my HealthScore

Polygenic risk screening for common diseases

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What is myHealthScore?

myHealthScore is the genetic screening test that provides **information about the patient's risk of presenting with common multifactorial diseases.** The test determines a previously unperceived genetic risk, enabling the detection of a greater number of people at risk.

What advantages does it have?

- Allows the quantification of the aggregated genetic risk, scattered along the genome, associated with a particular disease.
- It estimates the disease risk and how it varies throughout a person's lifetime.
- It can be performed before the onset of clinical risk factors, which allows a more effective preventive approach.
- It is carried out once in a lifetime and the inclusion of the result within risk calculators improves their predictive power.
- Information that is independent and complementary to traditional risk factors and the study of gene panels.

Who is it intended for?

The test is suitable for adults who are proactive about their healthcare. The results provide information about the lifetime risk of presenting the diseases analysed, in order to establish **preventive strategies and lifestyle** changes that will help to reduce the risk.

What is a polygenic risk?

The majority of common diseases have a polygenic component. In other words, there is a hereditary risk factor that is not associated with just one variant in the genome, but with hundreds or thousands of variants that represent the risk carried by a multitude of biological pathways.[1] Each variant carries a small or moderate risk which is included in a unique global score that can be evaluated with other risk and lifestyle factors.

What type of sample is required?

The test can be carried out with a saliva or blood sample. Subsequent sequencing is carried out using NGS technology and analysis using EC branded software.

Genetic factors account for around 40% of the risk in common diseases, such as type 2 diabetes or coronary artery disease. [2,3]

Which diseases are included?

myHealthScore enables to know the patient's risk of presenting with the following diseases:

Cardiovascular disease	Type 2 diabetes	Breast cancer	Prostate cancer
			
> 2 million variants	> 600.000 variants	> 550.000 variants	> 650.000 variants

myHealthScore can be requested for cardiovascular disease, type 2 diabetes or cancer risk, either separately or together.

Clinical application

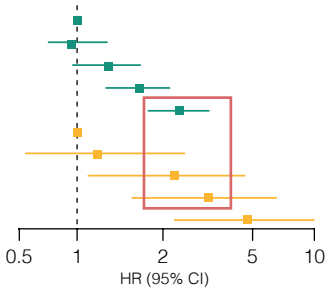
Cardiovascular disease

This includes the risk of a patient to present coronary artery disease (CAD), atrial fibrillation, lipid profile (triglycerides, LDL and HDL cholesterol) and hypertension.

1 in every 4 people suffering from coronary artery disease is not detected through evaluation of clinical factors.[5]

Current protocols for the prevention of CAD recommend the use of statins in people with LDL-c >190 mg/dL. This approach may exclude from the primary prevention strategy about 4% of the population at high polygenic risk.[6] These are the people who obtain the greatest benefit from the implementation of strategies to reduce LDL-c levels. [7,8] In patients with a high-risk result, it is possible to offset the lifetime risk of CAD by up to 50% through lifestyle changes.[9]

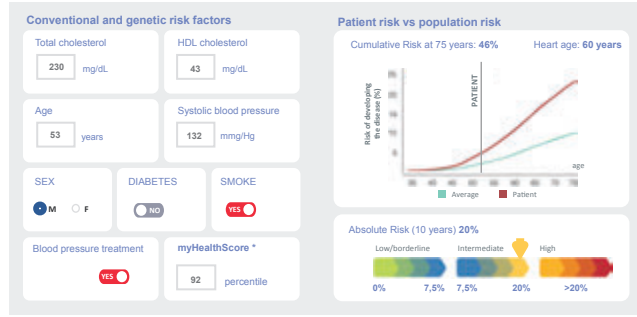
Group	LDL–C (mg/dL)	HR (95%CI)
Int PRS	<100	1
	100 – <130	0.94 (0.71–1.24)
	130 – <160	1.25 (0.95–1.63)
	160 – <190	1.62 (1.23–2.13)
	≥ 190	2.34 (1.75–3.14)
High PRS	<100	1
	100 – <130	1.15 (0.54–2.46)
	130 – <160	2.23 (1.08–4.59)
	160 – <190	3.14 (1.52–6.5)
	≥ 190	4.71 (2.23–9.94)



People with mid-level of LDL-c (130-160 mg/dL) with an elevated **myHealthScore** result present a CAD risk similar to that of people with elevated levels of LDL-c (>190 mg/dL) with average myHealthScore results.[10]

Graphic adapted from Bolli et al 2021.

Veritas has a calculator on its website that allows the integration of **myHealthScore** with other risk factors in order to estimate the patient's absolute risk.



myHealthScore can identify up to 20 times more people with a risk of CAD that is comparable or greater than the risk associated with familial hypercholesterolemia mutations.[4]

Type 2 diabetes

Type 2 diabetes can present in middle-aged and in older people. The likelihood of developing type 2 diabetes is higher after the age of 45 and the risk increases with overweight or family history. [11]

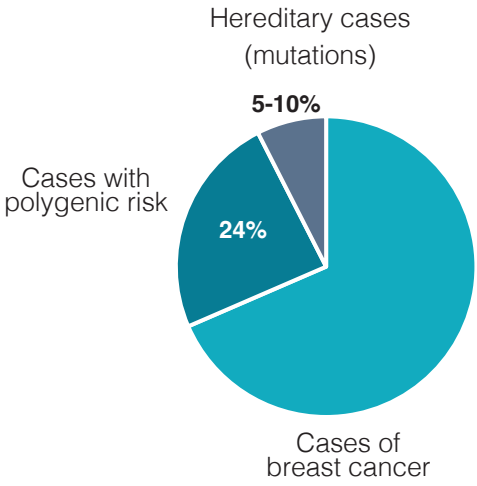
myHealthScore provides the risk of type 2 diabetes in order to start a dietary, lifestyle or pharmacological strategy for prevention.

8 in every 10 people with pre-diabetes are unaware of their condition and the possibilities for prevention.[12]

Breast cancer

Only between 5-10% of breast cancer cases are considered hereditary, the rest are considered to be sporadic.[13] Among the sporadic cases, **myHealthScore** evaluates a genetic component which has been unperceived until now, and which acts as an additional risk factor to other clinical factors. The test results enables to:

- Start breast cancer screening in high-risk patients at a younger age.
- Improve the precision of advanced risk calculators that include polygenic risk as an enhancing risk factor.[1]
- Reflect a hereditary risk in the absence of mutations.
- Provide additional information on the risk of disease in women who present with low penetrance mutations.[14,15]



Women presenting with higher percentiles of risk may present up to **double the risk of women with average myHealthScore results.**

Through myHealthScore it is possible to detect up to an additional 24% of breast cancer cases that are considered to be sporadic.[16]

1 in 8
women will be diagnosed with breast cancer throughout their lives.[17]

7 in 10
women diagnosed with breast cancer do not have a family history of the disease.[18]

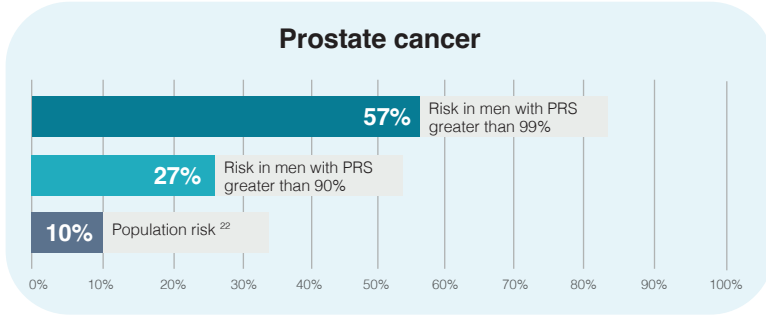
2 in 10
women diagnosed with breast cancer are under 50 years of age.[19]

Prostate cancer

Prostate cancer risk assessment is opportunistic and mainly focussed on family history, PSA levels and physical examination. The results generally imply a high rate of overdiagnosis and overtreatment.[20]

Carrying out **myHealthScore** allows the integration of polygenic risk to the medical checkups, providing more precise and complete information on patient risk.

Men with the highest polygenic risk have approximately 5.7 times higher risk of suffering from prostate cancer than men with an average result. Men in the highest 10% of polygenic risk have 2.7 times more risk than the general male population, making this an important screening tool.[21]

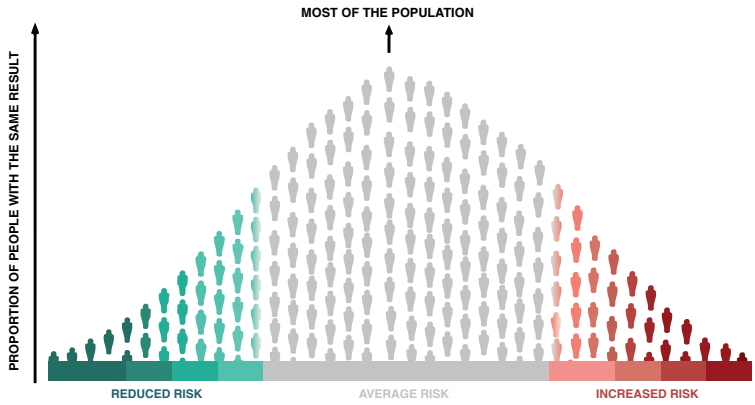


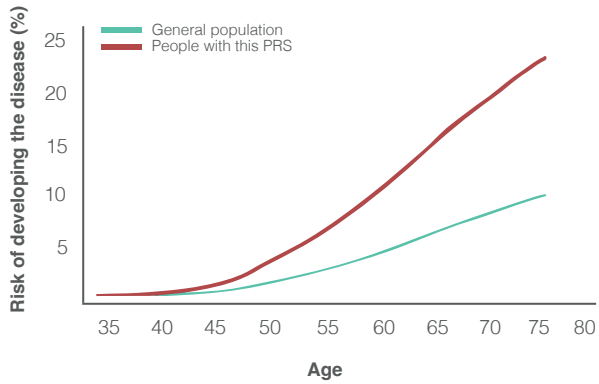
Prostate cancer lifetime risk

Polygenic risk score tests identify more people at risk of presenting with common diseases than monogenic mutations with a comparable level of risk.[4]

How are the results presented?

The results include the patient's percentile of risk related to the general population, as well as their lifetime risk. Additionally, a basic analysis of the patient's ancestry is carried out in order to adjust the risk analysis based on this information.





Complex diseases generally have a late onset, and the risk accumulates over time with ageing and environmental exposure. The polygenic risk can modify this risk path, increasing or reducing the tendency. myHealthScore allows to know if there is an increased risk based on genetics, which enables the implementation of prevention or risk reduction strategies before the onset of symptoms.

Genetic variation in human diseases

Among the common diseases that affect a high percentage of the population, genetic risk takes different forms. On one hand, mutations capture the risk associated with a specific altered pathway and substantially increase the risk of disease, but they are very infrequent within the population. On the other hand, there is a more dispersed risk throughout the genome, but it affects a much higher percentage of the population. This risk is determined through the aggregation of common variants which pose a small risk individually but together, represented as a score, imply a significant risk which, until now, had gone unnoticed.

Genetic variation in coronary artery disease

Rare variants which have a major effect		Common variants with minor effect
Family studies	⟷	GWAS studies
Variant in *LDLR, PCSK9, APOB*	⟷	From hundreds to millions of variants
< 1 in every 300 [7,23] ~ 1 in every 200	Population with high genetic risk	~ 1 in every 10 [1]

Why now?

Large genetic databases with patient data, along with advances in computing and bioinformatics, have made it possible to develop these risk scores and incorporate them into clinical practice.

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About Veritas

Veritas Genetics, a *LetsGetChecked* company, is one of the world leaders in advanced genetic sequencing and clinical interpretation of the exome and whole genome, driving the transition to personalized and preventive medicine.

Using state-of-the-art technologies and the highest safety standards, Veritas Genetics helps individuals, healthcare professionals and institutions worldwide to understand and anticipate genetic risks, enabling more informed and proactive health decisions.

With a focus on innovation and accessibility, Veritas Genetics transforms the way we understand and care for health at every stage of life.

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