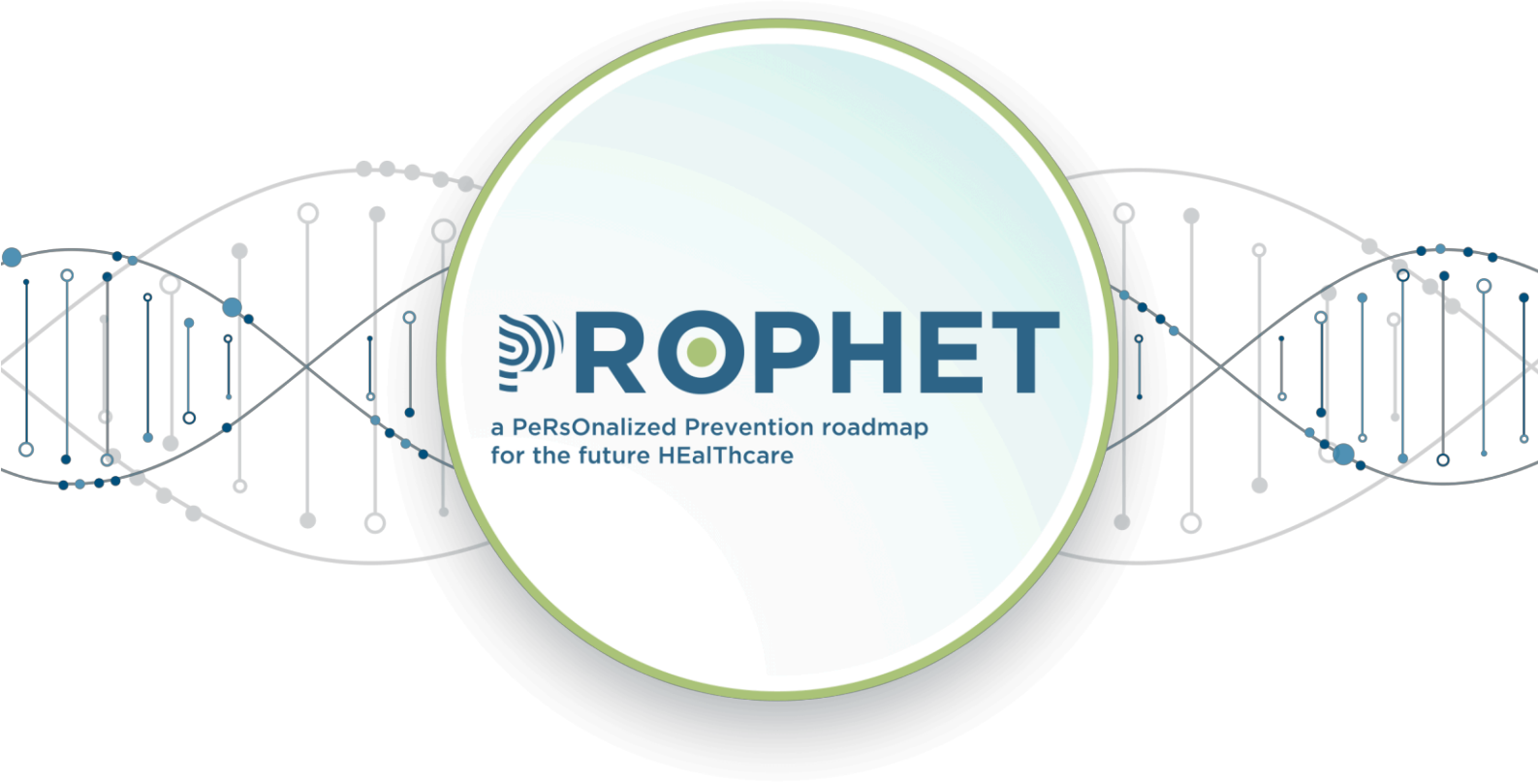

2.4. Report on critical factors for the successful adoption of Personalised Prevention approaches by healthcare systems

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Deliverable Abstract

Personalised prevention (PP) has gained prominence in the healthcare priorities of many nations, driven by advances in life sciences and digital technologies. This deliverable explores the outcomes of an extensive scoping review focused on personalised prevention approaches (PPA) and the insights from interviews and a survey targeted to stakeholders to identify primary bottlenecks and gaps that hinder PPA implementation, in Europe and beyond.

This activity has been conducted within the European Commission-funded project PROPHET (A PeRsOnalised Prevention roadmap for the future HEalThcare), that guides health systems in adopting innovative strategies for preventing chronic diseases sustainably.

Findings reveal that cancer is the primary target for PPA, followed by cardiovascular diseases, diabetes, and other diseases. Notably, tertiary prevention, including personalised target therapies, is prominent in cancer, while primary prevention, emphasising lifestyle changes for high-risk individuals, prevails in cardiovascular diseases and diabetes.

However, many of these approaches are still in the trial phase and not completely implemented and adopted in clinical practice.

Bottlenecks to PPA implementation, identified through literature and stakeholders consultations, encompass the lack of clinical utility and evidence, challenges in data management, limited omics science knowledge among healthcare professionals, and deficiencies in public health literacy and trust.

This work underscores the immense potential of PP to enhance population health and reduce chronic disease burdens on healthcare systems. To unlock these benefits, prioritising PP on research and policy agendas is crucial, ultimately benefiting citizens and patients alike. Addressing the identified bottlenecks is pivotal in realising the full potential of PPA and its transformative impact on public health.

Keywords

Personalised prevention, precision medicine, omic sciences, common diseases, chronic diseases, bottlenecks, gaps.

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Executive summary

This document, titled "Deliverable D2.4 - Report on Critical Factors for the Successful Adoption of Personalised Prevention Approaches in Healthcare Systems," is a product of the *A Personalized Prevention roadmap for the future Healthcare* (PROPHET) project, funded by the European Union's Horizon Europe Research and Innovation Programme under grant agreement No 101057721.

In this deliverable, PROPHET undertook a comprehensive mapping exercise, which included a scoping review, to collect information on all existing and ongoing personalised prevention approaches. Additionally, the project aimed to identify bottlenecks hindering the implementation of these approaches in healthcare systems. This mapping exercise encompassed various research methods, including expert interviews and engagement with stakeholders. An online survey was also administered to end users, such as healthcare professionals, citizens, patients, and policymakers.

The purpose of this document is to consolidate the findings from this extensive mapping exercise. These findings are essential for identifying critical factors that influence the successful adoption of personalised prevention approaches within healthcare systems, paving the way for their effective implementation and impact.

1 Introduction

1.1 Background

During the last three decades, the topic of personalised medicine has gained a crucial importance in disease diagnosis and targeted care provision (1), this was enabled thanks to the several progresses made so far in analysing, processing, and integrating huge amounts of data from different sources. As population health concerns the work on all determinants of health (e.g. genetic, biological, social, and environmental factors) for disease prevention and health promotion, this field has expanded its horizons to give rise to "Precision Public Health", which scales up personalised medicine applications to populations with a specific focus on prevention, especially through the use of genomic profiles and big data. (2)
Personalised prevention aims to prevent the onset, progression, and recurrence of disease by the adoption of targeted interventions that consider biological information, environmental and behavioural characteristics, socio-economic and cultural context of individuals. (3) These interventions should be timely, effective, and equitable in order to maintain the best possible balance in lifetime health trajectory. (4) Such opportunities have the potential to reduce the burden of chronic diseases on a broad scale, which account for 80% of the overall burden of diseases in Europe and deserve specific interventions due to their growing incidence, mortality, and impact in terms of disability-adjusted life years (DALYs). (5)
Despite a considerable body of evidence showed that personalised prevention (6) has the potential to foster positive health outcomes at the population level, the extent national public health systems use personalised preventive approaches is comparatively limited and varies significantly worldwide. (7) This is mainly due to a diverse availability of services, reimbursement mechanisms, regulatory frameworks, provider organisation policies and other issues. (6)
Given these assumptions, personalised prevention, is one of the main priorities on the research agenda of the European Commission, which has funded the project "a PeRsonalised Prevention roadmap for the future HEalThcare" (PROPHET) (8), a Coordination and Support Action of the International Consortium for Personalised Medicine (ICPerMed). (9) This project has the objective to support health systems in the implementation of innovative, sustainable, and high-quality personalised strategies for preventing chronic diseases. In this context, one of the aspects on which current research is focused is on the mapping of the state-of-the-art, and bottlenecks, of the implemented personalised preventive approaches in Health Systems for common chronic diseases in Europe and beyond.

1.2 Context and aims

The "PeRsOnalised Prevention roadmap for the future HEalThcare" (PROPHET) project, funded by the European Union's Horizon Europe research and innovation program and linked to ICPerMed, seeks to assess the effectiveness, clinical utility, key success factors and existing gaps in current personalised preventive approaches, as well as their potential to be implemented in healthcare settings. The overall objective of PROPHET is to co-create with stakeholders a Personalised Prevention Roadmap for the future healthcare, in order to

support the definition and implementation of innovative, sustainable, and high-quality personalised strategies that are effective in preventing chronic diseases. This will be achieved through the implementation of a Strategic Research and Innovation Agenda (SRIA) on Personalised Prevention. (8) In the scope of Work Package 2 (WP2), activities to gather evidence on the use of personalised approaches on primary, secondary, and tertiary prevention are conducted. This is done to provide inputs to the SRIA development by identifying main concepts, main research and innovation orientations, key priority areas for Personalized Prevention adoption in the health systems as well as main gaps and bottlenecks to overcome. This document shows the results of Task T2.2.1, which aims to map the state-of-the-art of personalised preventive approaches in Health Systems in Europe and beyond. It also wants to highlight main critical factors that preclude effective implementation of such approaches at local, regional, national, or global level, as appropriate. The exploration of personalised prevention approaches and the examination of impediments to their implementation have extended beyond Europe, encompassing a global perspective to uncover advancements achieved in countries outside Europe, fostering cross-border insights. This broader scope is motivated not only by a quest for innovation but also by the recognition that diverse healthcare systems can offer unique solutions. For this purpose we carried out a scoping review on the major scientific databases, a set of interviews and an online survey targeting end users, including health professionals, citizens, and policymakers. These deliverable details the methodology applied and presents together the main results of the mapping exercise and survey to experts, as well as the general findings that we got from the work as a whole.

2 Methods

The overarching approach of the work on mapping personalised prevention strategies and identifying implementation bottlenecks is structured into two main components.
Firstly, it entails a scoping review of the available scientific and grey literature, enabling a comprehensive analysis and synthesis of existing research. This review aims to unearth valuable insights, trends, and potential gaps in personalised prevention approaches.
Secondly, the study involves soliciting input from experts, including end users such as citizens, healthcare professionals and policymakers, through a survey. This consultation process allows for a focused and in-depth exploration of their perspectives, experiences, and viewpoints concerning personalised prevention strategies. By integrating findings from both the scoping review and expert consultation, the research endeavours to provide a holistic understanding of the current landscape of personalised prevention and key factors impacting its successful implementation.

2.1 SCOPING REVIEW METHODOLOGY

The scoping review follows the 5-stage methodological framework described by Arksey and O'Malley. (10) We also considered the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist. (11) The protocol of this scoping review has been uploaded to the Open Science Framework for public consultation (12), with registration DOI: https://doi.org/10.17605/OSF.IO/M4SZ3

2.1.1 Search strategy and definitions

Firstly, we conducted a preliminary search on PubMed, to define the search strategy and to identify eligibility criteria, through the study of relevant publications found.
Through this preliminary research, together with the consortium experts consultants and approval, we defined various terms and concepts crucial for the aim of the project and this specific task, listed below:

- ***Common chronic disease***: a common disease was defined as a condition with a high prevalence, affecting more than 5 out of 10,000 individuals, according to the definition of rare diseases of the European Union (13); while a chronic disease is a long-term health condition or illness that typically lasts for an extended period and results from the interplay of genetic, physiological, environmental and behavioural factors (5);
- ***Personalised prevention approach***: a personalised preventive approach is an action, or a set of actions, in which the information provided by genetic and/or other omic biomarkers testing, combined with demographic, environmental and behavioural characteristics, socio-economic and cultural context of individuals, guides the decision-making process regarding one or more interventions aimed at preventing the onset, progression and recurrence of diseases. In this context, the level of prevention is determined by the subsequent intervention following the predictive test, as outlined below:
    - ***Personalised primary prevention***: primary prevention entails a comprehensive set of measures, strategies, or interventions aimed at proactively averting the onset of diseases before they manifest. These initiatives revolve around diminishing disease incidence and mitigating risk factors through education and the advocacy of a health-conscious lifestyle. The personalisation of primary prevention is defined by interventions such as lifestyle adjustments, that are tailored to individuals who exhibit genetic predispositions for certain conditions. Genetic or other omic testing for primary prevention can be applied to individuals belonging to high-risk categories, such as specific age groups, as well as through cascade screening. This method involves testing healthy relatives of affected individuals with identified genetic variants, allowing for the identification of potential disease predispositions that may develop over the course of their lives;
    - ***Personalised secondary prevention***: secondary prevention involves implementing measures to detect and treat existing diseases or health conditions at an early stage in asymptomatic individuals, aiming to minimise their impact and prevent future complications; in this scenario, personalisation is achieved through the utilisation of genetic or omics testing on high-risk subjects to identify predisposed individuals, followed by in-depth diagnostic assessments. Furthermore, the application of cascade testing for relatives also remains a method in this context;
    - ***Personalised tertiary prevention***: tertiary prevention refers to interventions and measures aimed at reducing the impact of a diagnosed disease, as well as preventing further deterioration and disability; it focuses on rehabilitation, management, and support to enhance the quality of life for individuals with chronic conditions or disabilities; in this context, personalisation is facilitated through various genetic and omics testing modalities employed on the

diagnosed patient. This comprehensive approach completes the diagnosis, anticipates predispositions to potential complications, and forecasts responses to more tailored therapies, with the aim of averting the worsening of the individual's condition.

- ***Bottlenecks for the implementation***: any barriers, limitations, or obstacles to the implementation of personalised medicine approaches in health systems, concerning laboratory and clinical research, health professionals' and citizens' knowledge, ethical, legal and social issues and operational aspects.

Structuring our scoping review on these preliminary research and definitions, we searched on scientific databases, such as PubMed, Scopus, Web of Science, Google Scholar, and grey literature, such as existing networks in the field of personalised medicine and genomics, and relevant organisations websites, including governmental bodies, international public health institutions, national ministries of health, and similar entities. The search, extended from 2017 to date (last 5 years), aimed to identify all studies and reports related to the adoption of personalised prevention approaches in health systems in Europe and on a global scale.

The search algorithm was the following: *((“personal* prevention” OR “individual* prevention” OR “predictive prevention” OR “precision prevention” OR “stratified prevention” OR “tailored prevention”) AND (intervent* OR activit* OR approach* OR path* OR program* OR strateg* OR plan*) AND (genomic* OR epigenomic* OR metabolomic* OR transcriptomic* OR pharmacogenomic* OR radiomic* OR omic*))*, based on keywords such as: “individual”, “individualized” or “individualised”, “personalized” or “personalised”, “precision”, “tailored”, “targeted”. In the search query, synonyms for chronic and common diseases were intentionally omitted to facilitate a broader range of results from scientific databases.

2.1.2 Eligibility Criteria

The articles identified were uploaded into the Rayyan software (14) and underwent a two-phase assessment to determine their eligibility, first as a screening through title and abstract, second full text. During each phase, the records were thoroughly evaluated based on the following inclusion criteria: publications in English, citing policies, programmes, interventions, and structured approaches related to personalised prevention of common chronic diseases (e.g. diabetes, cancer, cardiovascular diseases, neurological diseases, etc.). In this context, the choice was made to include all common chronic conditions, even those originating from rare genetic variants. An example frequently encountered involves tumours, classified as common diseases, which upon diagnostic investigation and genetic testing, might unveil underlying rare conditions like Peutz-Jeghers syndrome or similar disorders. In such cases, these conditions were still integrated into the review. All research articles (e.g., randomised controlled trials, observational studies with intervention, etc.) including predictive omic tests and preventive interventions were included. Additionally, documents and publications concerning bottlenecks, gaps, and barriers for the adoption and implementation of personalised prevention approaches, as previously defined, were considered. Exclusion criteria encompassed publications in languages other than English, pre-prints, and study protocols, as well as studies solely exploring the clinical validity of genetic or other omic tests (e.g., genome-wide association studies, correlation studies, etc.), articles not involving omic sciences in prevention of common chronic diseases, and studies conducted on animals.

2.1.3 Data charting

From each eligible article, three independent researchers extracted information about first author, journal of publication, year of publication, study source, type of approach (e.g., genomic oncological screening, use of pharmacogenomics for tertiary prevention, nutrigenomics for metabolic diseases), sample size if available, disease/health condition and level of prevention (e.g., primary, secondary, tertiary). Moreover, whether available, data on country and healthcare system model and any outcome related to the approaches of interest (e.g., survival, avoided mortality) and health expenditure measures have been extracted; furthermore, we extracted, whether possible, bottlenecks, barriers, and facilitators for the adoption of the approach (e.g. regarding target population, social and economic aspects of the country, healthcare system model, and others).

2.1.4 Double-blinded evaluation

All previously mentioned steps of the study employed a double-blind evaluation and data extraction process. Four researchers independently assessed article eligibility based on titles, abstracts, and full texts, resolving any disagreement through discussion. Furthermore, three independent researchers extracted data from eligible articles to ensure unbiased information retrieval. This robust double-blind approach fosters objectivity, minimises biases, and enhances the credibility and reliability of the study's assessment of personalised prevention approaches in healthcare systems.

2.1.5 Collating, summarising and reporting the results

We reported in next sections descriptive statistics for all the items assessed using STATA software for Windows, v.16.1 (Stata Corp., College Station, Texas, USA, 2019). Results were presented narratively as well.

As for the part concerning personalised prevention approaches eligible studies were categorised according to pathology of interest and level of prevention. Then we undertook a synthesis, in accordance with the definitions previously described, identifying existing approaches as pathways that incorporated a specific predictive omic test for a target population and a corresponding preventive intervention. The intervention could have focused on lifestyle modifications for primary prevention, or it might have involved directing individuals to screening programmes with more frequent intervals for secondary prevention, while also considering personalised therapies for tertiary prevention. All these interventions are personalised precisely because they are tailored to individuals who have undergone the predictive tests, and as a result, they are targeted towards those with higher risk.

With regard to gaps and bottlenecks concerning the implementation of personalised prevention approaches, the extracted data were synthesised based on a set of categories identified through thematic analysis and subsequent consensus by the research team. An initial extraction of the content of the included articles provided an overview of the topic, each researcher then independently coded the main bottlenecks present; these codes were then unified through consensus by the research team and further grouped into 5 main categories.

2.2 STAKEHOLDERS CONSULTATIONS METHODOLOGY: EXPERTS INTERVIEWS AND SURVEY

The stakeholder consultation included experts' interviews and an online survey, developed based on the interview's outcomes. The interviews and online survey study protocol was approved by Ethical Committees from INSA and FPG (approval number 5658).

2.2.1 Experts interviews

i) Interview development

We were interested in learning more about the main perceived barriers and enablers of personalised prevention (PP) therefore we conducted semi-structured interviews with experts in the various fields related to personalised medicine.
We initially defined the main groups of stakeholders with expertise in the barriers and enablers of personalised prevention: health professionals, citizens and patients, researchers, and health policy decision-makers. Based on a literature review and the expertise of the research team, interview guides were designed to gather insights from each of the four stakeholder groups. The interview guides were directed at each of the expert groups, with common questions but also more specific questions for each group that explored their singularities.
We selected and invited 26 experts representing each of these stakeholder groups for an interview. Experts were invited by email, explaining the objectives of the interviews, and seeking consent for recording.
Most interviews were carried out online, using the Teams platform, and recorded with the individuals' permission for later transcription. Interviews were conducted in national languages (Portuguese, Italian, Spanish) or in English. The transcription was handled automatically by the Teams platform, and subsequently carefully reviewed by the interviewer. Recordings were deleted after the interview analysis. In some instances, experts chose to respond in writing. The interviews took place between April and July 2023, by elements of INSA and UCSC.

ii) Data analysis

Qualitative data content analysis of interviews transcriptions was carried out using the thematic analysis method. Thematic analysis is a qualitative research method that entails searching across a data set to identify, analyse, and report repeated patterns. (15) The three main goals of thematic analysis are:

1. To identify important themes from the data;
2. To understand how themes relate to one another and how they are manifested in the data;
3. To use themes to generate insights about a particular phenomenon.

Thematic analysis involved: (i) carefully reading through the interview transcripts multiple times, (ii) creating a systematic coding framework, defining, and naming themes, (iii) categorising all the data accordingly, and selecting compelling illustrative examples.
In detail, team members transcribed all interviews and worked independently at an initial stage. Transcriptions were read multiple times to establish preliminary impressions among team members. The team proceeded with line-by-line coding of transcripts. Initial codes were

refined interactively, and classified into themes and sub-themes, and relevant illustrative citations were identified for each theme. Team members discussed the findings and achieved consensus on a final thematic structure.

2.2.2 Survey

A cross-sectional online survey was designed to collect the perceived barriers and enablers for the adoption of personalised prevention strategies in the EU and beyond, among citizens and patients, health professionals, researchers and health policy makers. The survey content was developed based on the potential barriers and/or enablers to a wider adoption of personalised preventive strategies raised by interviewed experts. The survey was web-based and administered via the REDCap platform. Data collection took place between June and August 2023.

i) Instrument

Questions were iteratively developed by the research team, based on the results of the thematic analysis of the interviews, complemented with findings from the literature.
The survey includes five sections. It starts with an introductory description of the project, aims of the activity, and introduces the definition of personalised prevention discussed by the PROPHET team. Consent to participate is asked at the end of introduction, and progression to the survey is contingent on approval.
After the introductory section, participants were asked to position themselves in one of the following categories: 1) Citizens and patients, 2) Health professionals, 3) Researchers and 4) Policy makers. Citizens and patients were additionally asked: “Do you suffer from any chronic disease?”.
Section one consisted of the assessment of the individual understanding of personalised prevention, with three generic questions:

> [1] Have you ever heard of personalised prevention prior to this survey?
> [2] Do you believe that personalised prevention is a beneficial health intervention to prevent disease, and reduce disability or mortality?
> [3] Do you believe there are benefits in using pharmacogenomics for preventing adverse drug reactions and improving drug response?

Sections two and three were dedicated to assess perceived barriers and enablers to the adoption of personalised prevention strategies. A total of 112 items were scored on a 6-point Likert scale. Participants were asked to indicate their level of agreement with a set of sentences, addressing the potential barriers or enablers. The level of agreement was assessed as: 1) Strongly disagree, 2) Disagree, 3) Neither agree nor disagree, 4) Agree, 5) Strongly agree, 6) Don’t know. For citizens and patients the set of items related with barriers were differently asked, with a more appropriate language to this target group.
Sociodemographic characteristics were collected in section four. Variables assessed included gender, age, country, and educational level.

ii) Data analysis

Descriptive statistics were used to analyse the sample sociodemographic characteristics. Likert-scale answers were analysed as categorical data with frequencies and proportions represented by bar charts. Perceptions of barriers and enablers were categorised in two major categories: disagreement vs. agreement. The two categories were obtained with the sum of

Likert-scale answers of Strongly disagree + Disagree and the sum of Strongly agree + Agree, respectively. Neither agree nor disagree and Don't know were analysed separately.

3 Results

In this section, we present the findings of our research, which encompasses both scoping review and interviews and survey results separately, in order to maintain clarity and facilitate targeted analysis and comparisons between the two research methodologies. This ensures a clearer understanding of the overall study's comprehensive insights and implications.

3.1 Scoping review results

The scoping review involved an extensive examination of 11,793 records, comprising 10,404 from scientific databases and 1,389 from grey literature. After removing duplicates, 10,379 records underwent initial screening based on titles and abstracts. From this, a subset of 2,158 records progressed to the full-text evaluation stage. After meticulous assessment, 303 records met the inclusion criteria for the final analysis, as presented in the PRISMA flowchart (Figure 1). (16)

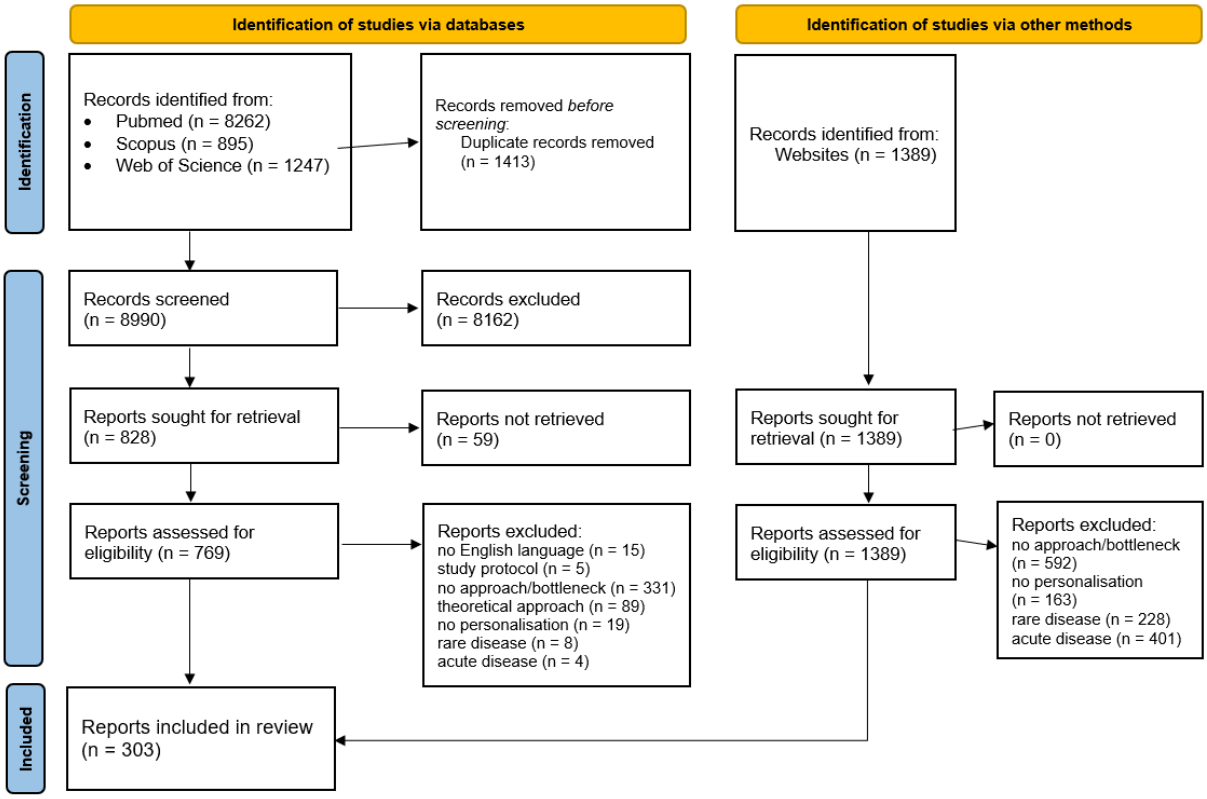


Figure 1. *Prisma 2020 flow diagram for the review, included searches of databases, registers, and other sources* (16)

Among the total 303 records, 82 incorporated personalised prevention approaches for common chronic diseases (17–98), 204 reported bottlenecks or barriers to the implementation of personalised prevention (99–302), and 16 presented both personalised

prevention approaches and identified barriers or gaps in their implementation(303–318), resulting in a total number of 98 records for personalised prevention strategies and 220 records for obstacles to their adoption.

In the following sections, we present a comprehensive depiction of the detailed results concerning personalised prevention approaches, as well as an examination of bottlenecks and barriers hindering their implementation. Furthermore, we provide a narrative synthesis of the findings, integrating key insights to offer a cohesive understanding of the topic.

3.1.1 PERSONALISED PREVENTION APPROACHES

Among the 98 included records, which reported one or more personalised prevention strategies, 58 were reviews or commentaries, 12 were guidelines or recommendations, 7 were reports and 22 were primary studies, comprising randomised controlled trials (RCT) and observational studies. Out of all the 98 articles where the country of the study or the location of the implemented approach was explicitly specified, 45% were conducted in the USA, 38% in Europe, 14% in Asia, with the remaining 3% distributed across various other countries, including Australia, Brazil and Russia. From these, 215 complete approaches were identified, incorporating a predictive omic test and a consequent preventive intervention. The majority of all approaches focused on cancer (62%), followed by cardiovascular diseases (27%), metabolic diseases (7%), and other chronic diseases (4%) (Figure 2)

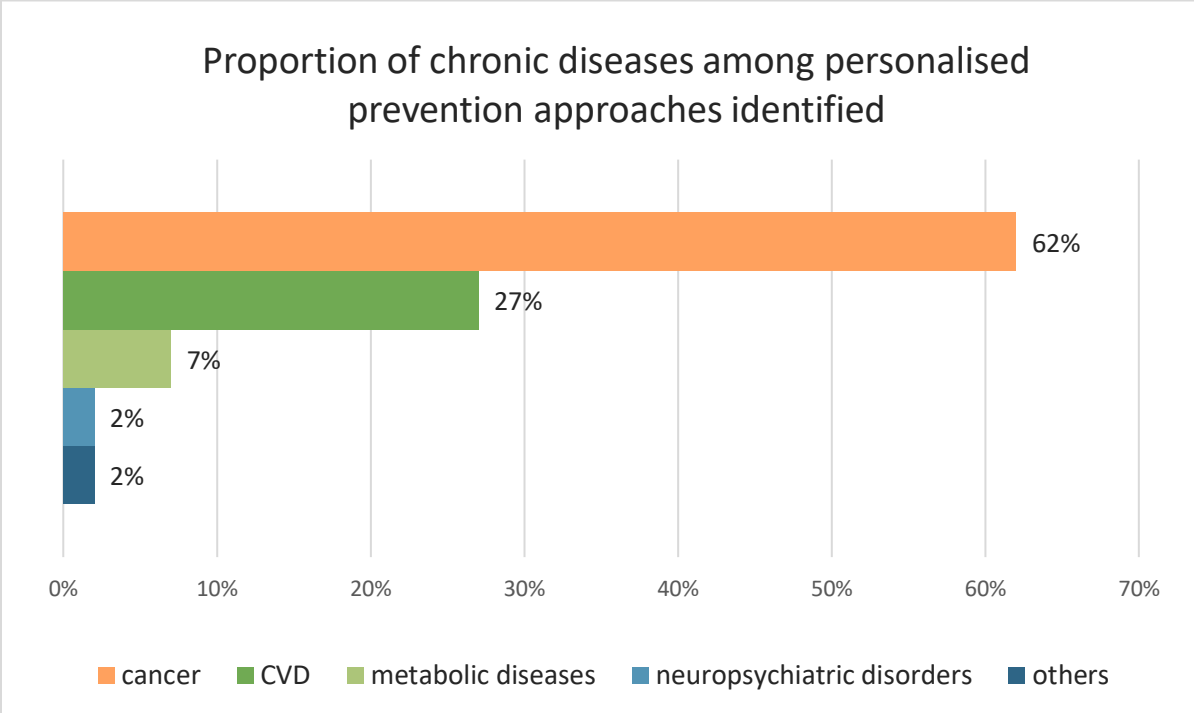


Figure 2. *Proportion of chronic diseases among the 215 identified personalised prevention approaches*

According to the level of prevention, we found that the majority of interventions, accounting for 51% were classified into tertiary prevention, followed by 27% of secondary prevention approaches and 23% of primary prevention approaches. (Figure 3)

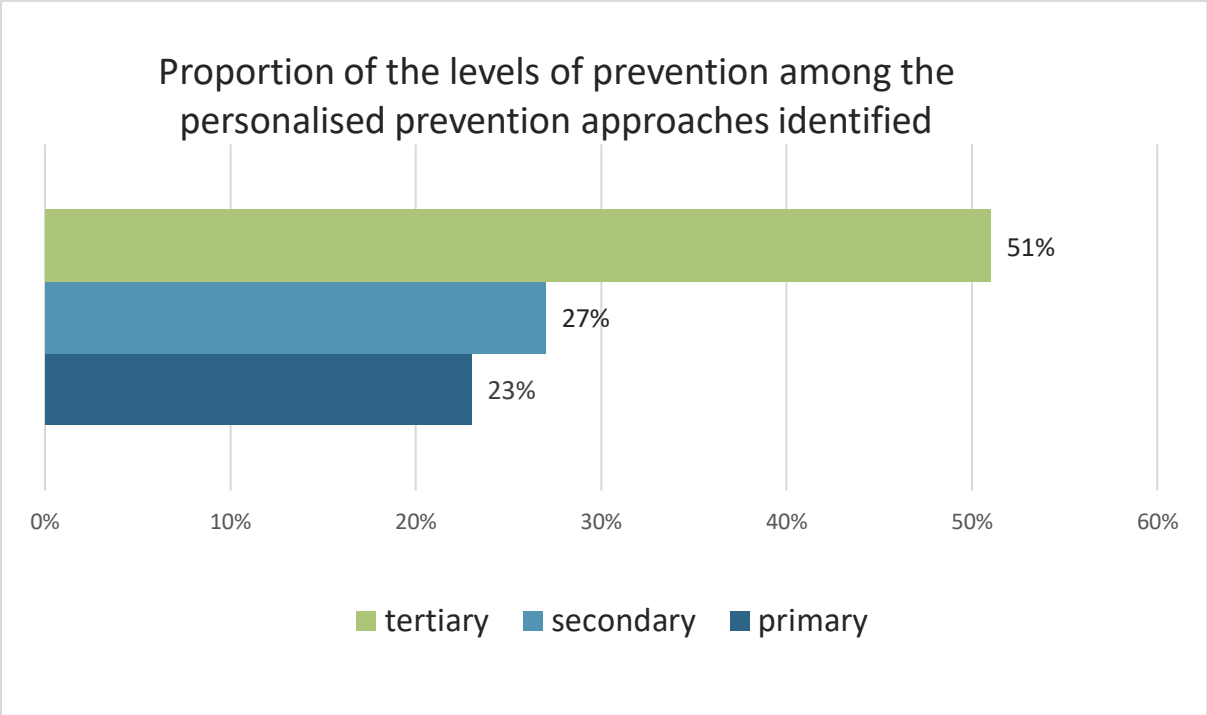


Figure 3. *Proportion of levels of prevention among the 215 identified personalised prevention approaches*

The subsequent sections will provide detailed insights into the results concerning personalised prevention approaches, systematically classified based on the groups of chronic pathologies, such as cancer, cardiovascular, metabolic, neurodegenerative, and psychiatric disorders, and other diseases. Each section will thoroughly examine the specific approaches adopted within these categories, presenting a comprehensive overview of the cutting-edge developments in personalised prevention, fostering a deeper appreciation for the potential advancements in population health management.

3.1.1.1 CANCER

Prevention of cancer

Cancer is a global health burden characterised by its diverse manifestations and significant impact on individuals, according to the World Health Organization (WHO) it is one of the leading causes of death worldwide, responsible for about ten millions of deaths in 2020, second only to cardiovascular disease.

The most common cancers are breast, colorectal, lung and prostate, contributing to about half of the new cases each year and about half of global cancer deaths. Lung cancer is the leading cause of cancer-related deaths worldwide, accounting for nearly two million deaths annually, and it is the most frequent in the male population while breast cancer is the most commonly

diagnosed among women. Colorectal cancer completes the group of the top three most frequent cancers, and it is second for overall mortality.

Traditional one-size-fits-all prevention strategies have limitations in addressing the heterogeneity of cancer risk factors and individual responses to treatment. Personalised prevention, on the other hand, tailors interventions to an individual's specific characteristics, and holds the potential to transform cancer prevention by offering targeted strategies that could help identify high-risk individuals earlier, facilitate early diagnosis, and ultimately reduce the burden of disease.

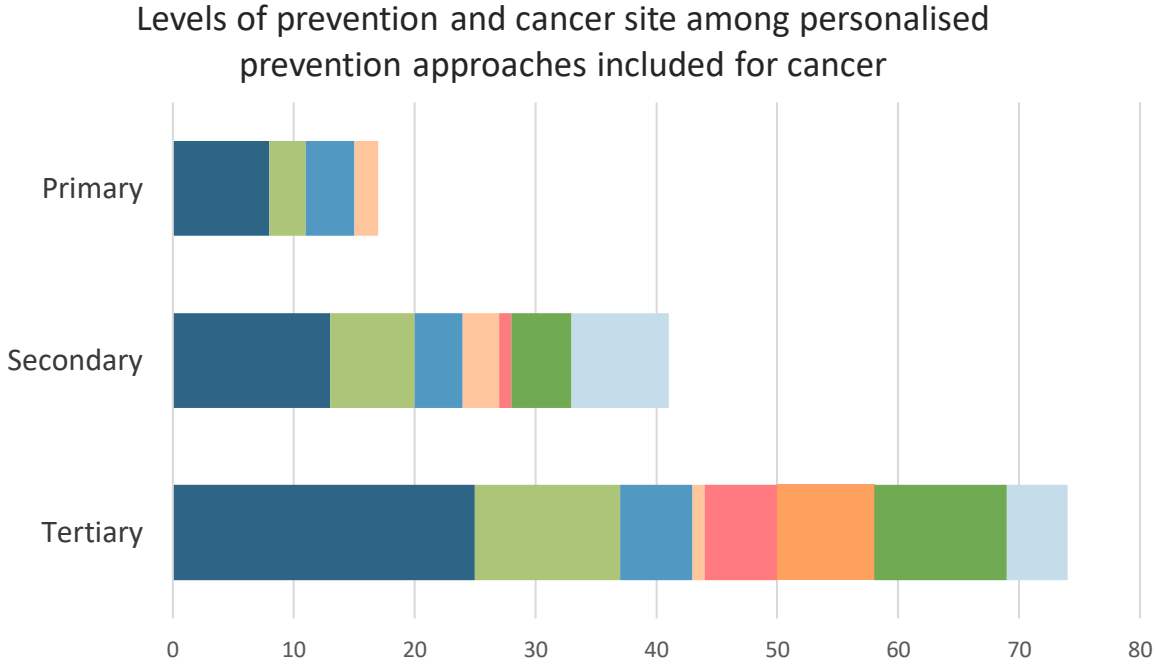
In this section, we explore the landscape of personalised prevention strategies for various cancers in order to highlight the promising developments in this field and identify gaps that warrant further investigation. Through a better understanding of personalised prevention, we aspire to contribute to the advancement of cancer prevention and ultimately improve the health outcomes and quality of life for individuals at risk of or affected by these cancers.

Specific features of cancer records

A comprehensive analysis was conducted on 49 records focused on cancer, which collectively addressed various aspects of personalised prevention approaches. Among these, a total of 133 distinct personalised prevention approaches were identified and subjected to in-depth examination.

The totality of the identified approaches utilised genomics-based testing and, according to the intervention, they were categorised based on their level of prevention. Primary prevention strategies were represented by 17 approaches (12.8%), secondary prevention was evident in 41 approaches (30.8%), while the majority of the approaches (75) were classified under tertiary prevention (56.4%). (Figure 3)

Regarding the cancer type, breast neoplasms received relevant attention with 53 approaches directed towards this specific type (39.8%). Other addressed neoplastic diseases included colorectal neoplasms (17.3% of the total, 23 approaches), ovarian neoplasms (10.5% of the total, 14 approaches), and lung neoplasms (6% of the total, 8 approaches). (Figure 3) Additionally, there were approaches aimed at other neoplastic diseases such as biliary, bladder, cholangiocarcinoma, endometrial, gastric, haematological, head and neck, hepatic, melanoma, pancreatic, prostatic, renal, sarcoma, testicular, and thyroid neoplasms.



	Tertiary	Secondary	Primary
Breast	25	13	8
Colorectal	12	7	3
Ovarian	6	4	4
Melanoma	1	3	2
Prostate	6	1	0
Lung	8	0	0
Digestive system	11	5	0
Others	5	8	0

Figure 4. *Levels of prevention and cancer site among the 133 personalised prevention approaches for cancer*

One identified approach focused on the utilisation of multigene panels on general population, investigating their predisposition to developing various types of tumours, such as breast, lung, colorectal cancer, and others. (44) These panels allow for primary prevention interventions in individuals found to be predisposed, involving lifestyle modifications or prophylactic measures. Additionally, they enable personalised follow-ups over time for secondary prevention. Furthermore, two additional approaches were used independently with respect to the cancer type for tertiary prevention: one involved a multigene panel (32), while the other focused on specific DPYD variants (76), and they were both used on cancer patients to find actionable and targeted treatments.
The following sections provide detailed descriptions of specific approaches for each type of cancer.

Breast Cancer

A total of 29 records were included for breast cancer personalised prevention. Among these, 16 records were reviews on different types of personalised prevention for breast cancer or various toumors, 7 were primary studies (observational, RCT) already concluded, 4 were recommendations and 2 guidelines, focusing on the use and implementation of *BRCA 1/2*

testing. About countries, 13 studies were conducted in USA, 10 in Europe, 5 in Asia and 1 in South America.

Among the 53 identified personalised prevention approaches targeting breast neoplasms, 15 specifically focused on detecting mutations in the *BRCA1* and *BRCA2* genes. These genes are associated with an increased risk of developing breast cancer and other malignancies. All but one of the identified approaches specifically refer to the search for germline mutations in the genes in question. The results of these tests lead to various types of preventive interventions, including primary prevention measures such as prophylactic unilateral or bilateral mastectomy. Additionally, secondary prevention strategies involved personalised surveillance through frequent screening methods. Furthermore, tertiary prevention approaches incorporated targeted therapies aimed at specific molecular targets, such as the use of *PARP* inhibitors. The only case of somatic testing for *BRCA1/2* fits within this level of prevention.
Furthermore, several approaches involved the analysis of *BRCA* mutations and the utilisation of the BOADICEA test to create personalised screening plans for patients. Seven approaches incorporated the Oncotype DX test, which allows to identify somatic mutations within the tumour and is utilised to predict the likelihood of cancer recurrence and guide the adoption of targeted therapy for breast neoplasms. The Oncotype DX test analyses the expression of certain genes in breast tumour tissue and provides a recurrence score, enabling physicians to tailor treatment plans to individual patients.
In addition to *BRCA*-related approaches, three of the identified strategies targeted the detection of mutations that make it possible to diagnose specific syndromes, including Hamartoma Tumour Syndrome, Li-Fraumeni Syndrome, and Peutz-Jeghers Syndrome. These syndromes predispose individuals to breast cancer and other malignancies, making early diagnosis crucial for both the patient and their family members. Early identification of these mutations allows for proactive preventive measures and cancer surveillance, reducing the overall burden of disease and improving patient outcomes.
Among the 53 identified personalised prevention approaches targeting breast neoplasms, the remaining strategies focused on the identification of genes that can guide targeted therapy for already diagnosed neoplastic conditions. In these approaches, the aim was to identify specific mutations that have implications for treatment decisions. Some of the key genes investigated include *HER2*, *PKB*, and *AKT1*, which play critical roles in guiding personalised therapy for breast cancer.
The *HER2* gene, for instance, is associated with a subtype of breast cancer known as *HER2*-positive breast cancer. This subtype tends to be more aggressive, but targeted therapies such as trastuzumab (Herceptin) have been developed to specifically inhibit *HER2* overexpression, leading to improved outcomes for patients with this mutation. Similarly, the *PKB* and *AKT1* genes are involved in cell signalling pathways that regulate cell growth and survival. Mutations in these genes can contribute to the development and progression of breast cancer and may influence the response to certain targeted therapies.
In addition to investigating specific gene mutations, other approaches utilised advanced tools and technologies to guide personalised therapy decisions. Mammaprint and Endopredict, for example, are genomic tests that analyse the activity of multiple genes in breast tumour tissue. These tests provide valuable information about the likelihood of disease recurrence and help in determining the most appropriate treatment options for individual patients. By using such genomic profiling tools, healthcare providers can optimise therapeutic choices and tailor treatments to suit the unique characteristics of each patient's breast cancer.

All the approaches focused on breast cancer prevention are synthesised in Table 1.

	Application	Intervention	Ref
Primary Prevention	***BRCA 1/2*** **Multi Gene Panel (*PTEN PALB2*)** **Genetic testing for healthy relatives of affected individuals**	**Programmes for Risk Reduction** **Prophylactic mastectomy**	(24,38,46, 57,66,76, 99,114)
Secondary Prevention	***BRCA 1/2*** **Genetic testing for healthy relatives of affected individuals**	**Active Surveillance Personalised Screening (mammography)**	(38,46, 65,98)
	BOADICEA **Peutz-Jeghers Syndrome** ***PTEN*-Hamartoma Tumor Syndrome** **Li-Fraumeni Syndrome** **TrueRisk gene panel** **Multi Gene Panel (*ATM PALB2*)** **Genetic testing for healthy relatives of affected individuals**	**Personalised Screening (MRI and mammography)**	(23,44, 46,48, 58,69,75)
Tertiary Prevention	***BRCA 1/2*** **Oncotype DX** ***PKB/AKT1/HER2* expression** **Multi gene panel** **Mamma Print** **Blue Print** **Prosigna (PAM50)** **Breast Cancer Index** **Genomic Grade Index** **Endopredict**	**Target Therapy**	(20,25,30, 32,38,45, 53,55,63, 66,68,75, 78,100,115)

Table 1. *Personalised prevention approaches for breast cancer*

Colorectal Cancer

Among the 22 identified personalised prevention approaches targeting colorectal neoplasms, 3 (13.6% of the total) focused on primary prevention, specifically aiming to identify genetic alterations associated with syndromic conditions such as Familial Adenomatous Polyposis (FAP), Lynch syndrome (Hereditary Nonpolyposis Colorectal Cancer - HNPCC), Peutz-Jeghers Syndrome, and Juvenile Polyposis Syndrome. These syndromes are characterised by inherited mutations that predispose individuals to an increased risk of colorectal cancer. The primary preventive strategies identified for these conditions involved surgical interventions to remove affected portions of the colon (in one case) or polyps (in two cases) to reduce the likelihood of cancer development and programmes for risk reduction.

Furthermore, 7 approaches (31.8% of the total) focused on secondary prevention, with an emphasis on the previously mentioned syndromes. The preventive strategies in this category included serial screening through endoscopy or MRI. These screening methods allow for the detection of polyps or early-stage cancerous lesions, enabling timely intervention and improved patient outcomes.

The majority, 12 out of 22 approaches (54.6% of the total), concentrated on tertiary prevention through the identification of specific mutations to guide the choice of therapeutic interventions. Among these, mutations in *ABC, SLC, EGF*, and *VEGF* genes play significant roles in guiding treatment decisions for colorectal cancer. Based on these mutations, healthcare providers can tailor treatments using agents such as fluoropyrimidines, irinotecan, and oxaliplatin.
Additionally, the FoundationOne CDx tool is utilised to identify KRAS and AXL mutations, informing the use of Cabozantinib therapy. Cabozantinib is a targeted therapy that inhibits multiple tyrosine kinases involved in tumour growth and progression.
The adoption of the Promega test, which assesses microsatellite instability, guides the use of pembrolizumab therapy. Pembrolizumab is an immune checkpoint inhibitor that activates the body's immune system to target cancer cells with microsatellite instability.
Another significant focus was on the identification of *RAS* mutations. These mutations impact the response to treatment with panitumumab in combination with *FOLFOX4*, a chemotherapy regimen that includes 5-fluorouracil, leucovorin, and oxaliplatin. Panitumumab is a monoclonal antibody that specifically targets the epidermal growth factor receptor (*EGFR*), and its efficacy is influenced by the presence or absence of *RAS* mutations.
All the approaches focused on colorectal cancer prevention are synthesised in Table 2.

	Application	Intervention	Ref
Primary Prevention	**FAP Syndrome** **Lynch Syndrome** **Peutz-Jeghers Syndrome** **Juvenile Polyposis Syndrome** **Genetic testing for healthy relatives of affected individuals**	**Colectomy** **Polypectomy** **Programmes for risk reduction**	(57,58)
Secondary Prevention	**FAP Syndrome** **Lynch Syndrome** **Peutz-Jeghers Syndrome** **Juvenile Polyposis Syndrome** **Hamartoma Tumor Syndrome** **Multi gene panel (*PMS2, APC*)** **Genetic testing for healthy relatives of affected individuals**	**Personalised endoscopy** **Personalised MRI screening**	(44,56–58,63,75)
Tertiary Prevention	**Multi gene panel (*ABC, SLC, EGF, VEGF, RAS*)** **Multi gene panel (*DPYD* and *UGT1A1*)** **FoundationOne CDx** **Multi gene panel for 73 genes** **FAP Syndrome** **Lynch Syndrome** **Promega (MSI Analysis System)**	**Target Therapy**	(19,28,36,43,53,54,58,64,68,100,111)

Table 2. *Personalised prevention approaches for colorectal cancer*

Lung Cancer

All eight identified personalised prevention approaches targeting lung neoplasms focused on tertiary prevention. These approaches utilised Next-Generation Sequencing (NGS)

technology, which plays a crucial role in identifying multiple gene panels that can influence therapeutic choices for this neoplastic condition.
NGS is a high-throughput sequencing technique that enables the simultaneous analysis of multiple genes, providing a comprehensive view of the genetic landscape of a tumour. By analysing a wide range of genes in a single test, NGS allows for the identification of various genetic alterations associated with lung cancer, including mutations in the *EGFR* and *KRAS* genes. Mutations in the *EGFR* gene are a known driver of certain lung cancers, making it a key target for personalised therapy. Drugs known as anti-*EGFR* agents and tyrosine kinase inhibitors (TKIs) are utilised in personalised treatment plans for patients with *EGFR* mutations. These drugs work by specifically targeting the *EGFR* protein, inhibiting its activity, and interfering with cancer cell growth and proliferation. Similarly, *KRAS* mutations are common in lung cancer and can influence treatment responses. In the context of personalised prevention, identifying *KRAS* mutations guides treatment decisions and helps in the selection of appropriate therapies, often involving targeted therapies and personalised combinations of anticancer drugs. All the approaches focused on lung cancer prevention are synthesised in Table 3.

	Application	Intervention	Ref
Tertiary Prevention	***EGFR, KRAS*** **Multi gene panel (143 genes) - NGS**	**Target Therapy**	(28,32, 53,54, 61,67, 68,83)

Table 3. *Personalised prevention approaches for lung cancer*

Ovarian Cancer

Out of the 14 identified personalised prevention approaches targeting ovarian neoplasms, 4 focus on primary prevention. Three out of these 4 approaches target the search for *BRCA1/2* mutations, which are known to play a significant role in the development of ovarian cancer. These approaches propose interventions such as prophylactic oophorectomy for carriers of these mutations or cascade testing for family members at risk. *BRCA1/2* mutations are associated with an increased risk of ovarian cancer, and identifying carriers of these mutations allows for proactive preventive measures to reduce the likelihood of cancer development.
One approach in the primary prevention category searches for mutations in the *BRIP1* and *RAD51D* genes. Mutations in these genes have also been linked to an increased risk of ovarian cancer, and this approach proposes a prophylactic surgical intervention as a preventive measure.
Regarding secondary prevention, 4 approaches targeted the search for mutations related to specific syndromes such as Peutz-Jeghers Syndrome or Lynch Syndrome or are based on multigenes panels for various tumours. These approaches propose high-frequency screening using techniques like ultrasound to detect early signs of ovarian cancer in at-risk individuals.
Lastly, 6 approaches focused on tertiary prevention, involving the search for *BRCA1/2* mutations to guide therapeutic interventions.
This includes the adoption of *PARP* inhibitors, a class of drugs specifically targeting cancer cells with defective DNA repair mechanisms. In addition, these approaches propose the use of multiple gene panels analysed through Next-Generation Sequencing (NGS) to inform personalised therapeutic interventions.

All the approaches focused on ovarian cancer prevention are synthesised in Table 4.

	Application	Intervention	Ref
Primary Prevention	***BRCA 1/2*** **Multi gene panel (*BRIP1* and *RAD51D*)** **Genetic testing for healthy relatives of affected individuals**	**Programmes for risk reduction** **Salpingo-oophorectomy**	(38,65,75,317)
Secondary Prevention	***BRCA 1/2*** **Lynch Syndrome** **Peutz-Jeghers Syndrome** **Genetic testing for healthy relatives of affected individuals**	**Ultrasound screening**	(25,44,56,58)
Tertiary Prevention	***BRCA 1/2*** **Multi gene panel (*KRAS, EGF/EGFR, VEGF/ VEGFR, IGF/IGFR, PDGF, FGF, RAS/ RAF/ERK/MAPK, PI3K/AKT/ mTOR, Wnt/* beta-catenin)** **FoundationOne CDx**	**Target Therapy**	(25,28,38,53,54)

Table 4. *Personalised prevention approaches for ovarian cancer*

Prostate Cancer

Among the 7 identified personalised prevention approaches targeting prostate neoplasms, all but one falling into tertiary prevention strategies, seeking genetic mutations that can inform therapeutic management of prostate cancer. For example, mutations in genes such as *ETS, PTEN, BRCA2*, and *ATM* are explored for their potential role in prostate cancer development and progression. Understanding the genetic basis of these neoplasms can guide treatment decisions and help identify patients who may benefit from specific therapeutic interventions. Additionally, one approach is based on multigene panels searching for the predisposition of diverse cancers, followed by personalised follow-up.

All the approaches focused on prostate prevention are synthesised in Table 5.

	Application	Intervention	Ref
Secondary Prevention	**Multi gene panel** **Genetic testing for healthy relatives of affected individuals**	**Personalised screening**	(44)
Tertiary Prevention	***BRCA1/2*** ***ETS/PTEN/ATM*** **Multi gene panel - NGS**	**Target Therapy**	(25,28,32,53,64,67)

Table 5. *Personalised prevention approaches for prostate cancer*

Melanoma

Among the 6 identified personalised prevention approaches targeting melanoma, 2 were focused on primary prevention. In particular, in both approaches the genetic test or the genetic profile of risk, was followed by behavioural interventions.
Behavioural interventions to reduce the risk of melanoma involve personalised strategies, such as dietary changes, minimising sun exposure, and implementing specific measures to reduce the absorption of UV rays by the skin. By incorporating this knowledge, individuals can make informed decisions to reduce the impact of genetic risks and promote healthier outcomes. Additionally, behavioural intervention may encompass counselling and education to empower individuals with the tools needed to proactively manage their health.
Three approaches constituted secondary prevention strategies, characterised by close dermatologic screenings and self-examinations for individuals at high genetic risk. One of them was for a specific syndrome, the Hamartoma Tumour Syndrome, related to the *PTEN* gene.
Only one approach regarded tertiary prevention. It is an application of a NGS for the identification of specific mutations to guide the choice of therapeutic interventions.
All the approaches focused on melanoma prevention are synthesised in Table 6.

	Application	Intervention	Ref
Primary Prevention	***MC1R*** **PRS** **Genetic testing for healthy relatives of affected individuals**	**Lifestyle modifications**	(17,307)
Secondary Prevention	***PTEN*** **– Hamartoma Tumour Syndrome** **PRS** **Genetic testing for healthy relatives of affected individuals**	**Self-examination** **Personalised dermatological screening**	(17,44,58)
Tertiary Prevention	**Multi gene panel - NGS**	**Target Therapy**	(54)

Table 6. *Personalised prevention approaches for melanoma*

Other Digestive System Tumours

A total of 15 approaches were identified, all for secondary (4) and tertiary prevention (11).

Biliary tract cancers: three approaches were identified, all of them regarding tertiary prevention, involving the search of mutations in key genes to guide the therapy.

Pancreatic cancer: among the 6 approaches identified, 3 concerned secondary prevention, in particular early screening for familial syndromes. The other 3 were about tertiary prevention, for the identification of specific mutations to guide the choice of therapeutic interventions.

Gastric cancer: 3 approaches concerned tertiary prevention, using multi-gene panels for the identification of actionable targets. Only one was about secondary prevention, considering a close screening with the endoscopy in gastric cancer related syndromes.

Hepatic cancer: 2 approaches were identified, both of tertiary prevention and target therapy.

The approaches focused on digestive system cancers prevention are synthesised in Table 7.

	Application	Intervention	Ref
Secondary Prevention	**Peutz-Jeghers Syndrome testing** **30-gene hereditary cancer panel** **Pancreatic cancer syndromes testing** **Gastric cancer syndromes testing** **Genetic testing for healthy relatives of affected individuals**	**Endoscopy screening** **MRI screening** **Genetic counselling**	(44,58,70,311,313)
Tertiary Prevention	**Multi gene panel – NGS** ***IDH R132C* - FoundationOne CDx** ***CLDN18-ARGAP26/6*** ***MSI*** ***EGF/EGFR, VEGF/VEGFR, IGF/IGFR, PDGF, PGF, RAS/RAF/ERK/MAPK, PI3K/AKT/mTOR, WNT/beta catenin*** ***BRCA 1/2***	**Target Therapy**	(25,32,33,43,53,83)

Table 7. *Personalised prevention approaches for digestive system tumours*

Other cancers

Among the remaining 13 approaches, 8 concerned secondary prevention and 5 tertiary prevention. Three approaches relate to the ***thyroid cancer***, two provide for the adoption of monitoring programs in individuals for whom a predisposing form of familial syndrome has been identified for the development of these cancers (secondary prevention)(28,58), and one regards testing for *BRAF* mutation and target therapy (tertiary prevention). (32)

As regards the 6 remaining secondary prevention approaches, they regard personalised screening for hereditary syndromes, for ***testicular cancer*** in patients with Peutz-Jeghers Syndrome(58), and for ***endometrial and renal cancer*** in patients with Hamartoma Tumour Syndrome (*PTEN* mutation)(44,58). Additionally, multigene panels are used to identify individuals at risk for other cancers, such as ***endocrine neoplasms*** and those affecting the ***central nervous system***(44), in order to structure personalised follow-up pathways.

Tertiary prevention approaches, on the other hand, regards genetic testing for the identification of actionable targets and target therapy in ***haematological malignancies, head and neck cancer, sarcoma, and bladder cancer.***(28,29,54,82)

3.1.1.2 CARDIOVASCULAR DISEASES

Prevention of cardiovascular diseases

Cardiovascular diseases (CVDs) represent a critical global health challenge, being the leading cause of mortality worldwide. This category includes diverse heart and blood vessel disorders, affecting individuals across all age groups and demographics. In 2020 alone, an alarming 31% of global deaths, approximately 17.9 million lives, were attributed to CVDs.(320) Risk factors like sedentary lifestyles, unhealthy diets, tobacco use, excessive alcohol consumption, and genetic predispositions compound this burden, necessitating targeted preventive measures.

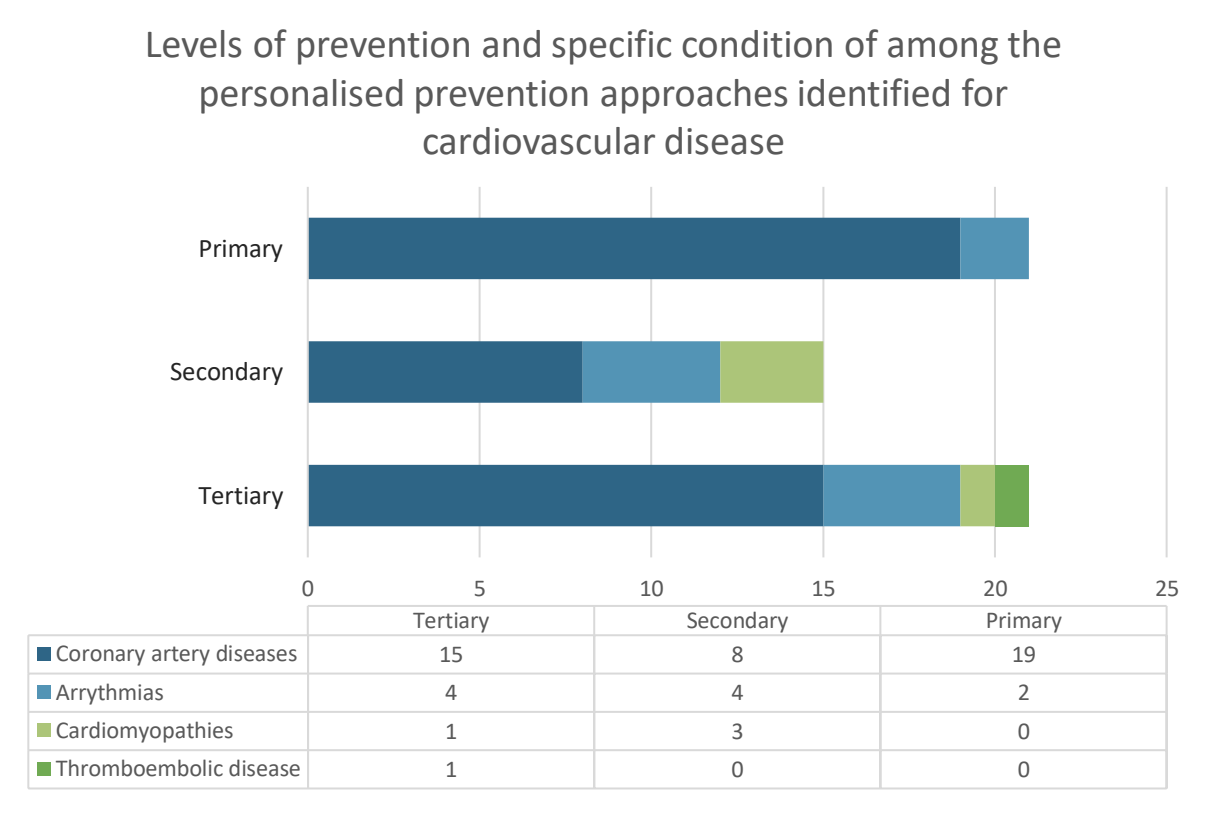
Current clinical practice utilises predictive models for cardiovascular risk that focus on modifiable risk factors and individual data, aiding in preventing 80% of cardiac events. (321) However, these models may not fully identify individuals with high risk due to genetic factors.

Thus, a paradigm shift towards personalised prevention is gaining recognition, fuelled by advancements in medical science and increased awareness. Personalised prevention shows promise in tailoring preventive strategies to each individual's unique genetic makeup, lifestyle choices, and medical history. By identifying high-risk individuals and implementing targeted interventions, personalised prevention aims to reduce the global burden of CVDs and enhance overall public health.

Specific features of the CVD records

A comprehensive analysis was conducted on 33 records focusing on cardiovascular diseases (CVDs), which collectively addressed various aspects of personalised prevention approaches. Among the records included a total of 57 distinct personalised prevention approaches were identified and subjected to in-depth examination. In these approaches, a wide range of cardiovascular diseases (CVDs) were targeted, including but not limited to coronary artery disease, myocarditis, atrial fibrillation, and stroke. Notably, a significant focus was observed on the management of hypertension, familial hypercholesterolemia, and other types of dyslipidaemias, which will be considered and examined as risk factors for myocardial infarction within the context of this research.

The majority of approaches were based on the use of pharmacogenomics and genomics, and focused on primary prevention (21 approaches, 36.8%) and tertiary prevention (21 approaches, 36.8%), in comparison with a smaller proportion of secondary prevention approaches (15 approaches, 26.4%). (Figure 5)



	Tertiary	Secondary	Primary
Coronary artery diseases	15	8	19
Arrythmias	4	4	2
Cardiomyopathies	1	3	0
Thromboembolic disease	1	0	0

Figure 5. *Levels of prevention and specific condition among the 57 identified personalised prevention approaches for cardiovascular diseases*

Coronary Artery Diseases

Coronary artery diseases (CAD) encompass a group of conditions that affect the blood vessels supplying the heart muscle, often leading to severe consequences, such as acute myocardial infarction. Among the 29 records included, 19 were reviews on different types of strategies for CAD personalised prevention, 4 were recommendations on the use of pharmacogenomics for treatment of people with past cardiac events, 5 were primary studies, including observational studies and RCT and 1 was a strategy implemented in a hospital. About countries, 14 studies were conducted in USA, 11 in Europe, and 4 in Asia.

The review identified 42 approaches aimed at preventing CAD, with a primary focus on averting acute myocardial infarction. Among these, 19 approaches concentrate on primary prevention. In particular, 13 approaches identify genetic variants associated with familial hypercholesterolemia or other dyslipidaemias (*PCSK9, APOB, LDLR, SLCO1B1*5*), while an additional 4 approaches target the management of hypertension and atherothrombotic conditions, in order to detect these diseases early and intervening through lifestyle modifications and targeted therapies, reducing the risk of acute myocardial infarction and other complications. Moreover, an alternative approach involves utilising Polygenic Risk Scores (PRS) to stratify patients based on their cardiovascular risk, thereby enabling primary prevention through lifestyle adjustments and healthy behaviours.

There are an additional 8 approaches dedicated to secondary prevention, primarily focusing on cascade screening through genetic testing for healthy relatives of affected individuals. Subsequently, regular cardiac screenings and follow-up are conducted for those identified as being at risk, enabling early diagnosis and appropriate management.

Moreover, 15 tertiary prevention approaches aimed at reducing CAD risks, not in healthy individuals but in those who have previously experienced CAD or undergone a PCI (percutaneous coronary intervention), pharmacogenomics plays a significant role. These approaches focus on genotyping a series of genes involved in the metabolism of various drugs used for the continuous treatment of CAD subjects. Notably, one recurrent example is the genotyping of *CYP2D19*, a crucial enzyme responsible for metabolising *P2Y12* receptor inhibitors. These medications play a crucial role in inhibiting platelet aggregation, preventing blood clot formation, and reducing the risk of thrombotic events, such as heart attacks.

Furthermore, these approaches can be applied to various genes and drugs, including antihypertensives, statins, vitamin K inhibitors, and others, enabling the precise dosage of the drug to make it as effective as possible in reducing the risk of recurrent heart attacks.

All the personalised prevention approaches focused on CAD are summarised in Table 8.

	Application	Intervention	Ref
Primary Prevention	**Genetic test for hypercholesterolemia or other dyslipidaemias (*PCSK9, APOB, LDLR, SLCO1B1*5*)** **Genetic testing for hypertension and atherothrombotic conditions** **PRS**	**Lifestyle modifications** **Target therapy**	(18,34, 35,37, 49,50, 72,92, 93,97, 303,309, 310,312, 322)

Secondary Prevention	**Genetic testing for healthy relatives of affected individuals**	**Regular cardiac screenings and follow-up**	(18,34, 35,37, 92,97, 310)
Tertiary Prevention	**Genetic testing of *CYP2D19, CYP2D9, VKORC1*, others**	**Adjustment of dosage of various drugs (*P2Y12* inhibitors, vitamin K inhibitors, b-blockers, etc.)**	(22,26, 41,42, 51,79, 81,86, 88,89, 303,305, 308,316, 318)

Table 8. *Personalised prevention approaches for coronary artery diseases (CAD)*

Arrhythmias

Arrhythmias are irregular heart rhythms that can disrupt the normal electrical activity of the heart, leading to potential health risks.

The review identified 10 personalised prevention approaches, with a primary focus on managing atrial fibrillation, one of the most common types of arrhythmias. These approaches primarily concentrate on secondary prevention strategies, ensuring continuous monitoring and follow-up of genetically predisposed individuals. Additionally, cascade screening for relatives is emphasised to identify potential risk factors and provide timely interventions. Moreover, the personalised strategies focused on atrial fibrillation include tertiary prevention, utilising pharmacogenomic testing to tailor therapies based on individual genetic profiles. This approach, for example, involves genotyping CYP2D6 to adjust the dosage of propafenone, aiming to reduce the risk of complications, such as stroke, by implementing more effective treatments.

These approaches involve genetic identification of syndromes associated with channelopathies, such as Brugada syndrome (with the search for mutations in the gene *SCN5A*) and Long QT syndrome (with the search for mutations in genes *KCNQ1* and *KCNH2*). Secondary prevention approaches for these conditions involve regular visits and check-ups for individuals predisposed to these channelopathies, while tertiary prevention emphasises personalised therapies based on individual needs and genetic makeup.

All the approaches focused on personalised prevention of arrythmias are listed in Table 9.

	Application	Intervention	Ref
Secondary Prevention	**Genetic testing for Brugada syndrome and Long-QT syndrome (*SCN5A, KCNQ1, KCNH2*)**	**Cascade genetic screening** **Monitoring and follow-up**	(40,92,309)
Tertiary Prevention	**Genetic testing (*CYP2D6, SCN5A, KCNQ1, KCNH2*)**	**Target Therapy**	(40,60,81,92)

Table 9. *Personalised prevention approaches for arrythmias*

Other cardiovascular diseases

Among the remaining 5 approaches for cardiovascular diseases, 4 are dedicated to cardiomyopathies, and 1 focuses on thromboembolic disease.

Cardiomyopathies are a group of heart muscle disorders that can lead to abnormal heart function and enlargement of the heart chambers. The primary focus of the identified approaches is on the identification of genetic variants in several genes (*MYBPC3, MYH7, MYL2, MYL3, TNNT2, TNNI3, CSRP3, TCAP, TPM1, ACTC1, TNNC1*) associated with hypertrophic cardiomyopathy in individuals presenting a compatible clinical picture. These approaches concentrate on secondary prevention and involve cascade genetic screening of healthy relatives to establish personalised follow-up pathways and cardiac monitoring for those predisposed.

On the other hand, thromboembolic disease refers to conditions where blood clots (thrombi) form in the blood vessels and can travel to block other blood vessels in the body, leading to serious complications such as pulmonary embolism or stroke. The identified approach is focused on tertiary prevention, aiming to prevent complications of the disease. This involves genetic testing of various genes, such as *VKORC1*, *CYP2C9*, and *CYP4F2*, to determine the proper dosage of medications like warfarin, a vitamin K inhibitor crucial for preventing the formation of emboli and clots. By tailoring drug dosages based on genetic information, the approach aims to reduce the risk of adverse events and optimise treatment outcomes.

All the approaches centred on personalised prevention of cardiomyopathies and thromboembolic disease are synthesised in Table 10.

	Application	Intervention	Ref
Secondary Prevention	**Genetic testing for cardiomyopathies (*MYBPC3, MYH7, MYL2, MYL3, TNNT2, TNNI3, CSRP3, TCAP, TPM1, ACTC1, TNNC1*)**	**Cascade genetic screening** **Personalised follow-up pathways and cardiac monitoring**	(39,59,309)
Tertiary Prevention	**Genetic testing for thromboembolic disease (*VKORC1, CYP2C9, CYP4F2*)**	**Adjustment of dosage of drugs (Warfarin)**	(309,312)

Table 80. *Personalised prevention approaches for cardiomyopathies and thromboembolic disease*

3.1.1.3 METABOLIC DISEASES

Prevention of Metabolic Diseases

Metabolic diseases encompass a group of disorders that disrupt the body's normal processes of energy production, utilisation, and storage. Among these conditions, type 2 diabetes mellitus (T2DM) stands as one of the most prevalent and significant public health challenges worldwide. T2DM is characterised by insulin resistance and impaired insulin secretion, leading to persistently elevated blood glucose levels. As a result, this chronic metabolic disorder poses a substantial burden on individuals, healthcare systems, and society at large. (323)

Another complex metabolic condition is obesity, which can be considered a chronic disease. It poses a substantial burden due to its association with various complications, such as cardiovascular issues, diabetes, respiratory disorders, and reduced life expectancy.
By tailoring preventive measures based on an individual's unique risk factors, genetics, and lifestyle, personalised prevention aims to provide more targeted and effective interventions for these chronic conditions.

Specific features of Metabolic Diseases records

Among all the identified approaches, a total of 15 approaches were identified for personalised prevention of metabolic diseases, with 10 specifically tailored for T2DM, one for non-alcoholic fatty liver disease (NAFLD), one for metabolic syndrome (MetS) and three for obesity, which was considered as a chronic disease in this review.
All the personalised prevention approaches identified for metabolic diseases are listed in Table 11.

Type 2 Diabetes

Six frameworks were dedicated to type 2 diabetes primary prevention, encompassing educational programmes designed to raise awareness about T2DM and to reduce its onset. These initiatives involved expert consultations, stakeholder engagement, and systematic evaluation of available evidence, while multiple frameworks highlighted lifestyle interventions, such as adopting a healthy lifestyle, engaging in physical activity, adhering to a balanced diet, and monitoring dietary intake. These interventions primarily targeted glucose intolerant patients, diabetic patients, individuals at risk of developing T2DM and healthy adults.
On the other hand, 7 approaches were identified, focusing on tertiary prevention primarily through targeted therapy for T2DM. This therapy involved using metformin (*ATM, SLC2A2, SLC22A1, SLC22A2, SLC47A1),* sulfonylurea (*PSMD6, CYP2C9, TCF7L2, ABCC8, KCNJ11, IRS1, CYP2C8),* repaglinide and thiazolidinediones (*PSMD6, PPARG)*. Furthermore, diabetic patients with established atherosclerotic cardiovascular or chronic kidney disease, and those at risk of hypoglycaemia or body weight-related issues, received additional treatment with glucagon-like peptide-1 (*GLP-1*) receptor agonists, sodium-glucose cotransporter-2 (*SGLT2*) inhibitors, and certain dipeptidyl peptidase-4 (*DPP-4*) inhibitors following initial metformin monotherapy, treatment was combined with lifestyle changes as a part of primary prevention strategy for individuals with very high risk of T2DM.

Other metabolic diseases

Five additional approaches were focused on tertiary prevention of other metabolic diseases.
Two approaches were identified for NAFLD and MetS target therapy, with a focus on statins targeting *APOE, SLCO1B1, PNPLA3.*(80)
Three other approaches were identified as personalised management of obesity, through the use of genomic or nutrigenetic testing and target therapies and diets, in order to reduce the complications linked to this condition. One of the key components in this personalised approach is the hormone leptin, produced by fat cells, which plays a crucial role in regulating appetite and energy balance. Understanding genetic mutations, such as deficiency or biallelic *LEPTR* mutations, allows for tailored management by targeting the leptin pathway and developing personalised therapies to address the specific genetic factors contributing to

obesity. One such drug utilised in this context is setmelanotide, which has been approved by the European Medicines Agency (EMA).

	Disease	Application	Intervention	Ref
Primary Prevention	**Type 2 Diabetes**	**Genetic testing**	**Lifestyle modifications**	(27,85, 90,91, 315,322)
Tertiary Prevention	**Type 2 Diabetes**	**Gentic testing (*ATM, SLC2A2, SLC22A1, SLC22A2, SLC47A1, PSMD6, CYP2C9, TCF7L2, ABCC8, KCNJ11, IRS1, CYP2C8, PSMD6, PPARG*)**	**Target Therapy**	(52,73,80,303)
	Obesity	**Genetic testing (*LEPTR*)**	**Target Therapy**	(31,94,95)

Table 91. *Personalised prevention approaches for metabolic diseases*

3.1.1.4 NEURODEGENERATIVE AND PSYCHIATRIC DISORDERS

Prevention of Neuropsychiatric Disorders

Neurodegenerative and psychiatric disorders encompass a wide range of debilitating conditions that significantly impact the overall health and well-being of individuals and societies. These disorders, which include neurological and psychiatric conditions, pose a substantial burden on global healthcare systems and social structures due to their complex aetiology and chronic nature.

The epidemiological burden of neurodegenerative and psychiatric disorders presents a compelling concern, as they significantly contribute to disability in affected individuals. Conditions such as Alzheimer's disease, Parkinson's disease, and depression, among others, profoundly reduce the quality of life for those afflicted. Neurodegenerative disorders, like Alzheimer's, often manifest with cognitive decline, memory loss, and executive dysfunction, leading to a heavy reliance on caregivers and impairing basic daily activities. Similarly, Parkinson's disease, characterised by motor symptoms like tremors and bradykinesia, can severely limit mobility and independence. Additionally, depression can cause profound emotional distress, social withdrawal, and challenges in maintaining personal and professional relationships. Consequently, these factors contribute to the high disability rates observed in individuals with neuro degenerative and psychiatric disorders worldwide. Understanding the magnitude of this burden is crucial for developing effective interventions and comprehensive care strategies aimed at improving the overall well-being and functional outcomes of those affected.

One promising avenue for tackling the challenges posed by neurodegenerative and psychiatric disorders is the advent of personalised medicine. Progress in genetics and neuroscience is paving the path for increasingly targeted and individualised interventions, albeit currently less prevalent for these disorders compared to other medical conditions.

Specific features of Neurodegenerative and psychiatric disorders records

Compared to the total number of approaches found, there are 5 approaches related to neuro degenerative and psychiatric disorders. In the context of neurological disorders, 2 approaches were identified for Alzheimer's disease. These approaches are respectively focused on primary prevention and tertiary prevention. Conversely, only one approach, pertaining to tertiary prevention, was found for Parkinson's disease.
Regarding psychiatric disorders, 2 approaches (40% of the total) have been documented, specifically concerning tertiary prevention of depression disorders and its subtypes.
All the approaches focused on neuro degenerative and psychiatric disorders prevention are synthesised in Table 12.

Alzheimer's disease

Alzheimer's disease imposes a substantial burden of disability on affected individuals. As the disease progresses, it results in a gradual deterioration of cognitive functions, memory retention, and problem-solving abilities, leading to profound impairment in performing daily living activities. Furthermore, behavioural changes and emotional disturbances can further hinder their independence and disrupt social interactions. The significant disability caused by Alzheimer's underscores the pressing necessity for improved diagnostic tools, targeted therapeutic interventions, and comprehensive support systems to enhance the quality of life for individuals grappling with this devastating condition.
ApoE is a crucial protein involved in lipid transport and metabolism within the brain, primarily known for its role in beta-amyloid clearance. It exists in different isoforms but the most important is ApoE4 because it represents the most well-known genetic risk factor for late-onset Alzheimer's disease. The intricate association of ApoE with Alzheimer's highlights its potential as a promising therapeutic target for tertiary prevention strategies. One of the approaches in this regard focuses on the development and utilisation of drugs in a mouse model of Alzheimer's disease, specifically those with retinoid-X receptor (*RXR*) nuclear agonist function. These drugs aim to induce the clearance of beta-amyloid, targeting the influence of ApoE4 and potentially mitigating its impact on disease progression.
Regarding primary prevention, subgroup analysis of the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) study indicated that subjects with the *ε4 allele*, identified through genetic testing, showed a more favourable response to multimodal interventions involving nutrition, physical activity, and cognitive engagement.

Parkinson's disease

Parkinson's disease is characterised by a significant level of disability, progressively impeding individuals' ability to perform daily activities due to a wide array of motor and non-motor symptoms. Motor symptoms, including bradykinesia, rigidity, tremors, and postural instability, often result in challenges with walking, dressing, eating, and executing fundamental tasks independently.
Additionally, non-motor symptoms, such as cognitive impairment, mood disorders, sleep disturbances, and autonomic dysfunction, substantially contribute to the overall burden of disability associated with this condition. Acknowledging the multifaceted nature of disability in Parkinson's disease is of utmost importance in optimising patient care and enhancing their overall quality of life. Early diagnosis and the implementation of interventions, such as targeted therapies, rehabilitation approaches, and supportive care, play a pivotal role in

mitigating disability and maximising functional outcomes for individuals living with this disease.

It is crucial to investigate novel therapeutic approaches with the potential to slow down or halt the progression of the disease. In this context, the dopaminergic neuronal pathways, which are primarily implicated in Parkinson's disease, offer promising opportunities for pharmacotherapy approaches. A multigene panel comprising genes encoding dopamine receptors (*DRD1, DRD2, DRD3*), dopamine transporters (*DAT, SLC22A1/OCT1*), and enzymes responsible for dopamine transformation and degradation (*COMT, MAO-B, DDC*) holds possible significance in addressing the burden of Parkinson's disease through targeted therapeutic interventions.

Depressive Disorder

Mental health disorders affect millions worldwide, leading to a range of disabling symptoms, including persistent low mood, loss of interest, cognitive impairments, and sleep disturbances. The burden of depression is multifaceted, encompassing not only the direct impact on affected individuals' quality of life but also substantial economic costs related to healthcare utilisation and productivity loss. Furthermore, depression can contribute to the development or exacerbation of other medical conditions, further compounding the overall burden.

Pharmacogenomic testing conducted by Myriad Genetics using the GeneSight panel offers a comprehensive interpretation of four pharmacodynamic gene variants (*SCL6A4, HTR2A, HLA-B1502, HLA-A3101*) and eight pharmacokinetic gene variants (*CYP1A, CYP2B6, CYP2C19, CYP2C9, CYP3A4, CYP2D6, UGT1A4, UGT2B15*). Of particular significance in terms of tertiary prevention strategies are the analyses focusing on pharmacokinetic genes, specifically *CYP2D6* and *CYP2C19*. These genetic variants play a vital role in determining an individual's metabolism status, determining whether they are normal, intermediate, poor, or ultra-rapid metabolizers of medications. Consequently, such variants have been incorporated into antidepressant dosing guidelines by expert groups, such as the Clinical Pharmacogenetics Implementation Consortium. This emphasises the crucial importance of personalised treatment approaches in optimising medication efficacy and minimising potential adverse effects for individuals diagnosed with depression disease.

	Disease	Application	Intervention	Ref
Primary Prevention	**Alzheimer**	**Apo E Genetic test**	**Lifestyle modifications and cognitive engagement**	(84)
Tertiary Prevention	**Alzheimer**	**Retinoid-X receptor (RXR)**	**Target Therapy**	(303)

	Depression	**Multi gene panel (*SCL6A4, HTR2A, HLA-B1502, HLA-A3101, CYP1A, CYP2B6, CYP2C19, CYP2C9, CYP3A4, CYP2D6, UGT1A4, UGT2B15*)** **Multi gene panel (*CYP2D6, CYP2C19*)**	**Target Therapy** **Adjustment of dosage of various antidepressant drugs**	(78,304)
	Parkinson	**Multi gene panel (*DRD1, DRD2, DRD3, DAT, SLC22A1/OCT1, COMT, MAO-B, DDC*)**	**Target Therapy**	(87)

Table 102. *Personalised prevention approaches for neurodegenerative and psychiatric disorders*

3.1.1.5 OTHER CHRONIC DISEASES

Five remaining approaches, identified from three included records, are focused on other chronic diseases described below. One approach targets the management of asthma, a chronic respiratory disease characterised by airway inflammation primarily mediated by IgE. This particular approach focuses on tertiary prevention, aiming to prevent the progression of the disease by utilising Omalizumab, an anti-IgE antibody. The dosage of Omalizumab is adjusted based on body weight and basal IgE levels, to achieve the desired reduction in IgE levels.(317)

Two additional approaches use the polygenic risk score (PRS) to identify individuals with low bone mineral density (BMD), indicating an elevated risk of osteoporosis, a chronic condition that results in increased bone fragility and high susceptibility to fractures. These individuals may benefit from primary prevention measures, such as lifestyle modifications or osteoporosis treatment.(306)

The last two approaches focus on primary and secondary prevention of age-related macular degeneration. A multigene panel is utilised to identify disease-related genetic factors (*ARMS2, CFH, IL8, VEGFA, TIMP3, SLC16A8, COL8A, RAD51B*), and targeted interventions address modifiable risk factors like smoking, lifestyle, and diet for carrier patients. These individuals undergo personalised eye examinations and follow-ups as part of secondary prevention strategies.(47)

3.1.2 BOTTLENECKS AND GAPS FOR PERSONALISED PREVENTION ADOPTION

Analysis of the 220 articles included led to a categorisation of bottlenecks made up of 24 main elements, which were then further traced to 5 main categories. Table 13 shows the categories of bottlenecks identified, along with the percentage of articles that reported each of them.

Category	Bottlenecks	% of articles
Research	Lack of clinical evidence	33%
	Lack of economic evaluations	17%
	Lack of clinical utility	16%
	Difficult applicability across populations	20%
	Insufficient funds for research	7%
Technologies	Difficulties in test choice	13%
	Lack of technologies standards and regulations	26%
	High technologies costs	16%
Healthcare workers	Poor knowledge from healthcare professionals	34%
	Limited acceptance from healthcare professionals	14%
	Absence of specialised healthcare professionals	15%
ELSI and Implementation	Health provision inequalities/accessibility/social disparities	33%
	Policy-makers poor knowledge	12%
	Inequalities between countries	6%
	Data sharing management concerns	19%
	Privacy issues	19%
	Lack of resources and cost-effectiveness	14%
	Lack of guidelines and standards	19%
Citizens and Patients	Psychological impact of results and communication concerns	29%
	Trust issues	19%
	Lack of belief in personal benefit	13%
	Discrimination and stigmatisation	18%
	Poor knowledge and education	28%
	Lack of willingness to participate in research	12%

Table 113. *Bottlenecks for the implementation of personalised prevention approaches (scoping review)*

Research Bottlenecks

In the domain of research bottlenecks, one recurring issue that prominently surfaced in our analysis was the dearth of clinical evidence concerning the practical utility of the personalised prevention approaches under scrutiny. This deficiency serves as a pivotal obstacle in the pathway toward implementing these preventive strategies on a larger scale within healthcare systems. The underlying cause of this deficiency can be attributed to the intricate challenges

researchers encounter when trying to structure robust studies that unearth the true clinical potential of these prevention tools.
This bottleneck not only hinders the advancement of personalised prevention but also impacts the decision-making process within healthcare systems. Without substantial clinical evidence, healthcare providers and policymakers may be reluctant to endorse and incorporate these approaches into mainstream medical practices. Furthermore, it highlights the need for investment in research infrastructure, methodologies, and collaborative efforts to generate the requisite evidence for informed decision-making.
Another noteworthy challenge within this category is the lack of applicability of personalised prevention approaches across diverse populations. While certain strategies may prove effective in specific contexts or demographic groups, their generalizability to broader populations remains uncertain. This issue underscores the need for research efforts aimed at tailoring these approaches to ensure their effectiveness across various demographic, cultural, and socioeconomic contexts.

Technologies Bottlenecks

Moving on to the realm of technological bottlenecks, a prevalent issue that emerged prominently, accounting for 26% of the analysed articles, relates to the absence of standardised practices and regulations governing the use of technologies in personalised prevention, especially in the context of applied omics testing. This technological heterogeneity poses significant challenges as it leads to inconsistencies in data quality, interpretation, and comparability across studies.
The lack of standardised practices not only impedes the seamless integration of these technologies into healthcare systems but also raises concerns about data reliability and interoperability. To address this bottleneck, collaborative efforts within the scientific community are imperative. The development and implementation of standardised protocols, data-sharing mechanisms, and quality control measures are essential steps toward harmonizing technological practices in the field of personalised prevention.
Furthermore, establishing a framework for shared regulation and guidelines is crucial to ensure the ethical and safe use of these technologies. This is particularly important given the sensitive nature of personal health data and the potential consequences of misinterpretation or misuse of omics information.

Healthcare Workers Bottlenecks

Regarding the challenges faced by healthcare workers, a prominent bottleneck relates to their insufficient knowledge about the tools, opportunities, and regulations surrounding personalised prevention strategies currently available to them. This deficiency was identified in a substantial 34% of the articles analysed.
This knowledge gap among healthcare professionals is a critical concern, as their understanding and acceptance of personalised prevention approaches are pivotal for successful implementation. Without adequate awareness and training, healthcare providers may be hesitant to embrace these novel approaches, potentially limiting their integration into routine clinical practice. Addressing this bottleneck necessitates targeted educational initiatives, training programs, and continuous medical education to equip healthcare professionals with the requisite knowledge and skills to effectively utilize personalised prevention tools.

ELSI and Implementation Bottlenecks

Within the Ethical, Legal, Social, and Implementation (ELSI) domain, a significant issue that stands out is the existence of inequalities in terms of accessibility to healthcare services, which was highlighted in 33% of the analysed articles. The integration of personalised prevention methods into healthcare systems brings the risk of exacerbating existing disparities by making these resources accessible primarily to populations with greater means and resources.
This dilemma underscores the ethical dimension of personalised prevention. It raises concerns about fairness, justice, and equity in healthcare delivery. Policymakers and healthcare stakeholders must be vigilant in ensuring that these innovative strategies do not inadvertently widen the healthcare gap but rather contribute to reducing disparities by offering equitable access to cutting-edge preventive measures.
Additionally, the lack of common guidelines for the sharing of health data and the associated privacy concerns, which were cited in 19% of the articles, represent crucial implementation bottlenecks. The sharing and protection of health data are central to the success of personalised prevention. Establishing clear guidelines, regulations, and safeguards for data sharing while respecting individual privacy rights is paramount for building public trust and facilitating the responsible use of health data in the context of preventive approaches.

Citizens and Patients Bottlenecks

Lastly, within the domain of citizens and patients, two salient bottlenecks emerged prominently. First, there is the potential psychological impact related to the communication of omics test results used in preventive strategies, cited in 29% of the articles. This psychological aspect reflects the profound implications of genetic or omics information on individuals' well-being and mental health. It underscores the need for robust communication strategies, genetic counselling, and support systems to help individuals navigate the emotional and psychological aspects of receiving such information.
Secondly, issues concerning trust in the effectiveness of these preventive strategies among citizens and patients, as mentioned in 19% of the articles, are of paramount importance. Trust is a cornerstone of successful healthcare interventions, and individuals must have confidence in the efficacy and safety of personalised prevention approaches. Building and maintaining this trust necessitate transparent communication, evidence-based practices, and rigorous monitoring of outcomes to demonstrate the tangible benefits of these strategies.

3.2 Stakeholder Consultation Results

3.2.1. Expert interviews: perceived barriers to the adoption of Personalised Prevention Strategies

Twenty-six interviewees, including 5 Policy makers, 6 Researchers, 11 Health professionals and 4 Patient representatives, 13 females and 13 males, participated in this stakeholder consultation phase. Experts were from different European organisations and multiple countries. Experts provided their individual opinions and were not representing any particular country or organisation.
Table 14 provides an overview of the experts' perceived barriers to the adoption of personalised prevention. Barriers to a wider adoption of personalised prevention strategies were systematised in 5 main levels:

(i) ***Healthcare system***: refers to the main cross-cutting components of a healthcare system, based on the WHO healthcare system building blocks framework;

(ii) ***Research***: refers to the main components of the research and innovation sector;

(iii) ***Implementation***: refers to the multiple processes and activities associated with the translation of scientific findings to clinical practice;

(iv) ***Awareness, education and literacy***: refers to understanding and competences of each of the stakeholder groups regarding personalised prevention;

(v) ***Personal attitudes****:* refers to individual attitudes of end-users to personalised prevention.

Overall, 13 themes with 28 associated sub-themes captured the stakeholders' perceived barriers to the adoption of personalised prevention (Table 14). Each theme was categorized in one of the five main levels. For each of the sub-themes that emerged, codes allow a better clarification of the sub-theme scope. For illustration purposes, we additionally selected example sentences quoted from the interviews. The 13 themes recurrently raised as barriers to personalised prevention, by most or all groups of stakeholders were: 1) Health strategy, 2) Inequities in access, 3) Clinical practice, 4) Scientific strategy, 5) Scientific funding, 6) Translational gaps, 7) Synergies between healthcare, research and industry, 8) Ethical, legal and social issues (ELSI), 9-11) Awareness, education and literacy of policy makers (9), health professionals (10), and citizens and patients (11) and 12-13) Personal attitudes of health professionals (12), and citizens and patients (13). We highlight below some of the outstanding barriers suggested at each main level:

Healthcare system

Within the Healthcare system organisation and functioning level, some aspects were highlighted as barriers to a wider implementation of personalised prevention strategies in clinical settings.

The current healthcare strategy itself, organised around disease treatment instead of prevention, is perceived by the majority of experts from every stakeholder group as a major constraint. One researcher says: "I think most of the healthcare systems are simply not oriented at prevention. They are oriented at curing or first diagnosing and then curing disease." A decision-maker adds: "(...) preventing is not an urgent business and that's why it doesn't get the sufficient political attention nor the investments that are needed". Most stakeholders also pointed to the predominance of the curative model of clinical services over prevention and the way it impacts on other building blocks of healthcare systems, such as financing, a critical factor for policy implementation. Experts considered that current funding in personalised prevention is insufficient, with "(...) only 3% goes to prevention and health promotion (...)". The low investment in prevention is also due to a strong competition with other priorities and demands for public investment in health, in what an expert called "a crowded fiscal space". The curative medicine approach is still the healthcare systems status quo, and a global change of perspective is needed towards prevention. The existing economic models developed for health technology assessment (HTA), a prerequisite for the market introduction of health devices and technology, are not the most appropriate for prevention. Some experts mentioned a lack of demonstration of the cost-benefits of personalised prevention strategies, due to inappropriate or absent economic models, contributing to a generalised scepticism of personalised prevention utility and effectiveness.

Linked with the focus in disease treatment, another relevant aspect mentioned is the lack of a solid strategy for personalised prevention, where actual implementation is fragmented, involving many uncoordinated actors, with unclear roles and responsibilities.
Existing health inequities in access to preventive strategies are another issue perceived as a barrier to its wider adoption, especially with the recognition that the current state of implementation "in no way ensuring universal and equitable access" with an emphasis on restrictions in access due to economic issues (e.g. out of pocket expenses, reimbursement gaps, etc.) and other social factors. Many stakeholders considered that equity is insufficiently taken into consideration in the actual model of delivery of personalised prevention, leaving some people behind, especially those with a lower socioeconomic status. The routine implementation of preventive approaches must consider the issue of equity, guaranteeing that health inequalities were no further deepened.
Actual clinical services organisations present some issues that are perceived as barriers to personalised prevention. The shortage of resources, the overload of health professionals, including the administrative tasks requested to physicians, and logistic problems are fracturing the relationship between patients and health professionals, considered "a major obstacle to personalised medicine". Personalised prevention relies on a set of expensive technologies and diagnostics, and some countries have difficulty guaranteeing widespread access to these, with an impact on clinical services delivery and coverage, and ultimately hindering citizens and patients to benefit from its use.
Personal health data are the basis for the development of individualised health devices and enable the production of evidence to support tailored personalised strategies, such as polygenic risk scores calculations, personalised drug therapies, etc. Most of this data is collected in the context of health service delivery (e.g. consultations, diagnostics, imaging, etc.), however, the collection of health data in clinical settings suffers from a lack of standardized norms that are limiting the quality of these technologies. The lack of standardisation of health data is perceived as a barrier to personalised prevention.

Research

At the Research level, a main barrier was the focus of the current strategy and investment on disease treatment discovery as opposed to prevention strategies. The low interest in prevention research is eventually due to the time length required for studies and the very high costs of studying large population cohorts over long times. There is also a negative impact on research teams working on supporting aspects needed to produce evidence for implementation, which "are highly unexplored: assessing clinical utility, exploring feasibility from an organizational point of view, understanding its comprehensibility for the citizen, assessing the readiness of the health professionals (...)". Current streams of research funding aren't focused on prevention, leading the core research to stray from personalised prevention.

Implementation

Several translational gaps were mentioned as holding back implementation of personalised prevention. Namely, the lack of regulatory frameworks and guidelines supporting health professionals in the adoption of personalised approaches. The length of time and costs of translation of personalised prevention is another barrier mentioned by experts. Personalised prevention is frequently perceived as complex, resulting from interactions between biological

factors, environmental exposure and individual behaviours, and therefore still in the realm of research. It is also perceived as expensive, with limited application in clinical daily practice: "Despite efforts (…) personalised medicine is not perceived as the medicine of the moment but rather as an emerging research field with potential benefits in the future (…)". This quote illustrates the current state of awareness for personalised prevention. Others may feel that "(…) in recent years, the potential of personalised medicine has been much hyped, promising great benefits always just around the corner. This corner, however, has not yet been well materialised and defined". End-users are not very aware of sufficiently robust evidence supporting the adoption of preventive approaches.

Synergies between healthcare, research and industry are insufficient and there are some resistances to collaboration, although these are much needed for the implementation of individualised approaches, which require that all stakeholders work in close collaboration. Feelings of distrust can explain the perceived resistance from all sides, hindering the translation of scientific knowledge into clinical practices or technological products.

Personalised prevention approaches, especially when supported by genetic or genomic data, raises ethical, legal and social implications (ELSI) that impact citizens and patients. Experts mentioned ELSI concerns as a barrier to the adoption of preventive measures: "(...) people are afraid to share their personal data because they're afraid it can be used against them, (…) people don't think the systems in place are robust enough from a cyber security perspective (...)". Since citizens and patients are the ones who mostly benefit from personalised prevention, at any level of prevention, distrust in the healthcare system due to a perceived lack of security and privacy can be a major barrier to a wider public acceptance, compromising the benefits.

Awareness, Education And Literacy & Personal Attitudes

One of the main barriers mentioned by almost all experts was a generalised lack of awareness, education and literacy for personalised prevention, especially for policy-makers, health professionals, and citizens and patients.

Health professionals mentioned recurrently that a lack of education and training on the concepts that underlie personalised prevention strategies are hindering its adoption in the clinics, and this impacts on citizens and patients enrolment and acceptance. Health professionals also mentioned that training for the development of skills to better communicate with patients is lacking. Moreover, a professional resistance towards preventive approaches was mentioned by some experts, noting a resistance to change current medical practices. This resistance can be linked with a perception of personalised prevention "(...) as a field of research and something that is more of a future concept rather than something that can already be implemented" and something in the realm of research, with little impact on current health services delivery.

For citizens and patients, a low health literacy level is considered a barrier to public acceptance of personalised prevention approaches. Health literacy implies the achievement of a level of knowledge, personal skills and confidence to take action to improve health. Adequate access to accurate health information will empower citizens and patients to make well-informed decisions about their health. Reduced capacity to judge the quality of information, specially found on the internet, has an impact on perceived relevance of personalised strategies to prevent a disease and can create feelings of distrust in health systems and science. Health professionals and the media have an important role at dissemination of reliable messages, and misinformation can be a problem. Combined with a low health literacy level, some

personal attitudes and fears can stray people from adhering to prevention practices, especially when they perceive themselves as healthy individuals for whom disease prevention isn't an urgent concern.

Experts also pointed to a lack of awareness and literacy of policy makers regarding personalised prevention. On one end, policy makers feel they don't have sufficient evidence regarding the cost-benefit of personalised prevention. Additionally, a low interest in the field of prevention may arise due to its medium-long term outcomes, which are longer than the political cycles (3-4 years). Other experts also highlighted that low interest of policy-makers can also be due to a lack of demonstration of personalised preventive approaches effectiveness compared with other available strategies: "probably there are low hanging fruits to improve the general health of the population that cost less, and decision-makers prefer to invest in cheaper strategies." Awareness can be increased if scientific evidence is better communicated to policy-makers.

LEVEL	THEMES	SUB-THEMES AND CODES	REPRESENTATIVE QUOTES
HEALTHCARE SYSTEM	HEALTH STRATEGY	**FOCUS ON DISEASE TREATMENT NOT PREVENTION** • Lack of a sense of political attention and priority for prevention • Generalized resistance to prevention • Investment focus on treatment • Limited and low visibility of personalised preventive strategies • Tertiary prevention focus **LACK OF STRATEGY FOR PERSONALISED PREVENTION** • Limited support from supra-national institutions • Lack of assessment of medium/long term impact of current options • Lack of an overarching framework for prevention including other determinants of health and health in all policies approach • Siloed perspective of health care expenditure • Lack of clear roles and responsibilities of all stakeholders involved in personalised prevention • Lack of coordination between different actors **INSUFFICIENT INVESTMENT** • Insufficient funding for implementation of personalised prevention strategies	"I think most of the healthcare systems are simply not oriented at prevention. They are oriented at curing or first diagnosing and then curing disease. (...) the education of people is pointed at diagnosing and curing. The reimbursement system is pointed at diagnosing." [R1] "(...) preventing is not an urgent business and that's why it doesn't get the sufficient political attention nor the investments that are needed" "(…) implementation (…) is very fragmented, you have different authorities, organizations, (…) different actors, but it is not in a really coordinated order. There it's not one big strategy yet." [DM2] "(…) fail to fully assess the medium- and long-term impact of choices that weigh today but could save a lot tomorrow, this is due to a siloed perspective of health care spending". [CP4] "We need to shift the perception, particularly among politicians, policy-makers, and the general public, that personalised prevention is a burden on the healthcare (…) it is essential to reframe personalised prevention as an

		• Competition for scarce resources • Competing priorities and demands for public investment **INADEQUATE ECONOMIC MODELS** • Inadequate economic models for personalised prevention • Lack of a business model for prevention • Insufficient research on economic models for personalised prevention • Lack of demonstration of cost benefits of personalised prevention • Insufficient awareness of benefits due to inadequate business models • Skepticism on the cost-effectiveness of personalised prevention strategies • Personalised preventive strategies are perceived as costly and difficult to implementation in a short-time frame	investment rather than a cost. This will help generate more support and funding for public health initiatives, including research, thereby calling for increased investments in these areas." [DM5] "(...) an issue to overcome is related to the financing. (…) should we argue a shift of money from care to personalised prevention (…)? And should we ask money from other sectors to pay for personalised prevention? That is, indeed, an issue to see what strategically would work best." [DM2] (...) it's not seen by everyone that prevention pays off, so we need to be better at demonstrating the costs and the calculation of the return on investment. And that health outcomes will improve by investing in prevention." [DM2] "I don't think it's lack of evidence but skepticism on the cost-effectiveness, probably there are low hanging fruits to improve the general health of the population that cost less, and decision-makers prefer to invest in cheaper strategies. [DM3]
	INEQUITIES IN ACCESS	**ACCESS CHALLENGES** • Existing access asymmetries across regions • Need to travel to have access to personalised prevention strategies	(...) personalised prevention is very dependent on access to a set of diagnostics that are expensive and that we are in no way ensuring universal and equitable access to. (…)." [DM1]

		• Access to personalised prevention strategies is often not reimbursed • Patient and citizens out-of-pocket expenses are individually supported costs • Effect of socio-economic status • Impact of the political determinants of health in access and health outcomes	"There are some barriers that need to be addressed (…) accessibility and affordability to personalised prevention programs, that can be limited by several barriers, such as geographical, financial, logistical(…)" [DM5]
	CLINICAL PRACTICE	**PATIENT DOCTOR RELATIONSHIP** • Organizational problems fracture the doctor-patient relationship (overload, time shortage, waiting lists, administrative tasks, infrastructure)/organizational problems due to resources shortage • Lack of adequate communication with patients/citizens/ Communication failures with patient/citizens • Low accurate information provided to patients/citizens **CLINICAL ORGANIZATION** • Insufficient service delivery and coverage • Lack of integration with primary care/ lack of GPs involvement • Lack of coordination between medical specialities • Insufficient access to technology/diagnostics • Dependence of access to high-cost technology • Insufficient evidence to support implementation into clinical practice • Tertiary prevention focus	"(...) the way in which the patient interacts with the doctor (...) especially for specialist visits, doctor has 15 minutes to talk to the patient; of these 15 minutes, most of the time is spent entering all the patient's data into the system. This creates great frustration both in the patient, who has to deal with a professional who merely enters data into a system, and in the doctor, who feels his profession has been betrayed. So this severely fractures doctor-patient relationship, again due to logistical issues, is a major obstacle to personalised medicine." [HP3] "The easy access to technology (where to go and costs) must be improved."[HP8] "I think the big mistake that is being made (at least in 50%) is the little involvement of primary care physicians." [HP9] "The use of genetic testing, especially for common chronic diseases, is not widespread in clinical practice. (...) even

		LACK OF TOOLS AND STANDARDS ● Insufficient standardization of clinical and laboratory reporting for genomic tests ● Lack of harmonized clinical data quality standards ● Lack of interoperability of data and clinical data standards	where there is evidence, it is probably not sufficient for the adoption of personalised prevention strategies (…).” [HP3] “Difficulties in the integration of data with existing health systems (…).” [HP5]
RESEARCH	***SCIENTIFIC STRATEGY***	**INSUFFICIENT RESEARCH ON PREVENTION** ● Insufficient research on prevention ● Lack of incentives for research teams working on prevention ● Insufficient research to demonstrate benefit and clinical utility ● Lack of robust evidence reduce credibility and uptake, create skepticism and raise concerns about efficacy, potential harms and cost-effectiveness among health providers, policy makers and general public ● Insufficient evidence to support implementation **LACK OF STANDARDS ON PREVENTION RESEARCH** ● Low awareness regarding quality standards	“The lack of robust evidence supporting personalised prevention strategies (...) that can demonstrate efficacy and safety, reduces the credibility of these interventions and can impact the uptake of these strategies. It is possible that this lack of evidence on the effectiveness of personalised prevention approaches can create skepticism among healthcare providers, policymakers, and the general public. Without solid evidence, there may be concerns about the efficacy, potential harms, or cost-effectiveness of these strategies.” [DM5] “(…) in the field of treatment there are gold standard in terms of methodology and good practice (...) in the field of prevention, nothing equivalent exists. (...) people have also to pay attention to the quality of the methodology.” [R2]
	SCIENTIFIC FUNDING	**INSUFFICIENT FUNDING STREAMS** ● Lack of funding for prevention research	(...) funding incentives. If there is no funding source, there will be no team working on this.[R2]

		• Insufficient economic incentives leads to lack of motivation and/or interest in developing prevention research • Low interest from industry • Low investment in large cohorts • Low investment in genomic research • Lack of vision for a long-term sustainability of data generated by healthcare systems	"Among the main problems has always been the lack of large funding in the area of research for personalised prevention aimed at building large studies. (...) funding has always been concentrated in the area of therapy." [R4] "(...) people are not thinking about the sustainability and the long term monitoring of the data that are being generated by the healthcare system(...)" [R5]
IMPLEMENTATION	***TRANSLATIONAL GAPS***	**LACK OF IMPLEMENTATION FRAMEWORKS** • Lack of a regulatory system for translation of prevention research outputs • Scientific knowledge is not sufficiently translated into clinical guidelines • Lack of organization and harmonization of standards for personalised prevention • High dependence of international guidelines or consortium **LENGTH OF TIME AND COSTS OF TRANSLATION** • Personalised prevention strategies take time to enter into practice • Personalised prevention strategies are perceived as expensive	"(…) very little activity in the field of HTA for assessing the power of risk scores when compared to other clinical outcomes." [R5] "We still have a huge problem for lack of verification of the data sets that come from the healthcare domain (...) the lack of a clear regulatory route for medical devices." [R5] "(…) there's a lot of knowledge but it's not in the guidelines. (...) we do nothing because it's not in the guidelines." [R1] "(…) for biomarkers risk scores and AI solutions healthcare systems are still not aware of the importance of funding for validation of these tools to bring them to clinical practice or technical decision-making process."

		COMPLEXICITY OF PERSONALISED PREVENTION OPERATIONALIZATION • Low promotion of implementation due to misconstrued concept of personalised prevention as not ready for healthcare • Complexity of personalised prevention implementation (many layers of intervention) • Lack of an effective communication of scientific evidence to non-scientific audiences	"Genetics-based screenings are expensive and difficult to implement in a short time frame (…)" [HP9] "The perception regarding personalised medicine is that it is associated with complex and expensive studies and that it will only be something of the distant future." [HP2] "Despite efforts (…) personalised medicine is not perceived as the medicine of the moment but rather as an emerging research field with potential benefits in the future (…)."[HP6] "(…) an issue to overcome is still the complexity of personalised prevention. (…) you give someone a pill and the person can get better. Personalised prevention is linked to behaviours of healthy people, which are very difficult to control. (...) it gets very complex and I think the complexity may shy away (...)" [DM2] "The low uptake of personalised strategies is certainly due to a lack of perceived benefit of these, but a real lack of evidence is also a cause. (…) the potential of personalised medicine has been much hyped, promising great benefits always just around the corner. This corner, however, has not yet been well materialized and defined." [HP3]
	SYNERGIES BETWEEN	**LOW COLLABORATION**	(…) health sector is not proactive enough in cooperating with other sectors. (…) there is no time allocation or financial or

	HEALTHCARE, RESEARCH AND INDUSTRY	• Inertia to collaborate with other sectors • Absent incentives for collaboration with other sectors • Resistance to collaborate with industry • Gap between research and entrepreneurship	human resources allocation nor mandate or responsibility to actively network and liaise with other sectors." [DM2] "Evidence for personalised prevention has existed for many years (...), as well as recommendations (...). However, in practice, things don't happen due to the inertia of healthcare systems. [HP6] "it require us to work with industries and there is a need to understand and accept this." [R3] "(…) first gap is turn an academic into a product or a test (…) takes a long time. The second gap (…) you need to persuade the health system to use it." [R3] "(…) getting academics to understand entrepreneurship. [R3]
	ELSI	**LACK OF DATA GOVERNANCE AND REPORTING REGULATION** • Lack of a legal and regulatory framework for health data • Lack of governance, legal and ethical frameworks • Lack of ELSI guidelines for reporting research findings to patients **DATA PROTECTION ISSUES** • Data privacy and security issues	" (...) problems with the governance, legal and ethical there are many questions unanswered, and many countries are very far from having real strategies." [DM3] "(...) reason to report back to the participant, but there's no guideline on it." [R1]

		• Insecurity regarding data protection • Guarantee compliance with GDPR • Discretionary adoption of GDPR at the national level relative to access to genomic and health data	"(...) people are afraid to share their personal data because they're afraid it can be used against them, (…) people they don't think the systems in place are robust enough from a cyber security perspective (...)" [DM3] "The fact is that the GDPR has been adopted differently by different member countries, which is certainly an obstacle to the uniform development of research." [R4]
AWARENESS, EDUCATION AND LITERACY	***POLICY MAKERS***	**LACK OF AWARENESS AND LITERACY** • Low awareness and literacy of policy makers regarding personalised prevention • Low awareness of policy makers regarding personalised prevention benefits • Perception of personalised prevention approaches still in the research realm • Lower perception of the positive impact of personalised preventive strategies in health outcomes **LOW POLITICAL INTEREST** • Asynchrony between health outcomes and political cycles • Political influence on the allocation of resources/ political determinants of health	"I think that what is lacking is a greater perception on the part of political decision-makers, of the importance of prevention strategies, with regard to their results, the health gains that the population will have." [DM4] "When we talk about prevention strategies, we are talking about strategies whose results we will only be able to measure in the medium-long term. And if we are talking about political cycles of 4-5 years (…) they are not very attractive for a politician to implement." [DM4] "Evidence needs to be better communicated to policy makers, we are bombarded with too much information (…). (...) we still need to have the best scientific evidence to date and how we can act on it. (...) Academy has to get closer to policy makers, using easier language." [DM4]

			"We need to shift the perception, particularly among politicians, policy-makers (…) that personalised prevention, along with public health in general, is a burden on the healthcare system" [DM5] "it is very important to convey the concept that new technologies in the area of personalised prevention are not the preserve of a few from the scientific world, but are essential tools for everyone, this awareness can stimulate need and promote investment." [R4]
	HEALTH PROFESSIONALS	**LOW AWARENESS AND INSUFFICIENT KNOWLEDGE** ● Insufficient awareness of benefits of personalised prevention approaches / low perception of benefits and risks ● Perception of personalised prevention approaches still in the research realm ● Perception of personalised prevention approaches as very costly ● Perception of personalised prevention approaches as an emergent research field ● Stigma of genetics as dangerous ● Low awareness of personalised prevention in public health professionals **INSUFFICIENT TRAINING** ● Insufficient training and information about personalised prevention approaches for clinical practice	"(...) health care providers are often the first ones who are unaware of the possibility of personalised prevention (…)" [CP3] "The perception of doctors and decision-makers in the healthcare system regarding personalised prevention as a field of research and something that is more of a future concept rather than something that can already be implemented." [HP6] "(…) The perception regarding personalised medicine is that it is associated with complex and expensive studies and that it will only be something of the distant future." [HP2]

		• Insufficient knowledge of existing evidence • Insufficient communication skills of health professionals • Lack of training/knowledge about genetic information utility • Lack of training of medical students in a prevention setting • Lack of training on communication with patients • GPs low health literacy level	"The stigma of genetic as a dangerous issue and not to be considered as useful biomarkers like all the others." [HP8] "(…) the lack of education is a major barrier. General practitioners are not fully aware of the advances that the medical world is making, due to a lack of training. In fact, they tend to use outdated approaches and models, due to a lack of education." [HP3] " (…) the lack of specific training on doctor-patient communication strategies means that the doctor improvises when communicating with the patient/citizen." [HP3]
	CITIZENS AND PATIENTS	**LOW HEALTH LITERACY LEVEL AND KNOWLEDGE** • Low health literacy level of citizens • Insufficient health information and literacy • Lack of knowledge about the benefits and risks • Lack of training/knowledge about genetic information utility • Lack of knowledge hinders patients involvement • Lack of a widespread transmission of knowledge beyond doctor-patient relation • Unsatisfied patient information needs • Lack of health literacy programs • Lack of knowledge about current programs • Lack of education for prevention	" (…) many individuals may not be aware of the availability, benefits, and importance of participating in screening programs or other personalised prevention initiatives (…) lack of trust and perceived benefits in healthcare systems, concerns about privacy, and perceived low personal relevance of personalised prevention strategies." [DM5] "people only want to learn about a disease when they are directly or indirectly affected by it." [CP2] "Communication about personalised medicine and the amount of information provided are insufficient [to citizens/patients] in the context of an overcrowded

		LOW AWARENESS • Lack of awareness of non-attendance impact • Lack of awareness and/or knowledge about available personalised prevention strategies • A perception shift is needed for general acceptance of personalised prevention • Low awareness and/or understanding of health benefits of prevention • Low recognition of personal relevance **MISINFORMATION/DISINFORMATION** • Misinformation • Disinformation • Information biases influences patient/citizens attitude	information space, which includes fake news as well as incomplete or distorted information (...)" [HP6] "The information and advice source. (…) instead of asking qualified professionals for a second or third opinion, we [citizens/patients] ask a neighbour, a co-worker or, worse, the internet, without validating the source of the answer." [CP1] "It depends on how we communicate with patients (…) Usually patients embrace the initiative in a good way, but it is crucial how the information comes through." [HP9]
PERSONAL ATTITUDES	***HEALTH PROFESSIONALS***	**RESISTANCE TO CHANGE** • Resistance to change current medical practices • Professional resistance • Medical paternalism • Lack of motivation/resistance to change established practice • Professional conflicting interests • Lack of trust on the promised benefits of personalised prevention	"I believe that there is resistance from various sectors to these [preventive] programs. there can be competition for the same resources, at the limit. There may also be issues related to the resistance of professionals themselves to developing these programs." [DM1] "(…) the paternalistic attitude of the medical profession and the limited involvement of patients, and especially citizens, in co-creating pro-health solutions." [HP6]

			"Mistrust and distrust of the benefits of these technologies, due to lack of evidence." [HP3]
	CITIZENS AND PATIENTS	**STIGMA** • Fear of health data misuse • Fear of discrimination • Stigma related to genetic data • Perceived stigma **FEAR AND DISCONFORT** • Fear of results • Fears of health risks (radiation exposure) • Invasive nature of screenings • Patients' discomfort • Inconvenience for patients • Insecurity • Lack of confidence • Negative psychosocial impacts of results/information • Religious beliefs **LACK OF MOTIVATION** • Lack of motivation for prevention due to focus on treatment attitude • Lack of patients motivation • Lack of trust • Insufficient patient empowerment	"(...) there is a stigma on the use of genetics that may lead to community to a non accepting stage." [HP8] "(...) lack of awareness of the great advantage of an early diagnosis (…) combined with fear of finding something in the screening.(...) And then the inconvenience of the screening itself (...)" [CP2] "The psychological repercussions of screening results on patients. How will genetic-based risk information be handled." [HP5] (...) For prevention, you're healthy, you say, why should I bother? So, it's also a personal attitude of healthy citizens that is not helping implementation of prevention, not everybody is very aware and conscious." [R1] "Involvement of patients, in general, is not sufficient, both because of lack of information and knowledge, and because of lack of trust." [HP3]

		• Incapacity of family members involvement	"(…) reduced trust in doctors, the healthcare system, and science (…) among a large portion of the population." [HP6]

Table 14. *Main Barriers and Bottlenecks for the Adoption of Personalised Preventive Strategies (Interviews)*

3.2.2 SURVEY OUTCOMES

Participants Characteristics

Findings presented are drawn from the initial 200 responses received to the survey. Table 15 shows the percentage of responses from each stakeholder group in the survey: Citizens and Patients, Health Professionals, Researchers, and Policy Makers. The distribution reveals that the highest number of respondents belong to the Citizens and Patients category. The smallest number of responders were in the Policy Makers category, possibly aligning with its relatively lower frequency.

Table 15. *Stakeholders*

GROUPS	n	%
Citizens and Patients	73	37%
Health Professionals	41	21%
Researchers	67	34%
Decision Makers	19	10%
Total	200	100%

Table 16 examines the gender distribution among the participants. Around two-thirds of the respondents are female, suggesting a potentially greater interest in the subject matter among women compared to men.

Table 16. *Gender*

GENDERS	n	%
Male	66	33%
Female	132	66%
Non-binary	0	0%
Other	0	0%
Do not want to answer	2	1%
Total	200	100%

Table 17 shows the age distribution of the participants. The survey exclusively targeted adults aged 18 and above. The majority of respondents fall within the 40 to 60-year age range.

Table 17. Age

AGE GROUPS	n	%
18 - 29 yrs	21	11%
30 - 39 yrs	38	19%
40 - 49 yrs	50	25%
50 - 59 yrs	54	27%
60 - 69 yrs	30	15%
70 - 79 yrs	6	3%
80+ yrs	1	1%
Total	200	100%

Table 18 shows the educational backgrounds of the respondents. Remarkably, a highly educated cohort emerges, with 41% possessing a master's degree and 51% having pursued doctoral studies. This was expected for health professionals, researchers and policy makers but possibly unexpected for citizens and patients group. However, citizens and patients' respondents show a similar education level distribution, with an accumulated percentage of master's and PhD degrees of 86%, vs 92% for all participants. These results can be attributed to several factors: the survey was conducted in English, excluding citizens and patients with insufficient English proficiency; the subject matter is complex, and even though we attempted to make the questions more accessible, they may still be too difficult for citizens with lower education level; finally, it was difficult in this short time to disseminate the survey evenly among European citizens, and it must have reached predominantly those with higher levels of education.

Table 18. Education level

LEVELS	n	%
Primary education	0	0%
Secondary education	3	2%
Bachelor's degree	12	6%
Master's degree	82	41%
Doctoral studies	102	51%
Other	1	1%
Total	200	100%

Table 19 shows the geographic distribution of respondents by country. The survey, disseminated at the European level through the communication channels of PROPHET, and reinforced by the WP2 team, has garnered responses primarily from Portugal, followed by Bulgaria, The Netherlands, Belgium, the United Kingdom, and Italy. Other European countries have contributed fewer than 10 respondents each. The observed asymmetry in terms of nationality, with a substantially higher number of answers from Portugal compared to other countries, might be introducing a bias. However, for each target group, we did not find any major differences in classifications (% of agreements, % disagreement, % of "neither agree nor disagree" or % of "Don't know") between the overall respondents (including Portugal) and the respondents excluding those from Portugal. To enhance the robustness of the findings, the survey's online availability will be extended, and dissemination across Europe, after the summer vacation period is finished, will be intensified to encourage a more diverse participant base.

Table 19. *Country*

COUNTRIES	n	%
Austria	5	3%
Belgium	12	6%
Bulgaria	16	8%
Croatia	0	0%
Cyprus	1	1%
Czech Republic	2	1%
Denmark	1	1%
Estonia	4	2%
Finland	8	4%
France	9	5%
Germany	3	2%
Greece	1	1%
Hungary	1	1%
Ireland	2	1%
Italy	10	5%
Latvia	0	0%
Lithuania	0	0%
Luxembourg	1	1%
Malta	0	0%
Netherlands	14	7%
Poland	1	1%
Portugal	68	34%
Romania	1	1%
Slovakia	1	1%
Slovenia	2	1%
Spain	3	2%
Sweden	8	4%
UK	12	6%
Other	14	7%
Total	200	100%

Main Barriers and Enablers to the Adoption of Personalised Preventive Strategies

In this section, we present the most significant survey findings. We highlight the key barriers identified by each stakeholder group and analyse how distinct stakeholders respond to common pivotal questions.
The questions in the survey were developed based on barriers identified by experts in the interview phase, which were transformed into statements for the respondents to select a level of agreement or disagreement with the statement, using a Likert scale. To simplify the data analysis in this report, we have added the percentages of *Agree* with *Strongly agree*, as well as *Disagree* with *Strongly disagree*. Below we highlight the major agreement levels (% provided are for agreements, unless stated otherwise). We also stress the statements with higher rates of disagreement, which indicate that the survey responses did not validate the experts' views on a particular barrier.
The questions asked to citizens and patients (CTB) were specifically developed for this stakeholder group in a less technical language. For the other stakeholder groups there is a set of common questions (HDR) to which each of the groups answered, and a set of questions specific for Policy makers (PM), Health professionals (HP) and Researchers (R).

- ***CITIZENS AND PATIENTS***

The survey included a question allowing the separation of answers from respondents with a self-reported chronic disease (Patients, N=24 (33%)) from those from respondents without any known disease (Citizens, 49 (67%)). The Citizens and Patients stakeholder group answers were analysed together, and we expect to do a finer analysis later if numbers of respondents for each group increase.
Citizens and patients identified the most significant barriers in two main sub-themes: (i) *Inequities in accessing the healthcare system* and (ii) *Awareness and education among citizens and patients*.
Regarding access challenges, the survey reveals a strong agreement consensus among respondents in two statements. Firstly, "Insufficient access to primary care services may hinder adherence to personalised prevention approaches" (question CTB10), which garnered an 89% agreement. Secondly, "Citizens and patients might face limitations in accessing specific personalised prevention procedures due to their socio-economic status" (question CTB17), achieving a high 90% agreement (Figure 6).

The survey responses also underscore the substantial barrier posed by low health literacy levels among citizens and patients concerning personalised prevention. An overwhelming 86% express the viewpoint that "Citizens and patients lack sufficient information to decide whether they wish to engage in personalised prevention programs" (question CTB5). Furthermore, 89% believe that "Citizens and patients lack adequate information about available prevention programs" (question CTB4) and an even higher percentage, 95%, feel that "Citizens and patients are insufficiently informed about the importance of personalised prevention approaches based on their health indicators, biomarkers, or family health history" (question

CTB3). Additionally, 77% of respondents believe that "Health professionals do not adequately inform or recommend participation in personalised prevention approaches "(question CTB8), suggesting that communication between healthcare professionals and citizens and patients on the subject of personalised prevention may require improvement.

Regarding the sub-theme *Personal attitudes, fears, and discomfort*, Citizens and patients exhibit greater apprehension about "experiencing pain or adverse effects to personalised prevention approaches" (question CTB23 – 74%), as well as the possibility of "discovering disease or facing death when adhering to personalised prevention approaches" (question CTB24 - 74%), while there was no great agreement with feelings of "embarrassment or discomfort with some personalised prevention procedures" bing a barrier (question CTB22 - 33%).

Some questions gathered agreement levels below the expectation suggested by the interviews, indicating that the question subjects are not strong barriers. For question CTB21, "Citizens and patients fear discrimination from providers of personalised prevention approaches" the level of agreement was 47%, while 21% disagree and 33% were neutral (neither agree nor disagree or don't know). Similarly, the question CTB16 "Personal beliefs, cultural or religious, may prevent citizens and patients from participating in certain personalised prevention procedures" also received a relatively low level of agreement (59%), with 14% disagreement and 41% neutral. We did not collect any information on religion or ethnicity. To gain clarity on this matter, a larger and more diverse respondent pool will be instrumental. Finally, lack of trust in health professionals or the health system is also not an important barrier to adhesion to personalised prevention approaches, as shown by a 35% disagreement to CTB14, "Patients and citizens do not sufficiently trust health professionals, health systems or scientific research"

Figure 6. *Agreement rates for selected questions to the stakeholder group Citizens and Patients (CTB)*

2.4. Report on critical factors for the successful adoption of Personalised Prevention approaches by healthcare systems

- ***POLICY MAKERS***

Policy makers have identified barriers and bottlenecks primarily within the healthcare system, particularly concerning strategic sub-themes (i) *Clinical practices* and (ii) *Ethical, legal, and social implications (ELSI)*.

Among these challenges, two critical barriers (PM2 and PM4) stand out, both of which show a notable agreement rate of 95% among respondents. The first significant obstacle is "… the need to advance the legal and regulatory frameworks for sharing genetic data" (PM4). This underscores the complex ethical and legal considerations surrounding the exchange of such sensitive information, which have not yet been solved. The second pressing barrier refers that "Economic models that demonstrate costs and benefits for personalised prevention are lacking" (PM2). These models are pivotal in establishing the viability and rationale for personalised prevention strategies in healthcare systems and are thus fundamental to support decisions from policy makers (Figure 7).

The prevailing opinion, shared by 89% of policy maker respondents, is that healthcare systems do not sufficiently prioritise preventive medicine ("Healthcare systems are not sufficiently focused on prevention medicine" - HDR 14). This disproportionate focus on treatment warrants a paradigm shift towards emphasizing proactive prevention measures. Furthermore, a lack of strategies for personalised prevention in healthcare policies has been identified. A substantial 84% of policy makers agree that "There is a lack of strategy in health policies to support the implementation of personalised prevention approaches" (HDR12). A related concern is that "An insufficient coordination and cooperation among different governing sectors (health, social, environmental, etc.) hinders the formulation of personalised prevention policies" (PM1- 84% agreement).

A shortage in critical services, resources, and equipment required to operationalise personalised prevention strategies within healthcare systems was also highlighted by policy makers. Accordingly, the question "There is a lack of critical services, resources and equipment to operationalise personalised prevention strategies in health systems (HDR15), reached an 84% agreement consensus. Similarly, the scarcity of human resources available to work on personalised prevention initiatives is stressed: "There are limited human resources to allocate to personalised prevention programmes in health systems" (PM6) with 79% of respondents agreeing with this concern.

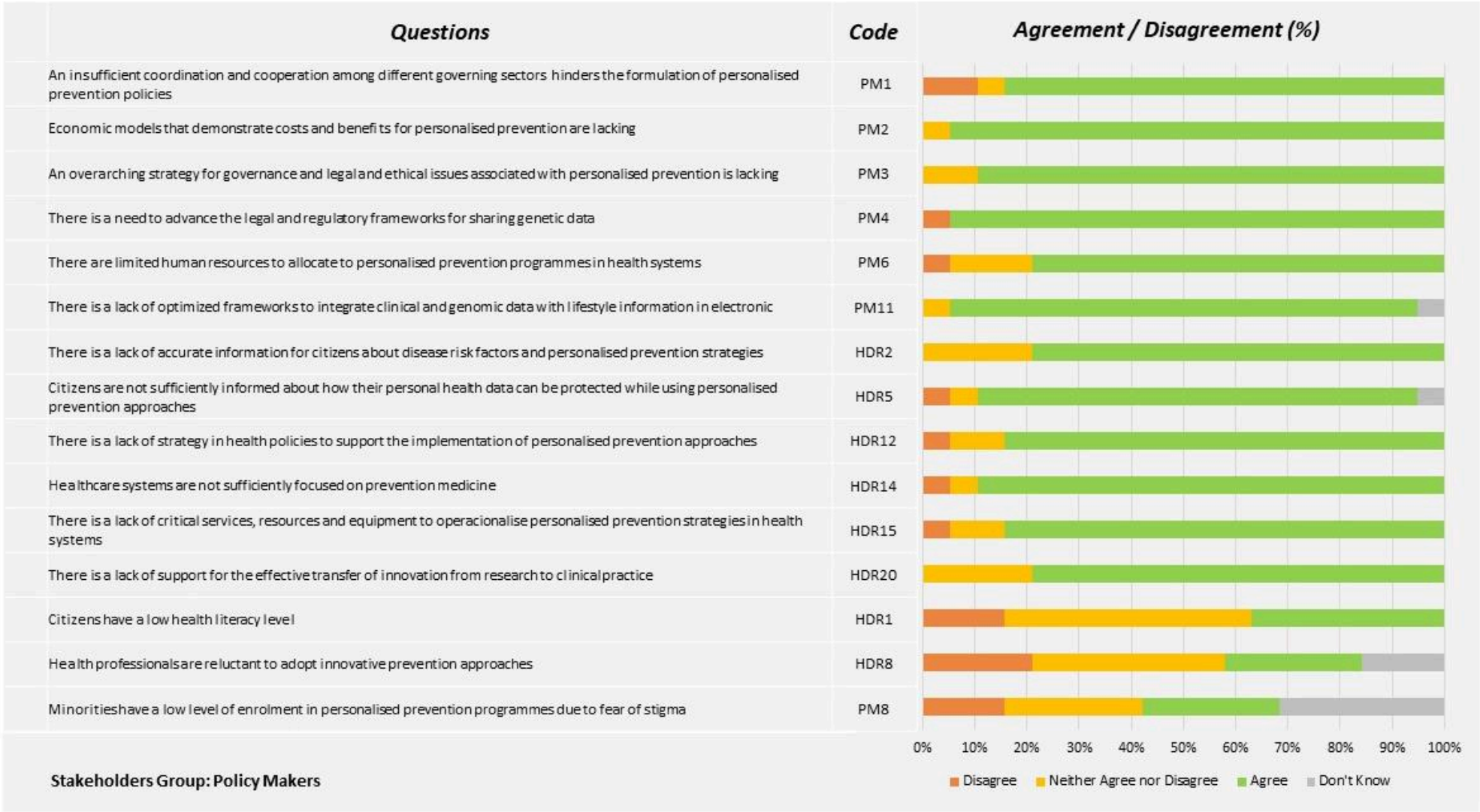


Figure 7. *Agreement rates for selected questions to the stakeholder group Policy Makers (PM and common questions HDR)*

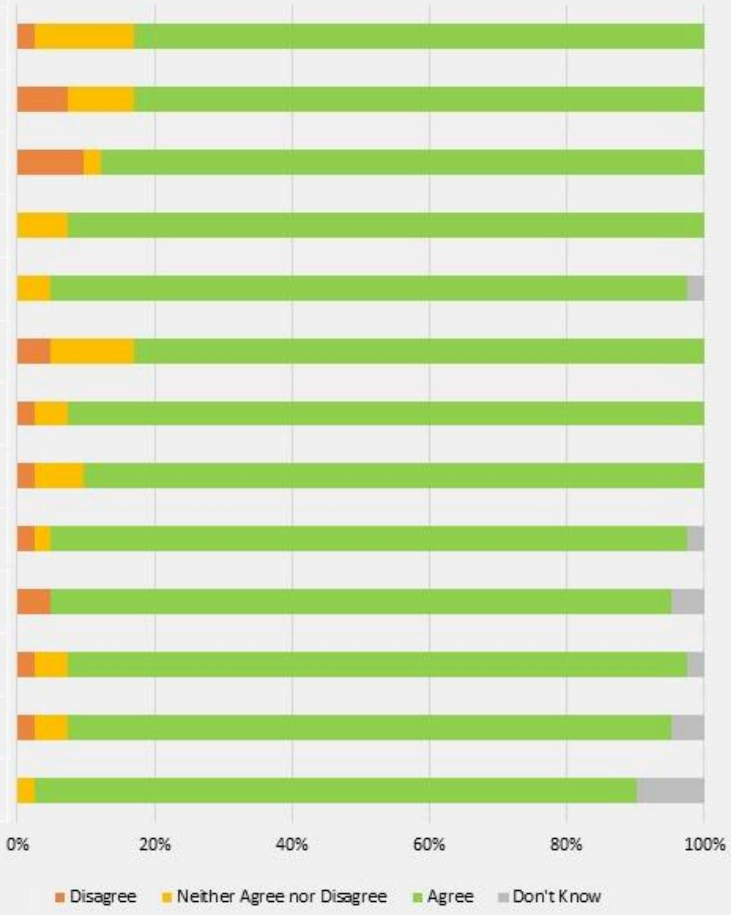
- ***HEALTH PROFESSIONALS***

Results for selected questions to health professionals are shown in Figure 8. Overall, health professionals demonstrated a remarkable consistency in identifying a set of barriers, with high agreement levels equal to or surpassing 90%. The leading concern is related to low investment levels, with a substantial 93% agreement on the statement "Governments do not adequately support or allocate funds for the implementation of personalised prevention programs" (HDR11). Echoing concerns emphasized by policy makers, another main barrier is the absence of a cohesive strategy for personalised prevention within the healthcare system, as highlighted by a 90% agreement for question “There is a lack of strategy in health policies to support the implementation of personalised prevention approaches” (HDR12). Also aligned with policy makers, a third concern emerging is related to ethical, legal, and social issues (ELSI), particularly concerning data protection information for citizens. Namely, 93% of health professionals agreed that "Citizens are not sufficiently informed about how their personal health data can be protected while using personalised prevention approaches" (HDR5).

Health professionals further strongly agreed with a lack of knowledge and awareness regarding personalised prevention, both among policy makers and citizens and patients. A meaningful 90% of health professionals agreed that "Policy makers have insufficient knowledge about personalised prevention strategies" (HDR9). Furthermore, 93% of health professionals believe that "Patients are not adequately informed about the available personalised prevention options for managing disease progression" (HDR4), while 88% agreed with the statement "Citizens aren't aware of the purpose and importance of personalised prevention approaches" (HDR3). An additional 83% concurred with the idea that "There is a lack of accurate information for citizens about disease risk factors and personalised prevention strategies" (HDR2).

Remarkably, 73% of health professionals, who are pivotal for the successful implementation of personalised prevention, agreed that "Health professionals lack a clear understanding of personalised prevention." This critical barrier identified by health professionals will have a cascading effect on other issues, raising additional barriers and bottlenecks for the adoption of personalised prevention strategies in health systems. Health professionals are also introspective about their own preparedness to confront the challenges associated with personalised prevention. A significant 83% agreement consensus emerged around the assertion that "Health professionals possess insufficient knowledge concerning personalised prevention strategies" (HDR6). Furthermore, an overwhelming 93% majority concurred that "Health professionals lack adequate understanding of the application of genetics and genomics in personalised prevention" (HDR7).

Questions	Code
Citizens have a low health literacy level	HDR1
There is a lack of accurate information for citizens about disease risk factors and personalised prevention strategies	HDR2
Citizens aren't aware of the purpose and importance of personalised prevention approaches	HDR3
Patients are not sufficiently informed about personalised prevention options to manage disease progression	HDR4
Citizens are not sufficiently informed about how their personal health data can be protected while using personalised prevention approaches	HDR5
Health professionals have insufficient knowledge about personalised prevention strategies	HDR6
Health professionals have insufficient knowledge about the use of genetics and genomics for personalised prevention	HDR7
Policy makers have insufficient knowledge about personalised prevention strategies	HDR9
Governments don't sufficiently support or fund the implementation of personalised prevention programmes	HDR11
There is a lack of strategy in health policies to support the implementation of personalised prevention approaches	HDR12
Healthcare systems are not sufficiently focused on prevention medicine	HDR14
There is a lack of critical services, resources and equipment to operacionalise personalised prevention strategies in health systems	HDR15
There is a lack of support for the effective transfer of innovation from research to clinical practice	HDR20



Stakeholders Group: Health Professionals

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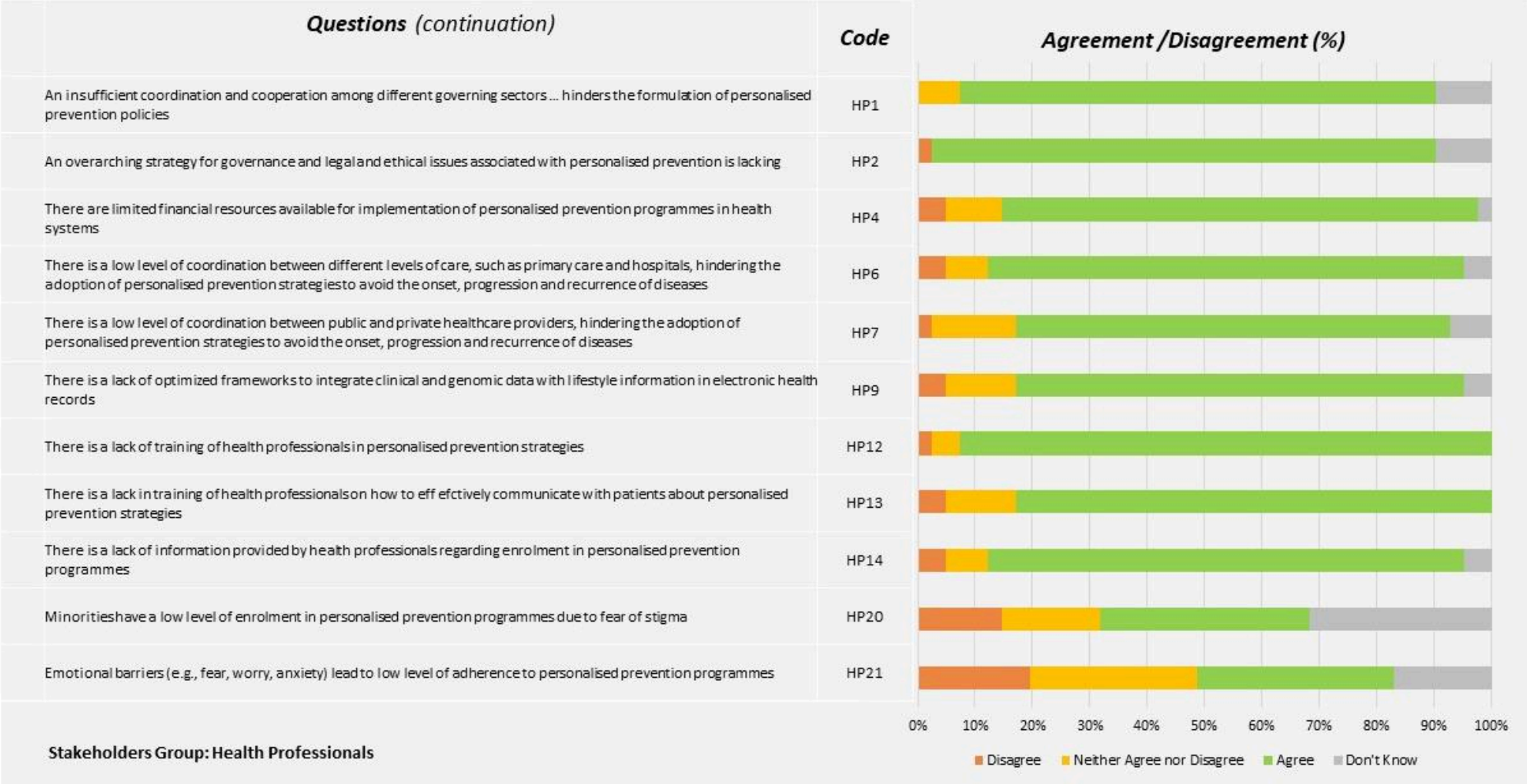

Figure 8. *Agreement rates for selected questions to the stakeholder group Health Professionals (HP and common questions HDR)*

Moreover, health professionals recognized that there is a shortage of opportunities for their training in personalised prevention strategies, as emphasized by a 93% agreement to the statement "There is a lack of training of Health professionals in personalised prevention strategies" (HP12). Equally relevant, 83% acknowledged the absence of training for health professionals in effectively communicating personalised prevention strategies to patients, as stated in "Health professionals lack training in effective patient communication regarding personalised prevention strategies" (HP13). These insufficiencies in professional training have further repercussions. The recognition that health professionals are not able to provide adequate information supporting citizen enrolment in personalised prevention programs, is evident from the 83% agreement with the statement "There is a lack of information provided by health professionals regarding enrolment in personalised prevention programs" (HP14).
In sum, the health professionals' acknowledgment of their own information gaps and limitations in effectively communicating personalised prevention strategies underscores the need for comprehensive training initiatives. Addressing these challenges is vital for fostering a more informed and engaged approach to personalised prevention among both health professionals and the broader public.
Overall, the health professionals' survey outcomes underscore the prevailing feeling that awareness and training, strategy development, and investment are pivotal factors in addressing the challenges posed by personalised prevention approaches.

- ***RESEARCHERS***

The levels of consensus of researchers to the survey statements were not as homogeneous at for the health professionals and policy makers stakeholders groups, with whom they shared 18 questions. Research did not reach a level of agreement equal to or greater than 90% for any of the barriers they were queried about, while such high levels of consensus were found for health professionals and policy makers (see Figure 9).
Researchers are in alignment with health professionals and policy makers regarding the assertion that "Healthcare systems lack sufficient focus on preventive medicine" (HDR 14, with 87%) and that "There is a lack of strategy in health policies to support the implementation of personalised prevention approaches" (HDR 12, with 85% agreement). They further corroborate health professionals regarding the "… lack of critical services, resources and equipment to operationalise personalised prevention strategies in health systems" (HDR15 - 79%). Additionally, researchers also identified barriers related to citizens and patients within the ELSI and Awareness themes: "Citizens lack sufficient information about ensuring the protection of their personal health data when utilizing personalised prevention approaches" (question HDR 5 - 81%), and "Citizens lack awareness regarding the purpose and significance of personalised prevention approaches" (question HDR3 - 79%).
Regarding the subset of questions addressed only to research (R), which focused specifically on research and innovation issues, this group agrees that "There is a lack of support for the effective transfer of innovation from research to clinical practice" (question R7, 73%). Their agreement levels were lower regarding the "… lack of knowledge about the initiatives and funding opportunities for encouraging personalised prevention" (question R6 – 54%).
For questions R1-R4 rates of agreement were comparatively lower, with a substantial proportion of neutral answers (don't know or neither agree nor disagree). For instance, the rate of agreement to "There is insufficient research in the area of personalised prevention" was relatively low (R3, 48% agreement, with 37% neutral), as was to "There are a limited number of

groups working on research about personalised prevention" (R2, 48% agreement, with 38% neutral).
The same pattern emerged for questions related to funding "There is a lack of competitive funding streams dedicated to research in the field of personalised prevention" (R1, agreement 46%, with 42% neutral) and quality of research "The quality of the methodology of research in the area of personalised prevention is insufficient" (R4, the agreement 37%, with 48% neutral). For all these questions the rates of disagreements are low, suggesting a lack of knowledge in the area.

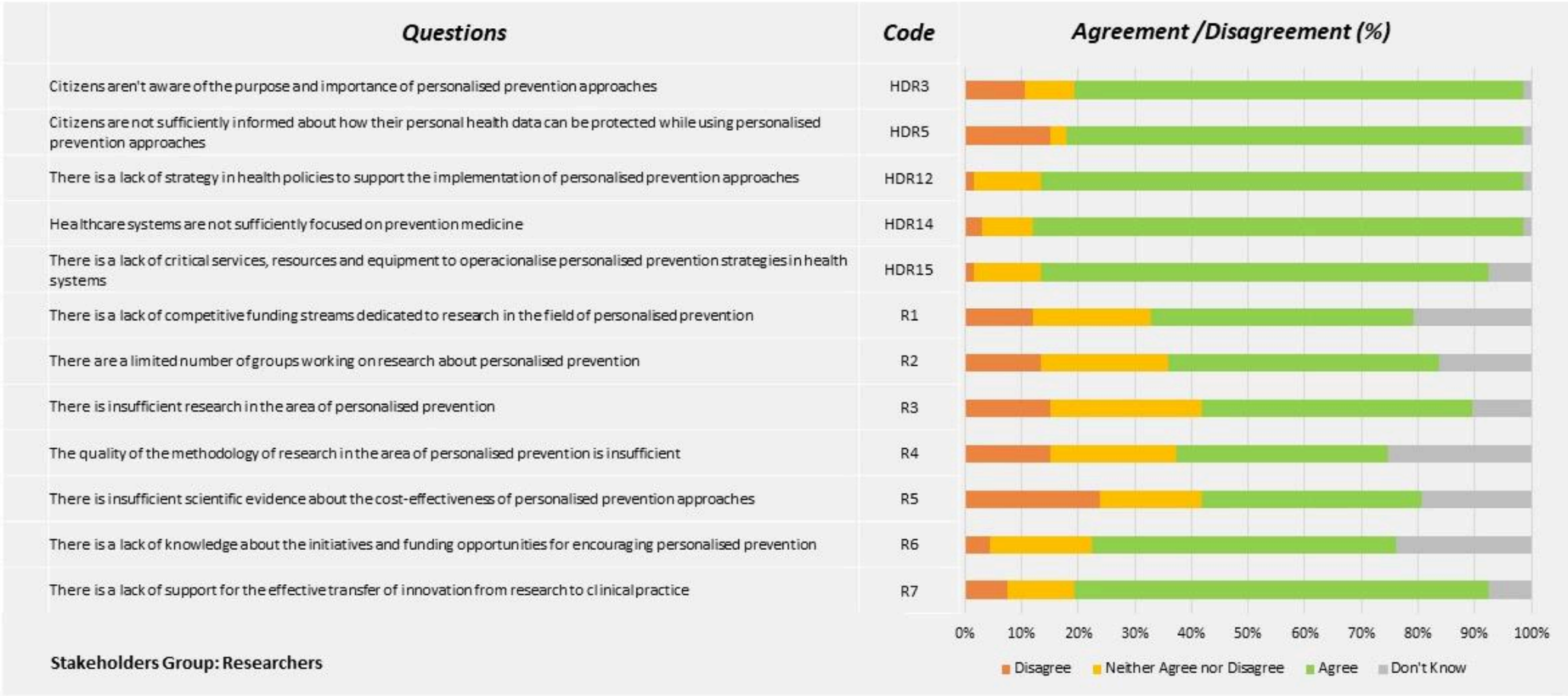

Figure 9. *Agreement rates for selected questions to the stakeholder group Researchers (R and common questions HDR)*

4 Discussion

Personalised prevention, a pivotal approach in the management of chronic diseases, has garnered significant attention in the research landscape. In a first analysis, through an extensive literature review, we observed a pronounced focus on cancer, followed by cardiovascular diseases, within the realm of personalised prevention strategies. This emphasis aligns with the extensive research and the more established understanding of the genetic aspects of underpinnings of tumour pathophysiology compared to the impact of lifestyle factors on genetic components in cardiovascular diseases. In this context, the research has particularly emphasised tertiary prevention strategies especially for cancers, exemplified by breast cancer, where therapeutic interventions have been extensively studied by analysing tissue samples from affected individuals, enabling targeted and personalised therapies. This underscores the growing emphasis on tailored treatment plans, designed to suit each patient's unique genomic profile, numerically exceeding primary preventive measures like prophylactic surgical interventions and secondary prevention tactics, such as increasing screening frequency in high-risk individuals.

Conversely, in the context of cardiovascular diseases, pharmacogenomics plays a vital role, driven by the need for personalised therapeutic approaches based on individual genetic profiles. However, primary prevention assumes greater significance in the overall management of cardiovascular conditions due to its emphasis on lifestyle interventions, such as dietary modifications and physical activity. As a result, genomics facilitates the identification of individuals with a heightened risk of cardiovascular diseases, a group that may not be identified by conventional clinical predictive models. This newfound identification empowers healthcare professionals to recommend personalised lifestyle modifications to these high-risk individuals, encouraging the adoption of healthier habits that effectively counteract or diminish the likelihood of cardiovascular events.

Moreover, our exploration of secondary personalised prevention strategies has revealed a comparatively lower volume of literature, compared to the tertiary prevention strategies. One possible explanation for this disparity may be the presence of effective screening methods already in place for certain chronic conditions, such as cancer screenings aimed at the general population, with particular reference to breast, colorectal and cervical cancer. Nevertheless, we acknowledge the potential for increased effectiveness and cost-effectiveness by implementing traditional screening on individuals identified as high-risk based on their genetic profiles, thus offering further stratification in the population and personalised clinical pathways. Examples in this regard currently include genetic testing to family members of individuals with conditions with a genetic aetiology. These include many of the conditions mentioned in the arc of the review study, including syndromes and predisposing mutations for the onset of oncologic diseases (*BRCA1/2*, Lynch, Li-Fraumeni, FAP, and many others), cardiomyopathies and arrhythmias, and metabolic type diseases. Performing cascade testing and the subsequent early identification of these conditions allows risk reduction strategies and individualised screening pathways to be set up in affected family members in order to mitigate their burden and promoting the effective use of resources from the perspective of a value-based system. Confirming this, these considerations are reflected in analyses conducted by the Center for Disease Control in the area of public health genetic applications. The CDC,

has identified applications for which there is strong evidence to support implementation, including analyses of the cost-effectiveness of the tools, which are collected within the Tier1 class. These include some of the very conditions we highlighted, including Hereditary Breast and Ovarian Cancer Syndrome, Lynch Syndrome, Familial Hypercholesterolemia. (324) In the area of applications to the general population, the same level of evidence is not available to date at the level of implementing large-scale personalised prevention strategies. Therefore, it is necessary to direct future efforts in assessing the health impact but also the sustainability of these approaches to the general population, focusing particularly on primary and secondary prevention.

However, it is worth noting that other chronic conditions, such as neurodegenerative and psychiatric disorders, have received comparatively less attention and research, despite their recognised substantial relevance for healthcare systems.

However, despite the vast number of results of this review, the state of implementation and adoption of personalised strategies for prevention of chronic disease are still far from being optimal. Infact, while some centres have made strides in adopting personalised prevention approaches, utilising targeted therapies, pharmacogenomics, and cascade testing for pathologies, such as breast cancer and Lynch syndromes, much remains to be accomplished in other areas. Indeed, despite the remarkable advancements in personalised prevention, it is essential to recognise that a considerable portion of these innovative strategies is still in the trial phase and requires further demonstrations in terms of effectiveness and health benefits. This highlights the need for sustained efforts to promote clinical studies and translational research, in order to widespread the adoption of personalised prevention strategies in various healthcare settings.

Amidst these challenges, there is undoubtedly a promising prospect for the future. The emergence of national genomic strategies in several European countries and beyond, particularly exemplified substantial genome sequencing efforts, marks a significant step forward in preventive healthcare. These groundbreaking advancements not only offer a deeper understanding of genetic predispositions to chronic diseases but also pave the way for personalised prevention strategies tailored to individual needs.

Concerning the bottlenecks hindering the implementation of personalised prevention approaches, a notable alignment emerges between the findings obtained through the comprehensive review of scientific literature and the insights obtained from consultations with stakeholders via interviews and surveys.

First and foremost, the results of our literature review underscore a critical issue: the deficiency of robust evidence supporting the clinical efficacy of personalised prevention approaches, particularly in the context of utilising omics technologies in primary and secondary prevention. This dearth of evidence poses a significant challenge to the widespread implementation of these techniques within healthcare systems. It calls for a concerted effort from the scientific community to generate the necessary data and evidence that can substantiate the clinical utility of these preventive strategies.

Moreover, the inherent complexity of studying the long-term clinical effects of preventive measures becomes evident. Such studies entail extended timelines, leading to increased costs and logistical complexities, including patient recruitment, managing information flow, and retaining participants within the study. These logistical challenges further emphasize the need

for sustained commitment and resources in research endeavours aimed at evaluating personalised prevention approaches.

Additionally, our study highlights the issue of healthcare inequalities, particularly those of a social nature, which hinder access to healthcare services. There is a legitimate concern that the implementation of personalised prevention approaches, without clear regulation and integration into existing healthcare systems, may inadvertently exacerbate these disparities. This underscores the importance of establishing well-defined pathways and reimbursement systems to ensure equitable access to personalised prevention for all segments of the population.

A third major bottleneck revolves around the potential psychological impact on patients and their families when confronted with information regarding their risk of developing chronic conditions. The receipt of such information should be accompanied by expert counselling and support to help individuals comprehend the actual risk and guide them toward meaningful preventive interventions. Managing this information independently may not lead to positive lifestyle changes and could even discourage individuals from taking beneficial actions.

Regarding the results the stakeholder consultations and survey, we found a remarkable consistency between the barriers identified by the interviewed experts and high levels of agreement from the survey respondents, for all four stakeholder groups.

Overall, there were four main barrier areas that were highlighted by all stakeholder groups, and that have cascading implications for adoption of personalised prevention:

1. The health systems are fully geared towards care and not towards prevention. This has enormous implications for development of strategies for personalised prevention, for funding and adequate resources, for reimbursement processes and equity of access, and for incentives for research, all of which were highlighted as barriers for personalised prevention;
2. Awareness and understanding of the personalised preventions concept is low for all stakeholder groups, explicitly acknowledged by citizens and patients, policy makers and health professionals, but also apparent in the neutral opinions to some questions to researchers. The implications of this lack of awareness and understanding are different for the different stakeholder groups, but warrant urgent tackling;
3. Following from the latter barrier, the lack of basic and life-long training for health professionals, of actions to document and raise interest of policy makers, as well as of a true interest in improving literacy of citizens and patients are also main challenges, and crucial to change the prevailing attitudes in health systems focusing almost exclusively on treatment and very little on prevention of disease;
4. Insufficient evidence of cost-efficiency, of research, of regulation for translation were also highlighted as main issues to be addressed that will have a major impact in the change of health systems focus from care to prevention.

Experts interviewed during our study often raised similar barriers and challenges, offering comprehensive insights. However, to ensure that survey respondents had the opportunity to address issues not addressed by the experts and/or adequately represented in the survey, we included an open-ended question soliciting additional thoughts and suggestions regarding additional significant barriers or challenges to the sustainable adoption of personalised prevention strategies.

2.4. Report on critical factors for the successful adoption of Personalised Prevention approaches by healthcare systems

The open responses raised several noteworthy barriers:

1. The long time required to realise the benefits of prevention investments;

2. The scarcity of emerging professions like bioinformatics and clinical data scientists, essential in multidisciplinary teams for research and implementation of personalised prevention strategies;

3. Questions about the feasibility of altering human behaviour,namely lifestyle and cultural habits changes for effective disease prevention, particularly among young people;

4. Uncertainty regarding the appropriate partners in healthcare systems to develop pharmacogenomics for preventing adverse drug reactions or lack of treatment efficacy;

5. The limited integration of personalised prevention into community-level healthcare systems, such as primary care or community pharmacies.

Some responses also emphasised that personalised prevention cannot solely rely on genetics but should address additional barriers and enablers, although these were not explicitly outlined.
These barriers are interconnected and addressing them collectively is essential for effective solutions. Many of these challenges are not exclusive to personalised prevention but apply broadly to prevention efforts at various levels and to personalised medicine in general.

In summary, the pursuit of solutions that pave the way for the real adoption of personalised prevention will necessitate a collaborative effort to enhance the visibility of this concept and involve all stakeholders in a shared mission to seamlessly integrate personalised prevention into healthcare systems.

5 Summary

Whithin the PROPHET project's, this deliverable represents a comprehensive mapping that sheds light on the landscape of personalised prevention approaches of chronic diseases and their implementation challenges in Europe and beyond. Despite the significance of chronic diseases and their burden on healthcare systems, our findings reveal a multifaceted scenario in which tertiary prevention takes precedence, while the emphasise on secondary and tertiary prevention remains limited. This trend is likely driven by substantial investments in therapeutic interventions, which are the main strategies for tertiary prevention, and the difficulty of implementing preventive strategies in healthy or asymptomatic individuals, funamental for primary and secondary prevention.

Furthermore, cancer prevention receives substantial attention due to a deeper understanding of genetic factors, while cardiovascular diseases receive less focus, underestimating the influence of DNA and underscoring the role of lifestyle factors.
Nevertheless, despite the wealth of insights into personalised prevention approaches, their current implementation within healthcare systems falls short of sufficiency. Several interconnected barriers contribute to this gap, including the prevailing emphasis on treatment over prevention within healthcare systems, a lack of awareness and understanding among healthcare professionals and the public, insufficient training, limited interest from policymakers, and low health literacy levels among citizens. Additionally, the absence of evidence on costs, research, and regulation further hinders the integration of these strategies.
In conclusion, our research highlights the need for tailored strategies that address unique challenges across disease categories and settings. This comprehensive mapping serves as a valuable resource for policymakers, healthcare professionals, and stakeholders aiming to advance personalised prevention efforts in Europe, showcasing both opportunities and challenges in the pursuit of improved health outcomes for all.

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