Precision Public Health Perspectives

7

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What Will You Learn in This Chapter?

By 2030, the primary focus of healthcare wants to shift to the optimization of healthcare systems with an integration of the societal perspective. In this way, the economic sustainability and societal benefits that PM can offer can help integrate new risk-sharing processes and PM approaches for the entire life cycle. From this perspective, this chapter illustrates the definition of public health, population health, and their link with personalized medicine. The objective is to describe the most significant points of this ecosystem such as risk definition, patient stratification, health promotion, and disease prevention strategies of particular value for aging societies. The chapter also describes the equity impact and citizen empowerment from a personalized (precision) perspective.

Rational and Importance

Personalized medicine looks to incorporate new technologies into healthcare, supported by data collection, integrating clinical phenotypes, and biological information from imaging to laboratory tests and health records. The analysis of data identifies, prevents, and treats better individual patient diseases. Indeed, the application of this approach to public health can improve the management and prevention of both communicable, or infectious diseases, and non-communicable or chronic diseases, starting from each person and reaching the whole community. In this chapter, the emerging field of "personalized" public health is reflected through the polygenic studies, epigenetics, omics, and citizens' involvement. Obstacles in public policy include uncertain regulatory requirements, insufficient insurance reimbursement for diagnostic tests linked to preventive care, incomplete legal protections to prevent genetic discrimination, and the lack of a comprehensive technology system.

7.1 Population Health Versus Public Health

Currently, there is some debate about the difference between population health and public health. For the scope of this chapter, both terms are considered in the same folder (gaps and challenges), with a previous clarification of both definitions.

Health system definition: The key structural arms of the Public Health system include the configuration and the design of health services influencing the way in which services are delivered (including health workers and mechanisms of governance and administrative decision making); the aspects of the behaviour (workers and population), performance, health facility and the

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nature of participation on the appropiate section; and, the last arm is the effect of the interventions provided by the health system, including facilities and personnel [1].[1]

Components:

1. Structure: design of health services that influence the way in which services are delivered, from the health workers to mechanisms of governance and administrative decision-making
2. Processes: aspects of the behaviour (workers and population) or performance or health facility and the nature of participation on the part of people it serves
3. Outcomes: result from the interventions provided by the health system, the facilities, personnel, and the actions of the targets of the interventions [1]

Primary care: It guarantees person-focused care over time to a defined population, accessibility to facilitate first care when needed, comprehensiveness, and coordination, such that it integrates all care facets (wherever received) [1].

Population health definition: This term refers to the health outcomes of a group of individuals, including the distribution of such outcomes within the group, including health outcomes, patterns of health determinants, and policies and interventions that link these two [2]. In other words, it focuses on understanding the factors influencing population health over lifetimes and measures occurrences of certain problems.

Public health definition: it is defined as the art and science of preventing disease, prolonging life, and promoting health through the organized efforts of society[2]. Both population and public health definitions work to improve health in the public itself [3].

7.2 Introduction to Public Health (PH) and Personalized Medicine (PM)

One of the initial definitions of public health (PH) was the science and art of preventing disease, prolonging life, and promoting physical health and efficiency. They will ensure every individual in the community has a standard of living adequate for health maintenance. This term includes organized community efforts for the sanitation of the environment, the control of community infections, the individual education in principles of personal hygiene, the organization of medical and nursing services for the early diagnosis and preventive treatment of disease, and the development of social machinery [4].

Later on, concepts such as "protect and improve" were added to the definition: "the science and art of preventing disease, prolonging life and promoting, protecting and improving health through the organized efforts of society." Indeed, the link between health and mortality was reflected, emphasizing the need to eliminate health inequalities [5].

Both definitions focused on improving health through society-wide measures like vaccinations, the fluoridation of consuming water, or policies such as the mandatory seatbelt and non-smoking laws. In this way, these terms are linked to the wider definition of health, found in the preamble of the constitution of the World Health Organization (1948), where health is referred to as "a state of complete physical, mental and social well-being and not merely the absence of disease" [6].

Nevertheless, the concept has changed over the years due to changes in the health status of the population and health-determining situations. Currently, PH is the science of protecting and improving the health of people and their commu-

[1]WHO adopted definition https://www.euro.who.int/en/health-topics/Health-systems

[2]WHO adopted definition https://www.euro.who.int/en/health-topics/Health-systems/public-health-services/public-health-services

nities; the status of health is achieved by promoting healthy lifestyles, researching disease and injury prevention, and detecting, preventing, and responding to infectious diseases.

The introduction of the discussion on population health term follows the understanding that policies and higher-level interventions are crucial in determining health together with genetics, levels of activity, nutritional intake, and other individual behaviors.

There are several definitions of personalized medicine and precision medicine already described in this book. Before 1990, patient management followed sociological, educational, and psychological bases. Then, the approach changed following the personalized medicine (interchangeably in this book with precision medicine) implementation, which has become more and more common. Currently, it includes mainly the term "genetic" and new biomarkers and their application in pharmacotherapy, molecularly targeted therapies in oncology, and the application of novel therapeutic agents. In 2015, in his State of the Union Address, President Barack Obama opened the door to the PM initiative that included "delivering the right treatments, at the right time, every time to the right person."[3]

In the context of this chapter, the definition of Horizon 2020 Advisory Group is applied: Personalized medicine is "a medical model using the characterization of individuals' phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention."[4]

Nowadays, public health has to find a balance among individualized approaches that focus on diseased individuals and on population-based preventive programs and health promotion that consider the behavioral, environmental, and social determinants of health.

7.3 Impact of Personalized Medicine in Public Health

Nowadays, medicine is moving from a reactive to a proactive discipline. Adapting to these changes, WHO developed a framework to promote an understanding of the attributes and objectives to strengthen a health system. It is useful to identify gaps for appropriate health interventions focused on an experienced health workforce; essential medicines, vaccines, health products; health information; and service delivery including health facilities, centers, clinics, and hospitals. In this way, a health system is effective if it has the ability to provide the ten essential public health functions defined by the WHO: surveillance; response to emergencies; health protection; health promotion; disease prevention; governance; workforce; finance; communication and social mobilization; and research.

For this reason, the P4 medicine, which includes predictive, preventive, personalized, and participatory medicine, needs to integrate the population/public perspective (5P) into each of the other four components [7].

Population perspective merges predictive medicine into the ecological model of health, applies population screening to preventive medicine, uses evidence-based practice (best examples) to personalized medicine, and supports participatory medicine with the three core functions of public health: assessment, policy development, and assurance.

Key elements of the personalized public integration are the right balance between "premature translation," leading to increased healthcare costs and potential for harm, and "lost in translation," leading to exacerbation of social, economic, and health disparities [7]. There is a clear need to evaluate the benefits, harms, and costs of person-

[3]Background and links related to personalized medicine initiative in the USA available from URL: https://www.genome.gov/about-genomics

[4]Background, conference reports, publications and links related to personalise medicine in EU available from URL: https://ec.europa.eu/research/health/index.cfm?pg=policy&policyname=personalised

alized interventions compared to the already existing ones.

One described example is the screening for prostate cancer [8]: the prostate-specific antigen (PSA) detects many cases of asymptomatic prostate cancer. The issue is that most asymptomatic cancers detected by PSA screening seem not to be able to progress or affect life span. However, this diagnostic involves serious treatment with surgery, radiation, or other therapy. The consequence is a loss of quality of life and higher societal investment.

There are also available commercially genomic risk tests (multiple single nucleotide polymorphism (SNP) profiles). These tests, sold directly to consumers, do not have a full clinical validation or formal assessments of benefits and harms, or the involvement of healthcare providers, with the evident issue [9].

Finally, the promise of molecular biomarkers, which can offer data to estimate the transition from health to disease, is frequently not used based on incomplete evidence. They need to be strictly evaluated for their potential benefits and harms at both the individual and population levels [10].

Subsequently, applying a personalized public health perspective, tests should be prioritized for validation based on principles of population screening, such as disease burden and the effectiveness and acceptability of interventions.

Noteworthy, nutrition is another example. It is now evident that nutrition participates in human development to ensure life expectancy and well-being, and it is not only related to food transformation into energy.

Moreover, according to the emerging health outlines, food intake should be assessed in relationship with social, safety, and sustainable dimensions. In this context, the global public health perspective and the precision-personalized nutrition paradigm are complementary and should be harmonized.

Indeed, precision nutrition considers factors involved in global quality of life and metabolic well-being depending not only on the genotype but also on the dietary intake and associated healthy lifestyles as well as environmental factors [11].

The current challenge for the healthcare system is to shift from a reactive healthcare system to a personalized health approach and from episodic and acute care models (where individuals presenting some symptoms receive a similar treatment) to the use of more individual care, predictive, and preventive tools for stratification of at-risk individuals. This stratification can facilitate the intervention before the onset of symptoms or identify the risk before symptoms appear.

Currently, the health system faces up to the coordination for implementing this new vision and the effective initial economic investments.

The recent pandemic is overwhelming the health system around the world, already with an ongoing increasing burden of health assistance and social needs mainly due to the ageing of the population, the health workforce shortages[5, 6] as well as other neurodegenerative or rare diseases. This complexity of elder patients is mainly due to chronic conditions of multi-morbidity associated to the rising burden of preventable, caused by risk factors such as tobacco, alcohol, and obesity. As example, in EU Member States Public, spending on health and long-term care is gradually rising and continuous in this direction. In 2014, €1.39 trillion has been the EU-28's total healthcare expenditure (10% of the EU's GDP). This is expected to increase to 30% by 2060. These trends are a hard problem for the sustainability of worldwide healthcare systems.[7]

Subsequently, and for easy comprehension, the impact of PM on public health can be grouped into two diverse impacts, direct and indirect.

- Direct impact: It includes the direct effects of new technologies on the reorganization of the public health system: mHealth, Internet of Things (IoT), artificial intelligence (AI),

[5] https://www.axios.com/2022/05/24/the-health-care-workforce-shortage-problem

[6] https://www.who.int/health-topics/health-workforce#tab=tab_1

[7] https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Healthcare_expenditure_statistics

imaging, data sharing, new -omics technologies, and the health technology assessment.
- Indirect impact: It includes all indirect effects of genetic information on preventive applications, diagnostic diseases, and targeted therapies.

7.4 Direct Impact

mHealth The use of applications and/or mobile-connected devices for supporting medical and public health practices is defined as mobile health (mHealth). Mobile health can play a positive role in various domains of health (well-being, prevention, care, monitoring or surveillance of diagnosed diseases, etc.) and in the healthcare system as a whole. To face the current financial difficulties of our health system, treating the patient at home (de-hospitalization) can be a solution. In this sense, the pandemic has accelerated the use of telemedicine and teleconsultation services.

mHealth has two kinds of software programs. One works as a medical device (SaMD), performing medical functions through software installation on generic devices such as tablets or smartphones. The second is a software program included in a medical device (SiMD) and a mHealth application as interface that interacts with a material medical device (MD). Both SaMDs and SiMDs must comply with the regulatory frameworks established by national and international authorities for marketing, quality, the safety of use, usability, and data security. Two international organizations, the World Health Organization (WHO) and the International Medical Device Regulators Forum (IMDRF)[8], have been developing regulations for MDs in collaboration with a group of Member States. The IMDRF proposes strategies, policies, and orientations for the deployment of MDs under different involved stakeholders' visions [12]. The 2018 World Health Assembly [13] adopted a resolution to develop a global strategy on mHealth to support efforts toward universal health coverage (2020–2025).

Material MDs have long been required to undergo certification by national and international regulatory systems. By contrast, the requirement for certification of SaMDs, particularly mHealth applications, was implemented only recently. Regulation (EU) 2017/745 on medical devices becomes applicable in the European Union in May 2021.[9] This MDR 2017/745 regulation includes a detailed list of safety and performance requirements that all medical devices placed on the market in Europe must comply with in order to guarantee a high level of quality, and it has been extended to a device for non-medical purposes. One of the objectives of the new EU regulation is the creation of a complete European bank of Medici devices – EUDAMED (European Databank for Medical Devices) – which is not only used for cataloging and medical devices but also for monitoring the life cycle. The new bank of EUDAMED will increase the transparency and the coordination of the information on its devices and represents an important openness to citizen engagement. If it becomes data interoperable, harmonized, adapted to international regulation, and under quality evaluation, the mHealth can become an important keystone of a successful personalized public health system.

Artificial intelligence: It has had an increasing role in the healthcare revolution and has shown great potential in developing effective prevention intervention strategies such as the prevention of HIV infection (see Chap. 13, Personalized Medicine in Infectious Diseases). With the aim to benefit from AI, the transformation of the market including new legal and ethical frameworks must be considered by public policy. In this direction, the European Alliance for Industrial Data, Edge, and Cloud was launched in 2021 by the European

[8]IMDRF. Work items. IMDRF, 2020, available from URL: http://www.imdrf.org/workitems/work.asp

[9]Background and links related to medical device regulation, available from URL: https://www.ema.europa.eu/en/news/medical-device-regulation-comes-application

Commission[10] with the aim to ensure Europe's competitiveness in the research and deployment of AI and to follow the associated social, economic, ethical, and legal. This Alliance has two main objectives, strengthening the position of the EU industry on cloud and edge technologies and meeting the needs of EU businesses and public administrations that process sensitive categories of data.

Imaging: The innovation in imaging has improved the diagnosis of disease and at the same time has been useful in different population-based screening such as for breast, lung, and prostate cancer. For example, on breast screening guidelines, the recommendations were based on age (following the age incidence) rather than on genetic factors. However, there are predisposing genetic variants with a polygenic risk score of breast cancer. New guidelines combine molecular testing with the current approach, with no clear consensus on how to lead with the different tiers of cancer screening risk and the knowledge and response of the public.

Data production and data sharing: Data from multiples sources and disciplines that need integrated solutions to enable cross-border data exchange; standardization for data sharing and analysis; and promote legal, organizational, semantic, and technical interoperability

Machine learning: The explosion of new concepts such as machine learning (e.g., transfer learning, distance metric learning, semi-supervised learning, structured ML meta-learning, multiview learning, and generative models), data processing techniques (e.g., new dimension reduction approaches, outlier removal methods, data augmentation techniques), and model validation methods (e.g., bootstrapping), if standardized, may facilitate follow-up research and subsequently public health implementation. Then, guidelines on the best approach to do available public knowledge and data sources can permit to take advantage of previous and new biomarkers and create robust and interpretable biomarker models, always with the integration of specific expertise in data analysis and regulatory and legal fields.

Electronic medical records (EMRs), based on *big data technology*, are improving predictive modeling, clinical decision support, and safety surveillance. EMR system starts as a small data repository of a patient receiving care under a given healthcare system (i.e., hospital, clinic, etc.) and offers clinicians a clear vision of patient care. The creation of a "big data" repository with the combination of other data sources facilitates data sharing with others. In this way, EMRs open all available information while determining diagnosis and patient prognosis. It would be possible to ensure the best and most timely treatment decisions on an individual basis. Indeed, the parallel development of training strategies is requested to support health workers and to ensure the implementation of innovation will be sustainable.

These technological developments involved directly the health industry. In this way, the PM development is also modifying the approach to the health industry as it operates to the benefit of the patient. Patient engagement is required for the health system decisions, so both the health system and health industry focus [14] on a user-centered approach "human-centered design (HCD)." This approach is based on principles such as the inclusion of the entire user experience. Users are involved during design and development, design that is guided by a user-centered assessment. Multidisciplinary skills and perspectives (e.g., doctor, nurse, citizen, designer) are involved interactively in the design process until satisfactory data results.

Technological innovation can help de-hospitalization, which improves the quality of care, thanks to medical devices. Thanks to these technologies, the doctor has an updated "image" of the patient's state and the actions already carried out, and inconvenience due to the movement of sick and disabled people, the social cost both for the patient and for the family members accompanying him, and the public and private cost of health care are reduced.

[10] Background and links related to the European Alliance for Industrial Data, Edge and Cloud 2021, available from URL: https://ec.europa.eu/growth/industry/strategy/industrial-alliances/european-alliance-industrial-data-edge-and-cloud_en

Indeed, new digital technologies such as wearable devices and interconnected products according to the Internet of Things (IoT) paradigm help maintain certain independence of patients, ensuring a valid and less expensive alternative to institutionalized care.

Each device can store and process the information on the network independently but also communicate with other devices belonging to the network and facilitate remote monitoring.

All are supported by robotics, artificial intelligence, and multidisciplinary teams composed of researchers in health, architecture, design, psychology, environment, and geological sciences and, of course, patients. Patients and general practitioners need to be involved as it has been demonstrated to have huge influence over daily decisions So, collaboration among all levels is needed to achieve changes in clinical practice, changes aimed at optimizing care and treatments for patients and their caregivers and prevention for all citizens.

Internet of medical things (IoMT) includes medical devices connected to a facility or healthcare provider via the Internet. Devices are able to generate, collect, analyze, and transmit health data such as smartphones and health apps, simple wearable devices, tools for remote patient monitoring, infusion pumps, drug tracking systems, specialized tools for monitoring, and medical equipment. Their impact on patient health management is increasing including diagnostics, bioinformatics collection, data sharing, rapid analysis, and timely therapy decisions. The impact of IoMT is higher and higher. Since IoMT started [15], it is growing exponentially to 10 billion connected IoT devices at present with a predicted increase to about 25 billion by 2025 [16]. In the current pandemic, intercommunication difficulties have been resolved using remote monitoring, telemedicine, robotics, sensors, etc. However, mass adoption seems challenging due to factors like privacy and security of data, management of a large amount of data, scalability, upgrade, etc., considering the start of economic involvement in the healthcare system.

Health technology assessment: An evidence-based process that enables competent authorities to determine the relative effectiveness of new or existing technologies, which in turn empowers national health authorities to make pricing or reimbursement decisions within health insurance. New rules for all these innovative health technologies and prevention and treatment methods are needed. So, in December 2021, the Regulation on Health Technology Assessment (HTA)[11] has been adopted. The Regulation will also ensure the efficient use of resources, strengthen the quality of HTA across the EU, save national HTA bodies and industry from duplicating their efforts, reassure businesses, and ensure the long-term sustainability of EU HTA cooperation. The new regulation, fully effective in January 2025, introduces a permanent framework. It will make it possible to unify procedures, work on joint and centralized clinical evaluations, promote unified scientific consultations, improve the identification of emerging health technologies, and favor voluntary cooperation mechanisms. This regulation includes the recommendation of patient input inclusion in all the regulatory decisions on the use of health technologies. One important point is the intention to facilitate faster authorizations, with centralized and more compatible criteria between countries, market unity, and, finally, more equitable access for all Europeans to innovation. So, Article 13 describes a joint clinical evaluation model through the collaboration of all countries and establishes that the Member States "shall pay due attention to the joint clinical evaluation report when carrying out a national HTA on health technology." In addition, for each national evaluation (undergone joint clinical evaluation), Member States will provide information on this development in their respective national processes. Indeed, each country will be able to complement the joint clinical evaluation with additional clinical analyses that may be necessary for their national regulations.

[11] https://ec.europa.eu/commission/presscorner/detail/en/ip_21_6771

7.5 Indirect Impact: Genetic Information on Preventive Applications, Diagnostic Disease, and Targeted Therapies

The appropriate function of health systems is in the pursuit of a standardized and rapid flow of digital information, including genomic, clinical outcome, and requested data. It will be feasible to drive treatments tailored to individuals' genetic structures, prescriptions could be analyzed in advance for likely effectiveness, and researchers will be able to study clinical data in real time to determine success.

Regarding this needed genetic information, important human genome map initiatives (Personalized Medicine Initiative in the USA,[12] 100000 Genomes Initiative in the UK[13], the Million European Genomes Alliance in Europe, and the Beyond 1 Million Genomes (B1MG) project[14]) have been launched worldwide. These initiatives include correlated populations' genetic information, environment, lifestyle, and clinical data. These combinations of information will help find lines of prevention and prediction and target better the treatment, and the health system can economize using therapies that will not be effective for a specific patient.

We need to consider that the advances in the field of genomics have led to substantial reductions in the cost of genome sequencing. The National Human Genome Research Institute (NHGRI) has carefully estimated the cost of whole exosome sequencing, and it is now less than $1.000. It is decreasing and is more accurate than the first human genome sequenced in 2001, which costs $95 million.[15]

Another important genetic data application is the surveillance and identification of genetic relatedness in outbreaks. For example, in a study of extensively drug-resistant tuberculosis (XDRTB), investigators used targeted and whole-genome sequencing to account for the geographic distribution of XDR-TB strains [17]. This study shows that the combination of PM tools with previous epidemiologic methods may rise to disease mapping and lead health policy decisions.

The other example is the actual advance of genomic surveillance in Africa. The continent is getting close to sequencing up to 50,000 genomes in 2021, thanks to investment and capacity building since the beginning of the pandemic, with successful implementation in South Africa, Angola, Nigeria, and Kenya and starting in Botswana. KRISP and CERI (working with WHO and Africa Centres for Disease Control and Prevention (Africa CDC)) are able to do genomic sequencing for many African countries. The most important is the share protocols with countries, as well as train technicians to boost their capacity.[16]

Personalized approach is also useful for improving the classification of diseases: Usually, cancer was divided into its histological subtypes and clinical phenotypes. Nowadays, molecular testing reclassifies subtypes providing a more precise classification of diseases, for example, with the abnormalities on the surface of the cancer cell such as the presence of the epidermal growth factor receptor (EGFR) in lung cancer, and compares its phenotype or histological group and the new targeted therapies [18]. Rare diseases can use the PM to analyze the hereditary condition and relate specific mutations with clinical phenotype. In this direction, molecular profiling can provide prevention strategies and prognosis information and drive treatment strategies. However, in some diseases without treatment options, a patient can receive early symptomatic and supportive care. The challenge

[12] Background and links related to personalised medicine initiative in the USA available from URL: to https://www.genome.gov/about-genomics

[13] Background and links related to 100000 Genomes Initiative in the UK available from URL: https://www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project/

[14] Background and links related to Million European Genomes Alliance in Europe available from URL https://digital-strategy.ec.europa.eu/en/policies/1-million-genomes; Beyond 1 Million Genomes (B1MG) project https://b1mg-project.eu/

[15] https://www.genome.gov/

[16] https://www.afro.who.int/news/why-genomic-sequencing-crucial-covid-19-response

for public health is that a more precise stratification of disease can increase the financial burden with little clinical benefit for overall population health. This is the case when the molecular classification of one disease fragments the management of this disease with more health services involved and more difficulty to apply a specific treatment [19].

Molecular profiling and biomarkers can identify persons at high risk of developing a disease, mainly among family members, and save an unaffected member from unnecessary routine screening procedures. One biomarker is more reliable than a clinical marker in predicting disease, for example, on family history of cancer, diabetes, or heart disease. However, it is not clear whether a person positive for genetic predisposition is able to decrease the risk through behaviors or lifestyle changes. In the same way, people can feel like not being able to decrease the risk for a disease or for addiction once the risk has been detected. On the other hand, biomarkers are sometimes difficult to validate in clinical settings, and it remains a lack generalizability. A recently systematic review regarding biomarkers for patient stratification illustrates how successful clinical biomarker translation is really providing applicable information for the design of new health public programs. However, it is far needed to guide clinicians involved in biomarker discovery with standard guidelines on methodologies for omics biomarker discovery [20].

The polygenic risk score (PGS) is the process by which people can learn about their risk of developing a specific disease. This score is based on the total number of changes in either one or many of their genes related to the disease across different populations, regularly coupled with environmental factors[17]. In general, the GWAS (genome-wide association study) estimates the polygenic risk as the result of the sum of risk alleles that an individual has, weighted by the risk-allele effect sizes on the phenotype. This estimation is considered a "relative risk" for a disease because it is independent of the baseline or timeframe for the progression of a disease. In addition, the clinical practice shows that the PGS needs to be integrated with other risk algorithms using environmental factors. Accordingly, people with polygenic high-risk percentage scores should discuss this risk with their medical doctor and or genetic counsellors for further health assessments.

Epigenetics Biomarkers Epigenetics is the study of altered gene expression without change in base pairs. The PGS with other omics data and environmental data for predicting programs will facilitate the implementation of PPH. Epigenetics biomarkers are any mark or altered epigenetic mechanism that:

- Can be measured in the body fluids or tissues
- Defines a disease (detection)
- Predicts the outcome of disease (prognostic)
- Responds to therapy (predictive)
- Monitors responses to therapy or medication (therapy monitoring)
- Predicts risk of future disease development (risk)

One example is the D-methylation changes described in neurodegenerative and neuropsychiatric diseases [21]. However, the adaptation of new technologies and methods will increase the adoption of epigenetic biomarkers in the diagnostic process.

Lastly, PM modern technology and therapeutics have the risk to create disparity among the population due to the cost of these services and the differences in healthcare system approach and the insurance that cannot cover genetic sequencing. In addition, genomic-wide association studies are doing an effort to include participants worldwide, but currently, there is a low representation of minorities that can drive a misclassification of disease in these groups, and for this, prevention strategies can be far from being effective in this groups.

In conclusion, the genetic risk approach cannot be predicted by genetic information without the combination with the clinical and familiar history and with an analysis of the environmental factors.

[17] https://www.genome.gov/Health/Genomics-and-Medicine/Polygenic-risk-scores

Gene Therapy and Gene Editing Techniques Targeting the mutated genes is becoming a therapeutic option. An example is a study for hemophilia B [22] using gene editing tools such as CRISPR/Cas9 or ZFNs (zinc finger nucleases), which correct the defective genes responsible for the disease. After that, adeno-associated viral (AAVs) or lentiviral (LVs) vectors carried by the "therapeutic gene" are administered systemically to the patient.

Another alternative therapy is done with stem cells, or already differentiated cells, transfected or otherwise, to correct a deficiency in the patient's physiological function.

Impact of personalized medicine in public health will follow the several genetic tests already available, medical device and biological date, mobile health application and data of behaviors, electronic health records, and clinical history. However, we need to consider onboard social inequities, poverty, and racism. In this way, the incorporation of data at multiple levels, including environmental data, can support the public health PM approach.

Lastly, a combined approach can improve the integration of PM in public health by extending the training and education of healthcare providers and citizens, opening access to genetic testing infrastructure, and increasing access to novel drugs.

Following this address, personal health suggests involving multidisciplinary stakeholders and listening to peoples' needs; the multiplicity of data sources available can drive the PM implementation to develop and foster the uptake of those technologies that meet peoples' needs.

As a result, integrating these technologies in the healthcare systems requires monitoring data use over time and the data outcomes. This continuous monitoring will promote risk minimization and assess the scientific validity of new technologies (Fig. 7.1).

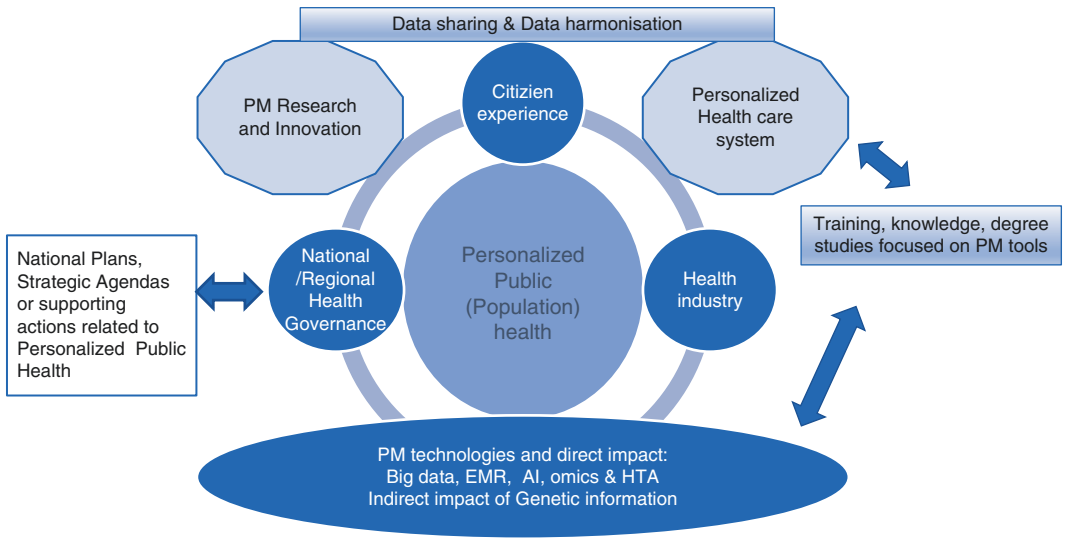

Fig. 7.1 Cooperation and coordination for personalized public health. Three main stones have been indicated for the PM interaction with public health and implementation aspects. Following the results of the research and the implementation of the healthcare system. Scientific and technological needs to enable personalized medicine implementation. All based on the successful PM technologies (starting from the center-left in the figure and proceeding clockwise); linked to the existence of national strategic plans, programs, and actions supporting PM-related basic, translational, and clinical research; infrastructures for PM research (i.e., biobanks, large-scale genomic databases, DNA sequencing facilities, etc.); data sharing and data harmonization and academia-industry relationships

7.6 Public Involvement in PM

It is needed to include here some already known definitions:

- Expertise: Convey a combination of specific education, training, or professional/personal experience
- Experience: Convey practical disease knowledge obtained from direct experience with the disease (affected person or close contact with affected person, e.g., family, carrier) or its treatment (e.g., healthcare professional)
- Advocacy: Act on behalf of the affected patients in defense of their rights; provide a patient-oriented public health/healthcare policy perspective
- Empowerment or engagement: Participate in the decision-making process within the committee; having access to information and process on behalf of patients and healthcare professionals

In the year 2000, The Council of Europe declared that the right of the public to be involved in the decision-making processes affecting healthcare is a basic and essential part of any democratic society [23]. The European Medicines Agency (EMA) considers that transparency and trust justify the participation of patient and citizen on their scientific committees, which improves the quality of the given opinion. In this way, patients are included as members in four of the six human EMA scientific committees: the Committee for Orphan Medicinal Products (COMP), the Paediatric Committee (PDCO), the Committee for Advanced Therapies (CAT), and the Pharmacovigilance and Risk Assessment Committee (PRAC). Their participation (i.e., members, alternates, experts, observers, or representatives) has been structured in four different features as indicated textually in the EMA report (which are not mutually exclusive)[18]:

[18]The role of patients as members of the EMA Human Scientific Committees, European Medicines Agency, 2011. https://www.ema.europa.eu/en/documents/other/role-members-representing-patients-healthcare-professionals-organisations-ema-scientific-committees_en.pdf

In the same direction, the personalised medicine approach promotes citizen's (patient and public in general) active participation in research and healthcare. Although there is a clear interconnection between PM research and healthcare, the role of public involvement is different in them. Citizen involvement in public health follows the concepts of consumer, service user, community, and the general public. The main scope of this involvement is to engage them actively in decision-making about large-scale health changes.

Consequently, the necessity of citizen involvement has been slowly increasing due to the difficulties to find the best model of implementation. Above all, citizens can be involved in the evaluation of public health programs trying to better identify needs and for improving the quality of these programs; also, the participation in the process of development of these public health programs adjusted to social and geographical aspects; and the participation in future health planning to increase their voice on the healthcare. There are diverse involvement methods that need to match the purpose of involvement, the social context, and the population. So, the strategy to involve individuals with experience of cardiovascular diseases in designing health education prevention programs is diverse from involving citizens in a public conference around the health danger of gambling dependence.

Additionally, new resources are needed to increase the knowledge and the involvement of citizens in the process of access to medical data. This involvement will improve the trust in its quality. One example of the impact of omics on citizens' health is the direct-to-consumer genetic test (DTC-GTc) and also the high request rapid test for the infection of SARS-COVID during the pandemic [24].

Community engagement: A systematic review [25] evaluated the community engagement effectiveness of public health interventions across diverse health issues and with a high positive impact on health outcomes without a definitive conclusion on the best effective model of intervention. The two related health interventions with positive impacts were divided into health

behaviors. Outcomes extracted were alcohol abuse, antenatal (prenatal) care, breastfeeding, cardiovascular disease, child illness, ill health, drug abuse, healthy eating, immunization, injury/safety, parenting, physical activity, smoking cessation, smoking/tobacco prevention, and health consequences.

Some of the significant recommendations for planning intervention are:

1. Involving the same community members in the delivery of the intervention. This is more effective if participants are classified as disadvantaged due to socioeconomic position (compared with those targeted to people based on their ethnicity, place of residence, or being at/high risk).
2. Single component interventions, both universal and targeted.
3. Consider personal skill development or training strategies or offer incentives.
4. Most effective in adult populations and less effective in general populations.

For a final reflection on the implementation of Personalised Medicine on Public Health: Patients' groups alone are not likely to change the prevailing pattern of public health, nor experts' groups at mechanisms for prioritization, neither would public funding alone solve the PM implementation. Suh as the Policies developed in the preapproval phase of drug development are needed, in the same way, the implementation of Personalised/ Precision Public health needs also a collaboration with industry and with input from the regulatory body [13].

In conclusion, the integration of every kind of PM innovation into Public health needs multidisciplinary public private engagement and the appropriate training of healthcare workers and of citizens.

Lastly, among the several ongoing projects, the International HundredK+ Cohorts Consortium IHCC[19] has as its main objective to increase the biological and genetic basis of disease and improve clinical care and population health. This consortium is currently working "to create a global platform for translational research, informing the biological and genetic basis for disease and improving clinical care and population health." In this way, this is an international-level project example of sharing of data, information, and resources linked to Population Health.

In conclusion, the integration of every kind of innovation into the health system needs engagement and appropriate training of healthcare workers and also of citizens.

7.7 Personalized Public Health and Equity

The CDC[20] defines health equity as "when every person has the opportunity to 'attain his or her full health potential' and no one is 'disadvantaged from achieving this potential because of social position or other socially determined circumstances'," describing their *goal to develop a set of priorities and actions that can help ensure that everyone has the opportunity to reap the health benefits of advances in genomics and precision medicine.* One of the primary goals of CDC's National Center for Chronic Disease Prevention and Health Promotion (NCCDPHP)[21] is to achieve health equity by eliminating health disparities and achieving optimal health for all.

Personalized public health wants to ensure equitable access to healthcare opportunities regardless of a person's age, gender, geographi-

[19] https://ihccglobal.org/

[20] Centers for Disease Control and Prevention Foundation. Atlanta, GA: Centers for Disease Control and Prevention. What is Heath equity

[21] https://www.cdc.gov/chronicdisease/healthequity/index.htm"https://www.cdc.gov/chronicdisease/healthequity/index.htm"/

cal origin, cultural, linguistic, religious background, communication, and accessibility needs. As a result of their application to public health, it can also provide a pathway to improve health equity across traditional barriers such as socioeconomic status, race/ethnicity, sex/gender, and geographical location. Considering that health disparities have often been linked to disparities in education, race, and income, several papers are concerned that the benefits of personalized medicine will go more to patients who have higher income and who are often not people of racial and/or ethnic minority groups, thus increasing the health disparities healthcare [26]. Based on the strategies proposed to optimize the benefits of personalized medicine [1] and lessen the potential worsening of health disparities, the priorities can be list as anticipated by Ward (Box 7.1) [27].

Box 7.1 Priorities to Optimize the Benefits of PPM Approach

1. Data must be collected in a systematic way, and it must be secured that health data flow in different socioeconomic statuses.
2. Dissemination models for developed therapies should include strategies that include outreach to patients who are not likely to have access to medications and healthcare, in other words an equitable access to public health service for all citizens.
3. Policies that foster the equitable development and access of prevention programs, medications, therapies, and devices that would be used in personalized medicine. Public health services are optimized in terms.

In this way, personalized public health should generate more specific and cost-effective prevention programs, enhance the impact of prevention and risk reduction campaigns, enhance coordinator among public health workers and the community, and request equity of access and service for all, including marginalized sectors and underserved citizens [27].

Healthcare and Personalized Medicine The process of the public health transformation needs to adopt the PM approach. In this way, the line of value based-health[22] needs to focus the personalized value and needs to understand how to measure this value. In this line, the value for patients cannot be assessed at the level of the hospital, a site of care, a medical specialty, a procedure, a primary care practice, or an entire population [28]. The value could look at the medical condition (unit of value) a patient has over the entire cycle of care for that condition. In primary and preventative care, value is created for segments of the population with similar needs. The most important practices in moving toward a value-based healthcare system were tried to be identified, and experts reached a consensus on the importance of outcome measurements, a focus on medical conditions, and full cycles of care. No consensus was reached on the importance of benchmarking with the purpose to improve efficiency, quality of care, patient safety, and patient satisfaction. More research studies through the value-based health concept are needed to assess the impact on the main quality of healthcare [29].

To sum up, the precision public health perspective is based mainly on two pillars, digital technology and genetic studies. The knowledge of the genetic diversity of the population will offer the needed background to guide decision-making concerning policies such as drug adoption, vaccination strategies, etc. However, crucial investments are needed for the appropriate implementation and sustainability [30], taking into account that the level of adoption will be variable and depending on regional geographic diversity, lifestyle population, and policies.

[22] https://hbr.org/2015/09/better-value-in-health-care-requires-focusing-on-outcomes

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