PROPHET

a PeRsOnalized Prevention roadmap for the future HEalThcare

D1.8 Update version of Strategic Research Agenda

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Executive Summary

Advancements in sequencing and genotyping technologies and the integration of digital resources in healthcare have ushered in a new era of medicine. This "precision-revolution" has opened possibilities for personalised prevention, where individualised risk profiles are identified through improved understanding of genetics, behavioural and socio-economic factors. According to PROPHET, "personalised 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 behavioural characteristics, socio-economic and cultural context of individuals. This should be timely, effective and equitable to maintain the best possible balance in lifetime health trajectory". By tailoring interventions based on this information, personalised prevention aims to delay disease onset, enhance quality of life and ultimately reduce the economic burden on healthcare systems. Although challenges exist in clinical implementation, genomics is the most advanced, providing examples of clinical utility such as genetic testing, polygenic risk scores, and pharmacogenomics.

This SRIA considers the intricacies of the personalised prevention paradigm and elucidates the reasons for its crucial integration into European healthcare systems. After reviewing the latest research and incorporating various stakeholders' perspectives, the SRIA identifies ten key challenges, including: The broad scope of promotion and prevention; Continuous evidence synthesis system supporting personalised prevention; The PROPHET Framework implementation; Data collection and integration, and Data Infrastructure; Community Engagement and trust; Health Professionals and Policy Makers involvement; Regulatory aspects and synergy with private sector; Access, Equity and Coverage; Ethical, Legal, Social Issues (ELSI); Changing behaviour.

The accompanying Roadmap provides a detailed blueprint for implementing tailored preventive strategies for each individual based on the latest scientific advancements and the specific needs of each context. The Roadmap outlines key goals, priority actions, implementation timelines, expected outcomes and output indicators, responsible entities, funding sources, and synergies with other EU initiatives, providing a structured plan for integrating personalised prevention into healthcare. For the ten challenges, we have identified 56 goals and 66 actions. These actions range from creating platforms and repositories for publications in the field of personalised prevention to improve evidence and interoperability across Europe, to the dissemination of the PROPHET framework in real-world settings, to the design and implementation of educational programs for professionals and citizens, and the establishment of regulations for data sharing and standardisation of data. The actions provide a detailed outline of what needs to be accomplished, as well as the potential obstacles that may arise. The anticipated implementation timeline is within the next five years, with the aim of long-lasting impact. The necessary funding for implementing these actions is expected to come mainly from the European Commission rather than from local or private sources. For most of the actions, the principal entities responsible for supporting implementation include the European Commission (DG SANTE), National Ministries of Health and related agencies, and the research community. Numerous synergies have been identified, particularly with ICPerMed and EPPeRMed, as well as connections to European projects. In a climate of severe budget cuts and redistribution of funding creative synergies and collaborations across domains and local, regional and national levels will need to be established.

The SRIA and Roadmap outline key areas to address for realising the potential of personalised prevention, ultimately empowering individuals to take control of their health.

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1. Executive Summary

The PROPHET Strategic Research and Innovation Agenda (SRIA) on Personalised Prevention reflects on the challenges for advancing personalised prevention in healthcare. With PROPHET, we are building the foundation to achieve the **final outcome** of **more effective, efficient and citizen-centered preventive approaches.** After extensive literature mapping on the latest research advancements in the field and after incorporating the consortium partners' views and the stakeholders' perspectives, the SRIA identified ten challenges for the implementation of personalised prevention, including: Challenge 1: The broad scope of promotion and prevention; Challenge 2: Continuous evidence synthesis system supporting personalised prevention; Challenge 3: The PROPHET Framework implementation; Challenge 4: Data collection and integration, and Data Infrastructure; Challenge 5: Community Engagement and trust; Challenge 6: Health Professionals and Policy Makers involvement; Challenge 7: Regulatory aspects and synergy with private sector; Challenge 8: Access, Equity and Coverage; Challenge 9: Ethical, Legal, Social Issues (ELSI); Challenge 10: Changing behaviour. For each challenge, state of the art, gaps, priorities and implementation, and final considerations are detailed.

Along the development of PROPHET, personalised prevention clearly emerges as a multi-faceted field that seeks to use individual information from various domains as safely and effectively as possible. This information includes an individual's lifestyle, health records, social habits, environmental exposures over time, individual omics data, role in the community, and more. Recognizing this, PROPHET endorses and strongly promotes this comprehensive definition of personalised prevention. However, to ensure the sustainability of evidence-systematization efforts, it was decided to focus on managing omics data within this ecosystem. This strategic decision aligns with the project's positioning within the International Consortium for Personalised Medicine ecosystem. Thus, while this SRIA acknowledges the importance of these diverse domains in defining personalised interventions, it primarily concentrates on policy development efforts on investigating the omics sciences sector.

Within this defined domain, we encounter additional complexity due to the multiple areas covered by omics sciences — such as genomics, metabolomics, proteomics, radiomics, epigenomics, and more. Despite their technical differences, certain shared elements allow us to propose common considerations across these fields, particularly regarding infrastructures required for omics data use. Issues related to data collection, integration, protection, and the development of data infrastructures thus have broad relevance across omics domains (Figure 1).

In contrast, when digging deeper to seek evidence of clinical utility that could inform implementation and scaling up by healthcare systems, the situation varies. In many areas of omics, there is a clear need for new, robust association studies to support biomarker candidacy as potential tools for personalised prevention. However, genomics stands out as the most structured in terms of implementation.

Given its early entry into scientific focus compared to other omics, genomics offers the primary examples upon which PROPHET has built its considerations around clinical utility and implementability, where examples of such utility are available, albeit with limitations. These examples form the core objectives of this SRIA, including applications such as genetic testing for high risk pathogenic variants, polygenic risk scores (PRS), and pharmacogenomics. These applications highlight the practical aims of this initiative and serve as focal points for advancing personalised prevention through clinically actionable genomics data.

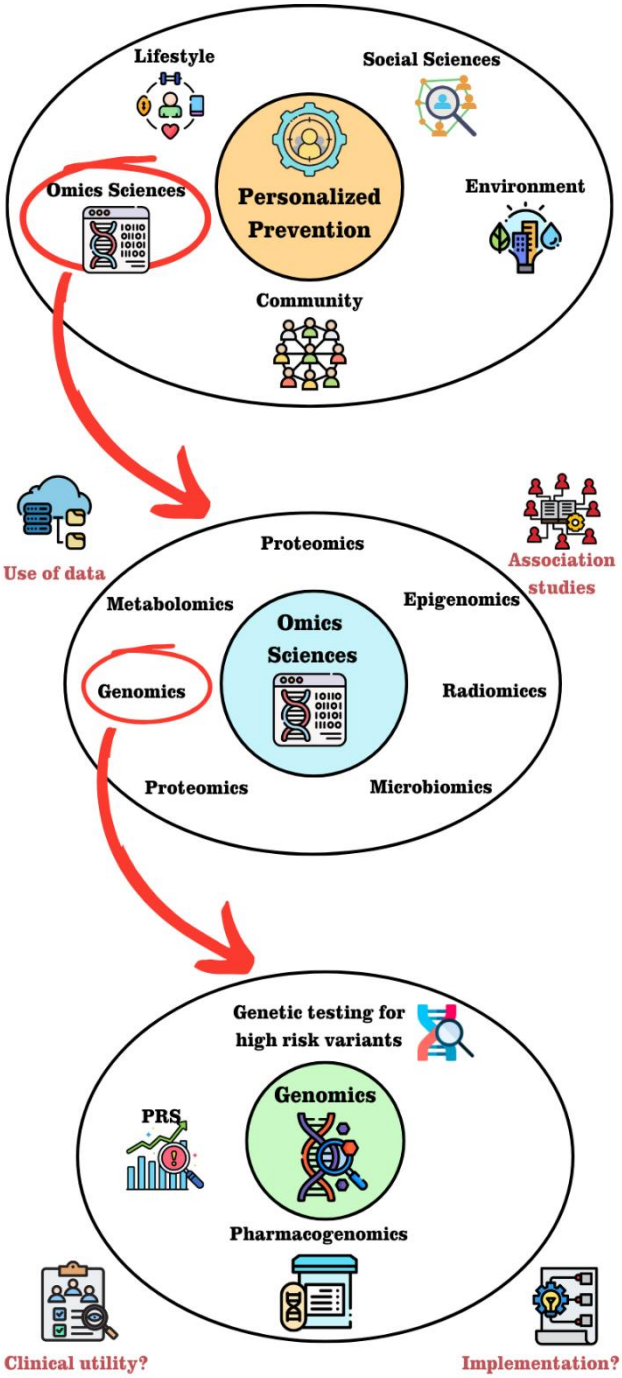

Figure 1. The PROPHET ecosystem

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In conclusion, PROPHET represents a significant step towards a future where prevention is truly personalised at all its' levels, empowering individuals to take control of their health and well-being. The SRIA outlines the major areas that must be addressed in order to fully realize the potential of personalised prevention.

2. Background and methodology

2.1 Definition and Vision: why is personalised prevention important?

The "*Health at a Glance: Europe"* report serves as a stark reminder of the overwhelming prevalence and impact of chronic diseases on the continent.[1] As these diseases continue to be the leading causes of morbidity and mortality, accounting for a substantial proportion of premature deaths, the burden on healthcare systems becomes increasingly apparent. Moreover, the socio-economic implications of chronic diseases, including diminished productivity and increased healthcare costs, highlight the urgency for innovative and sustainable solutions.

These elements pose a direct threat to the sustainability of European healthcare systems. The traditional reactive model of healthcare, focusing on treating established diseases, is proving to be economically unsustainable. As such, a transformative shift towards primary prevention and early diagnosis, together with more effective use of pharmacological therapy, is imperative for achieving a balance between effectiveness, efficiency and quality within the constraints of public budgets.

In the past two decades, advancements in sequencing and genotyping technologies and the integration of digital resources in healthcare have ushered in a new era of medicine. This "precision-revolution" has opened possibilities for personalised prevention, where individualised risk profiles are identified through a nuanced understanding of genetics, behavioural and socio-economic factors. By tailoring interventions based on this information, personalised prevention aims to delay disease onset, enhance quality of life and ultimately reduce the economic burden on healthcare systems. In this context, the need for a comprehensive and proactive strategy to mitigate the burden of chronic diseases is more pressing than ever. This Strategic Research and Innovation Agenda (SRIA) delves into the intricacies of the personalised prevention paradigm and elucidates the reasons for its crucial integration into European healthcare systems.

[1] https://health.ec.europa.eu/state-health-eu/health-glance-europe.en

The personalised PREvention of Chronic DIseases (PRECeDI) consortium, established in 2019, laid the groundwork for the integration of personalised prevention into chronic disease.[2] It emphasized the potential of preventive interventions targeting high-risk individuals and underscored the need for parallel changes in healthcare systems, while highlighting the large gap between therapeutic offerings and prevention tools in the field of personalised medicine.

By leveraging these premises, the "*A personalised Prevention Roadmap for the Future Healthcare*" (PROPHET) project aims to bridge these gaps by advocating for a holistic approach that considers not only solid biomedical knowledge but also economic sustainability, policy alignment and investments in cutting-edge technologies. PROPHET is a Coordination and Support Action of the International Consortium for Personalised Medicine (ICPerMed) and it involves 18 partners from 12 EU Member States, and the UK.

During the kickoff meeting of PROPHET in September 2022, personalised prevention was conceptualised as a targeted approach considering biological, environmental and behavioural characteristics, along with socio-economic and cultural context (*"personalised 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 behavioural characteristics, 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").*[3] **As PROPHET is a Coordinating and Support Action of the International Consortium of Personalised Medicine (ICPerMed[4]), it emphasizes the integration of genomics/biomarkers in personalized preventive approaches.** Various terms, such as Precision Prevention or Precision (Public) Health[5], are used interchangeably, emphasizing the need for precision and effectiveness in health promotion. The Fig. 2 depicts our vision of the three levels of personalised prevention in PROPHET.

[2] Boccia S, Pastorino R, Ricciardi W, Ádány R, Barnhoorn F, Boffetta P, Cornel MC, De Vito C, Gray M, Jani A, Lang M, Roldan J, Rosso A, Sánchez JM, Van Dujin CM, Van El CG, Villari P, Zawati MH. How to Integrate personalised Medicine into Prevention? Recommendations from thepersonalised Prevention of Chronic Diseases (PRECeDI) Consortium. Public Health Genomics. 2019;22(5-6):208-214. doi: 10.1159/000504652. Epub 2019 Dec 5. PMID: 31805565.

[3] Concept paper on Strategic Research and Innovation Agenda, available at https://prophetproject.eu/wp-content/uploads/2023/04/PROPHET-Concept-paper.pdf

[4] Home - ICPerMed

[5] Roberts, M. C., Holt, K. E., Del Fiol, G., Baccarelli, A. A., & Allen, C. G. (2024). Precision public health in the era of genomics and big data. Nature Medicine, 1-9.

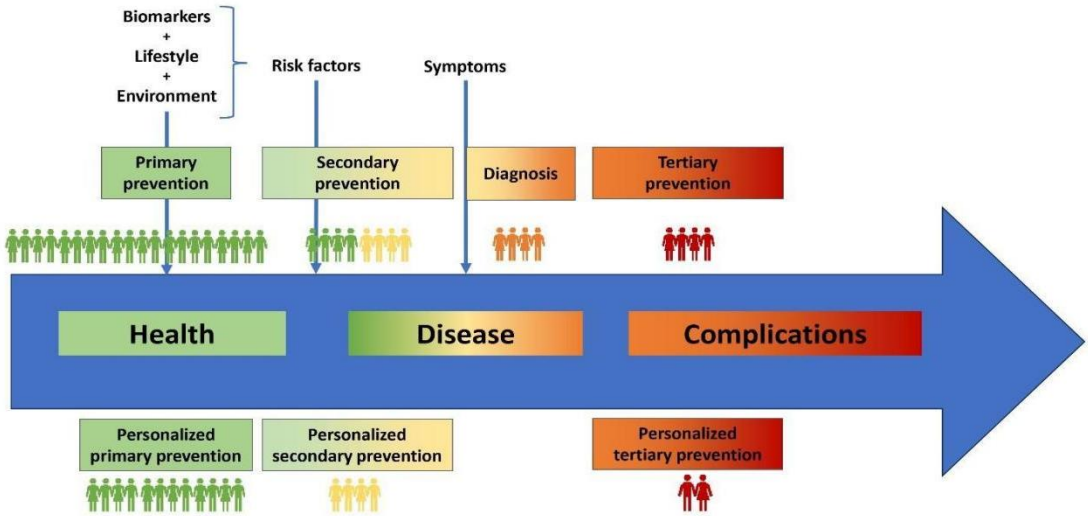

Figure 2. Description of the three levels of prevention, according to the disease stage.

Initiatives like PReCEDI and PROPHET chart a course towards the integration of personalised prevention into the fabric of European healthcare. The transition from reactive treatment models to proactive and individualised preventive measures holds the promise of a healthier and more sustainable future for all people across the continent. Embracing personalised prevention is not just a choice: it is a necessity for building resilient and effective healthcare systems that can withstand the complex health challenges of the 21st century.

2.2 PROPHET expected outcomes

The PROPHET project anticipates a spectrum of far-reaching outcomes and impactful contributions, strategically aligned with the overarching mission to innovate healthcare through the implementation of Personalised Prevention as an integral part of the current traditional approaches in prevention.

PROPHET employs a structured methodology, including the creation of a Stakeholder Platform, literature mapping, research gap analysis and the development of the PROPHET Framework. The outputs are disseminated through targeted communication strategies and capacity-building activities to maximize the impact of Personalised Prevention strategies across various stakeholder groups.

These expected outcomes encompass a multidimensional approach, addressing various domains and stakeholders, with a profound emphasis on sustainability, innovation and societal well-being.

Main expected outcomes are:

1. Comprehensive Personalised Prevention Roadmap
2. Strengthened Collaborative Ecosystem
3. In-Depth Research Advancements

4. Evaluative Frameworks and Indicators
5. Empowered Public Health Authorities
6. Raised Awareness among Citizens, Patients and Healthcare Professionals and Citizen Engagement
7. Informed policy makers thanks to Policy Briefs and Communication Strategies

A detailed description of expected outputs and outcomes is set out in Table 1.

In summary, the expected outcomes and impact of the PROPHET project extend beyond the development of a Roadmap; they encompass a holistic transformation of healthcare practices, stakeholder collaborations, research advancements and societal awareness.

The project's endeavors are poised to pave the way towards a future where personalised prevention is not just a concept but a tangible and integral component of healthcare excellence.

	Goal	Activities	Main Outputs	Expected Outcomes
Foster Collaboration, comprehensive personalised prevention Roadmap for effective prevention and Strategic Research and Innovation Agenda	Establish a comprehensive personalised prevention Roadmap. Establish collaboration among stakeholders in the field of personalised Prevention for the creation and implementation of a SRIA.	Create a Stakeholder Platform, to engage key stakeholders in order to contribute to the SRIA on personalised Prevention, to inform research funders and prospective partners. Develop a detailed Roadmap outlining actions, output and results indicators.	A Stakeholder Platform, a structured mechanism for SRIA co-creation and a comprehensive SRIA translating PROPHET's vision into a long-term systemic approach.	1. <u>Comprehensive personalised Prevention Roadmap</u> This accompanies the SRIA and details the actions and timelines by which this SRIA is expected to be implemented. The Roadmap provides a detailed blueprint for implementing tailored preventive strategies for each individual, based on the latest scientific advancements and the specific needs of each context. 2. <u>Strengthened Collaborative Ecosystem</u> A relevant activity of PROPHET is to strengthen the collaboration network among all stakeholders involved in the field of personalised prevention, aiming to create a robust and sustainable ecosystem.
Research Advancements in personalised Prevention	Gain a thorough understanding of research advancements in personalised Prevention through literature mapping, research gap analysis and mapping existing funded projects and programs.	Conduct literature mapping, research gap analysis and mapping of existing research projects and programs for personalised Prevention in Europe and beyond.	Mapping reports of the existing scientific literature in the domains of personalised Prevention.	3. <u>In-Depth Research Advancements in personalised Prevention</u> Literature mapping, research gap analysis and mapping of recent research projects and programs are expected to yield insightful reports in the domains of personalised Prevention. These outputs will not only inform the development of the personalised Prevention Roadmap but also contribute to the broader scientific community, advancing knowledge and guiding future research initiatives.
Provide instruments to evaluate the Effectiveness and Clinical Utility of personalised	Assess the clinical utility, key success factors and gaps of current personalised preventive approaches. Identify bottlenecks, analyze	Conduct literature reviews on the evaluation frameworks used to appraise omics technologies and extract the indicators to evaluate	Analysis of adoption of approaches in all domains, identification of facilitators / barriers and a list of indicators to	4. <u>Evaluative Frameworks and Indicators</u> A significant outcome of the project is the establishment of evaluative frameworks and indicators for personalised Prevention approaches. Through a meticulous analysis of existing bottlenecks, success factors and barriers, PROPHET will identify key process and

preventive approaches	evidence and evaluate successful implementations.	the relevant domains of clinical utility.	evaluate personalised Prevention approaches.	outcome indicators. These indicators will serve as essential tools for assessing the clinical utility and scalability of personalised preventive approaches, providing a tangible contribution to evidence-based healthcare practices.
Strengthen Public Health Authorities	Analyze how personalised Prevention can be delivered most effectively, efficiently and cost-effectively. Design a multidimensional framework (the PROPHET Framework) for appraising and adopting personalised preventive approaches.	Develop the PROPHET Framework and apply it to assess existing personalised prevention programs. Provide Capacity Building activities for Policy Makers and Health professionals through dedicated tool boxes and residential and educational efforts	The PROPHET Framework, 3 case studies and 4 Action Plans for personalised Prevention programs and Capacity Building activities.	5. <u>Empowered Public Health Authorities</u> The project aims to empower Public Health Authorities by providing them with a multidimensional framework for designing, assessing and implementing personalised preventive approaches. This framework, integrated into the SRIA, is expected to be a practical resource for policymakers and health authorities, enhancing their capacity to navigate the complexities of personalised Prevention and make informed decisions that benefit public health.
Raise Awareness among Citizens and Patients	Raise awareness among public and patients on the potential of personalised Prevention to improve quality of life. Engage them in defining, establishing and adopting personalised preventive services.	Implement awareness campaigns, capacity building for public and patients and develop tailored communication tools.	Guidelines for public and patient engagement, policy briefs and communication strategies tailored to stakeholders. Delivery of training courses, targeted awareness campaigns and capacity-building activities.	6. <u>Raised Awareness among Public, Patients and Healthcare Professionals and Patient Engagement</u> The project aims to empower individuals to actively engage in their health journey. This outcome extends to a broader cultural shift, where a patient-centric approach is encouraged, fostering open dialogues between health professionals, patients and their families.
Raise Awareness among Healthcare	Raise awareness among Health Professionals, Life	Stakeholder involvement via the Stakeholder	Guidelines for stakeholder engagement,	<u>Raised Awareness of healthcare professionals and policy makers</u> Through the elaboration of a policy brief and tailored

Professionals and Stakeholders	Sciences Companies, Insurers, Regulators and Policy Makers. Promote collaborative relationships for the quick adoption of personalised Prevention approaches.	Platform, awareness campaigns and capacity building for healthcare professionals.	policy briefs and communication strategies tailored to targeted stakeholders.	communication strategies, PROPHET aims to influence decision-makers, ensuring that the insights and recommendations derived from the project are disseminated effectively. This outreach is designed to catalyze policy changes that align with the vision of integrating personalised Prevention into the fabric of healthcare systems.

Table 1. PROPHET Goals, activities, main outputs and expected outcomes.

2.3 Building on lessons learned

One of the fundamental theoretical underpinnings of PROPHET is the "Vision Paper on Personalised Medicine Research & Implementation by 2030" by ICPerMed, a comprehensive and forward-thinking approach that envisions the integration of personalised prevention strategies as a fundamental element in the evolution of healthcare for all the public[6]. This vision is based on the idea that tailoring medical interventions to individual characteristics, including genetic, environmental and lifestyle factors, holds the potential to significantly enhance the effectiveness and efficiency of healthcare delivery[7]).[8] ICPerMed was created in 2015, bringing together over 50 European and international partners, working as a "think tank" focused on Policy and Strategy for Personalised medicine and on fostering Internationalization and Global cooperation. Over the past 10 years, ICPerMed produced several key documents to foster research and implementation in Personalised medicine, including an Action Plan (https://www.icpermed.eu/activities/action-plan/; 2017) and a ICPerMed's Vision 2030 reflects a concerted effort to engage a wide array of stakeholders, including experts from diverse professional backgrounds and sectors, to ensure that the implementation of personalised medicine is both inclusive and impactful. The emphasis on personalised prevention approaches within this vision aligns with the broader goal of empowering individuals to actively participate in maintaining their health and well-being. By integrating personalised prevention into the fabric of healthcare, ICPerMed envisions a future where individuals are equipped with the knowledge and tools to make informed decisions about their health, thereby contributing to improved health outcomes on a societal level. Furthermore, the ICPerMed's vision emphasizes the need for a paradigm shift in healthcare systems to accommodate the principles of personalised medicine. This includes fostering an environment that supports the responsible use of health-related data. By placing personalised prevention at the forefront of its vision, ICPerMed acknowledges the potential of these strategies to not only improve individual health but also to contribute to the sustainability and resilience of healthcare systems as a whole.[9]

[6] https://www.icpermed.eu/en/activities-vision-paper.php
[7] https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-020-02316-w
[8] https://www.eppermed.eu
[9] Aguilera-Cobos L, García-Sanz P, Rosario-Lozano MP, Claros MG, Blasco-Amaro JA. An innovative framework to determine the implementation level of personalised medicine: A systematic review. Front Public Health. 2023 Feb 3;11:1039688. doi: 10.3389/fpubh.2023.1039688. PMID: 36817923; PMCID: PMC9936069.

2.3.1 Promising stories in personalised prevention

In the countries where top level scientific expertise and universal countrywide coverage of health insurance and medical services are supported by forward-looking and timely established legislation, inspiring examples have been set as outgrowths of public-private partnership. To illustrate a real-life application in a well-studied area[10], personalised prevention in breast cancer includes tailoring screening recommendations to individual risk, initiating earlier surveillance based on Polygenic Risk Scores (PRS), offering additional genetic testing for high-risk variants when needed, and ensuring access to qualified medical support. These steps represent the foundation of personalised prevention and care in a field where delays can cost lives.Additionally, targeted analysis of specific patient pathways from prevention and pre-diagnosis to recovery or end-of-life care brings together key stakeholders from various sectors and effectively identifies key development needs, which can then be prioritized based on their importance and feasibility[11].

Making a change in paradigm takes time – however, this statement should not postpone the first steps to be taken as soon as possible. As an essential prerequisite to build a solid basis for a country-wide personalised medicine system, the medical and related data management must meet the highest level security standards, yet perform fluently. In Estonia, this is called the e-Health system. Its main success factors are clear governance, legal clarity, a mature ecosystem, agreement about access rights, and standardization of medical data and data exchange rules[12]. Consequently, more than 20 years of a general population biobank (EstBB, part of BBMRI-ERIC netwrok of biobanks) have created transversal competences in science, medical practices and healthcare governance both locally and internationally. The experience from several pilot projects carried out using the wide spectrum of the scientific capacities of EstBB[13], [14] now serve as examples of how far the best outputs from a biobank can reach to, and accelerate the medical practices in Estonia and elsewhere.

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[10] Padrik P, Puustusmaa M, Tõnisson N, et al. Implementation of Risk-Stratified Breast Cancer Prevention With a Polygenic Risk Score Test in Clinical Practice. Breast Cancer: Basic and Clinical Research. 2023;17. doi:10.1177/11782234231205700

[11] https://www.sm.ee/en/news/lung-cancer-patient-pathway-project-illuminates-gaps-cancer-care

[12] Klementi T, Piho G, Ross P. A reference architecture for personal health data spaces using decentralized content-addressable storage networks. Front Med (Lausanne). 2024 Jul 16;11:1411013. doi: 10.3389/fmed.2024.1411013. PMID: 39081693; PMCID: PMC11286498.

[13] Alver M, Palover M, Saar A, Läll K, Zekavat SM, Tõnisson N, Leitsalu L, Reigo A, Nikopensius T, Ainla T, Kals M, Mägi R, Gabriel SB, Eha J, Lander ES, Irs A, Philippakis A, Marandi T, Natarajan P, Metspalu A, Kathiresan S, Esko T. Recall by genotype and cascade screening for familial hypercholesterolemia in a population-based biobank from Estonia. Genet Med. 2019 May;21(5):1173-1180. doi: 10.1038/s41436-018-0311-2. Epub 2018 Oct 1. PMID: 30270359; PMCID: PMC6443485.

[14] Leitsalu L, Palover M, Sikka TT, Reigo A, Kals M, Pärn K, Nikopensius T, Esko T, Metspalu A, Padrik P, Tõnisson N. Genotype-first approach to the detection of hereditary breast and ovarian cancer risk, and effects of risk disclosure to biobank participants. Eur J Hum Genet. 2021 Mar;29(3):471-481. doi: 10.1038/s41431-020-00760-2. Epub 2020 Nov 23. PMID: 33230308; PMCID: PMC7940387.

Biobanks in several countries have started to return results of findings with implications for care and prevention. Pilots have been done and are ongoing on how best to deliver such information. For instance, participants can be contacted by the biobank or access their results via a portal.[15] Lessons from the Estonian biobank include participant reactions to such results and ways to deliver these results via counselling, which may prove to be time consuming.[16]

In Finland, participants can access their own 10-year absolute risk estimate for Type 2 Diabetes, which combines traditional risk factors (such as BMI and cholesterol levels) with Polygenic Risk Scores (PRS). Participants can compare their own total risk with a matched age population, their projected risk at age 60, and calculate changes to their risk if they would make lifestyle changes, such as stopping smoking. Such tools may help participants understand their own role in improving their health and promote citizen empowerment.

The P5.fi Study, based on Finland's FinHealth 2017 population-based study, assessed how individuals responded to personalized genetic risk information and its influence on health behaviors. Focusing on polygenic risk scores for coronary artery disease, type 2 diabetes, and deep vein thrombosis risks, it provided biobank donors with secure, personalized reports of the genetic and total risk for these diseases. Relevant pharmacogenetic and single variants for the diseases were likewise analyzed and the results returned. The study provided lifestyle guidance and information about the diseases and genetics through the MyP5 website. Participants' responses and health outcomes were monitored over years to evaluate the feasibility of integrating genomic data into public health, aiming to address challenges in applying predictive, preventive, and personalized health approaches.[17, 18]

The GenomeHealth project, a collaboration between Finnish hospital biobanks, aims to integrate genomic data from biobank samples into healthcare to advance personalized medicine. The study utilizes the genomic data created by the Finngen-study[19]. By screening high-risk genes like *BRCA1, BRCA2, and PALB2* for cancer susceptibility, the project developed a streamlined process for delivering significant genetic findings to biobank donors. The variants selected to be screened in the

[15] Estonian Biobank Launches Portal to Deliver Genetic Results to Biobank Participants - Research In Estonia. Frontiers | A Web Portal for Communicating Polygenic Risk Score Results for Health Care Use—The P5 Study (frontiersin.org).
[16] Lessons learned during the process of reporting individual genomic results to participants of a population-based biobank - PubMed (nih.gov)
[17] https://thl.fi/en/research-and-development/research-and-projects/the-p5.fi-study-genetic-information-for-health-support
[18] Ref: Marjonen H, Marttila M, Paajanen T, Vornanen M, Brunfeldt M, Joensuu A, Halmesvaara O, Aro K, Alanne-Kinnunen M, Jousilahti P, Borodulin K, Koskinen S, Tuomi T, Ilanne-Parikka P, Lindström J, Laine MK, Auro K, Kääriäinen H, Perola M, Kristiansson K. A Web Portal for Communicating Polygenic Risk Score Results for Health Care Use-The P5 Study. Front Genet. 2021 Oct 29;12:763159. doi: 10.3389/fgene.2021.763159. PMID: 34777479; PMCID: PMC8585790.
[19] www.finngen.fi

project are well-known, and there are clear action models and treatment recommendations for them, including enhanced follow-up, preventive surgery, and targeted therapy such as PARP inhibitors. Utilizing the MyBiobank digital service, donors were contacted and, with consent, informed of their genetic risks, then referred to clinical services for further testing and counseling. This approach not only supports early disease intervention but also demonstrates cost-effectiveness, highlighting Finnish biobanks' potential in preventive healthcare. Also cost-benefit analyses of the approach are being done.[20]

The vast majority of both the studies participants were satisfied with the provided services.

On top of health benefits, these studies as well as previous research showed that analyses of biobank samples can be done very cost-effectively, and in some cases, even saving costs.[21]

2.4 Synergies with other initiatives

During the different stages of project development, PROPHET will make contact and synergies with numerous initiatives.

First, PROPHET is fully matched and aligned in purpose with the Europe's Beating Cancer Plan, reflecting a resolute political commitment to comprehensively combat cancer. The plan is structured around key action areas and provides a holistic approach, addressing the entire spectrum of the disease pathway, from prevention to treatment and emphasizing the improvement of the quality of life for cancer patients and survivors. PROPHET's activities are intricately aligned with the nuanced Roadmap of action 31.2, the "Roadmap to personalised Prevention", making a substantive contribution to the overarching goals of the Europe's Beating Cancer Plan.[22]

The project supports personalised prevention within the cancer, that can serve as blueprint for successful initiatives in other chronic diseases, and extends its influence on pivotal European initiatives, notably collaborating with ICPerMed and the *European Partnership for Personalised Medicine* (EP PerMed was launched on October 5, 2023, marking a significant milestone in advancing research in personalised medicine across Europe., EP PerMed rallied 60 partners to contribute to its

[20] https://site.fingenious.fi/en/articles/genomehealth-project-returns-genetic-results

[21] Martikainen J, Lehtimäki AV, Jalkanen K, Lavikainen P, Paajanen T, Marjonen H, Kristiansson K, Lindström J, Perola M. Economic evaluation of using polygenic risk score to guide risk screening and interventions for the prevention of type 2 diabetes in individuals with high overall baseline risk. Front Genet. 2022 Sep 15;13:880799. doi: 10.3389/fgene.2022.880799. PMID: 36186460; PMCID: PMC95202

[22] https://health.ec.europa.eu/system/files/2022-01/2021-2025_cancer-roadmap1_en_0.pdf

development, with the primary goal of advancing innovative personalised medicine approaches in healthcare systems. EP PerMed's initiatives are underpinned by the SRIA for personalised medicine published in 2023[23], another key document useful in the construction of PROPHET's SRIA. This collaborative synergy enriches the landscape of personalised medicine, contributing significantly to the realization of a fortified European Health Union characterized by resilience, preparedness and sustainability in the face of evolving health challenges.

The concept of personalised prevention inevitably relies on the availability of data that allows for the individualization of healthcare interventions, as well as the creation of infrastructures that enable data sharing in a manner compliant with high European standards for both the effectiveness of healthcare systems and the protection of citizens' and patients' privacy and data security. To address these needs, the European Commission has funded three initiatives/projects: in 2018, the *1+Million Genomes (1+MG)*[24] initiative was launched. Twenty-six European countries have signed the declaration, aiming to enable secure access to genomic and corresponding clinical data across Europe for better research, personalised healthcare, and health policy making. In 2020, the *Beyond 1 Million Genomes (B1MG)*[25] project was initiated, focusing on the goals of the design and testing phase of the 1+MG Initiative. B1MG produced the 1+MG Framework[26] a user-friendly interface to navigate the guidelines and recommendations of the 1+MG initiative. As results of a common effort of 1+MG and B1+MG, **the 1+MG Roadmap 2023-2027** has been published.[27]

Subsequently, in 2022, the *Genomic Data Infrastructure (GDI)*[28] project began. This €40M co-funded project builds on the preparatory work of the 1+MG working groups, the B1MG project, and investments from EU countries. The GDI project is enabling access to genomic and related phenotypic and clinical data across Europe by establishing a federated, sustainable, and secure infrastructure for data access. Both projects are coordinated by ELIXIR, which acts as a neutral broker for the 1+MG countries and aims to sustain biological infrastructure to support the initiative's ambitions. The *Genome of Europe* project also supports the 1+MG initiative and started in October 2024. The project is bulding a European network of national genomic reference cohorts of 1,000,000 citizens, selected to be representative of the European population. It is worth mentioning in this context the latest report

[23] The EP PerMed: 'The Strategic Research & Innovation Agenda (SRIA) for Personalised Medicine' (2023)
[24] https://digital-strategy.ec.europa.eu/en/policies/1-million-genomes
[25] https://b1mg-project.eu
[26] https://framework.onemilliongenomes.eu/about-the-framework
[27] https://ec.europa.eu/newsroom/dae/redirection/document/99974
[28] https://gdi.onemilliongenomes.eu

from the WHO[29] that, by recognizing the importance and value of human genome data, provides guidance to realize the promise of genomics for all in a way that identifies and mitigates the ethical, legal, social and cultural issues that are likely to arise.

Lastly the *Transforming Health and Care Systems* (THCS) European Partnership, co-financed by the European Commission under the Horizon Europe Research and Innovation Framework, stands as a noteworthy initiative supporting personalised prevention advocated by PROPHET. By backing coordinated national and regional research, innovation programs, capacity development and networking, THCS actively contributes to the transformation of healthcare and care systems across Europe. In facing common challenges, healthcare and care systems in Europe necessitate harmonised solutions and THCS serves as a strategic opportunity to unite stakeholders and facilitate the digital transformation of healthcare services. With a goal to transition towards more sustainable, efficient, resilient, inclusive, innovative and high-quality healthcare and care systems, THCS aims to generate new knowledge, co-design solutions and strengthen healthcare systems through diverse activities.

The collective commitment of PROPHET and other initiatives enriches the landscape of personalised medicine, paving the way for a future where individualised healthcare becomes a cornerstone of the European healthcare system.

In conclusion, the integration of the results from different projects and initiatives is crucial to implement personalised prevention at European level and beyond.

2.5 Mission: the need of a SRIA on personalised prevention

The current document aims to support EU Member States when scaling up personalised preventive approaches for primary, secondary and tertiary prevention, interweaving the levels of biomarkers, individual behavior, and environment/societal factors. Unlike the traditional *one-size-fits-all* approach, which applies the same preventive measures to everyone, personalised prevention focuses on tailored interventions based on individual health profiles and risk factors. By considering the outcomes listed in Table 1, this SRIA seeks to address the key elements required to ensure that personalised prevention strategies are effectively implemented and that their benefits are realized across Europe.

[29] Guidance for human genome data collection, access, use and sharing: https://www.who.int/publications/i/item/9789240102149

2.6 Methodology for SRIA development

The SRIA is grounded in a highly multidisciplinary construction model, integrating the consortium's vision for personalised prevention (summarised in a Concept Paper described in 2.6.1), and the assessment and synthesis of various project outcomes through a co-creation process ensured by robust stakeholder engagement. In terms of evidence, the SRIA draws from all three major phases (and related Work Packages-WP) constituting the PROPHET approach: **Mapping**, which involves extensive research on the state of personalised prevention in Europe and beyond; the **Assessment** process, built around the PROPHET Framework, that provides decision-makers with a path and related indicators to evaluate personalised prevention approaches before implementation; the **Building** phase that presents results from the actual implementation of the PROPHET methodology in diverse health and social contexts. The stepwise approach for SRIA development is depicted in Figure 3.

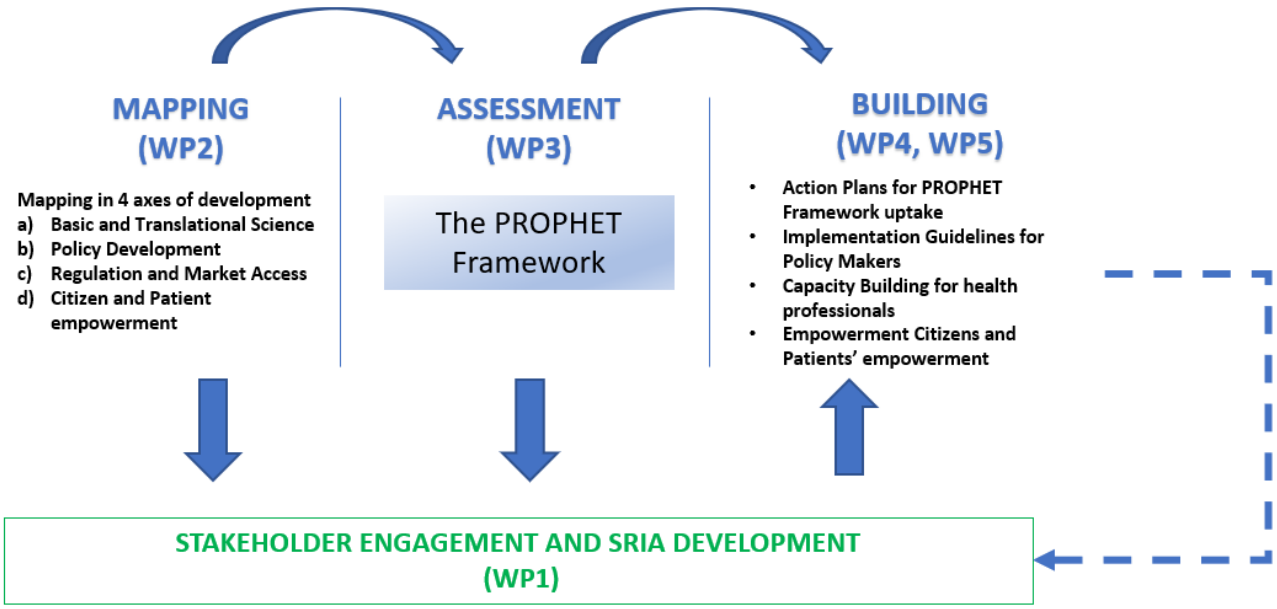

Figure 3. The approach for SRIA development in PROPHET.

2.6.1 The PROPHET Concept Paper

Efforts from the first year of activities of PROPHET have been summarized in a Concept Paper[30], which served as the foundation for the full Strategic Research and Innovation Agenda (SRIA) in the field of personalised prevention. This document encapsulates the consortium's vision, definition, and initial insights regarding the gaps and challenges of personalised prevention that need to be analyzed for its implementation. The Concept Paper has been informed by preliminary results of literature reviews, mapping analyses, and input from a wide range of stakeholder and key informant interviews and consultations at European and national levels.

The paper defines personalised prevention and its links with previous European initiatives in personalised medicine. It highlights PROPHET's role and the SRIA as a tool to support the implementation of innovative, sustainable, and effective personalised programs to prevent common chronic diseases in all European Member States. Precision in interventions implies predicting and addressing risk (at scale), in individuals as well as groups of individuals sharing different characteristics. Here the high-risk vs the population (subgroup) approach needs to be balanced recognizing Rose's prevention paradox[31]. In essence, effective public health prevention must strike a careful balance between precision targeting for high-risk groups and broader measures for the general population. This trade off depends on how much risk is confined to an identifiable population group, and the extent to which precision can be achieved in identifying this group and addressing this increased risk. This is likely to vary across risk factors and diseases, and across socioeconomic groups and whether these groups have access to health and social services.

The project's strategy involves engaging the broad health ecosystem and addressing individual risks within a community context, especially for primary prevention in healthy individuals (Fig.4). Data plays a central role in this approach, categorized into three subsections in PROPHET: biomarker, individual lifestyles and environmental/contextual factors. The disease and life-course stages, ranging from healthy to sick, involve actions across promotion/primary prevention, secondary prevention and tertiary prevention/treatment level.

[30] Concept paper on Strategic Research and Innovation Agenda, available at https://prophetproject.eu/wp-content/uploads/2023/04/PROPHET-Concept-paper.pdf

[31] Rose, Geoffrey, Kay-Tee Khaw, and Michael Marmot, Rose's Strategy of Preventive Medicine (Oxford, 2008; online edn, Oxford Academic, 1 Sept. 2009), https://doi.org/10.1093/acprof:oso/9780192630971.001.0001, accessed 26 Feb. 2024.

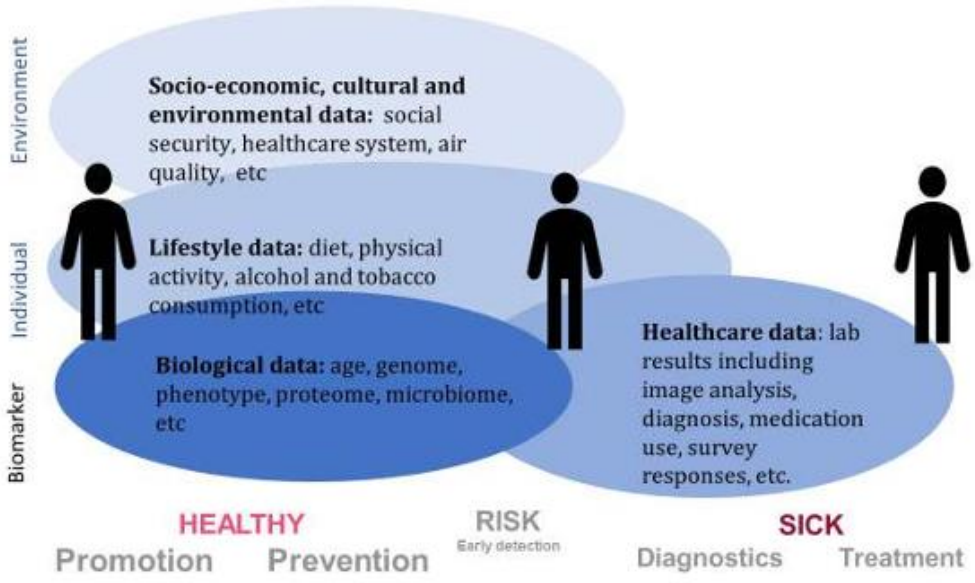

Figure 4. Potential source of information needed to achieve precision and personalization of prevention and treatment across the life course.

The Concept Paper also preliminarily identified preliminary challenges that constitute the core of the PROPHET project:

- The data challenge: practical and legal impediments currently hinder the potential to use and combine different types of data in prevention, which need to be addressed to increase precision in the identification of individuals, families, population groups, or neighborhoods at increased risk, combined with individual empowerment and health literacy.
- Trust, ethics, and community engagement: public health actions should focus on population-specific needs, policy development, and delivering effective and ethical interventions. Crucial activities include engaging communities, sharing data, building coalitions, improving health literacy, and developing a diverse educated workforce. A fundamental concern is whether precision technologies can exacerbate health disparities or create barriers to access for certain populations. Ethical principles of justice, fairness and equity in access will therefore need to guide assessment of precision technologies, in addition to various health technology assessments.

- Behavioral Science: personalised prevention assesses risk, which needs to be managed by the person exposed and stakeholders, including health workers, who can affect risk behavior and exposure. This suggests a behavioral science research agenda to develop an evidence-based approach to tackling risk.
- Health Sector integration and beyond: as personalised prevention interventions develop, they need to be integrated into health services, raising questions about health worker capabilities, systems support, financing/reimbursement, and incentive mechanisms to support prevention interventions.
- Technological advances add new markers that may help better identify subgroups of individuals with different risks of having a disease, which eventually could improve prevention strategies at the individual level. Integrating markers of risk into scalable intervention packages is key to achieve population impact.
- Political economy of prevention: what gets recognized, becomes policy and implemented, is not just a question of the evidence at hand, but also of the political economy, a social science conceptualisation of what gets done or not. During PROPHET stakeholder consultation it became evident that a stakeholder forum for multisectoral coordination and advocacy was desirable, at regional as well as national level. Such a forum could work on the narrative and positioning for prevention, and approach policymakers and stakeholders across sectors.
- Inequities in health and personalised prevention: Inequities in health outcomes are driven by differential risk mostly linked to biological and socio-economic factors. Measures across promotion, prevention, and treatment need to be adapted and highly contextualized to improve health.
- Scaling up- Implementation Research: As interventions are put into practice in complex health systems, issues around implementation and operational questions need to be addressed.

In summary, to realize its potential the precision field needs to take a life course, multisectoral approach using different types of data also to prevent disease and not restrict itself to using omic information to treat established disease. This implies a far-reaching research and innovation need, new governance mechanisms, and a balanced agenda assessing both individual utility and public health implications at population level.

2.6.2 Stakeholder engagement strategy

This specific activity will be completed and validated within the project lifespan. The stakeholder engagement strategy is implemented through the PROPHET Platform and the PROPHET Forum. One of the foundational elements of the PROPHET project, and subsequently the development of the SRIA, is the continuous engagement of stakeholders in the realm of personalised prevention, following a process defined as co-creation. This collaborative approach aims to bring together researchers, policymakers, healthcare professionals, patient and citizen representatives and other key stakeholders to drive advancements in the field. To achieve this, a thorough stakeholder mapping exercise, based on the "snowball methodology", was conducted to identify and categorise relevant stakeholders across Europe. This process started by identifying key stakeholders, suggested by partners, then extending the process to other stakeholders who mighthave an interest in the project. A (confidential) database of contacts was then established, which is continuously updated with new data, ensuring a thorough follow-up and involvement of stakeholders from all relevant groups. Access to this database is limited to PROPHET project partners.

The stakeholder engagement strategy outlines the approach to engage experts from various sectors, ensuring that the potential stakeholders' concerns and needs are considered in the development of the SRIA (Table 2).

Diverse channels and tools have been used to reach stakeholders, informing them about project activities and results, and encouraging their active participation in knowledge sharing activities such as workshops. At the heart of this engagement process is **the PROPHET Forum**, a stakeholder community that gathers stakeholders from all relevant categories. The Forum is managed and coordinated by the PROPHET project team, **with regular outreach to stakeholders to engage them in project events and ask them to contribute to the SRIA co-development process**. To facilitate exchanges and interactions among Forum members, the **PROPHET Platform** was developed as a **community platform**. The Platform offers members the ability to set up individual profiles, use features such as unity web platform bilateral exchange through a matchmaking tool, share information with peers and with the PROPHET team, access event information and recordings, and engage with co-developed documents, including the SRIA and related documents. This coordinated approach, supported by the PROPHET Forum and Platform, aims to maintain a stakeholder engagement process that is crucial for the success of the PROPHET project and the development of the SRIA.

Stakeholders	Concerns	Potential impacts
Patients & citizens	They are the most important key stakeholders as they are the ultimate beneficiaries of more targeted prevention and treatments. They may be concerned about the cost of personalised preventive treatments, access to genetic testing, etc.	Improved patients' and citizens' quality of life by adapting prevention to individual characteristics (including genomics and environment / lifestyle aspects).
Healthcare professionals	Concerns about the cost and feasibility of implementing personalised preventive approaches in health systems as well as the training and education on these new approaches.	Informed and trained professionals, emphasising prevention over treatment; early detection of potential risks among their patients and thus early approach to treatment where necessary; less overload in hospitals thanks to prevention and early treatment.
Researchers	Funding of research and collaboration with other stakeholders to advance in personalised prevention research.	New collaboration opportunities through research programmes to advance in the field of personalised prevention.
Policy makers & public authorities	Need to make new regulations or improve the existing ones as well as ensuring the safety and effectiveness of personalised preventive approaches and treatments. Validity of approaches across the EU and transferability of results.	Reduced burden on the health and social security systems thanks to prevention and early treatment, reducing costs. EU-wide approach and transferability tested through dedicated use cases which are nurturing the SRIA.
Insurers	Reimbursement processes of personalised preventive approaches.	Demonstrate the cost effectiveness & value of personalised prevention approaches, alleviating the burden on insurers.
Life Science Companies	Regulatory barriers for developing personalised prevention approaches and long processes.	Provide guidelines for the development of future personalised prevention approaches and "citizens" engagement.

Table 2. Anticipated key stakeholders concerns and potential impacts to be addressed in the development of the SRIA.

2.6.3 The Consultation Process for the Development of the SRIA

The development of the SRIA has followed a structured, multi-phase process since the early stages of the PROPHET project, combining conceptual elaboration, expert input, and progressive validation through stakeholder and public engagement.

The process began in August 2023 with the release of the Concept Paper (presented in detail in paragraph 2.6.1), which laid out the preliminary vision for personalised prevention and introduced a conceptual model for integrated, multilevel precision prevention. This document served as the foundation for subsequent development.

In September 2024, the first version of the SRIA was completed. It expanded on the conceptual model introduced in the Concept Paper and incorporated key findings from the mapping activities conducted in the project, as well as the main challenges to be addressed in the coming years. These challenges span multiple dimensions: from broadening the understanding and scope of promotion and prevention strategies, to establishing continuous systems for evidence synthesis that support personalised approaches. They also include defining practical pathways for implementing the PROPHET framework (Fig. 5) , ensuring robust mechanisms for data collection and integration, and building the necessary data infrastructure.

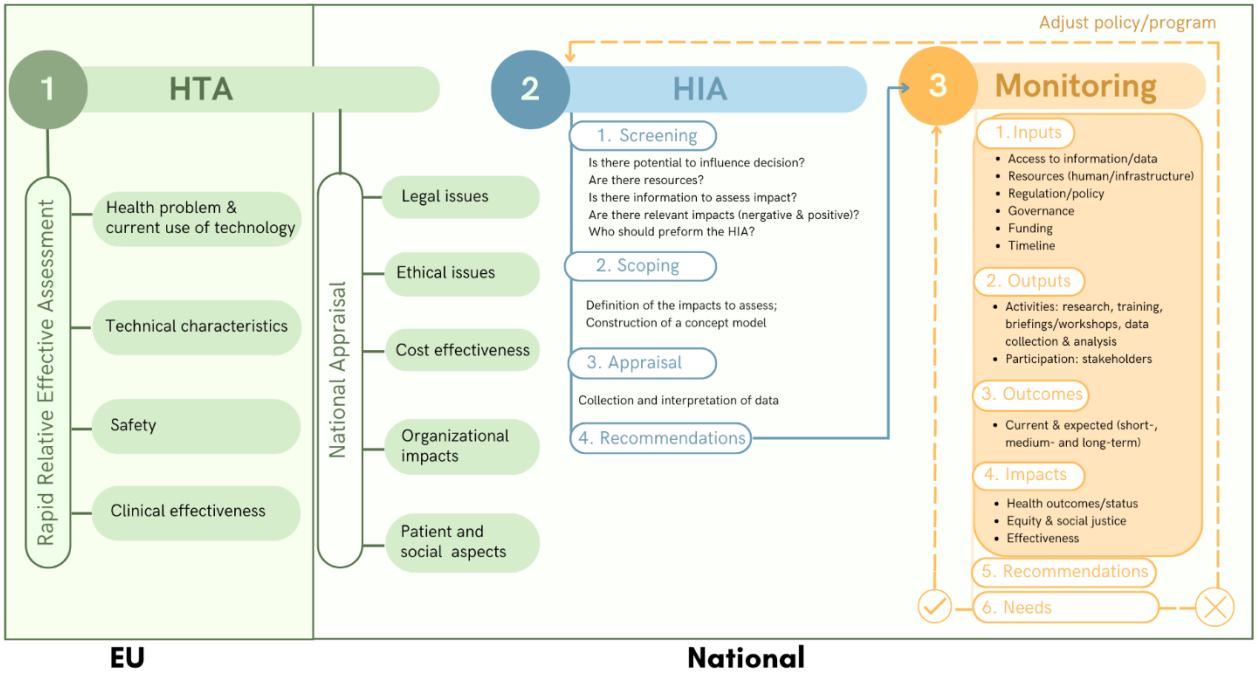

Figure 5. Overall PROPHET framework for genetic testing, including HTA complemented by HIA and a monitoring phase.

Furthermore, the process emphasised the importance of fostering trust and engagement within communities, ensuring the active involvement of health professionals and policymakers, and addressing regulatory issues while promoting synergies with the private sector. Equally crucial are efforts to guarantee equitable access and coverage, manage ethical, legal, and social implications, and develop strategies to support behavioural change among individuals and populations.

All these priorities were identified and selected through extensive internal discussion among stakeholders, ensuring that the SRIA reflects a shared vision and consensus within the PROPHET community.

To further refine the document, a dedicated workshop was organised in Stockholm in October 2024, where the first version of the SRIA was presented and discussed with stakeholders. In preparation for the consultation phase, a specific workshop on pharmacogenomics was held in Amsterdam in January 2025, bringing together experts and stakeholders to explore challenges and opportunities in one of the SRIA's key thematic areas.

PROPHET
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Funded by the European Union

Building on the insights gathered, an updated version of the SRIA was prepared, together with the drafting of a first version of the Roadmap, between October 2024 and March 2025. The Roadmap was designed to translate the strategic priorities outlined in the SRIA into actionable directions and milestones.

A subsequent phase of targeted stakeholder consultation was carried out between April and May 2025to gather further input on the updated versions of both the SRIA and the Roadmap. Feedback from a broad set of stakeholders helped validate the priorities and refine the implementation framework. Following this, a public consultation was launched to reach a wider audience across Europe. This phase provided additional insights from citizens, practitioners, researchers, and organisations who had not been previously engaged.

All these contributions are being integrated into the final version of the SRIA, which includes the Roadmap as an embedded component. While the SRIA outlines ten key challenges and corresponding priorities, described in detail later in this document (Section 3), spanning scientific, ethical, societal, organisational, and policy dimensions, the Roadmap complements it with an actionable implementation pathway. It identifies concrete steps, responsible actors, timelines, and enabling conditions needed to translate strategic priorities into effective interventions at both national and EU levels.

The final SRIA, to be published by November 2025, can represent a consolidated and shared vision for advancing personalised prevention in Europe.

3. The challenges of personalised prevention

Challenge 1: The broad scope of promotion and prevention

Status

Over the years, research on the prevention of chronic diseases has generated a substantial body of evidence. Effective strategies to reduce the risk of developing chronic diseases include lifestyle changes—such as healthy diets, exercise, sleep or smoking cessation-, reduction of occupational hazards and environmental exposures (e.g. air pollution or chemical contaminants), as well as primary care or public health preventive programs (e.g. screening, vaccination, metabolic risk factors

control).[32]These strategies can also be promoted or implemented through multilevel legal, societal, and public health measures that often extend beyond the health sector. The ambition, and potential, of a "precision dividend" is to reduce poor health and premature mortality by up to 70%. In this broader context, personalized prevention aims to advance efforts by incorporating the new possibilities offered by technological advancements in both biological and data science. A recent paper by Bian (2024) focused on lifespan, estimated that, while unfavorable lifestyles increased risk of death by 78%, those with an unfavorable genetic predisposition also had a 21% increased risk of death compared with a low genetic risk independent of lifestyle factor (Bian, 2024). However, today, technological advancements provide new opportunities to explore the drivers of illness and mortality. A recent study by Artengieri (2025) exemplifies this progress, utilizing exposome-wide association analyses in the UK Biobank cohort to assess the relative contributions of genetic susceptibility (polygenic risk scores) and environmental factors (the exposome). The study also incorporated -omic-derived biomarkers to examine proteomic aging and mortality. Findings revealed that, compared to basic demographic information like age and sex, polygenic risk scores for 22 major diseases accounted for less than a 2% increase in explained mortality variation, whereas the exposome contributed an additional 17%. In fact, an individual's risk of developing any disease is shaped by the interplay of sociocultural, economic, and physical environments (e.g education level, income, housing and employment conditions, cultural patterns and legal context, family and social networks, pollution and climate change). These factors influence lifestyles and behaviors (e.g dietary pattern, physical activity, tobacco or other substances use) that, combined with environmental exposures, genetic predispositions, and biological elements, determine disease susceptibility. While considerable research examines these factors independently, studies exploring their interactions are limited. Understanding these relationships is crucial for improving prediction accuracy and refining personalized preventive strategies. Since this SRIA primarily focuses on the omics sciences sector, a priority challenge for research should be to identify when these new resources provide real added value for prevention and how to integrate them effectively with existing knowledge and practical implementation strategies, without forgetting this global picture.

When it comes to omics, biomarkers are essential tools for identifying individuals at varying disease risk levels, whether in the general population or high-risk groups. They can function independently,

[32] Prüss-Üstün A, Corvalán C. Preventing disease through healthy environments: an estimate of the environmental burden of disease. Geneva: WHO; 2006.

be incorporated into predictive models, or work alongside digital tools like wearables and artificial intelligence for real-time monitoring. Traditional biomarkers, like blood pressure, blood sugar, and age, have guided prevention and treatment for decades. Now, advances in omics technologies—genomics, proteomics, metabolomics, microbiomics— provide additional data layers that enable finer risk stratification and tailored interventions. Furthermore, they can help estimate and refine risk exposures (e.g. exposomics). Molecular biomarkers, particularly genetic and genomic markers, dominate research in personalised primary and secondary prevention. However, genetic factors contribute moderately to disease origins and are less actionable compared to modifiable environmental and behavioral factors. Therefore, in addition to estimate the genetic risk of diseases, investigating gene-environment interactions is vital to understanding how genetic predispositions interact with external exposures and behaviors. This might expand the scope of the use of genetic data in prevention and pave the way for more personalised interventions. Emerging fields such as epigenetics and microbiomics also provide insights into modifiable risk factors. Epigenetic mechanisms, like DNA methylation, reflect how environmental exposures influence gene expression, linking modifiable factors like diet or stress to disease risk. Similarly, the microbiome -shaped by lifestyle and environmental influences- plays a relevant role in immune regulation, metabolism, and inflammation. Both epigenetics and microbiomics, as well as exposomics, may uncover actionable pathways for tailoring interventions based on individual and environmental contexts. Additionally, expanding the use of other -omic technologies like transcriptomics and metabolomics may provide new opportunities for improving preventive strategies. Beyond molecular biomarkers, other tools, such as imaging biomarkers can offer insights into disease-related structural and functional variations, while anthropometric and physiological biomarkers may also enhance diagnostic accuracy in complex predictive models. Given the multimodal type of data that can predict risk, as well as adherence to and effectiveness of interventions, increasingly we will need to rely on algorithms and artificial intelligence to integrate data sources, which also need to prove their added value. This is an important area for research and innovation.

Gaps

The true potential of personalized prevention in public health can only be realized by incorporating both personal and contextual factors, including socioeconomic, environmental, and commercial determinants of health. Insights from these -omic strategies should enhance and complement this

approach. However, our scoping review indicates that most biomarker research fails to consider these aspects. This is likely due to two key gaps: first, the lack of integration between non-clinical information and clinical or biological data, making their combination challenging; and second, the differing professional expertise required to interpret and manage each type of data. An integrative approach to personalized prevention should address these challenges.

Also, if personalised prevention strategies are primarily based on medical strategies delivered through health care, there is a risk of neglecting the social determinants of health. Omics-technologies applied through health services alone will achieve a smaller impact, particularly since vulnerable and high-risk individuals and groups tend to have less access and utilization of health services. However, data obtained from this integrative approach can also benefit and inform policies designed to address the broader factors mentioned above, and help them to achieve desired population impact, identifying high risk groups and promoting coverage.

It is the combined efforts of scientific advancements, including omics, as well as targeting social factors, and increased resource allocation that will be required for personalised prevention strategies to reduce disease burden and improve population health towards the ambition of preventing up to 70% of non-communicable diseases (NCDs). However, modelling and health economics research on incremental cost and health outcomes of -omics technologies in prevention beyond environmental/socioeconomic/lifestyle interventions would be useful. Also, the implementation part of the research and innovation agenda involves many sectors, and relies on several disciplinary areas, including political science. Nevertheless, these two issues are addressed in other challenges of this SRIA.

Among biomarkers, most current research focuses on identifying, quantifying and improving the estimation of genetic risk of diseases; however, while these efforts are particularly beneficial for individuals with inherited high-risk mutations, at the population level, polygenic risk scores currently have limited precision for individual risk prediction. While they may improve secondary prevention strategies, they are unlikely to serve as an effective guide for primary prevention. In contrast, the interaction between non-genetic risk factors and genes—a critical driver of disease development—

as well as the role of other omics that might also incorporate environmental exposures remains underexplored, despite its potential to refine and focus personalised primary prevention strategies.

Another important gap in this field is the issue of external validity. In many cases, biomarker research is highly context-specific, making it unclear how results can be extrapolated to the general population. There is a need for large, consistent, and reliable population-based data. While significant efforts have been made at the European level in genomics, such as the Genome of Europe initiative, non-genetic data in these projects remain scarce. Several national initiatives within Europe have established large population-based cohorts that include genetic, epidemiological, clinical, and contextual data. Providing structural support for these initiatives, while promoting their integration and combined analyses, can enhance their impact on personalized prevention research. Studying the complex field of chronic disease prevention requires robust cohort data to generate meaningful insights.

Finally, governments and healthcare systems often face tough choices about how to allocate limited resources. In the research field, while there is significant funding for clinical trials related to drugs and diagnostics, there is far less investment in lifestyle interventions and prevention research, with or without omics involved. Similarly, for service delivery health budgets across European countries typically spend 94% on care, and 6% on prevention. The imbalance between funding for clinical treatments and preventive strategies needs to be addressed, as greater attention to prevention could reduce the overall burden of disease and healthcare costs. A shift in funding priorities towards more preventive measures, to implement and scale preventive strategies, is needed for a more balanced and effective health system. This also implies the need for similar shifts in research and innovation.

Priorities and implementation

While this SRIA focuses mainly on genomics and its utility in a health systems context, there is need to address the multisectoral, and multilevel components to realize the potential of personalised prevention. This integrative approach will need to include also governance, and systems change of the physical-, food- and social- environments where citizens lead their lives. This will require also e.g. research and innovation agendas in political- and systems- science. But it also requires data and data integration. Many relevant sources of non-clinical information from different sectors (e.g.,

socioeconomic, environmental, and contextual) should inform personalized prevention, and omics research must incorporate them. The key challenges lie in making this information accessible and ensuring its compatibility with other data sources. Another priority should be the seamless integration of these diverse data types to enhance the effectiveness of personalized prevention strategies.

Also, prioritizing research into biomarkers that reflect modifiable factors is essential. Greater emphasis should be placed on improving methods for measuring relevant exposures, in studying gene-environment interactions and in understanding and incorporating omics that can help to understand the environmental origin of diseases, to develop personalised primary prevention. Context must also be incorporated as a key modulating factor. In addition, incorporating technologies like wearables and leveraging artificial intelligence will also be vital for interpreting and utilizing the data generated by omics studies.

Strengthening and combining existing large European population-based cohorts -which include genetic and clinical information, as well as rich epidemiological, contextual, and exposure data, and often have associated biobanks—may be an efficient way to conduct studies in this field. Supporting them and promoting the use of their data within the research community may be an effective way to achieve the necessary complexity and scale to produce robust results.

Furthermore, while -omic technologies have a focus on risk assessment and prediction of health outcomes, for prevention to be effective, both individuals and health-systems need to change behaviours to have an impact. How to use more precise and predictive information to effectively change behaviours is not yet known and this should be the focus of a behavioural science research and innovation agenda (see challenge 10).

Considerations

A central challenge in personalised prevention is how to integrate all of these diverse fields into a coherent strategy that improves health outcomes. In terms of omics sciences, they offer enormous potential, but they also face hurdles. Omics technologies generate vast amounts of complex data, raising issues of data management such as data safety, as well as interpretation, storage, and integration into clinical practice. The potential of and requirements to integrating such data with

contextual and environmental data, and the increasing amount of individual, user-generated data e.g. from wearables is one of the highlighted gaps.

More evidence is also needed to determine the accuracy and usefulness of omics data in power of predicting health outcomes in a way that can guide interventions. For example, non-genetic omics are highly sensitive to the type of analysed sample and how it has been handled (Huang, 2021). The findings from omics studies must further be proven to be valid, reliable and reproducible in real-world clinical settings, as stated in challenge 1.

These obstacles may thus hinder the ability of omics sciences to develop their full potential in personalised prevention, especially in terms of translating research into clinical practice. Among these omics, genomics is currently the most explored in personalised medicine. It has a well-established foundation in both research and clinical settings, with actionable insights already available in genetic risk assessments (Jukic, 2019; Dawed, 2023)[33] [34]Even though genomics is particularly valuable in advancing personalised prevention strategies, one must also consider broader socioeconomic and commercial determinants of health, such as inequalities in healthcare access, environmental conditions, in addition to the social determinants (e.g., housing, education, employment) to achieve the vision of reducing NCDs. Climate change also makes the broader determinants of health a moving target. This requires consideration of the additional utility omics offers towards realizing the potential prevention dividend.[35]

Challenge 2: Continuous evidence synthesis system supporting personalised prevention

Status

In the past decades, numerous genetic, genomic, and more general 'omics' technologies have been developed, significantly enhancing the accuracy of diagnosing health conditions and providing new

[33] Jukic MM, Smith RL, Haslemo T, Molden E, Ingelman-Sundberg M. Effect of CYP2D6 genotype on exposure and efficacy of risperidone and aripiprazole: a retrospective, cohort study. Lancet Psychiatry. 2019 May;6(5):418-426. doi: 10.1016/S2215-0366(19)30088-4. Epub 2019 Apr 15.
[34] Dawed AY, Mari A, Brown A, McDonald TJ, Li L, Wang S, Hong MG, Sharma S, Robertson NR, Mahajan A, Wang X, Walker M, Gough S, Hart LM', Zhou K, Forgie I, Ruetten H, Pavo I, Bhatnagar P, Jones AG, Pearson ERPharmacogenomics of GLP-1 receptor agonists: a genome-wide analysis of observational data and large randomised controlled trials. DIRECT consortium.Lancet Diabetes Endocrinol. 2023 Jan;11(1):33-41. doi: 10.1016/S2213-8587(22)00340-0.PMID: 36528349
[35] Marin M Jukic, Robert L Smith, Tore Haslemo, Espen Molden, Magnus Ingelman-Sundberg, Effect of CYP2D6 genotype on exposure and efficacy of risperidone and aripiprazole: a retrospective, cohort study. Lancet Psychiatry. 2019 May;6(5):418-426. doi: 10.1016/S2215-0366(19)30088-4. Epub 2019 Apr 15. PMID: 31000417, DOI: 10.1016/S2215-0366(19)30088-4

tools to predict disease onset and progression. Continuous evidence generation is crucial to support the implementation of personalised prevention approaches that adopt such technologies. Many studies have aimed to evaluate the ability of these tests to predict the presence or absence of specific genes, genetic variants or other biomarkers (analytical validity) and their accuracy in predicting future clinical outcomes (clinical validity). Although evidence on these dimensions, combined with safety data, may suffice to introduce a test to the market, demonstrating its clinical utility is essential for integration into personalised prevention strategies within national healthcare systems. As explained in par. 6.1, clinical utility, though not universally defined, generally refers to the test's usefulness (or value of the information) to provide actionable information that improve patient relevant health outcomes. While analytical and clinical validity provide foundational evidence for the potential of a test, clinical utility addresses the real-world effectiveness and impact of the test on individuals' outcomes (for instance, it is noteworthy to say that very commonly, the evidence on clinical validity of genetic tests are scanty across all the possible ancestries, that limit the transferability of evidence across populations). Demonstrating clinical utility involves proving the efficacy of the test in reducing the health burden of the condition for which it is used (clinical efficacy), as well as studying other dimensions crucial for its implementation. These include cost-effectiveness, acceptability of the test among clinicians and citizens/patients, organizational feasibility, and its impact on health inequalities. To date, although the evaluation of these dimensions is formally required within structured evaluation frameworks, like Health Technology Assessment (HTA) or other assessment models (par. 6.1), there is a **significant lack of primary evidence** on both the **clinical efficacy** of these tests **and all other dimensions.**

Gaps

The gold standard for studying the clinical efficacy of these tests is the development of randomised controlled trials (RCTs), which are considered the highest level of evidence in the evidence pyramid, ranking just below systematic reviews and meta-analyses of RCTs[36]. In these trials, the personalised preventive intervention (or strategy) incorporating the use of genetic or genomic tests is compared

[36] Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Harbour RT, Haugh MC, Henry D, Hill S, Jaeschke R, Leng G, Liberati A, Magrini N, Mason J, Middleton P, Mrukowicz J, O'Connell D, Oxman AD, Phillips B, Schünemann HJ, Edejer T, Varonen H, Vist GE, Williams JW Jr, Zaza S; GRADE Working Group. Grading quality of evidence and strength of recommendations. BMJ. 2004 Jun 19;328(7454):1490. doi: 10.1136/bmj.328.7454.1490. PMID: 15205295; PMCID: PMC428525.

with the standard of care to assess its efficacy in improving health outcomes. RCTs are highly valued for their ability to provide the most reliable evidence of clinical efficacy due to their rigorous methodological design, which includes randomization and controlled conditions to minimise bias. However, developing such study designs is challenging in the realm of genetic and genomic medicine due to the low prevalence of specific genetic conditions, the continuous development of promising technologies that might make a trial outdated before it is terminated, and the vast combinations of gene panels and interventions that need to be studied[37]. Moreover, limited sample sizes in trials and issues related to data sharing represent significant obstacles to achieving the statistical strength required to provide robust evidence on health outcomes. In primary and secondary prevention trials, these challenges are even more pronounced due to the substantial time lag between the implementation of the intervention and the observation of expected health outcomes, which complicates the measurement of long-term efficacy. Despite these challenges, generating solid evidence on the ability of preventive interventions that include genetic or genomics tests to reduce the health burden of these diseases remains crucial. Also, the studies on the impact of a test in terms of cost-effectiveness, patient acceptability, equity, and feasibility are likewise quite rare. One reason for this scarcity is that such evidence often necessitates prior proof of clinical efficacy, which is frequently absent or contentious. Without a solid foundation of clinical efficacy, it becomes challenging to justify and investigate these additional dimensions. Furthermore, the study of these impacts is sometimes context-specific, requiring research within the country where the test is intended to be implemented. Variations in healthcare systems, patient populations, and socio-economic conditions mean that findings from one context may not be directly applicable to another. Hence, there is a critical need for localised studies to ensure the technology's effectiveness and relevance in the target setting. Moreover, while these domains are formally included in HTA, clear criteria for their evaluation are often lacking, leading to their underestimation in formulating recommendations These research gaps—including the scarcity of sufficiently robust studies on clinical efficacy and the limited evaluation of broader impacts—are equally pronounced across other omics sciences, where the evidence base is even more constrained. Indeed, the mapping activities conducted within this project reveal a markedly lower volume of studies addressing clinical validity, clinical efficacy, and

[37] Rogowski WH, Grosse SD, Khoury MJ. Challenges of translating genetic tests into clinical and public health practice. Nat Rev Genet. 2009 Jul;10(7):489-95. doi: 10.1038/nrg2606. PMID: 19506575.

HTA reports in these fields compared to genetics and genomics, highlighting the need for further efforts to strengthen the evidence base in these areas.

Priorities and implementation

Strategies to study the clinical efficacy of personalised preventive approaches

Based on the considerations above on RCTs, it is essential for clinical and epidemiological expertise to assess the most suitable study design for each approach, considering both validity and feasibility. Different approaches are being developed to enhance evidence generation, particularly on genetic and genomic tests.

For example, while large-scale RCTs comparing test-based approaches with standard care are often challenging to implement, more focused RCTs can be designed to evaluate the efficacy of therapies or preventive interventions within specific risk categories identified by genetic tests. A classic example is the *BRCA1/2* test for women at risk for personalised breast and ovarian cancer prevention, recommended by major national and international guidelines. The high diagnostic accuracy of the test and the significant increase in incidence and mortality risk associated with the specific variants justified seeking the best possible evidence on the efficacy of various primary and secondary preventive interventions (such as prophylactic surgery or active surveillance) specifically in this high-risk population[38]. Other examples where RCTs have been implemented to study the efficacy of therapies on risk-stratified populations include the 21-Gene Expression Assay and the 70-Gene Signature for personalising breast cancer treatment. The multicenter MINDACT trial, initiated in 2007 across nine European countries, is an example of a non-inferiority RCT aimed at studying whether "high clinical risk, low genetic risk" patients have a non-inferior five-year survival without chemotherapy compared to with using it[39]. These targeted RCTs, while still requiring significant

[38] Pujol P, Barberis M, Beer P, Friedman E, Piulats JM, Capoluongo ED, Garcia Foncillas J, Ray-Coquard I, Penault-Llorca F, Foulkes WD, Turnbull C, Hanson H, Narod S, Arun BK, Aapro MS, Mandel JL, Normanno N, Lambrechts D, Vergote I, Anahory M, Baertschi B, Baudry K, Bignon YJ, Bollet M, Corsini C, Cussenot O, De la Motte Rouge T, Duboys de Labarre M, Duchamp F, Duriez C, Fizazi K, Galibert V, Gladieff L, Gligorov J, Hammel P, Imbert-Bouteille M, Jacot W, Kogut-Kubiak T, Lamy PJ, Nambot S, Neuzillet Y, Olschwang S, Rebillard X, Rey JM, Rideau C, Spano JP, Thomas F, Treilleux I, Vandromme M, Vendrell J, Vintraud M, Zarca D, Hughes KS, Alés Martínez JE. Clinical practice guidelines for BRCA1 and BRCA2 genetic testing. Eur J Cancer. 2021 Mar;146:30-47. doi: 10.1016/j.ejca.2020.12.023. Epub 2021 Feb 10. PMID: 33578357.

[39] Cardoso F, van't Veer LJ, Bogaerts J, Slaets L, Viale G, Delaloge S, Pierga JY, Brain E, Causeret S, DeLorenzi M, Glas AM, Golfinopoulos V, Goulioti T, Knox S, Matos E, Meulemans B, Neijenhuis PA, Nitz U, Passalacqua R, Ravdin P, Rubio IT, Saghatchian M, Smilde TJ, Sotiriou C, Stork L, Straehle C, Thomas G, Thompson AM, van der Hoeven JM, Vuylsteke P, Bernards R, Tryfonidis K, Rutgers E, Piccart M; MINDACT Investigators. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer. N Engl J Med. 2016 Aug 25;375(8):717-29. doi: 10.1056/NEJMoa1602253. PMID: 27557300.

sample sizes, long follow-up periods, and substantial costs, might represent a more practical approach than broad-based trials in the general population.

Specific considerations can also be made regarding the outcomes to be evaluated. While the final goal of any preventive intervention should be to reduce the incidence and/or mortality of a disease, intermediate endpoints can sometimes serve as effective measures for evaluating clinical efficacy. For example, the MyPeBS trial, designed to compare a personalised approach using a polygenic risk score (PRS) for breast cancer screening with the standard of care, focuses on an intermediate endpoint[40]. The trial's primary objective is to assess whether the personalised approach reduces the incidence of advanced breast cancer diagnoses. While intermediate endpoints, such as reductions in late-stage diagnoses, can be useful for evaluating preventive strategies, it is crucial to ensure that these endpoints reflect an impact on the ultimate outcome of interest, such as mortality, in the context of oncological screening programmes.

Some genetic and genomic tests have been developed to enhance the effectiveness of personalised prevention strategies that have already been studied. An example is the DNA stool test, which has been introduced as a more advanced alternative to the previously used faecal occult blood test for guiding individuals toward colonoscopy for early colorectal cancer detection[41]. However, while robust evidence of increased diagnostic accuracy in these trials has supported the recommendation of the DNA stool test, it is essential to conduct thorough assessments to ensure that the test's effectiveness applies to real-world clinical practice. This includes evaluating whether the test performs as expected in the target population and under routine clinical conditions.

Other strategies include the use of other methodological approaches, such as simulation models. For example, in 2021, a breast cancer simulation model developed by the Erasmus University Medical Center and the Georgetown University's Albert Einstein College of Medicine were used to evaluate

[40] S. Delaloge, P. Giorgi Rossi, C. Balleyguier, M. Guindy, F.J. Gilbert, J-B. Burrion, M. Roman, S. de Montgolfier, L. Giordano, D. Drubay, D.G. Evans, D. Keatley, E. Gauthier, A. du Bois d'Aische, C. Baron, A. Boland, H. Blanché, D. Couch, J-F. Deleuze, S. Michiels, 135P Real-time genotyping-based breast cancer risk assessment in MyPeBS, an international randomized trial in the general population comparing risk-stratified to standard breast cancer screening (BCS), Annals of Oncology, Volume 33, Supplement 3, 2022, Page S184, ISSN 0923-7534, https://doi.org/10.1016/j.annonc.2022.03.152.

[41] Imperiale TF, Porter K, Zella J, Gagrat ZD, Olson MC, Statz S, Garces J, Lavin PT, Aguilar H, Brinberg D, Berkelhammer C, Kisiel JB, Limburg PJ; BLUE-C Study Investigators. Next-Generation Multitarget Stool DNA Test for Colorectal Cancer Screening. N Engl J Med. 2024 Mar 14;390(11):984-993. doi: 10.1056/NEJMoa2310336. PMID: 38477986.

the lifetime effects of different risk-tailored screening strategies[42]. A similar approach was already employed by the established Cancer Intervention and Surveillance Modeling Network to develop models that were used to inform the current USPSTF breast cancer screening guidelines[43]. These approaches generally allow direct comparisons between preventive strategies and can benefit from the use of data from biobanks or other real-world data sources. Employing these methodological approaches can enable the study of the impact of introducing genetic and genomic tests into prevention strategies. However, the evaluation of their validity and their use in generating recommendations remains a highly debated topic. The validity of the generated estimates is contingent upon the quality of the data utilized and the robustness of the models developed. First, it is necessary to ensure transparency and reproducibility of the models; then, clear methods for assessing the model estimates are necessary. These methods should set standards for evaluating the credibility of the models, which are prone to bias since bias can arise from the input data and during the model calibration and validation phases[44].

Generating primary evidence on all the dimensions of clinical utility

To reduce the gap in evidence regarding the impact of the tests on various dimensions like cost-effectiveness, patient acceptability, equity, ethical aspects and feasibility, it is essential to invest in responsible research and innovation in this field. Funding programmes should allocate resources not only to clinical efficacy studies but also to investigations focusing on these broader impacts.[45] Certain dimensions of technology impact can be evaluated within the context of clinical trials designed to assess clinical efficacy. For example, incorporating patient-reported outcomes (PROs) into these trials can provide valuable insights into patient acceptability and quality of life. Similarly, assessing

[42] Van den Broek JJ, Schechter CB, van Ravesteyn NT, Janssens ACJW, Wolfson MC, Trentham-Dietz A, Simard J, Easton DF, Mandelblatt JS, Kraft P, de Koning HJ. Personalizing Breast Cancer Screening Based on Polygenic Risk and Family History. J Natl Cancer Inst. 2021 Apr 6;113(4):434-442. doi: 10.1093/jnci/djaa127. PMID: 32853342; PMCID: PMC8599807.

[43] Henderson JT, Webber EM, Weyrich MS, Miller M, Melnikow J. Screening for Breast Cancer: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2024;331(22):1931–1946. doi:10.1001/jama.2023.25844

[44] Brozek JL, Canelo-Aybar C, Akl EA, Bowen JM,…and Schünemann HJ; GRADE Working GRADE Guidelines 30: the GRADE approach to assessing the certainty of modeled evidence-An overview in the context of health decision-making. J Clin Epidemiol. 2021 Jan;129:138-150. doi: 10.1016/j.jclinepi.2020.09.018. Epub 2020 Sep 24. PMID: 32980429; PMCID: PMC8514123.

[45] Marschalek, I., Handler, K., Hofer, M., Schrammel, M., Unterfrauner, E. (2020). Responsible Research and Innovation (RRI): A Critical Reflection Toward Evaluation Standards. In: Carayannis, E.G. (eds) Encyclopedia of Creativity, Invention, Innovation and Entrepreneurship. Springer, Cham. https://doi.org/10.1007/978-3-319-15347-6_200035

the experiences and feedback of clinicians during these studies can shed light on feasibility and practical implementation challenges.

Synthesise and evaluate evidence quality

In order to implement effective personalised prevention approaches, a priority should be to ensure that the evidence produced is synthesised and that clear criteria for evaluating the quality and robustness of evidence are applied. These criteria must evaluate the quality of evidence, including its validity, study design, and potential implementation levels. Based on the level of evidence, the output of the synthesis should be categorised according to different levels of strength. Moreover, the scientific merit of testing technologies in personalised prevention depends on incorporating standardised methods for quality control, clinical validity, and overall utility. Ensuring that all testing technologies adhere to high standards is essential for producing reliable and actionable evidence.

To standardise and share it is necessary to invest in a system specifically designed to systematically synthesise evidence, ensuring that each piece of evidence is categorised based on its quality. This could be a dynamic, unified repository modelled on successful frameworks such as the U.S. CDC's Center for Precision Public Health, which utilises a tiered classification system for genomic medicine guidelines[46]. The system should allow for continuous updates as new evidence emerges, facilitating easy access to and retrieval of information.

Such a repository would serve as a valuable resource for healthcare professionals, policymakers, and researchers by providing a clear and structured overview of the evidence. This would support more informed decision-making and ultimately enhance the effectiveness and efficiency of preventive healthcare interventions.

Health Systems Integration

Health systems face numerous challenges when attempting to integrate and deliver personalised prevention approaches that are adapted to diverse local contexts. One of the primary obstacles is the creation of assessment tools that are tailored to the specific needs and structures of each healthcare system. The complexity of designing evaluation frameworks that account for local epidemiology,

[46] Center for Disease Control and Prevention, Work in Progress: Classifying Evidence-based Genomic Applications for Practice and Prevention, Available at https://blogs.cdc.gov/genomics/2018/02/28/work_in_progress/, Accessed on 25/07/24

resources, and healthcare infrastructure means that a one-size-fits-all solution is rarely feasible. Moreover, the challenge of data sharing is significant, as the effectiveness of personalised prevention relies on access to large, diverse datasets to enhance the accuracy of evaluations and evidence generation. Ensuring interoperability between different health systems, while safeguarding patient privacy and data security, is a critical hurdle. This lack of unified data can slow the development of robust methodologies for assessing new omic technologies, ultimately hindering their adoption. Therefore, fostering collaboration across regions and countries, and developing standardised yet flexible frameworks, is essential for realising the potential of personalised prevention in different healthcare settings.

Considerations

As we advance the integration of genetic and genomic tests into personalised prevention strategies, several critical considerations must be addressed to ensure their success and sustainability. It is essential to recognise the rapid pace of technological advancements in genetics and genomics, necessitating continuous evidence synthesis efforts and regular updates to evaluation frameworks and assessment guidelines. This dynamic landscape requires a flexible approach to research and policy-making, ensuring that emerging evidence is swiftly incorporated into practice.

Investing in primary research by funding studies that are both feasible and effective in evaluating clinical efficacy is necessary. These studies should be designed considering the progressive steps needed for implementation from bench to public health practice. While expert matter knowledge is necessary to ensure the accurate and comprehensive assessment of the intended outcomes, such implementation considerations are crucial to ensure that the studies are appropriately tailored to respond to the correct questions along the translational spectrum. Furthermore, additional primary studies are needed in the other omics sciences, which, while promising, still lack sufficient evidence, limiting their broader implementation and integration into clinical practice.

At the same time, it is important to establish clear parameters for evaluating this evidence. Creating standardised evaluation criteria will help ensure that the results of these studies are consistently and transparently assessed, facilitating their integration into healthcare decision-making processes.This

combined approach of robust primary research and clear evaluative frameworks will support the effective implementation of personalised prevention strategies.

Challenge 3: The PROPHET Framework implementation

Status

Since the early 2000s, various frameworks have been developed to evaluate the clinical utility of genetic and genomic tests. Despite many efforts, there is still no widely accepted criteria for evaluating preventive approaches that use genetic and genomic technologies. This lack of standardised criteria has caused inconsistencies in how different countries and regions evaluate and implement these technologies. Moreover, the varied methodologies and evaluation criteria in different frameworks have led to a fragmented understanding of clinical utility, making it harder to make informed decisions about adopting genomic technologies in healthcare systems, especially in resource-limited settings.

In 2021, the European Union made significant progress by approving a new HTA regulation[47]. The regulation aims to encourage streamlining of the assessment process, allowing member states to evaluate jointly the clinical data and evidence submitted for a health technology. This aims to address the lack of consistent methodology and processes across EU Member States, which leads to considerable variation in the evaluation of vaccines, drugs, and medical devices. The new regulation, set to be fully implemented by January 2025, marks a crucial step towards more unified and consistent assessments of health technologies across Europe.

Gaps

Despite the progress made with the new HTA regulation, significant gaps remain in the evaluation of genetic and genomic tests. One major challenge is the lack of primary evidence that informs any assessment, which makes it difficult to obtain informed decisions about adopting and implementing these technologies. This issue is compounded by the absence of consensus on the dimensions and

[47] Regulation (EU) 2021/2282 of the European Parliament and of the Council of 15 December 2021 on health technology assessment and amending Directive 2011/24/EU (Text with EEA relevance), available at https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32021R2282, accessed on 25/07/24.

indicators that should be used for recommendations. Without agreed-upon criteria, standardising evaluations and ensuring all relevant aspects is tough[48].

Moreover, the HTA has traditionally focused on evaluating the clinical efficacy and cost-effectiveness of tests, often overlooking or undervaluing other potential impacts that implementing a genetic or genomic technology can have[49]. Although clinical efficacy is a conditio sine qua non for assessing any test, the effective implementation of personalised preventive approaches also requires recognising that the decreasing costs of omics-based tests and data integration platforms call for a more dynamic consideration of economic evidence. Overemphasizing cost-effectiveness, without accounting for evolving cost trends, risks creating unnecessary barriers to the adoption of personalised preventive approaches. In this regard, modelling approaches should consider incorporating declining cost functions or, where appropriate, applying a specific discount rate to reflect the expected reduction in technological costs over time.

Effective implementation therefore requires a comprehensive evaluation framework that, alongside cost-effectiveness, also integrates factors such as feasibility, allocative value, patient acceptability, the personal value of the test information, legitimacy, and equity. These dimensions are often context-specific and can vary significantly across different countries and populations.

Priorities and implementation

The PROPHET framework aims to address the aforementioned gaps by providing a holistic approach when evaluating and implementing personalised preventive approaches. This framework includes all relevant aspects - professionals, tools, technology, resources, clinical and community pathways - to ensure a thorough and comprehensive appraisal of these approaches thanks to a full stakeholder engagement process. The goal is to guide public health authorities in adopting personalised preventive approaches using both health system and value-based perspectives.

[48] Hoxhaj I, Govaerts L, Simoens S, Van Dyck W, Huys I, Gutiérrez-Ibarluzea I, et al. A Systematic Review of the Value Assessment Frameworks Used within Health Technology Assessment of Omics Technologies and Their Actual Adoption from HTA Agencies. Int J Environ Res Public Health. 2020;17(21). Mario cosa è successo non ha il suo numeretto

[49] Love-Koh J, Peel A, Rejon-Parrilla JC, Ennis K, Lovett R, Manca A, et al. The Future of Precision Medicine: Potential Impacts for Health Technology Assessment. Pharmacoeconomics. 2018;36(12):1439-51.

The PROPHET framework builds on the HTA model promoted by the new European regulation, which mandates a joint assessment of the efficacy and safety of the technology at the European level and an evaluation of context-specific dimensions, such as economic aspects, feasibility, and acceptability at the national level (for further details please refer to Appendix 1, Section9.2). To comprehensively evaluate a personalised prevention approach, it is essential to ensure not only that the impact of the test on these dimensions is assessed, but also that these evaluations are conducted in collaboration with all stakeholder groups and are structurally considered when providing recommendations on implementation. The experience of using Health Impact Assessment (HIA) for non-health related policies provides valuable insights for a more holistic and context-specific evaluation of personalised prevention approaches[50,51]. In the context of genetic and genomic tests, these policies relate to determining the reimbursability of such tests and establishing the pathways for these decisions within the health system. Additionally they may include requirements for mandatory testing prior to specific medical interventions for making a test mandatory before certain medical interventions can be undertaken, similar to the model used for abacavir (drug used for the treatment of AIDS, based on a genetic testing before treatment). This approach will therefore improve equity in access to genetic and genomic tests. The HIA model emphasises the importance of structured and meaningful engagement of stakeholders throughout the evaluation process. This includes healthcare professionals, patients, policymakers, and community representatives, whose perspectives and concerns are vital for a thorough assessment. By involving these stakeholders, the evaluation process can capture a wide range of impacts and ensure that the outcomes are relevant and acceptable to all parties involved.

Furthermore, the HIA model requires a comprehensive consideration of impacts, including factors that are often overlooked, such as health inequalities. This approach allows for a broader assessment that goes beyond the immediate clinical and economic impacts of the test to include its effects on different population groups and social determinants of health. For instance, understanding how a new

[50] Harris-Roxas, B., Viliani, F., Bond, A., Cave, B., Divall, M., Furu, P., … Winkler, M. (2012). Health impact assessment: the state of the art. Impact Assessment and Project Appraisal, 30(1), 43–52. https://doi.org/10.1080/14615517.2012.666035

[51] Ádám B, Lovas S, Ádány R. Use of Genomic Information in Health Impact Assessment is Yet to Come: A Systematic Review. Int J Environ Res Public Health. 2020 Dec 15;17(24):9417. doi: 10.3390/ijerph17249417. PMID: 33334033; PMCID: PMC7765467.

genetic test might be perceived by different communities, its accessibility, and how it might exacerbate or mitigate health disparities is crucial for its successful implementation.

Additionally, HIA provides robust methodologies for developing programs that ensure the effective implementation and continuous monitoring of policies. This includes setting up systems for regular review and feedback, allowing for ongoing improvements based on new evidence and changing circumstances. The continuous monitoring aspect is particularly important as it helps identify any unintended consequences early on and provides opportunities to address them promptly.

In conclusion, the PROPHET Framework enhances the structured HTA evaluation implemented by the new European regulation with elements of HIA and a more structured monitoring plan. Implementing such comprehensive evaluations is undoubtedly complex and requires significant coordination and resources. Despite these challenges, our project has demonstrated that conducting these comprehensive evaluations is feasible within constrained budgets through three case studies in different countries and examining different tests and related policies.[52] This approach ensures a more holistic and continuous evaluation of personalised prevention approaches.

Considerations

The development and implementation of the PROPHET framework should consider several critical factors:

- For new in vitro devices or diagnostic tests, it would be beneficial to establish a voluntary early engagement mechanism involving HTA bodies, public health authorities, and developers. This mechanism would allow for early dialogue to jointly define evidence requirements, exchange expertise, and coordinate study designs, fostering alignment and efficiency in generating evidence to support both national and regional decision-making.

- Regulatory Alignment: It is essential to align the evaluations with the new HTA regulation, focusing on centralised clinical data assessment while addressing national

52 Valz Gris, A., Kannan, P., Costa, A., de Fátima Silva Lopes, M., Cardoso, M. L., Pezzullo, A., ... & Boccia, S. (2024). Health Impact Assessment in Personalized Prevention: three applications on pharmacogenomic testing. European Journal of Public Health, 34(Supplement_3), ckae144-1576.

context-specific impacts. This alignment ensures consistency and reliability in the evaluation process, and emphasises the importance of always using standardised and transparent methodologies to guarantee comparability and scientific robustness across assessments. Even when the evaluation does not fall directly under the HTA framework, for example, when it concerns broader public health programs or interventions rather than specific technologies, it remains important to ensure methodological consistency and to apply standardized approaches to maintain quality, transparency, and reliability of the assessment process.

- Stakeholder Engagement: Effective involvement of stakeholders in the evaluation process is crucial to ensure that all relevant impacts, particularly those related to inequalities, are considered. Stakeholders should be engaged in a structured manner to provide valuable insights and enhance the legitimacy of the evaluation process.
- Comprehensive Evaluation: The evaluation should use methodologies that incorporate both health system and value-based perspectives. This approach ensures a thorough assessment of personalised preventive approaches, considering all relevant dimensions and impacts.
- Policy Monitoring and Adaptation: Establishing programs for continuous monitoring and adaptation of policies is critical to ensure their effectiveness and relevance over time. These programs should include mechanisms for regular review and adjustment based on new evidence and changing contexts.

By addressing these considerations, the PROPHET framework can provide a robust and holistic approach to evaluating and implementing personalised preventive approaches.

Challenge 4: Data collection and integration, and Data Infrastructure

Status

A substantial increase in the creation of life sciences data has enhanced our understanding of disease risk, paving the way for preventative healthcare. To harness the potential of this data for personalised preventative medicine, integrating life science data is essential, drawing from previous European experiences, and co-creating with other sectors. Lessons from the COVID-19 pandemic demonstrate

the value of using unified frameworks and data-sharing structures. [53]. Research Infrastructures like ELIXIR, BBMRI, EATRIS, ECRIN, and EuroBioimaging have made progress, yet further efforts and investment are needed with a focus on three core areas: data quality and collection, data integration, and data infrastructure.

Healthcare-generated data, often clinical or ad-hoc, is typically not reusable. To overcome fragmented data collection it is crucial to identify and implement best practices using proven models as examples. Initiatives like Genomics England and disease registries (ERN-RND, The Danish Cancer Registry) aim to make clinical and genomic data accessible for research. Efforts in research and clinical-research settings have improved data management for access and reuse. Biobanks (e.g. The Estonian Biobank[54] and FinnGen[55]both part of the BBMRI-ERIC network) and repositories (e.g. the European Genome Phenome Archive (EGA) [56]) help support studies like Genome-Wide Association Studies (GWAS) investigating genetic disease components, aiding in polygenic risk score modelling for preventative approaches. However, it is not easy to extract actionable information immediately from omics data, as the complexity and variability of genomic data require significant curation, interpretation, and integration with other data types to yield meaningful insights.

The 1+MG initiative and the Genome of Europe project aim to unify national cohorts of genomic sequencing data, creating a key tool for understanding genetic disease drivers. However, fragmented, inaccessible, and inconsistent-quality data, especially from diverse sources such as socioeconomic, behavioral, and lifestyle data, present challenges for creating fully integrated, personalised preventive interventions[57]. Organisations such as GA4GH are working to cultivate a common framework of standards and harmonised approaches for effective and responsible sharing of genomic and related health data[58].

While substantial progress has been made, infrastructure and federated analysis tools at national and European levels remain insufficient for complex data integration—particularly with non-health data

[53] Collins FS, Varmus H. A new initiative on precision medicine. N Engl J Med. 2015 Feb 26;372(9):793-5. doi: 10.1056/NEJMp1500523. Epub 2015 Jan 30. PMID: 25635347; PMCID: PMC5101938.

[54] The Estonian Biobank: From Cohorts to Personalised Medicine" (Journal of Translational Medicine, 2019). Available at: https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-019-1977-4

[55] FinnGen: A Comprehensive Database for Genomic and Health Data from Finland" (European Journal of Human Genetics, 2020). Available at: https://www.nature.com/articles/s41431-020-00782-5

[56] https://ega-archive.org/

[57] Lovestone, S. (2020). The European Medical Information Framework: A novel ecosystem for sharing healthcare data across Europe. Learning Health Systems, 4(2). https://doi.org/10.1002/lrh2.10214

[58] GA4GH: International policies and standards for data sharing across genomic research and healthcare" (Nature Reviews Genetics, 2020). Available at: https://www.nature.com/articles/s41576-019-0170-0

like behavioral and lifestyle variables, increasingly captured by personal devices, wearables, and lifestyle apps. These data types require distinct privacy, consent, and quality considerations, and their integration with health and genomic data demands robust data harmonisation and governance frameworks. Standardised platforms inspired by successful commercial models are urgently needed to help healthcare providers and researchers navigate and share data responsibly while respecting patient consent. Frameworks like OMOP and HL7 FHIR are promising but require broader implementation, particularly as international and EU regulations evolve. With the exception of the BBMRI-ERIC Federated Platform, currently, national and European infrastructure and federated analysis tools are not advanced to deal with complex data integration and data coming from different sectors and sustained data infrastructure is limited. The European Health Data Space (EHDS), Genomic Data Infrastructure (GDI), and EUCAIM aim to integrate data and develop infrastructure that fits the necessary technical and ELSI requirements. Within GDI[59]15 countries have committed to establish a national node to manage human genomic data by 2026.

Gaps

Within the realm of healthcare data management, several significant gaps continue to pose challenges. One of the primary issues is the lack of standardization. The absence of widely accepted standards creates a fragmented ecosystem, which complicates the integration of data across different systems. It is necessary to consider how data from a wide range of biomarkers, including genomics, can be integrated and used to drive the development of personalised prevention interventions, and this fragmentation makes it difficult for researchers and healthcare providers to effectively work together and share information. The adoption of "minimal data sets" that distinguish "must-have" data from "nice-to-have" data is essential for guiding collection practices for both research and healthcare. To fully support prevention, consistent and longitudinal data collection needs to be supported, particularly from individuals when they are healthy, otherwise datasets will only address ongoing health challenges, rather than being useful to support prevention by flagging changes that may be indicative of the early development of disease. To address this issue, emerging standards like OMOP and HL7 FHIR hold great promise, yet they require broader implementation to truly make an impact, especially as new standards arise to accommodate multi-sectoral data integration. Another major

[59] European Genomic Data Infrastructure (GDI) project (onemilliongenomes.eu)

hurdle is the challenge of data discoverability. The HDR-UK health data gateway is an example of an initiative to tackle many of these challenges[60]. Researchers often struggle to find relevant datasets due to the fragmentation of resources, poor data quality, and inconsistent data management practices. While the establishment of unified health and genomic records could significantly enhance discoverability, there are still many barriers to their effective implementation. Furthermore, the situation is made more complex when we consider the integration of data from sectors beyond healthcare, including socioeconomic and environmental data, which only adds to the challenge due to variations in data structure, privacy concerns, and the contextual nature of these variables.

Accessing health and genomic data is critical for the advancement of personalised prevention and medicine. However, several obstacles continue to limit this access. Regulatory requirements can be daunting and create unnecessary hurdles, while the general lack of digital health literacy complicates the necessary administrative processes surrounding consent procedures and data-sharing policies. Additionally, the availability of high-quality data is often scarce, which underscores the need for clearer guidelines and practices that could facilitate better access.

Data reproducibility presents yet another challenge in this landscape. Gaps in quality assurance and the absence of comprehensive metadata can significantly impede research reproducibility, which in turn limits the applicability of research findings within clinical settings.

Moreover, effective data use mandates robust infrastructure and stringent security measures. For data to be integrated successfully into clinical environments, it must align with existing regulatory requirements, which is essential for safeguarding patient information.

Finally, translating research into clinical practice is not without its challenges. This process necessitates specialised training, fostering collaboration across various sectors, and ensuring alignment with regulatory processes. Additionally, it also requires the necessary tools and training for healthcare professionals to use whilst providing patient care. Addressing these multifaceted issues is crucial for unlocking the full potential of health and genomic data, ultimately enhancing patient care and outcomes.

Priorities and Implementation

- Standardisation: Implement standardised practices at both international and national level as

[60] https://healthdatagateway.org/en

recommended in the 1+MG Framework and supported by global and EU standards by GA4GH and ISO, for data structure and standardisation in health systems to overcome challenges arising from the use of unstructured formats and competing standards.

- Discoverability: Develop unified health and genomic records, as best practices, to enhance data discoverability at local, regional, national, and eventually international level. Efforts should focus on creating tools and platforms that facilitate easy and effective search and validation of appropriate datasets.
- Accessibility: Address variations in data accessibility across nations by establishing clearer and consistent regulations and consent mechanisms.
- Reproducibility: Ensure the availability of high-quality datasets with comprehensive metadata. Attention should be given to addressing metadata gaps for different types of health data to support research, regulatory purposes, and personalised prevention methods[61].
- Data Sharing: Establish secure approaches to data sharing, addressing reidentification and privacy concerns, ensuring patient and data safety at all times. Encourage organisations to adopt best practices for data sharing and enhanced digital health literacy to improve collaborative efforts.
- Data integration: Ensuring that data integration adheres to FAIR (Findable, Accessible, Interoperable, Reusable) principles is crucial. This involves creating secure, standardised, and interoperable services under a common framework that respects jurisdictional boundaries for datasets while centralising and making metadata discoverable through common APIs. Multisectoral data integration: integrating socioeconomic and contextual data on e.g. environments need development.

Considerations

To realise preventive medicine, there is a need to systematically connect and access population, clinical, genomic, and lifestyle data to perform research at a larger scale. Due to the heterogeneity of clinical data, sustained curation and accessible research data are critical. The use of standards like Beacon V2 (being expanded to support DICOM queries) will facilitate the generation of virtual

[61] Kho, A. N., Rasmussen, L. V., Connolly, J. J., Peissig, P. L., Starren, J., Hakonarson, H., ... & Roden, D. M. (2019). Practical challenges in integrating genomic data into the electronic health record. Genetics in Medicine, 21(9), 1918-1927.

cohorts for linking data across different modalities. The utilisation of interoperable metadata models, data standards and semantic annotation will facilitate data analysis and training of AI models across different modalities of data and data sources.

To implement the infrastructure and data management required, capacity needs to be increased for the five functionalities of data management: data discovery, data reception, storage and interfaces, data access management, and processing. Additionally, infrastructure in the healthcare setting needs to be interoperable with the research domain, paying particular attention to cybersecurity and privacy. Capacity development in data discovery, reception, storage, access, and processing is necessary, particularly as AI/ML-driven prevention models become more prevalent. To support actionable insights, investment in clinician-friendly tools is vital so that providers can interpret validated models for personalised prevention.

Interdisciplinary cooperation is needed to set shared data standards, reduce bureaucratic obstacles, and enhance healthcare efficiency.

Challenge 5: Community Engagement and trust

Status

Personalised medicine and prevention, in which genomic information plays an important role, envisions and requires active and informed patients and citizens who take an active role in managing their own health and care. They need to be well-informed to be empowered to make decisions regarding their health and prevention that reflect their personal values, and be aware of options for contributing to research, such as via data sharing [62]. However, what such engagement and empowerment entails may differ per domain relevant for personalised prevention: research, care or governance. To this end, we are aware that at the population level, 40% of health outcomes depend on socioeconomic status, with education playing a major role. This is why increasing health literacy in general, and in (personal) prevention is an asset. In research, patients with personal experience of a disease offer a unique perspective that, if explicitly incorporated, leads to science that is more relevant and translatable. Roles may range from "passive" study participants to "active" patients and the public being involved in all phases of research. In the care domain, individuals should feel empowered to make optimal decisions regarding their health and prevention that align with their

[62] www.EPPERMED.eu

personal values and preferences, leading to more culturally sensitive and patient-centred care. The governance domain emphasises the involvement of the public and patients in decision-making processes regarding personalised prevention policies and programs, encompassing their participation in policy development, guideline formulation, and organisational governance structures.

For citizens and patients to become active partners in prevention, they must be systematically and meaningfully engaged in the planning, delivery and evaluation of these three domains.[63,64] In recent years a range of instruments has been developed for engaging and empowering citizens and patients in various ways and to various degrees, ranging from one-directional methods, such as interviews to more collaborative participation in patient forums. Currently the former instruments are more frequently reported than the latter. The effectiveness and outcomes of engagement are often not measured.

Gaps

- Studies and reviews consistently report a lack of knowledge among citizens and patients regarding genetic information, while new concepts such as personalised medicine are not well-known. Lack of awareness and potential benefits may hinder acceptance and implementation of personalised prevention.
- Health care providers can help patients navigate genomic and personalised information, but often are also not sufficiently educated on these topics, and lack time for such additional tasks.
- Though elements of good engagement practices are more widely recognised (e.g. meaningful engagement needs iterative or continuous involvement, support and remuneration for patient input), evaluation towards specific goals for engagement is often lacking or patchy.
- Meaningful engagement requires dedicated funding and resources.
- Multisectoral governance poses a gap in community engagement as it requires effective coordination and communication between diverse sectors, such as healthcare, education, and

[63] Menear M, Girard A, Dugas M, Gervais M, Gilbert M, Gagnon MP. Personalised care planning and shared decision making in collaborative care programs for depression and anxiety disorders: A systematic review. PLoS One. 2022 Jun 10;17(6):e0268649. doi: 10.1371/journal.pone.0268649. PMID: 35687610; PMCID: PMC9187074.
[64] Schuster AL, Hampel H, Paskett ED, Bridges JF. Rethinking patient engagement in cancer research. The Patient-Patient-Centered Outcomes Research. 2023;16(2):89-93.

policy-making, which often have different priorities and operating structures. This fragmentation can lead to inconsistent messaging, delayed decision-making, and challenges in aligning goals, ultimately hindering meaningful and cohesive community involvement. Bridging this gap requires creating unified strategies that foster collaboration across sectors while ensuring that community voices are adequately represented.

Priorities and implementation:

- Co-create with Citizens and Patients: engage citizens and patients through their organizations (NGOs and Patient Advocacy Groups) in co-designing personalised prevention policies, decision-making processes, and communication activities. This engagement is essential for addressing public concerns, fostering trust, and ensuring that prevention strategies are aligned with the needs of the individuals and communities.
- Enhancing Community Engagement: Prioritise and improve community engagement, as defined by the WHO: "a process of developing relationships that enable stakeholders to work together to address health-related issues and promote well-being to achieve positive health impact and outcomes." This approach is fundamental to the successful implementation of personalised prevention strategies. [65] Need to support the active participation of community in awareness campaigns, prevention programs, and research initiatives.
- Generate more structural funding for citizen and patient engagement in research, care and public health, and their governance. Education and raising awareness of options for personalised prevention and taking part in health research.
- Amplify lived-experience stories (with consent) from patients/citizens via community ambassadors and multimedia campaigns to build trust and illustrate prevention benefits, ensuring diversity and avoiding overpromising.
- Develop and study online information and communication tools to disseminate knowledge on genetic testing and preventive options for citizens, patients, and their family members.

Considerations

[65] WHO community engagement framework for quality, people-centred and resilient health services", https://apps.who.int/iris/bitstream/handle/10665/259280/WHO-HIS-SDS-2017.15-eng.pdf

- Currently more engagement practices focus on care and research by patients, rather than citizens. Citizens may be more difficult to reach and may need other information tools. Awareness of prevention may also be more prominent in school curricula.
- Accessibility of information might be an issue: online tools for information and communication may be difficult to access and understand for persons with low digital literacy and health literacy, potentially exacerbating health inequalities. More specific attention to inform and engage such persons may be needed, e.g. by using more images for clarity and trustworthiness, as well as other individuals and communities that are marginalised or vulnerable and may have less access to or more distrust towards (health) institutions.
- Personal contact with and information by health professionals may increase trust in personalised prevention and data sharing, and such contact with e.g. primary care physicians and pharmacists would be also easily accessible for citizens.
- Robust structures for responsible health data sharing data may boost trustworthiness (see also Challenges 3 on Infrastructure and 9 on ELSI)
- As research and care become more interconnected, good communication to patients and citizens is necessary to help them understand what they can and cannot expect from their contribution in regard to their own health and prevention.

Challenge 6: Health Professionals and Policy Makers involvement

Status

At an institutional, national and international level, both health professionals and policymakers are essential in enabling the implementation of personalised preventive approaches in healthcare systems. Collaboration among stakeholders is critical to address regulatory, resource, and technological challenges. Policymakers should be encouraged to use stakeholder input and evidence-based research to guide their decisions. Ultimately, policymakers have the potential to create and support robust infrastructures and responsible practices that drive meaningful change towards a future healthcare system in which the overall strategy focuses not only on treatment but also on prevention. Through

engagement and collaboration, barriers to implementation can be overcome, resulting in a healthcare system that is more personalised, preventive, patient-centred and supported by the public.

Capacity building, education and information are important elements of engagement: well-informed policymakers and health professionals are better equipped to draft and discuss policies regarding personalised prevention with other relevant stakeholders and sustain further responsible implementation across disciplines, domains and national borders.

A variety of policymakers should be distinguished because they have different roles and responsibilities regarding aspects of personalised prevention, as they influence research agendas, funding priorities, guideline development, education, and the implementation of clinical innovations. Their educational needs may differ accordingly. For instance, professional organisations of medical specialists decide on guidelines for implementation of specific tests, public health (screening) organisations may decide on e.g. stratification of screening programmes based on biomarkers, governmental HTA organisations may decide on the thresholds for added value used in the assessment, reimbursement experts may decide on economic aspects. Key components of this engagement include capacity building, education, and access to accurate information. This process also necessitates addressing diverse and sometimes conflicting professional interests. Engaging stakeholders within and outside the HIA exercises, and fostering dialogue are vital for sound policymaking, enhancing public trust in data sharing, and supporting the ethical implementation of personalised prevention.

Increasingly, education on genomics (as a tool in personalised prevention) focusses not only on genetic experts, including clinical geneticists, genetic nurses [66] and genetic counselors, but also on non-genetic health care professionals. In primary and secondary care well-trained health professionals, such as general practitioners, nurses, pharmacists or pediatricians will be able to inform citizens and patients on personalized prevention options. The number of education initiatives targeting policy makers in public health programmes is limited. As a good example, USA cancer

66 Association of Genetic Nurses and Counsellors (AGNC). Professional Development Framework for Genetic Nurses and Counsellors in the United Kingdom and Ireland. AGNC, 2018.

programmes (integrating a.o. *BRCA* testing) illustrate how state cancer genetics programs have partnered with cancer registries, clinical facilities, health-care providers, health systems, public and private payers, policymakers, other state, regional, and federal programs, academic institutions, community organisations, advocacy groups, and industry.[67] Empowered, well-trained clinicians become "clinical champions" who advocate for and normalize personalised prevention in their organisations.[68]

Gaps

- Knowledge on economic models that assess cost-effectiveness of personalised prevention is lacking. Resources for and education on HTA are thus needed.
- In assessing the evolving landscape of educational initiatives for non-genetic health professionals relevant for personalised prevention in healthcare, several gaps have surfaced:
    - ✓ Appropriate training is required to increase genetic literacy among healthcare professionals to allow for effective information provision and counselling of patients, patient support, referral and efficient stratification in public health screening.
    - ✓ There is a need for training in new categories such as somatic genomics related to the tumour.
    - ✓ Introduction of new methods of assessment of competences such as Entrustable Professional Activities (EPAs) will allow for a focus on applying knowledge and know-how in addition to know-what.
    - ✓ Incorporation of public and patient involvement in education for health professionals.

[67] Green 2019

[68] Monahan KJ, Ryan N, Monje-Garcia L, Armstrong R, Church DN, Cook J, Elghobashy A, Lalloo F, Lane S, McDermott FD, Miles T, Hardy SA, Tyson A, Wang VYW, Kim A, Gelinas S, Faravelli F, Elmslie F, Shaw AC. The English National Lynch Syndrome transformation project: an NHS Genomic Medicine Service Alliance (GMSA) programme. BMJ Oncol. 2023 Oct 30;2(1):e000124. doi: 10.1136/bmjonc-2023-000124. PMID: 39886501; PMCID: PMC11315360.

Priorities and implementation

It is important to train healthcare professionals in personalised medicine, but also in epidemiology and statistics so that they can understand the concept of risk and determinants of health in a broader context, also including environmental and climate challenges, and properly communicate health risks to citizens and patients. The new generation of health care professionals, but also those in the workforce aged 50 and more, need to understand the concept of personalised prevention, be aware of the available approaches, and be aware of the relevance of data collection and use in health. Health systems might want to expand arrangements, for instance, via dedicated professionals such as nurses or screening programmes, to explicitly assign responsibility for risk communication, with clear referral pathways and documentation standards.

A very important aspect is to allow health professionals time for professional education and shared decision making. This can take the form of protected clinical time (and reimbursement) for healthcare professionals to complete training and conduct shared decision-making conversations, Also, health systems should make these things easy for general practitioners without overburdening them.[69] [70] An "enhanced" patient-doctor relationship is key to supporting behavioural change and ensuring patients have the information they need to make informed decisions about their health[71]. Health systems might also seed clinician-champion networks and encourage peer-to-peer training within professionals societies. In 2026, the PROPHET project will publish the Action Plans for the uptake of the PROPHET framework, fostering engagement and capacity building for health professionals and policy makers. A toolbox for capacity building will be developed, including a range of materials for the various types of health professionals and policymakers. It will include factsheets, policy briefs, webinars, conference presentations. It is important to link to other initiatives and existing information materials and online tools also for non-genetic health professionals that are made available by e.g. professional organisations and citizen and patient organisations[72]

In terms of the topics to be covered, the capacity building will need to include ethical and legal aspects related to big data and data infrastructures, evaluation of clinical utility including cost effectiveness, and pathways for prevention and treatment.

69 Martin SA, Johansson M, Heath I, Lehman R, Korownyk C. Sacrificing patient care for prevention: distortion of the role of general practice. BMJ. 2025 Jan 21;388:e080811. doi: 10.1136/bmj-2024-080811. PMID: 39837625.

70 Gray M. Prevention in primary care: more of the same is not the answer. BMJ. 2025 Mar 5;388:r413. doi: 10.1136/bmj.r413. PMID: 40044229.

[71] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5296930/

[72] European Society of Human Genetics: Genetic Educational Materials and Sources:

Funded by the European Union

Consideration

To support personalised prevention in our European health and care systems, health care professionals and policymakers need to be engaged and therefore have specific training. Education can take the mode of face-to-face training sessions but, given the large number and variety of policymakers and health care professionals involved, online training modules and materials are increasingly more effective in disseminating knowledge. Further research is necessary to evaluate training modes and materials for specific purposes and target groups. More time and facilitation for health professionals to complete training and shared decision making is a resourcing requirement.

It is to be expected that clinical geneticists will play an important part in being available for advice and coaching other professionals on more complex health problems.[73] The fields of public health and genetics may be separated by different traditions and practices (e.g. regarding prevention, screening, and one-size-fits-all approaches), requiring time for alignment and integration.

Challenge 7: Regulatory aspects and synergy with private sector

Status

The implementation of prevention strategies requires synergy between public and private sectors. Public-private partnerships (PPP) are important for utilising the strengths and capabilities of businesses. These partnerships involve shared investments in research and development initiatives leveraging the strengths and resources of both sectors to address health challenges and create targeted measures.

Engaging with the private sector plays a role in advancing personalised prevention for various reasons:

[73] Tobias ES, Avram E, Calapod P, Cordier C, den Dunnen JT, Ding C, Dolzan V, Houge SD, Lynch SA, O'Byrne J, Patsalis P, Prokopenko I, Soares CA, Tobias AP, Newman WG. The Role of the European Society of Human Genetics in Delivering Genomic Education. Front Genet. 2021 Sep 3;12:693952. doi: 10.3389/fgene.2021.693952. PMID: 34539735; PMCID: PMC8446627.

- Innovation and Technological Advancements: Private firms, such as those specialising in biotechnology and health technology can lead the way in applying innovation. Their contributions, such as cutting-edge tools like wearable health devices and genomic technologies have great potential for prevention efforts.
- Data Handling: Successful personalised prevention initiatives heavily depend on data collection, integration and analysis. Private sector organisations possess the infrastructure and expertise for sophisticated data management including utilising artificial intelligence (AI) to extract valuable insights from health data. A comprehensive data strategy may include gathering and integrating various types of information, such as personal device data (e.g., physical activity, heart rate, and sleep metrics from wearables); environmental data (e.g., air quality, noise, and access to green spaces); school data on nutrition and mental health; technical diagnostic data like breast density and microbiome analysis; and lifestyle data (e.g., shopping habits, screen time, and school lunch consumption).
- Financial Support and Resources: Collaborating with companies can offer financial support and resources that go beyond public funding capabilities. This can expedite research and development processes facilitating market access to preventive solutions.
- Execution: Involvement from businesses, historically and today, plays a role in expanding successful public projects into widespread healthcare solutions. Their expertise in commercialising and distributing health technologies ensures that advancements in prevention can effectively reach various healthcare settings.

Gaps

Ensuring the privacy and security of health information is a concern, especially when private entities are involved. The development of data-driven healthcare tools necessitates collecting sensitive data, such as genetic, racial, and sexual orientation information, raising privacy, discrimination, and stigmatisation concerns. Additional data types, such as screen exposure and social interaction metrics (evaluating depth and frequency of social connections) also present challenges, especially regarding

privacy. Furthermore, issues like inaccurate self-reporting and lack of standardised methods can introduce biases.[74]

- Including sensitive attributes can promote fairness by reflecting diverse populations, despite GDPR restrictions requiring strict safeguards like pseudonymization and consent.[75] Balancing these regulatory constraints with the need for fairness through data inclusion is crucial for creating equitable and effective healthcare tools.
- Implementing data protection measures and establishing clear regulatory guidelines can help mitigate these risks. However, differences in standards across regions can challenge the smooth integration of new technologies. Aligning regulations and setting guidelines for prevention tools can promote better collaboration.

The secondary use of health data for personalised prevention faces significant regulatory challenges, including the fragmented application of GDPR rules across EU Member States which creates barriers for cross-border research.[76] The European Health Data Space (EHDS) proposal aims to harmonise the framework for primary and secondary use of health data, but raises concerns about individual control over data and the risk of bias if certain groups opt out.

Wearable devices like smartphones and smartwatches offer continuous, real-time health data crucial for developing personalised prevention tools, but their use raises regulatory concerns. Ensuring data

[74] Andrus, M., Spitzer, E., Brown, J. & Xiang, A. 'What We Can't Measure, We Can't Understand': Challenges to Demographic Data Procurement in the Pursuit of Fairness. Preprint at https://doi.org/10.48550/arXiv.2011.02282 (2021); Bogen, M., Rieke, A. & Ahmed, S. Awareness in practice: tensions in access to sensitive attribute data for antidiscrimination. in Proceedings of the 2020 Conference on Fairness, Accountability, and Transparency 492–500 (Association for Computing Machinery, New York, NY, USA, 2020). doi:10.1145/3351095.3372877.; El-Azab, S. & Nong, P. Clinical algorithms, racism, and "fairness" in healthcare: A case of bounded justice. Big Data Soc. 10, 20539517231213820 (2023).; Lee, S. S.-J., Fullerton, S. M., Saperstein, A. & Shim, J. K. Ethics of inclusion: Cultivate trust in precision medicine. Science 364, 941–942 (2019).; Kristiansen, T. B., Kristensen, K., Uffelmann, J. & Brandslund, I. Erroneous data: The Achilles' heel of AI and personalised medicine. Front. Digit. Health 4, (2022).

[75] Žliobaitė, I. & Custers, B. Using sensitive personal data may be necessary for avoiding discrimination in data-driven decision models. Artif. Intell. Law 24, 183–201 (2016).; Veale, M. & Binns, R. Fairer machine learning in the real world: Mitigating discrimination without collecting sensitive data. Big Data Soc. 4, 2053951717743530 (2017).; Forti, M. The Deployment of Artificial Intelligence Tools in the Health Sector: Privacy Concerns and Regulatory Answers within the GDPR New Voices. Eur. J. Leg. Stud. 13, 29–44 (2021).; van Bekkum, M. & Zuiderveen Borgesius, F. Using sensitive data to prevent discrimination by artificial intelligence: Does the GDPR need a new exception? Comput. Law Secur. Rev. 48, 105770 (2023).; Dwork, C., Hardt, M., Pitassi, T., Reingold, O. & Zemel, R. Fairness through awareness. in Proceedings of the 3rd Innovations in Theoretical Computer Science Conference 214–226 (Association for Computing Machinery, New York, NY, USA, 2012). doi:10.1145/2090236.2090255.

[76] Slokenberga, S. Setting the Foundations: Individual Rights, Public Interest, Scientific Research and Biobanking. GDPR Biobanking 43, 11–30 (2020).

validity,[77] and addressing the accessibility and privacy disparities associated with wearables, especially those producing continuous data, will require an aligned regulatory framework.[78]. Data from wearables must meet high-quality standards and protect user privacy.

With regard to the private sector and PPPs making genetic tests available to patients across Europe, a number of regulatory considerations need to be assessed. This includes whether the EU Regulation on In Vitro Diagnostic Medical Devices provides adequately high standards of safety and performance for genetic tests[79], and the impact of diverse legal requirements regarding medical supervision, genetic counselling and informed consent across European countries[80]. In addition, other potential regulatory initiatives, such as self-regulation of the industry and patient education need to be explored.

Priorities and Implementation

- Stakeholder Platforms: Establishing platforms where stakeholders from the public sector institutions and academia can collaborate on prevention strategies promotes knowledge exchange, joint ventures and coordinated efforts toward common objectives. Moreover, arranging workshops and conferences to promote cooperation and knowledge exchange between public and private sectors builds up PPP networks. Additionally, it is essential to establish trust between institutions and private companies. Being transparent in communicating and involving stakeholders in decision-making processes can strengthen this trust and streamline cooperation. Establishing a culture of trust is paramount for patients and citizens to feel comfortable sharing their personal data, empowering them to become active participants in their own healthcare.
- Regulatory Sandboxes: These controlled environments allow for testing health technologies in various kinds of partnerships. This approach enables private companies to innovate while

[77] Cho, S., Ensari, I., Weng, C., Kahn, M. G. & Natarajan, K. Factors Affecting the Quality of Person-Generated Wearable Device Data and Associated Challenges: Rapid Systematic Review. JMIR MHealth UHealth 9, e20738 (2021).
[78] Canali, S., Schiaffonati, V. & Aliverti, A. Challenges and recommendations for wearable devices in digital health: Data quality, interoperability, health equity, fairness. PLOS Digit. Health 1, e0000104 (2022).; Cheung, S. Disambiguating the benefits and risks from public health data in the digital economy. Big Data Soc. 7, 2053951720933924 (2020).
[79] Niemiec E, Kalokairinou L, Howard HC. (2017) Current ethical and legal issues in health-related direct-to-consumer genetic testing. Per Med;14(5):433-45.
[80] Kalokairinou L, Howard HC, Slokenberga S, Fisher E, Flatscher-Thoni M, Hartlev M, et al. (2018) Legislation of direct-to-consumer genetic testing in Europe: a fragmented regulatory landscape. J Community Genet.;9(2):117-32.

ensuring compliance with health regulations, expediting the introduction of solutions to the market.

- Defining appropriate policies/regulations for the private sector. Stakeholders should assess the impact of current regulations on the private sector and consider whether additional policies/regulations, such as educational initiatives or transparent advertising, could improve responsible test implementation. These initiatives should foster a responsible partnership and proactively address future challenges in personalised prevention approaches.
- Encouraging Private Sector Engagement: Implement detailed incentives such as tax benefits, funding opportunities or exclusive research collaborations to encourage private businesses to participate in personalised prevention plans. These incentives should be accompanied by strong privacy protections to ensure data security. This can lead to development of health-promoting solutions integrated with individual data, like wearable devices, personalised nutrition, genomic testing services, and Direct-to-Consumer (DTC) products. The public sector must set guidelines for responsible marketing and verify the scientific validity, efficacy, and clinical utility of these products, ensuring their availability and presentation as options rather than necessities.
- Framework for Evaluation: Provision of specific indicators for the assessment of the successes of PPPs in personalised prevention. Proposition of a regular evaluation process to ensure consistent improvements.
- Public Awareness and Education: Utilise media, awareness campaigns, public forums and other methods to educate the public on the benefits and potential of personalised prevention through PPPs.

Considerations

Collaborating with the private sector may be beneficial in many ways to advancing prevention efforts. By encouraging innovation, providing resources, and ensuring solutions, private companies play a significant role in transforming preventive healthcare. Strategic partnerships, frameworks and a focus on ethical practices are vital for unlocking the full potential of this collaboration leading to more effective and personalised health outcomes. However, in dealing with PPP, the public sector should

set up indicators for assessing the success of partnerships between the involved entities in personalised prevention enabling regular evaluation of their impact and efficacy.

Challenge 8: Access, Equity and Coverage

Status

Similar to other healthcare initiatives, testing in personalised prevention should aim to maximise benefits while minimising potential disadvantages. Benefits may extend beyond clinical outcomes to include social and psychological impacts[47]. To fully realise the benefits of personalised prevention and fulfill the promise of universal health coverage in European healthcare systems, equitable access is a key challenge. Access can be defined through the 5As[81]: availability, affordability, accessibility (including geographic barriers), adequacy (including quality), and appropriateness (whether the service meets the needs of different population groups). Governments and health stakeholders must integrate these dimensions into personalised prevention strategies for successful implementation. Key elements include reimbursement, coverage of interventions, and integration into basic healthcare entitlements and routine preventive care to ensure availability and affordability.

Other factors impacting access to personalised prevention include lifestyle and behavioural modifications, awareness and understanding of personalised prevention, knowledge of family medical history, and availability of genetic information to inform disease risk understanding. These elements relate to health literacy and patient/citizen empowerment.

Population-based prevention strategies often fail to meet the specific needs of vulnerable groups. Lower income and socio-economic status, often affecting minority groups, are linked to reduced access to health information and healthcare, leading to poorer health outcomes. Personalised approaches can help reduce health inequalities by addressing individual needs based on environmental, behavioural, socio-economic, and cultural factors. However, access and equity considerations must be integrated into implementation strategies from the very start.

Gaps

[81] https://www.eu-patient.eu/news/latest-epf-news/2016/epf-position-paper-on-access-from-the-patients-perspective/

Insufficient focus on impact and investment in prevention across sectors: Low health literacy is often associated with limited awareness of the determinants of health, leading to less healthy behaviours, decreased participation in screenings and vaccinations, and healthcare avoidance. Increased investment in health literacy can help address the knowledge gap in prevention, especially for vulnerable groups. Additionally, climate change exacerbates existing health inequities while creating new forms of disparity based on geographic location and social vulnerability. There is a need to move towards more integrated health services, based on a lifecourse approach and selection of services based on the holistic needs of a certain population.[82] However, budget constraints across European countries may hinder the provision and reimbursement of additional health services, despite the potential long-term savings and improved health outcomes from preventive measures.

Limited utilisation of digital health technologies: Digital transformation in healthcare requires significant investment and is still in its early stages in many European countries. Access to digital health technologies is limited, especially for vulnerable groups at risk of digital exclusion, such as older people, socially excluded groups, people living in areas with limited internet coverage, etc.[83] The use of AI in healthcare poses challenges regarding health inequities, as algorithmic models often include errors and biases due to continuous under-representation of many ancestry groups in health datasets. Efforts to improve digital health literacy across the population are needed to build trust and understanding of health data collection and sharing.

Lack of harmonisation across Europe: Varying approaches to health data privacy, genetic testing, and insurance coverage mean that patients and citizens across Europe do not enjoy the same rights. Healthcare systems' management and organisation remain the sole competence of EU member states, with varying health budgets and priorities. As a result, inequalities within and between European countries in access to health and social services remain. More harmonised approaches and increased solidarity among member states could help close this gap and foster more equitable access.

Priorities and implementation

[82] https://www.who.int/docs/default-source/primary-health-care-conference/linkages.pdf
[83] https://www.england.nhs.uk/long-read/inclusive-digital-healthcare-a-framework-for-nhs-action-on-digital-inclusion/

A paradigm shift is needed to integrate personalised prevention into healthcare systems and achieve universal access to personalised prevention interventions. Three key priorities can help address the gaps outlined above: policymaking, collaboration and partnership among stakeholders, and outreach and training for communities and stakeholders. They overlap with priorities on community outreach/engagement (Challenge 5) and capacity building (Challenges 5 and 6) which are elaborated above. Further complementary priorities for implementation are:

- *Policymaking:* Support the use of digital health technologies in healthcare while prioritising a regulatory environment which prevents discrimination and bias and safeguards citizens' control over their personal data. Health and social policies should be complemented by regulatory frameworks that protect against discrimination based on socio-economic status, health status, race and ethnicity, religion, gender identity and sexual orientation, etc.
- *Policymaking:* Integrate preventive approaches into health systems and routine clinical practice, such as regular health checkups for the general population and better preventive counselling, providing adequate access to underserved communities and minorities. This includes integrating vulnerability mapping into health equity assessments , addressing geographic and cultural barriers to access to quality services, ensuring full coverage of relevant personalised preventive interventions by the national health insurance system, developing targeted interventions and reimbursement frameworks particularly for vulnerable populations, and earmarking funding for preventive health programmes, research, and infrastructure.
- *Collaboration and partnership:* Consider PPP with e.g. technology companies to develop and implement affordable digital health tools prioritising data security and privacy. Sustain the development and implementation of equitable personalised prevention interventions through diverse funding mechanisms and research programmes.
- *Outreach and training:* Prioritise awareness and health literacy programmes for the general public and patients about access to personalised prevention interventions. Specific efforts are needed to reach vulnerable populations through targeted/adapted messages and use of relevant media channels, including social media, television, radio, and community events.

Considerations

Integrating access and equity into the implementation of personalised prevention is essential to building citizens and patients' trust, a notion that is addressed across other aspects of relevance to this project, from the development of data collection tools and infrastructure to responsible research and innovation. Providing citizens and patients with accessible, affordable, appropriate, and high-quality personalised preventive care will help realise the potential of personalised prevention for improved health outcomes. This requires sustained investment, supported by potentially new funding approaches and evidence on the medium and long term cost-effectiveness of personalised prevention interventions.

Challenge 9: Ethical, Legal, Social Issues (ELSI)

Status

Advancements in genomic sequencing, extensive health data, and digital integration in healthcare have enabled personalised prevention through tailored risk profiles that analyse genetic, behavioural, and socio-economic factors. As personalised prevention evolves, research into ethical, legal, and social implications will be crucial.[84] [85]Current efforts address privacy concerns by strengthening data protection and giving individuals control over their health information. As mentioned earlier in the text, emerging regulatory frameworks like the European Health Data Space will shape the processing of health data for both primary and secondary purposes[86].

Gaps

Collaborative research will be essential to integrate ethical, legal, and social principles into personalised prevention, ensuring innovations are accessible and contribute to a fair and equitable healthcare system.

[84] Howard HC, Swinnen E, Douw K, Vondeling H, Cassiman JJ, Cambon-Thomsen A, et al. The ethical introduction of genome-based information and technologies into public health. Public Health Genomics. 2013;16(3):100-9.
[85] Borry P, Bentzen HB, Budin-Ljøsne I, Cornel MC, Howard HC, Feeney O, et al. The challenges of the expanded availability of genomic information: an agenda-setting paper. Journal of Community Genetics. 2018;9(2):103-16.
[86] Marelli L, Stevens M, Sharon T, Van Hoyweghen I, Boeckhout M, Colussi I, et al. The European health data space: Too big to succeed? Health Policy. 2023;135:104861.

Priorities and implementation

- Informed consent

Informed consent tools will be essential for ensuring citizens and patients understand the benefits, risks, and implications of personalised prevention strategies. These tools should provide clear, accessible information about the nature of the tests, potential outcomes, and subsequent healthcare decisions while addressing privacy concerns and data security.

- Responsible testing

We must consider factors such as disease prevalence, disease severity, financial constraints, and future implications to properly determine the appropriateness of certain tests over others. Though these considerations vary among individuals, the public and private sectors must make thoughtful decisions to prioritise addressing the most important health problems and how to budget resources in proportion to other healthcare demands.

- Maintaining trust and delivering effective communication

To maintain public trust in personalised prevention, it is essential to implement safeguards against misuse (e.g. discrimination, etc.). Furthermore, effectively translating and communicating knowledge to all stakeholders will be crucial for realizing the full potential of personalised prevention.

- Building evidence

The implementation of new technologies and research findings faces significant challenges, including limited evidence of clinical utility, varying interpretations of benefits, institutional resistance, data integration issues, a need for improved clinician understanding and patient-centered ecosystems, etc. To successfully implement personalised prevention strategies and enhance healthcare outcomes, it is crucial to address these challenges, improve data sharing, and incorporate public perspectives.

- Ensuring data privacy

In personalised prevention, key concerns include ensuring privacy, maintaining database integrity, and regulating data sharing and data access for authorised users and allowed purposes. Standardising

data formats, protecting against unauthorised access, and providing adequate storage and computational infrastructure are crucial for securely managing health information to advance prevention strategies effectively.

- Ensuring fair access

Ensuring fair access in personalised prevention requires equitable distribution of outcomes, balanced disclosure of sensitive attributes used to develop personalised prevention approaches, regulated commercial involvement, and fair distribution of potential benefits.

- Concerns regarding linking different sources of data

With increasing health data from personalised prevention, it is crucial to address the risks of cross-linking health information to derive new information about individuals. Robust guidelines are needed to ensure safety controls and protect sensitive patient information.

Considerations

To effectively integrate ELSI principles into practice, collaboration among researchers, healthcare providers, policymakers, industry leaders, and advocacy groups is crucial. Interdisciplinary research and dialogue can help develop comprehensive guidelines and frameworks that address these complex issues. This approach will enhance the ethical implementation of personalised prevention, build public trust, and ensure equitable access to advancements, ultimately promoting a fairer healthcare system.

Challenge 10: Changing behaviour

Status

For personalised prevention to reach its full potential, citizens and patients need to be aware of preventive options, and know how to take actions towards interventions or behaviour change to actually achieve prevention or better health. Increasingly, we are better able to personalize risk prediction for certain disorders, e.g. based on genetic information, but our understanding of behaviour change, and personalizing options for such change is limited. Merely providing information is not

enough to influence behaviour. People may not understand the information, they may not be interested or motivated to change their behaviour, they may not feel confident or in control of their behaviour, or face actual barriers to behaviour change.

Social sciences, health sciences and behavioural sciences have focused on various aspects of interventions to change behaviour[87]. Nudging behaviours has been shown to be effective in promoting healthy behaviour, for instance, in changing diet and smoking cessation. Nudging techniques include improving accessibility, adapting presentation of information and providing financial or emotional incentives for behaviour. Much research has focused on how to present risk information combining written text and numerical presentation with visual presentations to people with varying degrees of health and digital literacy.

Gaps

The discussion on promoting behaviour change in personalised prevention takes place across the domains of public health and clinical genetics, each with their own traditions. Whereas in public health behaviour is stimulated when the outcome is seen as to be in the best interest of all (e.g. exercise), in genetics the emphasis has been on making an informed choice requiring counselling. This is particularly important when genetic information on a familial disorder has consequences for reproduction or in the case of invasive interventions such as preventive surgeries for hereditary cancers. In practice also in public health it is important to ensure informed consent, for instance for participating in screening programmes. On the other hand, patient decisions regarding new applications of personalised prevention, such as pharmacogenomics and lifestyle-related advice based on genetic susceptibility may be more similar to traditional public health approaches. More research is needed on acceptability, ethics and effectiveness of information and health-related choices in these cases. This also pertains to the influence on motivation of the context of being offered a test or tool by the healthcare system versus buying a direct-to-consumer (genetic) test or health device[88].

[87] Nudging in Public Health Lifestyle Interventions: A Systematic Literature Review and Metasynthesis - PubMed (nih.gov)
[88] Nolan 2023 Clin Gen (review anclin validity consumer impact cons HCP exp att).pdf

ROPHET
a PeRsOnalized Prevention roadmap for the future HEalThcare
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Findings about consumers accessing e.g. cancer screening after receiving a test result may have been influenced by a prior interest in one's own health, underlying the purchase of such a test[89].

From the recent history of genetic testing we have learned that merely receiving genetic information on the risk to develop a disorder or susceptibility is not per se effective. About 40-50% of first-degree family members decide to have genetic testing themselves, after being informed about the diagnosis of an index patient in their family for monogenic subforms of common disorders, such as *BRCA*-related breast cancer, hereditary colon cancer or cardiovascular disorders. These first-degree family members have a 50% risk of having inherited the same pathogenic variant. Interventions have tried to increase uptake by a more pro-active role of health care professionals helping the patient to inform family members, while also digital tools for communicating information to family members have been introduced. Having an affected family member in these situations is nonetheless seen as an important incentive to seek out care. In the situation that less informative tests with lower risks are used for multifactorial disorders, without a family history, motivation for behaviour change or uptake of interventions may be low[90]. In recent years studies have been conducted on behaviour change after receiving polygenic risk scores that indicate a relatively modest risk for a variety of disorders, suggesting some positive changes[91] in adapting lifestyle, medication or screening, without increasing anxiety.

Implementation and priorities

Communicating personal risk information, such as gained via genetic tests, has the potential to stimulate healthy behaviour and prevention-related choices. It is important to better understand motivation for behaviour change by developing standards for best practices in communication of genetic information and of measuring relevant outcomes for behaviour change, such as uptake of screening, changing lifestyle, , et cetera[92]. To enhance the effectiveness of behaviour change interventions, individuals need to become aware of their personal objectives and feel confident it is possible to reach these. Behavioral interventions should help individuals to define clear, realistic

[89] Models of communication for polygenic scores and associated psychosocial and behavioral effects on recipients: A systematic review – ScienceDirect
[90] Can Communicating Personalised Disease Risk Promote Healthy Behaviour Change? A Systematic Review of Systematic Reviews - PubMed (nih.gov)
[91] Stewart KFJ 2018 J Comm Gen (review health beh resp psy impact follow-up Covolo).pdf
[92] Models of communication for polygenic scores and associated psychosocial and behavioral effects on recipients: A systematic review - ScienceDirect

and tailored behavioural goals, using the SMART framework (Specific, Measurable, Achievable, Relevant, Time-bound). Based on barriers, resources, and readiness or ability to change (e.g. through self-assessment tools or motivational interviewing), these goals could be adjusted.

For interventions to be effective various levels should be addressed and connected: the individual level and choices made, taking into account of the relevant (healthcare) context of the individual and their health needs and characteristics such as health literacy, the community level, and the societal level allowing for the accessibility of care and prevention via funding or regulation and public-private partnerships.

Considerations

In developing personalised prevention approaches, information and choice should be key cornerstones of promoting healthy behaviours, as behavioural interventions and encouragements should never be based on fear or force, and especially genetic risk information may be misunderstood. For instance a belief in genetic determinism may be connected to feelings of fatalism and reluctance to change behaviour, or overoptimism against changing lifestyle when perceived to be not at risk. The path forward aims to support citizens and patients in accessing and understanding information so they can make optimal health-related choices themselves, and help them sustain relevant behaviours..

4. List of abbreviations

Abbreviation, Acronym	Description
1+MG	1+Million Genomes
B1MG	Beyond 1 Million Genomes
CVD	Cardiovascular disease
DICOM	Digital Imaging and Communications in Medicine
DCT	Direct-to-consumer testing
EGA	European Genome Phenome Archive
EP PerMed	European Partnership for Personalised Medicine
GDI	Genomic Data Infrastructure
GoE	Genome of Europe
GWAS	Genome-Wide Association Studies
HIA	Health Impact Assessment
HTA	Health Technology Assessment
ICPerMed	International Consortium for Personalised Medicine
LEA	Essential Levels of Assistance
NCD	Non-communicable diseases
PDTA	Diagnostic Therapeutic Assistance Pathways
PPP	Public-private partnership
PRECeDI	PREvention of Chronic DIseases
PROPHET	A personalised Prevention Roadmap for the Future Healthcare
PROs	Patient-reported outcomes
PRS	Polygenic risk score
RCTs	Randomised controlled trials
SRIA	Strategic Research and Innovation Agenda
THCS	Transforming Health and Care Systems

5. The Roadmap for the "A Personalized Prevention roadmap for the future Healthcare" (PROPHET) Strategic Research and Innovation Agenda (SRIA)							
The broad scope of promotion and prevention (Challenge 1 of SRIA)							
Goal (Priority level*)	**Action (Expected Timeline for the implementation **)**	**Obstacle**	**Outcome**	**Responsible for the action**	**Other EU initiatives with the same objective**	**Funding sources**	**Output indicator**
Strengthen governance of health determinants across sectors (Immediate)	Support applied research and pilot projects across regions to test coordination models between health systems and other key sectors (e.g., environment, education, labor), engaging local authorities, healthcare providers, and academic institutions to integrate health	Multisectoral nature of determinants of health and disease	Benchmarking of best practices across sectors and countries	Research community, EU	One Health European Joint Programme (https://onehealthejp.eu/) Personalized CANcer Primary Prevention research through Citizen Participation and digitally enabled social innovation (4-PCAN) Project	EU calls	Inclusion of diverse determinants and sectors in research calls

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

	and non-health determinants in the policies. (Short term)						
Balance awareness and investment between prevention and care (Immediate)	Advocate to national governments for increasing research and innovation funding on integrated prevention programs Implement funding programmes for research to generate evidence and demonstrate value of prevention (health research, economic studies, etc. (Short term)	Lack of incentives and resources to systematically integrate prevention in healthcare (Around 6% of health budgets to care across EU is currently spent on prevention)	Research and Innovation investment in integrated prevention programmes Health benefits from preventive interventions not immediately observed, as outcomes from clinical care ones	EU/ national/ regional/ local policymakers in collaboration with healthcare professionals, patients, citizens, researchers, civil society (to ensure funding programmes adequately meet population needs)	Invest4Health project International Consortium of Personalised Medicine (ICPerMed) European Reference Network (ERNs) clinical care and expertise European Partnership for Personalized Medicine (EP PerMed)	European Commission, national, regional, local funding (health budgets, research budgets, etc.)	Percentage of research funding for prevention research Impact of funding programmes on health outcomes Availability of long-term plans for prevention funding at governmental level Number of scientific publications on prevention

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

Improving the scope of biomarkers used in personalised primary prevention beyond genetics (Mid-term)	Increase applied and clinical research on biomarkers that might represent actionable risk factors (e.g., gene-environment interactions, epigenetics, microbiome, exposome). Support the maintenance and integration of large european population-based comprehensive cohort studies that incorporate epidemiological, environmental, genetic and other omic data (Short term)	Lack of accessible data on non-genetic biomarkers and their interactions for prevention. Lack of quality population-based data structures that can have enough power and quality to address this challenge (to collect and analyse information) (Medium)	Identify new biomarkers that can be translated into preventive interventions Explore gene-environment and other biomarker interaction that might conduct to clear preventive actions Create strong european infrastructures that integrate such complex and large volume data	Research community Public Health organisations	European human exposome network; Partnership for the Assessment of Risks from Chemicals PARC; Exposome powered tools for healthy living in urban settings EXPANSE, Genome, Environment, Microbiome and Metabolome in Autism GEMMA & Oncobiome Projects;	European Commission (Horizon Europe, EU4Health)	Number of scientific publications reporting data on non-genetic biomarkers and their interactions Number of non-genetic biomarkers , and genetic and non-genetic interaction biomarkers assessed that can clearly improve and personalize preventive actions

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

Harmonize health data sharing regulations across EU member states to enable equitable access and collaboration (Mid-term)	Create a centralized platform to share best practices and lessons learned among EU Member States (Short term for setting up a platform Medium term for pilots and infrastructure improvement)	Fragmented governance, infrastructure, inequalities, and lack of regulation affects citizen trust	Increased policy alignment, interoperable systems, improved citizen trust and participation.	European commission, national governments, Horizon Europe/EU4Health Programme	EHDS implementation; TEHDAS; eHealth network; GDPR implementation the context of 1+Million Genome Initiative/Genome EDIC	European Commission and National budgets, public-private partnerships.	Number of Member states actively participating in platform development and use Number of citizen and patient representatives participating in platform development
Continuous evidence synthesis system supporting personalised prevention (Challenge 2 of SRIA)							
Goal (Priority level*)	**Action (Expected Timeline for the implementation **)**	**Obstacle**	**Outcome**	**Responsible for the action**	**Other EU initiatives with the same objective**	**Funding sources**	**Output indicator**
Generate robust evidence on the clinical efficacy and broader impact of omics-	Develop funding programmes for rigorous studies on clinical efficacy of	Difficulty in conducting robust trials (e.g., RCTs) and collecting	Conduction of studies on clinical efficacy of omics-based	Research community, EU and national funding agencies,	ICPerMed; EP PerMed	Horizon Europe, EU4Health, national research budgets.	Number of funded studies on clinical efficacy of omics-based preventive

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

based prevention approaches. (Mid-term)	personalised prevention approaches (e.g., Randomized Controlled Trial (RCTs) Support research generating evidence on the cost-effectiveness of omics-based prevention approaches. -Incorporate assessments of patient acceptability and implementation feasibility into clinical trials. (Medium)	comprehensive data on clinical efficacy and broader impacts (e.g., cost-effectiveness, acceptability, feasibility) of omics-based prevention tests.	preventive approaches valuation reports on cost-effectiveness, acceptability, and feasibility;Integration of the evaluation of patient-reported outcome measures (PROMs), clinicians' feedback, or mixed-method evaluations in current and new clinical trials.	clinical trial networks.			approachesNumber of cost-effective analyses of omics-based preventive approachesNumber of trials including PROMs and stakeholders feedbacks Number of reports evaluating the broader impact of omics-based approaches

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

Ensure a robust and transparent governance system for continuous evaluation of evidence in personalised prevention (Immediate)	Create an expert panel to steer, oversee and evaluate evidence curation activities. (Short term)	Ensuring the validity and transparency of the evidence evaluation process.	Biannual expert meetings, reviews and evidence curation process updates.	European Commission Directorate-General for Health and Food Safety (DG SANTE) in collaboration with national public health agencies.	ICPerMed EPPerMed; ERNs for collaborative clinical expertise Member State Coordination Group on HTA (HTACG) International Consortium for integrative genomics prediction (INTERVENE)	European Commission (Horizon Europe, EU4Health)	No. of assessments, revisions and updates to the evidence curation process by the expert panel
Guarantee the availability of high-quality and up-to-date curated evidence to support personalised prevention (Immediate, with continuous funding for team expansion in	Create an evidence curation team to manage and maintain a database under the guidance of the expert panel (Short term for curation team creation.	Recruiting and training specialized staff (informatics, genetic epidemiology, genomics experts) Developing standardized curation protocols and	Fully operational curation team with documented Standard Operating Procedures (SOPs) Monthly/quarterly curation cycles (number of new references	DG SANTE in close collaboration with the Expert Panel and national public health agencies	ICPerMed; EP PerMed ERNs for collaborative clinical expertise Member States (HTACG)	Initial funding through Horizon Europe or Digital Europe Programme; co-funding by participating member states and potential private/public partnerships	No. of curated publications added per cycle Adherence to SOPs and QA metrics Publication of annual curation reports Satisfaction/feed back from Expert Panel members

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

subsequent years)	Medium for ongoing curation with periodic expansions and updates to SOPs.)	Quality Assessment measures Ensuring coordination with existing national/international efforts to prevent duplication of work	curated and validated) Quality metrics (e.g., inter-rater reliability) for curated data, published annually				
Establish a common European standard for assessing the clinical utility and applicability of omics-based personalised prevention approaches. (Mid-term)	Develop an evidence classification framework based on clinical utility and translational considerations to tier the evidence (including modelled evidence) (Short term)	Ensuring that the evaluation of omics evidence is based on rigorous and transparent criteria.	Publication of omics evidence production and synthesis guidelines and classification framework.	European Commission, EMA, ECDC, BBMRI-ERIC, ELIXIR, EATRIS, ECRIN and ERN-EuroGen	EU Joint Actions on non-communicable diseases; EU best practices portal	European Commission (Horizon Europe, EU4Health funding)	Framework document published.
Enable timely access to synthesised evidence on	Build an open-access platform (regularly updated) for	Ensuring scalability and inclusivity of the evidence	Operational platform with tiered	European Commission Directorate-General for	EU Joint Actions on non-communicable diseases	European Commission (Horizon Europe,	Number of omics tests classified and available.

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

personalised prevention for researchers, clinicians, and policymakers (Mid-term).	synthesising, curating, and disseminating omics evidence for prevention. (Medium)	reporting, synthesis and classification system.	classifications for omics tests.	Health and Food Safety (DG SANTE) in collaboration with national public health agencies		EU4Health, national funding)	
Support research capacity and knowledge, to promote evidence-based adoption of personalised prevention (Mid-term) .	Develop training materials and workshops on the use of the platform and the guidelines to assess the evidence on omics-based preventive approaches and promote exchange programs for researchers on the field. (Medium)	Enhancing knowledge and skills for implementing omics-based prevention.	Number of workshops held, and participants trained.	ECDC, WHO-EURO, National Public Health Institutes	EP PerMed European Comission	European Commission (Horizon Europe, EU4Health, COST actions national institutions)	Participant feedback and post-training/exchanges application rates.
Ensure long-term accessibility and interoperability	Establish a comprehensive, EU-wide digital	Large volume of publications to screen.	Fully functional database pilot with thousands	DG SANTE in collaboration with national	ICPerMed EP PerMed	EU budget through Digital Europe / Horizon	No. of curated publications

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

of curated evidence on personalised prevention across Europe. (Immediate)	repository for personalised prevention to aggregate relevant published research (Short term)	Variety of data formats and metadata standards.Maintenance of data quality.	curated references focusing on personalised prevention within 2 years and continued curation onwards	public health agencies.	European Health Data Space (EHDS) Horizon Europe ERNs Member State HTACG	Europe/EU4Health; co-funding by participating member states.	Initial pilot usage metrics Database usage across member states
The PROPHET Framework implementation (Challenge 3 of SRIA)							
Goal (Priority level*)	**Action (Expected Timeline for the implementation **)**	**Obstcle**	**Outcome**	**Responsible for the action**	**Other EU initiatives with the same objective**	**Funding sources**	**Output indicator**
Create a network in support of the implementation of evidence-based personalised prevention approaches. (Immediate)	Invite Ministries of Health of EU Member States to identify national public health institutes and/or HTA/HIA/national guidelines bodies to be enrolled as partners in the network	Diverse national bodies may lack a unified vision for personalized prevention - Diverse legal and cultural contexts across EU Member States	Launch of the network "Vision & Scope" document, including initial goals & priorities Number of countries involved and partners agencies enrolled	European Commission (DG SANTE) National Ministries of Health and related agencies (national public health institutes, national HTA bodies, national	ICPerMed EPPerMed Transforming Health and Care Systems partnership (THCS) Building the EU Cancer and Public Health Genomics	European Commission (Horizon Europe, EU4Health) COST Action Co-financing by network partners	Number of signed partnership agreements between EC and national institutions in the established network .

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

	Agree on the Network's scope & goals (Short term)			HIA bodies where available) Network secretariat (once operational)	platform (CAN.HEAL) project JA PCM		
Establish a governance structure for the personalized prevention network. (Immediate)	Conduct a governance feasibility study reviewing EU & national laws to define the network' form, membership rules, and decision-making processes, aligning with the EU Better Regulation principles to ensure consistency and transparency (Short term)	Unclear governance and membership criteria can hinder sustainable collaboration	Publicly available feasibility report Recommended legal status (consortium vs official EU body) Defined membership criteria and governance structure	Commission-appointed legal experts National authorities' legal teams	ICPerMed EPPerMed THCS	European Commission (Horizon Europe, EU4Health) Co-financing by network partners	Feasibility report published Governance model endorsed by majority of EU Member States
Formalize the network's	Draft the Network's	Need standardized	Charter and MoU signed by at least	Commission-appointed legal	ICPerMed EPPerMed	European Commission	Official Charter ratified

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

operational frameworks (Immediate)	Charter, statutes, Memoranda of Understanding to clearly define roles, membership obligations, and conflict-of-interest policies (Short term)	documents to ensure clarity of roles and processes	8 Member States Defined roles for Secretariat, Steering Committees, membership fees, etc.	experts National authorities' legal teams	THCS	(Horizon Europe, EU4Health) Co-financing by network partners	Number of Member States signing the MoU Governance structure published
Secure long-term financial sustainability for the network. (Immediate)	Identify long-term financing (EU budget lines, membership fees, grants) and create a permanent Secretariat to coordinate activities and ensure the Network's continuity (Short term)	Reliance on short-term or project-based funding threatens sustainability	Full-time staffed secretariat Multi-year funding plan endorsed by 8 Member States Publicly available budget & resource allocation processes	European Commission (DG SANTE, DG Research) Member States (co-funding)	ICPerMed EPPerMed	European Commission (Horizon Europe, EU4Health) Co-financing by network partner	Secretariat's annual financial report Approved operating budget
Strengthen multi-stakeholder engagement in personalized	Strengthen stakeholder engagement (citizens,	Balancing interests of different stakeholders.	Stakeholder advisory committee(s) operational.	Secretariat National ministries of health	Large multi-stakeholders' initiatives in personalized/prec	European Commission (Horizon Europe, EU4Health)	Frequency of stakeholder meetings and feedback

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

prevention strategies. (Immediate)	patients, local public health authorities, healthcare providers, industry) through the establishment of formal advisory groups Define transparent processes for consultation (Short term)	Ensuring robust but feasible consultation	Public consultations on personalized prevention guidelines/reports.	DG SANTE	ision medicine at EU and national level	Co-financing by network partners Contribution by industry stakeholders	Integration of stakeholder inputs into the network outputs like HTAs reports or other reports on the implementation of PP approaches. final outputs
Integrate the main recommendations for evaluating personalized prevention approaches using the PROPHET Framework, into national standard procedures. (Mid-term)	Surveying national prevention processes for evaluating, designing, implementing, and monitoring preventive program (Medium)	Harmonize the heterogenousprocesses for evaluating and implementin prevention proposes, within which the use of the PROPHET framework must be adapted and integrated.	A report comparing existing processes across Member States Identification of key touchpoints for integrating PROPHET Framework principles in national workflows	Network Secretariat National public health agencies	ICPerMed EPPerMed THCS	Horizon Europe, EU4Health, Member State budgets	Published comparative report on prevention governance and managements in Member States. Number of Member States providing data on prevention governance and implementation

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

							mechanisms. Policy recommendations on how/where to integrate PROPHET framework in national personalised prevention processes
Test the adaptability of the PROPHET Framework in real-world settings. (Mid-term)	Promote & Pilot the PROPHET Framework in Multiple Countries to evaluate how it can be embedded in the development of national prevention programs (Medium)	Need real-world testing & demonstration of the framework's adaptability in diverse healthcare settings	Pilot-specific policy briefs documenting lessons learned Feedback loop to refine local implementation guidance	Network Secretariat National public health agencies	ICPerMed EPPerMed THCS Joint Actions for NCD or PCM, Prevent	Horizon Europe, EU4Health, Member State budgets	Pilot evaluation reports & policy briefs Adjusted, improved PROPHET implementation guidelines
Define metrics to assess the social impact of	Develop and integrate in the assessment	Measuring social impact in a comprehensive	Published social impact assessment tools,	Network Secretariat consulting social	ICPerMed EPPerMed THCS	EU grants, public health budgets	Number of assessment properly

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

personalized preventive approaches. (Mid-term)	framework social impact assessment tools, focusing on equity, access, sustainability in view or scarce resources, and public trust. (Medium)	and meaningful way, addressing diverse societal concerns.	increased use of these tools in evaluating personalised prevention initiatives.	scientists, public health experts, epidemiologist, regulatory bodies, civil society			evaluating the social impact of personalized preventive approaches.
Establish the PROPHET Framework as a guiding principle in national policy. (Mid-term)	Work with national authorities to adopt the PROPHET Framework main principles in the design monitoring revision of personalized prevention program (Long term)	Every country has various processes in place for evaluating and implementing prevention programs, within which the use of the PROPHET framework must be adapted and integrated.	Formal adoption in at least 8 Member States (policy statements, guidelines).	Network Secretariat National public health agencies		EU4Health, Member State budgets	Number of Member States with formal adoption Inclusion of PROPHET principles in national guidelines for design and implementation of prevention programs.

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Funded by the European Union

Improve monitoring in personalized prevention. (Mid-term)	Support national authorities in building monitoring guidelines for personalized prevention (Long term)	Lack of standardized guidance for tracking outcomes, cost-effectiveness, and equity impact in personalized prevention leads to inconsistent or incomplete monitoring.	Common metrics and data-collection protocols	Network Secretariat National public health agencies	ICPerMed EHDS	EU4Health, Member State budgets	Number of Member States formally developing guidelines Annual reports for data collection and analysis
Build capacity in national institutions for better integration of the PROPHET Framework. (Mid-term)	Organize training on the integration and specific components of the framework (HTA, HIA; policy monitoring) for National Institutions (Medium)	Diversity in methods, implementation strategies and training among different partners	Improved capacity among national stakeholders (health authorities, policymakers, etc.) to apply HTA and HIA in personalised prevention .	Network Secretariat Academic partners & professional societies	ICPerMed	EU4Health, Member State budgets	Number of trained professionals Pre-and post-training surveys (to gauge knowledge gain) Uptake of HTA/HIA methods in Member States' prevention program guidelines

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							Number of training sessions held (online/offline)
Stimulate research on understudies impacts of personalized prevention approaches (Immediate)	Launch of EU-funded research calls specifically targeting equity, patient acceptability, and ethical considerations (Medium)	Equity impacts and patient acceptability are often overlooked; insufficient data hinders policy decisions and real-world adoption of personalized prevention.	Priority setting and funding opportunities	European Commission (DG SANTE, DG RTD) Network Secretariat (advisory role) Academic and other research institutions NGOs	ICPerMed EPPerMed	– Horizon Europe, EU4Health Co-funding by industry Co-funding by nonprofit research foundations	Number of funded research projects focusing on equity & acceptability Peer-reviewed publications & policy briefs
Data collection and integration, and Data Infrastructure (Challenge 4 of SRIA)							
Goal (Priority level*)	**Action (Expected Timeline for the implementation **)**	**Obstacle**	**Outcome**	**Responsible for the action**	**Other EU initiatives with the same objective**	**Funding sources**	**Output indicator**
Standardise data structure across research and	Develop and implement **harmonised**	Fragmentation of data standards including	A unified set of standards for data management	European Commission (including	- Genomic Data Infrastructure (GDI)	European Commission, National Health	Percentage of organisations adopting

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healthcare sectors. (Immediate)	**data standards** for genomic, clinical, wearable, relevant environmental, and socioeconomic data, in collaboration with research communities and organisations such as Global Alliance for Genomics and Health (GA4GH) and International Standards Organisation (ISO) (Long-term)	inconsistent data formats, variability in storage, and different terminologies Resistance to change Differences in implementations of the standard across borders due to differences in data governance on a national level Technological barriers on the use of infrastructures hosting data which might result not being	across EU healthcare and research systems. Compliance across different countries resulting in accessible data for all Data quality standards will be better resulting in improved data analysis, thus safer, and maybe faster conclusions and results for patients, thus better precision and possible prevention Better data translation from	funded initiatives and projects: https://gdi.onemilliongenomes.eu https://digital-strategy.ec.europa.eu/en/policies/1-million-genomes https://ehds2pilot.eu), Research Infrastructures (e.g. ELIXIR) Standards setting organisations such GA4GH and ISO	- 1+Million Genomes Initiative (1+MG) - HealthData@EU Towards the European Health Data Space (TEHDAS 1&2) International consortium for integrative genomics prediction (INTERVENE) -Next generation tools for genome-centric multimodal data integration in personalized cardiovascular medicine (NextGen)	& Research Budgets, Research Infrastructures	standardised practices for genomic, clinical, wearable, relevant environmental, and socioeconomic data. Number of datasets compliant with the adopted standards. Number of publications citing the infrastructure or the data standards

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		accessible by everyone in health care or research It is also challenging to educate healthcare providers and researchers to implement the standards	research to medicine and alignment of data exchange				
Enhance data discovery, accessibility and quality of genomic and health data. (Immediate)	Implement metadata standards and data cataloguing practices to make datasets more transparent and easier to find (Medium)	-Inconsistent metadata practices and fragmentation of resources and efforts. Researchers, healthcare professionals might not able to	Standardised metadata practices adopted across EU repositories to improve data cataloguing. Increased discoverability and usage rates	Funding organisations such as the European Commission. Research Infrastructures, and Academic Research Institutions.	GDI, 1+MG, HealthData@EU	European Commission, National Research Budgets, Research Infrastructures	Percentage increase in the discoverability and usage of genomic and health datasets. Adoption rates of metadata

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		adopt the standards	of genomic and health datasets in research and clinical applications.				standards across EU repositories.
Integration of different data types: genomic, clinical, lifestyle, relevant environmental, and socioeconomic data. (Long-Term)	Create secure, standardised, and interoperable services under a common framework adhering to FAIR data principles (Long-term)	Heterogeneity of Data: Genomic, clinical, socioeconomic, relevant environmental, behavioural, and lifestyle data vary significantly in structure, quality, and context. Technical Barriers: Lack of interoperable tools and platforms to facilitate seamless integration across data types.	Increased research outputs using multi-sectoral integrated datasets.	European Commission, Research Infrastructures, Standards setting organisations	HealthData@EU -Population Health Information Research Infrastructure (PHIRI)	National Health Research Budgets, European Commission, Research Infrastructures,	Percentage of multisectoral datasets successfully integrated. Number of tools developed to support data integration.

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Integration of Artificial Intelligence (AI)/Machine Learning (ML) models for personalised prevention. (Long-Term)	Build infrastructure to support data discovery, storage, access, and processing. Develop clinician-friendly tools for interpreting validated AI/ML models (Long term)	Lack of necessary infrastructure, such as cloud-based storage, federated learning systems, and real-time data processing capabilities. Clinician training as healthcare professionalslack the necessary training to interpret and apply AI/ML models effectively in clinical practice. Security risks Cost	Increased adoption of AI/ML tools in clinical settings for prevention Increased capacity for analytics	Healthcare IT providers, Research institutions	Digital Cognitive Biomarker; LETHE project, Watching the Risk Factors: Artificial Intelligence (AI) and the Prevention of Chronic Conditions (WARIFA) Brain Health Tool Box: Facilitating personalized decision-making for effective dementia prevention	European Commission, National Research Budget, Academic Research institutions.	Number of clinician-friendly tools deployed Increase in AI/ML-driven personalised prevention applications.

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Improve the quality of evidence for personalised prevention through fostering of high-quality availability data for research beyond genomic information (Mid-term)	Provide logistical and structural support to existing large European population-based cohorts to aid in their maintenance and follow-up, promote their integration, and facilitate data sharing	Ensuring the availability & maintenance of high-quality population-based data for research to produce robust evidence for personalised prevention	Cohort Hub with personal and technical resources	European Commission Directorate-General for Health and Food Safety (DG SANTE) and DG research in collaboration with national funding agencies.	ICPerMed, 1+MG, Genome of Europe	European Commission (Horizon Europe, EU4Health) and member states	Access core data (common or federated) from main European cohorts with compatible data on environmental exposures, social determinants of health, clinical data and genetic and non-genetic biomarkers
Community Engagement and trust (Challenge 5 of SRIA)							
Goal (Priority level*)	**Action (Expected Timeline for the implementation **)**	**Obstacle**	**Outcome**	**Responsible for the action**	**Other EU initiatives with the same objective**	**Funding sources**	**Output indicator**
Actively engage citizens and patients in personalised prevention Policies	Each EU country should have a task force to oversee citizen and patients representatives	Citizens are more difficult to engage than patients	Recognizable representative of patients/ public in personalised prevention initiatives	Governments, health care funders, professional organisations who develop	ERNs for genomics / rare diseases 4P-CAN	EU via research funding, national funding bodies through e.g. partnerships with patient	Number of personalized prevention initiatives with recognizable

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(Immediate)	Ministers of EUMSs where personalised prevention policies are designed (Medium)			personalised prevention policies; patient organisations and civil society organisations		organisations and civil society organisations	engagement of citizens
Prioritise and improve community engagement (Immediate)	Identify relevant communities that could play a key role in promoting personalised prevention (Medium)	Engagement has to start before people are affected	Patient organization or community groups involved in personalised prevention initiatives	Governments, health care funders, professional organisations who offer or develop personalised prevention policies, patient organisations and civil society organisations	ERNs for genomics / rare diseases Genome, Environment, Microbiome & Metabolome in Autism: an integrated multi-omics systems biology approach to identify biomarkers for personalized treatment and primary	EP PerMed THCS	Number of patient organization or community groups involved in personalised prevention initiatives

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					prevention of Autism Spectr (GEMMA)		
Generate more structural funding for citizen and patient engagement in research, care and public health, and their governance (Immediate)	Generate funding for citizens/ patients in each personalised prevention Initiative (Medium)	Measures to evaluate engagement need to be streamlined	High percentage of personalised prevention initiatives with citizen/ patient engagement at higher IAP2 levels.	Governments or insurance companies who organize health care offers Funders of research,	ERNs for genomics / rare diseases	EU via research funding, national funding bodies, foundations	Number of funded personalised prevention initiatives with citizen/ patients engagement % of engagement level (IAP2)
Education and raising awareness of options for personalised prevention and taking part in health research. Develop and study online information and communication tools	Current communication focuses on affected people Current communication focuses on affected people, future communication should include citizens (Medium)	(Online) tools need to be accessible for people with low digital literacy and health literacy Family members need to be targetedFamily members and healthy citizens in general are	Tools to inform citizens, patients and research participants that are understandable and accessible also for persons with low (health) literacy; that can offer more information upon request (layered)	Governmental agencies who develop (online) tools to inform patients and public. Funders of research. Governments, health care funders, professional organisations	ERNs for genomics / rare diseases	National health budgets European Commission (Horizon Europe, EU4Health, national funding)	Number of tools that have specific low literacy version Number of tools to inform family members Percentage of health research projects with accessible

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(Immediate)		usually not approached by health care professionals	Tools to inform healthy family members of patients with a genetic disorder Health research projects with accessible awareness options. Personalised prevention tools for family members and healthy citizens Publications on the evaluation of these tools	Funders of research			awareness options Number of publications on the evaluation of these tools
Increase health literacy, especially among young populations (Immediate)	Design and implement programmes in schools to normalise regular health check-ups	Differences in health literacy leading to inequalities regarding access to and	- Availability of tool(kits) for education on prevention - Exchange of best practices	Wide range of stakeholders in health system and education system (government, public health	-Schools4Health project about prevention and health literacy in schools	EU, national, regional, local sources (health budget, council funding, education budget,	- Number of programmes implemented - Number of types of stakeholders

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	and inform about prevention (Medium)	participation in healthcare and health outcomes	among involved stakeholders - Increased number of routine health check-ups - Higher vaccination rates	authorities, education authorities, schools, civil society…)	- EU Health in Education: Transversal Projects to enable teachers to increase health literacy of school children	etc.) Funding source and scheme may vary between countries.	involved in programmes - Number of participants (e.g. no. of schools) - Ratio of funding for health prevention programmes compared to other educational programmes
Increase health literacy, especially among vulnerable populations (Immediate)	Design and implement educational programmes for adults (especially minority and vulnerable groups) to normalise regular health check-ups and inform about prevention (Medium)	Differences in health literacy leading to inequalities regarding access to and participation in healthcare and health outcomes	Availability of tool(kits) for education on prevention Exchange of best practices among involved stakeholders Increased number of routine health check-ups Higher vaccination rates	Wide range of stakeholders in health system and education system (government, public health authorities, education authorities, schools, civil society,…)	-'Prevention in Action' project to increase health literacy on NCDs among population, including vulnerable populations RISE-Vac project to increase vaccination uptake and health literacy among prison population	EU, national, regional, local sources (health budget, council funding, education budget, etc.) Funding source and scheme may vary between countries	Number of programmes implemented Number of types of stakeholders involved in programmes Number of participants (e.g. no. of institutions/organisations providing education)

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Funded by the European Union

					Action grants given under the EU Joint Action PreventNCD since some of them focus on vulnerable groups and groups of low socioeconomic status		Ratio of funding for health prevention programmes compared to other educational programmes
Increase public engagement and participation in the development and implementation of personalised prevention (Immediate) .	Implement public consultation processes, workshops, and forums to gather input from diverse stakeholders (Medium).	Ensuring meaningful and inclusive participation from all stakeholders.	Increased public awareness and involvement, policies and strategies that reflect public concerns and values.	Public health organizations, research institutions, patient advocacy groups/organisations, civil society organisations.		EU grants, public health budgets	Number of public engagement activities, level of stakeholder participation, survey results on public awareness and satisfaction.
Health Professionals and Policy Makers involvement (Challenge 6 of SRIA)							
Goal (Priority level*)	**Action (Expected Timeline for the implementation **)**	**Obstacle**	**Outcome**	**Responsible for the action**	**Other EU initiatives with the same objective**	**Funding sources**	**Output indicator**

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Education on HTA/HIA with special reference to economic evaluations of personalised prevention Approaches (Mid-term)	Develop HTA modules for personalised prevention in academia (Medium)	Few experts in EU members states.	Number of training modules	Academia (experts in economic modelling)	Healthcare- and pharma-economics in support of the International Consortium for Personalised Medicine (HEcoPerMed)	EU grants, national HTA bodies	Number of training modules
Appropriate training of non-genetic health care professionals for efficient stratification that include 'omics in public health screening (Mid-term)	Develop and implement personalised prevention training for non-genetic health care professional (Medium)	Limited interest	Availability of training modules with large numbers of participants	Genetic health care professionals, public health care professionals, EUPHA	European Union of Medical Specialists (UEMS) NHS Genomics education Programme Global Genomics Network in Education and Training (GGNET)	National and international professional organisations	Number of training modules, number of participants
Introduction of new methods for assessing practical competences	Include Entrustable Professional Activities (EPAs) in training for	Assessment often focuses on knowledge, what is needed is also focus on applying	Assessment including know-how	Organizations of genetic health care professionals,	European Board of Medical Geneticss (EBMG)	EU and national research grants on educational research	Number of assessment schemes including know-how

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aimed at the application of personalised prevention strategies. (Mid-term)	personalised prevention (Medium)	knowledge and know-how in addition to know-what		public health care professionals, EUPHA			
Incorporation of public and patient involvement in education for health professionals (Mid-term)	Include public/ patients in the development and implementation of personalised prevention training for non-genetic health care professional (Medium)	Training and education is often developed top-down	Personalised prevention training modules that incorporated public and patients' input	Organizations of genetic health care professionals, public health care professionals, EUPHA, patient organisations and civil society organisations	ERNs for genomics/ rare diseases Innovative Health Initiative	EU and national research grants on educational research	Number of PP training modules that incorporated public and patients' input
Regulatory aspects and synergy with the private sector (Challenge 7 of SRIA)							
Goal (Priority level*)	**Action (Expected Timeline for the implementation **)**	**Obstacle**	**Outcome**	**Responsible for the action**	**Other EU initiatives with the same objective**	**Funding sources**	**Output indicator**
Foster effective public-private partnerships (PPPs) to	Establish stakeholder platforms and	Building trust between stakeholders, including	Creation of functional stakeholder platforms	National Governments, European	Personalised Relapse Prediction (PARADISE)	European Commission, Public Private	Number and diverse types of stakeholders engaged

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advance personalised prevention strategies through innovation and resource sharing. (Mid-term)	workshops for collaboration between public institutions, academia, and the private sector (Medium)	patients and citizens, to encourage data sharing and collaboration. Addressing differences in operational priorities and practices between public and private entities, including funding sources and sustainability.	engaging a wide range of participants. Measurable increase in PPP-driven initiatives and projects in personalised prevention . Improved Data access and sharing due to collaborations that results in better technological advances improving prediction models.	Commission, and Private sector. Academic and Healthcare Institutions	project	Partnerships/Grants	Increase in collaborative PPP projects
Promote innovation in personalised prevention	Encourage private-sector engagement through	Balancing the need for innovation with stringent privacy	Increased private-sector investments in	-Private Sector Entities: Innovate and co-develop solutions.	Cancer Image Europe (EUCAIM)	European Commission (EU-Horizon	Number of innovative products

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by leveraging the technological expertise of private sector partners. (Mid-term)	incentives for example tax benefits, funding opportunities, and exclusive research collaborations. Leverage EU funding to support innovation in wearable devices, genomic technologies, and data integration tools for prevention efforts. (Medium)	and security requirements for sensitive health data. Addressing accessibility disparities in wearable technologies Ensuring that commercialised products meet safety and performance standards, and ethical standards.	personalised prevention technologies. Development and market introduction of validated, patient-centric health technologies Unified regulatory guidelines for personalised prevention across EU Member States. Increased collaboration agreements & strategic partnerships resulting in attracting more	- Regulatory Bodies: Design and monitor regulatory sandboxes. **Research Institutions:** Collaborate on validation and testing.		Europe), private-sector Research and Development funding, public-private partnerships.	developed and validated. Volume of private-sector investments in personalised prevention . No of projects involved as a results of partnership Adoption rate of standardized data frameworks and successful interoperability integrations

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			funding and into technological advancements.				
Strengthen public-private collaborations to accelerate the adoption of personalised prevention technologies. (Mid-term)	Launch an EU platform for regular dialogue between regulators, founders, researchers, and private sector stakeholders, with incentives such as tax-deductible contributions for industry associations, and share knowledge for new products development (Short term)	Enhance PPP to advance personalised prevention technologies	A functional platform with hybrid biannual meetings, opportunities and policy recommendations .	EC in partnership with national authorities and industry companies and associations.	Innovative Health Initiative (IHI)	EU grants, industry contributions by tax benefits	Number of meetings held; number of actionable policy recommendations . Private companies /industry/ researchers and national health authorities satisfaction survey results.
Harmonize regulatory standards across the EU to	Establish a working group to align EU regulations with	Regulatory environments that hinder innovation	EU-wide harmonized guidelines for regulatory	EMA and national regulatory authorities and	Digital Europe	EU grants, industry contributions by tax benefits	Number of harmonized regulatory documents

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facilitate private sector innovation in personalised prevention complying with GDPR, EHDS and ethical principles. (Mid-term)	innovative tools, products and approaches including AI for personalised prevention (Medium) .	through personalised prevention . Regulatory frameworks struggle to keep pace with rapid advancements in digital health technologies, delaying market adoption.	approval of personalised prevention products and solutions including AI use in development and update of the product.	PROPHET consortium as consultant.			published. Number of recommendations on personalised prevention published. - Number of new products, solutions for personalised prevention approved in a 10 year period. Private companies and national health authorities satisfaction survey results.
Access, Equity and Coverage (Challenge 8 of SRIA)							
Goal (Priority level*)	**Action (Expected Timeline for the implementation **)**	**Obstacle**	**Outcome**	**Responsible for the action**	**Other EU initiatives with the same objective**	**Funding sources**	**Output indicator**

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Ensuring sustained investment in prevention programmes (Immediate)	Implement funding programmes for patient/citizens involvement in research to ensure equity and accessibility of prevention to all Implement funding programmes for infrastructure to support prevention actions (e.g. to make routine check-ups more available and accessible) (Medium)	Lack of incentives and resources to systematically integrate prevention in healthcare (and encourage a paradigm/ cultural shift from care to prevention)	Increased uptake of prevention measures among entire population, including children and vulnerable groups (higher number of check-ups, vaccination rates, etc.) Increased involvement of patients/ citizens (in research, design of funding schemes, etc.)	EU/ national/ regional/ local policymakers in collaboration with health care professionals, patients, citizens, researchers, civil society (to ensure funding programmes adequately meet population needs)		EU, national, regional, local funding (health budgets, research budgets, etc.)	Number of new funding programmes for prevention (research, etc.) Comparative budget amounts for prevention programmes over time Impact and reach of funding programmes, determined through evaluations Availability of long-term plans for prevention funding at governmental level Number of scientific publications on prevention including

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							patient/citizen participation
Citizen access to, understanding of, and trust in digital health technologies (Immediate)	Trust – regulatory frameworks to ensure equitable and ethical data sharing to shared principles that support patient privacy, Access –ensuring analogue alternatives, accessibility through different platforms, understanding of national/ regional/local characteristics, and personal choice to disengage from digital health technologies	Health inequalities arising from access to digital technologies or from inherent biases within the technologies. Poor patient engagement in healthcare due to lack of trust in technologies; integration of health data use in HC/personalised prevention practice	Citizen engagement with digital healthcare technologies, to support general health management (staying healthy) and healthcare interventions when unwell.	Governments and health systems; patient and other civil society organisations; technology developers	GDPR; European Health Data Space/ eHDSI/ TEHDAS, AI act, EU Medical devices regulations; standardisation activities; EU action plan on the cybersecurity of hospitals and HC providers; eHealth network	Integrated with costs for implementing Personalised Prevention programmes – government level funding.	Proportion of citizens who engage with digital health technologies. E.g. population surveys of use and views on technology

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	Understanding and trust – educational programmes and engagement activities (Medium)						
Ensure fair and equitable access to personalised prevention (Mid-term)	Develop policies ensuring accessibility and equitable distribution in personalised prevention initiatives (Long term)	Risk of unequal access to benefits	Balanced and transparent distribution of benefits resulting from personalised prevention approaches	Governments, regulatory bodies, healthcare providers, research funders	Towards the European Health Data Space (TEHDAS & TEHDAS2)	EU and national funding	Number of equity and access assessment reports
Ethical, Legal, Social Issues (Challenge 9 of SRIA)							

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Goal (Priority level*)	Action (Expected Timeline for the implementation **)	Obstacle	Outcome	Responsible for the action	Other EU initiatives with the same objective	Funding sources	Output indicator
Strengthen public trust and prevent discrimination in personalised prevention (Immediate)	Implement safeguards against misuse, promote inclusive communication strategies (Medium)	Risk of discrimination and stigmatization, public concerns over data privacy	Increased public awareness, improved trust in personalised prevention ,	Governments, healthcare funders, researchers, patient advocacy groups	Beyond One Million Genomes (B1MG) SafePolyMed	EU and national funding	Number of public awareness initiatives and engagement activities
Ensure data protection and responsible use of health data (Immediate)	Implement regulations on data sharing, standardise data formats (Medium)	Risk of unlawful data processing, maintaining database integrity	Strengthened data protection and security measures	Data Protection Agencies, Health Data Access Bodies, Data Access Committees	HealthData@EU, Cancer Image Europe (EUCAIM), European Health Data Evidence	EU and national funding	Compliance with data protection frameworks

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					Network (EHDEN) HetERogeneous sEmantic Data integratIon for the guT-bRain interplay (HEREDITARY)		
Harmonize health data sharing rules and support equitable access across EU member states (Mid-term)	Fund pilot cross-border data-sharing programs to test interoperability, governance frameworks, and citizen engagement Align national legislation Provide targeted financial support to countries with underdeveloped infrastructure	Fragmented governance, infrastructure, inequalities, and lack of citizen trust affect harmonization.	Increased policy alignment, interoperable systems, improved citizen trust and participation.	European commission, national governments, Horizon Europe/EU4Health Programme	EHDS implementation; TEHDAS; eHealth network; GDPR implementation	EU and National budgets, public-private partnerships.	No. of successful pilots No. of citizens and patients engaged in pilots No. of Member states adopting standards No. of financial support initiatives

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	(Short term for setting up a platform Medium for pilots and infrastructure improvement)						
Address risks of linking different data sources (Immediate)	Develop robust guidelines for cross-linking safeguards (Medium)	Potential privacy breaches and misuse of data	Ethical and legal framework for responsible data linkage	EU regulators	Towards the European Health Data Space (TEHDAS & TEHDAS2), European Health Data Evidence Network (EHDEN) SHAIPED Better Project	EU and national funding	Number of established guidelines and regulatory frameworks for secure data linkage adopted at national and EU levels.
Promote international collaboration to address ethical, legal, and social issues in personalised prevention (Immediate)	Establish international research consortia and partnerships to share knowledge, best practices, and resources (Medium)	Coordinating efforts across different legal and regulatory frameworks, managing cross-border data sharing, and	Established international research consortia, increased cross-border collaborations, and shared ELSI frameworks.	International research organizations, governments, academic institutions.	Global Alliance for Genomics and Health (GA4GH)	International research grants, EU funding programs	Number of international collaborations, joint research publications, shared ELSI guidelines.

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**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

.		aligning research priorities.					
Establish ethical guidelines for the use of emerging technologies in personalised prevention (Mid-term) .	Create a multidisciplinary task force to develop guidelines addressing the ethical implications of technologies such as AI, genomics, and digital health tools (Medium)	Keeping pace with rapid technological advancements and ensuring guidelines are comprehensive and up-to-date.	Published ethical guidelines, increased adherence to ethical standards in technology use.	Ethics committees, technology developers, regulatory bodies.	Towards the European Health Data Space (TEHDAS & TEHDAS2) EP PerMed	International research grants, EU funding programs	Number of guidelines published, compliance rate.
Ensure that public-private partnerships in personalised prevention adhere to high ethical standards. (Mid-term)	Create a task force to develop ethical guidelines for public-private partnerships, focusing on transparency, accountability, and equitable access (Medium).	Balancing commercial interests with ethical considerations and public good.	Increased adherence to ethical standards in public-private partnerships.	Regulatory bodies, industry associations, patient organisations, civil society organisations	Towards the European Health Data Space (TEHDAS & TEHDAS2) IDERHA	EU funding programs, private sector investment	Compliance rate among public-private partnerships.

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

Behavior challenge (Challenge 10 of SRIA)							
Goal (Priority level*)	**Action (Expected Timeline for the implementation **)**	**Obstacle**	**Outcome**	**Responsible for the action**	**Other EU initiatives with the same objective**	**Funding sources**	**Output indicator**
More research is needed on acceptability, ethics and effectiveness of information and health-related choices regarding pharmacogenomics and lifestyle-related advice based on genetic susceptibility (Immediate)	Research on acceptability, ethics and effectiveness of information and health-related choices on pharmacogenomics and lifestyle-related advice based on genetic susceptibility (Long term)	Fields of public health, genetics and pharmacy are different pillars Communicating the risk is not sufficient to change behavior Joining data from various sources is challenging and potentially over-regulated	Publications on acceptability and effectiveness of health information based on genetic information	Academia Funders of research Regulators EMA	Implementation of Personalized risk stratification for cancer and other NCDs - JA PreventNCD	COST action EU and national research grants	Number of publications
Understanding the influence on motivation of the context of being offered a test or	Research to understand the influence of potential contexts (Long term)	Communicating the risk is not sufficient to change behavior	Publications on (motivation for) behaviour change	Academia Funders of research	add Ethical, Legal, and Social Aspects and Implications of Direct-to-	EU and national research grants	Number of publications

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tool (e.g. commercial versus healthcare system) (Immediate)					Consumer Genetic Testing | ELSAIDTCGT |		
Personalized prevention should target non-affected family members of affected individuals (Immediate)	Develop strategies/ tools respecting confidentiality to inform family members (Medium)	Inform family members at high risk and motivate them for behaviour change Some countries forbid passing genetic information to relatives, even next-of-kin	Modules to inform family members	Public health, Academia, Professionals from organisations who offer or develop personalised prevention policies, ESHG, Regulators, lawmakers, Patient advocacy groups	add Can.Heal | Building the EU genomics platform	add EU and national research grants	Number of modules to inform family members Implementing or improving regulation
Personalised prevention should integrate polygenic risk scores (PRS) where and when	Determine clinical utility of risk prediction with PRSs (Long term) alone and in combination with other	PRS usually confer only a part of the total risk and it gives somewhat limited scope of the genome.	Assessment of PRS or integrated risk prediction tools disease prediction	Academia Funders of research Professional medical	Can.Heal | Building the EU genomics platform	EU and national research grants	Number of publications on clinical utility of specific PRSs (integrated in combined risk modules)

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clinically utility has been proven (Mid-term)	environmental risk factors	It is population-specific and is hard to apply in mixed populations.		organizations (ESHG, ASHG)			

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Funded by the European Union

List of acronyms and abbreviations

European Union (EU)

Artificial Intelligence (AI)

European Reference Networks (ERNs)

Member State Coordination Group on HTA (HTACG)

Standard Operating Procedures (SOPs)

Entrustable Professional Activities (EPAs)

Personalized CANcer Primary Prevention research through Citizen Participation and digitally enabled social innovation (4-PCAN)

International Consortium of Personalised Medicine (ICPerMed)

European Reference Network (ERNs)

European Partnership for Personalized Medicine (EP PerMed)

Member State Coordination Group on HTA (HTACG)

International Consortium for integrative genomics prediction (INTERVENE)

*** Priority level (goal):** Immediate : within 2 years Mid-term: within 5 years Long-term: within 10 years

**** Expected timeline (action):** Short term (1-3 years) Medium (4-6 years) Long-term (7-10 years)

Funded by the European Union

JUNE 2025

STRATEGIC RESEARCH AND INNOVATION AGENDA (SRIA) ON PERSONALISED PREVENTION

PROPHET

a PeRsOnalized Prevention roadmap
for the future HEalThcare

Abstract

What is personalised healthcare ?

Personalised prevention is an emerging approach that uses individual data—such as genetics, lifestyle, and environment—to help prevent diseases before they develop. It shifts healthcare from reactive treatment to proactive risk reduction, empowering citizens and improving population health.

What the roadmap is trying to achieve ?

The Strategic Research and Innovation Agenda (SRIA), developed by the PROPHET project, identifies the main challenges and priorities for integrating personalised prevention into healthcare systems across Europe. It presents a roadmap based on the latest scientific evidence, stakeholder engagement, and policy analysis. Ten key challenges are explored, including data integration, ethical and legal issues, health equity, public engagement, and behaviour change.

What's next ?

We are now opening a public consultation to collect feedback on the draft SRIA. Professionals, policymakers, and citizens are invited to review the document, suggest additional priorities, and propose actions to enhance its relevance and impact. Your input will help ensure that the SRIA reflects shared societal needs and supports effective, fair, and sustainable implementation across Europe.

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Rapid SRIA overview

Strategic research and innovation agenda (SRIA) on personalised prevention

The paper reflects on 10 challenges for the implementation of personalised prevention in healthcare, empowering individuals to take control of their health and well-being.

The 10 challenges were identified on the basis of the latest research advancements in the field and after incorporating the views of the consortium partners and stakeholders.

The final outcome is a **more effective, efficient and citizen-centered preventive approach gathered in a document called concept paper.**

For each challenge, state of the art, gaps, priorities, implementation, and final considerations are detailed.

The SRIA outlines the major areas that must be addressed in order to fully realize the potential of personalised prevention.

- **Challenge 1 : The broad scope of promotion and prevention**
- **Challenge 2: Continuous evidence synthesis system supporting personalised prevention**
- **Challenge 3: The PROPHET Framework implementation**
- **Challenge 4: Data collection & integration, & Data Infrastructure**
- **Challenge 5: Community Engagement and trust**
- **Challenge 6 : Health Professionals and Policy Makers involvement**
- **Challenge 7: Regulatory aspects and synergy with private sector**
- **Challenge 8: Access, Equity and Coverage**
- **Challenge 9: Ethical, Legal, Social Issues (ELSI)**
- **Challenge 10: Changing behaviour**

I) The challenges of personalised prevention

Challenge 1 : The broad scope of promotion and prevention

📌 Context & Importance

- Chronic disease prevention involves complex interactions between lifestyle, environment, biology and social context
- The potential of a “precision dividend” lies in combining -omics advances (genomics, exposomics, microbiomics…) with public health strategies
- Emerging technologies must be integrated with broader social and environmental determinants to realise effective, personalised prevention

🔍 Research Gaps

- Limited integration of clinical, environmental and socioeconomic data
- Underexplored interactions between genes and modifiable risk factors (diet, pollution, stress…)
- Lack of external validity and representativeness of biomarker research
- Societal determinants under-addressed in omics-based prevention studies

🎯 Priorities & Implementation

1. Integrate omics with social, environmental and behavioural data
2. Strengthen population-based cohort studies with diverse, multimodal data
3. Focus on biomarkers reflecting modifiable risk factors
4. Leverage AI and wearables for data interpretation and real-time feedback

🚀 Key Considerations

- Multi-level integration: Prevention must operate across individual, community, and systemic levels
- Behavioural science is essential: predictive knowledge is insufficient without strategies for behavioural change
- Political, social and infrastructural barriers must be addressed for equitable access and implementation
- Climate, commercial determinants and inequalities are evolving and must be accounted for in personalised approaches

Challenge 2 : Continuous evidence synthesis system supporting personalised prevention

📌 Context & Importance

- Advances in genetic and ‘omics’ technologies improve disease prediction, but robust and continuous evidence is needed to demonstrate their real-world effectiveness (clinical utility)
- Integration requires not only clinical validation, but also consideration of ethical, contextual and societal dimensions

🔍 Research Gaps

- Lack of robust data on clinical efficacy
- Limited evidence on cost-effectiveness, equity, feasibility, ethics
- Insufficient quality control across omics fields
- Findings often not transferable across healthcare systems

🎯 Priorities & Implementation

1. Develop alternative study designs (e.g. focused RCTs, modelling)
2. Expand primary evidence (including PROs, contextual data)
3. Standardise & synthesise evidence with clear quality criteria
4. Integrate into health systems: interoperability, privacy, local adaptability
5. Include ethical and societal dimensions in evaluation

🚀 Key Considerations

- Adaptability to rapid technological change requires dynamic frameworks
- Investment must support both efficacy and broader impact studies
- Standardised methods are essential for transparency and reliability
- Ethical concerns (e.g. informed consent, equity) must guide implementation
- Multisectoral coordination is key to system-level integration

Challenge 3 : The PROPHET Framework implementation

📌 Challenge

- No widely accepted criteria for evaluating genetic & genomic tests in preventive healthcare, leading to inconsistent adoption across countries
- New EU HTA regulation (2025) aims to unify assessments but still lacks comprehensive evaluation beyond clinical efficacy and cost-effectiveness

🔍 Key Gaps

- Limited primary evidence makes informed decision-making difficult
- Lack of consensus on dimensions and indicators for evaluation
- Traditional HTA undervalues feasibility, acceptability, equity, and social determinants
- Broader societal impacts and stakeholder perspectives often neglected

🎯 The PROPHET Framework: A Holistic Approach

1. Expands HTA evaluations to include health system & value-based perspectives
2. Integrates Health Impact Assessment (HIA) to assess feasibility, equity, and social implications
3. Engages diverse stakeholders (patients, clinicians, policymakers, communities) in the evaluation process
4. Includes structured monitoring to guide policy adaptation based on emerging evidence
5. Supports context-specific assessment (e.g. reimbursement policies, mandatory testing requirements)

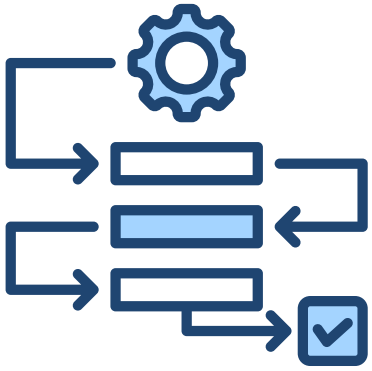
🚀 Key Considerations for Implementation

- Regulatory Alignment
- Stakeholder Engagement
- Comprehensive Evaluation
- Continuous Monitoring

Challenge 4 : Data collection & integration, & Data Infrastructure

📌 Challenge

Rapid expansion of life science data offers new opportunities to personalised prevention, but fragmentation, limited accessibility and poor integration hinder its potential.Infrastructure and data-sharing frameworks remain insufficient for complex, multi-sectoral data.Improved data management is essential.



🔍Key Gaps

- Lack of standardisation & poor data discoverability
- Limited accessibility due to legal, technical, and literacy barriers
- Fragmented and low-quality data impedes integration
- Low reproducibility due to missing metadata and inconsistent formats
- Data-sharing concerns (reidentification, security, consent)
- Limited infrastructure for federated, multi-modal, multi-sectoral data analysis

🎯 Priorities & Implementation

- Standardisation
- Discoverability
- Accessibility
- Reproducibility
- Secure Data Sharing
- Integration
- Clinician-Friendly Tools
- Interdisciplinary Cooperation

🚀Key Considerations

- Link diverse data for prevention research.
- Build capacity in key data functions.
- Improve metadata for AI integration.
- Ensure secure, interoperable systems.
- Align standards through joint governance.

Challenge 5 : Community Engagement and trust

📌 Challenge

- Personalised prevention requires well-informed citizens and patients actively involved in research, care, and governance.
- Yet awareness of genetics and participation options remains low, and engagement practices are fragmented across sectors.

🔍 Key Gaps

- Limited public knowledge and information on genetics and personalised prevention
- Health professionals lack training and time to guide patients
- Engagement efforts lack structure, evaluation, and continuity
- Coordination across sectors (health, education, policy) is weak
- Vulnerable groups face barriers due to limited digital and health literacy

🎯 Priorities and implementation

1. Engage and empower citizens,patients and their associations
2. Boost education and awareness
3. Ensure structural funding for engagement
4. Develop inclusive digital tools
5. Foster cross-sector coordination

🚀 Why It Matters

- Building trust and engagement is essential for personalised prevention. Informed citizens and patients can better understand risks, participate in decisions, and contribute to research—leading to more inclusive, culturally sensitive, and effective healthcare.

Challenge 6 : Health Professionals and Policy Makers involvement

📌 Challenge

Healthcare professionals and policymakers are key to implementing personalised prevention but lack training, resources, and coordinated engagement.

🔍 Key Gaps

- Lack of economic models and cost-effectiveness evidence
- Gaps in training for non-genetic professionals
- Fragmented policymaking and insufficient coordination

🎯 Priorities & Implementation

- Train professionals on personalised prevention, equity, and data use
- Build policymaker capacity through tailored education tools
- Develop national action plans to align practices and policies

Challenge 7 : Regulatory aspects and synergy with private sector

📌 Challenge

- Public-private partnerships (PPPs) are essential for innovation in prevention, but fragmented regulations, privacy concerns, and lack of trust hinder collaboration.

🔍 Key Gaps

- Inconsistent regulations across countries
- Unclear data-sharing and secondary data use rules
- Public scepticism toward private sector engagement

🎯 Priorities

- Create regulatory sandboxes and shared platforms
- Incentivise responsible private partnerships with safeguards
- Align EU-level rules for wearable data, DTC tests, and PPPs
- Evaluate PPPs regularly and educate citizens on benefits

Challenge 8 : Access, Equity and Coverage

📌 Challenge

- Personalised prevention must be universally accessible, but socio-economic inequalities, health literacy gaps, and digital exclusion hinder fair implementation across Europe.

🔍 Key Gaps

- Low health literacy and limited preventive care uptake among vulnerable groups
- Digital exclusion and underuse of e-health tools
- Unequal reimbursement and access across EU countries

🎯 Priorities and implementation

1. Strengthen health & digital literacy through targeted outreach and inclusive communication
2. Integrate personalised prevention in national health systems with equitable reimbursement
3. Support affordable digital tools via cross-sector partnerships (incl. private sector)
4. Promote EU-level harmonisation to ensure fair access and rights

Challenge 9 : Ethical, Legal, Social Issues (ELSI)

📌Challenge

Personalised prevention depends on sensitive data, raising concerns over consent, privacy, fairness, and ethical use.

🔍Key Gaps

- Unclear consent and data-sharing practices
- Risks in linking datasets and commercial use
- Limited public trust and unclear benefit evidence

🎯Priorities & Implementation

- Strengthen informed consent tools
- Build trust with transparent communication
- Address equity, access, and fair use of outcomes
- Promote collaborative ELSI research

Challenge 10: Changing behaviour

📌Challenge

- Behaviour change is crucial for prevention but complex—mere information is not enough to drive action.

🔍Key Gaps

- Misunderstandings of genetic risk and determinism
- Low uptake of preventive actions and testing
- Lack of personalised, motivating communication

🎯Priorities

- Improve communication tools using behavioural science
- Design tailored, multi-level interventions (e.g. nudges, reminders)
- Promote informed, autonomous decision-making with ethical messaging

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II) Background and Methodology

About PROPHET

48 months

18 partners

12 countries

Funded by the European Union

develop a comprehensive roadmap for integrating personalised prevention into European healthcare systems

10 expected oucomes:

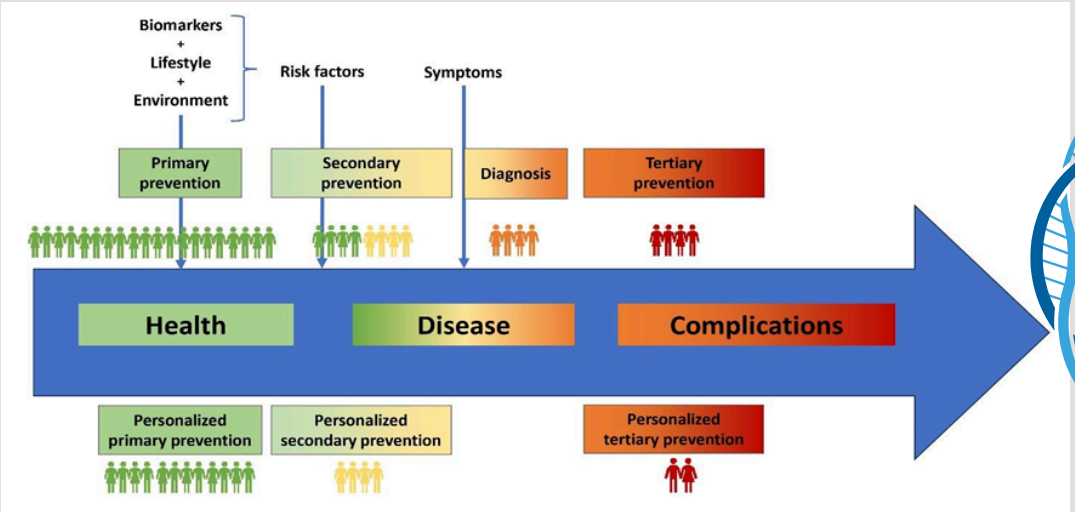
- Comprehensive Personalised Prevention Roadmap
- Strengthened Collaborative Ecosystem
- In-Depth Research Advancements
- Evaluative Frameworks and Indicators
- Empowered Public Health Authorities
- Raised Awareness Among Citizens, Patients and healthcare profesionals + citizen engagement
- Informed Policymakers & Stakeholders
- Drafting of the Strategic Research and Innovation Agenda (SRIA) on Personalised Prevention

Why personalised prevention?

Chronic diseases remain the main cause of morbidity and mortality in Europe.

The traditional reactive healthcare model, which focuses on treating established diseases, must evolve into personalised prevention, which prioritises early diagnosis and risk reduction.

to learn more, click here



Description of the three levels of prevention, according to the disease stage

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3 types of prevention

- 🏥**Primary Prevention:** Aims to prevent the onset of diseases before they occur by addressing risk factors (e.g., vaccination, healthy lifestyle promotion).
- 🩺**Secondary Prevention:** Focuses on early detection and timely intervention to prevent disease progression (e.g., cancer screening).
- 💊**Tertiary Prevention:** Seeks to reduce complications and improve the quality of life in individuals with established diseases (e.g., rehabilitation programs, personalized treatments).

What data drives PROPHET's personalised prevention?

One of the fundamental theoretical underpinnings of PROPHET is the "Vision Paper on Personalised Medicine Research & Implementation by 2030" by ICPerMed.

PROPHET personalised prevention focus on individual omics data :

genomics, metabolomics, proteomics, radiomics, epigenomics

Clinically actionable applications

- 🚀 **Genetic Testing for High-Risk Pathogenic Variants** – Identifying individuals with significant genetic predispositions.
- 📊 **Polygenic Risk Scores (PRS)** – Estimating disease susceptibility based on multiple genetic markers.
- 💊 **Pharmacogenomics** – Tailoring drug therapies to individual genetic profiles for enhanced treatment efficacy.

These applications highlight the practical aims of this initiative and serve as focal points for **advancing personalised prevention through clinically actionable genomics data.**

Promising Stories in Personalised Prevention

Estonia

The e-Health system and national biobank facilitate secure access to medical data and enhance healthcare practices.

Finland

Tools allow citizens to assess their risk of type 2 diabetes and adapt their lifestyle accordingly.

Studies like P5.fi and GenomeHealth integrate genetic data into preventive medicine.

PROPHET Synergies with Other Initiatives

The EU Cancer Plan

Promotes personalised prevention, particularly within the framework of the 31.2 Roadmap to Personalised Prevention.

ICPerMed and EP PerMed

Bring together 60 European partners to advance personalised medicine in healthcare systems.

The 1+Million Genomes (1+MG) and Genomic Data Infrastructure (GDI) initiatives

Facilitate secure access to genomic data to enhance research and healthcare services.

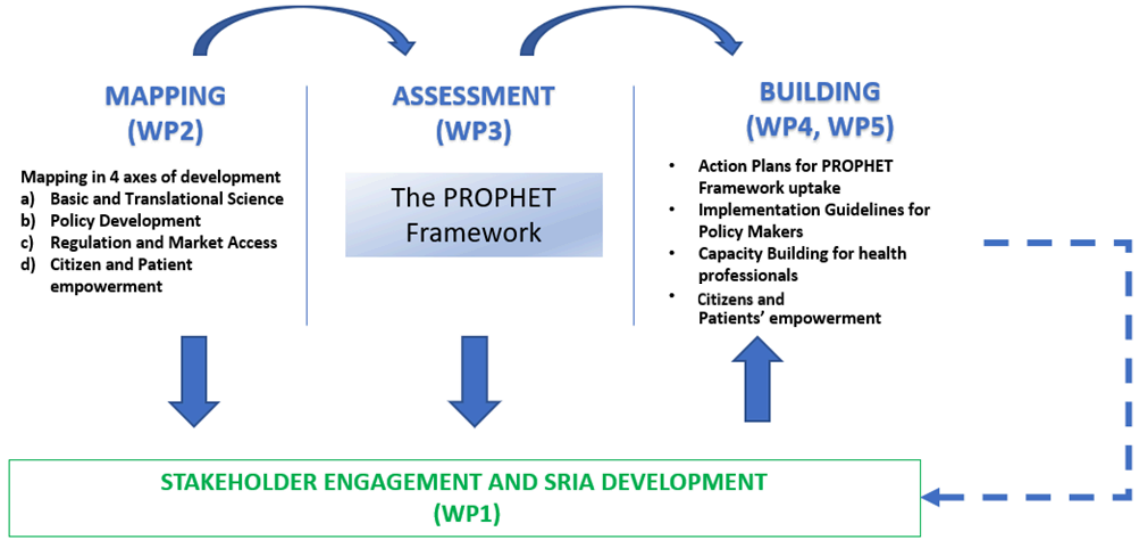
The European THCS Partnership

Supports healthcare system transformation by promoting digitalisation and innovation for a more sustainable and efficient care model.

Methodology for SRIA Development

The SRIA is based on three key phases of the PROPHET project:

- **Mapping**: In-depth analysis of the state of personalised prevention in Europe and beyond.
- **Assessment**: Evaluation of approaches before their implementation.
- **Building**: Presentation of the results from the concrete application of the PROPHET methodology.



Concept Paper for Personalised Prevention

Need

Balance between targeted interventions for high-risk groups and preventive actions for the general population.

Challenges

- data access
- ethics and community engagement
- integration of interventions into the healthcare sector
- health inequalities
- large-scale implementation

Strategy

Based on data integration (biomarkers, lifestyles, environmental factors) and a multisectoral approach, involving all healthcare stakeholders.

To maximise its impact, PROPHET advocates for a comprehensive prevention approach, combining technological advances and data integration into public health policies.

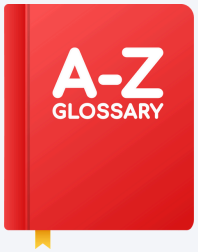
Stakeholder Engagement Strategy

1. Stakeholder mapping process
2. Engagement strategy
3. PROPHET forum

Delphi Consultation

The Delphi consultation was a structured, multi-phase process designed to gather expert insights and build consensus on the SRIA, ensuring it addressed key priorities for personalised prevention. It began with the Stockholm 2024 workshop, during which stakeholders reviewed the draft SRIA, engaged in discussions, and provided feedback through structured rounds, refining priorities over five months before progressing to the next phase.

This inclusive approach ensures the SRIA reflects diverse perspectives and leads to a more impactful and widely accepted strategy for personalised prevention.



Glossary box

- **Omics sciences**: A group of scientific fields that study different types of biological data (like genes, proteins, or metabolites) to better understand how the body works.
- **Biomarkers**: Biological indicators (such as molecules in blood or tissues) that can signal the presence of a disease or the effects of a treatment.
- **Genomics**: The study of all genes in a person's DNA and how they interact with each other and the environment.
- **Exposomics**: The study of all the environmental exposures a person experiences throughout life and how these affect their health.
- **Microbiomics**: The study of the microorganisms (like bacteria and fungi) living in and on the human body, and their role in health and disease.
- **Genetic**: Relating to genes or heredity—how traits and conditions are passed from parents to children through DNA.

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To find more about the PROPHET rapid scoping review, check the corresponding deliverable: **HERE**.

More about the project on our website: https://prophetproject.eu/
And follow us on LinkedIn:

@PROPHET.EU

JUNE 2025

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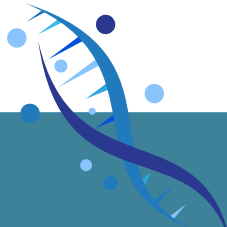

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Roadmap overview

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The final outcome is a **more effective, efficient and citizen-centered preventive approach gathered in a document called concept paper.**

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Challenge 1 : The broad scope of promotion and prevention

🧭**Context**:
Personalised prevention should move beyond genetic and clinical risks to incorporate behavioural, social and environmental determinants.

Priorities and actions:

- 🧬 Integrate omics, environmental, social and behavioural data
- 🧪 Strengthen population-based prevention studies
- 🔬 Use biomarkers to monitor modifiable risk factors
- 🤖 Leverage wearable technologies

Obstacles:

- 🔄 Fragmented data and governance
- 🧩 Disconnected preventive policies
- 📉 Limited behavioural data in health systems

Expected results:

- 🌍 Population-sensitive prevention strategies
- 📲 Scalable personalisation tools
- 🔗 Better coordination of services

Actors responsible:

- 🏛️ Policymakers, citizens, EU
- 🩹 Professionals
- 🎓 Research community

Funding sources:

- 🏛️Eu calls and European Commission fundings (Horizon Europe, EU4Health...)

Similar EU-funded initiatives:

- 🧬 PARC
- 🧠 EXPANSE
- 🌐 1+Million Genomes

Output indicators:

- 📌 Number of integrated prevention initiatives
- 📲 Uptake of digital and behavioural tools
- 🎯 Share of targeted populations reached
- 👥Number of member states, citizen, patient and scientific publications

Challenge 2: Continuous evidence synthesis system supporting personalised prevention

📌 Context

- Real-world, quality evidence is essential to validate the effectiveness and impact of personalised prevention tools.

🔍Priorities and actions

- Promote pragmatic and real-world study designs
- Systematise synthesis of population-specific evidence
- Link evidence generation with health system use
- Include ethical and social dimensions

🎯 Obstacles:

- Heterogeneity of methodologies
- Disconnection from implementation pathways
- Limited multidisciplinary frameworks

🚀Expected results

- Strong evidence base for decision-making
- Transparent validation procedures
- Scalable good practices

🏛️Actors responsible

- Research institutions
- HTA bodies
- Public health authorities

💶Funding sources :

- Horizon Europe
- Joint Programming Initiatives (JPI)
- EU4Health

🧬Similar EU-funded initiatives

- ICPerMed, EPPerMed
- EHDS, Horizon Europe ERNs
- Member State HTACG

📈Output indicators

- Number of context-adapted evaluations
- Guidance documents published
- Uptake of evidence by policymakers

Challenge 3 : The PROPHET Framework implementation

🧭Context:
A common evaluation framework is needed to assess personalised prevention tools beyond clinical outcomes, including feasibility, social value and ethical considerations.

Priorities and actions:

- 📊 Expand Health Technology Assessments (HTAs) to include system-wide and societal impacts
- ⚖️ Integrate Health Impact Assessment (HIA) criteria
- 👥 Engage citizens and stakeholders in evaluation processes
- 🔄 Create structured monitoring and policy feedback systems
- 🌍 Support context-specific assessments (e.g. reimbursement, accessibility)

Obstacles:

- 🧱 Lack of harmonised evaluation criteria across countries
- 📉 Weak integration of feasibility and social value dimensions
- 👥 Limited stakeholder involvement in decision-making

Expected results:

- 📊 Coherent and accepted evaluation methodologies
- 🧩 Improved policy alignment across Member States
- 📚 Broader inclusion of ethical and social impacts in assessments

Actors responsible:

- 🧮 HTA agencies
- 🏛️ Health ministries
- 🎓 Research institutions and universities

Funding sources:

- 🏛️ Horizon Europe
- 💡 Digital Europe
- 🩺 EU4Health

Similar EU-funded initiatives:

- ⚙️ EUnetHTA
- 🧠 PERMIT
- 🧬 IHI projects on precision prevention

Output indicators:

- 🟦 Number of evaluations using PROPHET Framework
- 🔍 Inclusion of equity, feasibility and acceptability in assessments
- 🔁 Monitoring and adaptation processes in place

Challenge 4: Data collection, integration & Data Infrastructure

📌 Context

- Secure, interoperable and FAIR-compliant infrastructure is vital for combining omics, clinical, environmental, and social data.

🔍 Priorities and actions

- Link multimodal data across platforms and institutions
- Improve metadata quality and data discoverability
- Ensure privacy, data security and governance
- Facilitate AI-ready, interoperable systems

🎯 Obstacles:

- Fragmented infrastructure and siloed data systems
- Legal, technical, and literacy-related barriers
- Low reproducibility and poor standardisation

🚀 Expected results

- Increased data integration across disciplines
- Higher data quality and reuse
- Infrastructure enabling personalised prevention research and services

🏛️ Actors responsible

- National and EU health data authorities
- Research infrastructure bodies (e.g. ELIXIR)
- Data protection agencies

💶 Funding sources :

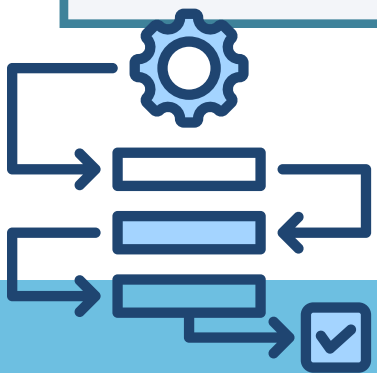
- Horizon Europe
- Digital Europe
- EU4Health

🧬 Similar EU-funded initiatives

- European Health Data Space (EHDS)
- TEHDAS
- 1+Million Genomes Initiative

📈 Output indicators

- Number of interoperable systems deployed
- Compliance with FAIR and GDPR principles
- Increase in data reuse for prevention



Challenge 5: Community Engagement and trust

🧭**Context**:
Public trust and informed participation are essential for equitable and effective implementation of personalised prevention.

Priorities and actions:

- 🧠 Raise awareness and improve health literacy
- 🤝 Engage citizens in co-design and decision-making
- 🌐 Develop inclusive and accessible digital tools
- 💶 Ensure structural funding for engagement
- 🔄 Promote intersectoral collaboration (e.g. education, municipalities)

Obstacles:

- 📉 Low awareness of personalised prevention
- 🌐 Digital and health literacy divides
- 📉 Weak continuity and evaluation of engagement

Expected results:

- 🧠 Improved citizen empowerment
- 🤝 More inclusive and trust-based healthcare models
- 📈 Increased participation and adoption of tools

Actors responsible:

- 👩‍🤝‍👨 Civil society organisations
- 🏛️ Local authorities and health ministries
- 🧫 Research institutions

Funding sources:

- 🏛️ Horizon Europe
- 🩺 EU4Health
- 🤝 Public-private partnerships

Similar EU-funded initiatives:

- 🔬 Genomics4All
- 💬 1Million Genomes' Citizen Juries
- 🌍 TEHDAS (engagement module)

Output indicators:

- 🧭 Number of citizens engaged
- 📊 Trust and literacy level improvements
- 💬 Stakeholder satisfaction indicators

Challenge 6 : Health Professionals and Policy Makers involvement

📌 Context

- Capacity building for professionals and policymakers is critical to foster system-wide adoption of personalised prevention.

🔍Priorities and actions

- Provide interdisciplinary training on genomics, data, ethics
- Develop educational tools for policymakers
- Promote national prevention strategies with coordinated action plans

🎯 Obstacles:

- Insufficient training in prevention for non-genetic professionals
- Fragmented or inconsistent policy frameworks
- Lack of integration between research and practice

🚀Expected results

- Enhanced health workforce capacity
- Better policy alignment and coordination
- Efficient translation of research into policy

🏛️Actors responsible

- Training institutions and health professional bodies
- Ministries of Health and Education
- Policy think-tanks

💶Funding sources :

- Horizon Europe
- EU4Health
- Structural Funds (ESF+)

🧬Similar EU-funded initiatives

- BeWell
- Ongoing IHI training modules
- EU Cancer Mission’s workforce strategies

📈Output indicators

- Number of professionals trained
- Availability of national guidance documents
- Adoption of national prevention strategies

Challenge 7: Regulatory aspects and synergy with private sector

🧭**Context**:
Clear regulatory frameworks and trusted public-private partnerships are key to advancing responsible innovation.

Priorities and actions:

- ⚖️ Develop EU-aligned regulatory sandboxes
- 🤝 Foster open platforms and co-regulatory mechanisms
- 💶 Align incentives and clarify liability and benefit-sharing
- 👨‍💼 Empower citizens with transparent communication on data use

Obstacles:

- 🔀 Fragmentation in national regulatory environments
- 🔐 Uncertainty on data sharing and secondary uses
- 💬 Public mistrust toward private sector

Expected results:

- 🧭 Harmonised and trusted regulatory pathways
- 💡 Responsible innovation in personalised prevention
- 📊 Increased citizen acceptance and participation

Actors responsible:

- ⚖️ Regulatory authorities and ethics councils
- 🏛️ EU and national policymakers
- 👨‍💼 Industry and innovation hubs

Funding sources:

- 🏛️ Horizon Europe
- 💶 InvestEU
- 🧪 National innovation funds

Similar EU-funded initiatives:

- 🔐 TEHDAS
- 🧠 IHI PPP projects
- ⚖️ EHDS governance pilot

Output indicators:

- ⚖️ Regulatory frameworks adopted
- 🟦 Co-regulation platforms created
- 🔍 Increased participation in innovation pilots

Challenge 8: Access, Equity and Coverage

📌 Context

- Access, equity, and trust in personalised prevention depend on sustained investment, fair digital inclusion, and the ethical use of technologies. There is a need to shift from treatment to prevention, supported by robust public funding, inclusive infrastructures, and citizen confidence in digital tools.

🔍 Priorities and actions

- Fund citizen involvement in prevention research.
- Support infrastructure for accessible check-ups.
- Ensure ethical rules and data privacy in digital health.
- Provide analogue and accessible options.
- Launch education campaigns on digital health.
- Develop policies for fair benefit distribution.

🎯 Obstacles:

- Few incentives to shift from care to prevention.
- Digital inequalities and biases in technologies.
- Low patient trust in digital tools.
- Unequal access to benefits of personalised prevention.

🚀 Expected results

- More people use prevention services (e.g. check-ups, vaccines).
- Citizens participate more in research and decision-making.
- Digital tools help people manage their health.
- Prevention benefits are distributed fairly & transparently.

🏛️ Actors responsible

- EU, national, regional, local policymakers.
- Health professionals, citizens, researchers, civil society.
- Technology developers, governments, regulators.
- Healthcare providers, research funders.

💶 Funding sources :

- EU, national and local health and research budgets.
- Government funding linked to personalised prevention.

🧬 Similar EU-funded initiatives

- EHDS, TEHDAS & TEHDAS2.
- GDPR, AI Act, eHealth Network.
- EU plan on hospital and provider cybersecurity.

📈 Output indicators

- Number and size of prevention programmes.
- Population use and views on digital health tools.
- Long-term funding plans at government level.
- Reports on access and equity.

Challenge 9 : Ethical, Legal, Social issues

🧭Context:
Personalised prevention raises new ethical and legal concerns. Action is needed to ensure trust, fairness, and data protection, especially in international and cross-sector contexts.

Priorities and actions:

- 🔒 Create ELSI guidelines and communication safeguards
- 📜 Harmonise data protection rules across borders
- 🤝 Align public-private partnerships with ethical standards
- 🌍 Support international ELSI cooperation and capacity building

Obstacles:

- ⚠️ Data misuse, privacy breaches, and discrimination risks
- ⚖️ Complex legal environments and lack of common standards
- 🧠 Ethical issues in fast-moving technologies (AI, genomics…)
- ⚙️ Difficulty in balancing public good and private interests

Expected results:

- ✅ Improved trust and awareness
- 🟦 Clear ELSI rules at EU and national levels
- 🛡️ Ethical data practices in R&I and health systems
- 🔗 Better international alignment on ELSI standards

Actors responsible:

- 🏛️ Governments, regulators, data protection agencies
- 👴⚖️ Ethics committees, academia, civil society
- 🏥 Industry, health funders, and patient organisations

Funding sources:

- 💶 EU and national public programmes
- 🏛️ Horizon Europe, EU4Health, Digital Europe
- 🏦 Private sector and international partnerships

Similar EU-funded initiatives:

- 🔗 TEHDAS, EHDEN, GA4GH
- 🟦 Towards EHDS, SHAI-PED
- 🧬 EP PerMed, EUCAIM, IDERHA

Output indicators:

- 📊 Number of guidelines published
- ✅ Compliance rates (data use, PPPs)
- 🌍 International ELSI collaborations and joint publications

Challenge 10: Changing behaviour

📌 Context

- More behavioural research is needed on personalised prevention. Existing disciplines (genetics, pharmacy, public health) remain siloed. Communicating genetic risk does not always change behaviour.

🔍Priorities and actions

- Study the acceptability and effectiveness of personalised prevention
- Research how context influences motivation and decision-making
- Investigate the behavioural impact of pharmacogenomics and lifestyle advice
- Develop strategies to inform and support high-risk family members.
- Determine when and where polygenic risk scores (PRS) have clinical utility

🎯 Obstacles:

- Difficulty translating risk communication into behaviour change.
- Legal limits on sharing genetic risk within families.
- Lack of coordination across scientific disciplines.
- PRS are population-specific and may misrepresent total risk.

🚀Expected results

- New evidence on behavioural drivers and motivation.
- Development of guidance modules for family communication.
- Validated tools for assessing PRS in clinical settings.

🏛️Actors responsible

- Academia and research funders.
- Public health authorities and regulatory bodies.
- Personalised prevention professionals and patient organisations.
- European agencies such as EMA, ESHG, ASHG.

💶Funding sources :

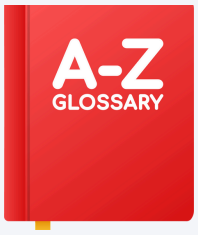
EU and national research grants.

🧬Similar EU-funded initiatives

- ELSAIDTCGT
- Can.Heal
- EU Genomics Platform

📈Output indicators

- Number of scientific publications.
- Number of modules developed to support family communication.
- Implementation of relevant regulation.
- Evidence on PRS use in combined risk tools.



Glossary box

- **Omics sciences**: A group of scientific fields that study different types of biological data (like genes, proteins, or metabolites) to better understand how the body works.
- **Biomarkers**: Biological indicators (such as molecules in blood or tissues) that can signal the presence of a disease or the effects of a treatment.
- **Genomics**: The study of all genes in a person's DNA and how they interact with each other and the environment.
- **Exposomics**: The study of all the environmental exposures a person experiences throughout life and how these affect their health.
- **Microbiomics**: The study of the microorganisms (like bacteria and fungi) living in and on the human body, and their role in health and disease.
- **Genetic**: Relating to genes or heredity—how traits and conditions are passed from parents to children through DNA.

PROPHET

a PeRsOnalized Prevention roadmap
for the future HEalThcare

To find more about the PROPHET rapid scoping review, check the corresponding deliverable: **HERE**.

More about the project on our website: https://prophetproject.eu/
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