NorthShore University HealthSystem

Prostate Cancer Genetic Risk Score Report

Prepared for: Martin McFly

Knowing your prostate cancer Genetic Risk Score can be helpful in developing a plan for personalized prevention, early intervention and treatment.

Please share your results with your doctor to discuss next steps.

Important Notes

- Results in this report are based on variations in your DNA which are known to be associated with prostate cancer.
- These results indicate whether you are at an increased or decreased risk for developing prostate cancer. They do not provide certainties about whether you definitely will, or definitely will not, develop prostate cancer.
- There are other factors that impact your risk of developing prostate cancer such as age, family history, lifestyle, ethnic background and variations in other known cancer causing genes.
- Please talk to a genetic counselor or your doctor about your results.

Prostate Cancer Genetic Risk Score Report

Patient Name:	McFly, Martin	**Ordering physician:**	Emmett Brown
Patient ID:	1234567890	**Physician Phone:**	(877) 688-0992
Patient Sex:	Male	**Date of report:**	03/15/2019
Date of Birth:	1 Nov 1959	**Specimen:**	Saliva
Self-reported race:	Caucasian American	**Test Ordered:**	Prostate Cancer GRS

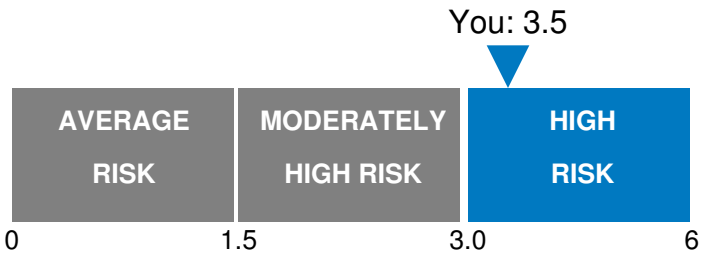
Sequencing done at: Helix OpCo LLC, 9875 Towne Center Dr., San Diego, CA 92121. (CLIA# 05D2117342)

Interpretation done at: NorthShore University HealthSystem, 2650 Ridge Ave., Evanston IL 60201

Your Genetic Risk Score (GRS) for Prostate Cancer is: 3.5

Interpretation of Your Score

- Your GRS for prostate cancer is 3.5, suggesting that your risk for prostate cancer is 3.5-times the risk of men in the general population.
- Based on GRS alone, you are in the 'high risk' category for developing prostate cancer.
- Based on your GRS, ethnic background and age, your risk for prostate cancer by age 85 is 49.8% (or 49 out of 100). In comparison, this risk is 14% (or 14 out of 100) for men of your age and ethnicity in the general population.

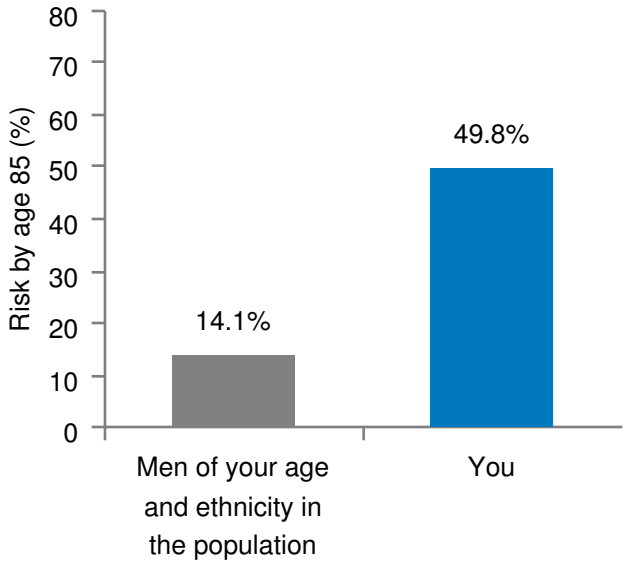


Your Risk Category: High Risk

Recommended Next Steps

- Please discuss with your physicians about potential benefits and harms of PSA screening for you. General guidelines (see page 7 for details) recommend that men with average risk start having a discussion with physicians about PSA screening for prostate cancer at age 55.
- Since your GRS is in the 'high risk' category, you may benefit from starting PSA screening 10 years earlier than general recommendations and/or more frequent screening.
- If you have a family history of prostate or other cancers, you may benefit from genetic counseling and other genetic testing.

Your lifetime risk for prostate cancer



Signed by: Peter Hulick, MD

Knowing Your GRS is Helpful

Primary use for GRS information: For men without prostate cancer

- The prostate cancer genetic risk score provides an estimate of your relative risk compared to the general population as well as lifetime risk by age 85, of developing prostate cancer. This score is based on your ethnic background, current age, and your genetic makeup.
- Knowing your risk of developing prostate cancer can help you make informed prevention management decisions like earlier screening and intervention. It is specifically helpful for deciding a plan for prostate cancer screening. Please share your results with your doctor and discuss the potential risks, benefits and limitations of prostate cancer screening.
- There are other factors that can impact your risk of developing prostate cancer that are not included in this test (like your family history, environmental exposures, etc) which should also be considered when making a decision about prostate cancer screening. Discuss your genetic risk score results with your doctor. If your doctors determine that further investigation is necessary after a PSA blood screening, they may perform a prostate biopsy to screen for the presence of prostate cancer.

Additional use of GRS Information: For men with moderately elevated PSA levels

- For men with moderately elevated PSA levels, your doctors can also use GRS information to supplement other clinical information for making the decision about performing a prostate biopsy.
- For men already diagnosed with prostate cancer, GRS can also be used to understand possible causes for developing the disease.

Explanation of risk categories

GRS can be directly interpreted as an individual's risk compared to the general population. The average GRS is 1.0 in the general population. A GRS higher or lower than 1.0 indicates a higher or lower risk of developing prostate cancer compared to the general population.

Depending on your risk scores, you can be in three different risk categories:

- **Average risk**

  Men with a score of 0.0 - 1.49 fall under this category. For example, if your GRS is 0.8, this means that your risk of developing prostate cancer is 0.8 times the general population risk. Men in this category can follow general population guidelines for screening

- **Moderately high risk**

  Men with a score of 1.5 - 2.99 fall under this category. For example, if your GRS is 2.0, this means that your risk of developing prostate cancer is twice as high when compared to the general population risk.
  Men in this category should talk to their doctor about earlier and more frequent screening than recommendations for the general population.

- **High risk**

  Men with a score of 3 or higher fall under this category. For example, if your GRS is 4.0, this means that your risk of developing prostate cancer is four times higher than when compared to the general population risk.
  Men in this category should talk to their doctor about earlier and more frequent screening than recommendations for the general population.

Sharing Your GRS results

Talk to a genetic counselor

Genetic counselors are board certified healthcare providers who are trained in medical and clinical genetics. We recommend that you speak with a Genome Medical genetic counselor who can help you understand your results. Additionally they can review your personal and family history, and give you information on how to approach your doctor with your Genetic Risk Score results. This service is provided to you at no additional charge.

Schedule an appointment:
A scheduling link for your complimentary appointment has been emailed to you ("Subject: Your genetic test has been authorized by your Genome Medical physician").

If you have questions or prefer to schedule by phone, contact Genome Medical's care coordination team at coordinator@genomemedical.com or (877) 688-0992.

Following a consultation with Genome Medical, it is also important to share your results with your doctor, so together you can determine your best plan of action.

Share your results with your doctor

Your prostate cancer genetic risk score can be an important tool in determining next steps for screening for prostate cancer. Your genetic risk score result along with your family history and other risk factors can assist your physicians to better recommend the frequency and the age to begin prostate cancer screening. Please share your prostate cancer genetic risk score with your physicians.

Consider impact on family members

This test looks at dozens of changes in the DNA. Each has a small impact on your overall risk of developing prostate cancer, but when combined, can have a larger impact. Each of these variations might be passed on to a future generation. Since, the genetic risk score is truly a personalized score and is calculated based on the combined effect of the variations you have, your family member's genetic risk score may be different than yours, based on the variations they have. This means that a high risk score for one person does NOT mean other family members will be in the same risk category. If one relative is in the 'average risk' category, there is a chance that other relatives could be in the 'high risk' category. That means each of your male relatives should have his own test to understand his genetic risk score and chance of developing prostate cancer.

If you have a personal or family history of prostate cancer, or other cancers that run in your family, your doctor or a genetic counselor can help determine if any additional genetic testing for other types of hereditary cancer risks may be appropriate.

Background Information

Genetic Risk Score is a powerful tool for genetic risk assessment

What is a genetic risk score?

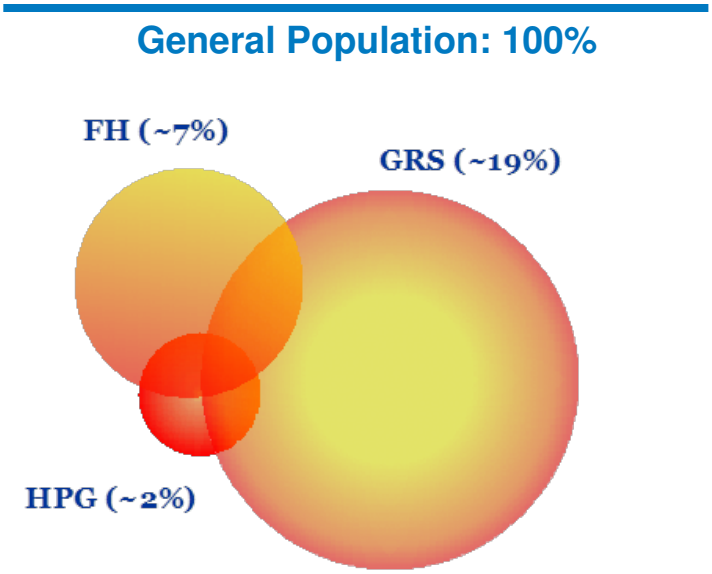
When thinking about your overall risk of developing a condition like prostate cancer, many different risk factors should be considered. These include age, family history, genetic makeup, personal medical history, lifestyle, and ethnic background.

Due to advances in medicine and genetics, we know that certain changes, called single nucelotde polymorphisms (SNPs), in the DNA can increase the chance of developing certain diseases, like prostate cancer. While most SNPs are of unknown significance, there are dozens of SNPs that have been shown to increase the risk of prostate cancer. Each has a small impact on your overall risk of developing the disease but when combined, can have a larger impact. The chance of developing prostate cancer increases based on the number of these harmful SNPs in a person. The Genetic Risk Score (GRS) is calculated by looking at the combined effect of these risk related SNPs. Knowing your GRS will allow you and your health care provider make informed medical management decisions, like early screening for prostate cancer.

How is this test different from other genetic tests for prostate cancer?

There are different kinds of genetic tests for prostate cancer. Some tests look at SNPs in major susceptibility genes such as BRCA2. These genes are also called high penetrance genes (HPGs) because having a single harmful change (mutation) in these genes can significantly increase the risk of prostate cancer.

Other tests, including this one, are GRS-based. They look at genetic changes that individually have low impact on overall risk but when combined with other genetic changes, a larger impact can be assessed.



Proportion of men in the general population identified as high-risk for prostate cancer by family history (FH), high- penetrance genes (HPGs), and genetic risk score (GRS)

Genetic risk score complements major high-penetrance genes and family history

A comprehensive genetic risk assessment should include all three genetic risk factors: family history, mutations in high penetrance genes, and GRS. The proportions of men in the general population having these risk factors are schematically shown in the Figure above. The size of circle indicates the proportion of high-risk men identified by each method. About 7% of men in the general population have a positive family history (FH), about 2% of men have mutations in high penetrance genes (HPGs), and about 19% men have high GRS (>1.5). The color indicates the degree of risk, with darker red denoting higher risk. These three risk factors are independent, and men who have any of them are considered to be at higher risk for developing prostate cancer.

Background Information (continued)

Distribution of GRS in the population

The average of GRS in a general population is 1.0, with a range from less than 0.1 to 6 or higher. As shown in the table below, the majority of men have scores less than 1.5 and are considered to have 'average risk'. Fewer men have scores between 1.5 and 3.0 and are considered to have 'Moderately high risk'. And considerably fewer men have a score greater than 3 and are considered to have 'high risk'.

		Percentage of men		
Range of GRS	Risk category	Caucasian	African American	East Asian
0.0 - 1.49	Average risk	84.6%	92.3%	84.8%
1.5 - 2.99	Moderately high risk	14.3%	7.6%	14.2%
3 or more	High risk	1.2%	0.1%	1.0%

Reliability and validity of GRS

Prostate Cancer Genetic Risk Score is calculated based on dozens of known prostate cancer risk-related SNPs. The relation of each of these SNPs to prostate cancer has been established and validated in independent populations (ref 1).

Validity of Prostate Cancer GRS (overall)

The validity of a GRS for prostate cancer risk assessment has also been consistently demonstrated and validated through large case-control studies with more than 140,000 study subjects, through retrospective analysis of clinical trials, through prostate biopsy cohorts, and through prospective population-based studies (refs 2,3).

Validity of This Prostate Cancer GRS

The validity of your GRS in this report is established through studies involving tens of thousands subjects. Our prostate cancer GRS test was validated in each ethnic background. The predicted risks (GRS values of test subjects) have been corroborated by observed risks in Non-Hispanic Whites (50,786 prostate cancer patients and 33,997 unaffected controls), in African Americans (4,185 prostate cancer patients and 3,985 unaffected controls), and in East Asians (1,233 prostate cancer patients and 1,048 unaffected controls).

For details, please visit the website: northshore.org/GeneticRiskScore

GRS is specific to a person's ethnic background

While the genetic makeup of all humans is more than 99% similar, it is that less than 1% that makes us unique. Some of the variations can have different effects on different ethnic groups, so it is important to study and validate what those genetic variants mean for each individual based on their ethnic background.

Currently, the Prostate Cancer Genetic Risk Score is available for men of three different ethnic backgrounds: Caucasians (Non-Hispanic Whites), African Americans, and East Asians. GRS has not yet been validated in other ethnic populations, but may be expanded in the future.

Background Information (continued)

About prostate cancer

Prostate cancer is a common cancer in men

Prostate cancer is the most common form of cancer besides skin cancer in American men. About 1 out of 7 men will develop prostate cancer by age 85. Although it can be diagnosed at a younger age, it is typically diagnosed after age 40 and the rate of diagnosis increases with age.

Prostate cancer usually grows slowly and is initially confined to the prostate gland, where it may not cause serious harm. However, while some types of prostate cancer grow slowly and may need minimal or even no treatment, other types are aggressive and can spread quickly. Prostate cancer that is detected early, when it is still confined to the prostate gland, has a better chance of successful treatment.

Screening for prostate cancer and recommendations

There are no symptoms associated with early stage prostate cancer. Therefore, screening for prostate cancer is important. Guidelines from professional societies, like the American Academy of Family Physicians (AAFP), recommend that men aged 55 to 69 years old should discuss the potential benefits and harms of PSA screening with their clinician (Ref 4-6). Although some debate remains in the medical community about the optimal use of PSA screening, it is an individual decision based on personal preference and personal risk.

Risk factors for prostate cancer

There are many factors that can impact risk for developing prostate cancer, such as age, family history of prostate and other cancers, lifestyle, environmental factors, and ethnic background. Inherited genetic factors play a leading role for developing prostate cancer, accounting for 57% of its risk.

The current approach to assessing a person's risk is to consider family history and ethnic background. Men with a family history of the disease as well as African American men have a higher risk of developing prostate cancer. However, with the advance of genetic technology, it is now possible to directly and more accurately measure the genetic risk using the GRS. Additional genetic testing for other hereditary forms of cancer, may also be appropriate. However, these are not included in this test.

For more information about prostate cancer, please visit the following websites:

- National Cancer Institute: cancer.gov/types/prostate
- American Cancer Society: cancer.org/cancer/prostate-cancer.html
- American Urological Association: auanet.org/guidelines/prostate-cancer-early-detection-(2013-reviewed-for-currency-2018)
- Prostate Cancer Foundation: pcf.org/about-prostate-cancer/what-is-prostate-cancer/the-psa-test/
- U.S. Preventive Service Task Force: uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/prostate-cancer-screening1

Disclaimers

GRS does not measure everything related to prostate cancer risk

GRS is one type of genetic test and is based on a combination of known genetic variations which are common in the population. There are also rare genetic variations that occur in a number of high-penetrance genes (HPGs) where having a single harmful change in the gene can mean a significantly increased risk for prostate cancer and, in some cases, other types of cancer. Most people who carry one of these types of genetic variations also have a family history of prostate or other cancers.

If you are concerned about your personal or family history of cancer, or want to learn more about whether additional genetic testing may be appropriate for you, talk to your doctor or you can speak with a Genome Medical genetic counselor at no additional charge.

What genetic risk score tells you
GRS provides information on the risk of developing prostate cancer. The risk is described in two ways:

1. Your chance of developing prostate cancer compared to the general population, and

2. Your remaining lifetime risk of developing prostate cancer.

What GRS does NOT tell you
1. It will not tell you whether you will, or will not, develop prostate cancer.
2. It will not tell you whether you have other, less common, genetic risks.

Disclaimer of liability

It is recommended that a genetic counselor or physician with expertise in genetic conditions help you interpret this report. The results of this test are best interpreted in a clinical context with respect to each individual's results. This test does not replace clinical assessment and must not be used as the only tool to estimate risk. This test has neither been cleared nor approved by the U.S. Food and Drug Administration (FDA). However, the FDA has determined that such clearance or approval is not necessary.

References

1. Conran, C.A., et al., Population-standardized genetic risk score: the SNP-based method of choice for inherited risk assessment of prostate cancer. Asian J Androl 18, 520-524 (2016).

2. Schumacher, F.R., et al., Association analyses of more than 140,000 men identify 63 new prostate cancer susceptibility loci. Nat Genet 50, 928-93 (2018)

3. Zheng S.L., et al., Cumulative association of five genetic variants with prostate cancer. N Engl J Med 358, 910-919 (2008)

4. US Preventive Services Task Force, et al., Screening for Prostate Cancer: US Preventive Services Task Force Recommendation Statement. JAMA 319, 1901-1913 (2018)

5. American Academic of Family Physicians, et al., Prostate Cancer: Clinical Preventative Service Recommendation. https://www.aafp.org/patient-care/clinical-recommendations/all/prostate-cancer.html.

6. American Urological Association, et al., Prostate Cancer: Early Detection (2013; reviewed for currency 2018). https://www.auanet.org/guidelines/prostate-cancer-early-detection-(2013-reviewed-for currency -2018)