ROPHET

a PeRsOnalized Prevention roadmap for the future HEalThcare

# D.2.6 Report on current practices of citizens', patients', health professionals and policy makers engagement in Personalised Prevention and their gaps/bottlenecks

Funded by the European Union

PROPHET

a PeRsOnalized Prevention roadmap for the future HEalThcare

# D.2.6(A) Engagement of patients and the public in personalised prevention using genomic information: Scoping review

Funded by the European Union

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## Abstract

**Background/Objectives:** Personalised prevention using genomic information requires active involvement from the public and patients, who need to be well-informed and empowered to make decisions reflecting their personal values in deciding on health care and sharing data. This underscores the importance of their active participation in care, research, education, and governance for meaningful engagement. We aimed to map engagement practices, and assess the extent and types of engagement methods utilised in the field of personalised prevention of common chronic conditions.

**Methods:** A scoping review selected literature (in Medline, Embase, Scopus, Web of Science, APA PsycINFO and IBSS) from 2015 to 2023 was performed. Articles included were practices of patient and public engagement in personalised prevention and genomics conducted in Europe focusing on cancer, cardiovascular diseases and neurodegenerative disorders.

**Results:** 23 engagement practices were selected. Analysis revealed diverse engagement levels, the majority falling into the low to medium engagement category, and showed mainly one directional methods of engagement, including dissemination and consultation. Most engagement activities related to cancer, and none to neurodegenerative diseases. The care domain exhibited the most publications, followed by research, research combined with care, and governance combined with education.

**Conclusion:** By elaborating on and implementing practices that engage and empower the patients and public at all levels of the engagement spectrum, fostering a more inclusive and participatory approach to personalised prevention, ultimately leads to improved health outcomes for individuals and communities.



**Keywords**

Public and patient engagement, empowerment, participation, personalised prevention, personalised medicine, genomics, chronic conditions, chronic diseases

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# Abbreviation List

| | |
|---|---|
| CAD | Coronary Artery Disease |
| CVD | Cardiovascular diseases |
| FH | Familial hypercholesterolemia |
| PROPHET | Personalised prevention roadmap for the future healthcare |
| PM | Personalised Medicine |
| PP | Personalised Prevention |
| PRS | Polygenic Risk Score |

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# Introduction

## Background

With the burden of chronic diseases growing and the population ageing, prevention has become paramount. The transition to "person-centered" disease prevention and early diagnosis has been suggested to foster the implementation of sustainable and high value healthcare [1, 2]. Chronic conditions are a significant focus in personalised prevention, as they currently affect one-third of adult European Union (EU) citizens [3] and lead to 900,000 premature deaths annually in EU countries [4].

In recent years a new vision of personalised prevention as a specific focus within personalised medicine has been developed, in which genomic information plays an important role, departing from one-size fits all approaches**.** Personalised prevention has been defined as aiming to 'prevent the onset, progression and recurrence of disease through the adoption of targeted interventions that consider the biological information (e.g. genetics, demographics, health condition), environmental and behavioural characteristics, the socio-economic and cultural context of individuals [5]. Personalised prevention, is closely connected to research as knowledge is continually developed via processing large quantities of data on biology, environment, and behaviour [6].
A personalised approach to healthcare requires the public and patients to be engaged with regard to healthcare, which implies being well-informed, willing to share data, and empowered to make decisions that reflect their personal values [7]. Empowerment, at its core, refers to ideas such as individuals' and groups' ability to take action and control their own health and their right to participate in any decision-making that affects them [8]. According to the EU Joint Action on Patient Safety and Quality of Care (PaSQ), empowerment is defined as a multi-faceted process that helps individuals gain control over their own lives and expand their ability to take action on matters they deem significant [9, 10].

Despite, or perhaps as a consequence of, increasing attention given to public and patient engagement, in recent years the meaning of the term - public and patient engagement - varies, especially across international settings and depending on the respective application or domain [11]. In this paper we have differentiated between the following domains to better grasp various engagement and empowerment practices relevant to personalised prevention. If the public, patients, and families are to be active partners, then they must be systematically and meaningfully engaged in the planning, delivery and evaluation of the following four domains of personalised prevention: care, research, education and governance.

In the **clinical care domain**, the aim of public and patient engagement is to increase the public and patients' active participation in health-care [12, 13]. Individuals should feel empowered to make health decisions that align with their personal values and preferences which leads to more culturally sensitive and patient-centred care. By being actively involved in the decision-making process, patients can ensure that their healthcare choices are aligned with their own beliefs, preferences and priorities. When patients feel heard, and are actively involved, they are more likely to take ownership of their health, engage in preventive measures, and adhere to recommended interventions [7]. As modern healthcare systems struggle with effectiveness, access, and resilience, patient empowerment is a vital enabler of sustainability [8].

With regard to **education**, it is critical for the general public and patients to have a clear understanding of their health risks and the potential to lower those risks through lifestyle modifications or other interventions [14, 15]. Individuals should be well-informed about the advantages and possible barriers associated with personalised medicine. This entails having a thorough understanding of the potential benefits that can be derived from the integration of genomics into healthcare, as well as being aware of any potential challenges or limitations that may arise. Engagement of the public, patients, and their families in shaping educational initiatives related to personalised prevention includes involving the stakeholders in the development of educational materials, training programs, and patient education resources. By actively engaging these stakeholders, educational initiatives can be tailored to meet their specific needs, preferences, and cultural contexts, leading to improved knowledge and awareness of personalised prevention strategies.

With respect to the **research domain,** literature on stakeholder engagement shows that patients with personal experience of a disease offer a unique perspective that, if explicitly incorporated leads to research that is more relevant and translatable [16]. The term patient engagement in research has been used to characterise patient and public contributions to research via roles that range from "passive" study participants to "active" patients and public involved in all phases of the research [17]. Individuals can also contribute to research and knowledge production by sharing their personal data [18]. There is much research on public and patient's willingness to share data and requirements, such as having reputable institutions and biobanks that prioritise data privacy and security. The collaboration between patients and researchers is crucial for advancing personalised healthcare, as it allows researchers and healthcare providers to gain valuable insights into individual health profiles and tailor treatments accordingly. By involving the stakeholders in the research design, participant recruitment, data collection, and dissemination of research findings, research becomes more patient-centred, relevant, and responsive to their needs and preferences.

Lastly, the **governance domain** emphasises the involvement of the public, patients, and carers in decision-making processes regarding personalised prevention policies and programs, encompassing their participation in policy development, guideline formulation, and organisational governance structures. Literature has shown that trust in scientific and medical

institutions is a concomitant for stakeholder engagement in the governance domain. In order to implement personalised prevention and genomics in the EU and gain the public's trust to contribute health data to science, stakeholders must be involved throughout the policy cycle [19]. By actively engaging these stakeholders, governance processes become more transparent, accountable, and responsive to the needs and perspectives of the communities they serve.

This scoping review takes a broad scope, to explore elements and trends of patient and public engagement in the field of personalised prevention across the common chronic conditions. We expect that by systematically and meaningfully engaging the public, patients, and families in these four domains of research, clinical care, education, and governance, the field of personalised prevention can ensure that initiatives are patient-centred, effective, and aligned with the needs and preferences of those involved.

## Aim and Context

It is vital to comprehend what kind of engagement practices exist in Europe to understand in what ways and to what extent citizens and patients are currently engaged, how such practices may relate to the concept of empowerment and where we find potential gaps in such empowerment, e.g. related to knowledge and education [20]. This scoping review, with its focus on the mapping of public and patient engagement practices in the field of personalised prevention and genomics in the EU, represents a pioneering effort in the exploration of an emerging area. Additionally, this paper seeks to conceptualise the term ‘’engagement” and the degree to which the public and patients are engaged in the personalised common chronic disease prevention arena. The mapping of literature allows for a better understanding of opportunities and bottlenecks of public and patient engagement. This research highlights the crucial role of providing understanding of how the public and patients can be empowered across the aforementioned four domains and aims to contribute to the successful implementation of personalised prevention.

Public and patient engagement in the field of personalised prevention is an embedded part of the European project “A PeRsOnalised Prevention roadmap for the future HEalThcare (PROPHET)” [5]. This scoping review is contributory to the PROPHET project, which aims to co-create a Personalised Prevention Roadmap for the future healthcare with stakeholders, in order to support the definition and implementation of innovative, sustainable and high-quality personalised approaches that are effective in preventing chronic diseases [5].

# Methods

A scoping review was conducted to systematically map the European public and patient engagement practices in the field of personalised prevention and genomics. We reported this scoping review in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR)-checklist (online supplemental file 1) [21].

## Eligibility criteria

*Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.*

According to the PICO framework, the research question and the requirements for inclusion in our study were developed.

**P**opulation: Patients and the general public in Europe
**I**ntervention: engagement practices: workshop, focus groups, websites, apps, games, capacity-building, forums, dialogue ongoing or concluded in 2023.
**C**omparator: not applicable
**O**utcome: Consultation, Collaboration or Patient/Public-Directed in the field of personalised prevention

Publicly accessible publications with regard to public and patient engagement practices were deemed eligible according to the PICO framework. The articles included are published solely in the English language. Publications based in Europe will be the focus due to the fact that this is a contributing article to a European project: PROPHET. The timeframe was limited to articles published between 2015 to August 2023 in order to display an up-to-date image of the state of the art of the existing engagement practices in the field of personalised prevention in Europe. Additionally, we restricted our search to documents that were published in 2015 or later, since the EU health ministry's first defined personalised medicine in the Council Conclusions on Personalised Medicine for Patients in 2015 [22]. In addition, in its 2015 report titled "Shaping Europe's Vision for Personalised Medicine," the EU-funded project "PerMed" listed raising awareness and empowering patients as one of the five challenges of personalised medicine [23]. The selection of studies are based specifically related to engagement practices in the field of the following common chronic conditions: cancers, cardiovascular diseases and neurodegenerative disorders. Rare metabolic/genetic hereditary diseases are excluded, as mandated by the scientific proposal's emphasis on "predominantly prevalent chronic diseases". Publications that do not pertain to the healthcare context (e.g. animal research or environmental studies) were excluded. Furthermore, studies with the incorrect research design, such as systematic reviews and literature, were removed, allowing for a more concentrated analysis of primary studies and the discovery of new insights into engagement practices. Studies outside of Europe were discarded as were publications which were not in English or no full text available. Furthermore, if the publications did not include a combination

of the following elements: genetics, preventive, engagement, or a chronic condition, it was eliminated. Within the scope of this article, publications which only call on patients and the public to be engaged in the abstract are excluded, as it was not reported whether the public or patients were actually asked about their preference or attitudes. We excluded review reports as they do not meet our criteria for showcasing meaningful engagement. Additionally, several protocols were excluded in the selection of articles, as they have not shown results or have not yet commenced. Only original studies with concrete results or ongoing research were included, thereby focusing on studies that contribute to the existing body of knowledge and provide meaningful findings for analysis and interpretation. In the data extraction sheet, studies that solely mentioned engagement practices without actually implementing or initiating them have been omitted. Only studies that involved active and existing engagement practices were included in the data extraction process. If an article discussed many practices, only the engagement methods for which results had already been reported were included. For example, in Delnord, Van Valckenborgh [24], the citizens' lab was merely mentioned and not launched or reported. Hence, it was not included in our analysis, but the working groups were included. Finally, articles on other stakeholders – such a policymakers or healthcare professionals – were excluded if the engagement did not involve patients or the general public.

## Information Sources and search strategy

A comprehensive search was performed in the databases: OVID/Medline, Embase.com, Elsevier/Scopus, Clarivate Analytics/Web of Science Core Collection, Ebsco/APA PsycINFO and Proquest/International Bibliography of Social Sciences (IBSS), from inception to July-August 2023 (see Appendix A for exact dates) in collaboration with a medical information specialist (JCFK). The search included controlled terms and free text terms for synonym terms for "public", "patient", "stakeholder", "community" in combination with "personalized prevention", "personalised medicine", "genetics", "genomics" and "engagement", "participation", "information", "consultation", "involvement", "collaboration", "empowerment" in the following three disease groups: "cancer", "cardiovascular diseases" and "neurodegenerative diseases". The search was performed without restrictions for methodology or language. The search was limited to publication date starting from 2015. The full search strategies can be found in Appendix A. Duplicate articles were excluded by a medical information specialist (JCFK) using Endnote X21.0.1 (Clarivatetm), following the Amsterdam Efficient Deduplication (AED)-method [25] and the Bramer-method [26] .

This search strategy resulted in 7,317 records. See Appendix A: Supplementary information for the full search strategies per database.

Engagement, as a concept, encompasses various dimensions and is widely discussed in the literature across different fields such as research, healthcare, and knowledge constructs. The

selection of relevant articles for this study was guided by the specific objective it aimed to achieve. The term "engagement" is multi-faceted and can be understood and applied in multiple ways, depending on the context and goals of the study. This highlights the need for a careful and nuanced approach in exploring the different facets of engagement and its implications in various domains. In this paper the working definition of engagement practices in personalised prevention of common chronic conditions involves strategies to actively engage individuals in their health and actively participate in research and governance domains. The goal is to empower individuals to make informed choices, adopt healthier lifestyles, and adhere to personalised prevention plans.

## Syntheses of results

Publications were clustered according to their type of public and patient engagement methods, with the use of a worksheet-based Excel model. The data synthesis process was conducted by a single researcher (LLK) using the Rayyan software, while another researcher (CvE) independently selected a sample of 25% of the articles in the Rayyan software. In cases of disagreement, the two researchers consulted each other to resolve any discrepancies, and if consensus could not be reached, two additional researchers (LH & MC) were consulted for additional input. Firstly, the articles were skimmed based on title and abstract, further the full-text was read to gain deeper insight on the relevancy according to the inclusion criteria. The screening of the articles found were manually selected through the Rayyan software. The articles were firstly screened based on their geographical region; all the articles outside of Europe were excluded, which is based on the title and abstract and, if not mentioned, the location of the first author's affiliations. Each reported public and patient engagement practice, including surveys, capacity-building, workshops, open discussions, and participation in governing committees, were given a qualitative synopsis using aggregate data. For each of the included reports, we extracted the following general input: first author, publication year; project name; funder and coordinator; aims/objectives; main outcomes; country; disease focus; participation characteristics/stakeholder group; extent of engagement, engagement method; degree of engagement, domains; and the evaluation/recommendations or key takeaways. The pertinent passages from the selected publications were allocated to the Data Extraction Sheet, utilising an Excel worksheet-based model (Table 5). For each publication and corresponding engagement practice, the engagement modalities, including the engagement method, engagement domains, and the extent of engagement, were assigned.

## Data items

### Extent of engagement

In order to analyse the level of public and patient engagement in the identified engagement practices, we used a modification of the International Association of Public Participation (IAP2) spectrum of public participation adapted by Shimmin [27]. In our study, we extended the use

of the revised Shimmin model beyond research to include domains such as care, government, and education. While Shimmin's customised model was originally based on research, we realised its potential for use in other fields and used it to study and analyse other relevant aspects in the healthcare environment (Figure 1).

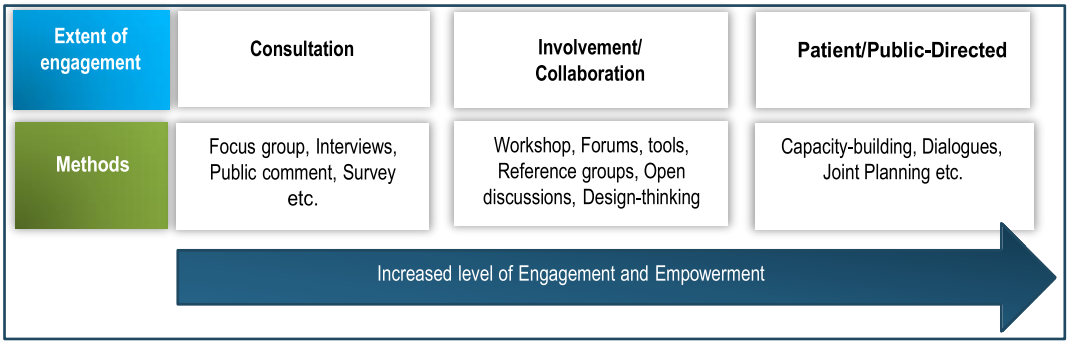


*Figure 1: Spectrum of engagement and empowerment of patients and the public in personalised prevention. Adapted model.*

The adapted model introduces three distinct levels or modes of engagement also referred to as the extent of engagement: Consultation, Involvement/Collaboration, and Patient/Public-Directed. At the Consultation level, the primary objective is to gather feedback and input from the general public, patients, families, and communities with first-hand experience of health conditions. We merged the categories of the Shimmin model "involvement" and "collaboration" in our analysis because we found significant overlap in the descriptions and outcomes of the engagement practices. The merged Collaboration level involves an ongoing partnership where decision-making is shared between stakeholders. Lastly, Patient/Public-Directed is referred to as "user-controlled" or "user-led research", patients and/or members of the public play a central role in decision-making throughout the process (Shimmin 2016).

Each of these modes describes the strength of the influence that engagement has on decision-making. The search terms were manually chosen based on the Shimmin model, engagement type (consultation, involvement, collaboration, patient/public-directed) as well as the matching methodologies of engagement also mentioned in this model (fact sheets; newsletters; websites; focus-groups; meetings; workshops; joint-planning; dialogue; Web 2.0 tools) and synonyms based on this (Figure 1)).

We classified engagement practices based on their level of involvement (low, medium, or high) and their influence on public or patient engagement and empowerment in research, care, governance, and education domain. Consultation is classified as low or medium, depending on the impact of engagement and empowerment. Collaboration is classified as medium or high, and patient/public-directed engagement is classified as high.

## Patient and public involvement

Patients and the public were not involved in this study, but input was sought from ACN and EPF on main concepts.

# Results

Figure 2 displays the screening and selection process of the scoping review. The total number of 7317 records was reduced to 4398 by removing duplicates. The abstract screening process resulted in 2320 titles being excluded as irrelevant, with 2078 articles remaining for full-text-screening. During full-text-screening we removed 1615 publications due to the content or outcome of the publication, or the source of information as described in our exclusion criteria, such as when there is no genetic element or no focus on prevention of chronic conditions. The publications with the other study design (n= 153) and other duration (n=222) were removed. In 56 publications a very heterogeneous sample was examined: policymakers, health care professionals, but also representatives of other groups that did not meet our inclusion criteria. The entire article selection procedure resulted in 23 engagement practices described in 23 articles for this review that were published between 2015 and 2023 and can be found in Appendix B.

The majority of the engagement practices were targeted to patients (10; 44%) [28] [29] [24] [30] [31] [32] [33] [34] [35] [36], three engagement practices focused on patient representatives (13%) [33, 37, 38], one on the combination of patients and families (4%) [39], one engagement practice targeted both patients and the public [40], compared to eight public engagement practices (35%) [41] [42] [43] [44] [45] [46] [47] [48]. Regarding the disease focus, most practices (18; 78%) focused on (hereditary) cancer, specifically breast cancer and ovarian cancer [29] [28] [42] [43] [40] [44] [30] [32] [34] [47] [35] [39] [49] [24] [38] [31] [33] [48] . Cardiovascular disease engagement practices were reported in two engagement practices (9%). No engagement practices (0%) were focused on neurodegenerative disorders. The three remaining practices (13%) focussed on personalised prevention or personalised medicine in general [41, 45, 46].

Across the geographical locations in Europe; four engagement practices (17%) were conducted in the United Kingdom [28, 34, 42, 43], four (17%) in France [29, 33, 38, 47]; three (13%) in Germany [32, 35, 48]; two (9%) in Switzerland [41, 46]; two (9%) in Italy [40, 49]; two (9%) in Denmark [39, 45]; two (9%) in the Netherlands [31, 37]; two (9%) in Estonia [30, 36]. Followed by one engagement practice (4%) reported in Sweden [44]; and lastly, one practice (3%) conducted in Belgium [24].

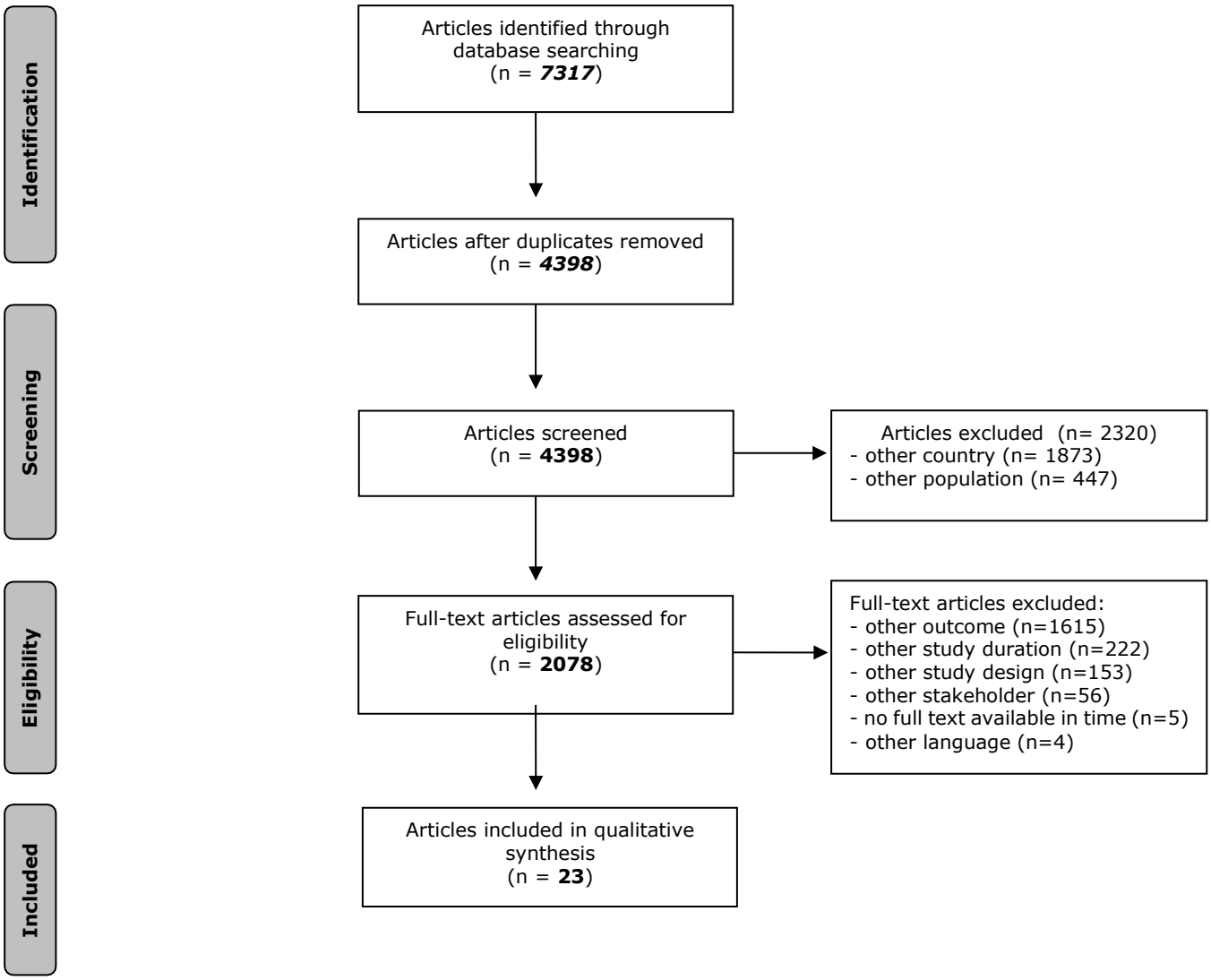


*Figure 2: PRISMA 2020 flow diagram for the selection and screening process in the scoping review (Page et al., 2021)*

## Extent and Methods of Engagement

The included articles described different public and patient engagement practices in the field of personalised prevention. Figure 3 displays that the majority of the practices were found at the consultation level of the engagement spectrum (18; 78%), by generally asking for input at set points in the process and not providing an ongoing opportunity for input. These include surveys; interviews; focus groups; a combination of questionnaires and genetic group counselling. The extent of engagement matched with the methods of engagement is portrayed in Figure 4. The second level of engagement is to partner and work directly with patients and the public throughout the process to address patient and public concerns. Four engagement practices were reported at this collaboration level (17%). Engagement practices included patient organisation representation; online decision aid tools with optional helpline as well as participation of patient representatives in working groups and establishing patient committees. One practice was reported in the public-directed level (4%) which included

empowerment app games which were co-created with citizens, by building on their feedback as well as engaging the public in the design and assessment of the digital game. Our analysis found that the majority of intensive engagement practices, found on the higher level of the engagement spectrum occurred between 2020 and 2023, suggesting a notable increase in proactive efforts during this period.

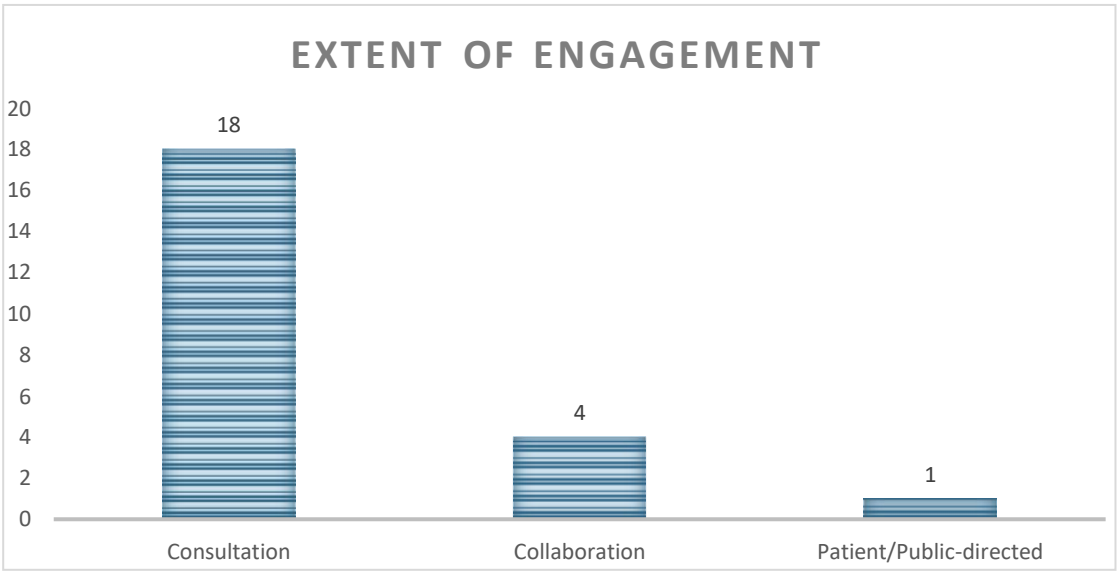


*Figure 3: Extent of public and patient engagement practices*

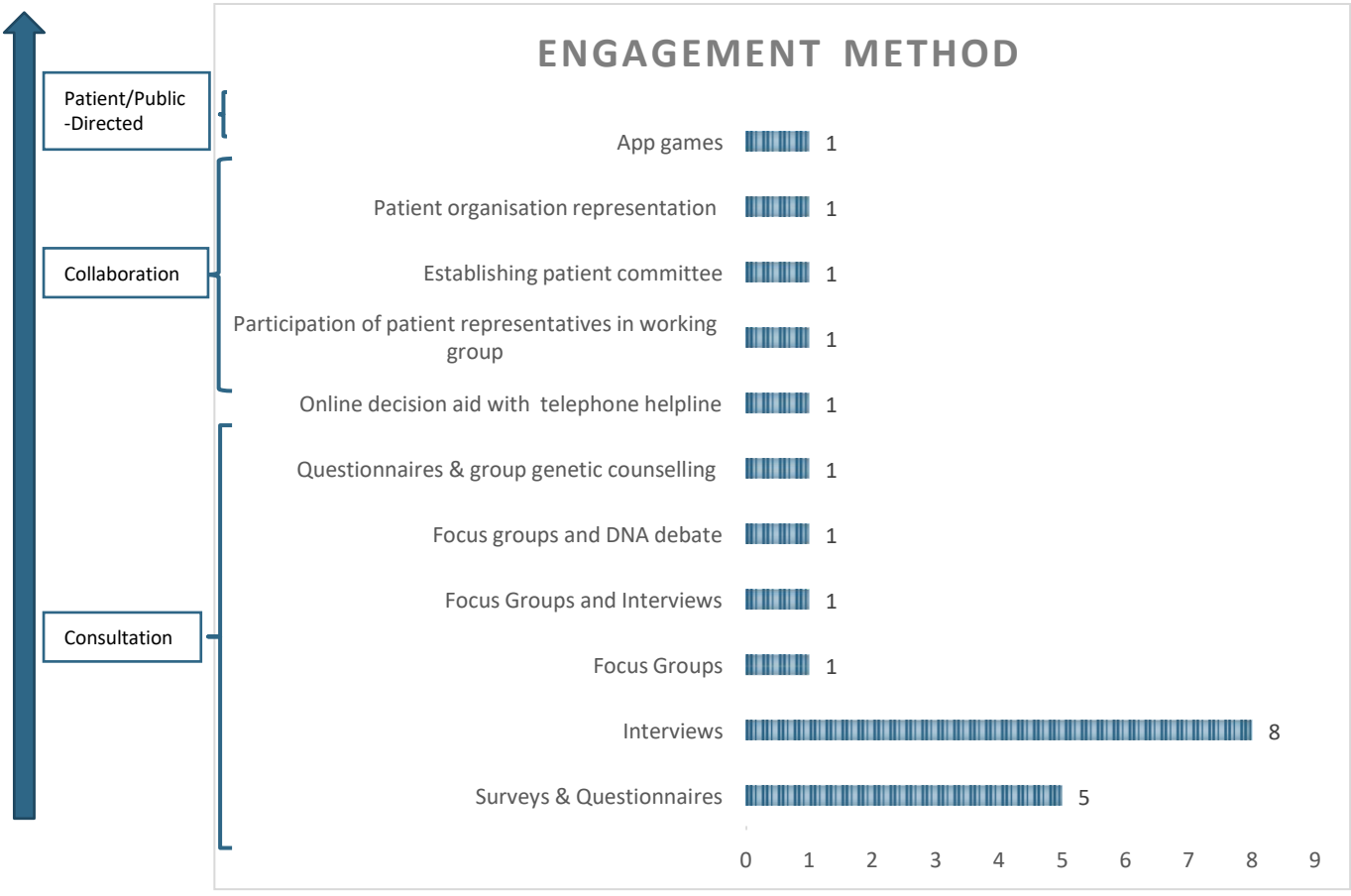


*Figure 4: Engagement methods matched with the engagement spectrum*

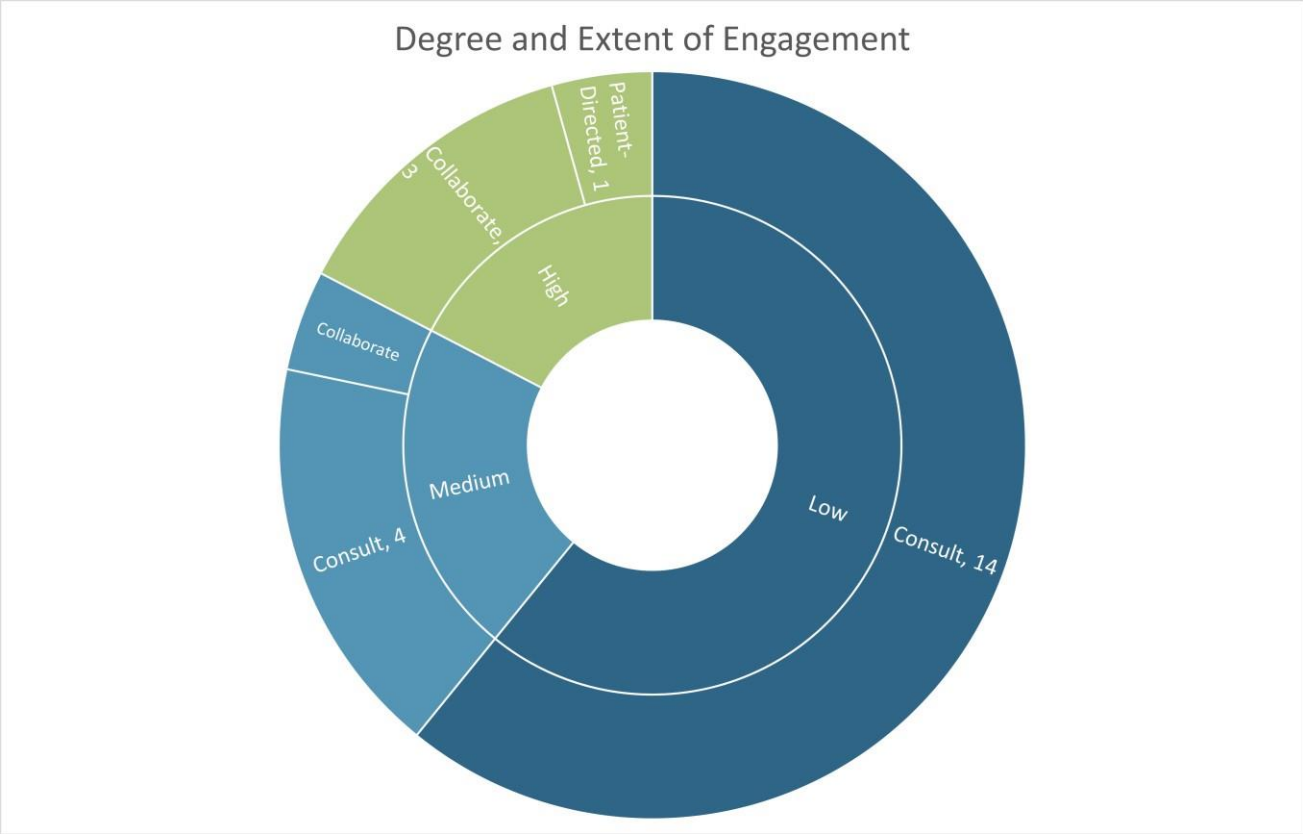


*Figure 5: Displaying the degree and extent of the identified 23 engagement practices in the field of personalised prevention*

Figure 4 displays the different levels and extents of engagement found in our analysis of engagement practices. The majority of practices fell into the low to medium engagement category, with fourteen practices classified as consultative and moderately engaged [28] [29] [41] [43] [44] [30] [46] [45] [31] [32, 34, 35] [37] [36] and four practices falling under the medium level of consultation [24, 42, 47]. In addition, we found one practice that was classified as collaboration [40]. Some practices (n=3) suggested a great deal of collaboration and we classified them as showing higher engagement levels [33, 38, 49]. Lastly, we discovered one practice that fits the definition of actively engaged and patient-directed care [48]. All things considered, these results show how different practices have diverse levels of engagement, using a variety of consultative, collaborative, and patient-directed methods.

## Primary, Secondary and Tertiary Prevention

Figure 5 presents an analysis of the categorization of personalised prevention engagement practices across the different levels of prevention. It reveals that one practice (4%) falls into all three categories: primary, secondary, and tertiary prevention. In this example, the parents' perspective on paediatric cancer families' participation in whole-genome sequencing (WGS) research were studied in Denmark. It is classified as primary prevention, as WGS may also identify potential genetic predispositions for diseases unrelated to the original indication. We classified this practice as secondary and tertiary prevention because it focuses on paediatric cancer early diagnosis and intervention [39].

The majority of practices fall into one or two categories; six practices (26%) are classified as primary prevention [29, 36, 41-43, 47], seven practices (30%) categorised as primary and secondary [30, 33, 35, 44-46]. Two practices (9%) are categorised as secondary [24, 40]. Furthermore, two engagement practices (9%) categorised as secondary and tertiary [28, 49], three practices (13%) are categorised as tertiary [31, 32]. This analysis highlights the diverse nature of personalised prevention engagement practices and the varying levels of prevention they encompass. The analysis displays that two practices (9%) cannot be clearly classified into a single category, or the information provided is insufficient to determine the appropriate classification [38, 48]. It is worth noting that the two engagement practices not classified are reported in the research domain; here the emphasis is typically placed on studying the overall effectiveness and impact of these practices.

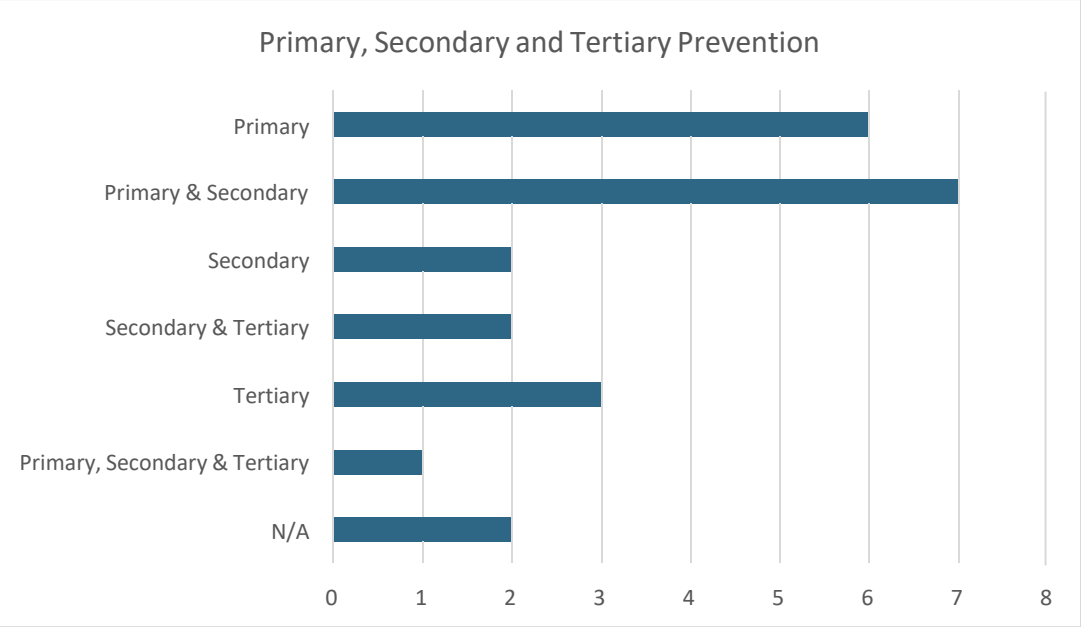


*Figure 6: : Proportion of levels of prevention among the 23 identified personalised prevention practices*

## Domains of Engagement

Figure 4 distinguishes the 23 reported engagement practices across the four domains we distinguished for our analysis: care, research, education and governance. The majority of the practices are found in the care domain (14; 61%). Two engagement practices were found in the research domains (9%). Six practices reported in the research to care domain (26%) and one in the domain of governance combined with education (4%).

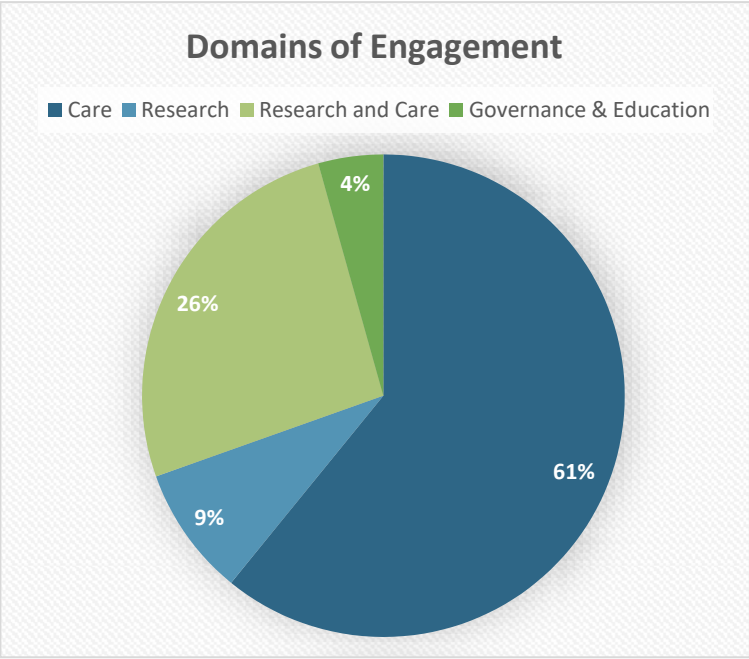


*Figure 7: Proportion of the identified personalised prevention practices across the domains of engagement*

## Care Domain

Fourteen identified practices engaged public and patients in the care domain. Eight out of fourteen engagement practices were targeted at patients or patient representatives; five engagement practices were focused on the public. One exploratory analysis focused on primary breast cancer patients as well as healthy subjects [40].

Five practices used interviews as a means to achieve patient or public engagement [31, 34, 35, 37, 43]. A mixed-method approach, which included interviews and examination of patient records and pharmacy information systems, is an illustration of a practice that used interviews as its engagement method [31]. Fifteen patients participated in the semi-structured interviews, designed to get their opinions on the dissemination of information about dihydropyrimidine dehydrogenase (DPD) testing. Patients who started fluoropyrimidines (FP) treatment- which are commonly used anti-cancer drugs- used in colorectal cancer and might experience adverse effects for this medication due to their genotype were selected. The aim of the study was to evaluate the level of DPD testing acceptance in the Amsterdam University Medical Centers and to identify the barriers and facilitators of integration of DPD testing in standard clinical care. The findings suggested that most stakeholders desired additional professional education on the practical uses and limitations of pharmacogenetic testing. Patients indicated they received adequate information, but want to be informed in simple wording. This is a prime example of patients being consulted to evaluate innovation.

Three practices focused on the method of asking for feedback with the use of questionnaires [36] [40, 45], while one practice used focus groups to investigate members of the Swedish public's attitudes and preferences for receiving genetic risk information about hereditary cancer risk [44].

Additionally, in order to address personal and family issues, consultations with a genetic counsellor and psychologist were conducted as a manner of patient and public education and engagement (n=1) [29], after which questionnaires were distributed to evaluate satisfaction and knowledge. Implementing a group approach to genetic counselling for hereditary breast and ovarian cancer has endured the rise in referrals, without compromising care. Patients' awareness of cancer genetics, genetic testing, and the significance of the results improved dramatically after attending the group session. Additional effects, such as group emulation and patient empowerment, were noted, albeit quantifying them proved difficult. The evaluation comprises analysing patient satisfaction and knowledge among the 210 patients who attended the group counselling sessions using a cancer genetics knowledge questionnaire [29].

Through focus groups and a DNA debate on cancer, patients' opinions, concerns, and expectations about Next Generation Sequencing (NGS) testing were collected [24]. A total of 1250 contributions were obtained from the focus groups and DNA debate sessions conducted. The topics covered included privacy concerns, personalised medicine uncertainties, and data governance. In order to enhance the harmonisation and quality of information conveyed to the patient when reporting secondary findings of genome sequencing in cancer genes, Pujol, Vande Perre [33] contended that the utilization of a video tool could offer crucial and cohesive assistance in interacting with the patient. The objective of the practice was to formulate guidelines on patient information and consent, and to create informed consent forms and an information media tool in the form of an animated movie. This is an example of a high level of engagement and empowerment of patients, as the participation of patient representatives in working groups provided the materials, educational guidelines, and ethical reflection. These guidelines provide essential information for physicians and laboratories to standardize their clinical practices for cancer-predisposing genes [33].

The Population Study of Ovarian Cancer Risk Prediction for Targeted Screening and Prevention utilised a customized ovarian cancer risk tool, to conduct a feasibility study on the stratification of women in the general population based on their ovarian cancer risk, and then implement risk management [42]. The study aimed to evaluate the acceptance, satisfaction, usage, psychological well-being, and quality of life of women undergoing population genetic testing risk stratification using an online/web-based decision aid and an optional telephone helpline [42].

In addition to the previously mentioned engagement practices, another notable practice was the Saghatchian, Abehsera [47] risk assessment clinic for breast cancer. This complete assessment comprised several components such as a questionnaire, mammogram with evaluation of breast density, consultations with a radiologist and a breast cancer specialist, and personalised approaches based on risk factors and calculated risk scores using MammoRisk®. This clinic's main goal was to give patients personalised risk assessments so that, based on known risk factors, breast cancer can be detected and treated early. Additionally, screening recommendations were tailored to the specific risk levels of each

individual, ensuring a more personalised and targeted approach to breast cancer prevention. The risk assessment consultation was reported to be a great opportunity to discuss with the patient on modifiable lifestyle risk factors, such as diet, physical activity and alcohol consumption. The authors state 'overall, the methodology of evaluating individual risk was well understood by the patients, who were very interested in the means to control the risk, especially in terms of diet. There was a need to clearly explain the difference, however, between the individual genetic risk (PRS) and hereditary risk (e.g., *BRCA*), especially to those with a family history of cancer. Patients classified as high risk understood the need for close surveillance'. The patient pathway was reported to be smooth and not in need of adjustments. The authors suggest that individual risk assessment is feasible in a specialised clinic setting, but more population-level research is required to determine the clinical utility of this method. Saghatchian, Abehsera [47] concludes that while a pathway session with a radiologist, nurse navigator and breast specialist might not be practical in every hospital setting, such risk assessment clinics would make the shift from treatment-oriented care toward early diagnosis, prevention and health promotion.

A variable degree of public and patient engagement practices was undertaken in the care domain, ranging from simpler open discussions and one-way communication such as questionnaires and interviews to online information media tool and participation of patient representatives in working groups as a more collaborative two-way communication. The most prominent extent of engagement of the general public and patients was reported at the consultation level (n=12), followed by two out of fourteen engagement practices which actively collaborated with the stakeholders.

*Table 1: The degree, extent and number of identified engagement practices in the care domain*

| Degree of engagement | Extent of Engagement | Description | N= |
|---|---|---|---|
| High | Patient & Public-Directed | Actively engaged | 0 |
| High | Collaboration/Involvement | Engaged | 1 |
| Medium | Collaboration/Involvement | Engaged | 1 |
| Medium | Consultation | Somewhat engaged | 3 |
| Low | Consultation | Somewhat engaged | 9 |

## Research Domain

Two identified practices engaged public and patients in the research domain. Both practices exemplify high levels of engagement and empowerment, with one engagement practice classified as collaboration and the other as patient/public-directed.

The study "Partnering with Patients in Translational Oncology Research: Ethical Approach" [38], underlined the necessity of creating a long-term collaboration and promoting a common understanding among all parties involved. To do this, the study used the engagement strategy of forming a patient committee. The goal of this engagement strategy was to increase the

involvement of patient advocates, in addition to health professionals, in the development of the translational research program. Patient representatives became full participants in this method, actively participating in knowledge dissemination to the public through conferences and publications. This empirical ethical research action sought to improve the integration of patient expectations and to ensure a collaborative and inclusive approach in translational oncology research [38].

The engagement practice of GENIGMA, an app designed for mapping the 3D genome of cancer cell lines via extreme citizen science, stands out as the highest form of engagement and empowerment in this study. This patient and public-directed example is a digital game co-created with the public and allows them to actively participate in producing data that surpasses the capabilities of artificial intelligence. The goal was to develop a digital game or smartphone app that would help researchers identify the most likely genome rearrangements in cancer cells. The procedure would entail presenting the concept to the public, acting on their suggestions, and incorporating them in creating and evaluating the game. After it was made, the citizens would play the game and contribute to the data's creation. Researchers are increasingly attempting to interact with the public by sharing their research in plain language and enlisting their help in gathering data for their work. Nonetheless, it is rare to witness public participation in the entire research project development process, which has been done in this study. When citizens are involved from the beginning, from game development to data production, "extreme" citizen science takes on a new form. This experiment within an experiment will solve the map of a cancer cell line and provide insights into how citizen science can help scientists.

The citizen feedback is utilised to help create new educational resources, videos, a weekly results summary, and a ranking of the top gaming clans that advance science for the website and social media. In addition, three introductory workshops were held to provide an overview of the fundamental ideas behind cell biology, cancer, and the genome. A wide range of people, including cancer patients, educators, artists, physicians, storytellers, scientists from various fields, and more, attended the workshops, which were held in Spain and Italy. In order to develop the game, efforts were made to identify metaphors that would aid in the citizens' understanding of these scientific ideas. Additionally, efforts are reported to incorporate schools in the #GenigmaChallenge, providing students the opportunity to contribute to scientific progress while learning new concepts in an ongoing project. It was downloaded by 31,000 users across 137 different countries in only four weeks [48].

*Table 2: The degree, extent and number of identified engagement practices in the research domain*

| **Degree of engagement** | **Extent of Engagement** | **Description** | **N=** |
|---|---|---|---|
| High | Patient & Public-Directed | Actively engaged | 1 |
| High | Collaboration/Involvement | Engaged | 1 |
| Medium | Collaboration/Involvement | Engaged | 0 |

| | | | |
|---|---|---|---|
| Medium | Consultation | Somewhat engaged | 0 |
| Low | Consultation | Somewhat engaged | 0 |

## Research and Care combination Domain

Six engagement practices could be regarded as a combination of research and care. Two practices were targeted at the public; three engagement practices were focused on patients and one was focused on the combination of patients and the family. This paper discussed paediatric cancer families in Denmark who participated in whole-genome sequencing research (WGS), where their family pedigree was mapped and were given the choice to select what information they would like reported regarding their child's WGS [39].

All the identified practices engaged public and patients at the consultation level of the engagement spectrum (n=6), by generally asking for input at set points in the process and not providing an ongoing opportunity for input. The most used engagement method found in the research and care domains was that of interviews (n=3); followed by surveys (n=2) and the remaining engagement method (n=1) combined focus group with interviews. The latter engagement practice explored perspectives of the general public on a hospital-based biobank aimed at supporting biomedical research, including genomics and personalised medicine. Some citizens expressed criticism towards the idea of 'personalisation' of medicine through the return of genomic information, citing concerns about individual dependence on medication and of the pharmaceutical industry's control. The results emphasize the ethical, social, and policy concerns related to disclosing data in biobanks that employ a broad consent model utilised for in-hospital biobank recruitment. Additionally, the public expressed a desire for more training in genomics and further information regarding the biobank effort [41].

An example of a study that used interviews to gather information about patient motivations for taking part in personalised cancer research focused on the patients' misconceptions about participating in a clinical trial that was aimed to study stratification [32]. Through a longitudinal empirical-ethical approach, semi-structured interviews were conducted with colorectal cancer patients involved in a biomarker trial for (neo)adjuvant treatment to analyse their viewpoints and comprehension of research and treatment (care). Based on the research findings, patients were found to be only partially aware of the main goal of personalised cancer research, which was to stratify responders and non-responders. Consent procedures might have inadvertently led patients to believe participating in research might be beneficial for their own treatment (therapeutic misconception) or their relatives' health, while patients may feel responsible for relatives due to the presumption of genetic kinship (genetic responsibility). The authors advocate for clinicians to be sensitive to possible misunderstanding in informed consent procedures and call for more training and the development of alternative measures to help improve such procedures [32].

The following engagement practice is another example of how the lines separating the care and research realms are becoming less distinct and more interconnected. The aim of this practice was to gain a deeper understanding of the practices and potential effects of stratified

medicine in a London breast cancer service [28]. Patient interviews were undertaken, with an emphasis on their individual experiences receiving cancer services being stratified as part of research. Most patients surveyed thought that early implementation of stratified medicine was doable. By integrating the viewpoints of diverse stakeholders involved in stratified medicine, including healthcare personnel, patients, and families, the study highlighted the shared high expectations for this new method. Nonetheless, patients, caregivers, and staff were impacted by the new and existing forms of stratification, leading to care that frequently felt less personal rather than more personal [28].

*Table 3: The degree, extent and number of identified engagement practices in the research and care domain*

| Degree of engagement | Extent of Engagement | Description | N |
|---|---|---|---|
| High | Patient & Public-Directed | Actively engaged | 0 |
| High | Collaboration/Involvement | Engaged | 0 |
| Medium | Collaboration/Involvement | Engaged | 0 |
| Medium | Consultation | Somewhat engaged | 1 |
| Low | Consultation | Somewhat engaged | 5 |

## Governance and Education Domain

In the domain of governance and education, an example of patient engagement is the Alliance Against Cancer (ACC), a network of Italian cancer centers dedicated to bridging research and care, which displays a high level of engagement and empowerment in the collaboration level. Through patient organisation representation, such as the Italian Cancer Patients' Organisation (AIMaC), the ACC states that they ensure a bidirectional exchange of information between patients and institutes. This collaboration aims to develop cost-effective processes, provide tailored information on concepts of contemporary personalised and precision medicine to cancer patients, and improve and expand the National Cancer Information Service (SION) to meet the increasing demand for information. The inclusion of patient associations among the association's active members is a standard practice in national and international associations, initiatives, and scientific societies dedicated to cancer care and research [49].

*Table 4: The degree, extent and number of identified engagement practices in the governance and education domain*

| Degree of engagement | Extent of Engagement | Description | N |
|---|---|---|---|
| High | Patient & Public-Directed | Actively engaged | 1 |
| High | Collaboration/Involvement | Engaged | 0 |
| Medium | Collaboration/Involvement | Engaged | 0 |
| Medium | Consultation | Somewhat engaged | 0 |
| Low | Consultation | Somewhat engaged | 0 |

# Discussion

The scoping review mapped the public and patient engagement practices in the area of personalised prevention across the following common chronic conditions: cardiovascular diseases, cancers and neurodegenerative disorders. The results show the variety of practices and approaches that may involve patients and the public at different stages of the engagement and empowerment spectrum in personalised prevention. The increase in articles included from later years suggests a rise in engagement practices, reaching a peak in 2022 amid the influence of the COVID-19 pandemic.

The disease focus across the various engagement practices was primarily focused on cancer, specifically (hereditary) breast cancer, and extensive literature and engagement practices are based on breast cancer initiatives with the general public. Literature states that the second leading cause of cancer death among females is breast cancer [50]. Our findings seem to echo advances in both research and implementation of Personalised Prevention in line with prior PROPHET deliverables D2.1 on biomarkers and D2.4 on implementation of personalised prevention, that found most articles reported on oncology. Other chronic conditions, such as neurodegenerative disorders, have received comparatively less attention, despite their acknowledged significant relevance for healthcare systems, as highlighted by Nielsen and Boenink (2019) who took a critical look at conditions for patient involvement in Alzheimer's biomarker research and beyond [51].

There is a promising prospect for the future as the emergence of engagement and empowerment practices has increased over time. International initiatives, such as the foundation of the International Consortium for Personalised Medicine in 2016, may have stimulated countries to develop national plans related to genomics and personalised medicine [52]. Therefore, it is likely that national and European authorities are becoming more interested in personalised medicine and personalised approaches to health. This has coincided with an increase in the number of (published) patient and public engagement practices in the EU in recent years.

The results show various forms of communication and discussion to be held with the participants across the spectrum of engagement throughout the four domains of care, research, education and governance. However, it is notable that the majority of engagement practices mapped in this analysis were in the lower spectrum of engagement and empowerment, referring to a more one-way communication with the patients and the public. Nabatchi [53], refer to one-way forms of communication, such as surveys or consultations, as indirect public involvement. It is apparent that on the low end of the engagement spectrum there are few opportunities for individuals to provide feedback on the conduct of the process. On the higher end of the engagement spectrum a two-way communication approach was described as direct public and patient involvement, including activities such as public and patient workshops, conversations, and deliberative and consensus conferences [53]. In this

discussion we will explore the various forms of engagement which may have their own merits and pitfalls, and may lead to specific forms of empowerment.

*Higher levels of engagement: the higher the better?*

Patient-driven health care is distinguished by greater information flow, transparency, customisation, cooperation, and patient choice and responsibility-taking, as well as quantitative, predictive, and preventative features [54, 55]. More intensive collaboration can be established as we saw in the case of Pujol, Vande Perre [33]; Mamzer, Duchange [38] and De Paoli, Ciliberto [49], through establishing more enduring forms of participation by inviting patients or patient representatives in e.g. working groups or committees. By involving patients and the public more structurally in decision-making processes, across various domains, their unique perspectives and needs can inform policies and practices. This fosters a sense of ownership and responsibility, empowering patients mostly represented by patient organisations to actively participate in healthcare decisions.

On the other hand, there are potential challenges and limitations associated with more high-end engagement practices including patient/public-led or patient/public-directed engagement and empowerment in personalised prevention. One challenge is ensuring representativeness or inclusion of diverse patient experiences, as not all individuals may have the resources or ability to participate actively. Patient organisations normally represent a broader perspective which encompasses a variety of individual experiences; however awareness is important that empowerment approaches, if not carefully implemented, may exacerbate existing inequalities. Some groups and individuals may be more in need of empowerment than others, and “one size” is not likely to fit all needs [56]. Additionally, balancing patient and public perspectives with scientific evidence and professional expertise can be complex, requiring well-informed ‘expert patients’, considering the innovation's nature, the professional and patient characteristics involved, and the social, organisational, political, and economic landscape [57]. Programs that provide education and training to enable patients to meaningfully participate are essential in this sense [58]. Furthermore, the scalability and sustainability of more intensive engagement activities may be limited, requiring ongoing support and resources from the organisations. Remuneration for patients’ expertise and resources also must be taken into account. There is a risk of tokenism or superficial involvement, where patient input is sought but not genuinely incorporated into decision-making processes. It is essential to address these concerns and ensure meaningful and equitable engagement and empowerment for all individuals involved [59, 60].

*Empowering the public*

It is important to note that the bulk of engagement and empowerment practices in this study were directed to patients, with only a handful of practices were directed towards the public. The observed bias toward directing engagement and empowerment practices predominantly to patients in the study may be grounded in the underlying fact that patients, being direct

beneficiaries of healthcare services, play a central role in personalised medicine. The assumption that patients are more directly engaged in decision-making processes related to their own healthcare might contribute to the prioritisation of patient-oriented practices over those targeting the broader public. In our study, the public, are more engaged in practices concerning biobanks and data-sharing topics, while being less involved in care and treatment-related practices. However, considering that the public may become patients themselves at certain points in their lives, it is crucial to engage the public in personalised medicine practices. Engagement practices targeting the public were often surveys as a means of measuring knowledge and opinion [45, 46]. For those who participate in the less intensive engagement methods, empowerment may be stimulated through increasing awareness of personalised medicine, while the findings of such surveys may be used to improve policy. There are several pathways for citizen engagement, and concomitant ways of achieving individual empowerment, including enhancing health literacy and capacity-building. These will be stronger in the more intensive engagement methods such as the development and dissemination of education and awareness tools and materials to educate the public on genetic concepts with the use of online apps and web-based decision aids [42, 48, 61].

*Empowering patients*

According to Steele et al (1987) patient empowerment is seen as a process of "activating" patients who, after rejecting the passivity of the sick role behaviour and taking ownership of their care, are "more aware of, satisfied with, and committed to their treatment regimens [62]. Empowerment can be defined as taking charge of one's health, and entails more than just finding one's voice [8]. As a result, there are numerous methods through which patients might be empowered. In our study, the most popular methods for engaging patients were the use of online discussions and questionnaires. The most intensive form of engagement method was the use of online/web-based decision aids; participation of patient organisation/representatives as well as app games which may presumably lead to empowerment. In order for a patient to be empowered, education, literacy and knowledge is essential. Allowing patients and patient organisations to share their perspectives on the quality of education and co-create information materials not only enhances information but can also contribute to an improvement in overall healthcare quality.

Patient engagement can relate to the micro (patient) level in terms of improved health, greater satisfaction with treatment options, and better quality of life and psychological state, which would constitute empowerment to take control of their own care. A well-informed patient is prepared for shared decision-making, equipped with a thorough understanding of their condition, treatment choices, and lifestyle implications, fostering a collaborative and patient-centred approach to healthcare. In practice, there is a need to shift from a paternalistic medical model to a collaborative model, where the healthcare provider welcomes patients' input and creates an enabling environment [56].

The concept of patient involvement refers specifically to the participant's rights and benefits to play a central role in the healthcare process; it extends beyond the availability of

information or health literacy; it is about the interaction between the patient and the healthcare provider [8]. In contrast, engagement can have an impact on the macro (community) level in terms of quality of health and social services and intervention design; policy prioritization, and cost-effectiveness [56]. For instance as Perry et al. (2017) and Pujol et al. (2018) showed, especially patient organisation can contribute to the development of effective consent forms and other relevant materials, highlighting the value of collaboration in decision-making processes to improve care [32, 33].

*Lack of Evaluation*

It is still unknown, how these practices impact patients and the public and whether improvements result in higher-quality care. During the mapping of patient and public practices in personalised prevention, it became clear that evaluation and feedback follow-ups were frequently missing or just briefly described. This oversight creates a huge gap in the implementation of these practices, making it difficult to measure their success and make necessary modifications. In light of the specified aims of engagement, we can stimulate continual development and get closer to optimising meaningful patient and public engagement in personalised prevention by recognising the importance of evaluation and embedding feedback mechanisms into these practices. Explain to patients how their feedback is used and is put into better practice is crucial to motivate patients to contribute. Furthermore, Nunn, Tiller [63] argues that more systematic methods of reporting and measuring involvement would be extremely valuable in developing best practices.

Murtagh (2021) provides a paradigm for supporting meaningful and effective engagement and involvement of participants, patients, and the general public in genomics research and health implementation. They propose an Engagement Framework recognising the importance of deliberative reflection on the purposes and strategies of engagement over the entire course of a project. Deliberative approaches also emphasise the necessity of assessing and evaluating engagement strategies in order to promote learning and improve future efforts [64].

Also, with respect to governance of personalised prevention, engaging with the public and patients during the various stages of the public health policy cycle is a crucial element for implementation and may help foster public trust of genomics initiatives in the EU [19, 60]. By involving patients and the public in decision-making processes, research and prevention strategies are tailored to the participant's unique needs, preferences, and circumstances, ultimately leading to improved health outcomes and a more sustainable healthcare system.

*Blurring boundaries between research and care*

In the context of personalised medicine, the traditional boundaries separating research and care become less distinct [65]. Research and care converge to drive improved patient outcomes and tailored treatment approaches. It is apparent that several patient and public engagement practices in our study, bridge both the research and care domains, indicating a growing recognition of the interconnectedness between these areas. Perry, Wöhlke [32] and Appelbaum [66] describe the perception among individuals that their contribution to research

automatically translates into benefits for their own care, also known as therapeutic misconception. However, this belief can be misleading, posing a potential pitfall for personalised prevention. It is crucial to avoid prematurely enticing individuals to participate in research without fully informing them of the complexities involved and of the objectives [32]. Embracing both domains of research and care in personalised medicine can introduce challenges, as highlighted by Day et al. (2017) who pointed out that the translation of new protocols based on biological research further complicated an already complex patient pathway. In exploring the integration of research and care, patients' experiences are crucial to help optimise the implementation of personalised prevention.

## Barriers and Facilitators of public and patient engagement

Engaging, educating, and empowering patients and the general public in personalised prevention is critical for achieving optimal healthcare outcomes. However, there are various barriers and facilitators to applying these principles. One key challenge is the lack of knowledge and comprehension of personalised preventative approaches among patients and the general public. Education and raising awareness are essential for providing accurate and easily available information on personalised preventative approaches. Providing clear and straightforward educational materials which address patients and citizen's needs, such as educational activities or online tools, can empower people to make informed health decisions.

Furthermore, healthcare personnel may confront difficulties in expressing complicated concepts and customizing information to the requirements of particular patients. This also requires healthcare professionals to have adequate knowledge and skills to help patients to take control of their health decisions which has been shown to be a barrier for implementing personalised prevention. Innovative ways of information provision can be helpful as Benusiglio, Di Maria [29] report increases in patients' knowledge and empowerment following a group counselling session.

During our search we came across several clinical trials that were excluded due to the fact that no engagement was reported. Clinical studies generally do not assess patient satisfaction or public response or do not report having done so. To address this gap, it has been recommended that studies place greater emphasis on involving patients, ensuring that feedback is actively sought and incorporated. This includes engaging them in trial design, informed consent processes, and trial monitoring [67]. But, also including the patients throughout the whole process, by actively contributing to the development of research questions before the trial takes place, which will improve trial enrolment, retention and adherence. By involving these stakeholders, clinical trials become more patient-centric, address relevant outcomes, and prioritize participant safety and well-being [68]. This integration has the potential to improve patient outcomes, since research findings can guide tailored treatment decision and care plans [69, 70].

Dedicated funding for patient and public engagement has been mentioned as an important prerequisite for enabling and enhancing the overall quality and relevance of research in personalised medicine and integration into health care systems [60].

### Study strengths and limitations

This scoping review has several limitations, as personalised prevention practices in Europe were retrieved via academic databases. Practices that are not publicly available or only reported in grey literature were not included. In the literature, the terms “engagement,” “participation,” and “involvement” are frequently used interchangeably and ambiguously, with their meaning appearing self-evident. Despite calls to develop evidence-based engagement, the literature's current lack of clear conceptualisations and definitions of engagement is a major impediment to valid measurement and analysis. We have tried to overcome this shortcoming by combining engagement in the four domains which may have resulted in overlooking other relevant aspects. It is worth noting that although the search strategy employed for identifying common chronic conditions could have been expanded, we deliberately used overarching MeSH terms rather than specific subheadings to avoid too many unrelated search hits detailing secondary factors.

We utilised a thorough methodology that allowed broad-scope investigations into the landscape of public and patient engagement practices in personalised prevention and genomics. Rather than covering engagement in detail, this method allowed for a better comprehension of the range of topics relevant for understanding patient and public engagement across various domains relevant for personalised prevention.

## Conclusions

In conclusion, this report has provided a thorough mapping of patient and public empowerment and engagement methods within the context of personalised prevention in the domains of research, care, education and governance. This scoping review, to the best ofour knowledge, is the first to map public and patient engagement practices in personalised prevention in Europe. The findings demonstrate the wide range of approaches and methods that can be utilised to engage patients and the general public at various stages of the empowerment and engagement spectrum. Recently, mainly one directional engagement methods were used (dissemination, consultation). Most engagement activities in our review were related to (personalised prevention of) cancer, and none to neurodegenerative diseases. It is evident that different methods are suitable for different purposes and objectives, as well as for engaging patients versus the general public. Engaging patients and the public in personalised prevention efforts is essential to empower individuals to take an active role in their own health and well-being. In order for patients and the public to be empowered, education, health literacy and knowledge need to be enhanced. Moving forward, it is crucial to invest in these various possibilities and to ensure that they are continually placed prominently on the agenda. Our research will form the foundation for the next PROPHET

deliverable, providing guidance on developing best practice models for engaging patients and the public. By elaborating on and implementing practices that engage and empower the patients and public at all levels of the engagement spectrum, we can foster a more inclusive and participatory approach to personalised prevention, ultimately leading to improved health outcomes for individuals and communities alike.

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# Appendix A

## Supplementary Information full search strategies

### Search strategy for OVID/Medline (28 July 2023)

*Ovid MEDLINE(R) ALL <1946 to July 27, 2023>*

| | | |
|---|---|---|
| **1** | "Citizen Science"/ or citizen-science*.ti,ab,kf. | **2,300** |
| **2** | exp Community-Based Participatory Research/ or exp Patients/ or exp Family/ or (public or publically or citizen* or communit* or population* or stakeholder* or stake-holder* or patient* or client* or famil* or outpatient* or inpatient* or index-case* or proband* or relative*).ti,ab,kf. | **12,382,485** |
| **3** | (((personalized or personalised or individual* or predictive or precision or stratif* or tailor* or targeted) adj3 preventi*) or (precision adj3 health*) or public-health-prevention or ((personalized or personalised) adj3 medicine)).ti,ab,kf. | **36,578** |
| **4** | 2 and 3 | **24,994** |
| **5** | 1 or 4 | **27,282** |
| **6** | exp "Consumer Health Information"/ or exp Internet/ or exp Patient Participation/ or exp "Webcasts as Topic"/ or webcast.pt. or exp Health Communication/ or exp "Surveys and Questionnaires"/ or exp Focus Groups/ or Communication/ or exp Public Opinion/ or (engagement* or intervent* or communicat* or educat* or empower* or literate* or literac* or initiative* or (ethic* adj3 legal* adj3 social*) or inform* or misinform* or consult* or involve* or collaborat* or dialogue* or internet or web-contest* or forum* or fora or capacity-building or workshop* or meeting* or website* or newsletter* or news-letter* or fact-sheet* or factsheet* or web-2-0* or social-media* or twitter* or instagram or tiktok* or tik-tok* or facebook or face-book or platform* or podcast* or pod-cast* or channel* or youtube or feeds or reference-group* or joint-plan* or blog* or bulletin* or circular* or social-network* or open-discussion* or digital-tool* or design-thinking* or public-action* or (concept* adj3 (framework* or frame-work*)) or public-participati* or patient-participati* or (online adj3 aware*) or survey* or focus-group* or questionnaire*).ti,ab,kf. | **8,151,032** |
| **7** | exp Genetics/ or exp Genetic Testing/ or exp Genetics, Population/ or exp Genetic Services/ or exp "Genetic Predisposition to Disease"/ or exp Genetic Counseling/ or exp Genetic Privacy/ or Genetics/ or exp Genetic Research/ or exp Human Genetics/ or Genomics/ or exp Pharmacogenetics/ or (genomic* or genetic* or pharmacogenetic*).ti,ab,kf. | **1,749,819** |
| **8** | Neoplasms/ or Myelodysplastic Syndromes/ or (tumor* or tumour* or cancer* or malignan* or carcinogen* or neoplas* or oncogen* or carcinoma* or oncolog*).ti,ab,kf. | **4,208,264** |
| **9** | Cardiovascular Physiological Phenomena/ or Cardiovascular Diseases/ or exp Stroke/ or (cardiovascul* or cardio-vascul* or cvd*1).ti,ab,kf. | **784,248** |
| **10** | Neurodegenerative Diseases/ or (neurodegenerative-disease* or neurologic-degenerative-disease* or degenerative-neurologic-disease* or nervous-system-degenerative-disease* or neurodegenerative-disorder* or neurologic-degenerative-condition* or degenerative-neurologic-disorder* or spinal-cord-degenerative-disease*).ti,ab,kf. | **106,770** |
| **11** | 8 or 9 or 10 | **5,018,736** |
| **12** | 5 and 6 and 7 and 11 | **1,744** |
| **13** | 12 not (exp Animals/ not exp Humans/) | **1,733** |
| **14** | limit 13 to yr="2015 -Current" | **1,205** |

### Search strategy for Embase.com (28 August 2023)

| No. | Query | Results |
|---|---|---|
| **#16** | #15 AND [2015-2023]/py | **3,071** |
| **#15** | #14 NOT ([animals]/lim NOT [humans]/lim) | **3,988** |
| **#14** | #12 NOT #13 | **4,014** |

| | | |
|---|---|---|
| **#13** | #12 AND ('Conference Abstract'/it OR 'Conference Paper'/it OR 'Conference Review'/it) | **2,393** |
| **#12** | #5 AND #6 AND #7 AND #11 | **6,407** |
| **#11** | #8 OR #9 OR #10 | **7,086,760** |
| **#10** | 'degenerative disease'/de OR 'neurodegenerative disease*':ti,ab,kw OR 'neurologic degenerative disease*':ti,ab,kw OR 'degenerative neurologic disease*':ti,ab,kw OR 'nervous system degenerative disease*':ti,ab,kw OR 'neurodegenerative disorder*':ti,ab,kw OR 'neurologic degenerative condition*':ti,ab,kw OR 'degenerative neurologic disorder*':ti,ab,kw OR 'spinal cord degenerative disease*':ti,ab,kw | **160,607** |
| **#9** | 'cardiovascular function'/de OR 'cardiovascular disease'/de OR 'cerebrovascular accident'/de OR cardiovascul*:ti,ab,kw OR 'cardio vascul*':ti,ab,kw OR cvd*1:ti,ab,kw | **1,291,696** |
| **#8** | 'neoplasm'/de OR 'myelodysplastic syndrome'/de OR tumor*:ti,ab,kw OR tumour*:ti,ab,kw OR cancer*:ti,ab,kw OR malignan*:ti,ab,kw OR carcinogen*:ti,ab,kw OR neoplas*:ti,ab,kw OR oncogen*:ti,ab,kw OR carcinoma*:ti,ab,kw OR oncolog*:ti,ab,kw | **5,777,822** |
| **#7** | 'genetics'/exp OR 'genetic screening'/exp OR 'population genetics'/exp OR 'genetic service'/exp OR 'genetic predisposition'/exp OR 'genetic counseling'/exp OR 'genetic privacy'/exp OR 'genomics'/exp OR 'pharmacogenetics'/exp OR genomic*:ti,ab,kw OR genetic*:ti,ab,kw OR pharmacogenetic*:ti,ab,kw | **2,910,744** |
| **#6** | 'consumer health information'/exp OR 'internet'/exp OR 'patient participation'/exp OR 'mass communication'/exp OR 'medical information'/exp OR 'questionnaire'/exp OR 'interpersonal communication'/exp OR 'public opinion'/exp OR engagement*:ti,ab,kw OR intervent*:ti,ab,kw OR communicat*:ti,ab,kw OR educat*:ti,ab,kw OR empower*:ti,ab,kw OR literate*:ti,ab,kw OR literac*:ti,ab,kw OR initiative*:ti,ab,kw OR ((ethic* NEAR/3 legal* NEAR/3 social*):ti,ab,kw) OR inform*:ti,ab,kw OR misinform*:ti,ab,kw OR consult*:ti,ab,kw OR involve*:ti,ab,kw OR collaborat*:ti,ab,kw OR dialogue*:ti,ab,kw OR internet:ti,ab,kw OR 'web contest*':ti,ab,kw OR forum*:ti,ab,kw OR fora:ti,ab,kw OR 'capacity building':ti,ab,kw OR workshop*:ti,ab,kw OR meeting*:ti,ab,kw OR website*:ti,ab,kw OR newsletter*:ti,ab,kw OR 'news letter*':ti,ab,kw OR 'fact sheet*':ti,ab,kw OR factsheet*:ti,ab,kw OR 'web 2 0*':ti,ab,kw OR 'social media*':ti,ab,kw OR twitter*:ti,ab,kw OR instagram:ti,ab,kw OR tiktok*:ti,ab,kw OR 'tik tok*':ti,ab,kw OR facebook:ti,ab,kw OR 'face book':ti,ab,kw OR platform*:ti,ab,kw OR podcast*:ti,ab,kw OR 'pod cast*':ti,ab,kw OR channel*:ti,ab,kw OR youtube:ti,ab,kw OR feeds:ti,ab,kw OR 'reference group*':ti,ab,kw OR 'joint plan*':ti,ab,kw OR blog*:ti,ab,kw OR bulletin*:ti,ab,kw OR circular*:ti,ab,kw OR 'social network*':ti,ab,kw OR 'open discussion*':ti,ab,kw OR 'digital tool*':ti,ab,kw OR 'design thinking*':ti,ab,kw OR 'public action*':ti,ab,kw OR ((concept* NEAR/3 (framework* OR 'frame work*')):ti,ab,kw) OR 'public participati*':ti,ab,kw OR 'patient participati*':ti,ab,kw OR ((online NEAR/3 aware*):ti,ab,kw) OR survey*:ti,ab,kw OR 'focus group*':ti,ab,kw OR questionnaire*:ti,ab,kw | **10,760,119** |
| **#5** | #1 OR #4 | **71,205** |
| **#4** | #2 AND #3 | **69,241** |
| **#3** | 'personalized medicine'/exp OR (((personalized OR personalised OR individual* OR predictive OR precision OR stratif* OR tailor* OR targeted) NEAR/3 preventi*):ti,ab,kw) OR ((precision NEAR/3 health*):ti,ab,kw) OR 'public health prevention':ti,ab,kw OR (((personalized OR personalised) NEAR/3 medicine):ti,ab,kw) | **103,337** |
| **#2** | 'participatory research'/exp OR 'patient'/exp OR 'family'/exp OR public:ti,ab,kw OR publically:ti,ab,kw OR citizen*:ti,ab,kw OR communit*:ti,ab,kw OR population*:ti,ab,kw OR stakeholder*:ti,ab,kw OR 'stake holder*':ti,ab,kw OR patient*:ti,ab,kw OR client*:ti,ab,kw OR famil*:ti,ab,kw OR outpatient*:ti,ab,kw OR inpatient*:ti,ab,kw OR 'index case*':ti,ab,kw OR proband*:ti,ab,kw OR relative*:ti,ab,kw | **17,099,954** |
| **#1** | 'citizen science'/exp OR 'citizen science*':ti,ab,kw | **1,987** |

**Search strategy for Elsevier/Scopus (28 August 2023)**

| History Count | Search Terms | Results |
|---|---|---|
| **9** | #8 AND PUBYEAR > 2015-2023 | **1,371** |
| **7** | #3 AND #4 AND #5 AND #6 | **2,045** |
| **6** | TITLE-ABS (engagement* OR intervent* OR communicat* OR educat* OR empower* OR literate* OR literac* OR initiative* OR (ethic* W/3 legal* W/3 social*) OR inform* OR misinform* OR consult* OR involve* OR collaborat* OR dialogue* OR internet OR web-contest* OR forum* OR fora OR capacity-building OR workshop* OR meeting* OR website* OR newsletter* OR news-letter* OR fact-sheet* OR factsheet* OR web-2-0* OR social-media* OR twitter* OR instagram OR tiktok* OR tik-tok* OR facebook OR face-book OR platform* OR podcast* OR pod-cast* OR channel* OR youtube OR feeds OR reference-group* OR joint-plan* OR blog* OR bulletin* OR circular* ORsocial-network* OR open-discussion* OR digital-tool* OR design-thinking* OR public-action* OR (concept* W/3 (framework* OR frame-work*)) OR public-participati* OR patient-participati* OR (online W/3 aware*) OR survey*OR focus-group* OR questionnaire*) OR AUTHKEY (engagement* OR intervent* OR communicat* OR educat* OR empower* OR literate* ORliterac* OR initiative* OR (ethic* W/3 legal* W/3 social*) OR inform* OR misinform* OR consult* OR involve* OR collaborat* OR dialogue* OR internet OR web-contest* OR forum* OR fora OR capacity-building OR workshop* ORmeeting* OR website* OR newsletter* OR news-letter* OR fact-sheet* OR factsheet* OR web-2-0* OR social-media* OR twitter* OR instagram OR tiktok* OR tik-tok* OR facebook OR face-book OR platform* OR podcast* ORpod-cast* OR channel* OR youtube OR feeds OR reference-group* OR joint-plan* OR blog* OR bulletin* OR circular* OR social-network* OR open- discussion* OR digital-tool* OR design-thinking* OR public-action* OR (concept* W/3 (framework* OR frame-work*)) OR public-participati* OR patient-participati* OR (online W/3 aware*) OR survey* OR focus-group* OR questionnaire*) | **20,405,004** |
| **5** | (TITLE-ABS (tumor* OR tumour* OR cancer* OR malignan* OR carcinogen* OR neoplas* OR oncogen* OR carcinoma* OR oncolog*) OR AUTHKEY (tumor* OR tumour* OR cancer* OR malignan* OR carcinogen* OR neoplas* OR oncogen* OR carcinoma* OR oncolog*)) OR (TITLE-ABS (cardiovascul* OR cardio-vascul* OR cvd*) OR AUTHKEY (cardiovascul* OR cardio-vascul* OR cvd*)) OR (TITLE-ABS (neurodegenerative-disease* OR neurologic-degenerative-disease* OR degenerative-neurologic-disease* OR nervous-system-degenerative-disease* OR neurodegenerative-disorder* OR neurologic-degenerative-condition* OR degenerative-neurologic-disorder* OR spinal-cord-degenerative-disease*) OR AUTHKEY (neurodegenerative-disease* OR neurologic-degenerative-disease* OR degenerative-neurologic-disease* OR nervous-system-degenerative-disease* OR neurodegenerative-disorder* OR neurologic-degenerative-condition* OR degenerative-neurologic-disorder* OR spinal-cord-degenerative-disease*)) | **5,748,587** |
| **4** | TITLE-ABS (genomic* OR genetic* OR pharmacogenetic*) OR AUTHKEY (genomic* OR genetic* OR pharmacogenetic*) | **2,250,453** |
| **3** | #1 OR #2 | **43,611** |
| **2** | (TITLE-ABS (public OR publically OR citizen* OR communit* OR population* OR stakeholder* OR stake-holder* OR patient* OR client* OR famil* OR outpatient* OR inpatient* OR index-case* OR proband* OR relative*) OR AUTHKEY (public OR publically OR citizen* OR communit* OR population* OR stakeholder* OR stake-holder* OR patient* OR client* OR famil* OR outpatient* OR inpatient* OR index-case* OR proband* OR relative*)) AND (TITLE-ABS ((personalized OR personalised OR individual* OR predictive OR precision OR stratif* OR tailor* OR targeted) W/3 (preventi*) OR (precision W/3 health*) OR public-health-prevention OR ((personalized OR personalised) W/3 medicine)) OR AUTHKEY ((personalized OR personalised OR individual* OR predictive OR precision OR stratif* OR tailor* OR targeted) | **34,439** |

| | | |
|---|---|---|
| | W/3 (preventi*) OR (precision W/3 health*) OR public-health-prevention OR ((personalized OR personalised) W/3 medicine))) | |
| **1** | TITLE-ABS (citizen-science*) OR AUTHKEY (citizen-science*) | **9,191** |

## Search strategy for Clarivate Analytics/Web of Science Core Collection (28 August 2023)

| | | |
|---|---|---|
| **5** | #4 AND #3 AND #2 AND #1<br>Refined by years: 2015 or 2016 or 2017 or 2018 or 2019 or 2020 or 2021 or 2022 or 2023 | **1,556** |
| **4** | TS=("tumor*" OR "tumour*" OR "cancer*" OR "malignan*" OR "carcinogen*" OR "neoplas*" OR "oncogen*" OR "carcinoma*" OR "oncolog*" OR "cardiovascul*" OR "cardio-vascul*" OR "cvd*" OR "neurodegenerative-disease*" OR "neurologic-degenerative-disease*" OR "degenerative-neurologic-disease*" OR "nervous-system-degenerative-disease*" OR "neurodegenerative-disorder*" OR "neurologic-degenerative-condition*" OR "degenerative-neurologic-disorder*" OR "spinal-cord-degenerative-disease*") | **5,776,990** |
| **3** | TS=("genomic*" OR "genetic*" OR "pharmacogenetic*") | **1,977,230** |
| **2** | TS=("engagement*" OR "intervent*" OR "communicat*" OR "educat*" OR "empower*" OR "literate*" OR "literac*" OR "initiative*" OR ("ethic*" NEAR/3 "legal*" NEAR/3 "social*") OR "inform*" OR "misinform*" OR "consult*" OR "involve*" OR "collaborat*" OR "dialogue*" OR "internet" OR "web-contest*" OR "forum*" OR "fora" OR "capacity-building" OR "workshop*" OR "meeting*" OR "website*" OR "newsletter*" OR "news-letter*" OR "fact-sheet*" OR "factsheet*" OR "web-2-0*" OR "social-media*" OR "twitter*" OR "instagram" OR "tiktok*" OR "tik-tok*" OR "facebook" OR "face-book" OR "platform*" OR "podcast*" OR "pod-cast*" OR "channel*" OR "youtube" OR "feeds" OR "reference-group*" OR "joint-plan*" OR "blog*" OR "bulletin*" OR "circular*" OR "social-network*" OR "open-discussion*" OR "digital-tool*" OR "design-thinking*" OR "public-action*" OR ("concept*" NEAR/3 ("framework*" OR "frame-work*")) OR "public-participati*" OR "patient-participati*" OR ("online" NEAR/3 "aware*") OR "survey*" OR "focus-group*" OR "questionnaire*") | **13,170,977** |
| **1** | TS=("citizen-science*" OR ("public" OR "publically" OR "citizen*" OR "communit*" OR "population*" OR "stakeholder*" OR "stake-holder*" OR "patient*" OR "client*" OR "famil*" OR "outpatient*" OR "inpatient*" OR "index-case*" OR "proband*" OR "relative*") AND (("personalized" OR "personalised" OR "individual*" OR "predictive" OR "precision" OR "stratif*" OR "tailor*" OR "targeted") NEAR/3 ("preventi*") OR ("precision" NEAR/3 "health*") OR "public-health-prevention" OR (("personalized" OR "personalised") NEAR/3 "medicine"))) | **37,567** |

## Search strategy for Ebsco/APA PsycINFO (28 August 2023)

| # | Query | Limiters/ Expanders | Results |
|---|---|---|---|
| **S 6** | S1 AND S2 AND S3 AND S4 | Limiters - Publication Year: 2015-2023 | **76** |
| **S 5** | S1 AND S2 AND S3 AND S4 | | **110** |
| **S 4** | DE "Neoplasms" OR TI(tumor* OR tumour* OR cancer* OR malignan* OR carcinogen* OR neoplas* OR oncogen* OR carcinoma* OR oncolog*) OR AB(tumor* OR tumour* OR cancer* OR malignan* OR carcinogen* OR neoplas* OR oncogen* OR carcinoma* OR oncolog*) OR KW(tumor* OR tumour* OR cancer* OR malignan* OR carcinogen* OR neoplas* OR oncogen* OR carcinoma* OR oncolog*) OR DE "Cardiovascular Health" OR DE "Cardiovascular Disorders" OR DE "Cerebrovascular Accidents" OR TI(cardiovascul* OR cardio-vascul* OR cvd*) OR AB(cardiovascul* OR cardio-vascul* OR cvd*) OR | | **177,177** |

| | | | |
|---|---|---|---|
| | KW(cardiovascul* OR cardio-vascul* OR cvd*) OR DE "Neurodegenerative Diseases" OR TI(neurodegenerative-disease* OR neurologic-degenerative-disease* OR degenerative-neurologic-disease* OR nervous-system-degenerative-disease* OR neurodegenerative-disorder* OR neurologic-degenerative-condition* OR degenerative-neurologic-disorder* OR spinal-cord-degenerative-disease*) OR AB(neurodegenerative-disease* OR neurologic-degenerative-disease* OR degenerative-neurologic-disease* OR nervous-system-degenerative-disease* OR neurodegenerative-disorder* OR neurologic-degenerative-condition* OR degenerative-neurologic-disorder* OR spinal-cord-degenerative-disease*) OR KW(neurodegenerative-disease* OR neurologic-degenerative-disease* OR degenerative-neurologic-disease* OR nervous-system-degenerative-disease* OR neurodegenerative-disorder* OR neurologic-degenerative-condition* OR degenerative-neurologic-disorder* OR spinal-cord-degenerative-disease*) | | |
| **S 3** | DE "Genome" OR DE "Genomic Sequencing" OR DE "Genetics" OR DE "Behavioral Genetics" OR DE "Genetic Engineering" OR DE "Genetic Processes" OR DE "Genomics" OR DE "Pharmacogenetics" OR DE "Population Genetics" OR DE "Gene Expression" OR DE "Mutations" OR DE "Polymorphism" OR DE "Genetic Testing" OR DE "Genetic Counseling" OR TI(genomic* OR genetic* OR pharmacogenetic*) OR AB(genomic* OR genetic* OR pharmacogenetic*) OR KW(genomic* OR genetic* OR pharmacogenetic*) | | **156,166** |
| **S 2** | DE "Digital Health Resources" OR DE "Digital Mental Health Resources" OR DE "Health Information" OR DE "Electronic Collaboration" OR DE "Social Media" OR DE "Online Social Networks" OR DE "Websites" OR DE "Blog" OR DE "Internet" OR DE "Client Participation" OR DE "Surveys" OR DE "Consumer Surveys" OR DE "Mail Surveys" OR DE "Online Surveys" OR DE "Telephone Surveys" OR DE "Questionnaires" OR DE "Communication" OR DE "Written Communication" OR DE "Oral Communication" OR DE "Verbal Communication" OR DE "Public Opinion" OR TI(engagement* OR intervent* OR communicat* OR educat* OR empower* OR literate* OR literac* OR initiative* OR (ethic* N3 legal* N3 social*) OR inform* OR misinform* OR consult* OR involve* OR collaborat* OR dialogue* OR internet OR web-contest* OR forum* OR fora OR capacity-building OR workshop* OR meeting* OR website* OR newsletter* OR news-letter* OR fact-sheet* OR factsheet* OR web-2-0* OR social-media* OR twitter* OR instagram OR tiktok* OR tik-tok* OR facebook OR face-book OR platform* OR podcast* OR pod-cast* OR channel* OR youtube OR feeds OR reference-group* OR joint-plan* OR blog* OR bulletin* OR circular* OR social-network* OR open-discussion* OR digital-tool* OR design-thinking* OR public-action* OR (concept* N3 (framework* OR frame-work*)) OR public-participati* OR patient-participati* OR (online N3 aware*) OR survey* OR focus-group* OR questionnaire*) OR AB(engagement* OR intervent* OR communicat* OR educat* OR empower* OR literate* OR literac* OR initiative* OR (ethic* N3 legal* N3 social*) OR inform* OR misinform* OR consult* OR involve* OR collaborat* OR dialogue* OR internet OR web-contest* OR forum* OR fora OR capacity-building OR workshop* OR meeting* OR website* OR newsletter* OR news-letter* OR fact-sheet* OR factsheet* OR web-2-0* OR social-media* OR twitter* OR instagram OR tiktok* OR tik-tok* OR facebook OR face-book OR platform* OR podcast* OR pod-cast* OR channel* OR youtube OR feeds OR reference-group* OR joint-plan* OR blog* OR bulletin* OR circular* OR social-network* OR open-discussion* OR digital-tool* OR design-thinking* OR public-action* OR (concept* N3 (framework* OR frame-work*)) OR public-participati* OR patient-participati* OR (online N3 aware*) OR survey* | | **2,593,153** |

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| | OR focus-group* OR questionnaire*) OR KW(engagement* OR intervent* OR communicat* OR educat* OR empower* OR literate* OR literac* OR initiative* OR (ethic* N3 legal* N3 social*) OR inform* OR misinform* OR consult* OR involve* OR collaborat* OR dialogue* OR internet OR web-contest* OR forum* OR fora OR capacity-building OR workshop* OR meeting* OR website* OR newsletter* OR news-letter* OR fact-sheet* OR factsheet* OR web-2-0* OR social-media* OR twitter* OR instagram OR tiktok* OR tik-tok* OR facebook OR face-book OR platform* OR podcast* OR pod-cast* OR channel* OR youtube OR feeds OR reference-group* OR joint-plan* OR blog* OR bulletin* OR circular* OR social-network* OR open-discussion* OR digital-tool* OR design-thinking* OR public-action* OR (concept* N3 (framework* OR frame-work*)) OR public-participati* OR patient-participati* OR (online N3 aware*) OR survey* OR focus-group* OR questionnaire*) | | |
| **S 1** | TI(citizen-science*) OR AB(citizen-science*) OR KW(citizen-science*) OR (DE "Patients" OR DE "Geriatric Patients" OR DE "Hospitalized Patients" OR DE "Medical Patients" OR DE "Outpatients" OR DE "Patient Safety" OR DE "Psychiatric Patients" OR DE "Surgical Patients" OR DE "Terminally Ill Patients" OR DE "Family" OR DE "Biological Family" OR DE "Family Members" OR DE "Family Relations" OR TI(public OR publically OR citizen* OR communit* OR population* OR stakeholder* OR stake-holder* OR patient* OR client* OR famil* OR outpatient* OR inpatient* OR index-case* OR proband* OR relative*) OR AB(public OR publically OR citizen* OR communit* OR population* OR stakeholder* OR stake-holder* OR patient* OR client* OR famil* OR outpatient* OR inpatient* OR index-case* OR proband* OR relative*) OR KW(public OR publically OR citizen* OR communit* OR population* OR stakeholder* OR stake-holder* OR patient* OR client* OR famil* OR outpatient* OR inpatient* OR index-case* OR proband* OR relative*)) AND (DE "Precision Medicine" OR TI((personalized OR personalised OR individual* OR predictive OR precision OR stratif* OR tailor* OR targeted) N3 (preventi*) OR (precision N3 health*) OR public-health-prevention OR ((personalized OR personalised) N3 medicine)) OR AB((personalized OR personalised OR individual* OR predictive OR precision OR stratif* OR tailor* OR targeted) N3 (preventi*) OR (precision N3 health*) OR public-health-prevention OR ((personalized OR personalised) N3 medicine)) OR KW((personalized OR personalised OR individual* OR predictive OR precision OR stratif* OR tailor* OR targeted) N3 (preventi*) OR (precision N3 health*) OR public-health-prevention OR ((personalized OR personalised) N3 medicine))) | | **5,758** |

**Search strategy for ProQuest/International Bibliography of Social Sciences (30 August 2023)**

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| **S2** | (MAINSUBJECT.EXACT.EXPLODE("Engagement") | OR | **1546708** |
| | MAINSUBJECT.EXACT.EXPLODE("Communication") | OR | |
| | MAINSUBJECT.EXACT("Education") | OR | |
| | MAINSUBJECT.EXACT.EXPLODE("Empowerment") | OR | |
| | MAINSUBJECT.EXACT("Health information") | OR | |
| | MAINSUBJECT.EXACT.EXPLODE("Information transfer") | OR | |
| | MAINSUBJECT.EXACT("Access to information") | OR | |
| | MAINSUBJECT.EXACT.EXPLODE("Information sharing") | OR | |
| | MAINSUBJECT.EXACT.EXPLODE("Internet") | OR | |
| | MAINSUBJECT.EXACT.EXPLODE("Social media") | OR | |
| | MAINSUBJECT.EXACT.EXPLODE("Reference groups") | OR | |
| | MAINSUBJECT.EXACT.EXPLODE("Patient participation") | OR | |
| | MAINSUBJECT.EXACT.EXPLODE("Polls & surveys") | OR | |
| | MAINSUBJECT.EXACT.EXPLODE("Focus groups") | OR | |

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| | MAINSUBJECT.EXACT.EXPLODE("Questionnaires")) OR noft(("engagement*" OR "intervent*" OR "communicat*" OR "educat*" OR "empower*" OR "literate*" OR "literac*" OR "initiative*" OR ("ethic*" NEAR/3 "legal*" NEAR/3 "social*") OR "inform*" OR "misinform*" OR "consult*" OR "involve*" OR "collaborat*" OR "dialogue*" OR "internet" OR "web-contest*" OR "forum*" OR "fora" OR "capacity-building" OR "workshop*" OR "meeting*" OR "website*" OR "newsletter*" OR "news-letter*" OR "fact-sheet*" OR "factsheet*" OR "web-2-0*" OR "social-media*" OR "twitter*" OR "instagram" OR "tiktok*" OR "tik-tok*" OR "facebook" OR "face-book" OR "platform*" OR "podcast*" OR "pod-cast*" OR "channel*" OR "youtube" OR "feeds" OR "reference-group*" OR "joint-plan*" OR "blog*" OR "bulletin*" OR "circular*" OR "social-network*" OR "open-discussion*" OR "digital-tool*" OR "design-thinking*" OR "public-action*" OR ("concept*" NEAR/3 ("framework*" OR "frame-work*")) OR "public-participati*" OR "patient-participati*" OR ("online" NEAR/3 "aware*") OR "survey*" OR "focus-group*" OR "questionnaire*")) | |
| **S3** | noft(("citizen-science*" OR ("public" OR "publically" OR "citizen*" OR "communit*" OR "population*" OR "stakeholder*" OR "stake-holder*" OR "patient*" OR "client*" OR "famil*" OR "outpatient*" OR "inpatient*" OR "index-case*" OR "proband*" OR "relative*") AND (("personalized" OR "personalised" OR "individual*" OR "predictive" OR "precision" OR "stratif*" OR "tailor*" OR "targeted") NEAR/3 ("preventi*") OR ("precision" NEAR/3 "health*") OR "public-health-prevention" OR (("personalized" OR "personalised") NEAR/3 "medicine")))) | **1263** |
| **S4** | MAINSUBJECT.EXACT.EXPLODE("Genetic disorders") OR MAINSUBJECT.EXACT.EXPLODE("Pharmacogenetics") OR MAINSUBJECT.EXACT.EXPLODE("Medical genetics") OR MAINSUBJECT.EXACT.EXPLODE("Psychiatric genetics") OR MAINSUBJECT.EXACT.EXPLODE("Genetics") OR MAINSUBJECT.EXACT.EXPLODE("Genetic counseling") OR MAINSUBJECT.EXACT.EXPLODE("Genetic testing") OR MAINSUBJECT.EXACT.EXPLODE("Genetic family histories") OR ("genomic*" OR "genetic*" OR "pharmacogenetic*") | **69455** |
| **S5** | MAINSUBJECT.EXACT("Cancer") OR MAINSUBJECT.EXACT("Neurodegenerative diseases") OR MAINSUBJECT.EXACT("Cardiovascular diseases") OR ("tumor*" OR "tumour*" OR "cancer*" OR "malignan*" OR "carcinogen*" OR "neoplas*" OR "oncogen*" OR "carcinoma*" OR "oncolog*" OR "cardiovascul*" OR "cardio-vascul*" OR "cvd*" OR "neurodegenerative-disease*" OR "neurologic-degenerative-disease*" OR "degenerative-neurologic-disease*" OR "nervous-system-degenerative- disease*" OR "neurodegenerative-disorder*" OR "neurologic-degenerative- condition*" OR "degenerative-neurologic-disorder*" OR "spinal-cord-degenerative-disease*") | **55226** |
| **S6** | [S2] AND [S3] AND [S4] AND [S5] | **56** |
| **S7** | ([S2] AND [S3] AND [S4] AND [S5]) AND pd(20150101-20230831) | **38** |

# Appendix B

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| **First Author** | **Year** | **Title** | **Aim / Objectives** | **Country** | **Disease Focus** | **Stakeholder groups involved** | **Participation/ engagement characteristics** | **Engagement method** | **Engagement objective/ outcome** | **Domain** | **Extent of Engagement** | **Level of Engagement** | **P,S,T prevention *** |
| Barazzetti | 2017 | Still Rather Hazy at Present: Citizens' and Physicians' Views on Returning Results from Biobank Research Using Broad Consent | Discuss the ethical, social, and policy issues associated with returning results in the context of biobanks using a broad consent approach | Switzerland | PM | Public | Two focus groups with a total of 21 citizens | Focus groups and interviews | Focus groups investigated stakeholder perspectives on a hospital biobank for biomedical research, including genomics and personalized medicine. Some citizens criticized personalized medicine, fearing dependency on medication and doubting the usefulness of genomic data for biobank participants. | Research and Care | Consult | Low | P |
| Benusiglio | 2017 | Hereditary breast and ovarian cancer: successful systematic implementation of a group approach to genetic counselling | Due to increased demand, more efficient ways to deliver genetic counselling are urgently needed, and this research aims to investigate the effectiveness of group counselling | France | Cancer: Hereditary breast and ovarian cancer | Patients | 210 patients attended group counselling, up to eight simultaneously. Cancer genetics knowledge questionnaire. Satisfaction and knowledge are evaluated | Questionnaires & group genetic counselling | Information regarding the genetics of breast and ovarian cancer, genetic testing and the implications of different types of results is well understood as shown by the significant improvement in patients knowledge scores after the group session. Other potential benefits were observed such as group emulation and patient empowerment although these were more difficult to quantify. | Care | Consult | Low | P |
| Byrjalsen | 2018 | Paediatric cancer families' participation in whole-genome sequencing research in Denmark: Parent perspectives | A parent perspective study was conducted by a clinical geneticist and anthropologist to document pragmatic, social and ethical dilemma | Denmark | Cancer | Patients & Family | N = 30 parents to 15 patients | Interviews | Genetic counselling sessions are arranged for families interested in STAGING, where they learn about its components, map their family pedigree, and discuss options for reporting their child's WGS results. Most parents found early engagement feasible, driven by altruism and curiosity about their child's cancer development, although some disagreed on the extent of information they wanted reported back. | Research and Care | Consult | Medium | P,S,T |
| Day | 2017 | Stratified, precision or personalised medicine? Cancer services in the 'real world' of a London hospital | To understand the practices and potential effects of stratified medicine. | UK | Cancer: Breast cancer | Patients | Patients (n=23) participating in interviews ranged in age from 38 to 79 years (median: 58.7 years) and most were white (n = 26). Most were being treated for the first occurrence of breast cancer (n = 22) and had begun treatment fewer than 5 years previously (n = 23) | Interviews | The patients were interviewed about their own experiences of the cancer services using minimal structured prompts from a topic guide. | Research and Care | Consult | Low | S, T |
| De Paoli | 2015 | Alliance Against Cancer, the network of Italian cancer centers bridging research and care | To achieve high standards of care across Italy, to implement and harmonize principles of modern personalized and precision medicine, by developing cost effective processes and to provide tailored information to cancer patient | Italy | Cancer | Patient representatives | Many additional full and associate members joined ACC, that presently includes the National Institute of Health, 17 research-oriented hospitals, scientific and patient organisations. There is a focus on the inclusion of patients' associations in the active members and in the assembly of this association. | Patient organisation representation | The Italian Cancer Patients' Organization (AIMaC) provides a bidirectional information exchange between patients and institutes with a continuous stimulus to look after patient's needs. The ACC goal is to develop a cost effective processes and to provide tailored information to cancer patients. As well as facilitate SION (National Cancer Information Service) improvement and expansion to meet the increasing demand for information | Governance and Education | Collaborate | High | S, T |

*Primary, Secondary and Tertiary Prevention: P=Primary; S=Secondary; T=Tertiary

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| Delnord | 2022 | Precision cancer medicine: What has translated into clinical use in Belgium? | In 2016, Belgium launched the Next Generation Sequencing (NGS) Roadbook, consisting in 10 Actions, across the health care system, to facilitate the uptake of NGS in routine clinical practice. The feedback on deployment of the NGS Roadbook from governmental stakeholders and beneficiaries were compiled. | Belgium | Cancer | Patients | 11 Focus groups were held in 2018−2019, 2 h sessions and DNA debate (debatadn.be) with 1250 contributions | Focus groups and DNA debate | The feedback allowed for constructive exchange on the attitudes, doubts, and expectations of cancer patients to whom NGS testing is offered. Patients touched upon many topics: data governance, secondary use of NGS data, data access and privacy issues, uncertainties and lack of knowledge about precision medicine, etc. ACTION 8: Engaging patients on informed consent, legal and ethical implications of NGS use in (hemato-)oncology. Key pillar of the HI-Impact Framework is Stakeholder engagement and capacity building. | Care | Consult | Medium | S |
| Gaba | 2022 | Unselected Population Genetic Testing for Personalised Ovarian Cancer Risk Prediction: A Qualitative Study Using Semi-Structured Interviews | To understand the attitudes, experiences and impact on the emotional well-being of women from the general population who underwent unselected population genetic testing (PGT) for personalised OC risk prediction and who received low-risk | UK | Cancer: Ovarian Cancer | Public | OC-unaffected women > 18 years and with no prior OC gene testing were ascertained through primary care in London. In-depth, semi-structured and 1:1 interviews were conducted until informational saturation was reached following nine interviews. | Interviews | In-depth, semi-structured and 1:1 interviews were conducted until informational saturation was reached following nine interviews. All felt the telephone helpline was helpful and should remain optional. | Care | Consult | Low | P |
| Gaba | 2020 | Population Study of Ovarian Cancer Risk Prediction for Targeted Screening and Prevention | The aim was to perform a feasibility study of OC risk stratification of general population women using a personalised OC risk tool followed by risk management | UK | Cancer: Ovarian Cancer | Public | Volunteers were recruited through London primary care networks., Women >=18 years. N=123 | Online/web-based decision aid along with optional telephone helpline use | Population genetic testing (PGT)/OC risk stratification uptake/acceptability, satisfaction, decision aid/telephone helpline use, psychological health and quality of life were assessed using validated/customised questionnaires over six months. | Care | Consult | Medium | P |
| Gorini | 2015 | Development and psychometric testing of a breast cancer patient-profiling questionnaire | The aim of this study was to develop and test the psychometric properties of the ALGA-Breast Cancer, a new multidimensional questionnaire that assesses the breast cancer patient's physical and mental characteristics in order to provide physicians, prior to the consultation, with a patient's profile that is supposed to facilitate subsequent communication, interaction, and information delivery between the doctor and the patient. | Italy | Cancer: Breast cancer | Patients & Public | The exploratory analysis included 100 primary breast cancer patients and 730 healthy subjects. | Questionnaires | Being asked to provide feedback on the topics included and the readability of the questions, both patients and physicians gave a significant contribution to the preparation of the questionnaire. | Care | Collaborate | Medium | S |
| Hawranek | 2021 | A Focus Group Study of Perceptions of Genetic Risk Disclosure in Members of the Public in Sweden: "I'll Phone the Five Closest Ones, but What Happens to the Other Ten?". | Explored perceptions and preferences on receiving genetic risk information about hereditary cancer risk in members of the Swedish public. | Sweden | Cancer: Hereditary cancer | Public | Participants (n = 18) aged between 24 and 71 years, recruited from various social contexts. The focus group interviews were initiated with a brief presentation of participants and facilitators, followed by a very short introduction to the clinical context under study and how genetic testing can identify hereditary cancer risks. | Focus groups | There is a genuine will to share risk information that can benefit others, even if this is difficult and causes discomfort. Second, when the duty to inform becomes overwhelming, compromises are made, such as limiting one's own responsibility of disclosure or projecting the main responsibility onto another party. | Care | Consult | Low | P, S |

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| Jurgens | 2022 | Precise, Genotype-First Breast Cancer Prevention: Experience With Transferring Monogenic Findings From a Population Biobank to the Clinical Setting | The experience from a national pilot study (2018-2021) were described in which 180 female participants of Estonian biobank (of >150,000 participants in total) were re-contacted to discuss personalized clinical prevention measures based on their genetic predisposition defined by 11 breast cancer-related genes. | Estonia | Cancer: Breast cancer | Patients | 180 female participants | Surveys | Participants' responses to the receipt of genetic risk information were gathered using two surveys developed based on findings from analogous previous studies. The participants perceived the receipt of genetic risk information as valuable. Fluent cooperation of project teams supported by state-of-art data management, quality control, and secure transfer can enable the integration of research results to everyday medical practice in a highly efficient, timely, and well-accepted manner. | Research and Care | Consult | Low | P, S |
| Kalouguina | 2023 | On the determinants and the role of the payers in the uptake of genetic testing and data sharing in personalized health | The factors influencing the uptake and sharing of data from genetic tests were determined | Switzerland | PM | Public | The sample comprises 1,000 respondents from Switzerland evenly distributed by gender, by four age categories between 25 and 65 years | Surveys | Five sets of socioeconomic, lifestyle, health insurance, sentiment, and political beliefs variables were utilised. Furthermore, two framings assess the willingness to undertake a test and the readiness to share results with an insurer when the costs of the test are borne by the insurer or the individual. | Research and Care | Consult | Low | P, S |
| Leppin | 2022 | Readiness to Accept Genetic Testing for Personalized Medicine: Survey Findings on the Role of Socio-Demographic Characteristics, Health Vulnerabilities, Perceived Genetic Risk and Personality Factors | The present study investigated whether readiness to accept a hypothetical cost-free offer of genetic testing to personalize treatment depends on socio-demographic characteristics, health-related vulnerabilities, personal dispositions, and prior awareness about personalized medicine | Denmark | PM | Public | 50-80-year-old Danish citizens (n = 15,072), n = 6807 returned a fully answered web-based questionnaire. | Questionnaires | Investigated whether readiness to accept a hypothetical cost-free offer of genetic testing to personalize treatment depends on socio-demographic characteristics, health-related vulnerabilities, personal dispositions, and prior awareness about personalized medicine. | Care | Consult | Low | P, S |
| Mamzer | 2017 | Partnering with patients in translational oncology research: ethical approach | The aim was to promote common understanding and sharing of knowledge between all parties and to establish a long-term partnership integrating patient's expectations. | France | Cancer | Patient representatives | Two distinct committees were settled in CARPEM: an "Expert Committee", gathering healthcare and research professionals, and a "Patient Committee", gathering patients and patient representatives. | Establishing patient committee | An empirical ethical research action was developed aiming to improve patient representatives' involvement in the development of the translational research program together with health professionals. The included patient representatives became full partners and participated in the transfer of knowledge to the public via conferences and publications. | Research | Collaborate | High | n/a |
| Martens | 2019 | DPD Testing Before Treatment With Fluoropyrimidines in the Amsterdam UMCs: An Evaluation of Current Pharmacogenetic Practice | Assessed the uptake of dihydropyrimidine dehydrogenase (DPD) testing in the Amsterdam University Medical Centers over time and to evaluate stakeholder experiences to indicate barriers and facilitators of implementation in routine clinical care | Netherlands | Cancer | Patients | A mixed-method approach involving electronic patient records of 753 unique patients and pharmacy information systems analyses and fifteen semi-structured interviews | Interviews | Patients were asked about their experience and expectations about the information provision around DPD testing | Care | Consult | Low | T |
| Perry | 2017 | Why take part in personalised cancer research? Patients' genetic misconception, genetic responsibility and incomprehension of stratification-an empirical-ethical examination. | The first longitudinal empirical-ethical study was conducted based on semi-structured interviews with colorectal cancer patients enrolled in a biomarker trial for (neo)adjuvant treatment. | Germany | Cancer: Colorectal cancer | Patients | Colorectal cancer patients (n = 40) enrolled in a biomarker trial | Interviews | Analysing the patients' understanding of and perspectives on research and treatment with qualitative methods. | Research and Care | Consult | Low | T |

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| Pujol | 2018 | Guidelines for reporting secondary findings of genome sequencing in cancer genes: the SFMPP recommendations | The objective was to elaborate general recommendations on information related to patients and consent and to provide informed consent forms and an information media tool (animation movie). | France | Cancer | Patients | Patient representatives (n=3) | Participation of patient representatives in working group | Patients' representatives provided ethical reflection, information guidelines, and materials. | Care | Collaborate | High | P, S |
| Rattay | 2018 | The Patient Perspective on Radiogenomics Testing for Breast Radiation Toxicity | The purpose of this study was to explore patient attitudes towards future predictive radiogenomics testing for breast radiation toxicity | UK | Cancer: Breast cancer | Patients | Twenty-one semi-structured interviews were conducted with breast cancer patients | Interviews | Three main themes were identified regarding attitudes towards a predictive radiogenomics test for breast radiation toxicity: willingness to undergo the test, implications of the test, and impact on treatment decision-making. Patients generally support the test's validity but prefer results to be shared with healthcare professionals. Most participants felt that advance knowledge of their risk would not greatly affect their treatment decisions, except in cases of significant symptoms or damage. | Care | Consult | Low | T |
| Ruffell | 2022 | GENIGMA: an app to map the 3D genome of cancer cell lines through extreme citizen science | The aim was to map the 3D genome of cancer cell lines through extreme citizen science with the use of an app | Germany | Cancer | Public | It was downloaded by 31 000 users across 137 different countries in only 4 weeks. | App game | The feedback was used to produce new content and materials for the website and social media, such as educational material, videos, a weekly results summary, and ranking of the game clans that contribute the most to science. The GENIGMA team is trying to involve schools in the #GenigmaChallenge, as an opportunity for students to participate in an ongoing project while learning new concepts and contributing to scientific progress' | Research | Patient/public-directed | High | n/a |
| Saghatchian | 2022 | Feasibility of personalized screening and prevention recommendations in the general population through breast cancer risk assessment: results from a dedicated risk clinic | A personalized approach to prevention and early detection based on known risk factors should contribute to early diagnosis and treatment of breast cancer. A risk assessment clinic was initiated for all women wishing to undergo an individual breast cancer risk assessment. | France | Cancer: Breast cancer | Public | A total of 290 women underwent breast cancer assessment, among which 196 women (68%) were eligible for risk assessment using MammoRisk (median age 52, range 40-72) Women previously identified as high risk, those who received chest irradiation, those with a personal history of breast cancer, atypical hyperplasia, or lobular carcinoma in situ, and those with a strong family history of breast or ovarian cancer were not eligible for risk assessment using MammoRisk | Not reported | A complete breast cancer assessment, including a questionnaire, mammogram with evaluation of breast density, consultation with a radiologist who explained the mammogram and risk assessment, and a breast cancer specialist. The visit concluded with a consultation with a breast cancer specialist for a clinical examination, lifestyle questionnaire review, explanation about risk factors, how risk score is calculated using MammoRisk, and general prevention recommendations. | Care | Consult | Medium | P |
| Stracke | 2022 | Medical knowledge and information needs among women with pathogenic variants in moderate-risk genes for hereditary breast cancer attending genetic counseling at an academic hospital in Germany-A qualitative approach | This study aimed to identify the medical knowledge, further information needs, and the possible impact of a lack of information on dealing with everyday life for women with pathogenic variants in MBCG who have attended genetic counseling at an academic hospital in Germany | Germany | Cancer: Hereditary breast cancer | Patients | Women with pathogenic variants in one of the genes CHEK2, RAD51C, RAD51D, PALB2 or ATM, either with or without a personal history of BC and/or OC, and who were at least 18 years old and in a medically and psychologically stable condition, were eligible for participation. Twelve women carrying pathogenic variants in MBCG. Women were between 29 and 59 years old and carried pathogenic variants in the risk genes. | Interviews | A qualitative approach was chosen in order to gain first insights into the perspectives and ideas of these women. The participants were asked if they knew the meaning of certain medical terms that had been mentioned in the PTGC. The women's uncertainties concerning medical knowledge and their further information needs seem to have an impact on how they deal with the pathogenic variant in everyday life. | Care | Consult | Low | P, S |

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| van El | 2018 | Stakeholder Views on Active Cascade Screening for Familial Hypercholesterolemia. | By identifying and interviewing a range of relevant stakeholders, the aim was to clarify arguments for and against more proactive, direct approaches, and show varying responses to and requirements for informing family members, given a changing landscape with new regulatory restraints. | Netherlands | CVD: (FH) | Patient representatives | Interviews with six persons from five stakeholder groups were conducted. | Interviews | Stakeholders were interviewed on pros and cons of actively approaching healthy relatives. To benefit from predictive, personalized, and preventive medicine, the roles and responsibilities of stakeholders in genetic testing as a preventive strategy, and informing family members, need to be carefully realigned. | Care | Consult | Low | P S |
| Viigimaa | 2022 | Effectiveness and feasibility of cardiovascular disease personalized prevention on high polygenic risk score subjects:<br>a randomized controlled pilot study. | The aim of the study was to evaluate the effect of the intervention by proactively sharing a patient's high polygenic risk score (PRS) for coronary artery disease (CAD) | Estonia | CVD | Patients | Participants were selected from 26 953 Estonian Biobank cohort participants. This randomized controlled trial was conducted among middle-aged subjects with a top 20% CAD PRS in a family medicine setting | Questionnaires | Subjects were informed about their PRS and CAD risk using a visual tool across three visits: baseline, counselling session, and a final visit at 12 months. An interactive interface allowed users to simulate lifestyle changes' effects on their risk, such as quitting smoking. Feedback questionnaires assessed subjects' and physicians' opinions on polygenic risk knowledge and its usefulness. Most subjects reported that understanding their genetic risk improved lifestyle and medication adherence. The majority recognized lifestyle as a major factor in CVD risk, with over 90% finding the counselling session information sufficient. | Care | Consult | Low | P |

PROPHET

a PeRsOnalized Prevention roadmap for the future HEalThcare

# D2.6 (B) Mapping educational needs on personalised prevention for health care professionals: a narrative review

Funded by the European Union

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| **Project acronym** | PROPHET |
| **Project title** | A Personalised Prevention roadmap for the future Healthcare (PROPHET) |
| **Thematic priority** | HORIZON-HLTH-2021-STAYHLTH-01 |
| **Type of action** | CSA |
| Grant Agreement | 101057721 |
| **Deliverable number and title** | D.2.6(B) Mapping educational needs on personalised prevention for health care professionals – a narrative review |
| **Work package** | WP2 |
| **Due date:** | 29/02/2024 |
| **Submission date** | |
| **Start date of project** | 01/09/2022 |
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| **Organisation responsible of deliverable** | Amsterdam UMC |
| **Version** | 1 |
| **Status** | Ongoing |
| **Author name(s)** | CG van El, LL Kreeftenberg, C Louati, MC Cornel |
| **Contributing partners** | EPF, ACN |
| **Reviewer(s)** | ELIXIR-Europe |
| **Document type:** | **R – Report**<br>O - Other<br>E – Ethics |
| **Dissemination level:** | **PU – Public**<br>SEN – Sensitive, limited under the conditions of the Grant Agreement |

| Versioning and contribution history | | | |
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| Keywords |
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| Personalised prevention, precision medicine, education, bottlenecks, gaps. |

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# Table of Acronyms or Abbreviations

| | |
|---|---|
| ACMG | American College of Medical Genetics and Genomics |
| BRCA | BReast CAncer (gene) |
| CPD | Continuing Professional Development |
| EPA | Entrustable Professional Activity |
| GP | General Practitioner |
| PROPHET | Personalised Prevention roadmap for the future HEalThcare |
| PRS | Polygenic Risk Score |

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# Executive summary

Genetics training for non-genetics medical professionals has been developed for over a decade. Partly, this coincided with mainstreaming: supporting non-genetic experts in ordering certain DNA tests within their field of expertise and also providing the relevant initial genetic counselling. The traditional competencies from clinical geneticists to assess, identify, manage and support individuals with inherited genetic disorders or conditions remain essential for an increasing group of medical professionals. However, in recent years, personalised medicine has gained prominence. It also raises the question of integrating genomics knowledge into public health activities, prevention and screening programmes. Personalised prevention requires additional competencies required for risk-stratified prevention based on genetic profiling. New categories of genomics knowledge for which training is needed emerged, such as somatic genomics related to tumours. The assessment in medical education has evolved to include competencies in so-called entrustable professional activities. Finally, the engagement of patients and the public in developing competency frameworks has been stressed as a crucial factor in fulfilling the promises of personalised medicine and prevention.

# 1 Introduction

After the publication of the sequence of the human genome , expectations were that medicine would become more personalised, using information on genetics and genomics. As many health care professionals would be involved, several organisations, including the European Society of Human Genetics, developed common minimum standards for core competencies in genetics for genetic experts (clinical geneticists, genetic specialist nurses or genetic counsellors, molecular geneticists, cytogeneticists, biochemists/biomedical scientists), but also non-genetics health care professionals (general practitioners, general nurses/midwives, medical specialists in fields other than genetics, specialist nurses, specialist midwives and specialist allied health professionals, and specialist dentists) (1). Given the limited availability of genetic experts and the increasing possibilities to apply genetics in other specialties, mainstreaming was gaining prominence: non-genetic experts provide genetic services for specialized patient groups. To support professionals to develop these competencies, various forms of education have been developed, some of which might be more effective in obtaining knowledge, and others to develop skills, for instance, in communicating information about genetics in an understandable, comprehensible and sensitive way and others to develop attitudes, and finally others to integrate the knowledge into own practices. More than ten years later, genetics knowledge is increasingly being integrated into personalised medicine, and the competencies and skills needed have changed.

## 1.1 Genetics, genomics, personalised medicine

In **genetics** the focus is often on monogenic conditions, where one gene variant can confer a high risk of for instance oncogenetic or cardiogenetic conditions. Presymptomatic testing for these conditions makes it possible to offer surveillance to reduce the morbidity and mortality. Knowledge and skills needed include (a) Identifying individuals who may have or may be a carrier of a genetic condition (b) Communicating information about genetics in an understandable, comprehensible and sensitive way, helping patients to make informed decisions and choices about their care and (c) Managing patients with genetic conditions, using accepted guidelines (1). Oncogenetic patients might for instance start surveillance at a relatively young age, so that (precursors of) tumours are recognised early. Cardiogenetic patients might receive care to limit the risk of arrhythmia's and sudden death by medication or implantable cardioverter-defibrillators.

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

**Personalised medicine** separates people into different groups—with medical decisions, practices, interventions and/or products tailored to the individual patient based on their predicted response or disease risk. It uses an individual's genetic profile to guide decisions made regarding the prevention, diagnosis, and treatment of disease. For this report we will

use the definition adopted by the EU Horizon Europe project 'PROPHET': Personalised Prevention roadmap for the future HEalThcare. "**Personalised prevention** aims to prevent the onset, progression and recurrence of disease through the adoption of targeted interventions that consider the biological information (*e.g.* genetics, demographics, health condition), environmental and behavioural characteristics and the socio-economic and cultural context of individuals. This should be timely, effective and equitable in order to maintain the best possible balance in lifetime health trajectory " (2).

## 1.2 Objective

The PROPHET project aims to co-create a Roadmap for the implementation of personalised prevention in health care systems, via the development of a Strategic Research and Innovation Agenda together with stakeholders in and outside academia. The first activities of the project focus on mapping the state of the art regarding *e.g.*, biomarkers, clinical utility, personalised prevention programs and activities, and engagement of citizens and patients, health care professionals and policymakers. This report is part of Deliverable D.6 focusing in particular on the engagement of health care professionals in personalised prevention. This review aims to collect key studies, including review articles, that identify the knowledge and competencies of (non-genetic) healthcare professionals require to effectively fulfill their role in personalised prevention. The ultimate goal is to provide a reasoned overview of healthcare professionals' needs and knowledge gaps to facilitate optimal implementation of personalised prevention. The review will focus on understanding the skills and competencies mentioned, such as utilising family medical history, given the new developments in personalised medicine, focusing mainly on chronic conditions, such as hereditary cancers or cardiovascular disorders, such as familial hypercholesterolemia, also relevant for public health. Examples of relevant skills and knowledge gaps in primary, secondary and tertiary prevention will be discussed.

## 1.3 Methods

We started from several key studies published by scholars active in the PROPHET project on educational needs for non-genetic health care providers (3-10). We searched the references for relevant studies, and snowballed studies citing these studies for relevant publications. In addition, we considered references from other deliverables within PROPHET: a scoping review on patient and citizen engagement for PROPHET (D2.6A) yielded some papers that inadvertently focused more on health care professional engagement and therefore were useful for this narrative review. Similarly, a scoping review of implementation of personalised prevention (D2.4) yielded several papers relevant for the narrative review.

# 2 Domains

Within the PROPHET project, personalised prevention is studied relating to all stages of prevention (primary, secondary, tertiary). We will sketch the most relevant developments and requirements for specific professional groups per domain.

## 2.1 Primary prevention

We speak about primary prevention when interventions lead to disease(s) being avoided. Persons with a genetic variant leading to familiar hypercholesterolemia can take statins from childhood onwards to reduce the risk of premature cardiovascular morbidity and mortality (11). Persons with Lynch syndrome, the most common cause of inherited colorectal cancer, can profit from colonoscopy to remove polyps before they become colon cancer. Furthermore, studies indicate that aspirin may reduce their risk of cancer. After two successful trials, a dose-finding trial is now ongoing, and some suggest discussing with Lynch syndrome carriers the possibility of using low-dose aspirin for colorectal cancer prevention (12). For inherited breast cancer due to BReast CAncer (*BRCA*) pathogenic gene variants, preventive surgery can be considered to avoid breast- and ovarian cancer. This, however, requires the inclusion of *BRCA* testing in the routine management of patients with breast, ovarian, pancreatic and prostate cancers, and the implementation of individual and family prevention pathways (13). From a public health perspective, after identifying a first index patient with a pathogenic gene variant, informing relatives in systematic approach (also called cascade screening) can contribute to primary (and secondary) prevention, as the preventive options mentioned above are especially relevant for the mutation carriers who do not yet have disease symptoms. Most individuals with these genetic conditions have, however, not yet been recognised. This may be due to limitations to the uptake of family history and the sensitivity of the family history–based approach (14), implying that other public health approaches, such as DNA-based adult screening, may be considered. The majority of public health professionals think that in the future public health programs (e.g. cancer screening, chronic diseases prevention programmes) will make greater use of genetic information (15).

*Professional groups involved in primary prevention include public health professionals, general practitioners (GPs), oncologists, specialists e.g. in internal medicine. They will need knowledge and skills for risk communication and referral.*

## 2.2 Secondary prevention

Secondary prevention aims to identify disease at the earliest stage through measures such as screening. Currently, public health cancer screening programs often follow an age-based one-size-fits-all approach. There is growing evidence that the efficiency of these screening programs could be improved by risk-stratification, including data from common susceptibility gene variants (3). More frequent screening tests could be offered to those at higher risk. In comparison, those at lower risk would receive less intense interventions, potentially limiting the disadvantages that screening programs always have, especially a lower proportion of false positives and reduced over diagnosis. Family history-based screening, as discussed under 2.1, may also provide opportunities for secondary prevention, such as surveillance for breast cancer starting at a relatively young age in families with *BRCA* gene variants (14). Some genes confer a somewhat lower breast cancer risk, such as *CHEK2* (Checkpoint kinase 2) (16). For different genes, the surveillance scheme may be somewhat different, so that, in fact a

stratified breast cancer screening is already performed, though in regular health care, not as a public health screening programme. Apart from physicians, cancer nurses could also contribute to prevention for cancer families (17). A multidisciplinary consensus study summarised competencies needed in cancer, genetics and prevention, including "ability to identify individuals that may be potentially at risk of having a genetic predisposition to cancer", "health promotion and health education" and the "ability to communicate and support family members at risk" (17). Chen *et al*. (2018) developed a training programme for community health workers in Texas (18).

**Pharmacogenomics**

When medication is prescribed, pharmacogenetic information on individual patients may help to improve effectiveness and avoid adverse effects. Guidelines for combinations of medication/gene variants have been issued by organisations such as the *Clinical Pharmacogenetics Implementation Consortium* (CPIC) and the *Dutch Pharmacogenetics Working Group* (*DPWG*), which show a high rate of concordance (19). The implementation of pharmacogenomics is gradually improving.

*The professional groups involved in secondary prevention include public health professionals in screening programmes, general practitioners, oncologists and other medical specialists, cancer nurses, community health workers and pharmacists. They will need knowledge and skills to interpret genomic results for risk assessment and communication.*

## 2.3 Tertiary prevention

Tertiary prevention seeks to limit the impact of existing diseases. Effective patient treatment can be based on genomic results, somatic genomics, and microbial genomic information (5). For tumours of unknown origin, DNA testing may identify a significant fraction that responds to immune checkpoint inhibitors (20). Relapsing ovarian cancer in *BRCA*-positive patients may respond to Poly (ADP-ribose) polymerase (PARP) inhibitors, a finding that has transformed the management (21). Microbial genome sequencing supports decision-making for treatment by antimicrobial susceptibility testing, and supports monitoring and surveillance in epidemiology, including the COVID pandemic. Hoxhaj *et al*. (2022) described the Core Competencies in Cancer Genomics for Healthcare Professionals, based on a systematic literature review and a Delphi procedure (10). The competencies cover cancer care (tertiary prevention) but also some aspects of secondary prevention. A Spanish group elaborated core competences for personalised precision medicine (22). They defined a framework of 58 competencies structured into 5 essential domains: determinants of health, biomedical informatics, practical applications, participatory health, and bioethics, and specify six professional profiles: health care, laboratory, digital health, community health, research, and management and planning.

*Professional groups involved in tertiary prevention include oncologists, other medical specialists, and public health physicians. They will need knowledge and skills to interpret genomic results, risk assessment and risk communication.*

# 3 Examples of relevant studies on knowledge, skills and competencies

## 3.1 Primary prevention

Many studies have addressed how to improve genomic medicine in primary care. Often, studies focus on the lack of knowledge regarding identification and referral for specific disorders, such as hereditary cancers and familial hypercholesterolemia, in general practice.

Vassy *et al*.(2015) offered 18 primary care physicians and cardiologists brief genomics continuing medical education on whole genome sequencing before completing surveys and semi-structured interviews. Sequencing was discussed for "generally healthy" adults in primary care. Participants described sequencing as currently lacking clinical utility because of its uncertain interpretation and limited impact on clinical decision-making. They expressed the idea that its clinical integration was inevitable. Potential clinical uses for sequencing included complementing other clinical information, risk stratification, motivating patient behaviour change and pharmacogenetics (23).
Laaksonen *et al*. (2022) studied the genomics education of public health nurses in Finland. They are health promotors who could take genome-based knowledge into account in precision healthcare. Thus, preventive health counselling would continue naturally after testing. The process led to genomic nursing competence being integrated into the curriculum of Public Health Care studies and Nursing Care studies (24).Grill and Rosén (2021) discuss the ethical dilemma of informing relatives. They argue that healthcare professionals have a duty to make actionable genetic information available to their patients' at-risk relatives. Traditionally patients are invited to inform their relatives, and health care providers support this with *e.g.,* family letters. However, Grill and Rosén (2021) argue that health care professionals should not deflect their moral responsibility, although they recognise this may conflict with other duties, such as the duty of confidentiality or of not knowing one's genetic predisposition. Confidentiality and respect for private life are fundamental patients' rights, protected by international conventions and national laws. However, this raises complex questions however and highlights the need for ethical competencies (25). Ploem *et al.* (2023) developed a tool to help professionals decide whether or not to recontact an individual in specific cases. The tool is based on legal- and ethical aspects (26).

Mainstreaming genetic testing has been discussed primarily in oncology settings. Identification of index patients by oncologists or pathologists will make primary or secondary prevention in relatives possible. Pathways must be streamlined, tasks laid out clearly, and educational material needs to be developed. In the UK such a mainstream pathway including training resources was developed for genetic testing in ovarian cancer patients(27). Tutika *et al*. (2023) performed a nationwide survey in the UK of the genomics training needs of oncologists, reporting a need for additional training. 'In total, 71.3% self-reported having good

knowledge of defining somatic and germline mutations, falling to 35.3% for understanding gene expression and regulation principles. Knowledge of cancer-predisposing syndromes was highest for Lynch syndrome (40.7% good knowledge) and lowest for multiple endocrine neoplasia (14.0% good knowledge). Overall, 49.0% of respondents had consented to patients for germline testing, but 80.7% reported a lack of training in genetic counselling' (28).

## 3.2 Secondary prevention

Chowdhury *et al.* (2015) report on a workshop organized in 2012 on improving breast cancer screening using medium and low-risk variants for risk stratification (3). They studied published frameworks and guidelines on core competencies in genetics for non-genetic experts (including examples from Europe (1), the USA (National Coalition for Health Professional Education in Genetics), and the UK (Royal College of General Practitioners)), which they conclude do not vary substantially. Common themes are to assess, identify, manage and support individuals with inherited genetic disorders or conditions. These core-competencies are especially relevant for the monogenic subtypes of cancer. Increasingly the possibilities to stratify populations according to multiple risk factors are discussed. Risk factors might include age, family history and genetic susceptibility based on common gene variants. These common gene variants might be combined in a Polygenic Risk Score (PRS).
Risk calculators for preventing common diseases in primary health care tend not to refer to using genetic variant information. Only the UK Royal College of General Practitioners' guideline for genetic competence in primary care discusses the importance of knowledge on genetic susceptibility. Thus, a gap was identified in the current competencies for using genomic information in the context of risk assessment tools for the asymptomatic population. Additional competencies needed are summarised in a table:

*Table 1: Additional competencies required for risk-stratified prevention based on genetic profiling (from Chowdhury et al., 2015) (3).*

| | Competence Themes | Additional Competencies Needed if Genomic Profiling Included in Risk Stratification |
|---|---|---|
| 1 | Knowledge of genetics, signs, symptoms in genetic disorders | Be aware of the extent and weight of contribution of common genetic variants and other determinants in contributing to disease risk and of their relevance in a risk assessment tool |
| 2 | Identify individuals with or at risk of a genetic condition | Competence already recommended in established frameworks |
| 3 | Genetic risk and risk assessment (particularly in common diseases) | Understand the rationale and pathway of the risk-stratified prevention programs incorporating genomic information |
| 4 | Family history in assessing predisposition to disease | Be able to explain any discordance in the relationship between the results of patients' genetic test for common variants and their family history assessment |
| 5 | Communicate relevant genetic information to enable informed decision making | Be aware of the specific harms and benefits arising from incorporating genetics in risk assessment tools.<br>Understand and provide information on the range and relevance of key genetic variants included in the test including the difference in risk contribution by high penetrant (e.g., variants within *BRCA 1/2*) and low penetrant alleles (e.g. single nucleotide polymorphisms) |
| 6 | Manage patients with genetic conditions | Health professionals are assumed to be competent in tailoring prevention interventions according to risk category |
| 7 | Obtain specialist help on inherited conditions | Competence already recommended in established frameworks |
| 8 | Understand relevant ethical, social and legal issues and offer appropriate psychological and social support | Respond to concerns about implications of the genetic component of a risk assessment result for family members<br>Explain, as appropriate, how the information obtained, including genetic data, may be shared with others including researchers, and, as appropriate, with commercial organisations, insurers or employers, and respond to specific concerns<br>Explain how the information obtained, including genetic data, will be used and stored, and be able to respond to specific ethical, legal and social concerns of the patient |

After starting risk-stratification pilots in the UK breast cancer screening programme, next steps require a comprehensive assessment of the resources needed for risk-stratification versus current resource availability, upgrades to screening IT and building screening infrastructure (29). The role of primary care needs to be determined. Simplification and clarification of risk-based screening pathways is needed to support health care professionals agency and facilitate implementation. Forthcoming evidence from ongoing randomised controlled trials assessing effectiveness of breast cancer risk-stratification will also determineimplementation (29).

The current reluctance to discuss stratified screening was also reported by Woof *et al.* (2021). Health care professionals reported concerns regarding risk estimate accuracy, healthcare professional confidence, service infrastructure and public communication prior to introducing less frequent screening for low-risk women (30). Also, the American College of Medical Genetics and Genomics (ACMG) advocates against clinical implementation of polygenic risk score testing at this time, as there is currently limited evidence to support the use of PRSs to guide medical management (31).

Puzhko *et al*. (2019) performed a deliberative stakeholder consultation involving 11 health professionals (family physicians and genetic counselors) working in Montreal, Canada (32). They explored the feasibility of implementing strategies for Personalised Risk Stratification-based breast cancer screening. Their main conclusion was that participants lacked understanding of the two steps: a first step to assess the risk, and next a stratified screening. Furthermore, participants were uncertain whether women at near-population risk would benefit. In terms of competencies, they were unsure how to interpret the 10-year risk for breast cancer based on the communication tools, in line with the competence themes”genetic risk assessment” and “communicate relevant genetic information to enable informeddecision making” from Chowdhury *et al*. 2015 (Table 1).

Blouin-Bougie et al., (2021) studied the needs and concerns of health care providers on risk-based screening to improve breast cancer prevention and early detection at the population level. They highlight three main conditions that should be met to foster the acceptability of breast cancer risk stratification: respecting the principle of equity, paying special attention to knowledge management, and rethinking human resources to capitalise on the strengths of the current workforce (33). Some elements require clarification before participants are “on board”. The step to defining their educational needs is not yet addressed.

For secondary prevention of cardiovascular conditions “there is a pressing need for advanced cardiovascular genetic counselling training, along with innovative online services, telemedicine, and patient-facing digital tools, as the most effective way forward” (34). Apart from genetic counsellors, one might consider other health workers to be involved in secondary prevention, as is the case for familial hypercholesterolemia where patients are often treated in primary care and internal medicine (35). In Texas a curriculum was developed for

community health workers using family health history-based prevention strategies (18). They learned, for instance, to develop a plan to use family health history assessments to identify high-risk clients and direct them to genetic evaluation and testing. Krittanawong (2017) stresses the need to educate physicians about health informatics next to implementing genetics/bioinformatics courses in medical education in the development of precision cardiovascular medicine (36).

Regarding the implementation of pharmacogenomics in health care, reviews and case studies discuss the lack of knowledge as a barrier to implementation and stress the need for education. For instance, Varughese (2020) mentions pharmacogenomic testing for gastrointestinal malignancies point-of-care education via appropriately designed clinical decision support alerts is a favourable teaching method for disseminating new information, especially when linked to clinical guidelines and primary literature (37).
When assessing community pharmacists' educational needs for implementing clinical pharmacogenomic services Berenbrok (2019) found 5 key themes: enriched pharmacogenomic education and training; active learning to build confidence in using pharmacogenomic data in practice; robust and reputable clinical resources to implement pharmacogenomic services effectively; a team-based approach throughout the implementation; a readily accessible network of pharmacogenomic experts (38).

## 3.3 Tertiary prevention

Rahman *et al*. (2022) conducted a scoping review on the genetic and genomic learning needs of oncologists and oncology nurses in the era of precision medicine who will be increasingly responsible for genomic testing (39). 'Learning needs relating to the interpretation of genomic data, clinical decision-making, patient communication and counselling, and fundamentals of genetics and genomics were reported. There was a lack of empirical research specific to oncology nurses and their learning needs in tumor sequencing. Our findings suggest that oncologists and oncology nurses need tailored support, education and training to improve their confidence and skills in adopting genomic testing into clinical practice.' Also Daly *et al*. (2023) studied training needs for precision medicine in cancer treatment (40).

Many developments in precision medicine concern treatment. Personalised prevention might be a next step, if germline variants are identified and if oncologists encourage family members to be tested, but this is not the focus of most current training on genomics testing in oncology.

# 4 Mode

Education can take the mode of a face-to-face training session, but given the large number of health care professionals potentially involved, increasingly also online training modules have become available. Both can be combined in blended learning.

Houwink et al (2015) developed three oncogenetic modules: an online Continuing Professional Development (G-eCPD) module, a live genetic CPD module, and a "GP and genetics" website (huisartsengenetica.nl) providing further genetics information applicable in daily practice (4). Main outcomes showed long-term (self-reported) genetic consultation skills (i.e. increased genetics awareness and referrals to clinical genetics centres) among GPs who participated in the oncogenetic training course, and interest in and satisfaction with the supportive website. CPD modules achieved a sustained improvement in oncogenetic knowledge.

Paneque *et al* (2017) describe the GenEquip project: a project team from six European countries developed online training to equip primary care physicians for genetics in everyday practice. The team included representatives from primary care, clinical genetics and patient organisations. A website www.primarycaregenetics.org leads to information in seven European languages (English, Spanish, Icelandic, Czech, Dutch, Italian, Portuguese), with webinars, practical tools, patient stories and online learning modules. The case-based modules are built around a typical clinical consultation with a primary care professional (6).

Calabro *et al.* (2021) evaluated a distance learning course focussed on genetic/genomics testing, pharmacogenetics and oncogenomics. With Multiple Choice Questions (MCQ) knowledge was assessed before and after physicians did the course on the online platform. The course primarily targeted General Practitioners (GPs) and Family Pediatricians (FPs). The course included audio-video lectures and interactive clinical cases and was structured according to the main models of Problem-Based Learning and Case-Based Learning. It was highly effective in improving physicians' knowledge and self-perceived competence (9).

In Switzerland, Staüble *et al* (2021) introduced a blended learning initiative combining an online module, virtual classroom sessions, and a follow-up case to apply learned skills. The training was evaluated by assessing knowledge, competencies and attitudes towards Pharmacogenomic testing in the pharmacy setting, satisfaction and plans for implementing a Pharmacogenomic service. The evaluation showed significant improvement in knowledge and an increase in self-perceived competencies in applying Pharmacogenomic counselling (41).

Although the ACMG currently advocates against clinical implementation of PRSs, their statement of PRS is designed as an educational resource for medical geneticists and other clinicians to help them provide quality medical service (31).
WIn a study in primary care US physicians were unfamiliar with genomics and placed a low priority on incorporating pharmacogenomics into practice while completing other

interventions for electronic health record first. However current barriers such as those related to knowledge and workload could be overcome by the development of adequate clinical decision support systems (CDS) (42).

David *et al.* (2023) describe an integrated system of personalised medicine in a community health system. They integrated amongst others, family history, pharmacogenomics information, a hereditary cancer panel, and polygenic risk scores in a learning health system. Education included videos available for internal and external audiences, virtual town halls for questions and answers, and a Genomic Ambassadors Programme for 10 primary care physicians per year to innovate quickly and disseminate knowledge (43).

Nisselle *et al* (2021) developed a Reporting Item Standards for Education and its Evaluation in Genomics. This will help developers of genomics education to increase the quality of education and evaluation across diverse settings (44).

A trend can be noticed that distance learning is more prominent. The courses are often problem-based or case-based. Evaluation tends to focus on knowledge and skills. Other dimensions of evaluation of learning need to be on the agenda.

# 5 Gaps, relevant for agenda setting: towards evaluation of best practices

## 5.1 From competence to entrustable professional activities (EPA)

After developing core competencies and training modules, learning needs to be evaluated. Some activities described in Chapter 4 used multiple-choice questions to assess knowledge. The modules developed by Houwink (2015) used a theoretical framework based on Kirkpatrick's Evaluation Framework for Education Outcomes, where at the first level, satisfaction with training modules is evaluated, at the second level, change in knowledge (retention) and self-reported competencies of newly learned genetic consultation skills, at the third level change in practice behaviour by applying acquired genetic competencies and timely recognition of patients at risk, and finally at the fourth level impact on patient health and organization, sustained change in practice behaviour (i.e. referral) and use of acquired genetics competencies (4). To assess competence, colleagues or trainees can be asked to perform critical activities (45). These activities require several (groups of) competencies, for instance, the possession of medical knowledge and communication skills to provide adequate patient care. Once a curriculum is finished, patients and instructors should be able to trust that the trainee can demonstrate readiness to bear professional responsibility for a specified list of activities. These activities are called entrustable professional activities (EPA). In the USA, the Inter-Society Coordinating Committee for Physician Education in Genomics started proposing EPAs as of 2014 (5). EPAs that were defined for genomic medicine include the

categories of family history, genomic testing, patient treatment based on genomic results, somatic genomics, and microbial genomic information (5).

## 5.2 Public and patient involvement

Patient and public engagement have been stressed as crucial factors in fulfilling the promises of personalised medicine and prevention. Patients and family members can contribute both to basic and continuing education activities; their roles can range from sharing experiences to teaching professionals and helping shape institutional training curricula (46). Yet, in developing competency frameworks for health professions in general patients and the public are rarely represented (47). Furthermore, often, the engagement is only partially reported (47).

It is crucial to involve the public and patients in developing educational and training resources to help build the skills required by a shift to more person-centred healthcare and ensure the outcomes in healthcare practice are adapted to their needs.. To achieve this, it is vital to first inquire about their needs and expectations, ensuring that the resulting materials align closely with the preferences and requirements of the community. A study explored the preferences and perceptions of receiving genetic risk information related to hereditary cancer risk in members of the Swedish public (48). The findings revealed a discrepancy between public expectations and the actual services provided by clinical genetics. The expectations along with the desire for a more personalised process and shared decision-making, highlight a gap in today's risk communication and suggest a need for developed clinical routines with improved healthcare–patient cooperation.

With respect to the expectations and knowledge of patients, Benusiglio et al. (2017), examined the effectiveness of group counselling for patients with suspected hereditary breast and ovarian cancer. The study outlines the substantial increase in patients' knowledge scores following the group session indicating that information about genetic testing, the genetics of breast and ovarian cancer, and the significance of various test results is well understood. Although they were harder to measure, additional possible advantages like patient empowerment and group emulation were noted. More effective methods of providing genetic counselling are needed due to the surge in demand (49).

In the domain of Biobanks the systematic collection and storage of biological samples are central. In order for individuals to be able to position themselves as possible donors ,Barazzetti *et al*. (2017) emphasised the significance of providing the participants with improved knowledge about the biobank initiative, the disclosure of genomic information andoptions not to be informed, and utility for the patient. Informing individuals about how the data will be used is also critical to build trust. Doctors mentioned training needs not only regarding the meaning of genomic information but also regarding ethical competencies for the communication about genetic risks in order for them to be ready to help biobank members appropriately in the event that information is returned (50). The body of research already indicates that increasing genetic literacy among the general public and medical professionals is crucial for facilitating the application of genomic research findings to therapeutic settings (51).

Additionally, a pharmacogenetic study assessed the adoption of *DPYD* testing in the Amsterdam University Medical Center in the Netherlands before starting chemotherapy, analysing stakeholder experiences to identify implementation barriers and enablers in standard clinical care (52). Most stakeholders wanted more information about the benefits of pharmacogenetic testing as well as its drawbacks, while patients indicated to have received adequate information, but wanted information to be simpler to help with comprehension. Involvement of the public and patients in the development of information material helps ensure that it is relevant and meets the needs of those who will use it. Close collaboration with patient organisations is important in this sense; they have extensive experience in producing and reviewing health-related information and help make specialist disease-specific information accessible and comprehensible for patients (53).

## 5.3 Gaps identified

In assessing the evolving landscape of educational initiatives for non-genetic medical professionals relevant for personalised prevention in healthcare, several gaps have surfaced. In relation to earlier initiatives the following aspects need more attention:

- Appropriate training is required for efficient stratification in public health screening.
- There is a need for training in new categories such as somatic genomics related to the tumour.
- Introduction of new methods of assessment of competences such as Entrustrable Professional Activities (EPAs).
- Incorporation of public and patient involvement.

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# D.2.6(C) Policymakers Engagement in Personalised Prevention

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| Deliverable Abstract |
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| On an institutional, national and international scale, policymakers are essential in enabling the implementation of personalised preventive approaches in healthcare systems. Collaboration among stakeholders is critical to address regulatory, resource, and technological challenges. Policymakers should be encouraged to use stakeholder input and evidence-based research to guide their decisions. Ultimately, policymakers have the potential to help create and support robust infrastructures and responsible practices that foster significant change towards a future healthcare. Through engagement and cooperation, barriers to implementation can be overcome, resulting in a healthcare system that is more personalised, preventive, patient-centered and supported by the public. This report addresses what kind of policymakers should be engaged along the implementation process of personalised prevention and what barriers need to be overcome. |



| Keywords |
|---|
| Personalised prevention, personalised medicine, genomics, policymakers, policy, engagement |

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# Introduction

After the publication of the human genome sequence, expectations were that medicine would become more personalised, using information on genetics and genomics. Globally, at the European and national levels, dedicated initiatives were taken to stimulate both research in genomics and responsible implementation into health care. At the level of the European Commission, the innovative potential has been recognised, stimulating research and the development of health care applications through various funding schemes. In subsequent years policymaking and regulation around using and processing genomic and health care data intensified.

An International Consortium for Personalised Medicine (ICPerMed) including 30 European and international members representing research funders and policy-making organisations, together with the European Commission as an observer, was established in 2016. In these years EU countries were found to have varying national policies regarding the implementation of genome-based technologies and attention to ethical issues suggesting 'a need for a co-ordinated effort to foster development and harmonisation of dedicated policies across EU to responsibly integrate genomics policies into existing health systems' (1). National genomics initiatives were established in many countries, boosting national research activities and infrastructures, and in some countries also stimulating applications in medicine (2). The 1+ Million Genomes Initiative (1+MG) was established as a commitment of 24 EU countries, the United Kingdom and Norway to allow cross-border access to one million sequenced genomes. In 2023, the European Genomic Data Infrastructure (GDI) project was started to enable access to genomic and related phenotypic and clinical data across Europe. Meanwhile, in Europe and globally omics-based treatments were developed, such as by the Worldwide Innovative Networking (WIN) consortium (3, 4).

A broad vision of personalised medicine moves beyond the domain of genomics research and genetic health care to also incorporate other health-related and lifestyle data. An important step to address and regulate concerns related to privacy and autonomy was made when in 2018 the General Data Protection Regulation came into force in the European Union, setting security and privacy standards for the processing of personal data and the movement or sharing of such data. The regulation is an 'essential step to strengthen individuals' fundamental rights in the digital age and facilitate business by clarifying rules for companies and public bodies in the digital single market .' Additionally, in May 2022, the European Health Data Space was launched by the European Commission which sets out a common EU framework allowing for primary as well as secondary use of health data for research, innovation, public health, policy-making and regulatory purposes.

Personalised medicine includes different aspects of medicine, such as care, cure and prevention. The latter is studied in the EU Horizon Europe project 'PROPHET': PeRsOnalised Prevention roadmap for the future HEalThcare (5). The project partners established a working definition of personalised prevention as aiming 'to prevent the onset, progression and recurrence of disease through the adoption of targeted interventions that consider the

biological information (e.g. genetics, demographics, health condition), environmental and behavioural characteristics and the socio-economic and cultural context of individuals'.

Onstwedder et al. (2022) propose an adapted Public Health Policy Cycle to extract critical aspects for genomics initiatives in public health, to study how (a) an agenda is set, (b) strategies and approaches to achieve public health benefits are determined (c) governance of the policy makers involved (d) implementation, and (e) evaluation (2). Elements of this cycle are also instructive for the implementation of personalized prevention. In the process various stakeholders for different cases and phases of personalised prevention are involved, such as researchers, funders, health care professionals, public and patients, companies, insurers but also regulators, advisory bodies and governmental agencies (6). In this report, we will discuss the engagement of policymakers in personalized prevention and focus on a few examples to highlight their role in fostering implementation.

The questions we will address are:

- What kind of policymakers should be engaged, and how can they be engaged, along the implementation process of personalised prevention?
- What are the barriers of implementation that need to be overcome?
  The questions apply at national and international levels, within health care at different levels (primary, secondary and tertiary care)

# Who are the policymakers?

In this report, we will use a broad scope including various policymakers to discuss their engagement. Along the pathway from research to implementation in health care, many actors may either take part in developing policies (*e.g.*, as part of their professional role in the organisation or actual delivery of health care) or are designated policymakers (*e.g.*, as officials in governing bodies or regulators). Health care innovations are often developed after researchers propose plans for new research and promise useful applications. To develop such plans, research needs to be funded, and questions that are important before applications can be implemented in healthcare need to be put on the agenda.

For medicine and devices, a regulatory approval is needed. If the product proves successful and sufficient evidence has been developed, niches can start working with the innovation, developing protocols, after which the innovation can be scaled up to an entire health region or country or setting. Often (multidisciplinary) guidelines are agreed upon by (organisations of) medical specialists, sometimes with the involvement of patients (7). Part of the evidence needed before implementing an innovation relates to costs and effectiveness. Reimbursement will be agreed upon by policymakers in health care insurance or health services based upon the economic evidence that may be gathered by health technology assessment agencies.

For personalised prevention, some of the innovations could be implemented in public health screening programs. Governmental institutes, Ministries of Health or Public Health can be involved in decision making on population screening programs. As the organisation of health

care is mandated in each European Member state, different countries/legislations can have different routes to innovations, and have their own research funders, health technology assessment agencies, government advisory committees, organisations of medical specialists, reimbursement experts and public health screening decision makers (Table 1).

# Stakeholder engagement and capacity building

Policymakers play a crucial role in enabling and regulating innovations in health care systems. We highlight two important elements for policymakers engagement pertaining to personalised prevention: their role in stakeholder engagement and the need for capacity building.

## Stakeholder engagement

Policymakers have a vital role in engaging with relevant stakeholders to ensure various perspectives and interests are considered in devising adequate policies. As the European Observatory on Health Systems and Policies stated, to overcome ethical, legal and social (ELSI) challenges and guarantee that advancements in the genomics field are founded on shared values, cautious regulation and close and ongoing stakeholder engagement will be required. To establish broad societal trust in genomics, it is critical to maintain an active dialogue with all stakeholders (6). Such engagement also allows for realistic policies that make optimal use of the actors' unique knowledge and network regarding their discipline or remit. Policymakers should not only be open to or participate in stakeholder engagement, but also, ideally actively promote and sustain such stakeholder engagement. For instance, in the EU, policies have been established to promote patient involvement in medical research and the delivery and governance of health care (7) (8). Conversely, stakeholders should be open to engage with policymakers as interaction between policymakers and researchers is a crucial component of knowledge mobilisation (9).

## Capacity building

It can be challenging to participate meaningfully in stakeholder engagement; all stakeholders require a variety of knowledge and skills. It is critical to invest in capacity building programs for policy makers and civil servants, health professionals, researchers, patients and patient organisations, project coordinators and other key stakeholders of the health sector (10). In order to fulfil the task of policymakers, they need to be aware of ongoing discussions and developments, not only concerning biomedical research and data infrastructures, but also with regards to ethical and societal ramifications.

Personalised prevention relies on various data sources. Such data need to be collected (*e.g.* from health records, databases, wearables, et cetera) and combined and analysed on a large scale to produce data-driven tools and eventually to be used in the clinic to personalise

prevention and treatment options for a specific patient. While using and combining such varied sources can yield more precise information on health, many ethical, legal and social issues need to be addressed as health data is considered to be sensitive (see also PROPHET T.2.2.3). Adding genomic data adds another layer of complex sensitivities as genomic information is not only relevant to an individual, but also to genetically related family members and can be used in other contexts to identify individuals and their relatives. Combining such sensitive data with a host of other data from various sources for the whole population needs extremely high safeguards against discrimination and misuse. Discussions are ongoing regarding how to organise such data sharing processes in a responsible manner, while policies and regulations have been developed and implemented. EU policies, such as those related to the European health Data Space require national commitments to find ways to establish safe data sharing procedures also at the local level, facilitate connecting research infrastructures, enabling better use and reuse of health data for healthcare, research, innovation and policy making. National bodies and policymakers need to be aware of this European context and well informed to engage in initiatives to harmonise and integrate their national practices and policies.

Useful tools for informing policymakers and capacity building, in addition to published research articles and reports, are so-called policy briefs. For instance, B1MG,ICPerMed and the European Parliament have produced multiple useful policy briefs to inform policymakers on important aspects of data sharing and implementing personalised medicine in health care (11) (12).

*Addressing barriers*

In recent years, barriers and facilitators for genomic research and implementation in health care have been identified (13).
In WP T.2.2.1/D.2.4 of the PROPHET project, interviews were conducted with a diversity of stakeholders to map the main perceived barriers and enablers for the adoption of personalised prevention. Some structural barriers were identified, most notably, the need to advance legal and regulatory frameworks for sharing genetic data, and the need for infrastructure to analyse and leverage genetic data for personalised prevention. In addition, it was mentioned that economic models that demonstrate costs and benefits of personalised prevention are lacking. In an environment where resources are limited and healthcare costs and demand are growing, healthcare decision-making now heavily relies on health technology assessments and economic evaluations (14). Especially with new technologies being incorporated into clinical practice and policy, such assessments should be conducted in personalised prevention and medicine (15). In Table 2, we summarise some barriers to implementation extracted from our three examples discussed below.

*Real world examples*

In this document we will sketch a few real-world examples to illustrate the involvement and engagement of policymakers. (a) The screening for breast cancer is often organized as a “one-

size-fits-all" population screening program, but risk stratification is increasingly discussed as a potential scenario for primary or secondary prevention. In clinical care, patients at increased risk already receive surveillance starting at a younger age and using other imaging modalities (b) To prevent adverse effects and improve effectiveness, pharmacogenetic testing offers potential as a form of secondary prevention. An example is testing for DPD (dihydropyrimidine dehydrogenase) before administration of fluoropyrimidines (anti-cancer drugs). Treatment of tumours can be guided by genomic information as form of tertiary prevention. (c) Recognizing hereditary cancers may offer relatives the possibility of surveillance and, therefore, primary or secondary prevention.

## Engaging policymakers in breast cancer screening

The European Collaborative on Personalised Early Detection and Prevention of BreastCancer (ENVISION) brings together international research consortia working on personalised early detection and prevention of breast cancer (16). In a consensus conference in 2019 they developed key recommendations for assessment of breast cancer risk, breast cancer prevention, risk-stratified early detection and program implementation. They propose the engagement of all stakeholders to ensure a systems approach to implementation studies in real-world settings. Thus questions that still need to be researched can be integrated in a learning health-care system approach. They describe ongoing studies, some of which are pragmatic Randomized Controlled Trials in real-world, including MyPeBS that is being performed in five European countries (Belgium, France, Israel, Italy and the UK) and Israel, and thus might lead to insights for implementation in European countries (17). Also at WIN conferences trials are presented on stratified breast cancer screening (e.g. WISDOM trial) (4). Policy makers are not specified in these ENVISION recommendations, although from the text it is clear that research funders, organisations of medical specialists, reimbursement experts and public health screening decision makers all have a role to play (16).

The United Kingdom subsequently organized an agenda setting meeting to ascertain whether attendees (a) think risk-stratified breast screening should be implemented and (b) identify issues that would need to be resolved before implementation into the NHS Breast Screening Program could proceed (18). Clearly policy makers from a public health setting in the UK were involved, as participants included "those involved in policy and national implementation of screening (e.g., members of the UK National Screening Committee; UKNSC)". The research priorities identified include aspects of implementation. Staff training and primary care staff training are mentioned as well as IT system development, but how to train or engage the policy makers is not discussed.

Estonia provides an example of how national research facilities can be used to stimulate innovation in personalised risk-based breast cancer screening (19). The infrastructure of the Estonian Biobank was used and a polygenic risk score (PRS) test was registered as medical device (IVD). Tests were used in partner with health care institutions in Estonia. It was feasible

to include a PRS in clinical practice for over 2600 women. Policymakers are not specified, and from the publication it is not clear how this pilot will lead to decision making on national implementation.

# Engaging policymakers in pharmacogenomics

As evidence accrues about clinical validity and utility, in pharmacogenetic applications collaboration between various stakeholders is ongoing to establish where applications may best be administered, and how information from genetic labs can be made available for such purposes. Pharmacists are a key player, but also general practitioners and medical specialists need to be informed about options for pharmacogenetic testing to establish roles and responsibilities in prescribing drugs and ordering pharmacogenetic testing, interpreting results, and communicating with patients (20, 21). In hospital settings implementation would entail hospital leadership facilitating communication with payers, the pharmacy and therapeutics committees leading the process in conjunction with the hospital, molecular laboratory, and information technology (IT) departments, as well as communicating with drug regulators who authorize or mandate pharmacogenetic tests (20).

As an example of current pharmacogenetic practice, the testing of Dihydropyrimidine Dehydrogenase (DPD) before chemotherapy with fluoropyrimidines in Amsterdam UMC was studied (22). If testing is performed before the administration of the medication, 3-5% of the population will be identified who are at risk of severe and fatal toxicity. A scientific landmark paper establishing clinical utility had no effect on implementation of testing. The oncologists developed a national guideline for colorectal carcinoma (published in 2017) recommending *DPYD* genotyping before treatment, which subsequently was discussed at local meetings to achieve consensus between oncologists and pharmacists. In this case a multidisciplinary group of medical specialists who developed the guideline, followed by local groups of oncologists and pharmacists, together changed the policy.

Treatment of tumours can be guided by genomic information. A relatively new organisational structure is the molecular tumour board (MTB) (23). The MTBs are multidisciplinary working groups, including different professionals such as pathologists, molecular pathologists, geneticists, oncologists, pharmacologists, surgeons, radiologists, bioinformaticians, and molecular biologists. They decide on which genomics tests to use in clinical care, especially next generation sequencing, to find an individualized treatment, based on the molecular and genetic characteristics of the neoplasm. Clearly, if genetic variants are identified, some of them may be somatic but some also may be germline variants, inherited from one of the parents, and thus also potentially relevant for family members (see next paragraph). Currently MTBs focus on innovative treatments, not on prevention for relatives.

# Engaging policymakers in hereditary cancers

Hereditary breast and ovarian cancer are caused by variants in the BReast CAncer (BRCA) genes *BRCA1* and *BRCA2*. Grech *et al* (2015) mention hereditary breast cancer families as an appropriate context for *BRCA1/2* screening. Thus carriers of variants would be eligible for preventive measures. Lynch syndrome is a hereditary cancer syndrome causing colon- and endometrial cancer (24). In the USA the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) led to Lynch syndrome screening recommendations in 2009 and the United States Preventive Services Task Force (USPSTF) issued *BRCA1* and *BRCA2* testing recommendations in 2005 and 2013 (25). The Center for Disease Control and Prevention (CDC) funded selected states to build capacity to integrate these recommendations into public health programs. Similar to Europe where member states develop their own health policy, also US have different policies. State cancer plans varied in their coverage of genetics/genomics aims, inclusion of hereditary breast and ovarian cancer specific goals, Lynch syndrome specific goals (25). Educational activities were organised, and surveillance initiated. A diversity of stakeholders was involved. State cancer genetics programs have partnered with cancer registries, clinical facilities, health-care providers, health systems, public and private payers, policymakers, other state, regional, and federal programs, academic institutions, community organisations, advocacy groups, and industry (25). Several of the stakeholders had to decide on their policy. To identify the first Lynch syndrome patient in a family, nowadays often all young colon cancer patients are screened for Lynch syndrome, but the coverage turned out not to be universal. This may depend on policies of oncologists and pathologists. Non-genetic public health initiatives such as Healthy People 2020 (26) and Cancer Moonshot (27) sometimes provided the impetus for state health departments to implement hereditary cancer activities.

Grech *et al* (2015) suggest that several genes are “candidates for a testing program in specialized clinics to screen family members of patients, identify risk, and initiate preventive monitoring, or discuss possible clinical solutions to reduce the risk significantly”. Apart from Lynch syndrome and *BRCA1/2* they mention several other hereditary cancer syndromes. Which policymakers precisely would have to decide on the testing programs is not explicitly mentioned(24).

# Moving forward

*Changing infrastructure, changing practice*

In various studies the importance of IT infrastructure and the reorganisation of procedures for testing, reporting, informing and collaboration across disciplines are mentioned, requiring training and the establishment of shared protocols. Martens *et al*. (2020) described how the implementation of pre-treatment pharmacogenomics testing in a hospital setting was supported by clear protocols and simple procedures for ordering and reporting relying on IT infrastructure (22). Qureshi *et al* (2022) performed a qualitative systematic review and provided policymakers with recommendations for the implementation of pharmacogenomics in primary care. They mention the need for effective educational strategies for primary care

physicians and patients. They also mention effective decision tools, clear delegation of roles and responsibilities, and cost effectiveness of pharmacogenomics and infrastructure (28).

Walton and Christensen (2023) integrate many of the aspects discussed in previous paragraphs in an ambitious plan to realize genomic data being widely available at the point of care with systems in place to manage its efficient utilization (29). One genetic test would be done for various purposes (pharmacogenomics, therapies, prevention). The authors have experience in health services in the USA. Substantial changes in billing, reimbursement, and reporting as well as the development of new systemic and technical architectures within the healthcare system would be needed. Some existing regulation in the USA might hinder a fast way forward to this “genome first” approach. An aspect Walton and Christensen (2023) touch upon is how knowledge on new variants will reach patients, and draw attention to the need for large-scale functional studies, sharing of data in the clinical ClinVar database, and roles and responsibilities of clinicians vs. academics (29).

# Summary

*Table 1: What kind of policymakers should be engaged*

| **What kind of policymakers should be engaged?** | | |
|---|---|---|
| **Disease** | **Actors** | **Activities** |
| All examples discussed | Funders of research<br><br><br><br>Researchers<br>Professional organisations<br>Health Technology Agencies<br>Reimbursement experts | Set agenda<br>Make innovation possible<br>Develop innovative idea<br>Agenda setting<br>Assessment<br>Evaluate insurance economic aspects |
| Stratify breast cancer risk in population screening | Public health screening decision makers<br>Governments/Ministries of Health<br>Screening Committees<br>Staff | Decide on implementation |
| Pharmacogenetics | Medical specialists<br>Pharmacists<br>Hospital leadership | Develop guidelines<br>Decide on implementation in practice |
| Integrating hereditary cancers in public health screening | Public health organisations<br>Health care providers<br>Payers | Recommendations<br>Implementation<br>Funding |

*Table 2: Barriers of implementation*

| **Barriers of implementation** |
|---|
| Evidence of the utility |
| Evidence of cost effectiveness |
| Education of health care workers involved |
| Education of patients |
| Delegation of roles and responsibilities, clear protocols |
| Simple procedures for ordering and reporting pharmacogenomics testing supported by IT infrastructure |
| Allowing genomic data to be used throughout the life of the patient |
| Effective decision tools |
| Maintaining trust in institutions and professionals |

# Conclusion

For implementing personalised prevention using genetics and genomics information in health care systems, it has often been stated that policymakers must be engaged. There is a need to specify who the policymakers are for a specific application of genomics in personalised prevention. Different policymakers are involved in different aspects of research agenda setting, research funding, developing guidelines, education and implementing innovations in both clinic and public health screening programs, and evaluating outcomes, economic aspects, funding and reimbursement. Capacity building, education and information are important elements of engagement: well-informed policy makers are better equipped to draft and discuss policies regarding personalised prevention with other relevant stakeholders and sustain further responsible implementation across disciplines, domains and national borders. Also, the data infrastructure needs attention. While major developments such as the European Health Data Space might make sharing of data increasingly possible, the practicalities of informed consent, ordering and reporting, and insufficient support of decision tools for everyday practice currently are barriers of implementation of personalised prevention. In reorganizing practices to allow for the further integration of genomic testing in personalised prevention strategies not only designated policy experts and governing bodies, but also a wide range of stakeholders, including health care professionals and their organisations, IT specialists, patient representatives, funders and reimbursement experts will need to collaborate to establish viable new routines and shared visions to reduce barriers to responsible implementation. Inevitably this will entail addressing varying and at times diverging (professional) interests and viewpoints. Stakeholder engagement and dialogue is key to adequate policymaking and help sustain public trust in data sharing and foster responsible implementation of personalised prevention.

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