PROPHET TOOLBOX
FACTSHEET#7

JULY 2026

Polygenic Risk Scores (PRS) in Chronic Disease Prevention

PROPHET
a PeRsOnalized Prevention roadmap
for the future HEalThcare

What is Polygenic Risk Score?

A Polygenic Risk Score (PRS) is a numerical estimate of an individual's genetic susceptibility to a particular disease, based on thousands of common genetic variants, known as single-nucleotide polymorphisms (SNPs). These variants, identified through genome-wide association studies (GWAS), are combined into a single score that indicates how an individual's genetic risk compares with that of the general population.

A PRS is calculated from DNA obtained through a blood or saliva sample, typically genotyped using a SNP array, followed by bioinformatics processing to combine the effect of relevant genetic variants into an individual risk score. PRS values follow a normal distribution: most people cluster around average risk, with fewer at the high- or low-risk tails.

Unlike rare high-penetrance variants (e.g. *BRCA1/2*), PRS provides a probabilistic estimate of risk, capturing the polygenic background on which environmental factors act. Among carriers of monogenic variants, polygenic background can further modulate estimated disease risk.

Scientific societies, such as the American College of Medical Genetics and Genomics (ACMG) and the National Comprehensive Cancer Network (NCCN), currently recommend using PRS as a complementary tool alongside established clinical assessment, and emphasize that PRS should not guide patient care management outside research settings.

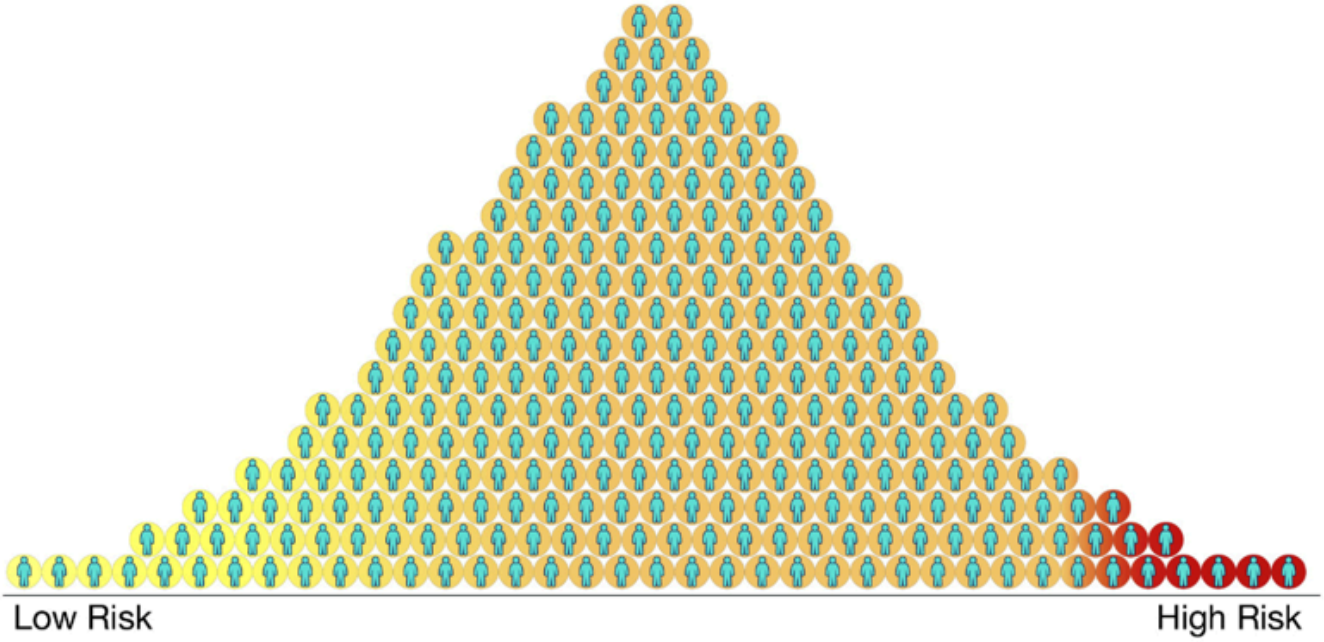

Fig 1: The graphic illustrates the distribution of PRS across a population, with most individuals falling around average risk and fewer individuals at the low- and high-risk tails. (From: National Human Genome Research Institute (NHGRI), Polygenic Risk Scores, https://www.genome.gov/Health/Genomics-and-Medicine/Polygenic-risk-scores)

Why PRS matters for Chronic Disease prevention?

PRS is a static, lifelong biomarker assessable from a single genetic sample at any age, offering predictive information well before conventional clinical risk factors emerge. This makes it a potentially powerful tool for early, targeted prevention.

Earlier screening:
a key advantage of PRS is its potential to enable targeted screening for high-PRS individuals. Modeling shows very high-PRS individuals can reach conventional screening thresholds 10.8 years earlier on average. PRS-guided screening is estimated to reduce premature mortality in high-risk individuals by 23.3%.

Overall risk is modifiable:
while polygenic risk itself is not modifiable, healthy lifestyle and pharmacological interventions can substantially reduce overall disease risk. Individuals with the highest polygenic risk derive the greatest absolute benefit from these interventions, highlighting their potential population-level impact.

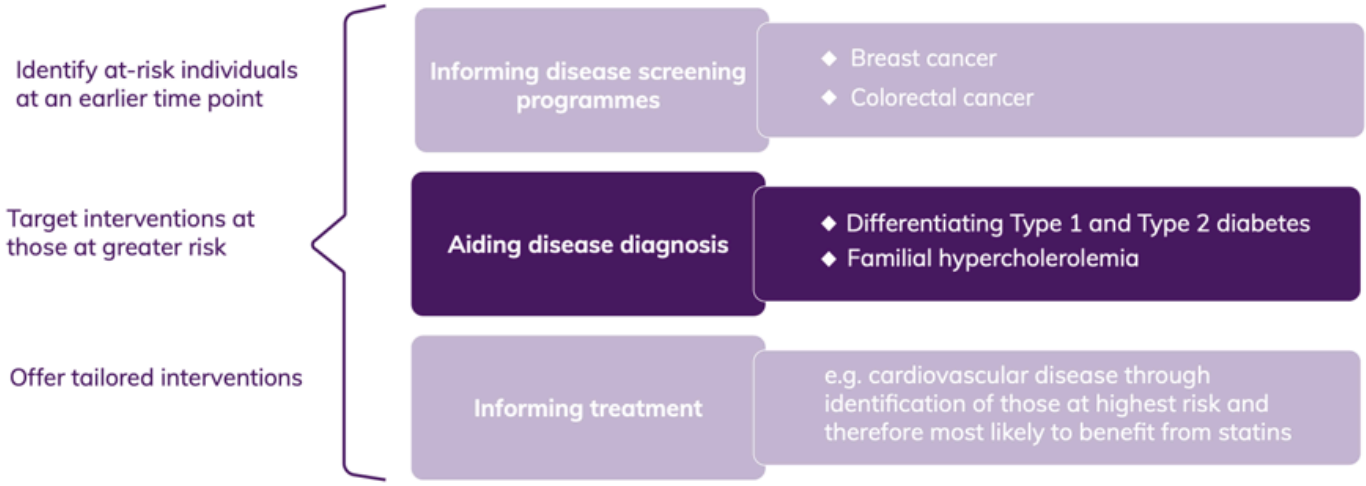

Fig 2. Applications of polygenic score information. (From Moorthie S. Application of polygenic scores in healthcare. PHG Foundation; 2023.)

Best-practice example: Estonia

In 2025, Estonia launched a national feasibility study offering PRS testing and tailored counselling to 1,000 women aged 40. The aim is to identify younger women whose breast cancer risk is comparable to that of women routinely invited to mammography from age 50, enabling earlier access to screening for those at higher risk. Developed through collaboration among the Estonian Cancer Network, the national health insurance system, universities and hospitals, the study served as a first step towards integrating PRS-guided screening into routine care. From 2026, the Estonian Health Insurance Fund is set to introduce nationwide PRS-based personalized breast cancer screening for all 40-year-old women, supported by a digital platform integrated into Estonia's e-Health infrastructure.

Limitations and challenges

Despite its promise, PRS faces significant scientific, ethical, and implementation barriers.

Limited predictive accuracy:
PRS captures only part of genetic risk and does not fully account for rare variants or gene-environment interactions; high scores do not confirm disease, and low scores do not exclude it.

Poor transferability across ancestry:
most GWAS have been conducted in European populations, reducing PRS accuracy in non-European groups, with the risk of exacerbating health inequities; multi-ancestry methods are emerging but have not closed the gap.

Lack of standardization:
different scores for the same trait use different methods, variants, and populations; clinically relevant risk thresholds are not consistently defined, and laboratory reporting practices vary substantially.

Ethical/legal concerns:
PRS may be misinterpreted as deterministic, raising concerns about fatalism; there is a risk of potential genetic discrimination, as well as data privacy, secure storage and secondary use of genomic information.

Implementation barriers:
clinical adoption is hindered by limited professional training, absence of workflows for generating PRS and integrating them into electronic health records, insufficient genetic counselling capacity, and a lack of clear guidelines for routine use.

Uncertain cost-effectiveness:
a systematic review of 24 cost-utility analyses found a positive trend toward cost-effectiveness, particularly for cancer screening optimization and preventive therapy eligibility, but current evidence is largely model-based; real-world data on implementation costs, delivery models, and long-term outcomes are needed.

Key Takeaways 

PRS holds promise as a population-level prevention tool, but its current use should remain primarily within research and pilot settings. Broader implementation requires investment in workforce capacity, equitable data infrastructure, clear regulatory guidance, and integration with evidence-based interventions.

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