Centre for Innovation in Medicine
Position Paper
on Europe's Beating Cancer Plan

State of Cancer in Romania

The prevalence of cancer constitutes the second leading cause of mortality worldwide. In 2018, the overall fatality rate was estimated to 9.6 million individuals (WHO, 2018). Europe accounted for 23.4% of global cancer cases and 20.3% of total deaths (Bray et al., 2018). According to the WHO, 30 to 50% of cancer cases could be prevented (WHO, 2017). Notwithstanding, the lack of information and appropriate screening services, are amongst the main causes leading to the late detection of the disease (Insider, 2019). For instance, in 2018, Romania faced 83,461 new cancer cases and roughly 50,902 total deaths. The number of 5-year prevalent cases was further estimated to 202,230 individuals and, the most common and prevailing cancer types are still characterized by the following: lung, breast, colon and prostate (The Global Cancer Observatory, 2019).

In 2018, the most affected counties by new cancer cases were represented by Bucharest, Hunedoara and Iași. Furthermore, the incidence for every 100,000 residents, ranged from 82.9 to 699.7 individuals (INSP et al., 2019). Currently, Romania is facing a progressive increase in the number of cancer patients despite the fact that Romania's population is steadily decreasing (Medichub, 2018). The number of cancer deaths has doubled from 2009 to 2018 and, according to the Federation of Cancer Patients Associations, cancer kills approximately 140 Romanian individuals daily (Insider, 2019). Thus, in light of these observations, novel prevention and treatment strategies are urgently needed (InoMed, 2019).

Main challenges for cancer patients in Romania

The disease burden of cancer in Europe has been progressively increasing over time. The total health expenditure in 2018 equalled €103 billion, corresponding to €195 per-capita or accounting for a mean of 6.2% of the total national health expenditure budget. All European countries spent between 4 and 7% of the total health expenditure. Yet, significant differences were observed in light of per-capita health spending, ranging from 50€ in Romania to 500€ in Switzerland (Hofmarcher et al., 2020).

The *2014-2020 Romanian National Health Strategy Plan* acknowledged that socio-economic factors underlie important discrepancies in regard to the national health level and national health expenditure budget (Buţiu, 2016). 35.7% of Romanian citizens are currently at risk of social and/or poverty exclusion (Eurostat, 2019). Thus, poor healthcare infrastructure and unequal access to medical treatment and services are still persistent determinants. In light of cancer as the second leading cause of morbidity and death in the country, Romania also faces cancer care and control challenges, delays in early diagnosis, shortage of trained and specialised medical personnel and low capacity to supply long-term care (Popa, 2017).

At present, Romania provides public support and assistance to cancer patients throughout the *National Programme for Cancer* (NCP). The NCP is operated by the Health Ministry and the National Health Insurance Fund. Over the years, the program has continuously evolved (Popa, 2017). Work on cancer policies has progressively accumulated, illustrating the need for an immediate and organized response to cancer. A review completed in 2017 where, all policies included in the NCP between 2001 and 2016 were analysed, determined that Romanian policies are predominantly concentrating on screening and treatment. Per contrary, policies are focusing significantly less on cancer prevention, research and surveillance and not at all on palliative care (Popa, 2017). In fact, in 2017, roughly 160,000 cancer patients were in need of palliative care. Unfortunately, specialized centres were able to attend only 10% of total cases (Posirca, 2017). In addition, the NCP documents do not appear to be evidence-based. Empirical data on cancer incidence, prevalence and mortality is not considered. Furthermore, the NCP does not imply any reference to ensuring a fair and equal treatment for vulnerable patients. Similarly, health socio-economic determinants are not contemplated. Notwithstanding, the further examination of budget reports exposed a ten times increased in allocated budget between years 2001 and 2015. Nevertheless, these observations identified the allocation of the majority of financial resources on cancer treatment. Thus, whilst the total budget allocation on cancer has drastically increased over the years, a persistent lack of coordination between priority components and economic resources, led to a scarce financing of critical factors such as early detection and diagnosis of the disease (Popa, 2017).

Romania is amongst the top 10 European countries containing the highest mortality rates due to cancer (The Economist, 2019). Considering such evidence, in 2016 a comprehensive national cancer plan, the *Romanian National Integrated Multi-Annual Cancer Control Plan 2016-2020*, was developed. However, the plan was never implemented (InoMed, 2019). Yet, despite the nonexistence of standard national screening programs, the process for rolling-out screening programs for targeted breast, cervical and colorectal cancer patients was established (The Economist, 2019). Currently, Romania has a national mandatory state insurance coverage for individuals, consisting of the coverage for diagnosis, treatment and follow-up costs. Nevertheless, such coverage displays important inconsistencies. For instance, surgery represents a typical treatment for cancer in Romania. As such, patients diagnosed with rectal cancer, for example, are oftentimes directly getting surgery instead of being offered a combination of chemotherapy and radiation therapy. In addition, patients are generally hospitalized for weeks waiting to be performed a CT scan and, usually a few more weeks to get the results. Therefore, delays in diagnosis are usually frequent. The further absence of national cancer registries and the lack of strong cancer surveillance programs leads to a subsequent lack of awareness of the exact number of affected individuals in the country. At present, multidisciplinary committees are not common in Romania and, the usual scarcity of awareness, information and education amongst patients, as well as, the lack of accurately conducted informed consent, represent some of the barriers challenging Romania's experience towards cancer (Anghel, 2020).

For that reason, given the factors mentioned hereinabove, it is not surprising that other obstacles such as the shortage of medicine is not always high in the policy maker's list of priorities and agendas. According to the European Medicines Agency a medicine shortage "occurs when supply cannot meet demand at national level." Based on new reports conducted by the Romanian Health Observatory, over 2600 complaints about lack of medicines were filed with the National Medicines and Medical Devices Agency during 2015-2017 (Observatorul Român de Sănătate, 2018). Most of those medications are used for cancer care. During the study period, 24 medicines from the list included in the National Oncology Program were either facing shortages or being permanently withdrawn in Romania. A further 13 therapeutics were listed as at serious risk of discontinuance. As previously specified, the number of cancer cases in Romania may not be accurate due to insufficient screening and surveillance programs. Per consequence, the adequate number of medicinal products required cannot be acknowledged. Therefore, such lack of data may not cause direct shortages, but it might represent an issue when attempting to reduce supply deficits. Some of the reasons why these shortages may occur include parallel exports, lack of commercial incentives for manufacturers, inability to forecast demand for medicines and a reduced administrative capacity. Current initiatives to mitigate shortages of cancer medicines are short-term responses to a long-term issue. For that reason, the system needs to be proactive in recognizing when a shortage could occur (Observatorul Român de Sănătate, 2018; The Economist, 2019).

In general terms and despite the challenges presented, in recent decades cancer has seen prospective changes and improvement in the efficiency and accuracy of diagnostic procedures, surgery effectiveness, development of more precise radiation therapies and medical treatment (Aapro et al., 2017). However, cancer is complex and extremely heterogenous (Krzyszczyk et al., 2018). As a result, new more personalised approaches towards cancer innovation have emerged. The use of genomic information for cancer prevention facilitate the implementation of long-term management strategies that incorporate targeted screening and multiple preventive measures (InoMed, 2019). Personalized medicine (PM) improves treatment by progressively decreasing the recommendation of therapies based on blunt instruments such as chemotherapy, usually aimed at destroying all dividing cells in the body, with drugs designed to target molecules (Mukherjee, 2019). Nonetheless, although precision medicine is revolutionary, clinical practice is far from an ideal situation when it comes to testing biomarkers. The number of trials involving drugs without a biomarker is still higher than the number of trials concerning drugs associated with biomarker testing (InoMed, 2019). On the other hand, the insufficient number of diagnostic labs and test for precision, as well as the frequent absence of political support, low PM awareness and lack of information about new therapies to the public, are acting as further barriers (Chong et al., 2018). In 2020, a study completed by InoMed-Imas, concluded that 57.2% of the individuals participating in the survey had never heard about PM. In addition, 60.3% of the participants had never heard about immun-oncology and 56.2% did not know what the term biomarker stands for. Furthermore, 33.3% of the individuals perceive new therapies and personalized treatment as economically not accessible. Those participants strongly correlated cancer innovation with increased costs (InoMed-IMAS, 2020). In the context of cancer, knowledge is power. For that reason, education and awareness are critical for the prevention and prompt detection of the disease, as well as, it enables more accurate and informed treatment decisions (Southeast Georgia Health System, 2020).

Romanian citizens expectations from the EU Cancer Plan

Cancer patients in Romania face major challenges that need to be surpassed in order to ensure accurately designed prevention strategies, integrative care, support and rehabilitation. In this context, the Centre for Innovation in Medicine launched the following paper: *"A new vision for cancer in the European Union, based on data, technologies and human touch"*. Following the European Cancer Plan approach, this report aims to reflect on the patient as the new centre of a broader vision and the need of personalized and individualised approaches for prevention, early detection, further diagnosis, treatment and follow-up (InoMed, 2019). The primary scope of the *EU Beating Cancer Plan* is to enhance the prevention, detection, treatment and the management of the disease whilst inequalities between and within each MS are reduced (European Comission, 2020). Given that the EU Cancer Plan is patient-centred, the InoMed-Imas survey concluded in 2020 aimed to observe Romanian individuals perceptions towards the European initiative. The question asked by the interviewees was the following: *The European Commission will launch the European Cancer Plan in 2020. What do you think should be the main priority of this project?* From 1010 interviewed people across the country, 41% believe that the *European Cancer Plan* should mainly focus on increasing and improving early cancer prevention and diagnosis as, 78% of total participants consider that cancer can be prevented. In comparison, 21% of individuals prioritized the access of cancer patients to appropriate medical services and, 20% prioritized investments in medical research. On the other hand, actions such as increasing awareness and informing the population about cancer risks factors are indicated as a potential priority for 11% of the participants. A further proportion of 4.5% exposed other possible priorities whereas 2.1% of the individuals did not answered (InoMed-IMAS, 2020).

Cancer should be approached in a holistic manner. Prevention, diagnosis, treatment and palliative care are key phases that should be under control (Woods, 2017). However, it is important to note that a considerable percentage of cases can be prevented. Cancer prevention results essential in fighting the disease. Unfortunately, many cost-effective and affordable preventive steps at the same time, have yet to be adopted in many countries. Cancer prevention must be contemplated in light of other chronic disease prevention programs, in particular those in which cancer shares common risk factors such as cardiovascular diseases, diabetes, chronic respiratory diseases and alcohol dependence. Common underlying risks include alcohol consumption, tobacco use, reduced physical activity, overweight and obesity (Forman et al., 2018; WHO, 2007). On the other hand, innovation, optimization and the engagement of distinct stakeholders are key solutions in order to continue the *Beating Plan*.

For that reason and, in accordance with the information presented considering the current state of cancer in Romania, the major challenges and barriers faced by the patients and the Romanian citizens expectations from the *EU cancer plan*, a series of proposals will be presented hereafter.

Covid-19 indicated the need for change. Let's implement it in oncology

COVID-19 pointed to the need to transform the way the European Union relates to health. Although the Treaty of the European Union considers public health to be an area of competence of the Member States, mechanisms must be identified whereby health-related themes can benefit from more coordination, exchange of best practices, real-time communication between relevant actors, funding and innovation.

Through the initiatives already launched - the European Plan to fight cancer and Cancer Mission - cancer, must be the first disease that the European Union fights against, in a different way. Prevention, diagnosis, treatment and palliative care, the main pillars of the European Cancer Plan, are cross-sectionally intersected by a number of challenges: unequal access to services, digitalisation, cancer literacy, doctors' education, funding and the way the health system is organised.

The patient at the center of care

Personalized medicine has moved from the "nice to have" stage to the current stage, where any non-personalized approach to the cancer patient must be considered malpractice. No patient in the European Union should be treated any other way than considering all the data that can be generated about the tumor and its organism. Personalization of cancer management should not be limited to biomarker testing, instead, a broader personalised healthcare approach should be promoted. The PHC can be implemented on each level, as follows:

Cancer **prevention** must move from prevention based on the natural course of the disease and what the health system can offer, to a prevention based on the individual risk model of the person. In this context, we recommend the promotion of the *digital twin* concept, within the Cancer Mission, but aiming for a real-time implementation of the research results for each person. Translational medicine 4.0 must become a reality, we can no longer afford to keep the division between research and current medical practice. In this context, the development of cancer literacy must become a priority, for all age groups, through personalised educational and information programs.

Diagnosis. Any cancer patient should have a quick and accurate diagnosis. The development of comprehensive genomic testing offers the chance to obtain an accurate diagnosis, and for many types of cancers represents the chance to have a diagnosis and the chance of treatment. To turn comprehensive genomic testing into a reality for all patients in the European Union, several structural changes are needed to allow people access to this type of advanced diagnosis:

- development of genomic medicine infrastructure to ensure uniform coverage across the EU
- the development of molecular tumor boards at the EU level, which can facilitate patient access to telemedicine services (in the context that there are few Member States currently with the necessary skills)
- identification, at the EMA level, of ways for accessing treatments through clinical trials, compassionate use or off-label; establishing a single European register for clinical trials
- the creation, within the European Health Data Space, of a hub dedicated to genomic data on cancer; it must provide patients with the opportunity to donate their data, under informed consent and by respecting the confidentiality, security and safety of their personal data

- promoting research projects that are connected to the medical practice, in order to highlight the value of ‘omic’ sciences – genomics, transcriptomics, proteomics and metabolomics

Personalized treatment for cancer must become the rule, given the development of genomic medicine as well as the field of data in oncology. Genomic medicine has led to the emergence, development and approval in the EU of cell therapies (which provide the highest degree of personalisation in cancer treatment). Patients need equal access to these therapies in the Member States and not depending on the economic status or research and healthcare infrastructure.

On the other hand, data creates the conditions for the individualization of therapy, based on the biology of cancer, but also on the biological, demographic, psychographic characteristics of the patient. Each cancer patient, within a reasonable period of time, should benefit from a virtual twin to "test" therapies in silico before being administered in vivo.

Health systems at the center

Health systems need new models of governance, funding and evaluation of results in the fight against cancer.

- **Recognizing the role of new players: non-governmental non-profit organisations**

In addition to traditional players (public and private system), in recent years, especially in Member States where the development of health systems is not optimal, an important new category has emerged: non-profit non-governmental organisations. They contribute significantly (from the construction of hospitals, to the purchase of necessary equipment and medicines, to medical education programs and public policy actions). The role of these non-profit non-governmental organisations must be recognized at the level of health systems, ensuring equal access to decision-making, funding, and coordination of large-scale projects (funded by European funds) for the benefit of citizens and patients. This is important when it comes to access to innovation in oncology, which is lacking precisely in the Member States that have unreformed health systems.

- **Transfer of knowledge through twinning projects**

Equal access for citizens of all Member States to oncology medical services cannot be achieved as there are major differences in access to technology and knowledge between Western and Eastern Europe. The European Cancer Plan and the Cancer Mission promote knowledge transfer, in parallel with the creation of healthcare and research infrastructure, through institutional mentoring or twinming programs, between oncology centers of excellence and partners in Eastern European Member States.

- **Use of data through citizen involvement**

The European data space for cancer must promote data donation from European citizens, cancer patients or other patients, directly to a single hub at the European Union level, in order to avoid the existing barriers of the health systems (absence of electronic records, different standards, lack of involvement in EU projects on a voluntary basis of some Member States, etc.). This approach would have an even greater value in the context of obtaining data through comprehensive genomic testing, which is limited in many Member States due to lack of knowledge and technologies necessary to make it a valuable instrument.

- **Rethinking doctors' education and single European protocols**

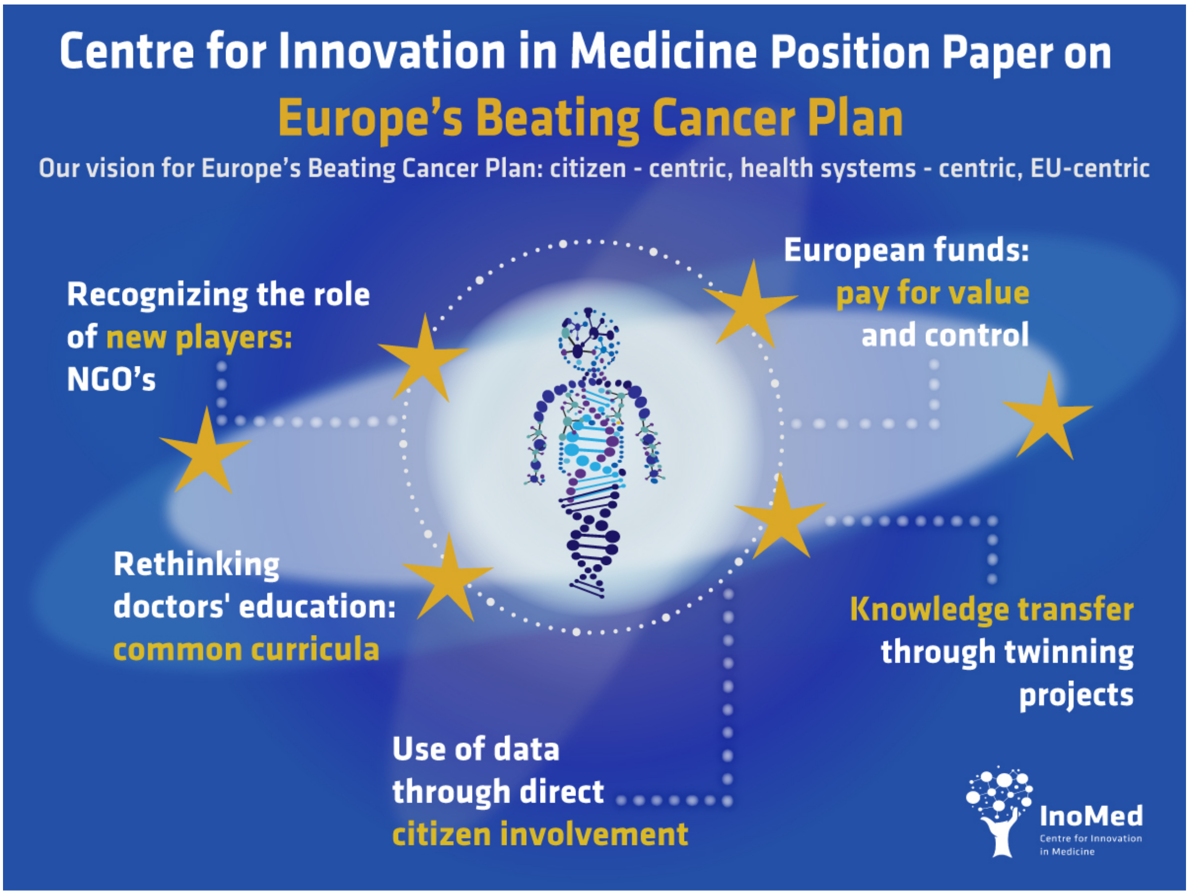
Oncology education needs to be rethought, by promoting a common European cancer curriculum, which should be compulsory in medical universities. Doctors in all Member States must have access to the same knowledge and a unique and continuously adapted understanding of scientific developments in order to be able to ensure patients that they will have the same type of access wherever they are treated in the European Union. In this context, the development of single European guidelines, through the involvement of ECO and ESMO, could help ensure the same high standard in cancer management and control in the European Union. Unified European standards on waiting time for a cancer patient for all the cancer care continuum.

- **European funds: pay for value and control**

The European funds allocated for the European Plan and Cancer Mission should be used at Member State level following the *pay for value* principle. Each entity accessing funds (public, private, non-profit) must bring value to citizens and patients through the projects it carries out. We recommend the implementation of a European Commission cooperation and verification mechanism for these projects, such as similar judiciary mechanisms implemented in Romania and Bulgaria. Prioritisation of funding and capacity buiilding support for Member States who experience lack of National Cancer Plans and strict monitoring of National Cancer Plan implementation.

The European Union at the center

Innovation must become a factor that unites Eastern and Western Europe, it must not be a factor that divides even more. No one should be left behind, let alone in the field of cancer.



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