

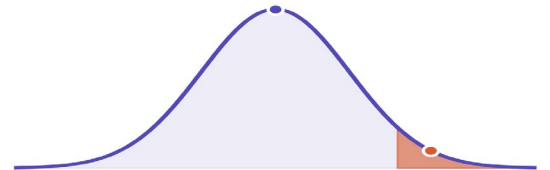
FOR THE PCORI PATIENT STAKEHOLDER GROUP

Polygenic risk scores

*A forecast written in your DNA,
and what it means for you.*

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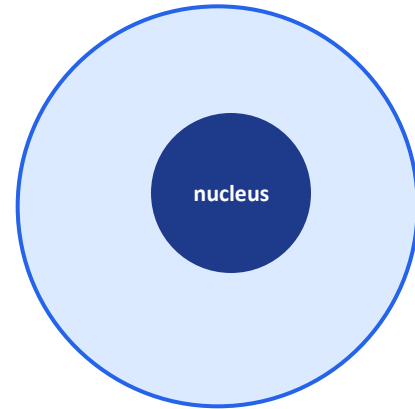
What is a gene?

A quick primer before we dive in

Your body is made up of tiny building blocks called **cells**. Inside each cell is a set of instructions called your **DNA**. A **gene** is one small piece of those instructions that tells your body how to do a specific job—like how to build a protein, which helps your body grow, heal, and function.



DNA (with genes)



Cell



Chromosome pair

Most risk hides in many genes, not one

Two very different ways genes shape what happens to us

RARE • MONOGENIC

One gene, one loud voice

A single flawed gene can raise disease risk dramatically on its own.

Familial hypercholesterolemia for the heart. BRCA1 and BRCA2 for breast and ovarian cancer.

Powerful, but uncommon. Roughly **1 in 250** people carry the classic high-cholesterol gene.

COMMON • POLYGENIC

Thousands of genes, whispered chorus

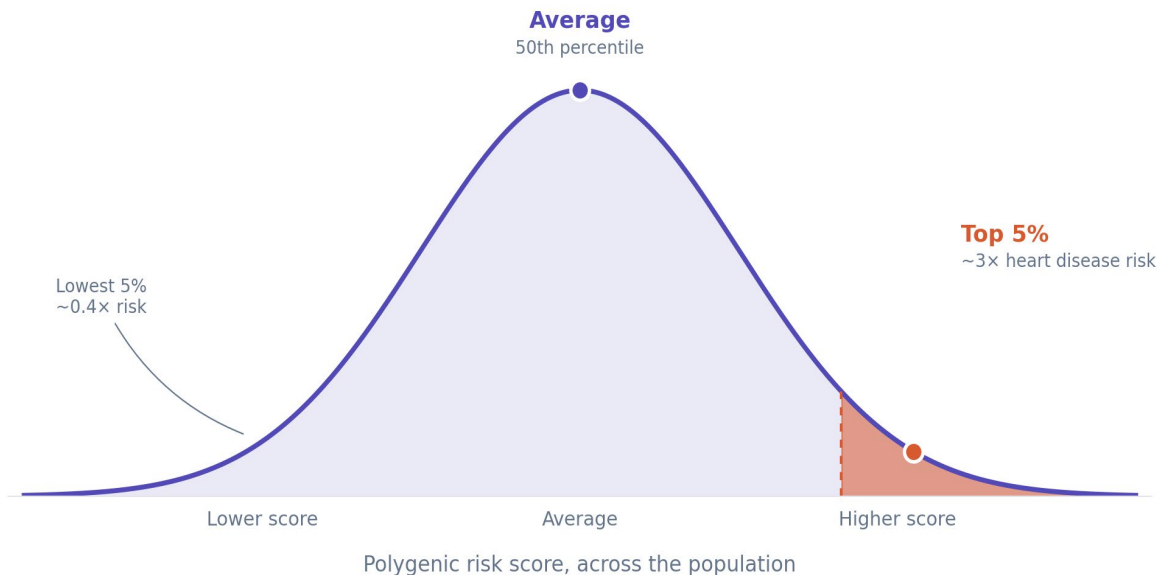
Each common variant nudges risk by a tiny/small fraction.

A **polygenic risk score** adds up roughly a million of those small signals into a single number.

Applies to heart disease, diabetes, many cancers, and most common conditions.

Where you sit on the curve

The same kind of curve that describes height describes genetic risk for most common diseases



~2-3x risk

Top 5% of polygenic score for heart disease, compared to everyone else

Set at birth

The score doesn't change. Your risk still responds to how you care for yourself.

Numbers based on published polygenic scores for coronary heart disease. Exact values depend on the specific score used.

What this could mean for you

01

Earlier warning

Your DNA carries the signal from the day you were born. A polygenic score can tell you something decades before the first symptom appears.

02

Adds to what you already know

A polygenic score complements family history and lifestyle information. It does not replace either one.

03

Can change what happens next

In the MI-GENES trial, people who learned their polygenic score for heart disease started lipid-lowering therapy more often, and their cholesterol went down.

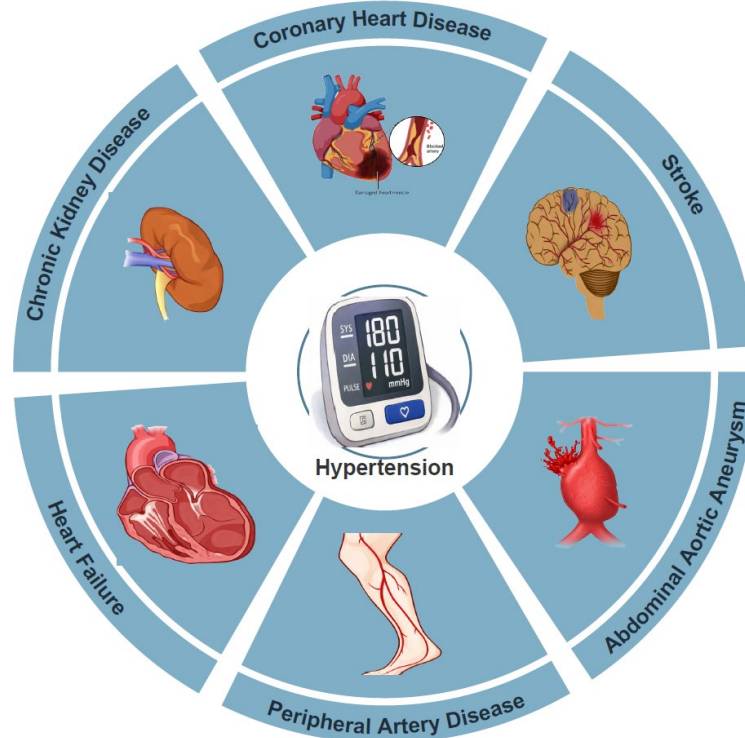
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Risk, not destiny

Statins, blood pressure control, exercise, and diet still lower actual risk, even for people with a high score.

Predicting Complications of High Blood Pressure

Identifying who will develop these hypertension-driven complications before they happen



A single test can stratify risk across all six major complications of high blood pressure — enabling earlier, targeted intervention.

Questions to ask

Patient-centered research needs patients in the room

Still being worked out

- Most scores were built in people of European ancestry. They work less well in other populations, and closing that gap is active work.
- Not yet standard of care for most conditions. Insurance coverage is limited.
- GINA protects you from health insurance and employment discrimination. Life and disability insurance are not covered.

Questions to bring to your doctor

- Would a polygenic risk score change what we do for me?
- How well has this score been tested in people with a genetic background like mine?
- What would we actually do if it comes back high, or low?
- Where does my sample go afterward, and how long is it kept?

Thank you. I'd like to hear your questions.