PROPHET TOOLBOX FACTSHEET#1

JUNE 2025

PERSONALIZED PREVENTION CONCEPTS AND LEVELS

PROPHET

a PeRsOnalized Prevention roadmap for the future HEalThcare

What is personalized prevention ?

Personalized Prevention aims to prevent onset, progression and recurrence of diseases through the adoption of targeted interventions that consider the biological information (e.g. genetic and other biomarkers, demographics, health conditions), environmental and behavioral characteristics, the socio-economic and cultural context of individuals. This should be timely, effective, and equitable in order to maintain the best possible balance in lifetime health trajectory.

Personalized medecine vs personalized prevention

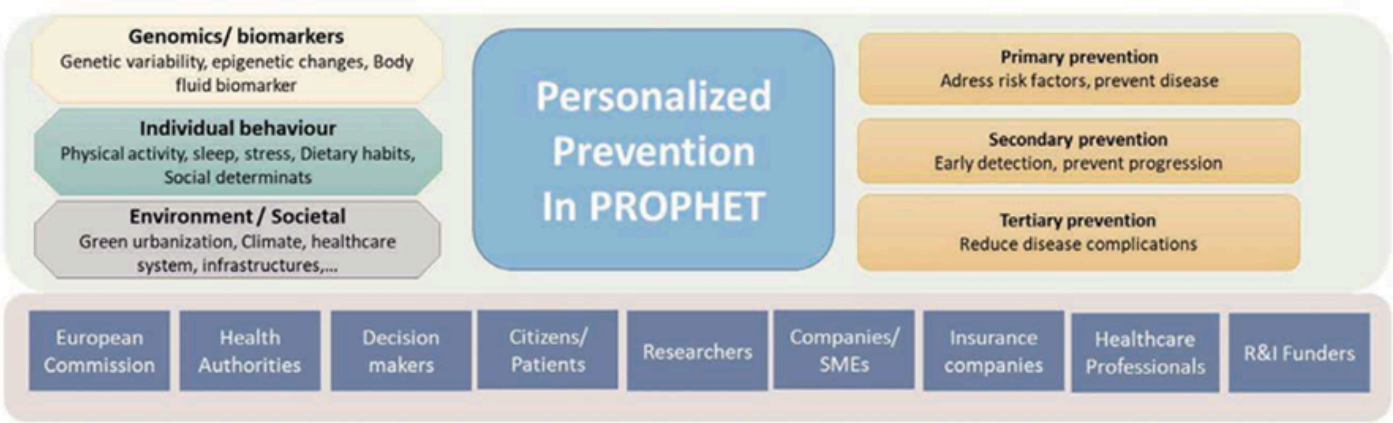
The Horizon 2020 Advisory Group defines **Personalized Medicine** as “a medical model using characterisation of individuals’ phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention.”

While personalized medicine encompasses the full spectrum of care (diagnosis, treatment, and monitoring), personalized prevention focuses specifically on pre-disease and early disease phases, integrating preventive strategies tailored on individual risk profiles.

As PROPHET is a Coordinating and Support Action of the International Consortium of Personalised Medicine (ICPerMed), it emphasizes the integration of genomics/biomarkers in personalized preventive approaches.

Personalized preventive approach and prevention levels

A **personalized preventive approach** is an action, or a set of actions, in which the information provided by biological information (e.g. genetic and other biomarkers, health conditions), combined with demographic, environmental and behavioural characteristics, socio-economic and cultural context of individuals, guides the decision-making process regarding one or more interventions aimed at preventing the onset, progression and recurrence of diseases.



Personalized prevention approach in PROPHET

In this context, the level of prevention is determined by the preventive intervention that follows the predictive biomarker:

Personalized primary prevention entails a comprehensive set of measures, strategies, or interventions aimed at proactively averting the onset of diseases before they occur and manifest. These initiatives focus on reducing disease incidence and mitigating risk factors through education, promoting a health-conscious lifestyle, and providing preventive medical treatments.

The personalization of primary prevention is defined by the listed interventions, such as lifestyle adjustments, that are tailored to individuals who exhibit predispositions for a certain condition, considering the individual characteristics. In the case of genetic or other testing for primary prevention, they can be applied to all the individuals regardless of any background risk, as well as to individuals belonging to certain high-risk categories, such as specific age groups, as well as through cascade screening.

For example, in the cardiovascular disease (CVD) setting, genetic testing for familial hypercholesterolemia (FH) in individuals with a positive family history or other risk factors allows early identification of those at high risk for CVD—while still asymptomatic. FH is commonly caused by pathogenic variants in genes such as *LDLR, APOB, PCSK9,* and *LDLRAP1*, which are involved in regulating blood cholesterol levels and can lead to elevated low-density lipoprotein cholesterol (LDL-C). Early diagnosis enables the timely implementation of lifestyle interventions and the initiation of lipid-lowering therapies, significantly reducing cardiovascular risk.

Personalized secondary prevention involves implementing measures to detect and treat existing diseases or health conditions at an early stage in asymptomatic individuals that belong to traditional high- risk categories, with the aim of minimizing their impact and preventing future complications; personalization is achieved by utilizing biomarker testing and individual information to further stratify high-risk individuals.

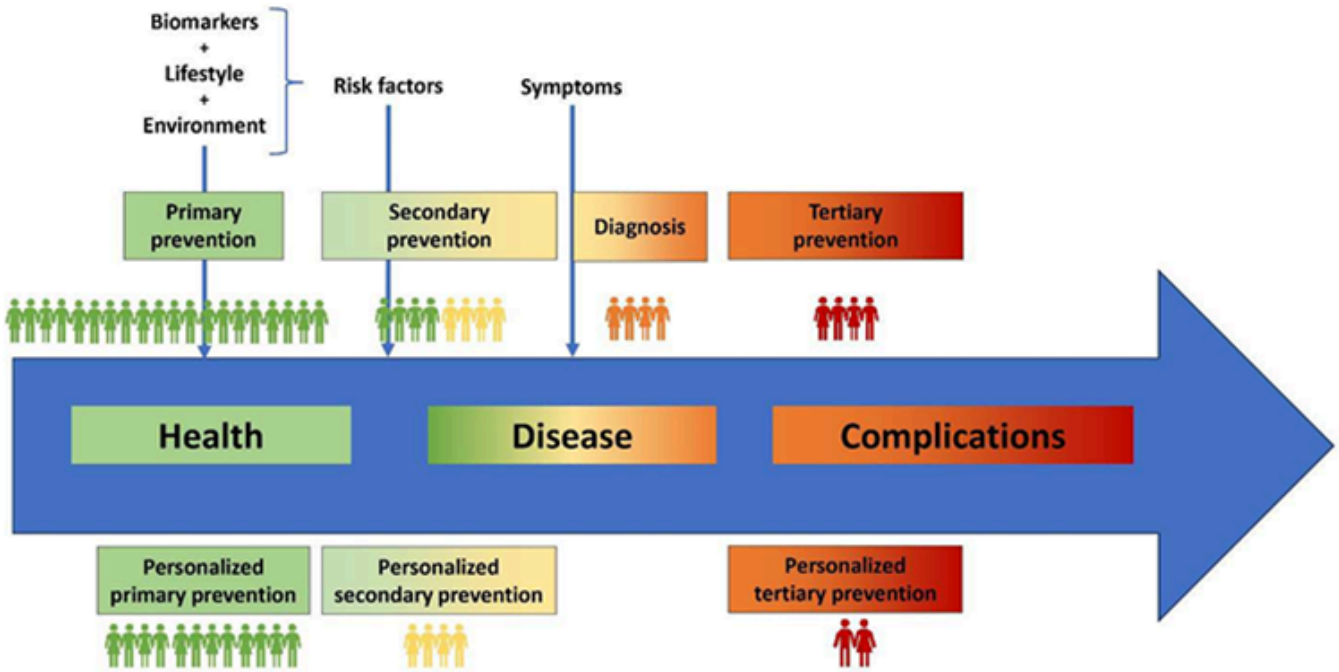
This identification can guide the implementation of in-depth diagnostic assessments, enabling early and effective disease detection. Furthermore, personalized secondary prevention, as well as primary prevention approaches, can leverage cascade screening, involving the relatives of individuals with specific characteristics. This enables the identification of heightened risks or conditions through predictive or diagnostic tests, ultimately guiding at-risk individuals towards more tailored screening programs.

For instance, cascade genetic screening and subsequent personalized follow up are recommended for individuals with a family history of colorectal cancer (CRC) or early-onset CRC. According to NCCN guidelines, multigene panel testing—including *APC* gene analysis for Familial Adenomatous Polyposis (FAP)—enables tailored surveillance and management strategies, as well as genetic screening for at-risk family members.

Personalized tertiary prevention refers to interventions and measures aimed at reducing progression and recurrence of a chronic condition, in order to enhance the quality of life for individuals dealing with such health challenges.

In this context, personalization is facilitated through various biomarker testing modalities, including pharmacogenomics, employed on the affected patient. This comprehensive approach anticipates predispositions to potential complications, forecasts the individual responses to therapies, and prevents adverse drug reactions by adjusting the dosage and using the most appropriate medication, all with the goal of averting the worsening of the individual's condition.

In neurological and psychiatric disorders such as depression, pharmacogenomic testing help determine the most effective drug and dosage. The Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines highlight the role of genotyping specific genes, such as *CYP2D6, CYP2C19, CYP2B6, SLC6A4,* and *HTR2A*, which are involved in the metabolism of many antidepressants, including Serotonin Reuptake Inhibitors. Individuals with genetic variants in these genes are at increased risk of adverse drug reactions and can benefit from an adjusted dosage tailored to their genetic profile.



The three traditional levels of prevention that integrates personalized prevention, according to the disease stage

Genetics, genomics and other omics sciences - Why they matter in personalized prevention

Personalized prevention is increasingly supported by the use of genetics and 'omics' sciences, a group of disciplines that capture different layers of molecular and biological information. These fields help us better understand disease mechanisms, stratify individual risk, and design preventive strategies tailored to a person's unique profile.

Genetics focuses often on monogenic conditions, where one gene variant can confer a high risk of for instance oncogenetic or cardiogenetic conditions.

For example, *BRCA1/2* mutations are linked to hereditary breast and ovarian cancer, and *LDLR* mutations cause familial hypercholesterolemia, increasing cardiovascular risk from a young age. Presymptomatic testing allows for timely interventions, such as enhanced surveillance, risk-reducing surgery, or statin therapy, that can significantly reduce morbidity and mortality.

Knowledge and skills needed include:

- Identifying individuals who may have or may be a carrier of a genetic condition
- Communicating information about genetics in an understandable, comprehensible and sensitive way, helping patients to make informed decisions and choices about their care
- Managing patients with genetic conditions, using accepted guidelines

Genomics makes it possible to investigate many genes simultaneously. Thus, risk estimates can be based on many genes and other relevant factors. Apart from germline testing, tumour samples can be investigated to decide on treatment options based on genetic variants in the tumour.

Genomics studies the full set of genes (the genome) and enables the simultaneous analysis of many genetic variants. This includes **polygenic risk scores** (PRS), which aggregate the effect of multiple low-risk variants to estimate an individual's predisposition to common complex diseases such as cancer, type 2 diabetes, or coronary artery disease.

Genomics also includes tumour genome profiling, used to guide treatment decisions in oncology, and whole-genome or exome sequencing in rare or undiagnosed conditions.

The other “omics” sciences beynd genetics and genomics include fields **such as transcriptomics, proteomics, metabolomics, epigenomics,** and **radiomics.** Each of these investigates a specific layer of biological information:

- **Transcriptomics** studies RNA transcripts to understand which genes are actively expressed in different tissues or conditions.
- **Proteomics** focuses on the full set of proteins produced by a cell or organism, which reflects real-time biological activity.
- **Metabolomics** analyses small molecules (metabolites) that result from metabolic processes and offer a snapshot of cellular function.
- **Epigenomics** examines chemical modifications, such as DNA methylation, that regulate gene expression without altering the DNA sequence itself.
- **Radiomics** uses advanced computational methods to extract large amounts of quantitative data from medical images, such as CT or MRI scans.

Together, genetics, genomics, and other omics sciences offer a multi-dimensional view of health and disease. When combined using multi-omic approaches, they allow for a more comprehensive understanding of individual risk by integrating information from different biological layers — such as genes, proteins, and metabolites. This integration is increasingly used to improve the precision and timing of preventive strategies, making personalized prevention more accurate and potentially more effective across a broad range of diseases.

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