

## Polygenic Risk Report

Patient: Sex:

Male

Emo J. Sharp

Ernst J. Schaefer, MD Laboratory Director / Chief Medical Officer Powered by **allelica** 



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## **CAD RISK REPORT**



#### RESULTS

Polygenic Risk Score

High (98<sup>th</sup> percentile)



#### CAD RISK OVER TIME

Everyone's CAD risk increases with age. The blue line on the chart shows this increase for a males with an average PRS. The PRS (orange line) of the tested individual shows that this person's risk rises more quickly than the average (blue line).





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## **CAD POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants spread throughout the genome. Lifetime risk of CAD is calculated by comparing the tested individual's PRS to a reference population. PRS above the 88<sup>th</sup> percentile is considered high because it confers a greater than 46% lifetime risk, which is three times the risk of disease compared to the remainder of the population. The chart shows how PRS translates to lifetime risk of coronary artery disease. This CAD PRS comprises 1,926,521 genome-wide variants.

#### RECOMMENDATIONS

The suggested next step is a conversation with a physician to discuss assessing the LDL cholesterol levels and 10 year absolute risk of cardiovascular disease\*. Additional non-genetic risk factors will also affect your lifetime risk. There are behavioral and dietary approaches to lowering risk, including following a healthy lifestyle and regular exercise. Major CAD risk factors include age, sex, race, high blood pressure, blood pressure treatment, diabetes, smoking, total cholesterol, and HDL cholesterol. In addition to lifestyle modification, subjects with a >7.5% 10-year CAD risk are candidates for statin therapy in addition to lifestyle change according to the American Heart Association.

\*Information on national heart disease guidelines can be found on the AHA website here: AHA Guidelines on management of blood lipids (2018) Circ 139:e1144–e1161\_





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## **STROKE RISK REPORT**



#### RESULTS

Polygenic Risk Score

Not elevated (90<sup>th</sup> percentile)



#### **STROKE RISK OVER TIME**

Everyone's Stroke risk increases with age. The blue line on the chart shows this increase for a males with an average PRS. The PRS (orange line) of the tested individual shows that this person's risk rises at around the same rate as the average (blue line).





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## STROKE POLYGENIC RISK REPORT



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants spread throughout the genome. Risk of an early menopause is calculated by comparing the tested individual's PRS to a reference population. PRS in males above the {90<sup>th</sup>} percentile is considered high because it confers a greater than 9% lifetime risk of disease. The chart shows how PRS translates to lifetime risk This Stroke PRS comprises 415,100 genomewide variants.

#### RECOMMENDATIONS

A number of lifestyle factors are known to increase risk of Stroke. These include smoking, high blood pressure and diet. To reduce lifetime risk of Stroke, as well as a number of other diseases, it is important to maintain a healthy lifestyle, reduce alcohol consumption and keep physically active.

\*More information on Stroke can be found on the American Stroke Association website here: https://www.stroke.org/





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## **ATRIAL FIBRILLATION RISK REPORT**



#### RESULTS

Polygenic Risk Score

Not elevated (89<sup>th</sup> percentile)



#### ATRIAL FIBRILLATION RISK OVER TIME

Everyone's AF risk increases with age. The blue line on the chart shows this increase for a males with an average PRS. The PRS (orange line) of the tested individual shows that this person's risk rises at around the same rate as the average (blue line).





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## ATRIAL FIBRILLATION POLYGENIC RISK REPORT



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants spread throughout the genome. Lifetime risk of AF is calculated by comparing the tested individual's PRS to a reference population. PRS above the 91<sup>st</sup> percentile is considered high because it confers a greater than 38% lifetime risk, which is twice the risk of disease of the average population. The chart shows how PRS translates to lifetime risk of Atrial Fibrillation. This AF PRS comprises 445,014 genome-wide variants.

#### RECOMMENDATIONS

Atrial fibrillation is a major risk factor for stroke and can be detected by an electrocardiogram or cardiac rhythm monitoring. If you are at high-risk, please discuss with your healthcare provider.





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## **TYPE 2 DIABETES RISK REPORT**



#### RESULTS

Polygenic Risk Score

Not elevated (40<sup>th</sup> percentile)



#### **TYPE 2 DIABETES RISK OVER TIME**

Everyone's T2D risk increases with age. The blue line on the chart shows this increase for a males with an average PRS.The PRS (orange line) of the tested individual shows that this person's risk rises at around the same rate as the average (blue line).





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## **TYPE 2 DIABETES POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic throughout the genome. variants spread Lifetime risk of T2D is calculated by comparing the tested individual's PRS to a reference population. PRS above the 90<sup>th</sup> percentile is considered high because it confers a greater than 34% lifetime risk, which is twice the risk of disease of the average population. The chart shows how PRS translates to lifetime risk of Type 2 Diabetes This T2D PRS comprises 620,162 genome-wide variants.

#### RECOMMENDATIONS

Average risk of Type 2 Diabetes can be maintained by following an active lifestyle and healthy diet to keep your BMI at a healthy level. If at high risk, please discuss with your healthcare provider and consider using our Life Plan for dietary modification.

\*Further information on the role of exercise, diet and therapeutics in preventing diabetes risk can be found here:

Precision medicine in diabetes: Consensus Report from the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) Diabetologia 63, 1671–1693 (2020)





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## HYPERTENSION POLYGENIC RISK REPORT



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic throughout the variants spread genome. Lifetime risk of hypertension (systolic blood pressure over 160 mmHg) is calculated by comparing the tested individual's PRS to a reference population. PRS above the 91<sup>st</sup> percentile is considered high because it confers a greater than 58% risk, which is twice the genetic risk of disease compared to the average of the population. The chart shows how PRS translates to lifetime risk of high blood pressure. This Hypertension PRS comprises 247,151 genome-wide variants.

#### RECOMMENDATIONS

Additional non-genetic risk factors will also affect your blood pressure. There are behavioral and dietary approaches to lowering risk, including following a healthy lifestyle and regular exercise. If at high risk, please discuss with your healthcare provider and consider using our Life Plan for dietary modification.

\*Information on blood pressure management approaches can be found here: https://www.nhlbi.nih.gov/files/docs/guidelines/express.pdf





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## **BODY MASS INDEX (BMI) POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic throughout the genome. variants spread Lifetime risk of high BMI (>30) is calculated by comparing the tested individual's PRS to a reference population. PRS above the 84<sup>th</sup> percentile is considered high because it confers a greater than 8% risk, which is twice the genetic risk of disease compared to the average of the population. The chart shows how PRS translates to lifetime risk of BMI. This BMI PRS comprises 543,656 genome-wide variants.

#### RECOMMENDATIONS

This BMI PRS provides an assessment of the contribution of genetics to bodyweight which is not an assessment of your actual BMI. High BMI is a risk factor for many common diseases. It is important to maintain a healthy weight to keep BMI low by following a healthy lifestyle and regular exercise. If at high risk, please discuss with your healthcare provider and consider using our Life Plan for dietary modification.





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## HIGH LDL CHOLESTEROL POLYGENIC RISK REPORT



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants throughout the genome. spread Lifetime risk high LDL-cholesterol of (>190mg/dL) is calculated by comparing the individual's PRS tested to a reference population. PRS above the 82<sup>nd</sup> percentile is considered high because it confers a greater than 12% risk, which is twice the genetic risk of disease compared to the average of the population. The chart shows how PRS translates to lifetime risk of high LDL cholesterol. This LDL PRS comprises 3,036 genome-wide variants.

#### RECOMMENDATIONS

Measure LDL Cholesterol after an overnight fast to assess baseline value.





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## HIGH LIPOPROTEIN (A) POLYGENIC RISK REPORT



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants throughout the genome. spread Lifetime risk high Lipoprotein of (a) (>125nmol/L) is calculated by comparing the individual's PRS to tested a reference population. PRS above the 76<sup>th</sup> percentile is considered high because it confers a greater than 10% risk, which is twice the genetic risk of disease compared to the average of the population. The chart shows how PRS translates to lifetime risk of high Lipoprotein (a). This LpA PRS comprises 39 genome-wide variants.

#### RECOMMENDATIONS

Measure Lp(a) to assess baseline value.





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## HIGH TRIGLYCERIDES POLYGENIC RISK REPORT



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic throughout the genome. variants spread Lifetime risk of high Triglycerides (>150mg/dL) comparing is calculated by the tested individual's PRS to a reference population. PRS above the 89<sup>th</sup> percentile is considered high because it confers a greater than 48% risk. which is twice the genetic risk of disease compared to the average of the population. The chart shows how PRS translates to lifetime risk of high triglycerides. This Triglyceride PRS comprises 68,880 genome-wide variants.

#### RECOMMENDATIONS

Measure Triglycerides after an overnight fast to assess baseline value.





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## LOW HDL CHOLESTEROL POLYGENIC RISK REPORT



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic throughout the genome. variants spread Lifetime risk of low HDL-cholesterol (<40mg/dL) comparing is calculated by the tested individual's PRS to a reference population. PRS above the 90<sup>th</sup> percentile is considered high because it confers a greater than 46% risk. which is twice the genetic risk of disease compared to the average of the population. The chart shows how PRS translates to lifetime risk of low HDI cholesterol This HDI PRS comprises 322,564 genome-wide variants.

#### RECOMMENDATIONS

Measure HDL Cholesterol after an overnight fast to assess baseline value.





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## ALZHEIMER'S DISEASE AND ALL-CAUSE DEMENTIA RISK REPORT



#### RESULTS

Polygenic Risk Score

Not elevated (45<sup>th</sup> percentile)



#### ALZHEIMER'S DISEASE AND ALL-CAUSE DEMENTIA RISK OVER TIME

Everyone's AD risk increases with age. The blue line on the chart shows this increase for a males with an average PRS. The PRS (orange line) of the tested individual shows that this person's risk rises at around the same rate as the average (blue line).





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## ALZHEIMER'S DISEASE AND ALL-CAUSE DEMENTIA POLYGENIC RISK REPORT



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants spread throughout the genome. Risk of AD is calculated by comparing the tested individual's PRS to a reference population. PRS in males above the 85<sup>th</sup> percentile is considered high because it confers a greater than 39% lifetime risk of disease. The chart shows how PRS translates to lifetime risk This AD PRS comprises 136,337 genome-wide variants, including some in and around APOE, a gene that contains polymorphisms that have been associated with increased risk of AD.

#### RECOMMENDATIONS

A number of factors are known to increase the risk of Alzheimer's Disease and all-cause dementia. These include age >70 years, having a stroke, diabetes, cancer, excess alcohol intake, low levels of plasma omega-3 fatty acids, and high levels of serum homocysteine.

\*More information on AD can be found on the Alzheimer's association website





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## **PROSTATE CANCER RISK REPORT**



#### RESULTS

Polygenic Risk Score

Not elevated (72<sup>nd</sup> percentile)



#### PROSTATE CANCER RISK OVER TIME

Every man's prostate cancer risk increases with age. This is shown for a man with average PRS by the blue line on the chart. The presence of a not elevated PRS means that risk rises at around the same rate as the average population (orange line).





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## **PROSTATE CANCER POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic throughout the genome. variants spread Lifetime risk of prostate cancer is calculated by comparing the tested individual's PRS to a reference population. PRS in individuals above the 83<sup>rd</sup> percentile is considered high because it confers greater than two times the lifetime genetic risk of disease of an average person. The chart shows how PRS translates to lifetime risk for prostate cancer. This prostate cancer PRS comprises 682,397 genome-wide variants.

#### RECOMMENDATIONS

A not elevated genetic risk of prostate cancer means that this man's genetics do not confer additional risk of disease. However risk increases over time and this man's risk may increase as a result of age as well as the presence of other, unmeasured risk factors.

\*Information on national screening guidelines can be found on the ACS website here:

ACS Prostate Cancer Early Detection Recommendations The National Comprehensive Cancer Network guidance on genetic risk can be found here: NCCN Guidelines for Genetic/Familial High-Risk Assessment





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## **BRAIN CANCER RISK REPORT**



#### RESULTS

Polygenic Risk Score

Not elevated (57<sup>th</sup> percentile)



#### **BRAIN CANCER RISK OVER TIME**

Everyone's brain cancer risk increases with age. This is shown for a males with average PRS by the blue line on the chart. The presence of not elevated PRS means that risk rises at around the same rate as the average population (orange line).





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## **BRAIN CANCER POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants spread throughout the genome. Lifetime risk of brain cancer is calculated by comparing the tested individual's PRS to a reference population. PRS in individuals above the 91<sup>st</sup> percentile is considered high because it confers greater than two times the lifetime genetic risk of disease of an average person. The chart shows how PRS translates to lifetime risk for brain cancer. This brain cancer PRS comprises 522 genome-wide variants.

#### RECOMMENDATIONS

A not elevated genetic risk of brain cancer means that this person's genetics do not confer additional risk of disease. However risk increases over time and this person's risk may increase as a result of age as well as the presence of other, unmeasured risk factors.

\*Information on brain cancer can be found on the National Cancer Institute website here: https://www.cancer.gov/types/brain





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## **PANCREATIC CANCER RISK REPORT**



#### RESULTS

Polygenic Risk Score

Not elevated (36<sup>th</sup> percentile)



#### PANCREATIC CANCER RISK OVER TIME

A not elevated genetic risk of pancreatic cancer means that this person's genetics do not confer additional risk of disease. However risk increases over time and this person's risk may increase as a result of age as well as the presence of other, unmeasured risk factors. Risk of pancreatic cancer is known to rise if you are a smoker, are overweight, or if you consume too much alcohol. Maintaing an active and healthy lifestyle is key to reducing overall risk of pancreatic cancer.





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## PANCREATIC CANCER POLYGENIC RISK REPORT



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic throughout the variants spread genome. Lifetime risk of pancreatic cancer is calculated by comparing the tested individual's PRS to a reference population. PRS in individuals above the 92<sup>nd</sup> percentile is considered high because it confers greater than two times the lifetime genetic risk of disease of an average person. The chart shows how PRS translates to lifetime risk for pancreatic cancer. This pancreatic cancer PRS comprises 22 genome-wide variants.

#### RECOMMENDATIONS

A not elevated genetic risk of pancreatic cancer means that this person's genetics do not confer additional risk of disease. However risk increases over time and this person's risk may increase as a result of age as well as the presence of other, unmeasured risk factors. Risk of pancreatic cancer is known to rise if you are a smoker, are overweight, or if you consume too much alcohol. Maintaing an active and healthy lifestyle is key to reducing overall risk of pancreatic cancer.

More information on early detection and testing for pancreatic cancer can be found on the ACS website:



<sup>\*</sup>More information on pancreatic cancer prevention can be found on the ACS website here:

https://www.cancer.org/cancer/pancreatic-cancer/causes-risks-prevention/prevention.html

https://www.cancer.org/cancer/pancreatic-cancer/detection-diagnosis-staging.html



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## **KIDNEY CANCER RISK REPORT**



#### RESULTS

Polygenic Risk Score

Not elevated (71<sup>st</sup> percentile)



#### KIDNEY CANCER RISK OVER TIME

Everyone's kidney cancer risk increases with age. This is shown for a males with average PRS by the blue line on the chart. The presence of not elevated PRS means that risk rises at around the same rate as the average population (orange line).





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## **KIDNEY CANCER POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants spread throughout the genome. Lifetime risk of kidney cancer is calculated by comparing the tested individual's PRS to a reference population. PRS in individuals above the 96<sup>th</sup> percentile is considered high because it confers greater than two times the lifetime genetic risk of disease of an average person. The chart shows how PRS translates to lifetime risk for kidney cancer. This kidney cancer PRS comprises 20 genome-wide variants.

#### RECOMMENDATIONS

A not elevated genetic risk of kidney cancer means that this person's genetics do not confer additional risk of disease. However risk increases over time and this person's risk may increase as a result of age as well as the presence of other, unmeasured risk factors.

\*More information on kidney cancer can be found on the ACS website here: https://www.cancer.org/cancer/kidney-cancer/about.html\_





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## **MELANOMA RISK REPORT**







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## **MELANOMA POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants throughout the genome. spread Lifetime risk of melanoma is calculated by comparing the tested individual's PRS to a reference population. PRS in individuals above the 93<sup>rd</sup> percentile is considered high because it confers greater than two times the lifetime genetic risk of disease of an average person. The chart shows how PRS translates to lifetime risk for melanoma. This melanoma PRS comprises 25 genome-wide variants.

#### RECOMMENDATIONS

A not elevated genetic risk of melanoma means that this person's genetics do not confer additional risk of disease. Melanoma is a form of skin cancer that is rare but more likely to spread. Knowing your own skin and regularly checking your skin is an important part of understanding if and when changes associated with melanoma could be present.

\*More information on melanoma can be found on the ACS website here: https://www.cancer.org/cancer/melanoma-skin-cancer.html





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## **INFLAMMATORY BOWEL DISEASE (IBD) RISK REPORT**



#### RESULTS

Polygenic Risk Score

Not elevated (64<sup>th</sup> percentile)



#### INFLAMMATORY BOWEL DISEASE (IBD) RISK OVER TIME

Everyone's IBD risk increases with age. The blue line on the chart shows this increase for a males with an average PRS. The PRS (orange line) of the tested individual shows that this person's risk rises at around the same rate as the average (blue line).





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## **INFLAMMATORY BOWEL DISEASE (IBD) POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants spread throughout the genome. Risk of IBD is calculated by comparing the tested individual's PRS to a reference population. PRS in males above the 87<sup>th</sup> percentile is considered high because it confers a greater than 6% lifetime risk of disease. The chart shows how PRS translates to lifetime risk This IBD PRS comprises 25,627 genome-wide variants.

#### RECOMMENDATIONS

The exact cause of IBD is unknown, but IBD is the result of a defective immune system. There are both genetic and environmental components to risk.

\*More information about IBD can be found on the CDC website here: <u>Centers for Disease Controls and Prevention</u>





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## **PSORIASIS RISK REPORT**



#### RESULTS

Polygenic Risk Score

Not elevated (65<sup>th</sup> percentile)



#### **PSORIASIS RISK OVER TIME**

Everyone's Psorasis risk increases with age. The blue line on the chart shows this increase for a males with an average PRS. The PRS (orange line) of the tested individual shows that this person's risk rises at around the same rate as the average (blue line).





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### **PSORIASIS POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants spread throughout the genome. Risk of an early menopause is calculated by comparing the tested individual's PRS to a reference population. PRS in males above the {65<sup>th</sup>} percentile is considered high because it confers a greater than 4% lifetime risk of disease. The chart shows how PRS translates to lifetime risk This Psorasis PRS comprises 250 genome-wide variants.





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## **CELIAC DISEASE RISK REPORT**

RELATIVE RISK OF CELIAC DISEASE	SUMMARY
Risk Threshold 2X average Not elevated High	Based on the PRS outlined below the risk of developing celiac disease is around 0.6 times the average, which is considered to be <b>Not elevated</b> risk.
RESULTS	
Polygenic Risk Score	Not elevated (11 <sup>th</sup> percentile)





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## **CELIAC DISEASE POLYGENIC RISK REPORT**



#### POLYGENIC RISK SCORE EXPLAINED

A polygenic risk score (PRS) measures the component of disease risk from many genetic variants spread throughout the genome. Risk of an early menopause is calculated by comparing the tested individual's PRS to a reference population. PRS in males above the {11<sup>th</sup>} percentile is considered high because it confers a greater than 1.6% lifetime risk of disease. The chart shows how PRS translates to lifetime risk This Celiac disease PRS comprises 228 genome-wide variants.



## **GENETIC ANCESTRY**

Genetic ancestry was assessed using principal components analysis (PCA) and iAdmix. The individual's genome was compared to a set of 26 global populations to provide an estimate of the components of their genetic ancestry. This ancestry inference is used to adjust an individual's PRS to account for their ancestry. The score is then aligned to ancestry specific PRS distributions built using populations from a range of genetic ancestries.





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#### Your genetic ancestry is: European: 100%

You inherit your DNA from your parents, who inherited their DNA from your grandparents. These generational links go back forever and so your genome contains a record of your ancestors. It is a unique history of past generations. You do not inherit DNA from all of your ancestors however, so your genetic ancestors will only ever be a small subset of your genealogical ancestors. Nevertheless, by comparing your genome to DNA from people across the world we can open a window into your past.

To assess your ancestry, we compared your genome to a reference dataset comprising more than 2,500 individuals from 26 global populations. We know from historical and archaeological studies that our ancestors moved around the globe and, although it's possible to extract DNA from people who were alive hundreds and even thousands of years ago, our ancestry assessment only compares your genomes to people alive in different parts of the world today. It is therefore best viewed as an estimate of your recent ancestry rather than a reflection of your deep history.





## **Technical Notes**

Genetic counseling is recommended for all patients undergoing genetic testing. Genetic testing does not replace standard biochemical testing, but is designed to augment such testing.



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#### **COMMON QUESTIONS**

#### What is PRS?

A PRS is a number calculated from a person's genetic data and is the sum of the number of risk alleles associated with the disease of interest weighted by the corresponding effect sizes (beta parameter) of those alleles on the disease.

#### How was the PRS percentile calculated?

The PRS Percentile was computed using an ancestry adjusted Z-score based on a distribution based on European individuals with known disease status from the UK Biobank.

#### What is a PRS percentile?

If you calculate PRS on a population the scores will form a bell shaped distribution. Most people will have scores in the middle of this distribution but a few will have high or low scores. This distribution can be split into 100 equally sized chunks, or percentiles. Because the risk of people in a reference distribution is known, we can assess the risk conferred by being in a particular percentile of the distribution and use this to assign disease risk in any individual.

#### How was age dependent risk calculated?

Risk by a given age (age-dependent risk) was computed using a Cox regression model using PRS as independent variable and adjusted for the first 4 principal components of variation.

#### What does it mean to have high lifetime risk?

A high PRS means that your score is higher than many in the population. This equates to your genes giving you a comparatively higher than average risk compared to the population. Having a high lifetime genetic risk does not mean that the disease will definitely develop, as there are numerous additional lifestyle and physiological factors that contribute to modify the absolute risk. Additionally, the risk for many diseases varies substantially with age.

#### **TEST LIMITATIONS**

It is important to note that the results of the PRS analyses presented here are not diagnostic. The aim of these genetic and bioinformatic analyses is to provide additional information to clinicians about the risk of disease to a patient that is conferred by their genes. Depending on the PRS, the analyses take into account a range of tens to millions of common genetic variants that have been robustly associated with the disease of interest. However, there may still be additional, as yet unidentified, genetic variants involved in genetic risk. In addition, this test does not take into account either known or unknown pathogenic variants in known prostate cancer susceptibility genes. These may be present but unidentified and may additionally contribute to an individual's genetic risk of developing disease.



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INTENDED USES	This test does not diagnose Prostate C test provides a quantitative assessmen This test should only be performed on used, and has no utility, to assess risk under the age of 18; in vitro fertilisation family planning.	cancer or any other health conditions. This ancer or any other health conditions. This to f an individual's future risk of disease. consenting adults and is not intended to be in any of the following situations: children embryo selection; carrier screening for
TECHNICAL DETAILS	This analysis was done on buccal swab or salivary DNA examining over 652,000 single nucleotide polymorphisms (SNPs) using the Illumina Global Screening Array version 3.0 at Clinical Enterprise Inc/Eurofins, Framingham, MA (CLIA number 22D1083041, CAP certified). Data analysis was carried out by Allelica to generate a polygenic risk score for breast cancer, the most common cancer in the United States in non-smoking women. Please note that this analysis does not include DNA sequencing for uncommon mutations in certain genes such as breast cancer genes 1 and 2 (BRCA-1 and BRCA-2) that can cause very premature breast cancer in certain affected families. The results of this analysis are being reported by Boston Heart Diagnostics/Eurofins, Framingham, MA (CLIA number 22D2100622, CAP certified). Patients should consult with their personal healthcare provider about the results of this testing, and what it means for the specific individual. We used Allelica's customised imputation module to impute this genetic data into a common set of 50 million genetic variants. The reference panel used for imputation comprises 2,504 fully sequenced and haplotypically phased genomes from Phase 3 of 1000 Genomes project. Our PRS have been calculated based on panels of varying numbers of Single Nucleotide Polymorphisms (SNPs). The sum of the number of risk alleles for each SNP is weighted by the corresponding effect size from the PRS panel. We select variants and associated effect sizes from the largest available Genome Wide Association Study (GWAS) available for a particular disease and use a suite of PRS methods to identify the best performing PRS.	
DISCLAIMER	This test was developed and its performance characteristics were determined by Allelica Inc. The test has not been cleared or approved by the Food and Drug Administration. This test should be interpreted in context with other clinical findings. All risk estimation is approximate and based on previously analyzed cohorts. Being identified as "high risk" is not a diagnosis and does not guarantee that a person will develop the disease. Mutations in other genes or regions not analyzed by this test can also impact an individual's risk to complex disease.	
LABORATORY INFORMATION	<b>Performing Lab:</b> Clinical Enterprise, Inc. 175 Crossing Blvd Framingham, MA, 01702 CLIA Number: 22D1083041	<b>Reporting Lab:</b> Boston Heart Diagnostics 200 Crossing Blvd Framingham, MA, 01702 CLIA Number: 22D2100622



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