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

Coriell Institute for Medical Research
403 Haddon Avenue
Camden, New Jersey 08103 USA
Phone: 888-580-8028
Fax: 856-964-0254
cpmc.coriell.org

CPMC Research Study Report

Name:	NATALIE DEMO	**Gender:**	Female
Date of Birth:		**Date Collected:**	11-30-2016
Coriell ID:	DEMONAT	**Date Received:**	11-30-2016
Lab Accessioning Number:	DEMONAT	**Date of Report:**	12-17-2014
Ordering Physician:	Dr. Edward Viner		

Risk of Developing Osteoporosis Based on:

- **CPMC Osteoporosis Variant 1 (rs3736228)**
- **Family History**
- **Smoking Status**

The CPMC is a research study investigating the utility of personalized genomic information on health and health behavior. Most common health conditions are caused by an interaction between multiple genetic variants and non-genetic risk factors such as lifestyle and environment. The genetic variant risk in this report is based on one genetic variant, but does not represent your complete genetic risk for osteoporosis. These results were generated as part of this research study in a CLIA-approved laboratory.

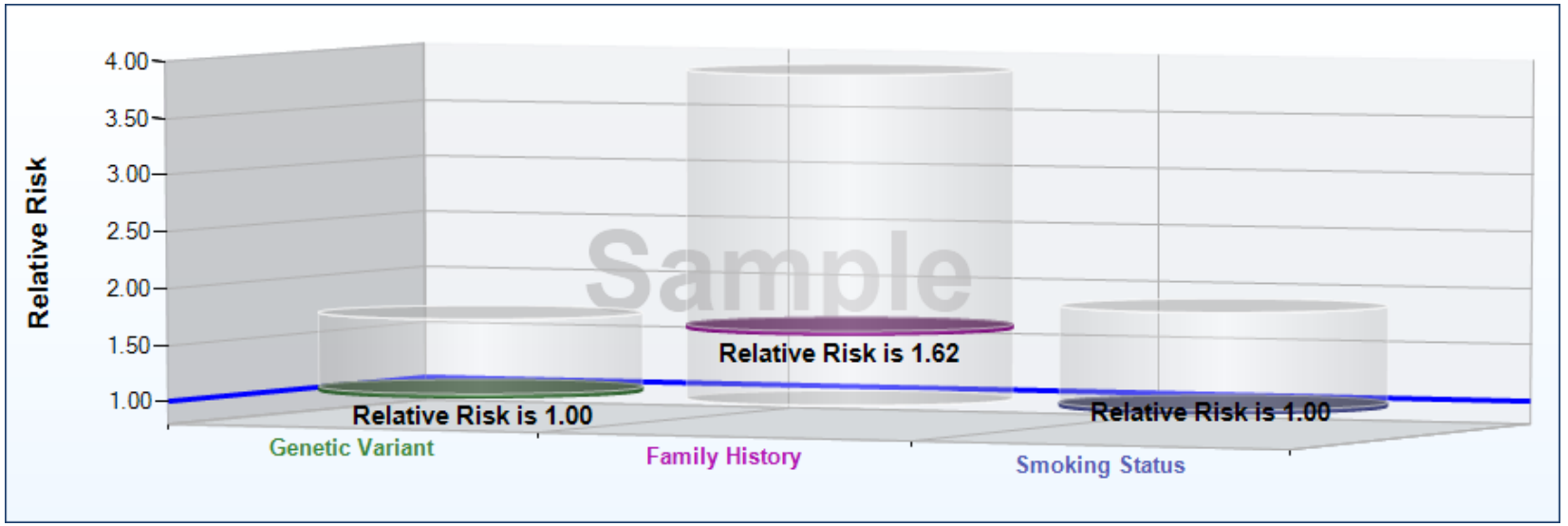
More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website http://cpmc.coriell.org or by contacting our genetic counselor. Participants may schedule an appointment with our board-certified genetic counselor through the web portal by clicking on “request an appointment”. Our genetic counselor also can be reached by email at 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

Osteoporosis

Risk factors may be related to each other and risk estimates cannot be combined.
This graph provides a summary of the relative risks for one genetic variant, family history and smoking status.



You reported you are a woman, between 18 and 49 years old; data for women in your age group are not available, however, an estimated 7 in 100 women aged 50-59 have osteoporosis.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	**1.00**	1.00	1.66	**You have 2 copies of the non-risk variant. Based on this result, you are at a lower risk to develop osteoporosis compared to someone with one or two copies of this variant.**
	Family History	**1.62**	1.00	3.86	**Based on your family history, you are 62% more likely (or 1.62 times as likely) to develop osteoporosis compared to a woman who does not have any parents, siblings or grandparents with osteoporosis.** ***Having either a parent, sibling or grandparent with osteoporosis contributes to your risk of osteoporosis.***
	Smoking Status	**1.00**	1.00	1.85	**Because you are non smoker you are at a lower risk to develop osteoporosis compared to women who have smoked more than 1 pack of cigarettes per day for eight or more years.**

Osteoporosis

Risk Due To Genetic Variant #1 (rs3736228)

Your Result: 2 copies of the non-risk variant were detected (CC)

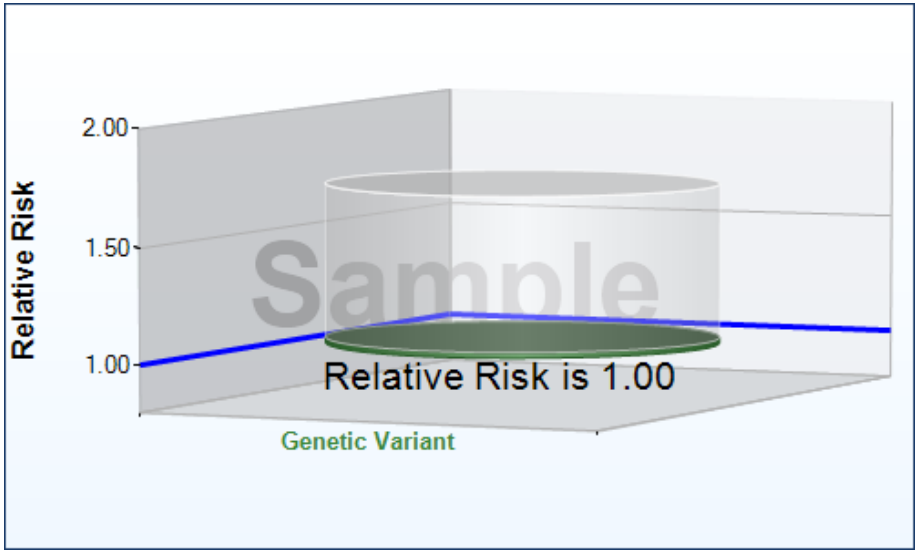
Non-Risk Variant = C Risk Variant = T

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	1.66	**You have 2 copies of the non-risk variant. Based on this result, you are at a lower risk to develop osteoporosis compared to someone with one or two copies of this variant.**

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

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

A relative risk greater than 1.00 indicates an increased risk.



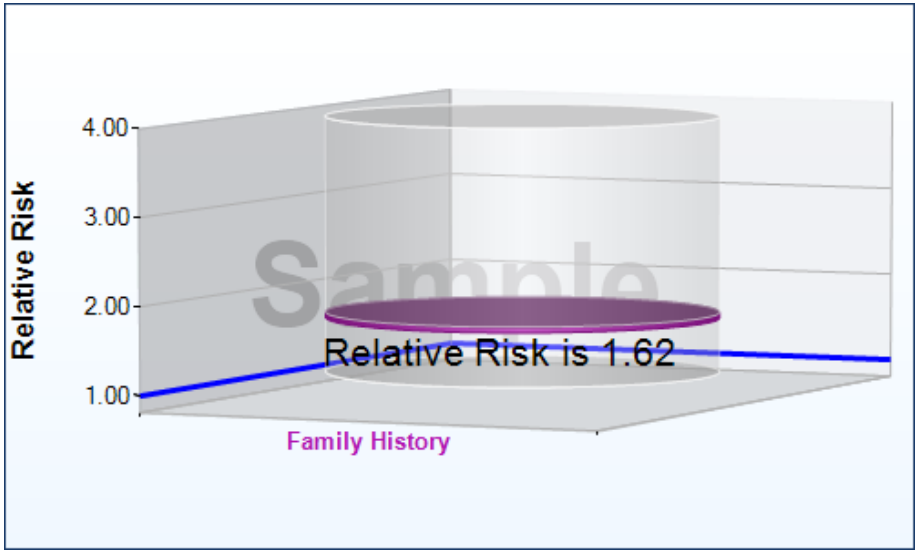
These results are based on a single study.

Osteoporosis

Risk Due To Family History

You reported that one of your parents, siblings or grandparents has been diagnosed with osteoporosis.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.62	1.00	3.86	**Based on your family history, you are 62% more likely (or 1.62 times as likely) to develop osteoporosis compared to a woman who does not have any parents, siblings or grandparents with osteoporosis.** ***Having either a parent, sibling or grandparent with osteoporosis contributes to your risk of osteoporosis.***



Risk is compared based on family history.

Women with at least one parent, sibling or grandparent with osteoporosis are compared to women with no parents, siblings or grandparents with osteoporosis to determine relative risk of developing osteoporosis.

A relative risk greater than 1.00 indicates an increased risk.

These results are based on a single study.

Osteoporosis

Risk Due To Smoking Status

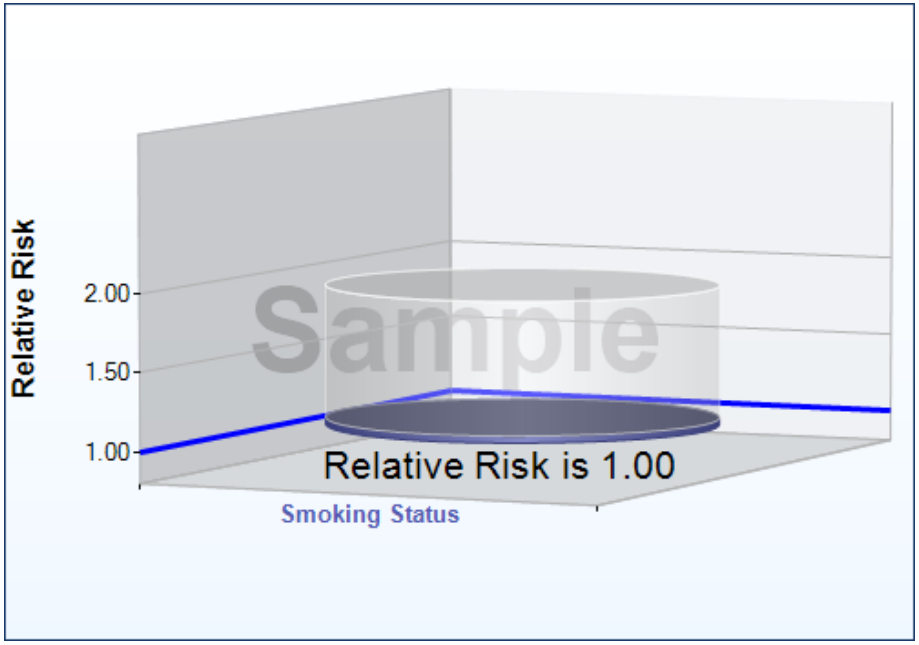
You reported that you do not smoke.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	1.85	**Because you are non smoker you are at a lower risk to develop osteoporosis compared to women who have smoked more than 1 pack of cigarettes per day for eight or more years.**

Risk is compared based on smoking habits.

Women who have smoked more than 1 pack of cigarettes per day for 8 or more years were compared to women who do not smoke, women who have smoked for 7 or less years, and women who have smoked less than a pack of cigarettes per day for 8 or more years to determine relative risk.

A relative risk of greater than 1.00 indicates an increased risk.



These results are based on a single study.

Osteoporosis - Variant #1 (rs3736228)

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** your risk for osteoporosis.

How Common Is This Variant?

Non-Risk Variant = C **Risk Variant = T**

CC - 90 in 100 people have 2 copies of the non-risk variant

CT - 10 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant

TT - 0 in 100 people have 2 copies of the risk variant

This frequency is based on data from an African American population.

Gene: LRP5 **Chromosome: 11q13.4**

Causes

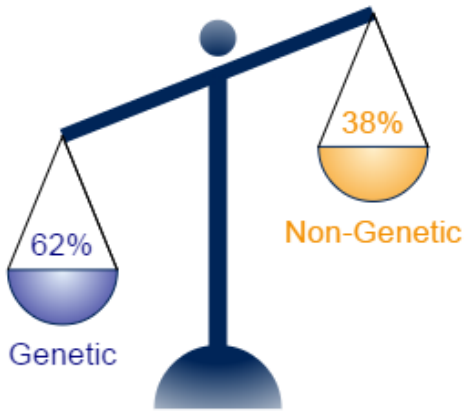
Genetic vs. Non-Genetic Risk Factors

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

It is estimated that **non-genetic** factors, like smoking, account for about **38%** of the risk of osteoporosis.

It is estimated that **62%** of the risk for osteoporosis is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

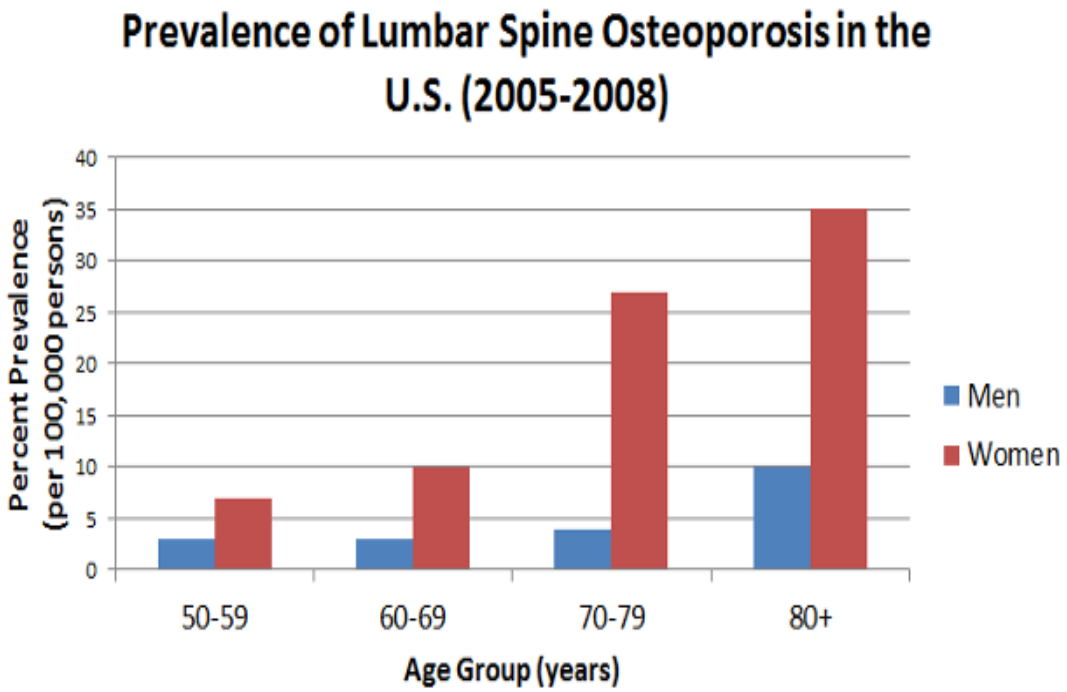
There are many different genetic and non-genetic risk factors that contribute to the risk of osteoporosis. We are only able to tell you about your family history risk, 1 genetic and 1 non-genetic risk factor at this time.



How Common

Age and gender contribute to the risk of osteoporosis.

You reported you are a woman, between 18 and 49 years old; data for women in your age group are not available, however, an estimated 7 in 100 women aged 50-59 have osteoporosis.



Limitations

Osteoporosis

- This result alone does NOT diagnose osteoporosis. Osteoporosis must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop osteoporosis.
- This result does NOT mean that you will not develop osteoporosis in the future.
- This result ONLY assesses your risk for developing osteoporosis due to the factors presented in this report and does not mean that other genetic variants or risk factors for osteoporosis are present or absent.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop osteoporosis 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.
- For some risk factors data may be provided by gender. Every effort will be made to provide you with risk information based on your reported gender. However, when risk data is not available for both genders, risk results for the available gender will be provided.

Methods

Osteoporosis

This condition and genetic variant was 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 Osteoporosis Risk Algorithm Version 1 (December 1, 2014)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. Genet Med. 13(2):131-139.
2. Looker, AC. et al (2012). Osteoporosis or low bone mass at the femur neck or lumbar spine in older adults: United States, 2005–2008. NCHS data brief no 93. Hyattsville, MD: National Center for Health Statistics.
3. Brook, JS. et al (2012). The smoking patterns of women in their forties: their relationship to later osteoporosis. Psychol Rep. 110(2):351-62.
4. Robitaille, J. et al (2008). Prevalence, family history, and prevention of reported osteoporosis in U.S. women. Am J Prev Med. 35(1):47-54.
5. Karasik, D. et al (2003). Age, gender, and body mass effects on quantitative trait loci for bone mineral density: the Framingham Study. Bone. 33(3):308-16.
6. Richards, JB. et al. (2008). Bone mineral density, osteoporosis, and osteoporotic fractures: a genome-wide association study. Lancet. 371(9623):1505-12.
7. McVean G.A. et al (2012). An integrated map of genetic variation from 1,092 human genomes. Nature. 491; 56-65.

Sample Results

Coriell Institute for Medical Research
Coriell Genotyping and Microarray Center
403 Haddon Avenue Camden, NJ 08103
Phone: 856-966-7377 Fax: 856-964-0254 www.coriell.org

Clinical Report for Osteoporosis Genetic Variant 1 (rs3736228)

Name:	NATALIE DEMO	**Sample Type:**	Saliva
Race/Ethnicity:	Black or African-American	**Gender:**	Female
Date of Birth:		**Date Collected:**	11-30-2016
Coriell ID:	DEMONAT	**Date Received:**	11-30-2016
Lab Accessioning Number:	DEMONAT	**Date of Report:**	12-17-2014
Ordering Physician:	Dr. Edward Viner		

Name of Gene/Region: LRP5		**Chromosomal Location:** 11q13.4
Variants tested	**Result**	**Reference Genotype**
rs3736228	CC	CC
Interpretation	**Individuals with this result are at a lower risk to develop osteoporosis compared to someone with one or two copies of this genetic risk variant.** These risk estimates are based on studies in European populations. When race/ethnicity specific risk estimates are not available, risk estimates based on Caucasian populations are provided.	
Other Risks	Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of osteoporosis. For additional information on other risk factors please see the accompanying CPMC research report.	

Risk interpretation based on Coriell's Osteoporosis Risk Algorithm Version 1 (December 1, 2014)

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 osteoporosis. This test is not diagnostic for osteoporosis and cannot rule out the risk of developing osteoporosis 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

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

References

1. Richards, J.B. et al (2008). Bone mineral density, osteoporosis, and osteoporotic fractures: a genome-wide association study. Lancet. 371(9623):1505-12.