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

Name:	STEVE CPMC	**Gender:**	Male
Date of Birth:		**Date Collected:**	11-30-2016
Coriell ID:	DEMOSTEVE	**Date Received:**	11-30-2016
Lab Accessioning Number:	DEMOSTEVE	**Date of Report:**	04-08-2013
Ordering Physician:	Dr. Edward Viner		

Risk of Developing Colorectal Cancer Based on:

- **CPMC Colorectal Cancer Variant 1 (rs6983267)**
- **Family History**
- **Alcohol Consumption**
- **Smoking**
- **Diabetes**
- **Inflammatory Bowel Disease**
- **Body Mass Index**
- **Physical Activity**
- **Screening (Colonoscopy)**

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 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 colorectal cancer. Some people have a rare genetic variant that can cause a high risk for colorectal cancer. The CPMC does NOT test for these rare genetic variants. If you have a family history of early onset colorectal cancer (before age 50) or 2 or more family members with either colorectal cancer or endometrial cancer diagnosed at any age, please contact a CPMC genetic counselor to determine if you are at risk for a hereditary form of colorectal cancer.

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

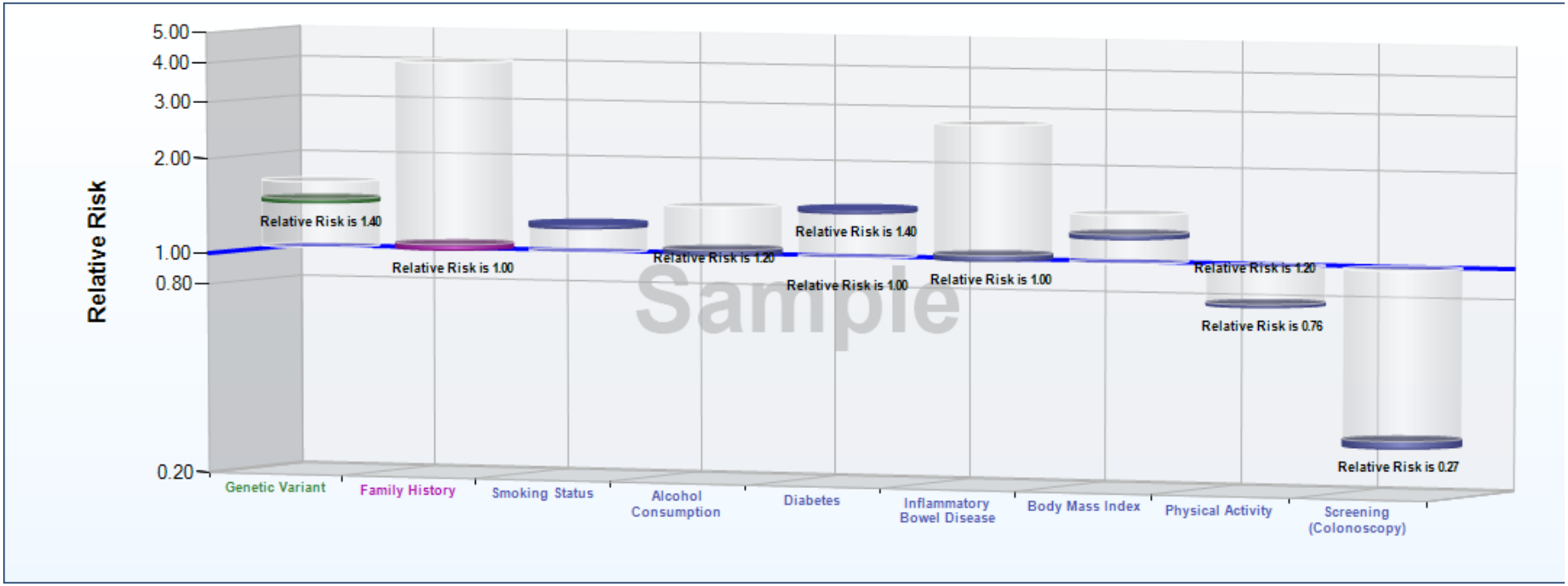
More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website http://cpmc.coriell.org or by contacting our genetic counselors. Participants may schedule an appointment with one of our board-certified genetic counselors through the web portal by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

Colorectal 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, smoking, alcohol consumption, history of diabetes, history of inflammatory bowel disease, body mass index, physical activity and screening for colorectal cancer.



You reported you are a Caucasian male, between 60 and 69 years old; 9 in 1,000 Caucasian males in your age group have colorectal cancer.

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Genetic Variant	**1.40**	1.00	1.60	**You have 1 copy of the non-risk variant and 1 copy of the risk variant. Based on this result, you are 40% more likely (or 1.4 times as likely) to develop colorectal cancer as someone with no copies of this variant.** *Having this risk variant contributes to your risk of colorectal cancer.*
	Family History	**1.00**	1.00	4.00	**Based on your family history, you are at a lower risk to develop colorectal cancer compared to someone with a first degree relative (parent, sibling or child) with colorectal cancer.**
	Smoking Status	**1.20**	1.00	1.20	**Because you are a current smoker you are 20% more likely (or 1.2 times as likely) to develop colorectal cancer compared to never smokers.** *Being a current smoker contributes to your risk of colorectal cancer.*
	Alcohol Consumption	**1.00**	1.00	1.40	**Based on the amount of alcohol you reported drinking you are at the same risk to develop colorectal cancer as someone who does not drink alcohol.**

Chart Color	Relative Risk Due To:	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	Diabetes	**1.40**	1.00	1.40	**Because you reported that you have type 1 or type 2 diabetes, you are 40% more likely (or 1.4 times as likely) to develop colorectal cancer as individuals who do not have type 1 or type 2 diabetes.** *Having type 1 or type 2 diabetes contributes to your risk of colorectal cancer.*
	Inflammatory Bowel Disease	**1.00**	1.00	2.70	**Because you reported that you do not have Crohn's disease or ulcerative colitis, you are at a lower risk of colorectal cancer compared to individuals who have Crohn's disease or ulcerative colitis.**
	Body Mass Index	**1.20**	1.00	1.40	**Based on your BMI you are 20% more likely (or 1.2 times as likely) to develop colorectal cancer as someone who has a BMI of less than 25 (not overweight).** *Being overweight (BMI of 25 to 29.9) contributes to your risk of colorectal cancer.*
	Physical Activity	**0.76**	0.76	1.00	**Because you are physically active, your risk to develop colorectal cancer is 24% lower (relative risk=0.76) than someone who is not physically active.** *Physical activity lowers your risk of colorectal cancer.*
	Screening (Colonoscopy)	**0.27**	0.27	1.00	**Because you have had colorectal cancer screening, your risk to develop colorectal cancer is 73% lower (relative risk=0.27) than someone who has not had colorectal cancer screening.** *Having colorectal cancer screening lowers your risk of developing colorectal cancer.*

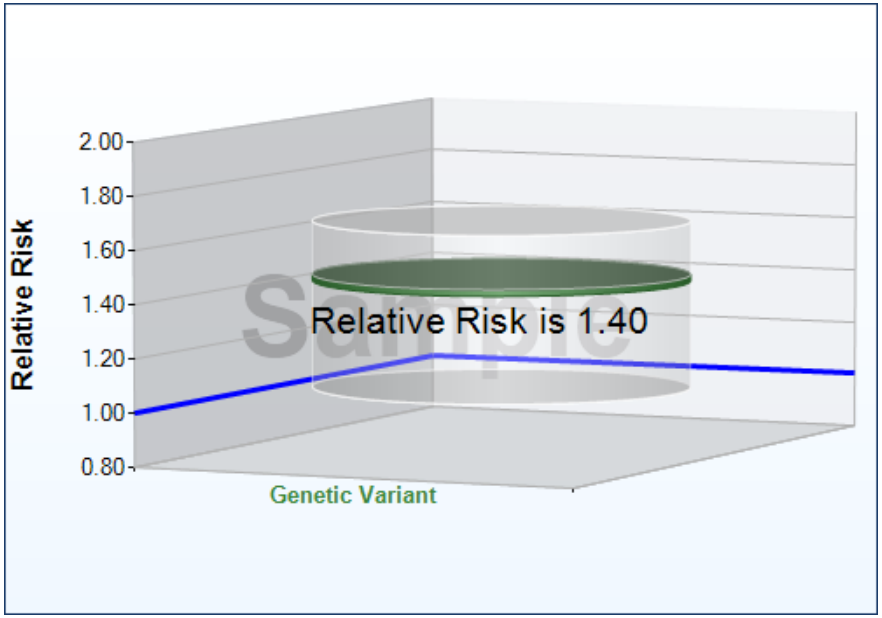
Colorectal Cancer

Risk Due To Genetic Variant #1 (rs6983267)

Your Result: 1 copy of the non-risk variant and 1 copy of the risk variant were detected (TG)

Non-Risk Variant = T Risk Variant = G

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.40	1.00	1.60	**You have 1 copy of the non-risk variant and 1 copy of the risk variant. Based on this result, you are 40% more likely (or 1.4 times as likely) to develop colorectal cancer as someone with no copies of this variant.** *Having this risk variant contributes to your risk of colorectal cancer.*



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 1.0 indicates an increased risk.

Some people have a rare genetic variant that can cause a high risk for colorectal cancer. The CPMC does NOT test for these rare genetic variants. If you have a family history of early onset colorectal cancer (before age 50) or 2 or more family members with either colorectal cancer or endometrial cancer diagnosed at any age, please contact a CPMC genetic counselor to determine if you are at risk for a hereditary form of colorectal cancer.

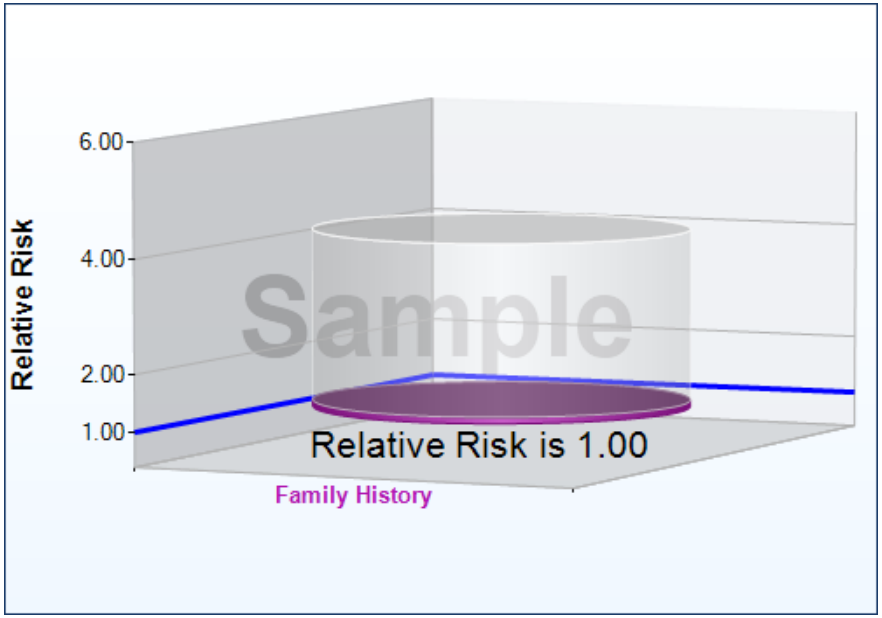
These risk estimates are based on studies in Caucasian populations.

Colorectal Cancer

Risk Due To Family History

You reported that none of your first degree relatives (parents, siblings or children) have colorectal cancer.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	4.00	**Based on your family history, you are at a lower risk to develop colorectal cancer compared to someone with a first degree relative (parent, sibling or child) with colorectal cancer.**



Risk is compared based on family history.

People with one or more first degree relatives (parents, siblings or children) with colorectal cancer are compared to people with no first degree relatives with colorectal cancer to determine relative risk of developing colorectal cancer.

A relative risk greater than 1.0 indicates an increased risk.

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

These results are based on studies in multiple populations of different racial and ethnic backgrounds.

Colorectal Cancer

Risk Due To Smoking Status

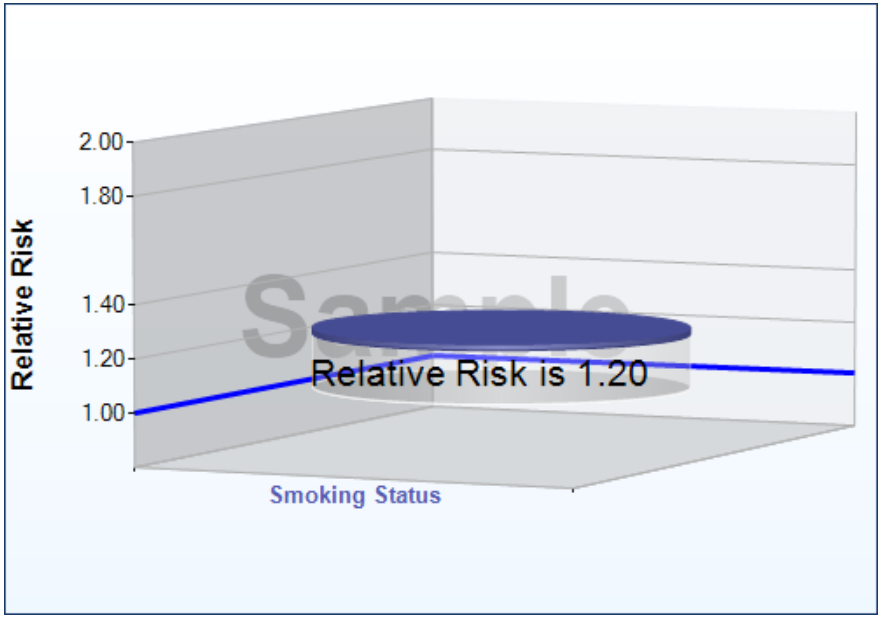
You reported that you are a current smoker.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.20	1.00	1.20	**Because you are a current smoker you are 20% more likely (or 1.2 times as likely) to develop colorectal cancer compared to never smokers.** *Being a current smoker contributes to your risk of colorectal cancer.*

Risk is compared based on smoking habits.

People who are current smokers or former smokers are compared to people who have never smoked to determine relative risk.

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



These results are based on studies in multiple populations of different racial and ethnic backgrounds.

Colorectal Cancer

Risk Due To Alcohol Consumption

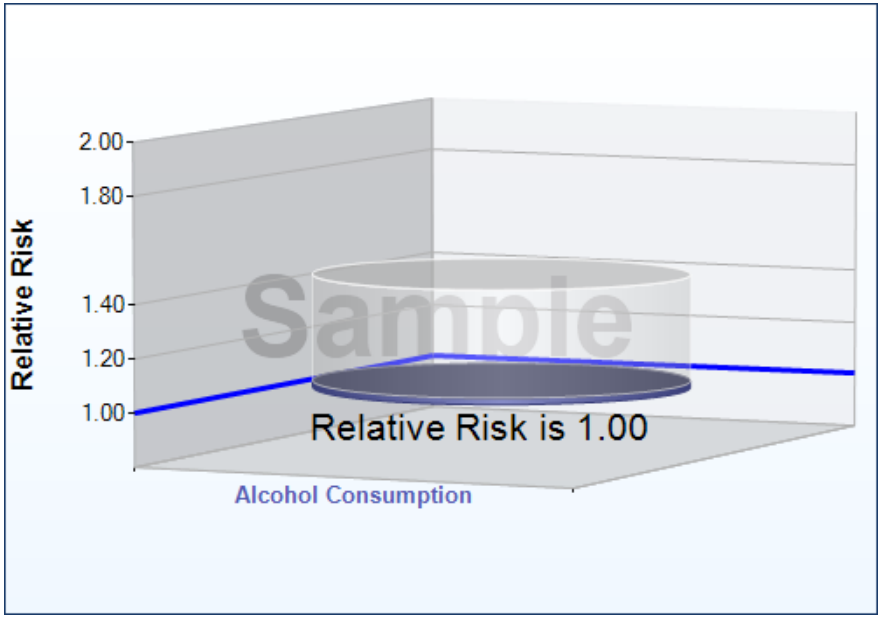
You reported that you drink alcohol.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	1.40	**Based on the amount of alcohol you reported drinking you are at the same risk to develop colorectal cancer as someone who does not drink alcohol.**

Risk is compared based on alcohol consumption.

People who drink alcohol are compared to people who do not drink alcohol to determine relative risk.

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



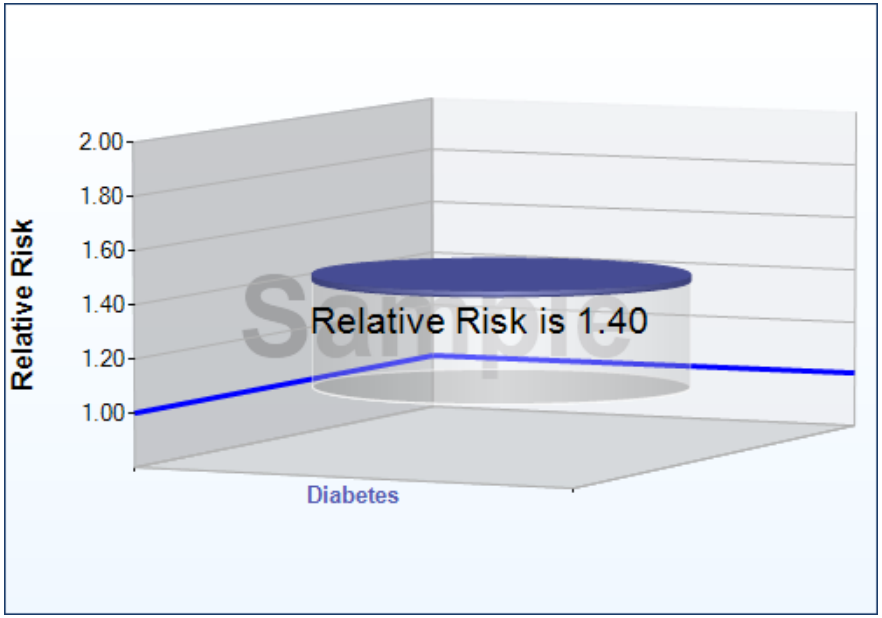
These risk estimates are based on studies in Caucasian populations.

Colorectal Cancer

Risk Due To Diabetes

You reported that you have either type 1 or type 2 diabetes.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.40	1.00	1.40	**Because you reported that you have type 1 or type 2 diabetes, you are 40% more likely (or 1.4 times as likely) to develop colorectal cancer as individuals who do not have type 1 or type 2 diabetes.** *Having type 1 or type 2 diabetes contributes to your risk of colorectal cancer.*



Risk is compared based on diagnosis of either type 1 or type 2 diabetes.

People who have type 1 or type 2 diabetes are compared to people who do not have type 1 or type 2 diabetes to determine relative risk.

A relative risk greater than 1.0 indicates an increased risk.

These results are based on studies in multiple populations of different racial and ethnic backgrounds.

Colorectal Cancer

Risk Due To Inflammatory Bowel Disease

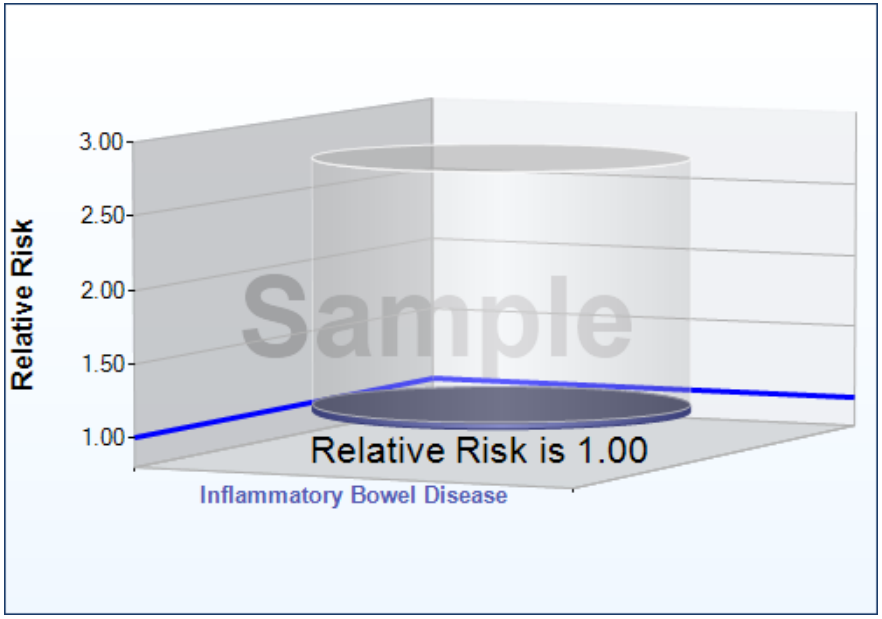
You reported that you do not have either Crohn's disease or ulcerative colitis.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.00	1.00	2.70	**Because you reported that you do not have Crohn's disease or ulcerative colitis, you are at a lower risk of colorectal cancer compared to individuals who have Crohn's disease or ulcerative colitis.**

Risk is compared based on diagnosis of either Crohn's disease or ulcerative colitis.

People who have Crohn's disease or ulcerative colitis are compared to people who do not have Crohn's disease or ulcerative colitis to determine relative risk.

A relative risk greater than 1.0 indicates an increased risk.



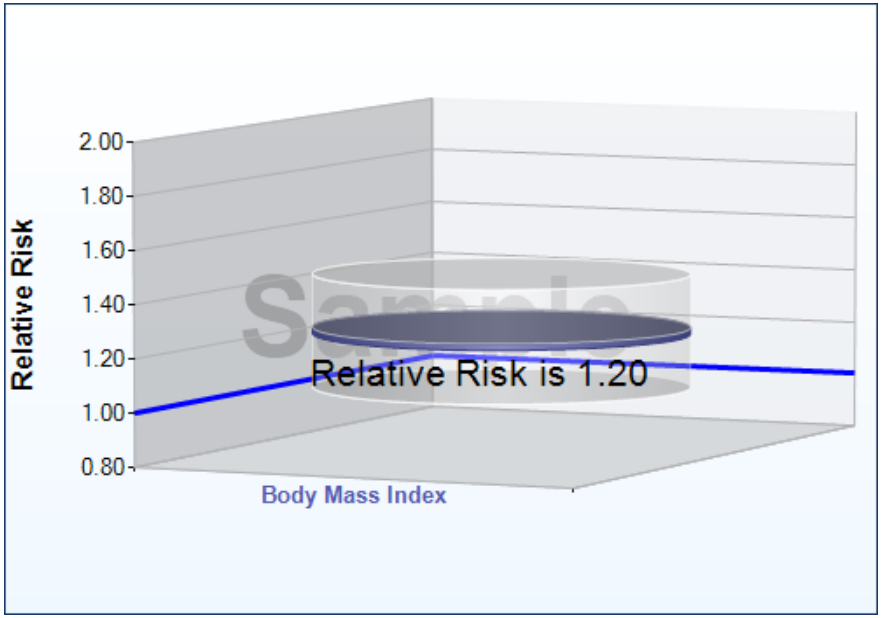
These results are based on studies in multiple populations of different racial and ethnic backgrounds.

Colorectal Cancer

Risk Due To Body Mass Index

According to the height and weight you reported, you may be overweight (BMI = 25.0-29.9).

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	1.20	1.00	1.40	**Based on your BMI you are 20% more likely (or 1.2 times as likely) to develop colorectal cancer as someone who has a BMI of less than 25 (not overweight).** *Being overweight (BMI of 25 to 29.9) contributes to your risk of colorectal cancer.*



Risk is compared based on Body Mass Index (BMI)

BMI is used to determine if someone is overweight or obese. Males who are overweight or obese are at increased risk of developing colorectal cancer. Females who are overweight or obese have not been found to be at increased risk of developing colorectal cancer.

Men who are overweight (BMI 25-30) or obese (BMI > 30) are compared to men who are not overweight (BMI < 25) to determine relative risk.

A relative risk greater than 1.0 indicates an increased risk.

These results are based on studies in multiple populations of different racial and ethnic backgrounds.

Colorectal Cancer

Risk Due To Physical Activity

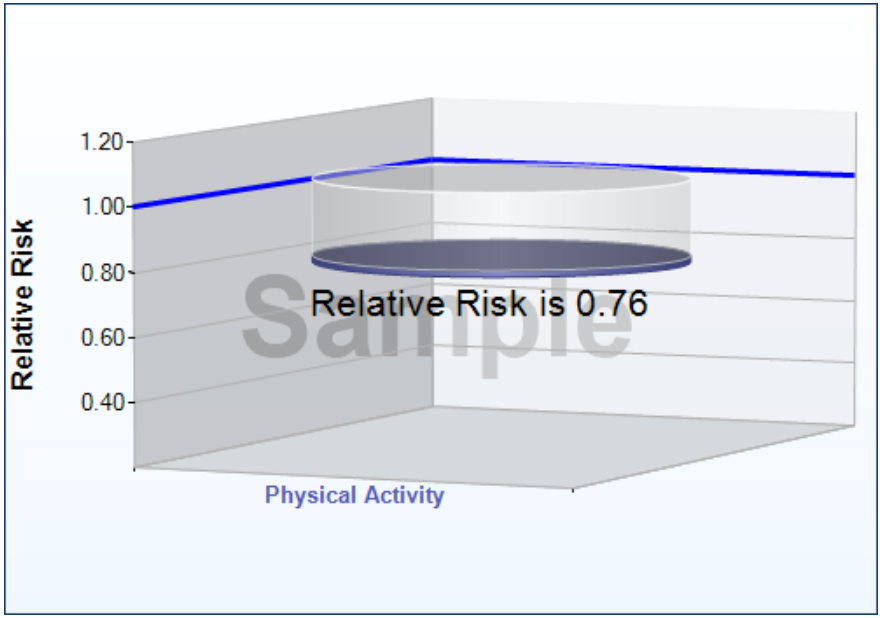
You reported that you are physically active.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	0.76	0.76	1.00	**Because you are physically active, your risk to develop colorectal cancer is 24% lower (relative risk=0.76) than someone who is not physically active.** *Physical activity lowers your risk of colorectal cancer.*

Risk is compared based on physical activity.

Men who are physically active are compared to men who are not physically active to determine relative risk.

A relative risk less than 1.0 indicates a decreased risk.



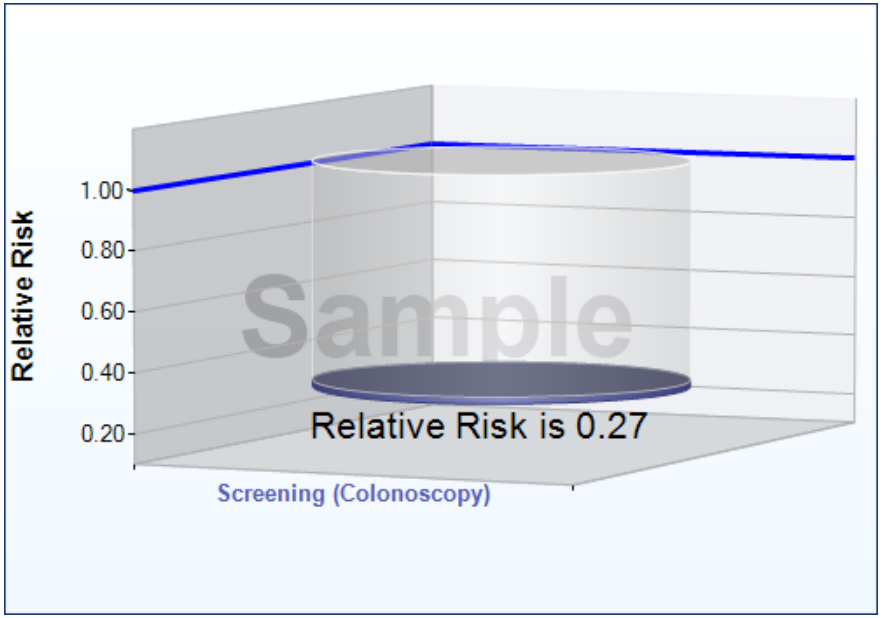
These results are based on studies in multiple populations of different racial and ethnic backgrounds.

Colorectal Cancer

Risk Due To Colorectal Cancer Screening (Colonoscopy)

You reported that you have been screened for colorectal cancer.

Chart Color	Your Risk	Minimum Risk	Maximum Risk	Interpretation
	0.27	0.27	1.00	**Because you have had colorectal cancer screening, your risk to develop colorectal cancer is 73% lower (relative risk=0.27) than someone who has not had colorectal cancer screening.** *Having colorectal cancer screening lowers your risk of developing colorectal cancer.*



Risk is compared based on whether or not recommended screening for colorectal cancer has been performed between the ages of 50 and 70.

People who have had recommended colorectal cancer screening are compared to people who have not had recommended colorectal cancer screening to determine relative risk.

A relative risk less than 1.0 indicates a decreased risk.

These risk estimates are based on studies in Caucasian populations.

Colorectal Cancer - Variant #1 (rs6983267)

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 colorectal cancer.

How Common Is This Variant?

Non-Risk Variant = T **Risk Variant = G**

TT - 27 in 100 people have 2 copies of the non-risk variant

TG - 50 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant

GG - 23 in 100 people have 2 copies of the risk variant

This data is based on studies in Caucasian populations.

Gene: This variant is not found within a known gene **Chromosome: 8q24.21**

Causes

Genetic vs. Non-Genetic Risk Factors

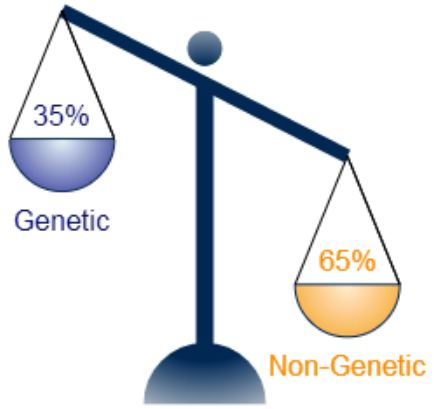
Colorectal cancer can be caused by both genetic factors and non-genetic (or environmental) risk factors.

It is estimated that **non-genetic** factors (like smoking, alcohol consumption and body mass index) account for about **65%** of the risk of colorectal cancer.

It is estimated that **35%** of the risk for colorectal cancer is based on **genetic** risk factors. This estimate accounts for both known and unknown gene variants.

Some people have a rare genetic variant that can cause a high risk for colorectal cancer. The CPMC does NOT test for these rare genetic variants. If you have a family history of early onset colorectal cancer (before age 50) or 2 or more family members with either colorectal cancer or endometrial (uterine) cancer diagnosed at any age, please contact a CPMC genetic counselor to determine if you are at risk for a hereditary form of colorectal cancer.

There are many different genetic and non-genetic risk factors that contribute to the risk of colorectal cancer. We are only able to tell you about your family history risk, 1 genetic and 7 non-genetic risk factor(s) at this time.

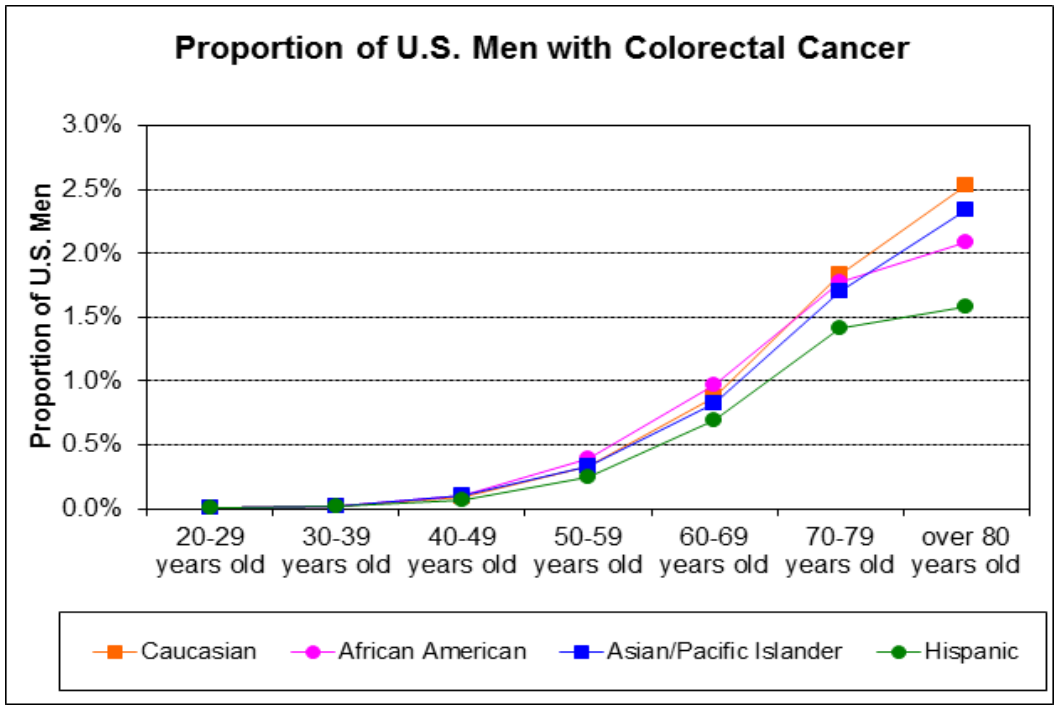


How Common

The risk of having colorectal cancer increases with age. Men have a slightly greater risk of developing colorectal cancer than women.

You reported you are a Caucasian male, between 60 and 69 years old; 9 in 1,000 Caucasian males in your age group have colorectal cancer.

Age and gender contribute to your risk of colorectal cancer.



Limitations

Colorectal Cancer

- This result alone does NOT diagnose colorectal cancer. Colorectal cancer must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop colorectal cancer.
- This result does NOT mean that you will not develop colorectal cancer in the future.
- This result ONLY assesses your risk for developing colorectal cancer due to the factors presented in this report and does not mean that other genetic variants or risk factors for colorectal cancer are present or absent.
- 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

Colorectal 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 Colorectal Cancer Risk Algorithm Version 1 (April 9, 2013)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. Genet Med. 13(2):131-139.
2. Tomlinson, I.P.M. et al. (2008). A genome-wide association study identifies colorectal cancer susceptibility loci on chromosomes 10p14 and 8q23.3. Nature Genetics. 40:623-630.
3. Horner MJ, et al. SEER Cancer Statistics Review, 1975-2006, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2006/, based on November 2008 SEER data submission, posted to the SEER web site, 2009.
4. Lichtenstein, P, et al. (2000) Environmental and Heritable Factors in the Causation of Cancer — Analyses of Cohorts of Twins from Sweden, Denmark, and Finland. NEJM, 343:78-85.
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12. Brenner, H. et al. (2011). Long-Term Risk of Colorectal Cancer After Negative Colonoscopy. Journal of Clinical Oncology. 29:3761-3767.

Sample Results

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Clinical Report for Colorectal Cancer Genetic Variant 1 (rs6983267)

Name:	STEVE CPMC	**Sample Type:**	Saliva
Race/Ethnicity:	White (Caucasian)	**Gender:**	Male
Date of Birth:		**Date Collected:**	11-30-2016
Coriell ID:	DEMOSTEVE	**Date Received:**	11-30-2016
Lab Accessioning Number:	DEMOSTEVE	**Date of Report:**	04-08-2013
Ordering Physician:	Dr. Edward Viner		

Name of Gene/Region: This variant is not found within a known gene		**Chromosomal Location:** 8q24.21
Variants tested	**Result**	**Reference Genotype**
rs6983267	TG	TT
Interpretation	**Individuals with this result are 40% more likely (or 1.4 times as likely) to develop colorectal cancer as someone with no copies of this variant.** 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.	
Other Risks	Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of colorectal cancer. For additional information on other risk factors please see the accompanying CPMC research report.	

Risk interpretation based on Coriell's Colorectal Cancer Risk Algorithm Version 1 (April 9, 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 colorectal cancer. This test is not diagnostic for colorectal cancer and cannot rule out the risk of developing colorectal 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. Tomlinson, I.P.M. et al. (2008). A genome-wide association study identifies colorectal cancer susceptibility loci on chromosomes 10p14 and 8q23.3. Nature Genetics. 40:623-630.

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