Personalized Medicine Literacy

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What Will You Learn in This Chapter?

The chapter provides an overview of the best practice model applied by the Center for Innovation in Medicine on reducing cancer fatalism in the Romanian population, as well as increasing the level of cancer literacy, including cancer innovations awareness, by periodical assessment of attitudes, perceptions, and behaviors, followed by personalized communication campaigns. Such a model can also be applied for a long-term sustainable increase in the level of personalized medicine literacy in any population.

Rationale and Importance

Classical health strategies aiming to raise awareness around the theme of cancer innovations have proven ineffective because they do not take into account people's perceptions, attitudes, and behaviors. By not looking at these essential factors, communication campaigns are conducted on the one-size-fits all model. At the Center for Innovation in Medicine, we conducted research during 2016–2020 aiming to understand people's knowledge and attitudes toward cancer innovation. Based on this research, we performed personalized communication campaigns aiming to reduce the fatalism of cancer in the Romanian population. Implementing personalized health communication campaigns focused on citizens' needs is essential for any effective cancer control strategy, and it should be prioritized in national cancer control plans and aligned with the European initiatives. The COVID-19 vaccination campaigns all over the world were a real-time simulation of what delivering the right messages, by the right influencers, to the right population can do. When you intersect the two dimensions, you obtain a highly personalized approach in communicating health innovations to the citizens. This approach should constitute the first step in the efforts of increasing personalized medicine literacy.

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12.1 Introduction

Health literacy is the degree to which individuals have the capacity to obtain, process, and understand health information needed to make health decisions that best suits their interest [1]. In time, the definition evolved to be more comprehensive—health literacy is not only about medical decisions, but it is also about healthcare and about health: one's health or a beloved one's health. As society evolved, the human's central meaning—*to live, to be alive*—transformed into *to be healthy*.

The COVID-19 pandemic showed us that the human race is now at the forefront of medical and technological advances. Even though humans are biased to perceive the negative side of events in a much more dramatic way [2], there was no better and safer time in human history to exist and be alive than now.

And this statement can be made in part because of the evolution of precision and personalized medicine, of health innovations in general. In order to be more holistic, we will refer to it as PHC—personalized healthcare. Because of PHC, the classical medical approach of one-size-fits-all is quickly disappearing—in some parts of the world faster than in others.

The omics sciences were first put in practice in oncology, but nowadays they are impacting nearly all dimensions of the response to the COVID-19 pandemic, including single-cell multi-omics analysis of the immune response at COVID-19 and multi-omics approach for the identification of potential therapeutic biomolecules [3].

Back to definitions. Although there is no universally accepted definition, the Horizon 2020 Advisory Group defines personalized medicine as "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]. This definition was also used by EU health ministers in their council conclusions on personalized medicine from 2015, during the Luxembourg Presidency of the Council of Europe [5].

According to the 2012 definition of the European Consortium for Health Literacy (HL) [6], "Health literacy is linked to literacy and entails people's knowledge, motivation and competencies to access, understand, appraise, and apply health information in order to make judgments and take decisions in everyday life concerning healthcare, disease prevention and health promotion to maintain or improve quality of life during the life course." In other words, an adequate level of HL is defined by the ability of an individual to access health data, to sort and choose the appropriate sources of health-relevant information, to understand this information, to personalize it for his situation, and to apply the information in order to obtain a benefit for his own health.

HL is a complex concept that needs to be defined in a context. According to a 2017 analysis, there were more than 100 specific types of HL [7], but four of them are usually used when referring to HL: personal health literacy, organizational health literacy, digital health literacy, and quantitative literacy. In recent years, the 2012's definition of HL as it is above becomes more defined for the concept of personal health literacy [8].

Although no official definition of PHC exists, we can define it by integrating PM and the person, the citizen, and the individual as a social human being [9, 10].

Having this information in mind and the unprecedented advance in omics sciences, it is reasonable to argue that personalized medicine literacy, or more correctly, personalized health and care literacy, should become the fifth main part of the HL concept, at least for now. Though no PHCL official definition exists, it could be summed up:

> PHC literacy entails people's knowledge, motivation, and competencies to access, understand, appraise, and apply omics and other clinical and laboratory data and psychosocial and lifestyle information in order to make judgments and deci-

sions concerning the modifiable determinants of their health and prevention, healthcare, and health promotion, in order to maintain or improve quality of life during the life course.

And so, even though HL refers to the individual capacity for assessing and using health information mostly, PHC literacy is an essential catalyst for the responsible and effective translation of genome-based information for the benefit of population health [11].

12.2   What Does Being Healthy Mean? The Determinants of Health During the Time

In the 2006 Constitution of the World Health Organization, health was defined as the physical, mental, and social well-being [12], and not merely the absence of disease or infirmity. Achieving the highest standard of health is a fundamental human right, regardless of race, religion, political vision, or social and economic status.

As with health, "disease" is difficult to define. The first definition referred to a disturbance that occurs in an organism: "Organic or functional change in the normal balance of the organism; a pathological process that affects the body." A simple, but abstract and circular, definition could be "lack of health." Therefore, the two terms are closely related, and the current understanding of the human being determines the need to constantly redefine the terms, as the "state of health" becomes increasingly difficult to understand, and the "perception" of the person is what differentiates in fact between illness and health.

According to WHO 1998, the determinants of health are defined as "The range of behavioral, biological, socio-economic and environmental factors that influence the health status of individuals or populations" [13]. On average, 89% of our health occurs outside of the clinical space through our genetics, behavior, environment, and social circumstances [14], leaving only 11% for the clinical setting. Individual behavior shapes 36% of our health; social circumstances, 24%;

genetics and biology, 22%; and the environment, 7%. These are the main categories, based on the understanding of the state of health almost three decades ago.

While the percentages above show a bigger behavioral and social burden for the state of health when compared to biology and genetics, this is not the case for every individual. The disease is individual, even when referring to global pandemics.

Although access to healthcare services usually means access to better health outcomes, scientific evidence shows that healthcare, as it is today, with a focus on treatment, is only part of the problem. For example, the United Kingdom has begun to recognize social prescribing as a basic tool for public health [15].

Therefore, a personalized approach to determining the individual risks of developing diseases, and further early detection of those diseases, must take into account both the genetic and the environmental components (which refers to the conditions of development of the disease in an individual) integrating genetic, clinical, and lifestyle data and a person's developmental environment [16].

And although the determinants of health were refined over time, the challenge of understanding how they interrelate with each other is still a great topic of research. Nowadays, because of technological and scientific advances, the complexity of biological factors/determinants (including those related to omics) cannot be classified altogether. There are very few scientific papers that aim at classifying them, leading to a greater amount of information hard to understand not only by the general population but by the scientists and specialists themselves—leading to an infodemic.

Because of this complexity, a new emerging integrative field was born in the last years—social epigenomics: the study of how social experiences affect our genes and biology. Though social epigenomics is a relatively new area of research, studies exploring the individual and mutual influence of social, environmental, and genetic factors on health have become increasingly abundant. Social epigenomics is uniquely positioned at the

intersection of population health and precision medicine, allowing us to understand how exposure to social and environmental stressors modifies the way in which genes are expressed and ultimately alters our risk for disease [17].

A recent study showed that the impact of genetic factors on the onset of disease decreases with age and other mechanisms are taking place as important, including those influenced by the environment in which the person lives [18].

Apart from the theoretical understanding of the determinants of health in the personalized medicine era that could lead to unimaginable long-term benefits for human health, there are more practical approaches that could be deployed, like meta-personalized public health interventions.

During the time, the majority of public health interventions were aimed at lifestyle, the modifiable factors—the classic understanding of primary prevention, without fully understanding the complex bond between these factors and the biological ones. It was acceptable 30 years ago, 20 years ago, but not in the last decade and not in the present, and not during our COVID-19 times. So the concept of personalized prevention emerged.

12.2.1 The Determinants of Health and Precision Cardiology

Let's look at cardiovascular diseases—the number one global killer. Cardiovascular diseases account for 36% of all deaths across the EU. Around 20% of all premature deaths (below the age of 65) in the EU are caused by CVD. CVDs are caused by so-called modifiable or non-modifiable (inherited, genetic) risk factors. The world's most common and non-modifiable CVD risk factor is familial hypercholesterolemia (FH). Less than 10% of those born with FH are diagnosed and adequately treated, leading to heart attacks, strokes, heart disease, and deaths, early in life, even as early as 4 years of age [19]. Interventions based on early screening of those at genetic risk might actually be the missing piece of the puzzle when it comes to CVD primary pre-

vention. And moreover, it would lead to a new understanding of the cardiovascular determinants and stimulate new therapies and preventive solutions development.

Although most of the cardiovascular medicine we see in Europe is mainly composed of classical prevention (targeting classical lifestyle factors) and treating the condition, cardiology benefits in practice from the personalized medicine approach in 3D modeling and simulation that can guide surgeons before cardiovascular surgery.

Artificial intelligence is also making its presence felt in CVD management—recently, a study showed that the predictive value of AI algorithms for determining the risk of developing cardiovascular disease using physiological data and laboratory results (such as blood pressure and cholesterol values) is much higher if data on the social determinants of health is added [20].

12.2.2 The Determinants of Health and Precision Oncology

On the other hand, in oncology, the other aspects of personalized medicine have been engaged: precision screening, personalized diagnosis, and personalized treatments. These are already a reality in many parts of the world. Genomics is already imposing major changes in cancer understanding and care, from redefining cancers to changing therapeutic standards.

When the sequencing projects for different types of tumors began, the aim was to create a "library" of mutations involved in cancer and to identify mechanisms that can be targeted therapeutically. Although this goal has been met, cancer is not a single disease; two tumors considered to be in the same category according to classical classifications may be completely different at the molecular level, and even cells in the same tumor may be different. Deciphering the human genome was only the first step. Over 300 different conditions are known as cancer nowadays.

Genomic tumor testing has evolved over time, from several biomarkers to extensive gene panels, which allow the analysis of all mutations that can be acted upon through targeted therapies.

Genomics also provides valuable insights into how the disease progresses and the response to a particular treatment can be anticipated.

Conventional oncological treatments, such as chemotherapy, involved the administration of cytotoxic agents that did not discriminate between a healthy and a pathological cell. New drugs appearing on the market are targeted at molecular alterations—at the level of DNA, and RNA, at the level of immune cells, etc. In the age of precision medicine, oncological therapies should be approached more and more from new perspectives, using molecular anomalies and not the organ in which the tumor appears for the choice of therapy.

Lung cancer is an important example of how genomic medicine has evolved. Up to 45% of patients with non-microcellular lung carcinoma have genetic mutations for which there are specific treatments already approved or under study. In recent years, several subgroups of patients with non-small cell lung cancer (NSCLC) have begun to be defined based on molecular abnormalities. There are already therapies approved by the authorities, targeting genetic abnormalities in the EGFR, ALK, ROS1, BRAF, NTRK, MET, and RET genes [21, 22].

12.2.3 The Determinants of Health and Precision Diabetology

Over the last two decades, many common diseases had to be rethought. Cancer has not only transformed and is continuously evolving in hundreds of distinct diseases but also forced the change from classification based on the primarily affected organ to classification by the mutations or biomarkers of the tumor (tumor-agnostic classification). Diabetes is another common disease that is in continuous change, from the glyco-centric approach to more complex mechanisms and new therapeutic approaches, putting high on the agenda the cardiovascular risk of the patient—these advances were so rapid in the last years that the American Diabetes Association approached them by a living guideline, updating it as new technologies emerged [23]. In 2018, the American

Diabetes Association and the European Association for the Study of Diabetes launched a consensus paper on the management of type 2 diabetes that underlined the patient-centered approach and evaluation of cardiovascular risk factors [24], and in 2021 a consensus paper on type 1 diabetes [25]. This deep understanding of diseases and health was possible through the personalized and precision medicine era we are in.

The major developments in the understanding of cancer, cardiovascular diseases, and other chronic diseases, based on the concept of personalized health and care, require a different approach as well as the doctor-patient relationship through the implementation of personalized communication and education as a part of the broader area of PHCL.

12.2.4 COVID-19 Pandemic and the Social and Behavioral Innovations

In a simple search on Google Scholar for "determinants of health," there are hundreds of papers from 2020 and 2021 analyzing the connection between *social determinants of health (including political and economical determinants) and COVID-19*. There are also hundreds of papers that estimate the lives lost because of people not having access to health services during the pandemic. On the other hand, researchers are trying to understand the complete biological burden of the COVID-19 disease—how long it will affect the body after the active phase, what kind of organs will be affected, and what is the genetic and biological predisposition to worse outcomes.

Being faced with such an emergency global state, the scientific world came up with more and more risk factors and new categories of determinants of health. In this complex context, adding the infodemic—too much information including false or misleading information in digital and physical environments during a disease outbreak [26]—it is impossible to continue to classify the determinants of health in an un-personalized manner. And arguably, it is even more impossible

to make public health decisions based on the classical approach of classification and assessment of the health determinants, which most of the time exclude the assessment of psychosocial determinants of health. Depending on the population and individuals, certain determinants weigh more than others. Using only statistics is not enough to understand the complexity of features of an individual.

While we have described above the understanding of the determinants of health through the lenses of personalized medicine, PHC is a more complex concept—it involves health and care, and PM is only a part of it, although the terms are usually used to describe the same concept.

While health literacy is usually understood through a preventive attitude, healthy lifestyle behaviors, and the ability to navigate through the health system a person inhabits, these groundbreaking changes in how certain diseases are defined make the assessment and the increase the health literacy level one of the biggest challenges of our century.

COVID-19, a disease that will probably remain in the public and scientific focus for many years from now on, pushed the idea of prevention and health literacy further and showed us that while health literacy is important, during a global health emergency, it is more important and effective to be able to influence human behavior by understanding the attitudes and perceptions of certain populations. By doing this, you can indirectly increase the level of health literacy through practical experience and by indirectly targeting key beliefs and attitudes, using influencers of the community at three levels—micro, meso, and macro. This model is described in detail below, based on our experience.

To add another layer of evidence to the need to go beyond or rethink health literacy as it is now: a recent study showed that the countries that performed the best in the pandemic from the perspective of the number of infection cases were the countries in which citizens reported a high level of confidence in society and their governments and not those with the best plans of pandemic preparedness. The results also suggest that increasing health promotion for key modifiable risks is associated with a reduction of fatalities in countries where citizens trust the society and their leaders.

Overall, governments and communities can maintain or increase the public's trust by providing accurate, timely information about the pandemic, even when that information is still limited, and by clearly communicating the risk and relevant vulnerabilities [27]. The identity of the messenger in risk communication can also improve or damage trust.

The major point to be underlined here is that in countries with a very low level of trust in their leaders and a history of distrust in society, like ex-communist countries, timely, effective, and well-delivered communication might not still be enough. To take advantage of the full potential of personalized communication, a more sustainable approach is needed, based on citizens' perceptions and attitudes.

12.3 The Role of Attitudes and Perceptions Assessment for Influencing Pro-health Behavior of the Citizens: Two Case Studies on Cancer Literacy and Vaccination Literacy

Abstract In the following, we will present two case studies in the Romanian population—the seventh member state in the European Union in terms of population: one will focus on increasing the level of cancer literacy by assessing the attitudes and perceptions of the population on the subject and develop personalized communication and educational campaigns and the other on COVID-19 vaccination and HPV vaccination (two major vaccination campaigns in Romania from the public health perspective).

12.3.1 Cancer Literacy in Romania

Health literacy entails the knowledge, motivation, and competencies to access, appraise,

understand, and apply information for making decisions concerning healthcare, disease prevention, and health promotion and to maintain and improve quality of life during the life course. In the context of cancer literacy, it refers to the knowledge and skills needed to find, understand, evaluate, and use the information and advice the health system has to offer with regard to prevention, diagnosing, and treatment [28]. A low level of cancer literacy has been shown to hinder patients at every stage of the disease journey. Improving cancer literacy in Europe can help save lives, time, and ultimately, costs.

As inequalities in cancer care are an international reality and a European reality, in the case of cancer literacy, we can observe the same trends and gaps. As innovations enter the clinical stage in countries with a low level of health literacy, health education, and literacy overall, the gaps between the EU Member States become more evident. Besides the influence that HL has on healthy behavior [29], a correlation can be drawn between the quality of healthcare services and the health literacy level of the population. The relationship between demand and supply is compromised in the healthcare system—healthcare providers will not be motivated to offer the best available quality of service if the patients are not empowered to request it and understand their rights.

The cancer domain, being the most positively impacted area by personalized medicine development, represents a key model for understanding how a high level of cancer literacy impacts and stimulates PHC literacy in a country at all levels. But as the pandemic highlighted, adding the attitudes and perceptions of a population on a certain subject, cancer in this particular example represents the missing essential piece of the puzzle for influencing human behavior in populations with a low level of HL and impacted by high inequalities in cancer care.

Moreover, in the current understanding of health, diseases, and the scientific advances in cancer, the actions that aim at increasing cancer literacy level should no longer address the patient, but the citizen, recognizing his role in society before, during, and after the cancer diagnosis.

12.3.1.1 Cancer Burden in Romania

Romania has some of the highest rates of avoidable deaths from both preventable and treatable causes in Europe [30]. Romania's cancer burden is high, with 83,461 newly diagnosed cases and roughly 50,902 total deaths occurring in 2018 [31]. Romania is also among the top ten European countries in terms of cancer mortality rates [32]. The lack of information and adequate screening and diagnosis services, together with the unstandardized cancer patient path, are some of the main causes of the late detection of cancer cases.

Although the access to new cancer treatments has improved in the last 6 years, the improvement was not reflected in the survival rate of the cancer patients. Romania provides public support and assistance to cancer patients through the National Programme for Cancer (NPC), operated by the National Health Insurance House. Over the years, the program has continuously evolved to include more patients and more types of cancer, but results are not published.

Besides the faulty healthcare services, at the macro level, the overall situation as shown by statistics is complex: half of the Romanian population live in the rural area, Romania has one of the lowest rates of education in Europe and some of the highest rates of school dropout, and Romania is an ex-communist country, with very conservative views, and many vulnerable populations living in poverty.

Going back to cancer statistics, Romania has also the biggest rate of mortality from cervical cancer in the European Union. Every year, in Romania, there are 1800 deaths from cervical cancer and 3400 new cases. At the European level, Romania ranks first in terms of incidence and mortality: the incidence is 2.5 times higher than the European average, and the mortality rate is over four times higher [33].

But seven out of ten cases of cervical cancer can be prevented with the HPV vaccine [34]. The HPV vaccination rate will be discussed in the next case study.

The guidelines of the European Society for Medical Oncology recommend mammography screening for breast cancer, annually or every 2 years, with priority for women in the 50–69 age

group [35]. Moreover, in women with a family history of breast cancer, with or without knowledge of BRCA carrier status, annual MRIs and/or annual mammograms are recommended. The relative 5-year survival rate has increased by up to 90% due to the expansion of screening programs and therapeutic advances. Participation in screening programs is associated with a reduction in mortality of at least 30% and a reduction in the risk of severe disease by 40% [36].

Romania launched the first breast cancer screening pilot program in 2018 [37]. However, according to the latest Eurostat survey, only 9% of women in Romania aged between 50 and 69 reported in 2019 that they had a mammogram in the last 2 years [38]. Once again, Romania ranks last in the EU. For Bulgaria, which is on the penultimate place, the percentage is 36%—four times more than in Romania. In Sweden, the percentage is 95%, about 11 times higher.

12.3.2 Attitudes, Perceptions, and Behaviors on Cancer: National Survey (2016, 2018, 2020) in the Romanian Population

Increasing the overall health literacy level (including cancer literacy) has become more and more complex because of the unprecedented scientific development, at an unprecedented speed. But influencing health behavior through targeted interventions after assessing attitudes and perceptions seems to be a more sustainable approach.

In order to understand how the Romanian population relates to cancer and the degree of awareness of cancer innovations, the Center for Innovation in Medicine, a civil society organization with an interest in research, innovation, policy, personalized communication, and education at the European level, measured the level of citizens' awareness and their perception on prevention, diagnosis, and treatment of cancer, in 2016, 2018, and 2020 (pre-pandemic), through telephonic interviews (CATI—computer-assisted telephone interviewing): 1010 participants in

each study, sociologically relevant at the national level.

One of the major outputs of this study was to find that approximately 5% of Romanians had cancer at some point in life, and one in three people had a direct or indirect experience with cancer during their lifetime. These data are very valuable because there is no cancer registry at the national level and the IARC data on Romania is based on estimates from the Northern Region, where there is a functional cancer registry.

Another two major outputs consist of the fatalism rate in relation to cancer in the Romanian population and the drop observed from 2018 to 2020 in awareness of cancer innovation (personalized medicine and immuno-oncology), correlated with an actual increase of the information campaigns (but with poor and non-targeted messages), which led to a cancer infodemic.

12.3.2.1 Fatalism

Measuring fatalism in relation to cancer is important because it can indicate people's willingness to take action in all the areas of the cancer continuum, from prevention to palliative care. In other words, the higher the fatalism in relation to the disease, the more people will resign and no longer participate in screening programs, will not adopt preventive measures, and will not try to find and access diagnosis and therapeutic options in case of a cancer diagnosis.

Despite the fact that they say, to a large extent, that they know that there are cancers that can be cured, when asked if a cancer diagnosis always leads to death, almost 48% (2020) agree. This indicates fatalism, a condition in which many citizens try to cope with the prospect of cancer, considering that the health system, for various reasons, cannot provide them with access to the means of screening, diagnosis, and treatment they may need (Fig. 12.1).

The rising rate of fatalism is also reflected in the knowledge about cancer innovation (personalized medicine, immuno-oncology, or biomarkers)—common terms in current cancer management. Another set of questions also assessed people's perceptions of access to medi-
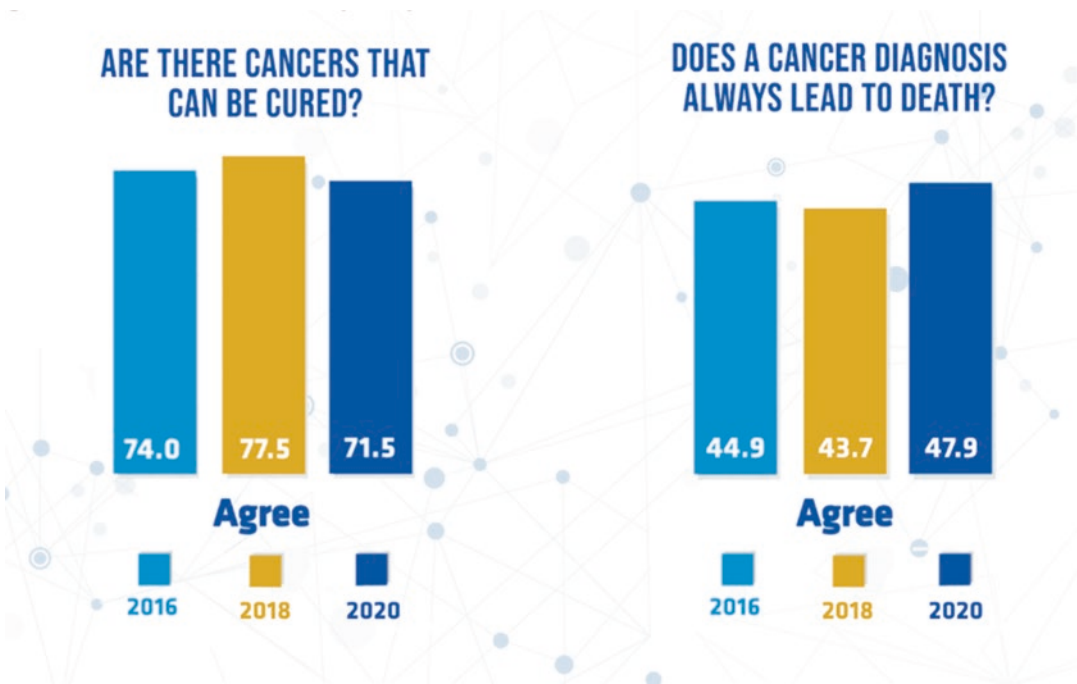
Fig. 12.1   Fatalism results from the three studies. Property of Center for Innovation in Medicine

cines and therapies. The general conclusion is that most respondents did not know the price of therapies or how to access them.

The data show that although access to healthcare and new therapies has improved in Romania between 2016 and 2020, people's perceptions and fatalistic attitudes have worsened, despite multiple information campaigns. There has also been a decline in awareness of cancer innovation (immuno-oncology, biomarkers, and personalized medicine). One explanation could be the development of infodemia in relation to cancer—a multitude of incomplete, irrelevant, poor quality, and scientifically invalid information posted online and beyond, especially on social media and forums, which causes people to be confused and unable to identify the right message.

Independently, a recently published study in the United States had similar findings between 2016 and 2020, comparing two types of major populations in a state: *Rural Residents Tend to Hold Fatalistic Beliefs and Perceive More Cancer-related Information Overload Than Urban Residents* [39]. To assess whether cancer beliefs vary between rural and urban adults in the

United States, Jensen and colleagues analyzed the results of a survey conducted between 2016 and 2020 in 12 US National Cancer Institute-designated cancer centers.

Similarly, in the Romanian study conducted by the Center for Innovation in Medicine, the participants were asked to rate four statements related to:

- Prevention-focused cancer fatalism ("It seems like everything causes cancer" and "There's not much you can do to lower your chances of getting cancer").
- Cancer information overload ("There are so many different recommendations about preventing cancer, and it's hard to know which ones to follow").
- Treatment-focused cancer fatalism ("When I think about cancer, I automatically think about death").

The researchers found that, compared to urban participants, rural participants in the study exhibited higher levels of cancer fatalism and cancer information overload—a trait of cancer infod-
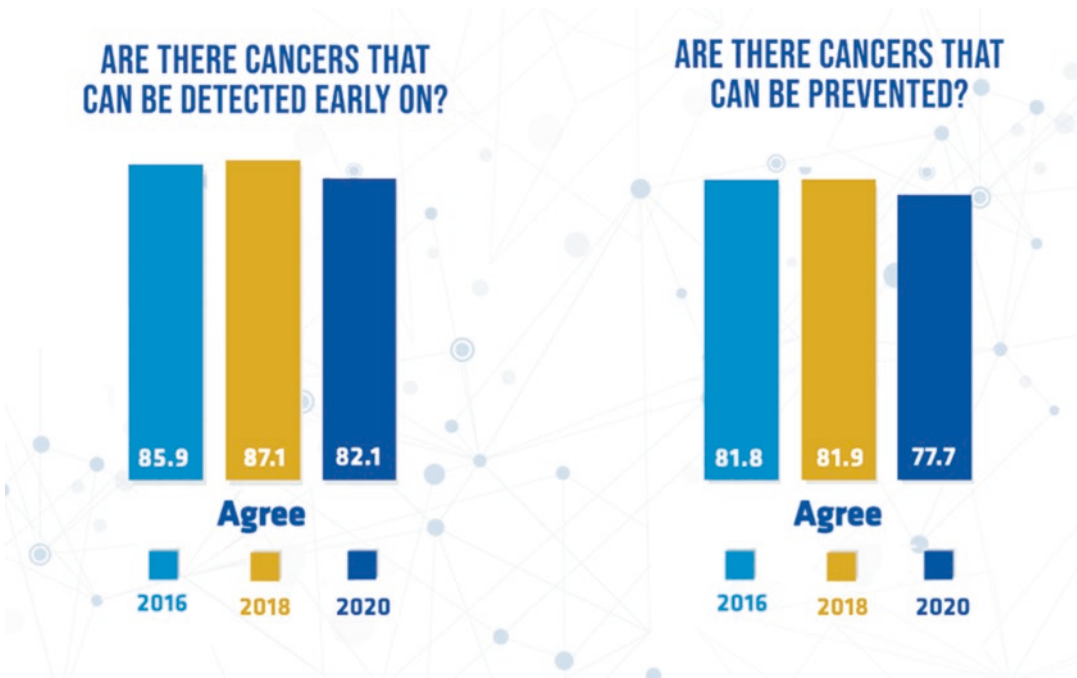
Fig. 12.2 Prevention and diagnosis results from the three studies. Property of Center for Innovation in Medicine

emy. In particular, rural participants were 29% more likely to agree that everything causes cancer, 34% more likely to agree that prevention is not possible, 26% more likely to agree that there are too many different recommendations about cancer prevention, and 21% more likely to agree that cancer is always fatal (Fig. 12.2).

In 2020, 78% of the Romanians that participated in the study believed that cancer can be prevented, compared to 82% (in 2016 and 2018) (see Fig. 12.2). This belief was rather present in the segment that had no experience with the disease. Over 80% of respondents (85.9%, 2016; 87.1%, 2018; 82.1%, 2020) believed that the disease can be detected in early stages. Despite all this data, Romania has the lowest screening rates in the EU for cervical and breast cancer (the only types of cancer screening implemented so far).

12.3.2.2 Personalized Medicine and Cancer Innovation Awareness

Further data assessed levels of knowledge on immune-oncology and personalized medicine,

with varying trends being reported across the three studies (Fig. 12.3).

As of March 2020, approximately 42% of study participants said they have heard of the term "personalized medicine" (see Fig. 12.3). Comparably, in May 2018, there was a percentage of 44.0% when the notoriety of the term "personalized medicine" was evaluated among the adult population of Romania, and almost 40% of Romanians knew this term in 2016.

Regarding immuno-oncology, 39.1% of the respondents in March 2020 heard about this notion; the notoriety of the term "immunooncology" is also comparable with the data from previous waves (42.5% in 2018, respectively 37.1% in 2016).

The notoriety of the term "biomarkers" is also maintained at a constant value (42.8% in 2020, respectively 42.2% in 2018).

The 2020 study, similar to research conducted in 2016–2018, shows that new personalized therapies such as immuno-oncology and targeted therapies are associated with high prices/costs—only 20.9% of respondents estimate that they
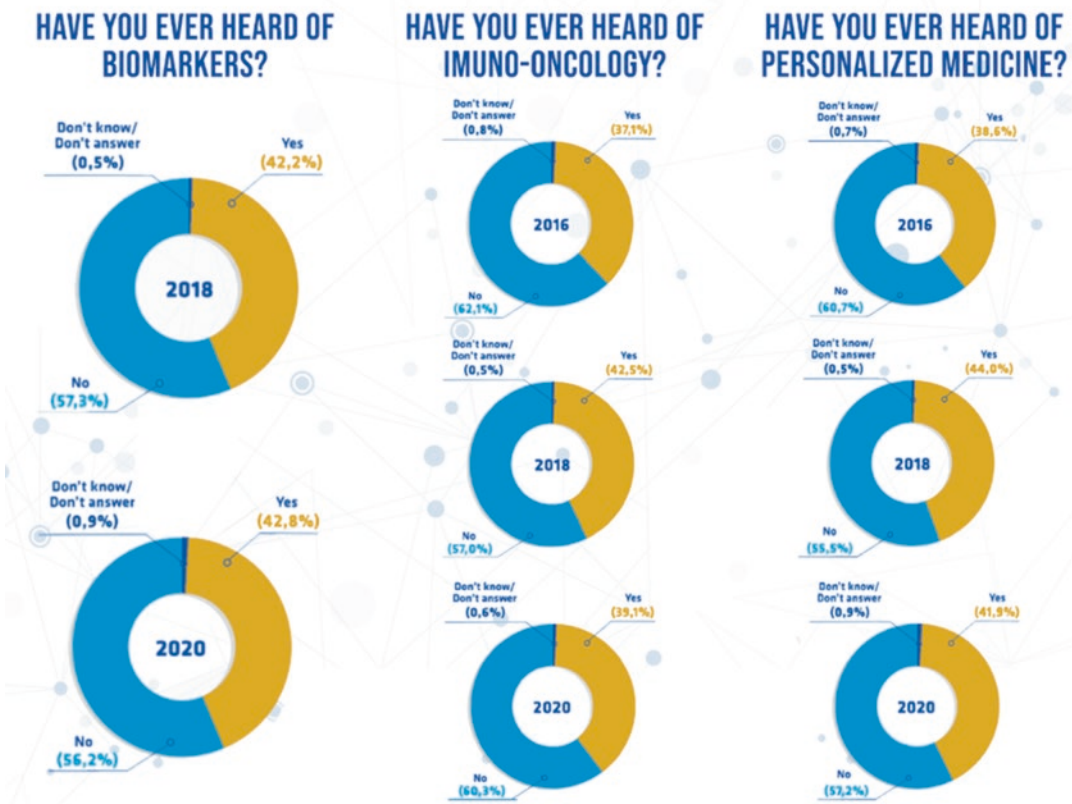
Fig. 12.3 Health innovation awareness results. Property of Center for Innovation in Medicine

could afford it, and 33.3% of those surveyed consider that these treatments are not affordable at all (see Fig. 12.4). It should be noted that the percentage of those who consider that the new treatments are not accessible at all is still decreasing, from 44.1% in 2018, fueling the development of an increasing rate of fatalism.

12.3.2.3 Quality of the Cancer Information Campaigns: From One-Size-Fits-All to Personalized Communication

According to the *Digital News Report* [40], conducted by the Reuters Institute and Oxford University, in the last 3 years (2017–2020), television and the online environment have been and continue to be the main sources of information for Romanian citizens.

According to the data obtained from our surveys, the top five sources from which Romanian citizens are informed about cancer prevention, diagnosis, and treatment are represented by medical staff (doctors or nurses), the online environment blogs, medical forums, social networks, etc.), television, information materials (reports, posters, brochures, leaflets, etc.), and the written press. In 2020, the medical staff was responsible for informing a percentage of 68.2% of citizens, while the online environment reached a percentage of 61.3%, television 61%, news materials 53.5%, and print media 39.6%.

In 2017, after the results of the first round of the survey (2016) showed a high grade of fatalism (almost one in two Romanians believed that a cancer diagnosis always leads to death), and that the main source of information on cancer was the physician (usually itself being fatalistic
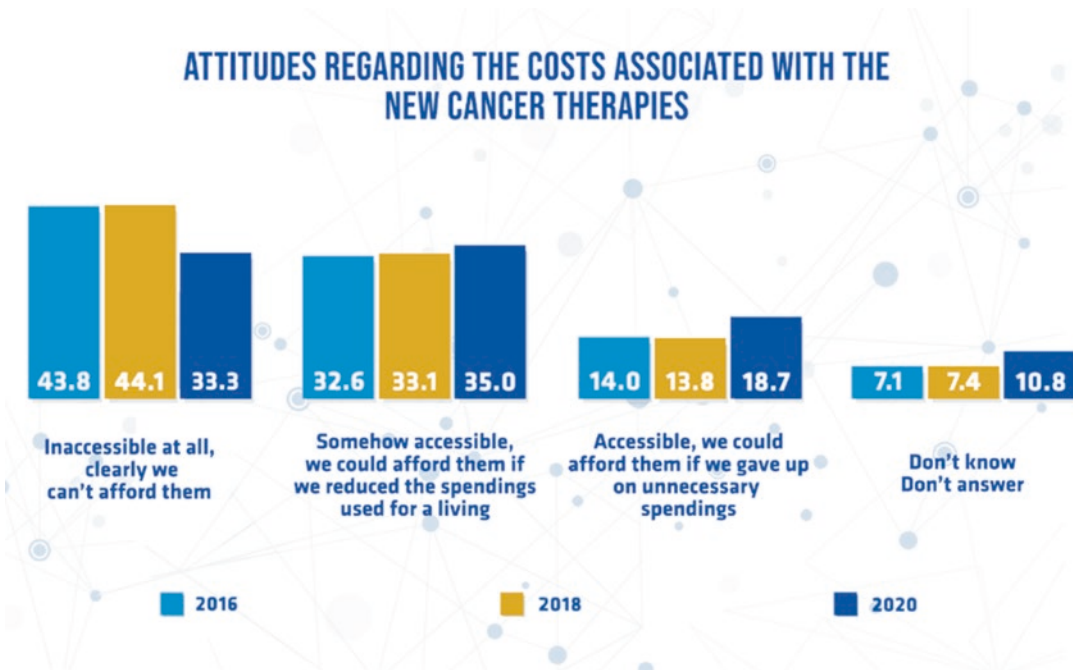
Fig. 12.4 Associated costs of the new cancer therapies. Property of Center for Innovation in Medicine. Property of Center for Innovation in Medicine

when it comes to cancer topic), with the second place being held by the mainstream media (but no channel that actually referred to innovation in oncology, but rather presented the death cases and exclusively criticized the Romanian healthcare system), the Center for Innovation in Medicine decided to implement a personalized multilayer communication and educational approach on cancer in Romania.

This study and the newly adopted definition of personalized medicine in Europe (2015) led to the first Personalized Medicine Conference organized in Bucharest, Romania, by the Center for Innovation in Medicine, in partnership with the presidential administration. The time for the conversation around cancer to change has come. The conference has been held annually since then. This was the first step at the macro level (politicians, decision-makers, mainstream health influencers, and mainstream media) to change perceptions around cancer by highlighting the benefits of innovations.

Less than a year later, at the beginning of 2017, the Center for Innovation in Medicine

launched the course *Innovation in Communication. Communicating the innovation* that aimed at training medical students, journalism students, and health engineering students to become health innovation communicators. The participants were thoroughly selected and 4 months later, the innovation communication platform, in Romanian, Raportuldegardă.ro [41] emerged, a platform that offered a different perspective for Romanian citizens that aimed at decreasing fatalism not only on cancer—another block was added to the macro level.

Based on the same findings from the 2016 national survey, at the end of 2017, the "Let's differently talk about cancer" campaign was launched, involving authorities, key opinion leaders, medical doctors, patients, cancer survivors, and citizens.

Adding another layer to the macro level of changing the perception of cancer and other fatal diseases in the Romanian population, the Center for Innovation in Medicine launched the initiative—science meets politicians—in partnership with the Romanian Parliament, consisting of the

launch and debates around the *State of Innovation Annual Report of the Center for Innovation in Medicine* [22].

As a result, in 2018, the perceptions and attitudes were measured again, and we noticed that the fatalism rate experienced a decrease and the notoriety of cancer innovation-related terms "personalized medicine," "biomarkers," and "immuno-therapies" increased.

But between 2018 and 2020, another phenomenon happened in Romania. The media platform influencers became more vocal, and many health websites and platforms were launched, many of them engaging in mostly disease awareness campaigns mainly paid for by the industry. The cancer infodemic was reaching new heights. While "disease awareness campaigns" are not bad, the qualitative analysis we conducted showed us that these campaigns mostly fuel the fatalism and the infodemic around cancer. The messages followed the same pattern: *This percent of Romanians have died because of cancer in a year, get tested now*. While the conversation around death shouldn't be taboo, messages like these cannot be so bluntly delivered to a population in which one in two people believe that a cancer diagnosis always leads to death.

And so, the positive effect gained by the Center for Innovation in Medicine and partners between 2016 and 2018 at the macro level was neutralized and downgraded by the infodemic and indirectly negative effect at the macro and meso level.

On the other hand, as the social media platforms grew in popularity, many websites, pages, and health influencers promoted all sorts of wonder treatments, fueling the conspiracy theories around Big Pharma.

So in 2020, before the pandemic, when we measured the attitudes and perceptions again, the decrease in the fatalistic approach observed from 2016 to 2018 not only was not maintained but increased.

The work continues, with Raportuldegardă.ro being a source of information for approximately 2000 unique Romanian users daily, weekly covering the most important news on pandemic control and daily publishing the most relevant health innovations and trends at the international and European levels.

12.3.3 Vaccination Literacy in Romania

Two major vaccination campaigns can be identified in Romania in the last two decades: the HPV vaccination campaign that first started in 2008 and the SARS-CoV-2 vaccination campaign. The first one can briefly be described as a big international and national failure, and the last one can be described as a big European failure, but national relative success when compared to the previous experiences.

Both vaccination campaigns have the following key elements in common:

- The propagandistic approach and the alignment of the messages with the political agenda led to the misappropriation of public trust (a government trust already very low in public polls [42]).
- The incapacity of convincing the health professionals to deliver the pro-vaccination messages, as most of the people expected according to the national surveys.
- The failure of delivering the key messages: from the beginning of the COVID-19 vaccination campaign, the official message was that the vaccine will get you the normal life back and not that the vaccine protects you and your dear ones against complications and hospitalization.
- The oversimplified messages that did not refer to the unique genetic and biological traits of a person led to the false impression that everyone should react and get the same level of protection.
- The failure of complying with the people's needs, using the dissemination, channels, and influencers that reached people that had access and followed certain official pages, when the lowest rate of vaccination was among those who do not have access to these channels or are compliant to the fake news spreading channels.

12.3.3.1   HPV Vaccination Literacy

The major problem when it comes to preventing disease by vaccination (particularly in Romania) is the inadequate communication that derives from a low level of understanding of the particularities of the population you are addressing. By adding the low level of health literacy and the fake news and conspiracy theories that arise from it to the low capacity of the authorities to communicate and engage with the citizens, a major gap in HPV vaccination rates and cancer survival rates was created between countries in Europe.

HPV vaccination is a very sensitive subject because it involves the prevention of a possible sexually transmitted disease from an early age. In societies with a strong traditional and religious background and in which around half of the population lives in rural areas, it is very difficult to communicate these messages properly. Romania has a strong communist background—a recent study showed that more than 60% of the respondents believe that the actual situation in Romania is worse than 30 years ago (7 years ago, only 40% of Romanians had that opinion). Over 60% of Romanians prefer traditional values to modern rights and freedoms [42].

At the EU level, Romania ranks first in terms of incidence and mortality for cervical cancer: the incidence is 2.5 times higher than the European average, and the mortality rate is over four times higher. When referring to HPV, this information can be explained partly by the following data, according to the national survey organized by the Center for Innovation in Medicine, Renaşterea Foundation, and National Institute for Public Health:

- (2018) 48% of women respondents said that in the last 3 years, they were not tested for HPV.
- (2018–2020) no less than 67% of women and girls from rural areas, aged 15–65, have genital infections.
- (2020) only 36% of Romanian women have heard of the HPV virus, and only 31% associate this infection with cervical cancer [43].

Currently, after the 2008's HPV vaccination failure (less than 2% of the target population was vaccinated at that time), Romania is trying to implement a new HPV vaccination program for girls aged 11–18 and a National Screening Program for Cervical Cancer, but these need to be strengthened by sustainable and highly personalized communication and training courses for the people involved in the process (from family doctors to school teachers).

In 2020, the Romanian Ministry of Health announced its intention to introduce free HPV vaccination also for boys. But as HPV infection is perceived as women's health issue exclusively in countries with a profile resembling Romania, the mere fact that there are free vaccines available for boys does not guarantee their vaccination (similar to COVID vaccination—doses available for the entire population, but the majority refused to get the vaccine).

Inequalities in vaccination in general and HPV vaccination rate, in particular, exist not only between countries but also within countries, communities, and groups. For example, a total of 41 counties, along with the municipality of Bucharest, constitute the official administrative divisions of Romania but based on Renaşterea Foundation's experience with their cancer screening projects, in the North and North-East of the country, the level of cervical cancer and HPV vaccination literacy is very low, being hard to get access to the people through classical methods. Different communication vectors and messages are needed.

Two Sides of the Story About HPV Vaccination Efforts in Romania

The Center for Innovation in Medicine measured the level of citizens' awareness and their perception of prevention, diagnosis, and treatment of cancer, in 2016, 2018, and 2020 (before the pandemic). In 2018, 48% of women respondents said that in the last 3 years, they were not tested for HPV. Sixty-one percent stated that they had heard of the HPV vaccine. Fifty-four percent documented the subject but did not get the vaccine and only 2% have been informed and vaccinated.

According to data from the Renaşterea Foundation, no less than 67% of women and girls from rural areas, aged 15–65, have genital infec-

tions. In the urban areas, the percentage was 65%. Forty-one percent of girls aged 15–19 had a genital infection, and the percentage rose to 71% for girls aged 20–29. Moreover, only 17% of women in Romania took a Pap test, while at the EU level, the average is 70%.

Only 36% of Romanian women interviewed in an IRES (Romanian Institute for Evaluation and Strategy) survey conducted at the request of the National Institute of Public Health have heard of the HPV virus, and only 31% associate this infection with cervical cancer. Romania has the highest incidence and highest mortality rate from cervical cancer compared to European Union countries, although it is one of the few types of cancer that can be prevented by vaccination. Every 5 h, a Romanian woman in the 20–50 age group dies of cervical cancer.

In 2012, Romania launched its first cervical cancer screening program, targeting approximately six million women aged 25–63 (in a period of 5 years). By 2015, only 7% of the target population was tested [44].

In 2008, Romania was among the first countries to introduce HPV vaccination (for girls aged 10–11), simultaneously with the United Kingdom. However, the campaign was a total failure—only 2.6% of eligible girls were vaccinated and the program was suspended. In 2009, an information campaign was launched, followed by a second vaccination program, targeting girls aged 12–14. A catch-up program was also launched, where adult women were given the opportunity to get the vaccine free of charge through their health provider. Despite the accessibility of the vaccine, uptake remained low and the school-based program was discontinued at the end of 2011. The program was launched for the third time in April 2013 and for the fourth time in 2019.

In 2020 and 2021, according to preliminary data, less than 50,000 girls were vaccinated; no Romanian county has a vaccination rate higher than 5% of the target population, and the average vaccination rate in Romania in 2020/2021 is 2%.

The numbers speak for themselves—cervical cancer is not prevented by vaccination in Romania, and many women don't know about the virus and don't get tested for the infection. But in a parallel universe, a communication campaign ("Protect her wings") launched in 2017 to encourage HPV testing and to raise awareness of the disease caused by the infection with the virus, which, according to the jury that gave the award "contributed to the decision announced by the Ministry of Health to resume HPV vaccination," was awarded an international distinction for "Best in show" campaign in the entire CEE region.

Despite the fact that a pro-HPV awareness campaign implemented in Romania was awarded one of the most distinguished prizes for communication campaigns, the vaccination rate has not increased. One possible explanation was the one-size-fits-all approach of the campaign that did not include the assessment of behavior, perceptions, and attitudes in the Romanian population. Having a low HPV vaccination rate does not guarantee that if you just start communicating on the subject it will increase. It's that simple, but complex after all.

12.3.3.2 COVID-19 Vaccination Literacy

This kind of approach was also seen during the COVID-19 vaccination campaign. Again, the communication campaign was awarded a prize for its creativity, but Romania has one of the lowest COVID-19 vaccination rates in Europe. We can easily assume that the people that got the vaccine were not impressed by the campaign, since the campaign was carried on Facebook exclusively and sometimes on TV, mixed with political messages, but were convinced by the health emergency.

In 2020, COVID-19 was the cause of death for approximately 16,000 people in Romania—no less than 5% of the total number of registered deaths [30]. Approximately 18,500 COVID-19 deaths were recorded by the end of August 2021. COVID-19 mortality calculated by August 2021 was 12% higher in Romania than the EU average. Rates are calculated based on reported deaths, but the number may be much higher, not to mention the indirect burden.

The COVID-19 pandemic overlapped with an already overwhelmed health system and high-

lighted the need to increase the HL level of Romanian citizens. According to the results of the most recent Eurobarometer on the attitude of European citizens toward science and technology, only three out of ten Romanians know in 2021 that antibiotics have only an antibacterial effect and not an antiviral effect. Their percentage decreased compared to 2005 [45]. The data must be interpreted in the context in which the COVID-19 pandemic brought to the public discussion more than ever the subject of viruses and bacteria, but also considering the media coverage of nosocomial infections in Romanian hospitals and the antibiotic resistance crisis, which launched extensive communication campaigns 5–6 years ago.

Multiple sociological studies conducted by various institutions provide a number of information on the limited level of health literacy among the general population of Romania. Cancer is not the only disease impacted. In the Center for Innovation in Medicine's study from 2016 regarding another chronic disease, diabetes, patients did not seem to have long-term disease management skills, as 20% did not visit a diabetes specialist in the previous year. The results of another sociological study (2017) identified a low level of literacy in mental health and a negative attitude toward those diagnosed with mental illness among Romanians.

The low level of health literacy, the infodemic, and the impact of fake news were reflected in the results of the vaccination campaign against COVID-19 in Romania. According to the Public Health Barometer of October 2020 [46], 21% of Romanians would get vaccinated if a vaccine had been available, a third choice to be immunized only if they heard that there were no side effects, and 8% would have wanted to know more information to make the vaccination decision. In context, nine out of ten Romanians declared that they got a vaccine at some point in life.

Another study, conducted by IPSOS in September 2020 [47], showed that only 29% of Romanians in urban areas were determined to get vaccinated if a vaccine was available. The repetition of the study in early February 2021 showed that the intention to vaccinate increased by 7% among those over 16 years in urban areas.

An IRES (Romanian Institute for Evaluation and Strategy) study [48] conducted at the beginning of 2021 underlined that individuals who are pro-vaccination (declaring that they will certainly or probably be vaccinated) tend to come from urban areas (58%) and that anti-vaccination are mostly from rural areas (53%). Moreover, over 60% of the undecided respondents were willing to take the vaccination advice if it will come from their medic or a healthcare professional. The percentage was 20% in the case of those against vaccination. This finding is consistent in many sociological studies—the healthcare professionals are the main vectors that could recommend the vaccination.

Independently, this trend is observed in studies from other states and countries [49]. In the United States, the vaccination rate in people that received the recommendation of getting vaccinated against COVID-19 from their doctor was 15% higher than in people who did not receive such information from their doctor.

And although sociological studies show those rates, the gap between declared willingness and action is still important. One of the explanations can be drawn from the CDC study that showed that direct referring is very important. Even if doctors publicly recommended vaccination, the citizens expected that this would come from their physician or a physician they trust. In Romania, the vaccination rate of healthcare professionals had a slow increase when compared with other EU countries.

In May 2021, Romania was already vaccinating the general population, but only 3.5 million people were vaccinated with the two doses full scheme. From May to the end of October, another 2.4 million people were added, given that the indications for certain vaccines have been extended to children over 12.

In July 2021, only 16% of the 80+ population had the full scheme of vaccination, but Romania reported to ECDC that it had no difficulties with vaccinating the elderly population [50].

From October 2021 to February 2022, the number of people vaccinated with the full scheme (considered two doses in Romania) reached eight million (target population 5+), with less than

2000 people getting a first dose of the vaccine daily. Moreover, only two million of the eight million Romanians vaccinated got their booster dose. Almost 2 years since the vaccines were available, Romania recently reached the 50% vaccination rate against COVID-19 (two doses scheme). In the context of VOCs and Omicron variants, vaccine protection offered by the two doses vaccination scheme is low, and only two million Romanians got their booster doses since they became available. In this scenario, the 50% vaccination coverage doesn't have the same value as it would have 1 year ago.

The failure of the vaccination campaign and of the vaccination communication campaign can be partially explained by Eurobarometer data on Romanian's attitudes and perceptions about innovation and data from various national surveys. The pro-vaccination communication campaign failed to exceed the percentage of about 30% of people who constantly stated in opinion polls that they will be vaccinated.

On the other hand, the COVID-19 pandemic directed, in the first phase, public attention in Romania to the subject of health and health education and had a positive effect on discovering the communication and the applied importance of HL at the authorities' level. But after multiple waves of COVID-19, and after political messages of incertitude and measures that were not based and explained at the scientific standards required, the public opinion in Romania diverted, and the citizens turned their back to the individual protective measures in the face of the disease.

12.4 Conclusions and Discussions

Romania has the highest rate of preventable deaths among European countries (80.1% compared to 68% EU average) [51]. While these rates can briefly be explained by the limited access to health knowledge, healthcare, and technology, the extensive explanations are infinite.

While more and more therapies entered the Romanian market in the last years and were reimbursed, with cancer being one of the most active areas, the survival rates did not improve in accor-

dance. This can be partially explained by the high fatalistic attitudes, the low level of government trust, and the reticence in accepting innovations, the traditional and conservative beliefs of people, etc.

Despite multiple efforts to stimulate the adoption of a healthy lifestyle and increase the adherence to screening and treatment, in Romania and in other countries with a similar profile, the results did not meet the expectations. From our experience with HPV vaccination, COVID-19 vaccination, and cancer, we argue that there were three main general reasons for this: (1) lack of proper understanding of the behavior of individuals (based on micro, meso, and macro assessment) as the key determinant for pro-health behavior and implementation of the one-size-fits-all communication strategies, (2) the low level of health literacy within these countries, and (3) the failure of authorities in identifying the proper channels and personalize the messages for every group, as well as the failure of authorities to engage with relevant NGOs in order to improve the situation.

Overall, during more than 10 years of experience in the field of personalized health and care communication, we noticed that the lack of data and capacity to use data for public health decisions, as well as the lack of human touch and empathy (in some countries derived from the long history of communism), were the main drivers of this situation at the level of the decision-makers.

Time showed us that in populations with these characteristics, just offering better-structured information will not change the behaviors of the citizens, at least not fast enough for the speed of scientific advance of the moment. Many levels and actions need to be employed. We propose a concept of a personalized communication model based on the matrix with the social and behavioral determinants of health (see Fig. 12.5).

Based on the experience gained in our research studies done at the national level in Romania, we propose a new model, based on the individual behavioral health determinant matrix, for influencing pro-health behavior and indirectly increasing the overall health literacy and the faster
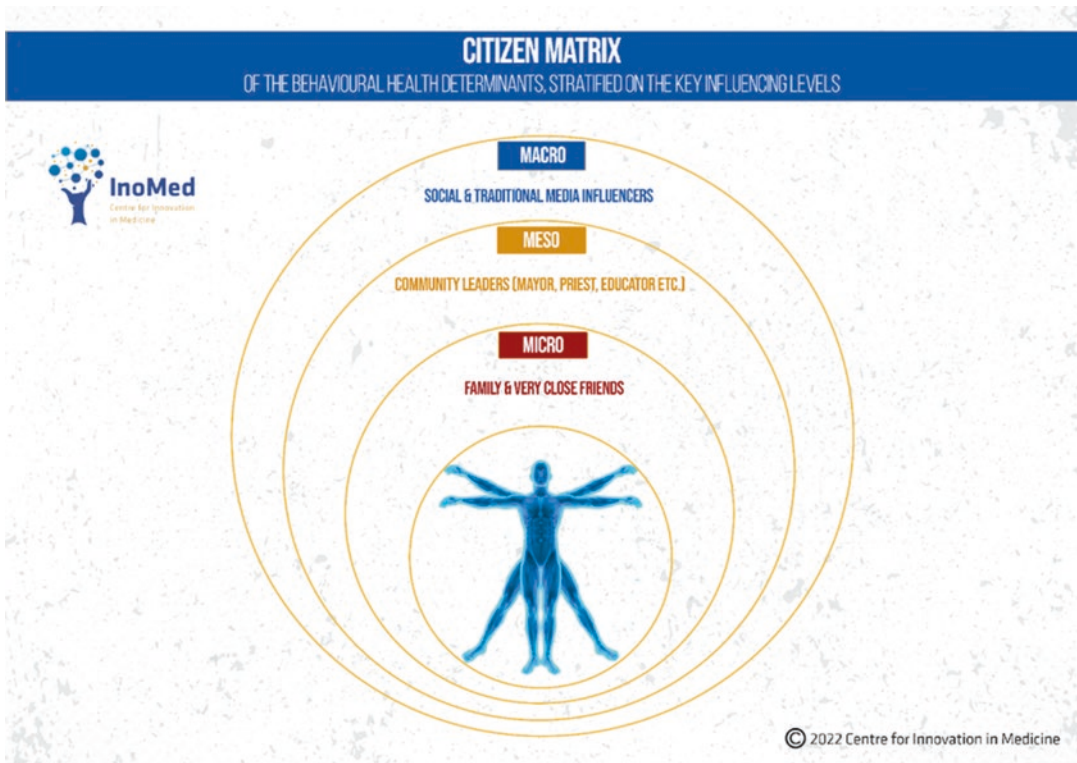
Fig. 12.5 Citizen matrix. Property of Center for Innovation in Medicine

adoption of relevant and evidence-based health innovations.

The matrix has three layers:

- Micro-dimension—family members and inner circle of close friends who can influence behavior.
- Meso-dimension—community influencers who can influence pro-health behavior (e.g., religious leaders, family doctors, or mayors, especially in rural areas).
- Macro-dimension—(inter)national influencers driven by traditional media and social media who can influence behavior.

The citizen behavior matrix (micro, meso, macro) above represents an innovation in terms of health communication because it is based on a deep understanding of the high granularity of the reasons for the high level of fatalism. Another social innovation consists of the unique approach in using the citizens' perspectives and perceptions for influencing their behavior and not expecting that by only delivering the information, they can assimilate it and use it to make better decisions about their health (the one-size-fits-all approach) (Fig. 12.6).

The main motif of the personalized communication model revolves around health literacy, education, and communication based on personalized and sustained efforts in understanding the specific needs of the communities and individuals addressed. In countries with a medium-high literacy and education level, with at least a medium level of trust in the national and regional authorities, this level of detail might not be
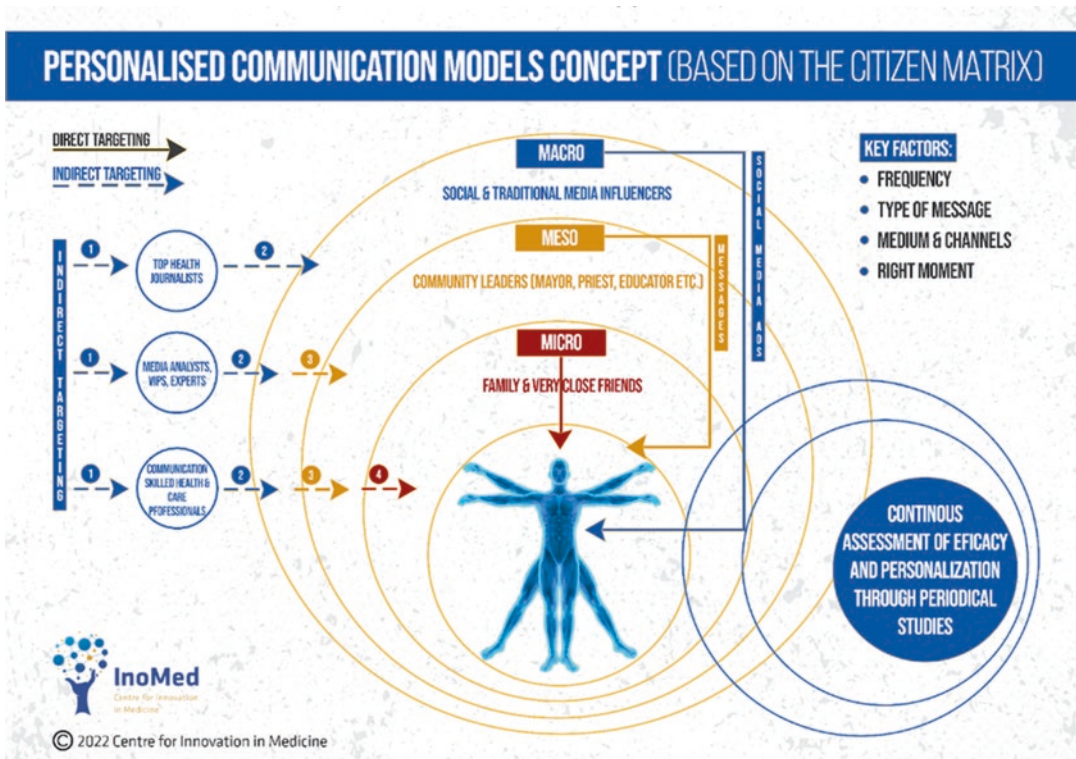
Fig. 12.6 Personalized communication models concept. Property of Center for Innovation in Medicine

needed, but in countries like Romania, the experience and the time showed us that there is, unfortunately, no other way of doing it.

We have already validated the model of assessing the attitudes, perceptions, and behaviors of cancer every 2 years at the national level and take actions based on the survey results in our campaigns. We argue that this measurement could be a valuable tool for understanding the social determinants of health in a population and that by closing the community circle and assessing the level periodically, you can have a correct evaluation of the willingness of people to exercise a healthy behavior on main areas like getting vaccinated or participating in screening programs.

The same applies to the intake of innovations and personalized medicine understanding. If you are able to identify, target, and then sustainably address the meso influencers in the communities,

their messages will penetrate and settle better at the citizen, individual level. This is not a one-time approach; you need to periodically reassess the quality of interventions—the 2-year span could become standard.

To sum up the concept:

- Assess attitudes, perceptions, and behaviors every 2 years.
- Conduct qualitative evaluation of health communication campaign at the national level.
- Take actions based on the information obtained from the surveys (launch a new platform, start a training course, construct a different communication campaign, etc.).
- Engage with the mainstream media and key macro stakeholders.
- Consult with communication and health literacy analysts (Fig. 12.7).
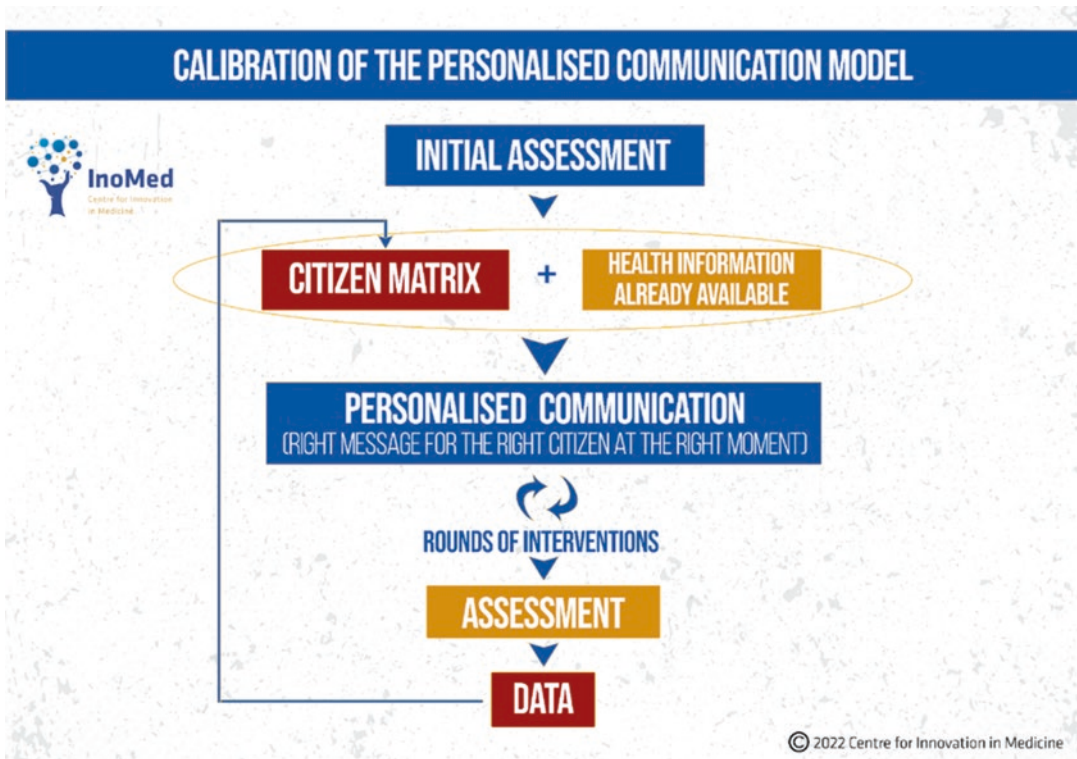
Fig. 12.7 Calibration of the personalized communication model. Property of Center for Innovation in Medicine

12.4.1 Future Perspectives on Increasing the Individual Level of Health Literacy by Periodically Assessing Attitudes, Perceptions, and Behaviors, in Synergy with the European Opportunities

While following the concept and scheme presented above can bring great value to a population, collaboration at the national, European, and international levels is crucial. The good practice model needs to be shared, adapted, improved, and enriched with new data and scientific evidence.

Improving cancer literacy and changing health behavior following the model presented above can be a best practice model for improving or starting building on PHCL in certain populations. Europe's Beating Cancer Plan [52] and the Mission on Cancer [53] are key drivers in the fight against cancer at the European level. Though we refer to cancer literacy, the new vision in cancer battle has the citizens in the middle: it is no longer possible to fight cancer with what decision-makers perceive as being important. We need to take everything to the next level—identify the needs of patients and citizens and work with them to meet those needs (Table 12.1).

The "Missions" are a new tool in Horizon Europe—the European Union's Framework Program for Research and Innovation. Inspired by the Apollo 11 mission to send one man to the moon, EU missions are a commitment to addressing major social challenges. The five missions for the period 2021–2027 are fighting cancer, adapting to climate change, living in greener cities, ensuring healthy soils, and protecting the oceans.

The Cancer Mission, launched on September 29, 2021, together with Europe's Beating Cancer Plan (February 3, 2021) and the 2023 expected European Partnership for Personalised Medicine (EP PerMed), aims to improve the lives of more

Table 12.1 European initiative to support health literacy and citizens' engagement in cancer information extracted from the European Mission on Cancer and Europe's Beating Cancer Plan: Implementation Roadmap (updated version | January 2022) [52, 53]

Initiatives and programs	Actions to support health literacy and citizens' engagement in cancer	When
Cancer Mission	UNCAN.eu – improve the understanding of cancer	2021–2030
	European Cancer Patient Digital Centre	2021–2023
	Support quality of life (living labs)	2021–2025
Europe's Beating Cancer Plan: Implementation Roadmap	Knowledge Centre on Cancer	2021–2025
	European Code Against Cancer	2021–2025
	"Health Literacy for Cancer Prevention and Care project"	2021–2025
	Propose mandatory front-of-pack nutrition labeling	2021–2022
	EU Clinical Trials Portal and Database	2021–2025
	Set up Partnership on Personalised Medicine	2021–2025
	Roadmap to personalized prevention	2022–2022, 2024
	Cancer Inequalities Registry	2021–2025
	EU Network of Youth Cancer Survivors	2021–2025

than three million people affected by cancer by 2030. The four goals of the Cancer Mission are understanding cancer, preventing and detecting it early, optimizing diagnosis and treatment, and supporting quality of life.

Identifying the synergies and opportunities on how to better engage with citizens and let their voices be heard is crucial for a structured and sustainable approach over time. The table below sums up those actions and opportunities.

One first step is to adapt and include data on perceptions and attitudes in the Cancer Inequalities Registry, launched in February 2022. The initial framework of the Registry is based on the same classical approach to the disease and does not reflect the citizen's approach and inequalities' gap, but the change requires scientific evidence and new models of collaboration.

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