

What could be a cancer mission objective if we join our forces in the fight against cancer?

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Abstract

The European cancer burden is growing rapidly, with an estimated 2 million deaths a year according to the latest research. As almost half of cancers are diagnosed after the age of 65, and considering the aging European population, a tidal wave of cancer cases will sweep across Europe within the coming decades. Without major action, the additional number of annual cancer cases is expected to rise from 4.2 million to 5.2 million by 2040. If we are to reach plateauing numbers by 2040 (as a minimum goal), this would require 0.75% annual reduction in risk and 1% reduction in risk of death. These challenges call for attack from various angles, coordinated efforts, rational strategies, initiatives throughout the cancer trajectory, activities to reduce inequities, and implementation of evidence-based measures. In order to defeat the societal challenges of cancer through innovation, Europe will need to join forces and connect the European Commission and the member states, politicians and citizens, industries and patient associations. A cancer mission should thus unite the public and patient viewpoint to the perspective of cancer professionals. The authors describe a plan that has been agreed upon among some of the major European Cancer organizations and associations. This plan uses a cancer mission as a tool and must deliver robust medical evidence to patients and doctors through high-quality research delivering sustainable and affordable strategies for prevention, treatment, and follow-up.

Keywords

Hematology–oncology, pediatric oncology, molecular oncology, epidemiology, prevention

Introduction

The European cancer burden is growing rapidly, with an estimated 2 million deaths a year according to the latest research. As almost half of cancers are diagnosed after the age of 65, and considering the aging European population, a tidal wave of cancer cases will sweep across Europe within the coming decades. Without major action, the additional number of annual cancer cases is expected to rise from 4.2 million to 5.2 million by 2040. If we are to reach plateauing numbers by 2040 (as a minimum goal), this would require 0.75% annual reduction in risk and 1% reduction in risk of death. These challenges call for attack from various angles, coordinated efforts, rational strategies, initiatives throughout the cancer trajectory, activities to reduce inequities, and implementation of evidence-based measures.¹

In order to defeat the societal challenges of cancer through innovation, Europe will need to join forces and

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connect the European Commission and the member states, politicians and citizens, industries and patient associations.^{2,3}

A cancer mission should unite the public and patient viewpoint to the perspective of cancer professionals. A certification of quality and truly integrated care should be the core of this endeavor, where new instruments such as artificial intelligence, machine learning, big data, molecular diagnosis, and single cell analysis will play a major role in a European plan to join our forces in the fight against cancer. This plan uses a cancer mission as a tool and must deliver robust medical evidence to patients and doctors through high-quality research delivering sustainable and affordable strategies for prevention, treatment, and follow-ups. The mission should inspire a generation by better addressing one of the primary and universal concerns: the common desire across countries and social groups to further combat cancer.^{2,3}

At a European level, cancer is a broad field of policy with, among other variables:

- Hundreds of individual tumor types, each with their own clinical presentations, molecular portraits, treatment strategies, and prognostic outlook
- Emergent science and technology impacting all treatment modalities and across all areas of the care pathway
- Deviation in health system organization and finance producing highly divergent outcomes

The list of potential missions that the European Union might therefore choose to apply in regard to cancer could be almost endless. Yet selection must be made. Temptation to choose a cancer mission based primarily on political considerations must be resisted if credibility and the widest buy-in from the expert community is not to be compromised. We therefore suggest that an EU cancer-related mission should be based on public and patient needs and implementation of evidence. In short, the evidence for the reason why a certain cancer mission was chosen, as opposed to other alternatives, must be given up-front and not left to others to fill in the blanks.¹ All should be provided with confidence that the correct mission was chosen while relying on the best information.

A war to defeat the rapidly increasing number of cancers in Europe will need attack from different angles, and may be divided into 3 parts.

Part I: To fight inequalities all over Europe for good prognosis tumors

The goal to reach 90% survival for some childhood cancers, hormone-positive breast cancer, prostate cancer, Hodgkin disease, testicular cancer, lip cancer, thyroid cancer, and uterine cancer is feasible only for a number of European countries.

First inequality: Access to prevention

Prevention is vital to cancer control and missions bring a unique option to integrate this fundamental aspect into the cancer trajectory. The potential to expand preventive intervention remains large and the evidence base for a number of measures has been summarized in the 4th edition of the European Code Against Cancer (ECAC) (<http://cancer-code-europe.iarc.fr/index.php/en/>).

The current situation in Europe is one of variable delivery of evidence-based preventive measures and research in this area may unlock unrealized potential. Cancer prevention has a broad scope, encompassing primary, secondary, and tertiary prevention, and research in this domain ranges from the submicroscopic study of the mechanisms of carcinogenesis to the supramacroscopic analysis of the causes of the causes, also known as the health social determinants. The latter are less relevant to pediatric cancer in the framework of primary prevention strategies. The focus in this age group needs to be on understanding what drives the predisposition to carcinogenesis in the child's host genome.⁴

Recent studies from France, the United Kingdom, and Germany have estimated that around 40% of cancers in these countries could be prevented and a Danish cohort estimated that 22% of deaths can be prevented if social inequalities are tackled.⁴ Established means of primary prevention include legislation and policies (e.g., on tobacco, alcohol, or hazardous agents, physical activity, and overweight preventive measures), vaccination programs (e.g., human papilloma virus and hepatitis B), and education about healthy lifestyles and behaviors (e.g., tobacco, alcohol, diet, and UV exposure), as well as other risk-adapted preventable pharmaceuticals (e.g., tamoxifen and aspirin). By cancer type, a proportion of 75% to 100% of all cancers of the lung, cervix, esophagus, oral cavity, melanoma, and stomach are suggested to be preventable as a consequence of changes in established risk and protective factors in Europe; similarly, 25% to 74% of all colorectal, bladder, kidney, liver, uterus, pancreas, and breast cancers are potentially preventable.

Primary prevention synergistically benefits other non-communicable diseases by reducing exposure to shared risk factors and creating healthy environments for current and future generations, and will likely generate knowledge of relevance for intersectorial policies related to city planning, transportation, food, and healthy life.

Other areas that merit interest are socioeconomic differences in cancer incidence and mortality across Europe, even within countries, that cannot be explained by behavioral risk factors alone.⁴

Furthermore, there is a lack of surrogate biomarkers for cancer to provide an early read-out of biological activity in early-phase trials and predict efficacy during late-phase

studies. This could be addressed by pooling biobank resources from trials across European partners and linking with the translational expertise available in biomarker discovery and validation. Better identification of high-risk populations would also enable smaller, less expensive, and more efficient clinical trials.

Secondary prevention through organized screening programs can significantly reduce mortality from breast, cervical, and colorectal cancers, as well as incidence of cervical and colorectal cancers; in Europe, however, implementation of secondary prevention is scattered, as recently assessed. For cancer types where effective screening strategies have been established, development and evaluation of strategies for risk stratification would help to provide more effective, targeted screening and early detection.

Developing and evaluating more sensitive approaches to early cancer detection based on noninvasive or minimally invasive biospecimens and imaging methods through research studies has an unrealized potential that may help attain our goals.⁵

Tertiary prevention refers to care aimed at reducing morbidity, disability, and risk of second primary cancer, as well as at restoring function and improving quality of life and participation in society. Evidence-based successful interventions and guidelines for effective management of symptoms will be crucial to improve patients' everyday life and may influence recurrence and prognosis.

The *ECAC* is an integrated instrument for cancer prevention that informs the general public how to avoid or reduce exposures to established causes of cancers, to adopt behaviors to reduce cancer risk, and to participate in vaccination and screening programs under the appropriate national guidelines. It also acts as a guide to aid development of national health policies in cancer prevention, as has been shown by the adoption of the *ECAC*-proposed structure in the comprehensive National Cancer Plans of several European countries.

Research is required to understand the factors that hamper their implementation within health care systems and in the community. In 2018, the international and multidisciplinary consortium Cancer Prevention Europe was created to develop world-class prevention research to be translated into effective cancer prevention guidelines and policies at the national and international level.

Second inequality: Outcomes

The survival difference between Western and Eastern countries and between Northern and Southern Europe is almost 30%. We should reach the same results all over Europe over the next 10 years. Furthermore, the role of member states, as well as regional and national governments, should be enhanced by acknowledging them as major actors. In order to reach this major objective, we should set up at least one Comprehensive Cancer Centre

(historical or within a university hospital) in each country, while in countries with a large population, we should define a Comprehensive Cancer Centre for every 5 million inhabitants. We should also define Networks around Comprehensive Cancer Centres to be able to provide the same survival expectations to all patients, regardless of the hospital in which they receive treatment.² Networks explain why we need a cancer center for every 5 million inhabitants in large countries.

Based on more than 10 years of operation of the Organisation of European Cancer Institutes (OECI) Accreditation and Designation Programme,⁶ and seeing the evidence of improvement in cancer care and treatment processes in centers, the Programme may be the major contributor to the creation of new Comprehensive Cancer Centres and the accreditation of all Comprehensive Cancer Centres in Europe (with the probable exception of Germany and Austria, which have their own national quality certification systems). In order to achieve these objectives, OECI should lead development in the following areas by:

- Extending the OECI Accreditation and Designation Programme to all Comprehensive Cancer Centres in Europe except for Germany and Austria (the Programme is well on the way to achieving this)
- Building a consultancy/advisory arm of OECI whereby we use the expertise we have amassed to help hospitals and other institutions become well-functioning cancer centers and networks that integrate care, education, and research
- Establishing a Programme of accrediting cancer centers based on a Network throughout Europe, which fosters improvement to patient outcomes and promotes better cooperation among cancer centers
- Developing better benchmarking systems across Europe (in connection with the European Joint Actions and the ISPRA European Joint Research Centre) so that improvements in the quality of cancer care can be consistently and objectively tracked, for the information of patients and policymakers⁷

These areas of development will require investment beyond the usual operational resources of the Accreditation and Designation Programme. We can obtain expertise through OECI's constituent or affiliated organisations.

The benefits of this work for patients and policymakers would be as follows:

- The creation of more cancer centers in Europe, where existing clinical expertise is brought together with research expertise, and innovations in cancer care and cure are accelerated into clinical practice
- The cancer centres so created would then network with other hospitals serving cancer patients to ensure consistency across geographical areas

- Patients would be empowered to identify accredited centers for high-quality care and to measure and compare quality indicators across health care providers
- Policymakers would have increased benchmarked data across member states to identify areas for improvement

Third inequality: Access to early diagnosis and screening

Cervical screening clearly reduces cervix cancer mortality, which can be eradicated through a combination of vaccination and screening. Colorectal mortality can be reduced by 20%–30% with stool test screening. Breast cancer screening allows us to find small tumors that are easily curable.¹

The ability to identify the disease at the earliest stage possible allows for treatment of the tumor before it becomes advanced. A European strategy for early cancer detection when small tumors may be cured by surgery \pm radiotherapy will reduce the economic burden and increase survival all over the European community.

With the growing demand for high-quality cancer care, we need to ensure that we are focusing on what offers the greatest benefit to patients. Based on the theory of value-based healthcare, health systems should maximize patients' outcome, defined as the health outcome per dollar spent. Surgery is still the first treatment to cure cancer. Radiotherapy is also central in cancer cure.⁸

Fourth inequality: Access to innovation, new instruments, and new drugs

In order to define a new standard of care, it is paramount to optimize clinical research. It is therefore crucial to establish an attractive environment for clinical research, commercial relationships, and drug development. The process should be balanced by an independent, noncommercial, and robust clinical research program for the management of patients in clinical settings so as to be able to recommend access to therapeutic strategies based on solid foundations. We should share our data using artificial intelligence, machine learning, and big data, but we should also link centers in rich countries with eastern and southern European ones to allow training, exchange of students, and cooperation to implement new techniques.⁹

Access to new and innovative medicines remains one of the most significant inequalities across Europe. Patients with cancer currently face the paradox of life-saving new medicines becoming available in Europe, yet not accessible to them, depending on which member state they reside in. While all cancer medicines must be authorized by the European Medicines Agency, based on evaluation of safety and efficacy data from clinical trials, for their marketing approval, health technology assessment (HTA) and pricing

and reimbursement (P&R) decisions are not centralized.¹⁰ The therapeutic value of innovative medicines for patients, healthcare systems, and societies is determined by HTA. It is a valuable tool that can establish the real value of medicines, taking into consideration not only clinical impact, but also the quality of life (QoL) and social and societal impact. Maintaining or improving QoL can allow many patients to return to work and hence, in conjunction with extended survival, it can confer economic benefit to both patients and society. In the European Union, there are more than 50 national HTA bodies, all embedded in different institutional settings. Each member state decides individually which medicines should be reimbursed by the health systems, and at what price, attempting to balance the goal of improving access to innovative medicines with the need to ensure the sustainability of healthcare systems, and the efficiency of care. In this scenario, many cancer patients in the European Union cannot access life-saving medicines. The European Cancer Patient Coalition (ECPC), established in 2003, is Europe's largest cancer patient umbrella organization, with over 450 cancer patient organizations in 46 countries. The ECPC vision is a Europe of equality, where all European patients with cancer have timely and affordable access to the best treatment and care available throughout their life. The ECPC plays an essential role in Europe by effectively acting as the voice of patients with cancer. The ECPC has extensively advocated for HTA harmonization in the European Union.¹⁰

The ECPC white paper "Challenging the Europe of disparities," launched in 2015, called for a harmonized HTA relative effectiveness assessment as a potential to reduce workload, create efficiencies, and underpin speedier patient access to life-preserving medicines by reducing delays.¹¹ The ECPC has created momentum on EU cooperation in HTA during the process of amending regulation 726/2004, "laying down community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency," when the proposed amendments were voted by the European Parliament in March 2016. The ECPC response to the European Commission (EC)'s 2017 consultation on "Strengthening of the EU cooperation on health technology assessment" stated that increased EU cooperation will not only significantly reduce costs and duplication across HTA bodies, but decrease delays in access to innovative medicines, facilitate participation of patient organizations in the HTA decision-making process, and facilitate access to market.¹⁰

In January 2018, the EC set out a proposal on the joint work on clinical aspects of HTA, which are typically based on global evidence, while the nonclinical aspects remain at member state level. This framework is called the Joint Clinical Assessments (JCAs), which paired with nonclinical assessment would inform the real value of medicine for P&R at the member state level. The European Parliament

has already unanimously approved its position in February 2019 and strongly supports the EU JCAs. The challenge remains with member states. Up to now, what is established in the proposed EU regulation was not welcomed by all member states, several of which have expressed strong reservations in the mandatory uptake of the JCA reports. Patient involvement in the HTA at the national level must be mandatory, due to legal, ethical, patient, and social aspects, which are evaluated for P&R. It is increasingly recognized that patients can contribute to the HTA process in 2 areas: the experience of living with the particular condition that the new technology is intended to treat and preferences for general therapeutic approaches or specific attributes of the technology.¹⁰

Artificial intelligence (AI) and its many related applications (ie, big data, deep analytics, machine learning) have entered medicine's magic bullet phase.

Desperate for a solution for the challenges of cost, quality, equity, and access, a steady stream of books, articles, and corporate pronouncements make it seem like health care is on the cusp of an AI revolution, one that will finally result in high-value care.¹²

Final inequality: Legal protection for survivors

The French and now Belgian law, which enable children and adult survivors to forget their cancer history after 5 and 10 years, respectively, should be implemented at a European level.

Furthermore, value, inclusiveness, and collaboration should be the core principles of the vision of a mission. The community should go beyond the concept of curing cancer. "Optimal" relates to what matters to patients, not only in terms of cancer outcome in the broad sense, but also considering all other aspects that impact on patients' well-being and quality of life. The term "for all" highlights the need to be inclusive: on one side, ensuring that all patients, despite where they live and who they are, have access to the care they need, and on the other side, considering the whole cancer care pathway, ensuring multidisciplinary and multi-professional care, collaboration, and appropriate communication. Finally, "together" encourages stakeholders to build partnerships, covering the whole spectrum of optimal health: oncology societies, other health care professionals and organizations, healthcare providers, patients, industry, research organizations, and policymakers.

Part 2: To double survival for intermediate and poor prognosis tumors

The intermediate prognosis group of tumors includes colon and rectum cancers, head and neck tumors, urinary bladder cancers, kidney cancers, and lymphomas. The poor prognosis groups of tumors include stomach cancer, lung cancer,

liver cancer, pancreatic cancer, esophageal cancer, brain tumors, and some hematologic malignancies.

For those tumors, prevention and prevention of relapses will be a major priority and early diagnosis with or without screening a major goal to improve survival.¹

Advances in genomic research (and the reduction of cost of DNA sequencing) will allow us to stratify tumors and predict their prognoses. The addition of big data, artificial intelligence, and machine learning will allow new techniques for early diagnosis and to define prognosis factors.²

The creation of a European platform for telemedicine and e-learning, together with the specific patient right to privacy in Europe, will be an essential tool to strengthen prevention research and the new strategy, as well as to diagnose small tumors.² Innovation should be redefined. Indeed, producing multiple sets of complex data is not the challenge that lies in the appropriate understanding of the data and transforming those into therapeutic progress for patients.

However, a group of tumors with very poor prognosis and no major progress will still exist and for these we need innovation and wide access to personalized medicine and immunotherapy, the next revolution in cancer treatment.⁹

Access to innovation needs translational research from laboratories to the clinic. This does not solely refer to testing new drugs. Proof of concept in laboratories or animal models, the creation of start-ups, cooperation between these start-ups and major pharma, will be key to this. Benchmarking ourselves against the United States and China would bring better processes into Europe and quicker access to innovative treatments after positive clinical trials.⁹

Independent and academic clinical research is a key priority for major patient-centered questions informing the access process for daily treatments and ensuring long-term outcome research.⁹ Clinical trials remain the best available standards for changing practice. Modern clinical trials increasingly have innovative as well as complex designs that allow stepwise evaluation and insights from small patient sets to important lessons from single patients based on an integration of precision medicine. Whereas this development allows for small-scale studies, the actionable alterations may apply to small subsets of diagnostic subsets, which call for large-scale collaborations. Multiple challenges such as those related to precision oncology in selected groups of patients but also identifying appropriate combination, integration with other treatment modalities, as well as addressing patterns of relapse and resistance will require re-engineering the process from early drug development into care and access into real life to the majority of European patients, leaving no one behind. It will require new organization and mode of cooperation between all those involved, sequencing expertise in the process to the committed deliverables. This is up to that level of ambitions that the mission and the plan will subscribe.

By associating everyone, building on existing transborder solutions, clinical research, and access to innovation could be improved all over Europe with clear links between networks from rich countries and networks for countries where survival and quality of life have not reached average values, in comparison with other parts of Europe.

Over the years, the evolution of technologies as well as the integration of translational research into clinical trials have enriched existing datasets with biological and imaging data that continue to build up as complex trials continue to develop. Data sharing therefore cannot be dissociated from the evolving role of independent networks in society and in revisited healthcare systems.¹² The technological revolution has led to new types of clinical trials, generating different and multidimensional datasets that require novel bioinformatics solutions for appropriate interpretation. However, the fragmentation of clinical datasets across different commercial and noncommercial stakeholders is an impediment to knowledge development, notably to address the patterns of relapse and resistance to numerous multiple agents being made available, often with limited intrinsic values. Therapeutic progress calls naturally to swift exchange of datasets but existing competing forces at both the commercial and noncommercial stakeholders tend to protect these sets from hypothesized future research, which may or may not happen. Before anticipating what may be an optimal framework for data sharing, it may be valuable to develop views on what is the role of independent networks in the continuum of clinical research, to structure new datasets in a re-engineered environment.⁹ New types of datasets such as large screening platforms to address the biology of the cancer to late trials into healthcare systems, together with the collection of human biological material, force the various stakeholders to re-address completely their role in an ecosystem that is more interoperational, based on data agility. While data are infinite, biological samples are finite, and therefore sharing principles raise different challenges. The stakeholders must leave their comfort zone to create new workable trustworthy zones. The European Organization for Research and Treatment of Cancer (EORTC) has developed a data-sharing policy offering access to its collections: since 2001, 310 data-sharing exercises (recipients) conducted on 261 datasets have been shared 568 times. Leveraging existing datasets should be seen as an opportunity to pay tribute to patients who volunteered for clinical trials. New vision on existing datasets can lead to new hypothesis and innovation. Nevertheless, data-sharing has proven to be a challenging exercise. Prompted by the International Committee of Medical Journal Editors, many organizations have implemented data-sharing policies. The challenges raised by dataset holders lie in appropriate use of datasets and proposed methodologies by requestors, protecting ethics of sensitive information under the General Data Protection

Regulation. Managing activities such as data sharing is not cost-free, and it implements the paths for decision process. Finally, incentives to share data are often lacking and Comprehensive Cancer Centres are the best candidates to do this.⁹

It has been claimed that there is no regulatory or technical difficulty in sharing datasets, but the reluctance to share some or all of the datasets could be due to the lack of incentives and the fear of sharing. Whatever the solution might be, it is crucial that the scientific community tackles precisely the problems that are yet to be solved. Data sharing may be applicable to divergent datasets that contribute differently to the drug development process and to clinical research in general. The stakeholder role should be redefined according to a continuum in which the patient is at the center from beginning to end. A new type of dataset, generated in early or late clinical trials, should be placed in a public health improvement perspective and where datasets could be reinterrogated indefinitely in the context of the new science.

Personalized medicine refers to a medical model that tailors the therapy to the patient's molecular profile and other individual information. The principles apply to medicines as well as other treatment modalities, including surgery and radiotherapy. The concept though has specifically emerged due to the increased number of drugs targeting specific proteins responsible for a specific disease. The commercial promotion of genome-wide analyses has led to an increasing expectation among patients.⁹

On the other hand, there are numerous drugs authorized on the market, with limited knowledge on how to use them for dose, sequence, combination, and duration of treatment. Suboptimal administration of costly treatments may generate unnecessary toxicity for the patients and negatively affects national healthcare budgets. Thus, there is a need to investigate the best way to use medicines (applied research or treatment optimization).

In Europe, most of the clinical research dedicated to therapeutic innovations aims primarily at regulatory approval. Once a drug enters the common market, each member state determines its real world use based on its own criteria: pricing, reimbursement, and clinical indications.⁹

Such a regulatory approval-centered clinical research landscape may neglect patient-relevant issues in a real-world setting, such as comparative effectiveness of distinct treatment options or long-term safety monitoring.

There is call for reforming the current system to a truly patient-centered paradigm with systematically coordinated treatment optimization in conjunction with drug development and the EORTC Manifesto for a new approach for better medicine in Europe is an important document to help establish such treatment.

Europe in partnership with member states should establish treatment optimization research as an official and mandatory step in the treatment access path to market,

while ensuring this does not lead to further delays in patients' access to innovative treatment optimization.

National legislation should include provisions allowing for publicly funded international research to address collective therapeutic challenges. Member states should agree on a framework for joint optimization research whenever there is need for an international approach.⁹

The European Union's next mission-oriented Framework Programme for research and innovation, Horizon Europe, should provide funding opportunities specifically aimed at supporting treatment optimization and academic trials such as those of the EORTC.¹¹

Clinical research and access to innovation could also be improved all over Europe with clear links between networks from rich countries and networks for lower-income countries.

Cancer research is the first hope for patients with dismal prognosis. Success with immunotherapy is a direct consequence of mechanistic research achievements. European universities and research organizations should be helped to attract the best researchers and the ERC Programme should be a major tool in the cancer fight.

The cells of our body are constantly changing. But which alterations are part of healthy development and which ones lead to serious diseases? This is what the cross-national and cross-disciplinary initiative called LifeTime wants to explore. Leading European researchers and clinicians have joined forces to lay the foundations for tomorrow's precision medicine. While they are currently exploring the choice of the diseases on which the initiative will focus, it is essential to explore how its tremendous potential can best link to a cancer mission.¹³

Indeed, the new generation of scientists not only from Western Europe but in all EU member states could help to invest in the new emerging technologies around big data and artificial intelligence but also in chemistry, physics, mathematics, single cell studies, epigenetics, immunology, and biology to bring new mechanistic concepts to understand why some cancers have such poor prognosis and are so resistant to treatment.

The potential of single cell technology to map gene activity and to analyze data from many single cells individually instead of the average of many cells will provide novel insights into the development of diseases.¹³ The journal *Science* called these methods—and the contribution of LifeTime researchers to this field—"Breakthrough of the Year 2018."

New personalized disease models are emerging from organoids ("mini organs") obtained from the cells of patients and additional experimental technologies. Using these technologies, LifeTime researchers will track and decipher the changes in the activity of the genome in individual cells during disease and develop the appropriate treatment to correct the defects. Ultimately, LifeTime technologies should enable physicians to better diagnose

cancer and do so much earlier, to understand the molecular history of patients' tissues, to predict their future development, and to select optimal treatment for an individual patient.

Part 3: To include specific attention to pediatrics

Pediatric oncology is organized at both an international level (International Society for Paediatric Oncology [SIOP]) and a European level (European Society for Paediatric Oncology [SIOP Europe (SIOPE)]). SIOPE has a clear mandate to lead designated mission funding focused on the needs of children and adolescents with cancer. The pediatric cancer field is characterized by multiple rare types of cancer unique to this patient population with specific epidemiologic, biological, clinical, and policy considerations. Although individual types of childhood and adolescent cancers are rare, together they represent both a life-threatening disease and a major public health issue in Europe. With 35,000 cases and more than 6,000 children and young people dying every year,¹⁴ cancer remains the leading cause of mortality from disease in the pediatric population above the age of 1 in the region. Indeed, despite research progress that has enabled achievement of an overall 80% cancer-free rate at 5 years, there has been very little advancement for some types of pediatric cancers.¹⁵ In addition, inequalities in access to essential therapies account for differences in survival rates of up to 20% across Europe.¹⁴ Moreover, there are more than 300,000 European childhood cancer survivors (nearly half a million by 2020), two-thirds of whom experience adverse physical and psychosocial late side effects in adulthood,¹⁵ limiting their well-being and participation as EU citizens.

The rarity of individual pediatric cancers and their high collective burden often lead to limited market-driven innovation and an emphasis on cross-border academic cooperation to foster therapeutic progress. SIOPE has a long track record of research and clinical collaboration that goes back over 50 years. SIOPE represents the European professional pediatric hematology and oncology clinical and research community through its broad membership from 36 European countries. The SIOPE Clinical Research Council harnesses the expertise from 36 national childhood cancer societies and 19 disease-specific European clinical trial groups, facilitating state of the art research, education, and advocacy activities at the European level. SIOPE works in close partnership with the patient organizations Childhood Cancer International–Europe and Unite2Cure and has collaborative initiatives with multiple stakeholders including industry, regulators, and policymakers.¹⁶ As a continental branch of SIOP International, SIOPE activities are fully aligned with the global agenda.

With the support of project-based EU funding, the community has succeeded in building cross-border research initiatives. In particular, the EU FP7 project European Network for Cancer Research in Children and Adolescents (ENCCA) enabled the development of the long-term SIOPE Strategic Plan,¹⁵ which defines 7 key objectives towards achieving a substantial increase in the cure rate and the quality of survivorship for children and adolescents with cancer. The ultimate goal is to achieve disease- and late effect-free survival, with a medium-term vision of halving the deaths and halving the late effects burden in Europe by 2030. Integral to this vision are the following: fostering therapeutic innovation including for difficult-to-treat and refractory pediatric malignancies, eradicating inequalities in access to the best possible treatments and care that drive differences in survival across Europe, supporting full socioeconomic equality and participation of survivors in adulthood, and engaging in public policy to underpin all objectives.

The SIOPE Strategic Plan gives a detailed description of well-defined scientific, clinical, and policy objectives for children and adolescents with cancer as well as proposed implementation platforms to ensure translation into practice.¹⁵ Some are already operational but substantial progress has been constrained by lack of resources. Sustained public investment at the EU level could affect transformational change. It would enable delivery of the Strategic Plan and make life-saving differences for these patients. This research would contribute to synergistic areas with adult oncology that include but are not limited to basic science advancements and transfer of innovative cooperation models. The European dimension remains central to all efforts to address the urgent needs in childhood and adolescent cancers and to foster positive collateral benefits in other disease areas.

The SIOPE Strategic Plan and collaborative concepts thus provide a blueprint for an ideal Mission,¹⁷ with the following specificities:

- Being bold and inspirational with wide societal relevance
- Embracing a clear direction with targeted, measurable, and time-bound actions
- Consisting of ambitious but realistic research and innovative actions
- Upholding cross-disciplinary, cross-sectoral, and cross-actor areas
- Fostering multiple bottom-up solutions

As a collection of rare malignancies, pediatric cancer affects children and adolescents, adult survivors, and their families, and has negative repercussions for the European society and economy. These multifaceted issues can be addressed by a concerted European-level public investment into pediatric cancer research priorities defined by

clinicians and academia of SIOPE in cooperation with the parent and patient organizations Childhood Cancer International–Europe and Unite2Cure. Cooperative models and discoveries in childhood cancer can be highly relevant for the adult oncology field and other disease areas.

Conclusion

A cancer mission is an exciting opportunity to use the fight against cancer to re-excite the European public about what the European Union can achieve and re-engage them in EU activities. Prevention, early diagnosis and screening, fundamental research, clinical research, outcomes research, and patient perspective are the most important chapters to be included in a mission where both adult and pediatric tumors should be a priority.

A cancer mission must necessarily include a focus on pediatrics centered on 3 major goals:

1. Fighting inequalities all over Europe for good prognosis tumors
2. Doubling survival for intermediate and poor prognosis tumors
3. Including specific attention to pediatric cancers

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