risk of greater than 1.0 indicates an increased risk.



These risk estimates are based on a study of post-menopausal Caucasian women.

## Breast Cancer

### Risk Due To Hormone Replacement Therapy

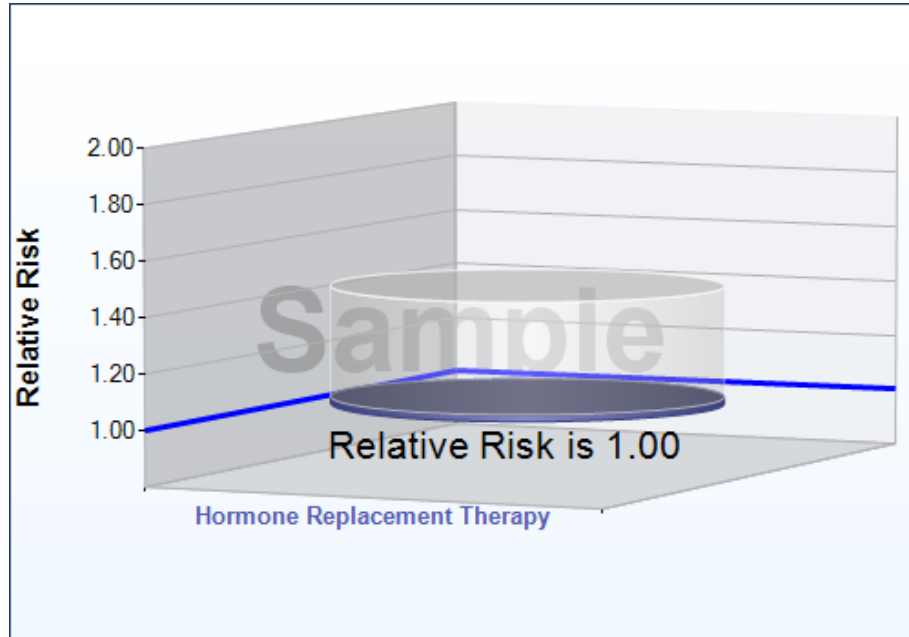
You reported that you have never used hormone replacement therapy.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	1.40	Because you reported that you have never used hormone replacement therapy, you are at a lower risk of breast cancer compared to women who have used hormone replacement therapy.

Risk is compared based on use of hormone replacement therapy.

Women who have ever used hormone replacement therapy were compared to women who had never used hormone replacement therapy to determine relative risk.

A relative risk greater than 1.0 indicates an increased risk.



These results are based on a study of postmenopausal women of different racial and ethnic backgrounds.

## Breast Cancer

### Risk Due To Age at First Menstrual Period

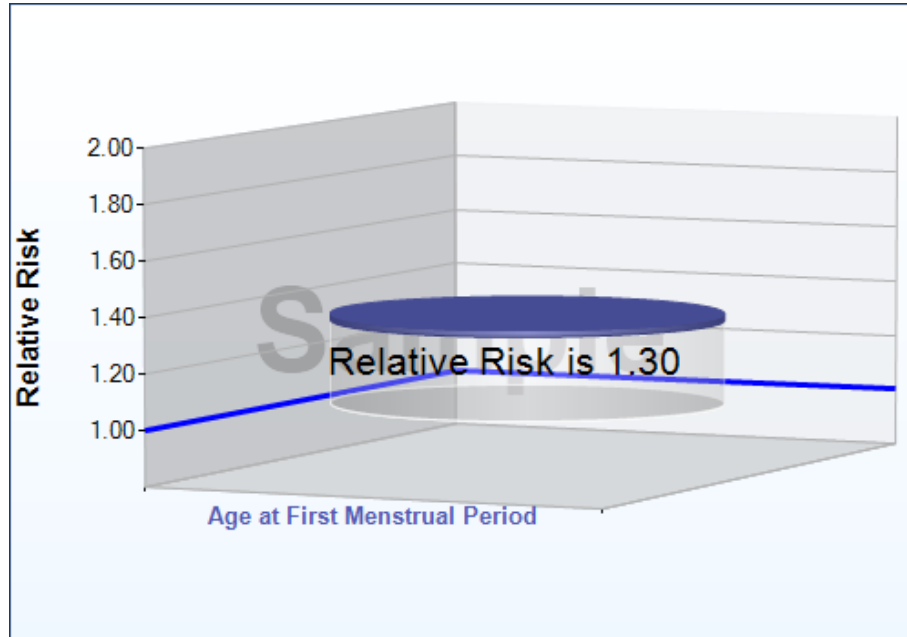
You reported that you had your first menstrual period at 13 years of age or younger.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.30	1.00	1.30	Because you reported that you were 13 years old or younger when you had your first menstrual period, you are 30% more likely (or 1.3 times as likely) to develop breast cancer as women who were 14 years of age or older when they had their first menstrual period.

Risk is compared based on the age you were when you had your first menstrual period.

To determine relative risk, women who had their first menstrual period at age 14 years or older were compared to women who had their first menstrual period before 14 years of age.

A relative risk greater than 1.0 indicates an increased risk.



These risk estimates are based on a study including both pre and post-menopausal African American women.

## Breast Cancer Risk Due To Childbearing History

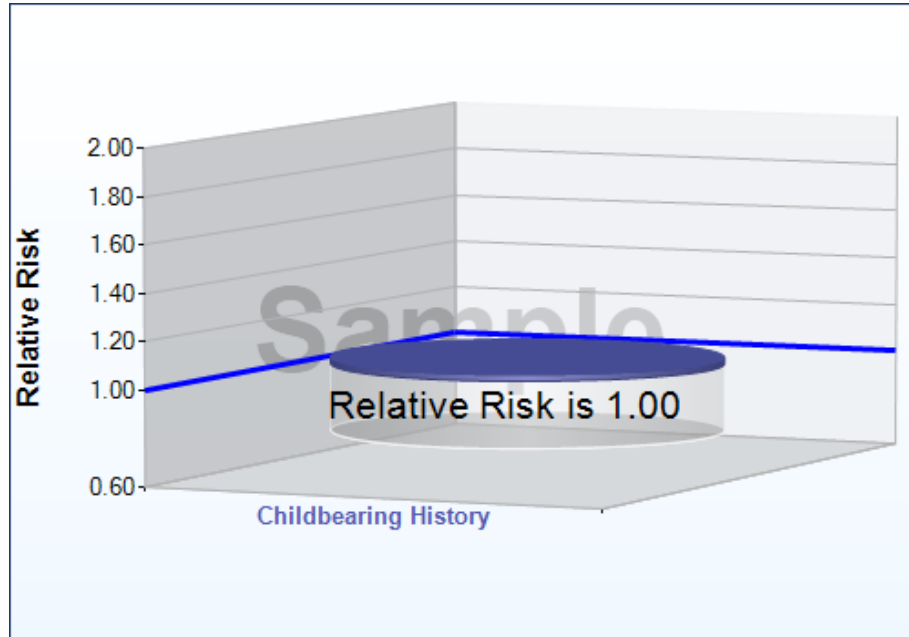
You reported that you do not have children.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	0.72	1.00	Because you reported that you have never given birth to a child, you are at a greater risk of breast cancer compared to women who have given birth to at least one child.

Risk is based on whether or not you have ever given birth to a child and at what age you had your first birth.

Women who have given birth to a child are compared to women who have never given birth to a child to determine relative risk.

A relative risk less than 1.0 indicates a reduction of risk.



These risk estimates are based on a study of post-menopausal Caucasian women.

## Breast Cancer - Variant #1 (rs2981582)

We all have 2 copies of every gene, one from each of our parents.  
Each copy may have small changes called genetic variants.  
Some genetic variants are associated with an increased risk of disease.  
Some genetic variants are associated with a decreased risk of disease.

Having one or two copies of this variant **increases** the risk for breast cancer in **women**.

### How Common Is This Variant?

Non-Risk Variant = G    Risk Variant = A

**GG** - 20 in 100 people have 2 copies of the non-risk variant

**GA** - 67 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant

**AA** - 13 in 100 people have 2 copies of the risk variant

This data is based on studies in African American populations.



Gene: FGFR2

Chromosome: 10q26.13

## Causes

### Genetic vs. Non-Genetic Risk Factors

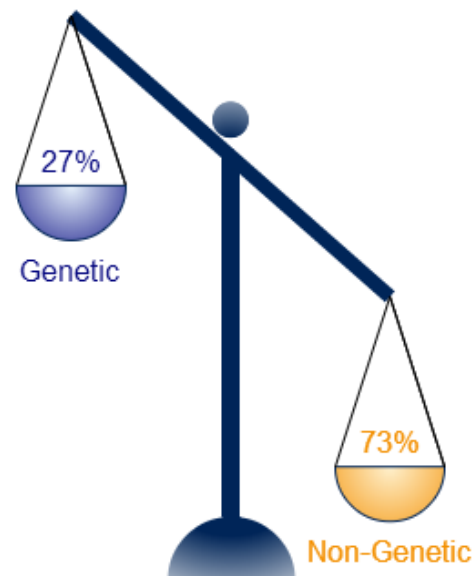
Breast cancer can be caused by both genetic factors and non-genetic (or environmental) risk factors.

It is estimated that **non-genetic** factors (like body mass index, alcohol consumption, etc.) account for about **73%** of the risk of breast cancer.

It is estimated that **27%** of the risk for breast cancer is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

In rare cases, breast cancer can be caused by a change in a single gene (like BRCA1 or BRCA2), not tested as part of the CPMC research study. If you have a family history of early onset breast cancer (before age 50), multiple family members with breast or ovarian cancer diagnosed at any age, or any male relatives with breast cancer, please [contact a CPMC genetic counselor](#) to determine if you are at risk for a hereditary form of cancer.

**There are many different genetic and non-genetic risk factors that contribute to the risk of breast cancer. We are only able to tell you about your family history risk, 1 genetic and 5 non-genetic risk factors at this time.**

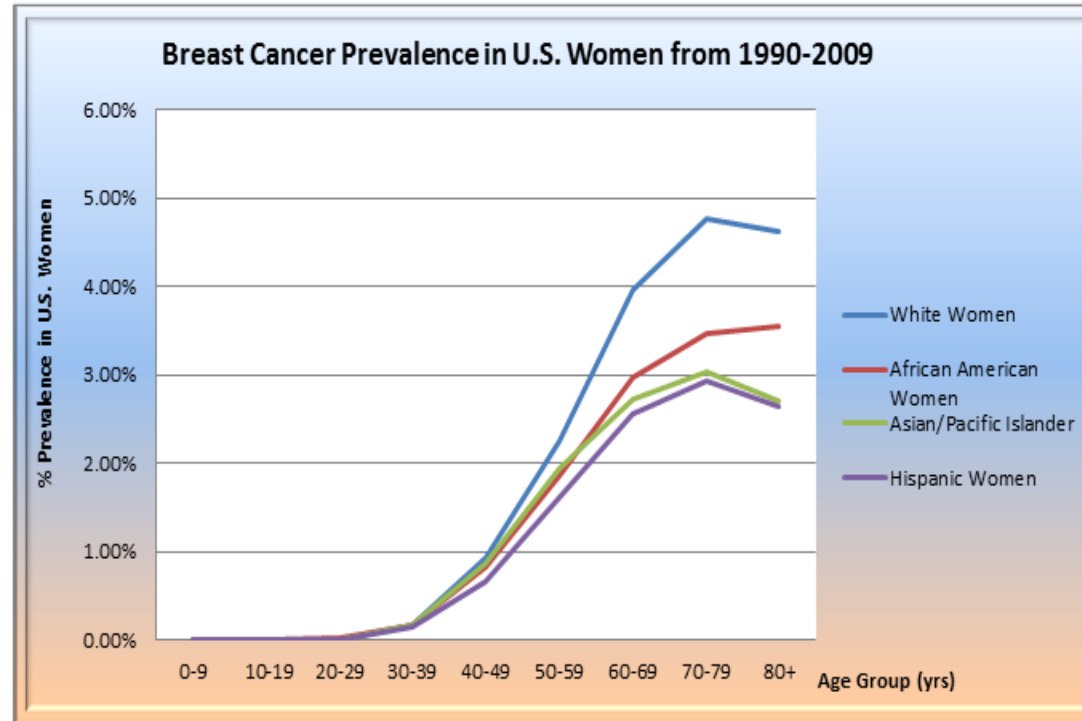


## How Common

The risk of having breast cancer increases with age and is more common among Caucasian women.

**You reported you are an African American woman, between 30 and 39 years old; 2 in 1,000 African American women in your age group have breast cancer.**

Age, gender and race/ethnicity contribute to your risk of breast cancer.



## Limitations

### Breast Cancer

- This result alone does NOT diagnose breast cancer. Breast cancer must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop breast cancer.
- This result does NOT mean that you will not develop breast cancer in the future.
- This result ONLY assesses your risk for developing breast cancer due to the factors presented in this report and does not mean that other genetic variants or risk factors for breast cancer are present or absent.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop breast cancer than any individual genetic variant.
- Risk estimates are based on current available literature.
- Although rare, it is possible that you may receive an incorrect result; 100% accuracy of reported results cannot be guaranteed.
- Occasionally there may be a specific variant on a gene chip that is not able to be read or interpreted. In this case you will not receive a result for that variant. It is expected that you will receive results for about 95% of variants approved by the ICOB.
- Relative risks used to estimate risk of disease for CPMC participants are based on groups of people with the same risk or protective factor as the individual CPMC participant. In some cases, the relative risk is estimated based upon an odds ratio and known or assumed disease prevalence.
- Separate risk estimates for each risk or protective factor have been given. Risk or protective factors may be related to each other and risk estimates cannot be combined.
- Risk information for non-genetic factors is based on information you provided in your medical, family, lifestyle questionnaire. If you did not provide answers or if you answered "do not know", risk estimates for some factors may not be available.
- Risk information for non-genetic factors is based on information you provided in your medical, family, lifestyle questionnaire and may not be reflective of your current risk if any of these factors have changed. You will be given the opportunity to update your medical, family and lifestyle questionnaire responses periodically.
- Every effort will be made to provide you with risk information based on your reported race/ethnicity. However, data may not be available for all races/ethnicities for all risk factors. Please see your individual results to determine which race/ethnicity the data given is based on.



## Methods

### Breast Cancer

**This condition and genetic variant(s) were approved by the Informed Cohort Oversight Board (ICOB)**

#### Test Methodology

Saliva samples were collected using Oragene DNA Collection Kits (DNA Genotek) and DNA was extracted manually according to the manufacturer's instructions. Purified DNA was quantified using UV absorbance at 260 nm. Five hundred nanograms of the resulting DNA from each sample were used as template in the Affymetrix Genome-Wide Human SNP Nsp/Sty 6.0 GeneChip assay. Data analysis was performed using Affymetrix Genotyping Console software.

See [CPMC Technical Paper](#) for genetic variant selection and reporting methodology.

[Risk interpretation based on Coriell's Breast Cancer Risk Algorithm Version 1 (May 14, 2013)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. *Genet Med.* 13(2):131-139.
2. Easton, DF. et al (2007). Genome-wide association study identifies novel breast cancer susceptibility loci. *Nature.* 447(28):1087-1095.
3. Travis, RC. et al (2010). Gene-environment interactions in 7610 women with breast cancer: prospective evidence from the Million Women Study. *Lancet.* 375(9732):2143-2151
4. Reeves, GK. et al 2007. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *BMJ.* 335(7630):1134S
5. Allen, NE. et al (2009). Moderate alcohol intake and cancer incidence in women. *J Natl Cancer Inst.* 101(5):296-305.
6. Saxena, T. et al (2010). Menopausal hormone therapy and subsequent risk of specific invasive breast cancer subtypes in the California Teachers Study. *Cancer Epidemiol Biomarkers Prev.* 19(9):2366-2378.
7. Beral, V. et al (2011). Breast cancer risk in relation to the interval between menopause and starting hormone therapy. *J Natl Cancer Inst.* 103(4): 296-305.
8. Gail, MH. et al (1989). Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J Natl. Cancer Inst.* 81(24):1879-1886.
9. Gail, MH. et al (2007). Projecting individualized absolute invasive breast cancer risk in African American women. *J Natl. Cancer Inst.* 99(23):1782-1792.
10. Schonfeld, SJ. et al (2011). Hormone related risk factors and postmenopausal breast cancer among nulliparous versus parous women: An aggregated study. *Am J Epidemiol.* 173(5):509-517.
11. Bevier, M. et al (2012). Risk of breast cancer in families of multiple affected women. *Breast Cancer Res Treat.* 132:723-728.
12. Lichtenstein, P. et al (2000). Environmental and heritable factors in the causation of cancer. *New Eng J Med.* 343(2): 78-85.
13. Howlader, N. et al. SEER Cancer Statistics Review, 1975-2009 (Vintage 2009 Populations), National Cancer Institute. Bethesda, MD, [http://seer.cancer.gov/csr/1975\\_2009\\_pops09/browse\\_csr.php?section=4&page=sect\\_04\\_table.25.html](http://seer.cancer.gov/csr/1975_2009_pops09/browse_csr.php?section=4&page=sect_04_table.25.html), based on November 2011 SEER data submission, posted to the SEER web site, April 2012.

## Sample Results



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#### Clinical Report for Breast Cancer Genetic Variant 1 (rs2981582)

<b>Name:</b>	NATALIE DEMO	<b>Sample Type:</b>	Saliva
<b>Race/Ethnicity:</b>	Black or African-American	<b>Gender:</b>	Female
<b>Date of Birth:</b>		<b>Date Collected:</b>	11-30-2016
<b>Coriell ID:</b>	DEMONAT	<b>Date Received:</b>	11-30-2016
<b>Lab Accessioning Number:</b>	DEMONAT	<b>Date of Report:</b>	05-07-2013
<b>Ordering Physician:</b>	Dr. Edward Viner		

<b>Name of Gene/Region:</b> FGFR2		<b>Chromosomal Location:</b> 10q26.13
<b>Variants tested</b>	<b>Result</b>	<b>Reference Genotype</b>
rs2981582	GA	GG
<b>Interpretation</b>	<b>Women with this result are 20% more likely (or 1.2 times as likely) to develop breast cancer than women with no copies of this variant.</b> These results are based on studies in Caucasian populations. When race/ethnicity specific risk estimates are not available, risk estimates based on Caucasian populations are provided.	
<b>Other Risks</b>	Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of breast cancer. For additional information on other risk factors please see the accompanying CPMC research report.	

Risk interpretation based on Coriell's Breast Cancer Risk Algorithm Version 1 (May 14, 2013)

#### **Test Limitations**

DNA-based testing is highly accurate, however there are many sources of potential error including: mis-identification of samples, rare technical errors, trace contamination of PCR reactions, and rare genetic variants that interfere with analysis. There may be other variants, not included in this test, that influence the risk to develop breast cancer. This test is not diagnostic for breast cancer and cannot rule out the risk of developing breast cancer in the future. Risk estimates are based on current available literature (see reference). This test or one or more of its components was developed and its performance characteristics determined by the Coriell Institute for Medical Research. It has not been approved by the Food and Drug Administration (FDA). The FDA has determined that such approval is not necessary. The Coriell Institute is regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988 as qualified to perform high-complexity testing.

#### **Test Methodology**

Saliva samples were collected using Oragene DNA Collection Kits (DNA Genotek) and DNA was extracted manually according to the manufacturer's instructions or automatically using a DNAdvance Kit (Agencourt). Purified DNA was quantified using UV absorbance at 260 nm. Five hundred nanograms of the resulting DNA from each sample were used as template in the Affymetrix Genome-Wide Human SNP Nsp/Sty 6.0 GeneChip assay. Data analysis was performed using Affymetrix Genotyping Console software.

electronically signed by

Marie Hoover, PhD, Laboratory Director

#### **References**

1. Travis, RC. et al. (2010). Gene-environment interactions in 7610 women with breast cancer: prospective evidence from the Million Women Study. *Lancet*. 375(9732):2143-2151

This clinical report only includes data generated in the CLIA approved genotyping laboratory, for additional information please see the CPMC research report.