European Commission

FORESIGHT

Mission Area: Cancer

Foresight on Demand
Brief in Support of the
Horizon Europe Mission Board

Research and Innovation

Mission Area: Cancer. Foresight on Demand Brief in Support of the Horizon Europe Mission Board

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Mission Area: Cancer

Foresight on Demand Brief in Support of the Horizon Europe Mission Board

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Foreword

In 1969, the first human set foot on the moon. "A small step for a man. A giant leap for mankind" was what audiences across the world heard. The Apollo mission showed the world what directed science, research and innovation could make possible. It proved what humankind can achieve in not even a decade, by setting a clear goal, which manages to capture public imagination, and by investing the necessary resources into it.

The mission approach, directing and combining different resources and actors towards a common goal, is becoming a key element of transformative R&I policies in a world of increasing global challenges. The Commission introduced missions as a new instrument in Horizon Europe and appointed Mission Boards to elaborate visions for the future in five Mission Areas: Adaptation to Climate Change, Including Societal Transformation; Cancer; Healthy Oceans, Seas, and Coastal and Inland Waters; Climate-Neutral and Smart Cities; Soil Health and Food.

EU R&I policy missions are ambitious, yet realistic and most of all desperately needed in light of today's challenges. They endeavour to bring together policies and instruments in a coherent, joined-up approach, and tackle societal challenges by setting and achieving time-bound, measurable goals.

In September 2020, the Mission Boards handed over their reports to the Commission. Five foresight projects carried out in close interaction with the Boards supported their work. These projects provided advice on trends in the respective areas, elaborated scenarios on alternative futures, scanned horizons, and made aware of weak signals, and emerging new knowledge and technology, helping the Boards imagine how the future may evolve and how to shape it.

With the launch of the five Missions in Horizon Europe, we are making this valuable work available for the broader public. I am confident that the comprehensive material, creative ideas and exciting examples in the Mission Foresight Reports will prove useful to all those engaged in the Horizon Europe Missions.

Jean-Eric Paquet
Director General
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BACKGROUND AND ACKNOWLEDGEMENTS

Missions and Horizon Europe

The notion of "missions" as one of the novel cornerstones of Horizon Europe, the European Framework Programme for Research and Innovation 2021-2027, was introduced in the course of the programmatic debates about the orientation of the EU's future R&I policy, in particular through the Lamy Report. This report, which was presented in July 2017, recommended adopting "a mission-oriented, impact focused approach to address global challenges". Missions would serve as targeted and longer-term ambitions around which to build a portfolio of Horizon Europe research and innovation projects.

The idea of mission-oriented research and innovation was subsequently further specified through various studies and reports, in particular also by two reports by Mariana Mazzucato, which inspired policy debates at European as well as national level. In line with this preparatory work, missions shall have a clear R&I content EU added value and contribute to reaching Union priorities and Horizon Europe programme objectives. They shall be bold and inspirational, and have scientific, technological, societal and/or economic and/or policy relevance and impact. They shall indicate a clear direction and be targeted, measurable, time bound and have a clear budget frame.

As a result of debates at European level, the European Commission (EC) proposed five initial broad Mission Areas in autumn 2018. This initial list was subsequently adjusted in interaction between the EC and Member States, leading to five Mission Areas:

i) Adaptation to climate change including societal transformation,
ii) Cancer,
iii) Healthy oceans, seas, and coastal and inland waters,
iv) Climate-neutral and smart cities, and
v) Soil health and food.

As spelt out in the specific request, these missions will be anchored in the pillar "Global Challenges and Industrial Competitiveness", but may well reach out to the other pillars of Horizon Europe.

Within each of these Mission Areas, a limited number of specific missions shall be defined in the context of the next framework programme, with a first set of missions to be launched in 2021. To this end, the EC has established Mission Boards of about 15 outstanding members for each of the five Mission Areas. Mission Board members were appointed in August 2019 and they started their work in September/October 2019. They presented their recommendations to the EC at the EU R&I days in September 2020. The titles and descriptions of the actual EU Missions launched by the European Commission are found here: https://ec.europa.eu/info/research-and-innovation/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/missions-horizon-europe_en

Foresight on Demand

Against this background, a request for services with five lots was put out under the Foresight on Demand Contract (FOD) of DG R&I to support the five Mission Boards. The five projects started in autumn 2019. For around a year they worked for and with the Mission boards, providing foresight expertise and methodology. They were aimed to feed the reflections of the Mission Boards with future-oriented inputs on challenges and options in the respective areas.

With the launch of the missions in Horizon Europe, this valuable work is now public as a part of the Foresight Papers Series. The five mission foresight reports give a detailed overview of the alternative futures, and the future perspectives in science and technology in the five mission areas build part of the basis for the considerations of the Mission Boards. They may serve as background material and a source for examples and idea for coming mission activities.

Mission foresight project "Cancer"

The foresight project "Support to the Mission Board Cancer" (Framework Contract 2018/RTD/A2/PP-07001-2018 – LOT1) focused on the contribution of foresight knowledge that should inform the

Mission Board strategies, and more specifically to support the reflections of the Mission Board concerning the identification of missions within the broader theme “Cancer”.

The EU has launched several strategies and programmes to fight and prevent cancer and to help cancer patients. Thus, such a Horizon Europe Mission should contribute to the goals of the Europe’s Beating Cancer Plan: “*A mission in this area will help set common goals aiming to reverse these frightening trends in cancer. By joining efforts across Europe, more people would live without cancer, more cancer patients would be diagnosed earlier, would suffer less and have a better quality of life after treatment*.” (https://ec.europa.eu/info/horizon-europe-next-research-and-innovation-framework-programme/mission-area-cancer_en)

The work was carried out in interaction with the Mission Board members and responsible Commission services. They provided important input to this report and the project team would like to thank all contributors. The report documents the scoping of trends and drivers for cancer, two future health scenarios targeted at fighting cancer and roadmaps of events and milestones in the future of fighting cancer. It formed part of the basis of the vision for a Horizon Europe Mission on cancer, outlined by the Mission Board in “Conquering cancer, mission possible” (2020).

MISSION AREA: CANCER.
FORESIGHT ON DEMAND BRIEF IN SUPPORT OF THE HORIZON EUROPE MISSION BOARD

INTRODUCTION

The activities reported in this foresight brief reflect the foresight knowledge in support of the Mission Board and its strategies towards a consolidated mission within the broader goal to fight cancer in the European Union. The support of the FOD Cancer project team consisted of several interactive events with the Mission Board, horizon scanning, and the provision of three specific reports. This synthesis report gives a concise overview of the deliverables, which are provided in full as annexes.

Based on the “Scoping Paper” (Annex I) this synthesis report demonstrates the challenges for future cancer research. It summarises some major aspects behind the urgency of the cancer topic – not only medical aspects but a broader spectrum that includes prevention, prediction, care, diagnosis and treatment as well as other economic and social aspects. The report is the result of a targeted literature review of recent documents where the future of the fight against cancer is discussed. The main goal of the review was to identify and assess both consolidated trends and drivers, and other phenomena at the periphery that are likely to have impacts on the future of cancer. Mission Board members revised the report and gave additional inputs online (since an onsite scoping meeting had to be sacrificed to meet the COVID-19 containment measures).

Building on the outcome of the revised Scoping Paper, two scenarios were developed discussing diverging directions of cancer development and the measures to fight cancer (Annex II). The two future health scenarios were based on scenarios from an earlier EU-funded project entitled "FRESHER - FoResight and Modelling for European HEalth Policy and Regulation", which aimed to identify future research policies to effectively address the burden of noncommunicable diseases (NCD) using emerging health scenarios with a time horizon up to 2050.

Within the online scenario workshop with members from the Mission Board on ‘Fighting Cancer’ and members from the European Commission, the two FRESHER scenarios were discussed, revised and feedback for desirable futures with regard to fighting cancer was collected. The two scenarios are briefly presented in this report as well.

Under the impression of the two scenarios, the Mission Board members and EC representatives were guided by the FOD Cancer team to discuss online in five focus groups - in parallel - different stakeholder perspectives with regard to desirable milestones that may be achieved in the future to make prevention, diagnosis, treatment and survival of cancer more effective. These stakeholder perspectives comprised “Members of the European Parliament against Cancer”, “General Practitioners”, “Pharmaceutical Companies”, “Patient Organisations”, and “Survivors”. Out of these discussions, the FOD team developed three roadmaps (Annex III): milestones for prevention, milestones for diagnosis and treatment, and milestones for survivorship. The roadmaps are also briefly summarised.

OVERVIEW OF THE “SCOPING PAPER ON TRENDS & DRIVERS FOR CANCER”

Cancer is the second leading cause of death worldwide and accounts for 9.6 million globally in 2018. With more than 3 million new cases and 1.7 million deaths each year, cancer is the most important cause of death and morbidity in Europe after cardiovascular diseases. There were an estimated 3.9 million new cases of cancer and 1.9 million deaths from cancer in Europe in 2018. Almost half of the patients diagnosed with cancer are passed 65 years old. Even though survival rates are also increasing, demographic change will contribute to an increase of incidents and deaths. Prognostic calculations expect that the annual diagnostics of currently 4.2 million will increase to 5.2 million in 2040 in Europe.

Cancer refers to any one of a large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue. This arises from a change in one single cell and may be started by external agents and inherited genetic factors and can affect almost any part of the body.

The transformation from a normal cell into a tumour cell is a multistage process where growths often invade surrounding tissue and can metastasize to distant sites. These changes can result from the interaction between a genetic factor and external agents such as the chemicals in tobacco smoke, or radiation, for example ultraviolet (UV) rays from the sun.[1]

The report which we summarize here, is designated to give an overview on three documents issued by the FOD Cancer team to support the current Mission Board on Cancer in reflecting the trends, drivers, developments and challenges influencing (1) our understanding of cancer, future approaches to (2) prevent, (3) diagnose, and treat cancer and finally (4) provide support for the survivors.

As the matter is very complex, the scoping report can only point out a few flash lights depicting some pressing issues and trends not only health policy makers have to take into account in order to turn the fight against cancer and the support of survivors into a mission. Still the scope of the report is quite broad. It explains latest trends in **medical innovations** – from the technological but also from the social side.

Innovation in prevention, detection, treatment and for survivors of cancer are necessary and much research is going on to support the fight against cancer with innovation. The demographic trend of aging and shrinking societies in Europe and other countries in the world (opposed to still young and increasing populations in other parts of the world like Africa or Asia) has a large impact on the development of the number of cancer cases. In Europe, people are getting older, and more often reach very high ages over 100 years.

We also see a pseudo-informed society, in which people inform themselves via internet and social media.
Presently, the most effective cure to fight cancer is surgery. However, medical innovations and other activities focusing not only on treatment but also on prevention, diagnosis and survivorship will become more important in the future and are expected to be more effective.

Innovations for the health sector concern new ways of:

- Prevention: such as human genome mapping, genomic vaccination, personalized medicine
- Diagnostics: such as companion diagnostics, smart medical devices such as smart phone labs, artificial intelligence, machine learning and augmented reality

[1] https://www.euro.who.int/en/health-topics/noncommunicable-diseases/cancer/cancer

- and imaging: functional magnetic resonance imaging, molecular imaging, theranostics
- treating patients: for example, by gene editing, gene therapy, precision oncology, immune therapy, regenerative medicine, organoids, organ transplantation and 3D modelling in surgery, microbiota-based therapy; minimal invasive and robotic surgery, biohybrids

and also

- social innovation and new societal practices (e.g. in care, new business models, living together in a new way, administrative innovations etc.).

For all of the developments and initiatives mentioned above, hardware (e.g. medical technology and devices including advanced imaging technology, robotics), software (new applications of software, steering, sensoring, personal data use for research, "big data" approaches, artificial Intelligence etc.), pharmaceuticals and other approaches or combinations are under development. It is also important to remember that innovations will only be realized if there is a good cost-benefit ratio, and if they are accepted in the system.

Nutrition has an impact on the general condition of human beings, on the development or prevention of cancer and in supporting an active immune system or condition that supports curing cancer and thus survival. **Agriculture** and the way our food is produced play a large role in what we eat, what is available, how it is transported, packed and which ingredients or pollutants are included. It also plays a role how "secure" the food is in terms of availability (enough nutrition elements) and unwanted by-products. Invisible mildew, rotten or old food, pesticides, heavy metals or even radioactivity in our food can contribute to the development of cancer in humans. The microbiome of our land and later our food can also include substances, viruses or bacteria that have cancerous effects.

Chemicals, plastics, pesticides and fertilizers from agriculture (and industrial products) end up in our food - and we come into contact with these substances on farms, with our food or just when being outside "in nature".

Plasticizers like adipates and phthalates are often added to brittle plastics like polyvinyl chloride to make them pliable enough for use in food packaging, toys, and many other items. To sum up, there are still many opportunities, for finding alternative ways of transporting, logistics, avoiding fertilizers, pesticides etc. or replacing chemical substances with less harmful ones. Counter developments such as **certified organic farming** and more awareness raising for **healthy food** are optimistic developments with growing impact pointed out in the report, however the quantities of processed food are also growing. Some pessimistic aspects are that **undernourishment and malnutrition** in deprived areas of the globe have still not been contained and famine catastrophes are still sparking from time to time. The report points to several EU and WHO action plans to encounter the negative developments.

Many **innovations in food** (e.g. new cooking methods) and in food retail policies (e.g. labelling and taxation of unhealthy food) may need particular attention.

Somewhat related to nutritional aspects are also **environmental aspects**. The report points out that many scientific studies have recognised environmental factors as being relevant for cancer occurrence and also for promoting health. Substances in the environment causing cancer are generally labelled **carcinogens**. The US National Institutes of Health regularly update a long list of carcinogens that contains several hundred entries (US National Institutes of Health 2016).[2] Being exposed to carcinogens does not necessarily mean that a person is developing the disease. A number of complex factors, many of which are not yet scientifically researched, have to come to together, such as certain quantity and duration of exposure, genetic disposition, other environmental factors, life style. Cancer risk factors related to environment in a broader sense, include exposure to biological agents (infections), to synthetic chemicals through work or consumer products, and lifestyle factors such as exposure to sunlight, poor diet, being overweight, tobacco use and consumption of alcohol.

[2] https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html#toc1

In the context of environmental health factors, the report mentions also **urban development** as a critical determinant for cancer related aspects. Urbanization is associated with many health challenges including cancer and unhealthy life choices such as **tobacco use and alcohol abuse**. City dwellers are more exposed to stress through road traffic accidents, injuries, violence and crime. The urban poor suffer disproportionately because they often have less access to proper health care and prevention measures, because the health service infrastructure is insufficient in the poorer urban areas, but likely to be more frequented.

Apart from the above mentioned aspects on the micro level, the report discusses the significance of **access to European health systems** with regard to public health and cancer. Along with many variations in the organisation of health systems, the provision of primary and secondary care and the positioning of cancer diagnosis and care therein differs greatly across the Member States. In most countries, the **cancer screening programmes**, if available, are arranged at the level of primary care (general practitioners and other primary health services**). The diagnosis and care** are then performed at the level of secondary (specialist) care, which can be accessed by patients either directly or through a referral from primary care if the gatekeeping system is imposed. Overall, the health **expenditure on cancer care** has doubled from €52 billion to €103 billion in the EU between 1995 and 2018. The dramatic increase is caused by, among others, adoption on innovative treatments and subsequently increasing expenditure on cancer medicines: from €14.6 billion in 2008 to €32 billion in 20182. The costs of inpatient cancer care have, on the contrary, decreased due to a shift of cancer care to ambulatory and outpatient settings. At the same time, total country expenditure on health as well as cancer expenditure are largely disparate across the Member States.[3]

While every European MS can develop and adopt national clinical guidelines for cancer diagnosis and treatment, much progress has been achieved in developing **European clinical guidelines**. The European Society for Medical Oncology has developed a large database of clinical guidelines for various cancer types, which are available for clinicians through a simple and comprehensive online system[4]. To enhance harmonisation, ESMO and other European organisations are putting efforts into development and implementation of various platforms for knowledge exchange such as joint multi-country trainings, conferences, and workshops.

Among the social aspects with high significance to the prevalence of cancer, the report focuses on **inequity.** Cancer is, as many diseases, related to **socioeconomic differences**. Advances in medicine increase survival but unevenly between countries, regions and individuals. Inequalities are complex to tackle. In cancer survival, socioeconomic differences have been reported in many cancer sites and populations, with patients from lower socioeconomic groups having poorer survival. Differences between socioeconomic groups in the stage of disease at diagnosis and in access to optimal treatment clearly explain at least part of the association between social deprivation and cancer survival.

Socioeconomic factors play a strong role already in cancer prevention. It is often stated that **preventing cancer** is the most neglected part of the cancer continuum, lacking both financial support and public attention. Current estimation is that in Europe over 40% of all cancer cases could be prevented and among preventable cancers about 50% are due to tobacco. Those countries who have managed to reduce smoking prevalence, have demonstrated steep declines in lung cancer mortality.[5]

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[3] Hofmarcher, T., Brådvik, G., Svedman, C., Lindgren, P., Jönsson, B., Wilking, N. Comparator Report on Cancer in Europe 2019 – Disease Burden, Costs and Access to Medicines. IHE Report

[4] An overview of clinical guidelines is available at https://www.esmo.org/guidelines

[5] https://www.europeancancerleagues.org/ecl-annual-meeting-2019/ accessed 27.1.2020

Finally, socioeconomic determinants are also important for the **survival from cancer** that in Europe has increased steadily. However, as several recent studies have shown, survival in Eastern Europe was generally low and below the European mean, particularly for cancers with good or intermediate prognosis, whereas survival in the Nordic countries remained highest.

The report shows that advances in science are able to point out more and more carcinogenic substances and behaviours and at the same time are making great progress in understanding the causes of cancer. The report goes on making reference to cancer-related factors such as agriculture, nutrition, environment and urban developments. The subsequent chapter discusses the (economic) burden for cancer on our health systems and workplace and the difficulties of national programmes to cope with it. Finally, the report points out that cancer is a societal as well as a personal issue and that coping strategies are very much dependent on the socio-economic context. This means that even across the EU there are fundamental differences of countries (and also within countries), the quality of their health systems and the patients' accessibility to proper prevention, diagnosis and treatment, as well as care for the survivors. These differences are reflected in mortality rates as well as long-term cures, related to inequity and prosperity. Obvious differences exist also on the policy side. Some governments still have not been participating in population-based cancer registries, even though these tools can be used to evaluate the impacts of cancer prevention strategies and the effectiveness of health systems for all cancer patients. It this is a necessary task of the near future by all EU member states to find some common approaches in granting every citizen equal access to the latest advances in prevention, diagnosis and treatment, no matter from which country the patient comes from or what her/his socio-economic status is.

Schütz J, Espina C and Wild CP (2019) Primary prevention: a need for concerted action. Mol Oncol 13, 567–578 and presentation Schütz J Future of cancer prevention research in Europe 28.11.2019 https://www.europeancancerleagues.org/ecl-annual-meeting-2019/ accessed 27.1.2020

Thun, Michael, et al. Stages of the Cigarette Epidemic on Entering Its Second Century (2012). Tobacco Control, vol. 21, no. 2, 2012, pp. 96–101., www.jstor.org/stable/41515999. Accessed 27 Jan. 2020

OVERVIEW OF THE ”CANCER SCENARIOS”

This section summarises the adapted two future health scenarios with the aim of tailoring them specifically to possible futures in the fight against cancer. The original scenarios were developed in an earlier EU-funded project entitled "FRESHER - FoResight and Modelling for European HEalth Policy and Regulation" (https://www.foresight-fresher.eu/), which aimed to identify future research policies to effectively address the burden of noncommunicable diseases (NCD) using emerging health scenarios with a time horizon up to 2050.

Within a scenario workshop with members from the Mission Board on ‘Fighting Cancer’ and members from the European Commission, the two FRESHER scenarios were discussed and feedback for desirable futures with regard to fighting cancer was collected.

The specific objectives of the workshop were to

- produce sketches based on the Fresher scenarios with focus on the future of cancer (prevention, diagnostics & treatment, survivorship)
- outline desirable futures with regard to cancer (prevention, diagnostics & treatment, survivorship)

in order to support the Mission Board to identify future-oriented topics from multiple perspectives for their mission.

In a final step, the gathered ideas and future outlooks were discussed with experts of the project team and the scenarios were further developed with a special focus on the fight against cancer. The resulting final scenarios are presented in the scenario report.

1 Scenario “We will health you”

1.1 General Picture: Economy, Politics, Society

We celebrate the year 2050. Today’s priority is to guarantee access to adequate health care for all European citizens in a timely manner in a growth-oriented society. Governments and the private sector collaborate closely to maintain a healthy workforce and to keep Non-Communicable Diseases (NCDs) under control, with the aim of ensuring the continuation of economic productivity as well as the sustainability of the healthcare systems. Thanks to big data, pattern recognition, public and private investments effectively influence citizens’ behaviour towards healthy lifestyles. When meeting the “general standards“ of a healthy lifestyle, citizens get a reward and their insurance is kept at stable costs. By offering healthy working environments and care services, employers compete to attract talented, motivated and well-educated people. Employers are increasingly held accountable in case of not providing working conditions that are optimal for health.

Ambient 24/7 surveillance measures and a high degree of regulation and control of individual behaviours are made possible through personal implanted chips and other telemonitoring devices.

1.2 Innovations for “Healthing you”

In healthcare and for fighting cancer, this means, it is easy and normal to screen, monitor, gain data, or process data - or have them processed automatically.

EU countries enjoy a new era of economic growth and social progress founded on education, innovation and full employment, thanks to important government action, and the “European model”, which stands out in an increasingly competitive world. Tracking Apps are not only to monitor economic activities but also sports, visiting a hospital, using prevention measures etc.

Innovation in medicine supported the policy measures. There were promising breakthroughs for example in personalised medicine. Thanks to government-managed big data, implanted chips and gene scans personalised prevention and treatment, including organ or tissue regeneration, are now accessible and paid by insurances. New treatments are largely affordable because the drug pricing framework has been reformed to reflect a fair balance between intellectual property and public health rights. A strong governmental top-down policy on data and on drug pricing affected the fight against cancer dramatically. We now have a fair distribution of drugs and common affordable pricing.

Understanding the development of cancer and its containment has made big progress thanks to cancer-related open networks. In our paternalistic states, the public money is used for new ways of intervention also by regulators or authorities along the whole innovation process.

1.3 Between Citizen Empowerment and Big Brother

Equity, economic growth and redistribution lead to a relatively stable situation, in which most people can afford a healthy lifestyle and have equal access to tests for illnesses (like cancer), diagnosis and treatment. Thanks to a broad European change management programme in respective regions the new „culture“ of prevention and screening normality was successfully installed.

In our uniform society, online information is strictly controlled to avoid dilution or manipulation of information.

1.4 The role of Urbanisation, Climate Change and Environmental Issues in Fighting Cancer

Cities are the engines of ongoing growth and first and foremost places to work. Urban planning aims at offering the optimal conditions to work in cities (housing, transport and health services), especially as it is much easier to control employment and movements of people. Cities are a good environment to provide technical as well as social innovations in order to nudge people to a healthier lifestyle. However, air pollution, soil and other pollution are increasing, thus causing for example the spread of lung cancer.

Many people in big cities are stressed because of the mass of people living in small flats or apartments - even in Europe. Stress develops - often unnoticeable - at many different levels, by being tracked, by being observed by neighbours to obey all rules of state and society, by being exposed to new and ever more substances, by the lack of personal time, or by just living in small spaces.

Environmental change has led to the continuous outbreak of environmental emergencies (floods, cyclones, heat waves), the exacerbation of pandemics from time to time when a new virus or bacteria occur.

In the major parts of Europe, increases in production and consumption put a huge pressure on the ecosystems. Green investments were only undertaken if they were economically profitable in a rather short time. The direct impact was that the risk factors for cancer changed dramatically - not to the positive, so the cases of diagnosing cancer are still on the rise in numbers, but more can be cured. The governments tried to get hold of this by generally tracing whatever is possible (e.g. specific cancer-related substances) and for the individual by tracing the exposures of individuals in the environment, e.g. on workplaces to provide early treatments if necessary. On the other hand, the exposures of the individual are related to the life style habits that is highly related to the economic status. This means, the rich are not better off.

2 Scenario “The Rich Get Healthier”

2.1 General Picture: Economy, Politics, Society

The Europe of 2050 presents a very fragmented picture. It is fragmented in terms of equity as large income gaps exist across and within European countries and the distribution of wealth has been ever more uneven since 2020. It is also fragmented in terms of health and well-being, which parallel the social stratification of wealth and income.

2.2 Innovation in Medicine and the Health Care System

After the COVID-19 crisis in 2020, a window of opportunity had opened for strong governmental measures to be taken in order to prioritize health over economic measures. These measures, though subsided after a few years, have also affected the approach to fight cancer in the long run. Public hospitals and GPs have become part of a much tighter and efficient network governance by state health authorities. The basic supply for medication, hygiene etc. was improved. Most of these basic supplies incl. medication and medical appliances are produced within the country or in another EU core country. Besides, more expert occupations have emerged within the health sector, thus improving the overall health provision in the EU. Better provision is also the case for diagnostic and screening facilities. Though this is generally not affordable for the poorer part of society, patients with private insurance schemes benefit from the progress. Such provisions account for the fact that more cancer screenings among the better-off are done.

When it comes to rare cancer diseases national health systems are short of capacities. Access to the newest and most expensive medicines are limited to those who are employed or have an additional health plan or special insurances. Private health plans are offered by multi-national companies with mixed services and goods (conglomerates). People and organisations can buy shares to participate in the profits and to share the risk burden of high investments in personalized and the latest diagnostic services. Many cancers have become chronic and the most expensive medicines and diagnostics are prolonging life with fighting against metastatic tumours. These multi-national companies (MNCs) are joint ventures of former insurance companies, pharmaceutical companies, hospital providers, IT companies and miscellaneous investment companies.

2.3 Environmental Change and Urban Development

The EU wide campaigning to put a halt on carcinogenic emissions has improved the general health of the people and reduced the rate of cancer incidents among younger people. Most importantly, healthy lifestyles are fashionable and wealthy people are sportive, do not smoke or use alcohol. Smoking is concentrated in the poorest section of population coupled with many addictions (games, drugs...). Nonetheless, there is still an increase in the total number of cancer patients due to the fact that the people keep getting older. Younger people are less confronted with cancer.

2.4 Equity

It is obvious that this system of health provision has improved access to medical care only for the most basic treatments. Profit-driven health systems produce inequity instead of health outcomes. Especially economically marginalized people, unemployed, micro enterprises, the major part of the low-tech service sector, but also single person companies and those in precarious employment etc. are dependent on the basic provision for general care. Parallel to the rudimentary public health care system, the private health care system is growing. In addition, there are also private philanthropes and charities that raise money from profitable companies and private donors to support patients in need for special care.

2.5 Digitalisation and Empowerment

In the aftermath of the COVID-19 crisis, digitalization in the health sector experienced an unprecedented boost. Critics of private data collection were silenced by the argument that this is done in the name of public health. The digital hype is spurred by many individuals who “donate” their data to health companies and get the option of reimbursement for treatment – if necessary - in return.

A gene scan at child birth and big data give a statistical estimation of a person’s likelihood to develop cancer or other non-communicable diseases, if parents want it and can afford it.

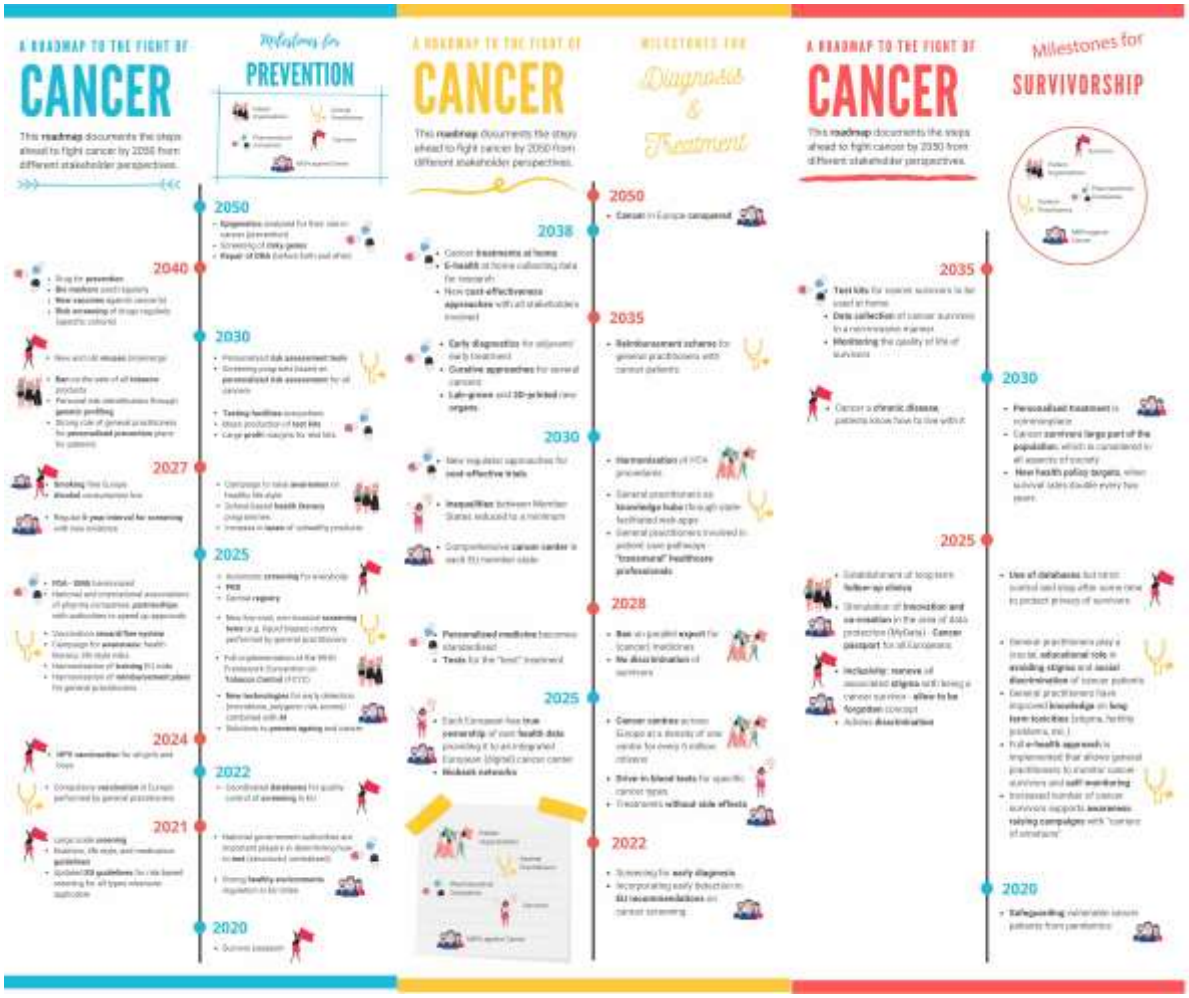
The high quantity of information available on cancer related issues makes it impossible to keep an overview on the latest breakthroughs, prevention and diagnostic measures or treatments. Patients have to rely on medical experts but often have difficulties to find the best specialist for their needs and often get contradictory or even false and fake information.

The public health sector is not providing any basic safety net such as vaccination programmes for the whole population but concentrates on expensive technologies to treat the healthiest and the wealthiest part of the population. These are also the people with the highest level of health literacy, enabling them to dedicate the necessary resources to their own health. At the same time digitalization enables better the empowerment of citizens and patients to engage in ‘communities of practice’ with peers and specialist. These ‘communities’ are dedicated to certain indications and develop new approaches to tackle cancer diseases, increase the survival rate and improve the quality of life of patients and survivors.

THE ROADMAPS

This part of the report covers the roadmap of events and milestones formulated and discussed by the Members of the Mission Board on Cancer in a virtual workshop that took place on March 31, 2020. The workshop was part of an interactive Foresight exercise on behalf of the "Foresight on Demand" (FoD) study in support of the Mission Board's work. It was organised and hosted in five parallel sessions by the FoD team. There were three to four participants in each session, some supported by experts from the European Commission who accompanied the work of the Mission Board. In the sessions, the participants were asked to assume the role of certain stakeholders such as cancer survivors, a patient organisation, Members of the European Parliament group against cancer, a large pharmaceutical company, and general practitioners. From these perspectives, the participants formulated crucial events and milestones to take place in the future on the pathway to fight cancer in the European Union.[6]

Annex III gives a brief overview of such events and milestones in form of three graphical roadmaps (see below graph), each summarising what needs to happen on a successful pathway in terms of prevention (roadmap 1), diagnostics and treatments (roadmap 2), and survivorship (roadmap 3). The stories behind the events and milestones are presented as part of the annex.



[6] Disclaimer: The roadmap report was made possible by the European Commission and the members of the Mission Board for Cancer on cooperation of the 'Foresight on Demand' team. It reports the results of a creative and interactive role play exercise as part of a larger foresight approach. The participants assumed the role of stakeholders but did not represent stakeholders. The statements and projections do not represent any official stakeholder group. Neither the European Commission nor any person acting on behalf of the Commission is responsible for the use that might be made of the following information.

ANNEX I - SCOPING PAPER ON TRENDS & DRIVERS FOR CANCER FOR THE MISSION BOARD ON CANCER

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INTRODUCTION

Cancer is the leading cause of death worldwide and accounts for two million death annually in Europe. Almost half of the patients diagnosed with cancer are passed 65 years old. Even though survival rates are also increasing, demographic change will contribute to an increase of incidents and deaths. Prognostic calculations expect that the annual diagnostics of currently 4.2 million will increase to 5.2 million in 2040 in Europe.

Cancer refers to any one of a large number of diseases characterized by the development of abnormal cells that divide uncontrollably and have the ability to infiltrate and destroy normal body tissue. This arises from a change in one single cell and may be started by external agents and inherited genetic factors and can affect almost any part of the body.

The transformation from a normal cell into a tumour cell is a multistage process where growths often invade surrounding tissue and can metastasize to distant sites. These changes result from the interaction between a genetic factors and external agents such as the chemicals in tobacco smoke, or radiation, such as ultraviolet (UV) rays from the sun.

This deliverable was designated to support the Mission Board on Cancer in reflecting the trends, drivers, developments and challenges influencing our understanding of cancer and future approaches to prevent, diagnose, and treat cancer and finally provide support for the survivors.

As the matter is very complex, the scoping can only shed a few flash lights pointing out some pressing issues and trends not only health policy makers have to take into account in order to turn the fight against cancer and the support of survivors into a mission. Still the scope of the report is quite broad. It points out latest trends in medical innovations – from the technological but also from the social side. The report shows that advances in science are able to point out more and more carcinogenic substances and behaviours and at the same time are making great progress in understanding the causes of cancer. The report goes on making reference to cancer-related factors such as agriculture, nutrition, environment and urban developments. The subsequent chapter discusses the (economic) burden for cancer on our health systems and workplace and the difficulties of national programmes to cope with it. Finally, the report points out that cancer is a societal as well as a personal issue and that coping strategies are very much dependent on the socio-economic context. This means that even across the EU there are fundamental differences of countries (and also within countries), the quality of their health systems and the patients' accessibility to proper prevention, diagnosis and treatment, as well as care for the survivors. These differences are reflected in mortality rates as well as long-term cures, related to inequity and prosperity. Obvious differences exist also on the policy side. Some governments still have not been participating in population-based cancer registries, even though these tools can be used to evaluate the impacts of cancer prevention strategies and the effectiveness of health systems for all cancer patients. It thus is a necessary task of the near future by all EU member states to find some common approaches in granting every citizen equal access to the latest advances in prevention, diagnosis and treatment, no matter which country the patient comes from or what her/his socio-economic status is.

1 WORKING DEFINITIONS

1.1 Defining Drivers & Trends

1.1.1 Drivers

We define drivers as developments causing change, affecting or shaping the future. A driver is the cause of one or more effects.[7] For example, taxation can be a driver for regulating alcohol consumption.

1.1.2 Trends

Trend is a general tendency or direction of a development or change over time. It can be called a megatrend if it occurs at global or large scale. A trend may be strong or weak, increasing, decreasing or stable. There is no guarantee that a trend observed in the past will continue in the future. Megatrends are the great forces in societal development that will very likely affect the future in all areas over the next 10-15 years, for example urbanization or demographic change.

“Trends are experienced by everyone and often in more or less the same contexts insofar as they create broad parameters for shifts in attitudes, policies and business focus over periods of several years that usually have global reach. What is interesting about trends is that normally most players, organizations or even nations cannot do much to change them – they are larger than the power of individual organizations and often nation states as well”.[8]

[7] Definition adapted from ‘Global Foresight Glossary and Drivers of Change in Ecosystems and Their Services’

[8] Definitions adapted from Saritas O., Smith J. (2011, p. 294): The Big Picture – trends, drivers, wild cards, discontinuities and weak signals, Futures, 43(3): 292-312, and from ‘Global Foresight Glossary and Drivers of Change in Ecosystems and Their Services’

2 KEY TRENDS AND DRIVERS FOR CANCER

2.1 Innovation in medicine

Innovation in prevention, detection, treatment and for survivors of cancer are necessary and much research is going on to support the fight against cancer with innovation. The major demographic trend of aging and shrinking societies in Europe and other countries in the world (opposed to still young and increasing populations in other parts of the world like Africa or Asia) have a major impact on the development of the number of cancer cases. In Europe, people are getting older, and more often reach very high ages over 100 years.

We also see a pseudo-informed society, in which people inform themselves via internet and social media. The information is more or less reliable, and sometimes contradictory to the recommendations of the doctors. It is getting more and more difficult for people to understand whom to trust. Many people trust in fake or just wrong information - because they read it somewhere in the social media. This is one of the reasons why wrong information spreads. It is also one of the reasons for resistance against vaccination in general, which is an increasing trend in some of the European countries so that for some vaccinations (e.g. measles), new “duties” were introduced, e.g. in Germany. That has an effect on the willingness to be vaccinated e.g. against the papillomavirus (or others) which may cause cancer. But this may change after the Covid-19 crisis when everybody seeks for vaccination.

The ambition in cancer has increased to curing people completely from cancer. There are important therapeutic approaches allowing to minimise treatment and treatment-free long-term survival. Some of these treatments are based on predictive diagnoses, others are genome-editing based. But this is very long-term as there are persistent problems with cancer stem cells, which serve as a reservoir for disease relapse and are hard to treat because of their relative refractiveness to therapy.

Innovations for the health sector concern new ways of diagnostics and imaging, treating patients but also social innovation/ new societal practices (e.g. in care, new business models, living together in a new way, administrative innovations etc.). For this, hardware (e.g. medical technology and devices including advanced imaging technology, robotics), software (new applications of software, steering, sensoring, personal data use for research, “big data” approaches, Artificial Intelligence etc.), pharmaceuticals and other approaches or combinations are under development. It is also important to remember that innovations will only be realized if there is a good cost-benefit ratio, and if they are accepted in the system. The following are some future innovation, which are expected on the markets in the medium- and long-term.

2.1.1 From Human Genome Mapping to Gene Editing

Thanks to the Human Genome Project researchers have sequenced all 3.2 billion base pairs in the human genome. This information is the basis for understanding genetic changes and principles in human beings that may lead to cancer. The latest progress in this field is the Cancer Genome Atlas. With it, the understanding of cancer has improved.

A new phase in innovation is **genome editing**: Genome editing, or **genome engineering**, or gene editing, is a type of genetic engineering in which DNA is inserted, deleted, modified or replaced in the genome of a living organism. This can develop innovative methods to understand the role of novel oncogenic pathways and potential treatment interventions. It may also be used to prevent a person who is expected to develop a specific type of cancer to be “cured in advance”. When the person’s genome shows a propensity for developing cancer, the specific part of the DNA is changed - no cancer appears. The special feature of genome editing is not that it is possible to change the DNA sequence and insert or remove DNA fragments (in principle, this has been possible for a long time), but that the new methods are so precise (pinpoint changes), easy to use and work in virtually all organisms. Thus, the technical possibilities of genetic engineering have expanded dramatically and will do that further.

Gene therapy has existed as a concept for a very long time, i.e. the attempt to repair genetic defects. In treatment, virus vectors to be transferred directly into tumours have reached better precision but the approach with the new tools (CRISPR/cas) open up ways to control even more precisely: In classical methods, the mutation in the actual gene is not corrected, but a functional copy of the gene is introduced into the genome. However, classical methods (e.g. using viral vectors) cannot control where the new copy is inserted into the genome, and further undesirable changes in the genome may occur. It has been observed that (new) cancer has frequently been the result (the classic example is the bubble babies) of the attempts, which is why gene therapy has fallen into disrepute after a hype around the year 2000. This could now be fundamentally changed again by CRISPR/cas technology, which makes it possible to "repair" one's "own" genes. However, many questions remain unanswered, especially regarding off-target effects, i.e. the extent to which these methods also cause undesired changes at other sites in the genome (see e.g. https://www.cancer.org/treatment/treatments-and-side-effects/treatment-types/immunotherapy.html).

Other trends are the application of **precision oncology** (see also below precision medicine), which is related to the knowledge about the personal genome: Identification of genetic markers for personalized therapy (this is not new in itself, but is increasingly being carried out in the routine), and in parallel: **companion diagnostics**, i.e. concrete tests (e.g. for a genetic marker) to identify those patients who are suitable for a certain therapy. This is highly relevant because resistance often occurs in cancer cells, i.e. certain therapeutic agents cannot be effective, or conversely, certain therapies are only effective in a small proportion of patients. Here the goal is no longer to test randomly, but to develop tailor-made therapy concepts. Particularly in the case of high-priced active ingredients, **companion diagnostics** are often a prerequisite for the costs to be covered. Of course, genetic knowledge is the essential basic prerequisite for the development of a genetic diagnostic test.

2.1.2 Immune therapies/interplay of immune system and cancer

Immunotherapy is a treatment that uses a person's own immune system to fight cancer. Immunotherapy can boost or change how the immune system works so it can find and attack cancer cells. CART T-cell therapy is a new form of immunotherapy, which was recently approved and has received great attention: Here, T-cells are taken from patients and genetically reprogrammed to specifically target cancer cells. These are retransferred into the patient in the hope that the altered T-cells will destroy the cancer cells.

However, in contrast to gene therapy, it is NOT about repairing a specific genetic defect. It is therefore a more classical therapeutic intervention when cancer has occurred already, in contrast to preventive treatment. Immune therapies promise a cure with a long-term memory. There are several approaches which seem to be promising, but immune therapies and their interplay in the immune system are highly complex and still poorly understood. At individual basis it is often ex ante unclear who will benefit, what are the side effects, or what are influencing factors such as the personal microbiome.

Genomic Vaccines is another approach: "The typical vaccines deployed against infectious diseases use dead or weakened pathogens or subunits thereof – in the case of cancer vaccines, directly the relevant proteins – to activate the body’s immune system. The latter recognizes the foreign pathogen through the antigens it carries (in some modern vaccines, just the antigen is provided in fact) and hits back on the next encounter. Genomic vaccines, also known as “DNA vaccines”, take a different approach: they inject genes, specifically DNA or RNA that encode for the needed protein, which then cause cells to produce the protein in question. This has many advantages: producing the genes should be easier than manufacturing the proteins (which need entire cell cultures); more proteins can be crammed in a single vaccine; and they can be adapted as the pathogen goes through the mutations we are familiar with from, for example, the annual flu." (Warnke et al. 2018)

2.1.3 Epigenetics

is defined as the study of heritable phenotype changes that do not involve alterations in the DNA sequence. Epigenetics has already been used to refer to changes in gene expression, which are heritable through modifications not affecting the DNA sequence (Mason and Dunnil 2008). Any disturbance of a stable epigenetic regulation of the gene expression mediated by DNA methylation,

histone or chromatin modifications is associated with a number of human disorders, including cancer. Long non-coding genetic sequences are still poorly identified and are seen as potent regulators of gene expression and certainly involved in cancer initiation. Therefore, basic research in epigenetics still has to clarify many details for a better understanding of cancer (Weber et al. 2018).

Epigenetics can also be used to fight cancer but only recently some drugs are clinically tested. Humans have certain genes that can suppress cancer cells - the so-called tumour suppressor genes. They are responsible for our body's own defence against cancer. Cancer patients often have epigenetic changes, which disrupts the reading mechanism. However, if the tumour suppressor gene is not read off correctly, the body cannot prevent the cancer cells from growing. Epigenetic therapy is supposed to reactivate the gene by removing the epigenetic factors. The body then starts fighting the cancer cells again (Wilson & Humphreys 2020; Deutsche Krebshilfe 2017).

2.1.4 Regenerative Medicine

Human cells have the potential - the focal point of regenerative medicine - to replace or regenerate human cells, tissue or organs to restore or establish normal function in given conditions (embryonic stem cells, induced pluripotent stem cells, Mason and Dunnill 2008). Mason and Dunnill (2008) also state that "A successful regenerative medicine centered on human cells could be a 'disruptive technology' because it would potentially replace a number of major molecular pharmaceuticals and medical prostheses." Many new developments are expected in this field.

2.1.5 Organoids

One recent approach is using organoids, which are in vitro derived from stem cells and are used to portray organ development and disease (Wilson and Humphreys 2020). The three-dimensional structure that is only few millimetres in size is similar to that of organs. They may play a large role in organ replacement (Weber et al. 2018).

"**Single-cell RNA sequencing (scRNA-seq) technologies** are increasingly being applied to reveal cellular heterogeneity in kidney development and disease. In just the last year, multiple scRNA-seq datasets have been generated from kidney organoids, developing [...] kidney cancer. The data generated enables a much deeper understanding of biological processes within and between cells. It has also elucidated unforeseen cell lineage relationships, defined the presence of off-target cell types in kidney organoids, and revealed a diverse inflammatory response in a human kidney allograft undergoing rejection." (Wilson and Humphreys 2020).

2.1.6 Organ transplantation and 3D modelling in surgery

Artificial organs are an option in medical treatment. In the future, many human organs already may exist in artificial versions, on chips or as organoids and can be reproduced and replaced at least once. Organoids and in-silico models can be used to quickly develop effective treatments for existing organs; other solutions are based on genetic engineering or require therapeutic cloning and breeding (i.e. xenotransplantation). The bio-printing of organic tissues presents a third avenue for human tissue replacement. Bio-printed organs and tissues could give future opportunity of preventive transplants instead of solution of last resort (Weber et al. 2018).

If organ transplantation is affordable, artificial organs will become an option for public health care systems. Through the common usage of this surgery the life span of people will increase dramatically. Replacing the 'market' for human organs with a market for artificial organs that involve less side-effects and have better performance is an important vision for the medical devices industry, an industry in which Europe is very strong. (Weber et al. 2018). Bioprinting is also an option with high expectations. Bioprinting, also referred to as organic printing, is a special purpose of 3D printing. This technology produces tissues and organs by using polymers or genetically engineered biomaterials. Bioprinting has the benefit of individual adaptation of the material and fewer side effects, such as implant rejection (Warnke et al. 2018).

2.1.7 Microbiota

Microbiomes are defined as "an ecological system of commensal, symbiotic, and perhaps pathogenic microorganisms that reside in the human body." (Liu 2016). Those microorganisms occur in humans, animals and plants. In contrast to the microbiome, that "refers to the collection of genomes from all the microorganisms in the environment", the **microbiota** is used to describe the accumulation of certain microorganisms in a specific location for instance bacteria. Within a person, the microbiota severely vary with each different location in the body (Fios Genomics 2020). Microorganisms can affect our health in very different ways. Inter alia microbes cause proneness to cancer, as well as they affect the results of therapeutics. Hence, the microbiome is also an objective for cancer therapy. Research on next-generation biotherapeutics is undertaken to examine microbial consortia and to alter the microbiota (Helmink et al. 2019). "Given that the human body hosts trillions of microbes, it is not surprising that bacteria have been detected within tumours themselves; lung, breast, colon, gastric, pancreatic, cholangiocarcinoma, ovarian, and prostate cancers have all been found to harbor microorganisms." (Helmink et al. 2019). Also nutraceuticals (bio-ceuticals) as a pharmaceutical alternative which claims physiological benefits are discussed in this context.

In-depth future studies aiming at the link of the human microbiome and cancer may find solutions in form of prevention, detection and methods of recovery (Vogtmann and Goedert 2016) but there are ex ante differences to be tackled: "Microbiome associations with cancer may differ across many host factors, including sex, age, smoking, alcohol consumption, diet, obesity, physical inactivity, and polymorphisms in major human oncogenes." (Vogtmann and Goedert 2016).

2.1.8 Functional (MR) Imaging, Molecular Imaging, and Theranostics

Advances in high resolution planar imaging technology (CT, MRI) have resulted in detailed morphological information on the extent and stage of the tumour. More recently functional MR imaging has been introduced in clinical practice. The combination of morphological information and information of the underlying tumour biology provides a comprehensive picture of the tumour behaviour. Increasing evidence shows the high sensitivity of targeted tracer imaging in oncology (molecular imaging). Smaller tumours can be detected and response to targeted treatment more accurately assessed. Theranostics is a new area where imaging and treatment take place in parallel, using nuclear tracers. MR imaging will have huge potential for diagnostics when combined with Artificial Intelligence for tumour recognition (pattern recognition), which is improving in accuracy (see below).

Hyperspectral Imaging also belongs to this category of imaging devices. It is an attractive technique in medical treatment and diagnosis thanks to its non-contact and minimally invasive nature. Searching for cancer tumours, researchers obtained a very good correlation between the real positions of the tumours seen by clinicians and the automatic predictions made by a hyperspectral imaging system (Warnke et al. 2018).

Theranostics combines specific targeted therapy based on specific targeted diagnostic tests."With a key focus on patient centred care, theranostics provides a transition from conventional medicine to a contemporary personalised and precision medicine approach. The theranostics paradigm involves using nanoscience to unite diagnostic and therapeutic applications to form a single agent, allowing for diagnosis, drug delivery and treatment response monitoring." (http://theranostics.com.au/what- is-theranostics/) and is performed at the interface to personalized medicine (see e.g. https://www.ema.europa.eu/en/documents/presentation/presentation-theranostics-nanoparticles-peter-dobson-oxford-university_en.pdf).

2.1.9 Minimal invasive and robotic surgery

Minimal invasive treatment has been widely adopted in today's oncological practice. Image guided radiotherapy enables precise targeting of the tumour allowing higher effective doses to the tumour while sparing the doses to normal tissue. Recently developed MR Linac equipment is promising for daily adaptation of the fields while the patient is on treatment. Laparoscopic and robotic surgery aims to achieve successful resection, minimise the surgical field and hospital stay while minimising per- and postoperative morbidity with better functional outcome and quality of life. Increasingly interventional

oncological procedures are part of the spectrum of local treatment that can be offered to the patients. Some examples are percutaneous freezing or burning of tumours (ablative treatment) and intra - arterial therapies.

2.1.10 Smart medical devices

Smart medical devices of very different kinds are developed. For example, scientists at Washington State University developed a mobile **Smartphone-Lab** for cancer biomarkers. The optical spectrometer can detect a signaling substance which gives evidence for certain types of cancer. The technique is based on antibodies and an enzymatic color reaction (Wünnenberg 2016). In the project RIBRI for the European Commission (Warnke et al. 2018), drug delivery and lab-on-a-chip are mentioned in connection to cancer:

"**Drug delivery** represents the administration of a healing agent or pharmaceutical complex to humans or animals in order to reach a therapeutically operative range of medication. Advances in drug delivery technologies generally aim to increase the efficacy and absorption of a drug, while decreasing its side effects. Nanomaterials and new materials are revolutionizing the field. When a sensor embedded into a transdermal drug-delivery device detects a significant change, like an abnormal variation in temperature, the device will release drugs as programmed and precisely to the relevant location. Such treatment deployment will decrease the time spent in hospitals for patients suffering from cancer and chronic diseases and thus substantially cut the costs of therapy." (Warnke et al. 2018)

"A **lab-on-a-chip** (LOC) integrates laboratory functions such as chemical analysis within a single device of small dimensions. LOCs, which are a subset of micro-electro-mechanical systems (MEMS), can handle very small fluid volumes and thereby allow for high throughput analysis with fast responses. Microfluidics, i.e. the physics, manipulation and study of minute amounts of fluids, is an important basis of LOC development. Lab-on-a-chip technology promises a rapid improvement in healthcare due to better, faster diagnostics, especially in areas with poor healthcare infrastructure. At the same time, the technology may allow for a more active role of patients in monitoring their own health. In a similar way, LOC may enable citizens to engage in environmental monitoring, for example via citizen science projects." (Warnke et al. 2018)

Liquid biopsy chip: A chip developed by mechanical engineers can target and capture cells originating in metastatic tumours in blood samples of patients. The device uses antibodies attached to an array of CNTs (carbon nanotubes) at the bottom of a tiny well. Cancer cells settle at the bottom of the well, where they selectively bind to the antibodies based on their surface markers. Unlike other devices, the chip can also trap tiny structures called exosomes produced by cancer cells. This “liquid biopsy” could become the basis of a simple lab test to quickly detect early signs of metastasis and help physicians select treatments targeted at the specific cancer cells identified.

There are many other new technologies in physics and chemistry that allow more performant analysis of cell structural complexes and also in vivo imaging. One example are incremental improvements in nuclear medicine, also in PET (position emission tomography) scans to detect cancer as well as new ways in `Radiomics’.

2.1.11 Biohybrids

Biohybrids are expected to be more and more relevant in many application fields, also for cancer research and in treatments (Warnke et al. 2018): "A biohybrid typically refers to a combination of artificial components and at least one biological component. This kind of systems can be applied in a large array of domains, from health to nanotechnology, robotics or even consumer goods – such as fresh produce." [...] "An international team of researchers developed biohybrid magnetic robots for site directed drug delivery. They used microscopic algae that have approximately the same size as red blood cells, called Spirulina platensis. After functionalizing the algae with biocompatible magnetic particles, they tested the micro-robots by magnetically guiding them to the cancer site in the stomach of a rat. The therapeutic substances that the algae released killed only the cancer cells. By controlling the coating of the algae, the researchers are able to control the biodegradation process and the

release of therapeutic substances. These biohybrid magnetic robots could be used in the future for not only cancer treatment, but for diagnostic or for the treatment of other illnesses." (Warnke et al. 2018)

Further developments can be found in:

Biodegradable sensors/ Biodegradable electronics are electronic components with a limited lifetime subject to disappearing via hydrolysis or biochemical reactions. Such devices can be used as medical implants for temporary in-body sensing, drug delivery, tissue engineering, microfluidics, etc.

Bioelectronics is defined as the use of biological materials or architectures inspired by biological systems to design and build information processing machinery and related devices. A crucial dimension of this area of research is the envisaged complementarity and interaction between biological materials and extremely miniaturized electronics; in vivo memory storage systems can be used not only to store data, but also to record events and processes in human cells, tissues or engineered organs (from Warnke et al 2018).

2.1.12 Artificial Intelligence, Machine Learning and Augmented Reality

Artificial Intelligence (AI) is widely acknowledged as a potentially disruptive innovation with impact on the way we live and provide medical care. The exponential increase in digital data (big data) has led to a rapid evolution of AI and the implementation of AI in many fields of healthcare and research. Machine and deep learning algorithms surpass the accuracy of human brains to detect and diagnose cancer and predict (calculate) responses to treatment using CT's, MRIs, conventional mammography, endoscopy, digital histology skin pictures etc. Algorithms also exist and used for genomic sequence analysis. (Cuhls et al. 2007)

Powerful graphical processing units (GPUs) have enabled the intensive computations required for machine learning (particularly, deep learning), drastically reducing the running time of training algorithms and enabling new applications (Warnke et al. 2018). Deep learning is promising to help in the very complicated practice of identifying cancer from tissues, as this process is more difficult for the human cognition than for a machine intelligence. Consequently over- and under-diagnoses and faulty treatment resulting from this could be prevented in the future (Hipp and Stumpe 2018). Image recognition in combination with deep learning and interpretation of the pictures will be a major application for cancer diagnosis. A new way called "deep convolutional neural networks" (CNNs) has succeeded for the first time in creating an automated image recognition program that can identify malignant skin tumours more reliably than the majority of clinically experienced dermatologists. This is a revolutionary development in the field of dermatological image recognition. CNNs are simply structured, adaptive programs that can be implemented in any smartphone. It is estimated that there will be 6.3 billion smartphones in use worldwide by 2021. This technology has enormous potential for dermatological cancer screening. One could imagine a skin cancer app that would give everyone the opportunity for self-monitoring at home. Comprehensive secondary prevention in the field of dermatological early detection could be guaranteed, especially for people who do not make use of cancer screening by dermatologists. Skin cancer could be diagnosed in earlier stages (Wolfsperger and Yazdi 2017).

The expectations for diagnosis, treatment and support by AI are high. Currently, huge data sets for algorithmic training are necessary for applications. A barrier for introducing AI is the requirement of transparency and also legal responsibilities. This is why AI systems learn under control (weak AI). Machine learning, computer vision, natural language processing, robotics (Warnke et al. 2018) and many other new applications will help in medical treatment or for cancer survivors together with self-learning systems – however all this is also contested due to severe impacts on health care and legal systems. Capsule networks and other neural network designs will significantly increase the power of learning systems, while also accelerating their development and deployment. That means search platforms and information providing for cancer patients and their relatives as well as for doctors or others in the system may be facilitated and easily accessible. It is also expected that many standard bureaucratic procedures, e.g. in the health system, may be more automatized also with help of Artificial Intelligence (Opiela et al. 2017). Regulation and ethical considerations play a huge role in the

area. Anywhere, where the detailed analysis of pictures is needed like radiographs, the development of self-learning algorithms is advancing. First applications of deep-learning systems in the fields of radiology, pathology and dermatology seem promising though (Krebsinformationsdienst und Krebsforschungszentrum 2019).

AI is discussed in many different contexts and combinations with helpers in cancer research, even to support precision medicine which has to handle huge amounts of data, which is impossible by humans. The combination with sensors, different data bases (digital health approaches) and technologies like organ-on-a-chip will allow new and fast ways of diagnostics and treatment (Weber et al. 2018).

Augmented Reality (AR) overlays computing images (or even sound) on real world perception. Doctors are already using augmented reality to better guide them during surgery, and it is hoped that this will drastically reduce the duration of surgeries (Warnke et al. 2018). Many other devices and solutions are expected, e.g. smart tattoos (Warnke et al. 2018: 89-90) that represent an all-in-one sensing platform, also known as paper skin, e-skin, or electronic tattoos. They consist of wearable epidermal skin electrodes which enable real-time and simultaneous sensing of various environmental stimuli (pressure, touch or proximity). In medical applications, paper skin promises to be a flexible platform for applications such as health monitoring, where sensing diversity, surface adaptability, and large-area mapping are all essential. The e-skin platform is suitable for measuring instantaneous UV (ultra-violet) exposure (a major risk for skin cancer) and skin temperature, providing precise dosimetry in the UV-A and UV-B spectrum.

2.1.13 Personalized (Precision) Medicine

Personalised medicine (precision medicine) promises the ability to anticipate, diagnose and cure illnesses on an individual basis, and in a targeted way, while limiting potential harm. The diagnostics and therapeutics are based on the patient's' own genetic, biomarker, phenotypic, characteristics of the tumours. A milestone in precision medicine are targeted therapies and the assessment of response with targeted imaging: Some of these concentrate on anticancer drug development or on pharmacogenomics. One of the major aims in precision medicine is the integration of comprehensive multi-omic tumour characterization. The aspirations of precision medicine are to open to personalized medicine, and give a boost to biology and biotechnology, which are essential competencies for the medium and long-term future. The application combines mass data analyses, genetic engineering, epigenetics, and knowledge about the personal microbiome and the biotic environments. In particular, advances such as cell sorting, epigenetics, proteomics, metabolomics, and more are converging with informatics and other technologies, rapidly expanding the scope of this field (Weber et al. 2018).

To accelerate the applicability of precision medicine, it needs increased knowledge of biological phenomena. Understanding and mapping out the interactions between human organisms and their environment is still a huge project, as is the mapping of the human and non-human microbiome. Progresses in this field are issues of ethical and regulatory concern. That is why medical regulation, research and ethics and organization of health and insurance systems are important. Precision medicine approaches are still expensive and rare and until now, no regulation for the predictive treatments exist (e.g. amputations in case of the threat of cancer). As in precision medicine, many personal data are generated, related, hosted in databases and retrieved, policies concerning data and their security are as important as the health considerations to avoid potential misuse of personal data.

A milestone in precision medicine are targeted therapies[9] and companion therapies (see above). Some of these concentrate on anticancer drug development. Drugs prevent "the growth and spread of cancer by interfering with specific molecules ("molecular targets") that are involved in the growth, progression, and spread of cancer." In contrast to standard therapies that aim to kill normal and cancerous cells, targeted cancer therapies are devised to act on their targets affected by cancer. FDA

[9] https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies/targeted-therapies-fact-sheet

(Food and Drug Administration) approved many targeted cancer therapies. Other targeted therapies that have been permitted "include hormone therapies, signal transduction inhibitors, gene expression modulators, apoptosis inducers, angiogenesis inhibitors, immunotherapies, and toxin delivery molecules." One of the major aims in precision medicine is the integration of comprehensive multi-omic tumour characterization, “dynamic monitoring of liquid biopsy samples, annotation that is automated through advancements in artificial intelligence but guided by experts’ clinical input, the enrollment of patients into innovative clinical trials that not only test molecular profile–drug matching but also investigate the utility of different drug-assignment algorithms” (Malone et al. 2020). Real-time access of these information would be another step to create a global knowledge basis.

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2.2 Social Innovations

Social innovations can be entirely new ideas, emerging social practices like sharing online opinions, experiences, photos or peer-to-peer advice (Warnke et al. 2018). They can also be everyday inventions that are improving existing practices (Taipale 2013), for instance how to keep appointments and take medicines. When focus is on cancer, quality improvement and appropriate quality assurance practices are especially important ways to advance both prevention, early detection and care.

In emerging practices, food circles or community gardening could introduce more healthy diets (Warnke et al. 2018). Citizen engagement, collaborative or co-creational practices and patient-reported outcome measures are examples of social innovations aiming towards more patient-centric approaches. Comprehensive policies are the most effective ones. In prevention, polygenic risk scores could be in the future one way to prevent cancer with individual risk profiles but these new methods will need support from health policies to succeed, for instance so called societal nudging towards healthier lifestyles. (Alemanno 2019) Society is needed to encourage and support individual efforts.

Quality improvement in cancer screening looks for social innovations. There are at least three different levels in innovations:

- goods, equipment, tests or services
- process innovation
- applicability according to specific criteria of the process.

In cancer screening programmes social innovation mean ways to improve coverage of the programme, more efficient evaluation of the screening programme or improving practices of data collection (Anttila et al. 2019). These innovations might stay local unless mapped and distributed across borders. With their social contexts, some social innovations are not easily transferable, even if necessary for implementation.

Vaccination programmes, suffering from rumours and low-quality reporting of media and social media channels, are in need of social innovations to keep the coverage in a level where herd immunity is reached. Cancers are linked to viruses and the European Code Against Cancer (more about the Code under title Inequity and prosperity) evidence recommend that both HPV and Hepatitis B should be included in national vaccination programmes and the coverage monitored.

Social innovation can be a widely established, effective practice of influencing dietary habits of children. Finland has made free school meals mandatory for municipalities since1948. Every child between 6-16 years gets school meals in both primary and secondary school (Pellikka et al. 2019). Free school meals are integrated into nutrition education.

Social innovations are needed when evidence-based research has difficulties in reaching out policy makers or it is not well implemented into policies. One example from prevention comes from Australia, when it introduced generic cigarette packages, taking off branding elements marketing the product. This move was successful, because it clearly reduced smoking initiation among young people (Müller 2014).

Regulations to protect people from carcinogenity in the workplace also show that social innovations are essential and especially if social practices differ widely. It may be socially easy to introduce legislation to protect workers from asbestos, but carcinogenic tobacco smoke might be a more difficult task, even if it would expose workers or young children to a mix of carcinogenic substances. This is partly due to strong commercial interests and anti-regulatory actions from tobacco companies. Similarly radiation may raise concerns but exposure to UV-radiation as an occupational health hazard does not cause similar worry.

In large Nordic Occupational Study (NOCCA) of cancer incidence up to 45 years by occupation, 15 million people aged 30-64 years were studied and 2,8 million incident cancer cases diagnosed in these people until about 2005. Waiters were in highest risk among men and priests and farmers in the

lowest risk: those professions where smoking and drinking alcohol has been acceptable, carry increased risk (Pukkala 2009).

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2.3 Agriculture and Nutrition

2.3.1 General aspects

Nutrition has an impact on the general condition of human beings, on the development or prevention of cancer and in supporting an active immune system or condition that supports curing cancer and thus survival. Agriculture and the way our food is produced play a large role in what we eat, what is available, how it is transported, packed and which ingredients are included. It also plays a role how "secure" the food is in terms of availability (enough nutrition elements) and unwanted by-products. Invisible mildew, rotten or old food, pesticides, heavy metals or even radioactivity in our food can contribute to the development of cancer in humans. The microbiome of our land and later our food can also include substances, viruses or bacteria that have cancerous effects.

2.3.2 Chemistry and pesticides

Chemicals, plastics, pesticides and fertilizers from agriculture (and industrial products) end up in our food - and we come into contact with these substances on farms, with our food or just when being outside "in nature". Many of these substances may cause cancer, in some cases, there is an evidence-base, in others, there is none. The background trend is that the occurrence of these substances will rather increase and even more diversified substances are on the market. Starting with fertilizers, it is reported that overall consumption in Europe was rather stable over last decade on a high level. In 2017, 11.6 million tonnes of nitrogen fertilizer was used in EU agriculture, an increase of 8 % since 2007 (10.7 million tonnes). In 2017, 1.3 million tonnes of phosphorus was used in EU agriculture, a reduction of 9 % since 2007 (1.5 million tonnes)[10]. Even though there are decreases in some fertilizer use, the differences between European countries are significant and still on a high level. The use of chemical pesticide use has rather increased since the 1960s and is increasing fast (Agrios 2005), mainly herbicides, but also insecticides and fungicides. Especially in China, where a huge amount of our food is produced, the increase is dramatic - in 2016, it reached three times the global average and has an impact on our European food. Zhang (2018) indicates that in 2013, Greenpeace reported that 70% of all pesticides used in China was not absorbed by plants, but ended up in soil and groundwater - humans were directly in contact with them. Plastics are another increasing problem - with a large volume of waste generation. Plastics can be found everywhere on the planet and the production is still increasing. Annually, more than 300 million tonnes of plastics are globally produced, the number of 2018 is 61.8 million tonnes[11].

Plasticizers like adipates and phthalates are often added to brittle plastics like polyvinyl chloride to make them pliable enough for use in food packaging, toys, and many other items. Traces of these compounds can leach out of the product. Owing to concerns over the effects of such leachates, the European Union has restricted the use of DEHP (di-2-ethylhexyl phthalate) and other phthalates in some applications, and the United States has limited the use of DEHP, DPB, BBP, DINP, DIDP, and DnOP in children's toys and child care articles with the Consumer Product Safety Improvement Act. Some compounds leaching from polystyrene food containers have been proposed to interfere with hormone functions and are suspected human carcinogens (Yang et al. 2011). Whereas the finished plastic may be non-toxic, the monomers used in the manufacture of the parent polymers may be toxic. Small amounts of those chemicals can remain in the product. For example, the World Health Organization's International Agency for Research on Cancer (IARC) has recognized vinyl chloride, the precursor to PVC, as a human carcinogen and it was early on the agenda (WHO 1999). Bisphenol A (BPA) also seems to be linked to cancer causing the United States FDA to spend $30 million to investigate indications of BPA being linked to cancer in 2010.[12]

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[10] https://ec.europa.eu/eurostat/statisticsexplained - 20/05/2019

[11] https://www.plasticseurope.org/application/files/9715/7129/9584/FINAL_web_version_Plastics_the_facts2019_14102019.pdf

[12] https://www.latimes.com/archives/la-xpm-2010-jan-16-la-na-fda-bpa16-2010jan16-story.html

To sum up, there are still many opportunities, for finding alternative ways of transporting, logistics, avoiding fertilizers, pesticides etc. or replacing chemical substances with less harmful ones.

2.3.3 Organic Farming

Organic farming is a long existing alternative agricultural system already introduced 1924 as "biodynamic farming" in reaction to rapidly changing farming practices. It includes many measures that are intended to ensure a better balance in agriculture (sustainability principle) and that food does not include chemicals, artificial fertilizers and unintended substances. Principles are: no plant protection with synthetically produced chemicals, cultivation of less-susceptible varieties in suitable crop rotations, using beneficial species and mechanical weed control measures such as hoeing and flame weeding; no utilisation of easily soluble mineral fertilisers, ...the preservation of soil fertility through intensive humus management; varied and long crop rotations with many crop rotation links and intermediate crops; no application of synthetically produced chemical growth regulators; and limited stocking density based strictly on the area of land available; where possible feeding of animals on farm-grown feed, few purchased feed as well as largely dispensing with the use of antibiotics (all cited from Federal Ministry of Food and Agriculture 2019).

Certified organic agriculture accounts for 70 million hectares globally (Paull 2019) and is on the rise[13], sometimes coupled with the concept of "agroecology"[14]. According to the result of the representative survey on the 2019 Nutrition Report one person in two "always" or "usually" pays attention to the organic production logo when shopping. The annual Ökobarometer (organic barometer) confirms this trend: more than one quarter of respondents now regularly buys organic food.[15] If this really prevents from cancer on the consumer side, still needs research, but it definitely does not expose farmers to the risks of pesticides etc. in huge amounts that might cause cancer.

2.3.4 General nutritional aspects, guidelines

Nutrition has an enormous effect on the development or prevention of cancer. Together with enough physical education (sports or movements in daily life) it is a factor that may prevent cancer on the one hand, help curing it and support the general condition of cancer survivors on the other hand. In food and nutrition behaviour, two controversial trends can be observed:

1. Standardisation of our food and the consumption of fast food with differing content, but in most cases with an overconsumption of salt and saturated fats. This trend seems to continue, especially in parts of the population with low income, limited knowledge on food and food quality and by the trend of still eating fast food and less cooking at home. In some houses, kitchens do not exist, anymore. People are infiltrated by an industry that wants to sell junk food and is permanently exploring new markets (Kruchem 2017). These foods are less expensive and as they are comfort food, they are fashionable and please the young. We are moving from a system where women stayed all day at home and cooked to a new system, where no one has made food when you all arrive at an empty house in the evening.
2. Diversifying nutrition patterns are found in other groups of the society, where dietary habits are rapidly changing. Currently, we observe an increasing number of people shifting towards vegetarian, vegan or gluten free diets. Major drivers behind these changes are climate change and sustainability considerations, but also health explanations are given (even though e.g. for gluten free diets, no effects are scientifically proven for persons without celiac conditions). It is unclear, if this remains a niche or a fashion or if the numbers are growing steadily.

[13] https://www.organic-world.net/yearbook/yearbook-2016.html

[14] https://stats.oecd.org/glossary/detail.asp?ID=81

[15] https://www.bmel.de/EN/Agriculture/SustainableLandUse/_Texte/OrganicFarmingInGermany.html

There is a discrepancy in developments. On the one hand, undernourishment[16] (even in the European Union) and malnutrition still exist, and on the other hand in the same regions and at the same time, the trend of rising adiposities is ongoing (WHO 2017)[17]. Two billion people around the world are estimated to be overweight (body mass index greater than 25), a third to be obese (BMI>30) and rising obesity rates by 1% every three years are observed. By 2022, more children may be obese than undernourished. (Bentham et al. 2017) This presents a fearsome prospect for all health systems and is a special problem in wealthy Europe, where more than half the population is overweight and a fifth is obese. Compared to the 2,500 calories a day recommended for an adult, Europeans eat on average 3,700. (EAT-Lancet Commission 2019) Overweight is one of the risk factors for developing cancer and other diseases.

A healthy diet is recommended to prevent cancer, but the behaviour of human beings changes slowly, is often forgotten on the way (remember the good intentions around New Year) and cannot be prescribed in the same way for all because the reactions of each individual on his or her nutrition is different. The EAT Lancet Commission (2016) gives some general recommendations but there seems to be individualistic reactions to every diet. Paternalistic prescriptions (Do not eat...!) evoke rather resistance of people than long-term commitment. The EAT- "Lancet Commission on Healthy Diets from Sustainable Food Systems" (EAT 2016) evaluated the shifting toward healthy diet as of one the three targets needed to meet the challenge of providing healthy food for 10 billion people by 2050 while creating a sustainable food production to ensure stable earth system. But the affordability of such a diet for all is doubted (Hirvonen et al. 2020). General recommendations include the achievement of an energy balance and a healthy weight by the limitation of salt consumption, free sugars and total fats (possibly shifting fat consumption away from saturated fats to unsaturated fats and towards the elimination of trans-fatty acids). An increase in consumption of fruits, vegetable, and legumes, whole grains and nuts is recommended.

There are already policies for more nutritious and safe food, e.g. the Treaty of Amsterdam that obliged the EU to ensure "high level of human health protection (...) in the definition and implementation of all Community policies and activities". Health is now included as transversal requirement in the EU Treaty on the Functioning of the EU. Concerning nutrition and healthy diet strategies there are a Strategy for Europe on Nutrition, Overweight and obesity related health issues (2007), the EU Action Plan on Childhood Obesity 2014-2020 or the WHO European food and Nutrition Action Plan 2015-2020. However, on the whole the "current EU food systems and policies are failing to address the root of unhealthy diets while austerity policies are further undermine the social safety net". The main question behind is how to make healthy food accessible to all. In 2015, 23.7% of EU citizens were at risks of social exclusion and 8.7% were affected by food insecurity in 2011 (IPES-Food panel: February 2019).

2.3.5 Innovations in Food

There are many innovations in nutrients and food components as well as food additions, for example insects or algae as food or ingredients (Wells et al. 2017; Borowitzka 1997), but also 3D printing of food or local food circles (Warnke et al. 2018).

Nutrigenomics are a field of focus, the application of the human genome to nutrition and personal health to provide individual dietary recommendations. There is however an asymmetric development: healthier cooking methods on the one hand, a shift to packaged processed unhealthier food, especially in urban areas, on the other hand. For the recommendations and the personalisation, big data analysis are already used and will be used even more often in the future. Artificial Intelligence is supposed to support in the future by finding patterns of personalized use, patterns in genome and functions, and giving recommendations based on databases (Weber et al. 2018; Warnke et al. 2018).

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[16] http://www.fao.org/sustainable-development-goals/indicators/211/en

[17] http://www.euro.who.int/de/media-centre/sections/press-releases/2017/new-who-study-on-health-and-well-being-of-europes-youth-reveals-that-obesity-continues-to-rise or http://www.euro.who.int/__data/assets/pdf_file/0003/98247/E89858G.pdf

2.3.6 Food labelling

It is often unknown, which ingredients are in prepared food or ready-made food. Even though there are numerous labels, they are difficult to understand, some of the logos are unknown to the consumers or it is difficult to trust them as they are no “official” labels. Often, the imprint of the ingredients on the package is too small to be readable or too detailed and complicated to be understandable. Nevertheless, there is a trend to labelling food according to easy-to-understand signals, e.g. the “Bio Siegel” (Federal Ministry of Food and Agriculture 2019) or labels like traffic lights or “Nutriscore”, so that consumers understand at a first glance that something is too salty, includes too many fats, too much sugar, or a lot of “E”s (all food components of an unhealthy diet).

2.3.7 Taxation of unhealthy foods and drinks (and tobacco)

The taxation of unhealthy foods and drinks is discussed (e.g. Mytton et al. 2012, Rajagopal et al. 2018 or Smith et al. 2018) but it is uncertain how this development will unfold. The idea started with tobacco as smoking is one of the cancerogenic habits. When high taxation of tobacco was not enough incentive to prevent people from smoking, there are now “warning pictures” on the packages and smokers are discriminated (they are not allowed to smoke in public areas like stations, not in restaurants and pubs etc). If e-cigarettes as the alternative are less risky has to be proven, some of the ingredients seem to cause cancer, too, but as these habits are rather new, the empirical data are still missing. First countries (e.g. Mexico, Hungary, Denmark, France, Peru etc.) have high taxation on sugar already[18], it can be expected that others might follow. With increasing evidence of the usefulness of health taxes, not just for tobacco but for foods high in sugar, saturated fats, salt and sugar sweetened beverages may be introduced by several countries (precautionary principle).

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2.4 Environment

Many scientific studies have recognised environmental factors as being relevant for cancer occurrence and environmental factors that are promoting health as well. Substances in the environment causing cancer are generally labelled carcinogens. The US National Institutes of Health regularly update a long list of carcinogens that contains several hundred entries (US National Institutes of Health 2016).[19] Being exposed to carcinogens does not necessarily mean that a person is developing the disease. A number of complex factors, many of which are not yet scientifically researched, have to come to together, such as certain quantity and duration of exposure, genetic disposition, other environmental factors, life style. WHO's International Agency for Research on Cancer (IARC) has classified 107 agents, mixtures, and exposure situations as carcinogenic to humans. These include all forms of asbestos and a number of agents found in the environment such as benzene, arsenic in water, cadmium, ethylene oxide, benzo[a]pyrene, silica, ionizing radiation including radon, ultraviolet radiation including tanning devices, aluminium and coke production, iron and steel founding, or the rubber manufacturing industry (WHO, 2011; WHO Regional Office for Europe, n.y.).

Cancer risk factors related to environment in a broader sense, include exposure to biological agents (infections), to synthetic chemicals through work or consumer products, and lifestyle factors such as exposure to sunlight, poor diet, being overweight, tobacco use and consumption of alcohol. These risk factors are reported to collectively contribute to the development of 70–95% of all cancers. While the specific contribution from chemicals to cancer is difficult to quantify with certainty, a number of estimates have been made as such: diet (30–35%); tobacco (25–30%); obesity (10–20%); alcohol (4–6%); others, including air pollutants and radiation (10–15%). Infections may contribute by 15–20% (Madia et al. 2019).

However, it should be emphasized that as individuals we are exposed in real life to mixture of chemicals. To this end the exposome concept was elaborated recently. The exposome is defined as the measure of all the exposures of an individual in a lifetime, which begins before birth and includes insults from environmental and occupational sources. The impact of exposures to health varies with the individual's stage of life. A key factor in describing the exposome is the ability to accurately measure all exposures and effect of such cumulative exposures.

There is a great need of developing new tools and technologies for exposure assessment in making the exposome initiative to succeed. These tools and technologies range from exposure strategies to the development of direct reading devices for exposure, novel biomarkers of effects or artificial intelligence tools for tracking past exposures. In addition, the "omics" technologies offer great promise to help elucidate the exposome both in identifying exposures and response to exposures.

Of special importance there are biomarkers that may indicate past exposures. They are important to determine the effect that lifetime exposures have on present health status. These biomarkers may pinpoint to a specific chemical or insult or may pinpoint to specific damage that occurred due to exposure to a certain class of chemicals. Antibody formation, metabolites, adducts, genetic mutations, epigenetic changes, toxicogenomic effects, etc. may all provide information about past exposures.

Different environmental exposures have been linked to specific kinds of cancer (UPMC 2017)[20] so far: For example, exposure to asbestos is linked primarily to lung cancer, whereas exposure to benzidine, a chemical found in certain dyes is associated with bladder cancer. In contrast, smoking is linked to cancers of the lung, bladder, mouth, colon, kidney, throat, larynx, oesophagus, lip, stomach, cervix, liver, and pancreas.[21]

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[19] https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/roc/index.html#toc1

[20] https://share.upmc.com/2017/03/carcinogens-in-environment/

[21] https://www.niehs.nih.gov/health/materials/cancer_and_the_environment_508.pdf

Breast cancer has been associated with the cumulative exposure to pesticides and other chemicals. Several key studies have been reviewed, suggesting higher breast cancer risk for exposures during breast development to dichlorodiphenyltrichloroethane (DDT), dioxins, perfluorooctanesulfonamide (PFOSA) and air pollutants and, for occupational exposure, to solvents and other mammary carcinogens such as gasoline (Rodgers et al. 2018).

Approximately 5% of childhood cancers have also been estimated to result from environmental exposure to pollutants (Prüss-Ustün, et al. 2016).

The annual burden of disease caused by indoor air pollution alone, including polluted outdoor air used to ventilate indoor spaces, is estimated to correspond to a loss of over 2 million healthy life years in the European Union. Based on measurements of the European Environment Agency (EEA), approximately 90 % of EU citizens live in areas where the World Health Organization guidelines for air quality of particulate matter sized <2.5 mm (PM2.5) are not met. This burden of disease, caused mainly by exposure to PM 2.5, is dominated by cardiovascular (CV) diseases, but the second largest contribution comes from lung cancer (23%).

The implementation of the REACH[22] have led in Europe to a gradual decrease of production of highly toxic and CMR (Carcinogenic Mutagenic Reprotoxic) chemicals. The restriction of cancerogenes such as chromium (VI), dichloroethane, lead, cadmium, trichloroethylene and more recently decaBDE, PFOA, PFOA-related substances and PAHs has resulted in reduced risk for workers and consumers. It has been shown that the strongest legislative impact has been primarily the reduction of occupational cancers, resulting from reduced exposure to occupational carcinogens by as much as 7% per year. In relation to 13 well known carcinogens for example, it is estimated that over 1 million deaths from cancer have been avoided (Amec Foster Wheeler Environment & Infrastructure UK, Directorate-General for Environment, 2017).

However, it seems that it may change in coming years. For years chemical production which posed high risk to human health, including carcinogenic, has been moved from Europe to China, India and other non-European countries. It is estimated that e.g. production of almost 70-80% of active drug ingredients is produced now outside Europe. Economic policy changes in China and Covid-19 virus pandemics will reverse this trend, as it becomes obvious that such situation is posing a real threat to health security of European (and US) population. It means that exposure to different chemicals in the working as well as in general population will increase in coming years.

Compared with traditional pollutants, considerably less is known about engineered nanoparticles (ENP) as well as natural nanoparticles (NP) toxicity during tap water ingestion, and this uncertainty underpins public concern. Such perception is often influenced by aesthetics (taste, odour and colour). However, there are no published reports that show toxicity or human disease associated with ENP ingestion in drinking water at relevant exposure levels. Most available toxicology data related to NP ingestion is associated with either consuming nanomaterials in food or investigating ENP concentrations significantly higher than those present in drinking water. For some metals that are reported to occur as ENPs with high global usage potential, limited occurrence data exists for drinking water systems. These ENPs tend to be fairly insoluble in typical drinking water matrices and have high threshold concentrations before inducing toxicity in humans. Summing up ENP concentrations in tap water are extremely low and pose low risk during ingestion. However, after leaving drinking water treatment plants, corrosion by-products released from distribution pipes or in-home premise plumbing can release incidental nanoparticles into tap water. It seems that occurrence and toxicity of these incidental nanoparticles, rather than ENPs, should therefore be the focus of future research and concern of municipality (Westerhoff et al. 2018).

[22] https://ec.europa.eu/environment/chemicals/reach/reach_en.htm

Lung cancer is the most common form of cancer worldwide and cigarette smoking is the main cause of lung cancer. It is attributable for nine lung cancer cases out of ten. Global trends of smoking and lung cancer show that the prevalence of smokers is particularly high in Europe. Smoking among men is the highest in Eastern Europe. Furthermore, the prevalence of smoking among women in Europe is especially high compared to global estimates of female smoking. At the same time, Europe is also experiencing highest burden of cancer deaths attributable to smoking (Islami, Torre & Jemal 2015). Also, it should be noted that compared to smoking women, men who smoke have 61% higher risk of getting smoking-attributable lung cancer (Yu et al. 2014). Despite the fact that tobacco control regulations have achieved some significant decreases in the rates of smoking, it is still causing overwhelming harm (Torre, Siegel & Jemal 2015).

The box below gives five examples of carcinogenic substances identified by scientists:

Tobacco

Cigarette, cigar, and pipe smoking have been associated with cancers of the lung, mouth, bladder, colon, kidney, throat, nasal cavity, voice box, esophagus, lip, stomach, cervix, liver, and pancreas, and with leukemia; smokeless tobacco has been linked to cancers of the mouth; and Environmental Tobacco Smoke (ETS) has been implicated in lung cancer. Cigarette smoke contains more than 100 cancer-causing substances. Years of Life Lost (YLL) rates due to cancer showed limited or no change between 2010 and 2016. Despite recent declines in tobacco use among men, this lack of change may reflect, on the one hand, the chronicity and lag-time of cancer development and, on the other, the difficulty or limited effectiveness of treatment against some of the most aggressive forms of cancers related to tobacco use (trachea, oesophagus and lung). (according to a comparison documented by WHO 2011).[23]

Particulate matter[24]

According to the latest model calculations, 3.3 million people die every year worldwide as a result of particulate matter. Above all, the smallest particles with a maximum diameter of 2.5 micrometres and no larger than bacteria are considered harmful to health. Wherever there is a particularly high concentration of particulate matter in the air, not only the number of fatal strokes, heart disease and respiratory diseases such as asthma is increased but also the number of lung cancer (Lelieveld 2017).[25] For every 10 micrograms of increased particulate matter concentration per cubic meter of air, the risk of dying of cancer increased by a total of 22 percent. For tumours in the upper digestive tract, the experts found an increase of 42 percent. According to the study, the risk of dying of cancer of the liver, pancreas or gallbladder increased by 35 percent. In women, the risk of dying of breast cancer even increased by 80 percent, as the researchers explain (Wong et al. 2016).[26]

Benzene

Benzene is known to cause leukemia, Non-Hodgkin-lymphoma and other forms of cancer in humans. It occurs often 30 years after exposure. It has widespread use as a solvent in the chemical and drug industries and as a gasoline component, and also in many occupations in the manufacturing industry where it was not recognized as harmful for many years. Because benzene is present in gasoline, air contamination occurs around gas stations and in congested areas with automobile exhaust. It is also

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[23] http://www.euro.who.int/__data/assets/pdf_file/0009/402777/Tobacco-Trends-Report-ENG-WEB.pdf?ua=1

[24] Fine dust is defined as tiny particles down to a size of 10 micrometers. The pollutant particles can originate from diesel soot, tyre abrasion or exhaust gases from industrial, power plant or heating systems. The current study focuses on particles with a diameter of less than 2.5 micrometers (PM2.5), which can become lodged deep in the bronchi and pulmonary alveoli or even enter the bloodstream. The researchers collected the particulate matter values at the places where people live.

[25] https://www.nature.com/articles/nature15371

[26] bit.ly/1SX4se1 Cancer Epidemiology, Biomarkers and Prevention, released April 29, 2016. WHO: http://www.euro.who.int/de/health-topics/environment-and-health/air-quality/news/news/2013/10/outdoor-air-pollution-a-leading-environmental-cause-of-cancer-deaths

present in cigarette smoke. Virtually everyone in is exposed to benzene in gasoline (National Institute of Environmental Health Sciences et al., 2003).

Ultraviolet radiation

VR exposure is the main cause of skin cancer, including cutaneous malignant melanoma, basal-cell carcinoma, and squamous-cell carcinoma. Skin cancer is the most common cancer in fair-skinned populations, and its incidence has increased steeply over recent decades. In Europe, incidence rates are particularly high in the Nordic countries, Switzerland, the Netherlands, the Czech Republic and Slovenia, while Mediterranean countries, as well as the Baltic and Eastern European countries, tend to have lower rates. In most parts of Europe, the incidence rates are higher among women than among men. Recent findings indicate a uniformly increasing trend in European countries over the last decades, with the strongest increases seen among older ages and with strong North-to-South and East-to-West variation (higher incidences in the North and East) (Greinert et al. 2015).[27] In part due to its long latency, the number of malign melanoma has been rising and will continue this trend in the near future.

Radon

Radon is produced by the breakdown of uranium, which naturally releases low levels of ionizing radiation. Higher levels of radon can be found in certain types of rocky soil. The health effects of radon were first seen in the elevated levels of lung cancer found in underground uranium miners. Radon gas seeps into homes from the surrounding soil through cracks and other openings in the foundation. Even though the cancer risks for radon exposure in the home are much lower than for radon-exposed miners (National Institute of Environmental Health Sciences et al., 2003).

Comprehensive understanding of the relationship between health and the environment requires insight into the composite interactions among the physical, biological and social spheres (WHO 2013). An overview of impacts of environmental changes to health is given in Figure 1:

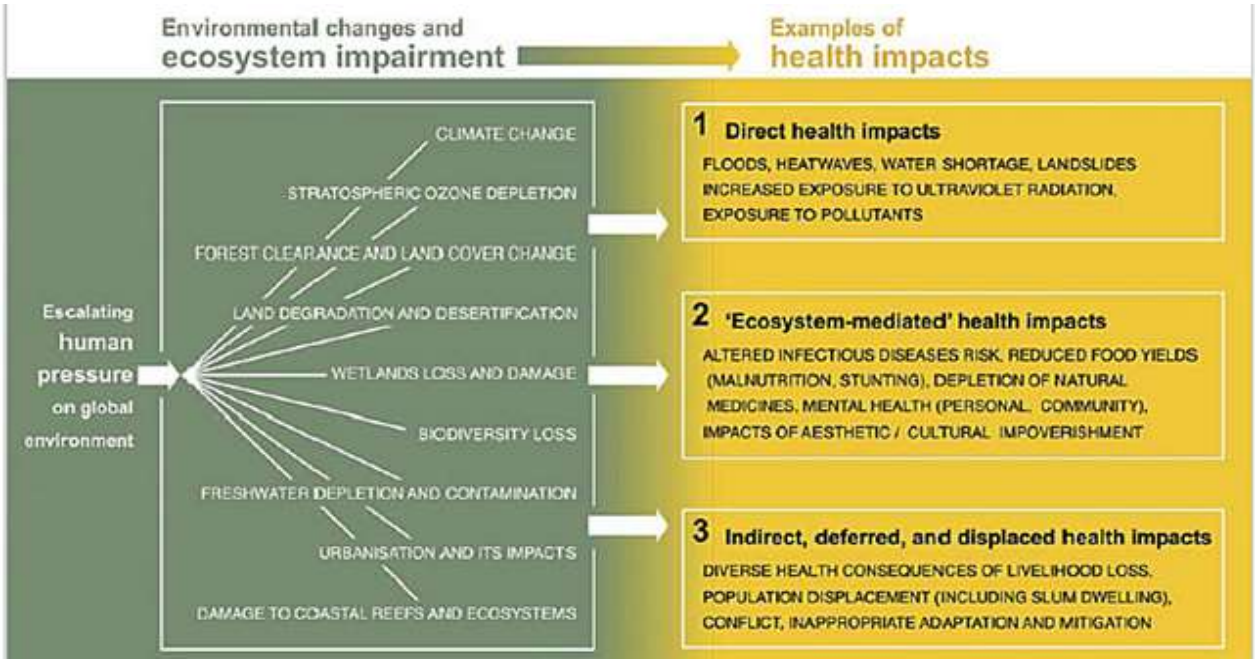

Figure 1: Millennium Ecosystem Assessment (2005) (Source: http://www.who.int/globalchange/environment/en/)

[27] https://www.sciencedirect.com/science/article/pii/S1877782115000028

What is included in the term “environment” can be best depicted by Figure 2, adapted by the WHO from Smith et al. (1999), but was defined in a more practical sense by the WHO: “the environment is all the physical, chemical and biological factors external to a person, and all the related behaviors, but excluding those natural environments that cannot reasonably be modified” (Prüss-Üstün & Corvalán 2006).

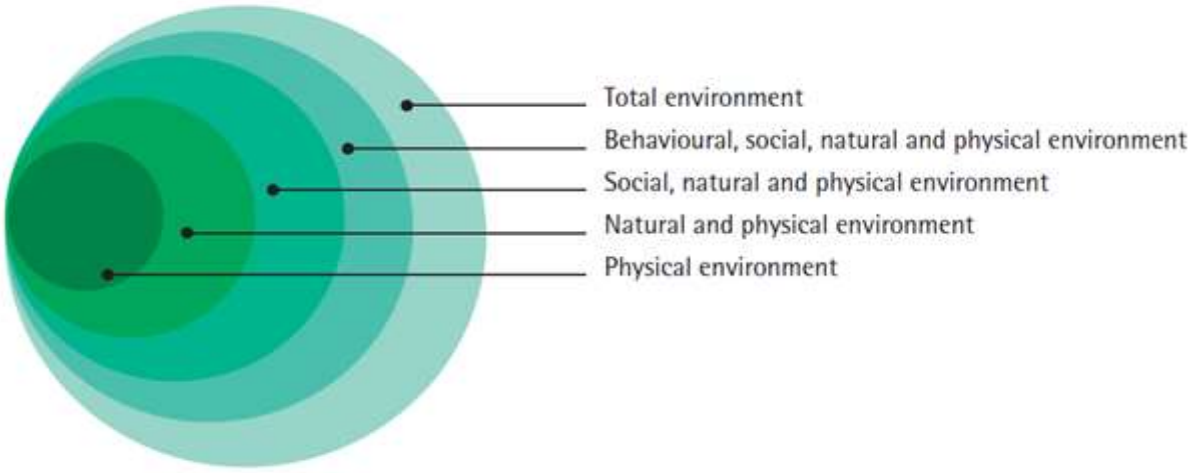

Figure 2: Definition of the environment (adapted after Smith et al., 1999)

Thus various factors need to be taken into consideration and the most important risk hazards are addressed by the global strategy of WHO Public Health & Environment (2011):

- Water, sanitation & hygiene guidelines to inform policy making and prevent waterborne diseases
- Indoor air policies Outdoor air policies to minimize the health impact of urban transport
- Housing standards and policies to reduce exposure to radon, lead, asbestos and other harmful chemicals
- Chemical regulation policies to restrict or stop the use of highly hazardous chemicals in industry, agriculture and in consumer products and promote the use of safer alternatives

Physical activity is influenced by **urban environments and transport policies**, which can promote cycling and walking for transport by developing safe infrastructure, as well as fostering the establishment of accessible green spaces for leisure-time physical activity and encouraging behaviour modification (see next chapter in this report) (IPEN Project 2017).[28] Occupational health and safety programmes can also be advocates for workplace wellness interventions. On a larger scale, lessons learned from the climate change and sustainable development movements serve as a model for developing advocacy for cancer development and prevention. There are deep connections with the causes of air and noise pollution and with efforts to control them. Sound and sustainable policies relating to the environment and health will contribute directly to reducing the burden of cancer: from agricultural practices and policies, to protection of children from adverse environmental exposures.

Agriculture influences health directly through the **quantity and the nutritional composition** of the foods available for consumption in the household and in the market (see also chapter in this report).

[28] http://www.ipenproject.org/

There has been an increasing awareness in recent years of the presence and potential impacts of **pharmaceuticals** increasing the prevalence of acquiring cancer, e.g. dimethylformamide, or DMF. Several blood pressure drugs have already been recalled due to concerns about other cancer-causing chemicals (Lovelace 2019).[29] Pharmaceuticals and other care products released to **the environment**, including surface water, groundwater, soil, bed sediment, and in tissue are under investigation for their carcinogenic effects. The potential routes of environmental entry include patient excretion either as parent compound or metabolites via the sewer system, direct release into the waste water system from manufacturing, hospitals or disposal via toilets/ sinks, and terrestrial depositions, for example via sludge application to land, leaching from solid waste landfills, or irrigation with treated or untreated wastewaters (Thatha Gower 2014).

Most of these environment-related cancers are however not easily detected and may be acquired during childhood and manifested later in adulthood. Improper management of solid waste is one of the main causes of environmental pollution and degradation in many cities, especially in developing countries. Many of these cities lack solid waste regulations and proper disposal facilities, including for harmful waste. Such waste may be infectious, toxic or radioactive (National Institute of Environmental Health Sciences et al., 2003).[30]

Air pollutants, taken as an example of environmental influence on health, such as carbon monoxide (CO), sulphur dioxide (SO2), nitrogen oxides (NOx), volatile organic compounds (VOCs), ozone (O3), heavy metals, and respirable particulate matter (PM2.5 and PM10), differ in their chemical composition, reaction properties, emission, time of disintegration and ability to diffuse in long or short distances. Air pollution has both acute and chronic effects on human health, affecting a number of different systems and organs, e.g. lung cancer (Kampa & Castanas, 2008).

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[29] https://www.cnbc.com/2019/06/18/fda-warned-of-cancer-causing-chemical-found-in-heart-pill.html

[30] https://www.niehs.nih.gov/health/materials/cancer_and_the_environment_508.pdf

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2.5 Urban Development

Over half the world's population now lives in cities, and urbanization will be among the most important global health challenges during the 21st century. A Eurostat report from 2016 projects that by 2050 the population of EU-28's urban regions will increase by 24.1 million persons and will provide home to almost half of the EU-28 population. For the same period, the population of predominantly rural regions is projected to fall by 7.9 million (Eurostat 2016). Thus, even though several factors speak for a healthier lifestyle in the country, there is no significant trend pointing in this direction. This does not imply, of course, that living in the countryside is per se healthier, as public transportation infrastructure is often limited and people use private motorization which contributes to sedentary behaviour.

Urbanization is associated with many health challenges including cancer and unhealthy life choices such as tobacco use and alcohol abuse. City dwellers are more exposed to stress through road traffic accidents, injuries, violence and crime. The urban poor suffer disproportionately because they often have less access to proper health care and prevention measures, because the health service infrastructure is insufficient in the poorer urban areas, but likely to be more frequented.

To reverse this trend, representatives of local and national governments are urged to develop policies to protect and promote health, across multiple sectors, including the environment, transport, education and urban planning (WHO 2010).[31]

2.5.1 Built Environment and Physical Activity

Built environment may influence health behaviours directly or indirectly (Cradock/Duncan 2014, p. 442). It is obvious that built environment can have some preventive effects from cancer by promoting physical activity via respective promoting facilities and environments, for example with regard to walkable community design, density, connected streets, mixed land uses, access to transit and public transportation, pedestrian and bicycle facilities, building designs such as stair cases, parking places; the location of workplaces and schools, parks and trails, playgrounds, landscape aesthetics, sidewalks and safety. Among children and adolescents, research suggests that walkability, traffic speed and volume, access and proximity to recreational facilities, and the urban form characteristics of land-use mix and residential density present important correlates of physical activity participation (Ding et al., 2011). A positive trend is also that building block have more mixed use, thus inviting to more physical activity and social exchange (e.g. Office Buildings with flats and/or shops, etc.).

Local stores, supermarkets, and fast food restaurants can influence nutrition-related behaviors via access and marketing of foods and beverages, e.g. with regard to distance and availability for special needs. There are some studies that indicate that perceived availability is linked to healthy nutritional behavior. Other correlations still need to be evaluated and researched more.

A growing body of studies shows that accessibility to **tobacco** retailers is associated with increased tobacco use (Chan & Leatherdale, 2011; Henriksen et al. 2008; Leatherdale & Strath 2007). Concerning **alcohol**, the issue is more complex. Research results concerning alcohol availability in the neighborhood and alcohol consumption are ambiguous (Halonen et al., 2011; Connor, Kypri, Bell, Cousins, 2011).

2.5.2 Built Environment and Depression

Depression may affect cancer patients in an indirect but nonetheless critical way. Some patients with cancer may experience depression before, during, or after cancer treatment. Depression may make it harder to cope with cancer treatment. It may also make it harder to make choices about one's own care (Cancer.net 2019). As a result, identifying and treating depression are important parts of cancer

[31] http://www.euro.who.int/en/health-topics/environment-and-health/urban-health/activities/healthy-cities/who-european-healthy-cities-network/meetings-of-the-who-european-healthy-cities-network/annual-meeting-of-the-who-european-healthy-cities-network-2010.-theme-the-hidden-cities-addressing-equity-in-health-and-inclusiveness-in-cities/quick-facts-on-urban-health

treatment. Built environment and depression are associated as several studies show. Greater access to social destinations and community design features in the built environment may promote socialization and prevent or work against symptoms of depression. No definite evidence is available yet concerning the walkable distance in a particular neighborhood and depression.

Interventions in the built environment are generally sustainable interventions, that is to say they influence the structure and function of the physical environment in which health behaviors occur but do not require repeated introduction in order to be maintained. It goes without saying that interventions of this kind are usually very costly, but since they last very long and can reduce the health care budget, they might often be the cheaper expenditure. Cost effectiveness studies of built environment interventions however are just lately becoming an area of research (Wu et al., 2011). Built environment interventions are increasingly becoming multi-disciplinary partnerships between urban planners, parks/recreation officials, transportation engineers, public health officials, and citizens.

2.5.3 Built Environment of Schools

Schools are an important for influencing health-related behavior of both students and teachers and other employees working at the school site. Interventions within the built environments of schools have been developed to address dietary behaviours as well as physical activity and tobacco consumption. Interventions in schools often include physical infrastructure change and also campaigns to raise awareness for the connection between built environment, behaviour and health. Many students consume food and beverages while on school property thus making the built environment of schools a popular setting for interventions to promote healthy eating and drinking (Giles et al. 2012).

School playgrounds and public playgrounds are a common device to promote play and physical activity among students and smaller children. Studies have shown that physical activity is more attractive to children if sufficient playground materials and space are provided (Hannon/Brown, 2008).

2.5.4 Attractive Environments

Built environment can also promote or hamper the physical activities of adults. Taking the stairs is one way to be more physically active in everyday environments and has proven to strengthen fitness over short intervention periods (Boreham et al., 2005). Examples of interventions promoting stair use in place of elevators and escalators have generally relied on point-of-decision signage frequently demonstrating statistically significant increases in stair use with potential for longer-term sustainability (Soler et al., 2010). Certain design characteristics can impede or promote stair use.

To make neighborhoods more attractive for walking they have to have a certain infrastructure and they have to be safe from accidents. There are several design features to help reduce speed of cars and to raise more awareness in car drives for the needs of pedestrians. Pedestrian crossing countdown signals, visual signals that provide information on the amount of time for the next green light, auditory information for pedestrians with visual impairment, installations of traffic calming measures (speed bumps, blocks on the road), and shared spaces are options to reduce traffic speed and grant more right to the pedestrians. (Dumbaugh/Frank, 2007; Bunn et al., 2009)

The other major strategy to improve or maintain health though intelligent neighborhood built environment is to support biking, e.g. by more biking lanes, off- as well as on-road, bike parking lots, bicycle sharing programs, public electric stations to charge e-bikes, etc.

There is quite some room for action at the political level to influence health behavior by regulating physical infrastructure, e.g. through local zoning policies. What is more, several studies have shown links between the density of tobacco retail outlets around schools or homes and smoking prevalence. (Mozaffarian et al., 2012; Center for Tobacco Policy & Organizing, 2011)

One approach for more physical activity of children in a safe environment is called “multi-component intervention” and comprises information campaigns for parents and children together with changes in the built environment. Within school buildings, multi-component intervention can ameliorate healthy

eating by designing teaching kitchens, storage of food, serving and eating zones, display of healthy foods and on-site food production facilities (Larson/Huang et al., 2016).

2.5.5 Health Equity and Built Environment

The health equity debate is based on the assumption that health inequities often occur among disadvantaged groups and are unjust. Built environment strategies can play an important role in promoting social and environmental justice and reduce health inequities be eliminating health-harming environments. As several studies have shown, low income populations and some racial/ethnic minorities are exposed to features of built environment that may contribute to cancer-related factors (Larson et al., 2009).

2.5.6 Healthy and Sustainable Cities

The WHO European Healthy Cities Network consists of cities around the WHO European Region that are committed to health and sustainable development: nearly 100 cities and towns from 30 countries. The WHO European Healthy Cities Network has six strategic goals[32]:

1. to promote policies and action for health and sustainable development at the local level and across the WHO European Region, with an emphasis on the determinants of health, people living in poverty and the needs of vulnerable groups;
2. to strengthen the national standing of Healthy Cities in the context of policies for health development, public health and urban regeneration with emphasis on national–local cooperation;
3. to generate policy and practice expertise, good evidence, knowledge and methods that can be used to promote health in all cities in the Region;
4. to promote solidarity, cooperation and working links between European cities and networks and with cities and networks participating in the Healthy Cities movement;
5. to play an active role in advocating for health at the European and global levels through partnerships with other agencies concerned with urban issues and networks of local authorities; and
6. to increase the accessibility of the WHO European Network to all Member States in the European Region.

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2.6 Health Systems

2.6.1 Organisation of EU health systems

The healthcare systems in Europe share the fundamental principle of universal health coverage but differ greatly in their organisation, service delivery and outcomes. Since 1990s many national health systems have undergone a great deal of re-organisation leading to a higher involvement of private sector in healthcare financing and delivery in many European countries. (Micheli et al. 2003) The tendency to involve private sectors in health care increased in many countries (Czech Republic, Estonia, Poland, Slovakia, Slovenia), while others (Denmark, Iceland, Finland, Norway, Sweden) confirmed and reinforced strong public sector health systems. Other countries (England, Scotland, Wales, Malta, and Italy) although reduced the role of the public sector, kept the health systems to a large extent public. Remaining countries adopted insurance-based coverage, with important involvement of the private sector.

Along with many variations in the organisation of health systems, the provision of primary and secondary care and the positioning of cancer diagnosis and care therein differs greatly across the Member States. In most countries, the cancer screening programmes, if such are available, are arranged at the level of primary care (general practitioners and other primary health services). The diagnosis and care are then performed at the level of secondary (specialist) care, which can be accessed by patients either directly or through a referral from primary care if the gatekeeping system is imposed. Policies for cancer care therefore need to incorporate multi-level perspective, following patient pathways through the system.

2.6.2 Expenditure on cancer

Overall, the health expenditure on cancer care has doubled from €52 billion to €103 billion in the EU between 1995 and 2018 (Hofmarcher et al. 2019a). The dramatic increase is caused by, among others, adoption on innovative treatments and subsequently increasing expenditure on cancer medicines: from €14.6 billion in 2008 to €32 billion in 20182. The costs of inpatient cancer care have, on the contrary, decreased due to a shift of cancer care to ambulatory and outpatient settings.

At the same time, total country expenditure on health as well as cancer expenditure are largely disparate across the Member States. While data shows that the total health expenditure ranges from 5% to 11.1% in EU28 (Figure 1) (Eurostat 2016), no systematically recorded data is available to measure the share of cancer expenditure therein. A recent study by the Swedish Institute for Health Economics estimates that the share of total health expenditure spent on cancer care in the EU ranged from less than 4% in Finland, Iceland and Sweden to over 7% in Bulgaria, Czech Republic, France, Hungary, Poland, Romania and Slovakia. However, the per capita spending on cancer reflect that the actual (direct) costs of care are the highest in Germany, Austria, Benelux, and France (€250-€350 per capita) and the lowest in Romania, Latvia, Bulgaria, Estonia, Hungary, and Poland (less than €100 per capita). These disparities in health and cancer financing are considered to be one of the driving forces behind variations in rates of cancer survivorship across the Member States.

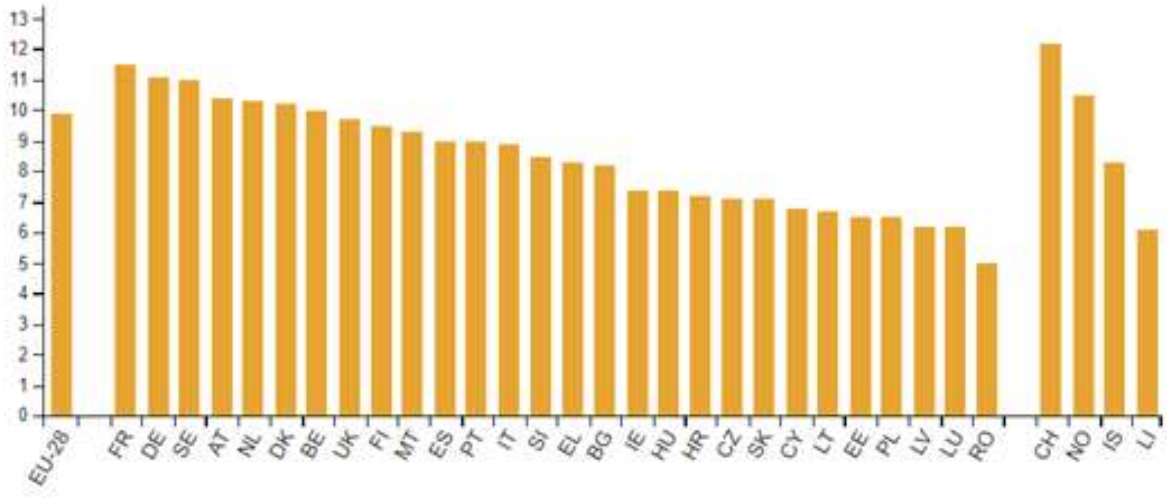

Figure 3: Health expenditure as a percentage of GDP across the Member States, 2016 (Eurostat 2016a)

The analysis of the growth of the expenditure on cancer care also poses a risk to the sustainability of health systems in the EU. With the growing expenditure on cancer and limited health budgets, national governments are faced with a dilemma to balance the affordability and quality of services. Greater efficiency is particularly needed in cancer care to ensure that governments can continue to finance high-quality affordable therapies and diagnostics (Wait et al. 2017).

2.6.3 Cancer burden in the EU

In 2018, there were an estimated 3.1 million new cases of cancer and 1.4 million deaths from cancer in Europe (EU) (Hofmarcher et al. 2019). Figure 2 represents the increase in cancer rates between 1995 and 2018. Overall, cancer incidence has increased by around 50% whilst mortality increased by 20% in Europe between 1995 and 20184.

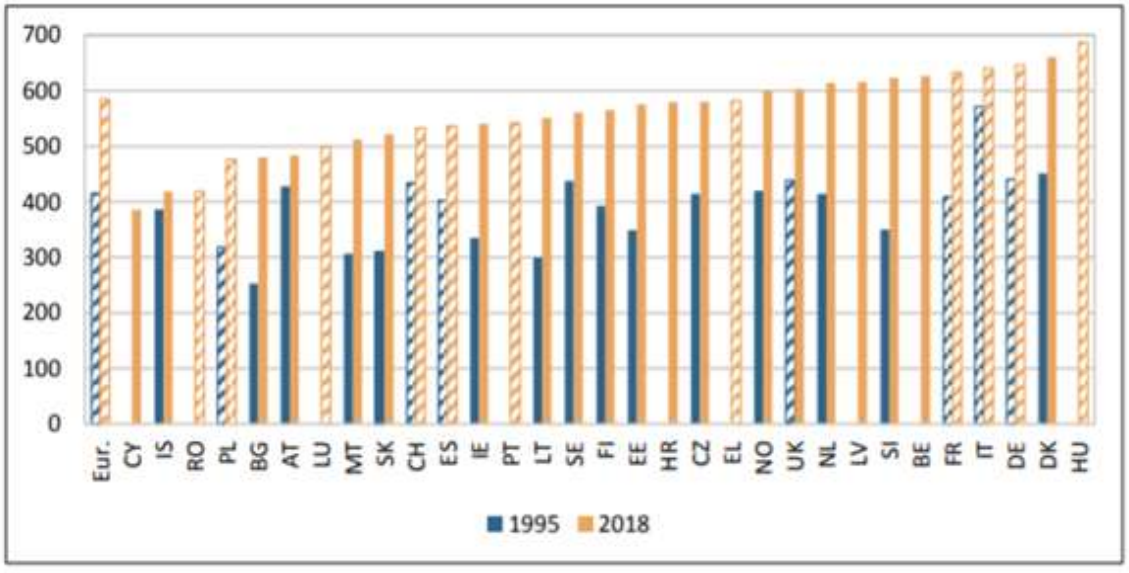

Figure 4: Estimated number of cancer incidence cases per 100,000 inhabitants (crude rates for both sexes), 1995-2018. Source: IHE Report, 2019 (Hofmarcher et al. 2019)

While the overall number of cancer cases has increased across all countries and sexes, the types of cancer and the age distribution of new cases varies. For instance, the share of male colorectal cancer has doubled since 1995, while the share of male lung cancer decreased by 7%. Cancer incidence in

children remained more or less stable, while there has been a rapid increase in the age group 40-64 years old. Incidence among people aged 65 and older has increased and can be expected to continue increasing in the future.

Along with an increase in cancer incidence, the total number of deaths from cancer has increased from 1.2 million cases in 1995 to 1.4 million in 2018 (Hofmarcher et al. 2019). However, the increase has been slow and deaths have been decreasing in the groups below 65 years old5. It is estimated that if not for population growth and population ageing, cancer mortality could have decreased in Europe between 1995 and 20185. The decrease in mortality rates in the groups below 65 is explained by improved quality and availability of treatments, leading to higher survival rates.

At the same time, the decrease in cancer mortality has been unequal across the Member States with countries from Central and Eastern Europe reporting higher mortality rates in comparison to those in Northern, Southern and Western Europe (Bray et al. 2018; Eurostat 2016b).

2.6.4 Cancer screening

Nearly half of cancers in the EU can be prevented through, among others, ensuring access to screening and early detection services leading to prompt treatment of common cancers at an early stage. Cancer screening is associated with a positive effect on survivorship and quality of life, and potentially to reduced healthcare costs (Ratushnyak et al. 2019). Screening may be performed nationally, as a part of population-based cancer screening programmes or can be available on-demand either in specialist or primary care services. To date, national screening programmes are recommended for breast, cervical, and colorectal cancers.[33]

All EU Member States, except for Bulgaria, Greece, and the Slovak Republic, implement population-based cancer screening programmes among women aged 50-69 years. In 2013 78.9% of women aged 50-69 have been invited for mammography screening and about half of them have been screened[34,35]. This is a significant improvement compared to the estimates from 2007. For cervical cancer, population-based screening exists in 22 Member States either nationally or regionally, while some countries (Denmark, Finland, Italy, Sweden, Romania, and Portugal) have already introduced HPV test as the primary screening method. In 2013 59.2% of target women aged 30-59 were invited for screening, out of which 53.2% were screened. Substantial progress has been made in the area of colorectal cancer screening: 20 countries have rolled out population-based screening programmes either regionally or nationally. Average invitation and screening rates (for 17 countries) were 32.6% and 14% respectively in 2013.

The existing gaps in the coverage and efficacy of screening programmes point that more needs to be done to expand access to screening to the entire population. Lack and incompleteness of recent data also show that countries are lacking national cancer registries which would include rigorous data reporting on screening rates and results in order to ensure effective and timely monitoring of advances and identification of challenges.

Another important development in the area of cancer screening is the emergence of genetic services and personalised medicine, and particularly the use of DNA testing to identify hereditary predispositions to cancers among relatives of cancer patients. Debates around the integration of the genomic approach into the national screening programmes are on-going. Stratified screening programs could include cascade screening and risk assessment based on family history (Cornel and

[33] Council Recommendation of 2 December 2003 on cancer screening

[34] Source: Report on the implementation of the Council Recommendation on cancer screening, 2017.

[35] Here and further: we use the latest average estimates calculated based on performance and data recorded for all countries participating.

van El 2017). There is limited data on the use of a genomic approach in the population cancer screening programmes across Europe.

2.6.5 Access to cancer diagnosis and care

The increase in cancer incidence in Europe can also be linked to, in part, improved diagnostic tools, such as population-based screening programmes and a wider availability of CT and MRI scanners. Although the possibilities for rapid and accurate diagnosis improved the spread and access to such diagnostic tools as well as the speed of diagnosis remains uneven across and even within the Member States. Figure 3 shows an example of the inequality in availability and access to lung cancer diagnostics in selected European countries (LuCE Report 2017).

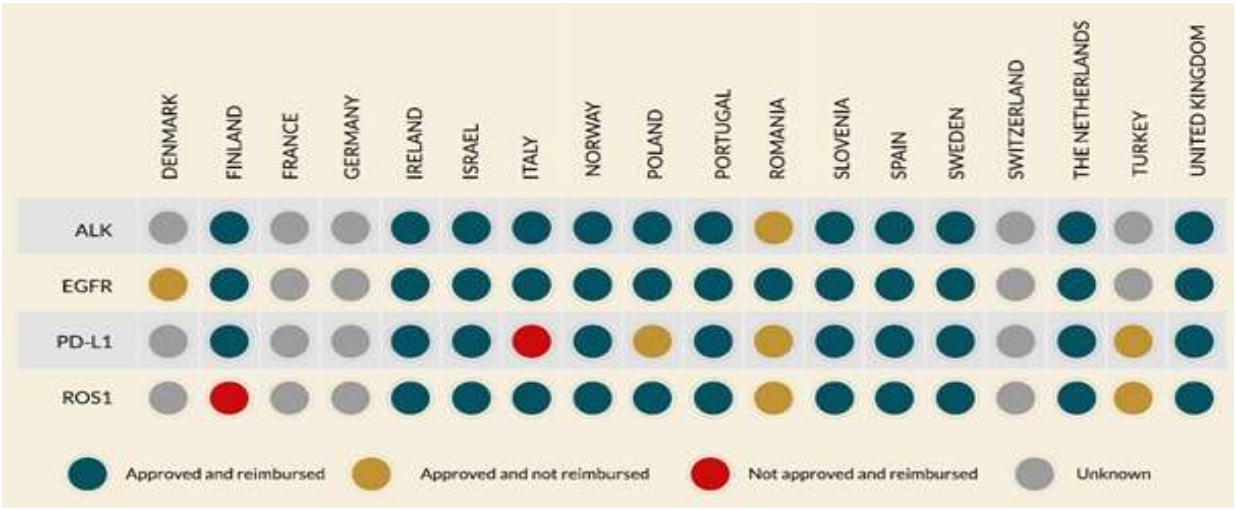

Figure 5: Availability of lung cancer molecular tests in Europe, 2017 (LuCE Report 2017)

Access to cancer medicines is also much greater in wealthier countries (see Figure 4): in 2018 the counties spending the most were Austria, Germany, and Switzerland (€92-€108 per capita), whilst the Czech Republic, Latvia and Poland spent the least (€13-€16 per capita). The differences in uptake rates are the highest for immuno-oncology medicines, for which uptake in the least wealthy countries is only 10-20% of that observed in the wealthiest states.

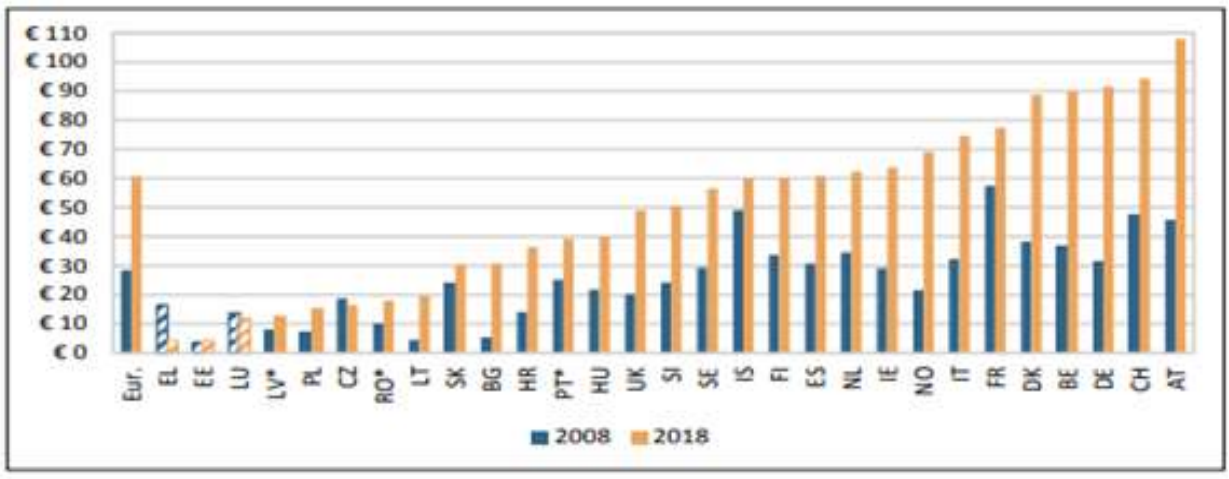

Figure 6: Cost of cancer medicines per capita, EU, 2018 (Hofmarcher et al. 2019)

The recent IHE analysis of the sales shows that access to novel therapies remains largely unequal among the Member States. Figure 5 shows cancer medicines sales by year of EMA approval in three groups of countries. This reflects a sizeable inequality in the availability and access to newly

authorised therapies, meaning that patients with a similar diagnosis from the upper-tier countries are substantially more likely to be treated with state of the art technologies than those from lower-tier countries.

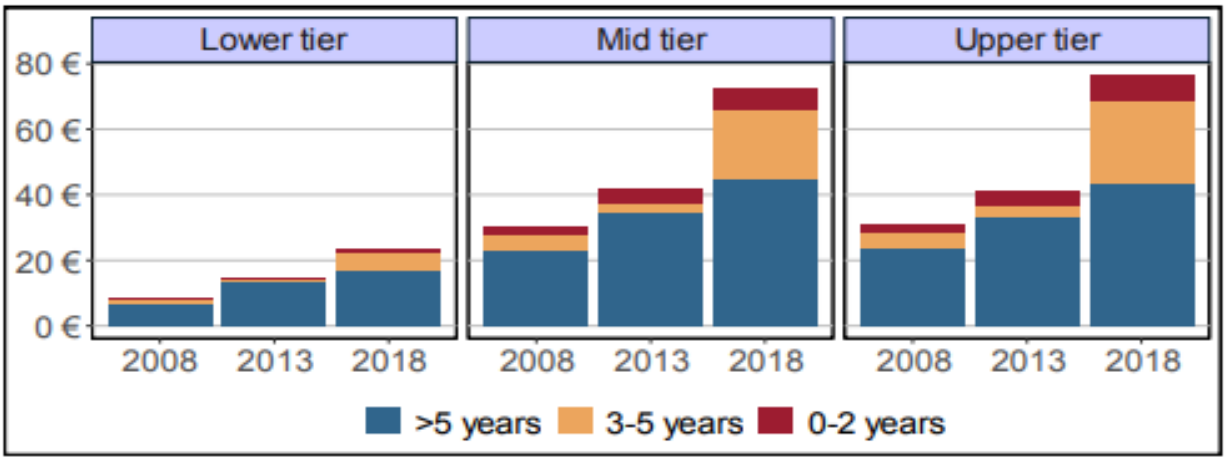

Figure 7: Sales of cancer medicines (in € per capita) by time since EMA approval by country groups (Hofmarcher et al. 2019)

There are various reasons behind the variation in access to novel health technologies across Europe. One issue is the lack of evidence of additional benefit for many newly approved cancer therapies, creating a need for follow-up clinical studies, adjustments in efficacy rates, and consequently in pricing and reimbursement schemes. Better availability of additional data of safety and efficacy, gathered in a real-world setting, could improve the uptake and use of novel valuable therapies.

Another issue is the difference in the level of affordability of new drugs for health systems across Europe. As mentioned earlier, the prices of cancer medicines increased dramatically over the past decades, making it unaffordable for countries with least health expenditure to procure the latest treatments. The similar problem persists for smaller European States, where the patient population is too small for the government to be able to negotiate better prices through bulk procurement. To fill the gap between affordability and access, novel methods for pricing, valuation and payment for health technologies are needed (Hormarcher et al. 2019). The use of generics and biosimilars can also serve to expand access to existing and new therapies in many countries, however, little examples of such radical policies exist.

To expand access to high-cost therapies, countries conduct (closed door) negotiations with pharmaceutical companies with an aim to negotiate a better price. Some countries have been involved in joint pharmaceutical policy schemes: e. g. Beneluxa Initiative[36] for cooperation in the areas of health technology assessment (HTA), pricing and reimbursement, information sharing and policy exchange, and horizon scanning. Beyond the multilateral country initiatives, joint HTA in Europe is steered by the European Network for Health Technology Assessment (EUnetHTA), which supports voluntary cooperation between HTA bodies across the Member States. Such collaboration programmes for HTA and reimbursement show promise to deliver greater access to novel cancer therapies to more patients across Europe though applying economies of scale and avoiding duplication of efforts. However bigger representation and closer collaboration of Member States is needed to advance existing efforts.

[36] Members: Netherlands, Belgium, Luxemburg, and Austria. More info: https://beneluxa.org/collaboration

2.6.6 Cross border cancer care

The EU Cross-Border Healthcare Directive[37] can also serve as a booster of patient access to cancer therapies (including surgical procedures and use of medical devices) in cases when cancer diagnostics and treatment are covered by national health systems but cannot be provided to the patient within medically justifiable time limit or because the technology is unavailable in the country. According to the directive, in such cases, patients are entitled to receive similar care in the other Member States, with national insurance covering costs up to the amount determined by the patient's reimbursement basket. The Directive can be effective in expanding the availability of cancer services, particularly in the areas of rare diseases. However, since the reimbursement is determined by the national regulations, the Directive does not cover patients for whom access is not granted in their home country thus it does not address the systemic problem of inequality in access across Member States.

2.6.7 Cancer care guidelines

While every European MS can develop and adopt national clinical guidelines for cancer diagnosis and treatment, much progress has been achieved in developing European clinical guidelines. The European Society for Medical Oncology has developed a large database of clinical guidelines for various cancer types, which are available for clinicians through a simple and comprehensive online system[38]. Little is known about the overall level of MS adherence to pan-European clinical guidelines for cancer care. To enhance harmonisation, ESMO and other European organisations are putting efforts into development and implementation of various platforms for knowledge exchange such as joint multi-country trainings, conferences, and workshops.

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[37] Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare

[38] An overview of clinical guidelines is available at https://www.esmo.org/guidelines

2.7 Social developments

2.7.1 Inequity and prosperity

In the forthcoming decades the number of new cancer cases in the European Union increases substantially, mainly because of the aging population of Europe. The risk for the most common cancers increases after 65 years. Projected cancer burden 2018-2040 could mean 100 million new cancer cases in the next 25 years. (Ferlay et al. 2018; Schütz et al. 2019). There is no easy way out. When nearly half of the cancer can be prevented, there is a push for societal action and preventing those cancers that are preventable.

Cancer is, as many diseases, related to socioeconomic differences. Advances in medicine increase survival but unevenly between countries, regions and individuals. Inequalities are complex to tackle. For instance, recent research in Finland showed how pediatric cancer patients whose parents have only basic education or whose mother tongue is not Finnish or Swedish have higher risk of dying than patients whose parents have higher education or are native Finns, even when access to cancer care is equal and treatment standardized (Tolkkinen et al. 2018).

According to findings of Eurocare 5 -study between European countries mean for instance that:

- In Eastern Europe, the mortality rates for many cancers are above the European average.
- Western and Northern European countries also have social inequalities in cancer care, such as low survival rates for lung, colorectal and ovarian cancers in the UK and Denmark as compared to Norway and Sweden.
- Some European countries have inadequate access to surgery, radiotherapy and essential and personalised medicines, treatments that have been shown to prolong lives and in many cases achieve long-term cures.
- Access to innovative treatment interventions, a number of which have demonstrated substantial therapeutic benefit, are also inadequate in some European countries. (Peiró et al. 2018; De Angelis et al. 2014).

2.7.2 Socioeconomic status and cancer control

In cancer survival, socioeconomic differences have been reported in many cancer sites and populations, with patients from lower socioeconomic groups having poorer survival. Differences between socioeconomic groups in the stage of disease at diagnosis and in access to optimal treatment clearly explain at least part of the association between social deprivation and cancer survival. Characteristics of the patient, such as nutrition, co-morbidity and health-seeking behaviours, may also interact with treatment decisions and, ultimately, with the outcome. Socioeconomic status is reflected in health illiteracy and thus cancer literacy. It is important to find out whether socioeconomic differences in how patients seek and obtain access to health services, or participate in screening, are associated with socioeconomic differences in cancer survival. (Woods et al. 2006)

As cancer is a heterogenic name for many diseases, inequalities exist in every level of cancer control. There is a remarkable diversity across EU member states and between individuals in cancer prevention, early detection, access to therapies and in survival.

Example 1: While cervical cancer rates in the Nordic countries have fallen markedly over the past few decades, there have been striking increases in parts of central and eastern Europe; these increases reflect changing sexual practices, an associated increased prevalence of human papillomavirus (HPV) infection, and a continued absence of effective screening programmes. For example, **incidence** rates in Bulgaria and Romania are now similar to those in several sub-Saharan African countries (Bray et al. 2018).

Example 2: Lung cancer is one of the main contributors to the differences between European countries in the magnitude of inequalities in cancer mortality. This is unsurprising because lung cancer is a very common cancer and tobacco smoking, its main risk factor, is strongly associated with socioeconomic status. In Europe, absolute inequalities in lung cancer **mortality** rates in men were

largest in central and eastern Europe, followed by Belgium and Norway, whereas inequalities in women were largest in Denmark and Norway. (Vaccarella et al. 2019)

Example 3: In breast cancer best **survival**, 85% or higher, are in 16 European countries, but in the range of 70-79% in Estonia, Lithuania, Croatia, Bulgaria, Poland, Romania and Slovakia (Allemani et al. 2018). In some countries survival rates are difficult to estimate, due to weak data management and lacking links to registers.

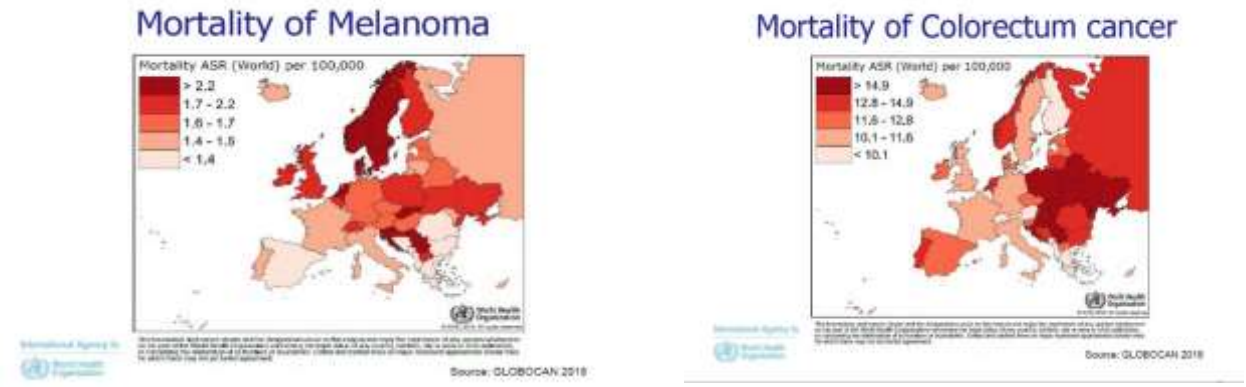

Figure 8: Mortality of melanoma and colorectum cancer (Soerjomataram 2019)

In general privileged groups have better cancer outcomes because:

- they have fewer risk factors for cancer and /or
- can take advantage of new interventions and screening programmes more quickly,
- more easily access health services, and
- can minimize the social and financial consequences of cancer when it occurs.
- higher education means also less exposure to tobacco consumption and obesity, both risk factors leading to cancer (Peiró et al. 2017)

Thyroid cancer and prostate cancer are examples of cancer types where overdiagnosis and overtreatments are common among more wealthy populations (Vaccarella et al. 2019). The cancer type associated with higher socioeconomic status is cutaneous melanoma. Melanoma mortality is higher in the north while UV radiation is stronger in the south. In colorectal cancer mortality eastern part of Europe is dominant. (see Figure 8).

2.7.3 Prevention, European Code Against Cancer

It is often stated that preventing cancer is the most neglected part of the cancer continuum, lacking both financial support and public attention. Current estimation is that in Europe over 40% of all cancer cases could be prevented and among preventable cancers about 50% are due to tobacco. Those countries who have managed to reduce smoking prevalence, have demonstrated steep declines in lung cancer mortality (Schütz 2019; Thun et al. 2012).

The evidence of health harms of tobacco is so strong that both the World Health Organization WHO and EU regionally have in the last decades put much work on regulation. On global level there is the Framework Concention on Tobacco Control, ratified by over 180 countries. EU was among the first 40 signatories of the global treaty. The newest Tobacco Products Directive (2014/40/EU) entered into force on 19 May 2014 and became applicable in EU countries on 20 May 2016.

Most preventable cancers are cervical cancer (100%), lung, oral cavity and oesophagus (90%) followed by melanoma and stomach cancers (75%) and colorectal cancer (55%), thus the potential to expand preventive interventions remains large.

WHO has called for a global elimination of cervical cancers in May 2018 because of its high preventability. (WHO call 2018). The evidence base of preventable cancers and for a number of measures has been summarized in the Cancer Prevention Europe website by IARC and on a dedicated website for the 4th edition of the European Code Against Cancer.[39]

Citizens' awareness of cancer risk factors is regularly monitored in the EU, for instance in France Baromètre cancer.

Currently there is a drive towards developing health policy at EU level and to support individual member states. For instance the European Code against Cancer (4th edition) recommendations are aimed at individual level, although health promotion and specific concepts like Health in all policies, emphasize comprehensive action across all policy sectors.

Important reason for slow progress in prevention is the strong role played by commercial determinants of health. There is a need to take robust, regulatory action against industries who wreak wholesale havoc on health at a population and individual level. Recognizing the need to broaden the scope from individual action to health policies is important because the environments we live in are shaped by commercial actors and politicians who refuse to protect their populations. The iPAAC Joint action (2018-2021) will produce a sustainability plan for the European Code Against Cancer, further developing evidence-based strategies of cancer prevention. This work is ongoing in collaboration with member states from iPAAC consortium, International Agency for Research on Cancer (IARC) and the Association of the European Cancer Leagues ECL. The scope of the Code is one of the main points under discussion.

The European Code Against Cancer (ECAC), 4th edition

1. Do not smoke. Do not use any form of tobacco.
2. Make your home smoke free. Support smoke-free policies in your workplace.
3. Take action to be a healthy body weight.
4. Be physically active in everyday life. Limit the time you spend sitting.
5. Have a healthy diet. Eat plenty of whole grains, pulses, vegetables and fruits. Limit high-calorie foods (foods high in sugar or fat) and avoid sugary drinks. Avoid processed meat; limit red meat and foods high in salt.
6. If you drink alcohol of any type, limit your intake. Not drinking alcohol is better for cancer prevention.
7. Avoid too much sun, especially for children. Use sun protection. Do not use sunbeds.
8. In the workplace, protect yourself against cancer-causing substances by following health and safety instructions.
9. Find out if you are exposed to radiation from naturally high radon levels in your home. Take action to reduce high radon levels.
10. For women: Breastfeeding reduces the mother's cancer risk. If you can, breastfeed your baby. Hormone replacement therapy (HRT) increases the risk of certain cancers. Limit use of HRT.
11. Ensure your children take part in vaccination programmes for: Hepatitis B (for newborns), Human papillomavirus (HPV) (for girls).
12. Take part in organised cancer screening programmes for: Bowel cancer (men and women), Breast cancer (women), Cervical cancer (women).

2.7.4 Early detection

The EU council recommendation on population-based cancer screening programmes (2003/878/EC) includes breast, cervical and colorectal cancers. Cervical cancer screening programme will change in the future the most, when human papilloma virus (HPV) vaccination programme reaches the age

[39] Cancer prevention Europe, accessed 27.1.2020. https://cancerpreventioneurope.iarc.fr/ and European Code Against Cancer, accessed 27.1.2020 https://cancer-code-europe.iarc.fr/index.php/en/

groups for screening. Pre-cancerous lesions or pre-cancers are precise entities for which early detection programmes exist. In population-based screening programmes the targeted population is asymptomatic. The programme is intended to find pre-cancerous changes before they give symptoms.

If detected early - either from screening programme or based on symptoms and early diagnosis in clinical settings - cancer can be less invasive, easier to care for and with better prognosis. Awareness of early warning signs of cancer helps in detecting cancer early.

A summary on implementation of cancer screening has pointed out several vulnerabilities of early detection which have effects on inequality among countries, groups or individuals (Anttila et al. 2019). Out of the 28 countries population-based screening in its implementation, roll-out, piloting or planning phase is on-going for breast cancer in 25, cervical cancer in 22, and colorectal cancer 20 EU member States (Ponti et al. 2017; Basu et al. 2018; Senore et al. 2019).

Among the estimated 32 million female annual population for breast cancer screening in the age group of 50-69 years in the EU, nearly 25 million have been invited to mammography screening in the population-based programmes in the index year (coverage by invitation 79%) and 16 million have been screened (coverage by examination 49%) (ibid.). Among the women invited in this age, on average 60% participated in screening though the participation rates varied remarkably, between 6.2% and 84%.

The quantitative information available from 19 of the countries on population-based **cervical cancer** screening programme showed that 59% (range 7.3 – 100.0) of the annual target women aged 30-59 years (the minimum age group targeted in the EU countries) were invited for screening and 53.2% (range 23.9 – 86.7) were tested in the index years. The mean participation rate to screening in the 30-59 years age group in the countries providing data was 51% (range 12 – 68).

The estimated coverage by invitation and by examination of the annualized EU population aged 50 to 74 years for **colorectal cancer** screening were 33% (range 1.4 – 112) and (as low as) 14% (range 0.5 - 65), respectively. The values of the other performance indicators differed with the target age, screening tests used and also the threshold of positivity used by the programmes.

While the evidence informing implementation of effective cancer prevention and early detection is strong, in addition to social determinants of cancer, there are commercial determinants of cancer prevention and early detection. In prevention, there is resistance to regulation while in early detection there is a push for practices that have not been researched enough (Kickbusch et al. 2016; Maani et al. 2020).

All public health measures, like organised screening programmes on population level, are continuously researched. The commercial sector markets new possible screening programmes with risk stratification, although all screening programmes identify risks for instance in defining age-groups of target populations or modifying screening intervals.

There is often a tendency to simplify screening programme into merely taking a test with technological improvements. There is also a strong push to introduce new programmes based on risk strategies. Before launching new programmes they need to be piloted, evaluated with balanced harms and benefits and monitored with proper follow-up. Target groups of screening activities should be clearly defined and identified, and ethical principles considered, even if scientific research and evidence support possible action.

In CANCON Joint Action quality assurance for cancer screening programmes was examined and recommendations given. Several points for improvement are needed within implementation, including data management and legislation.

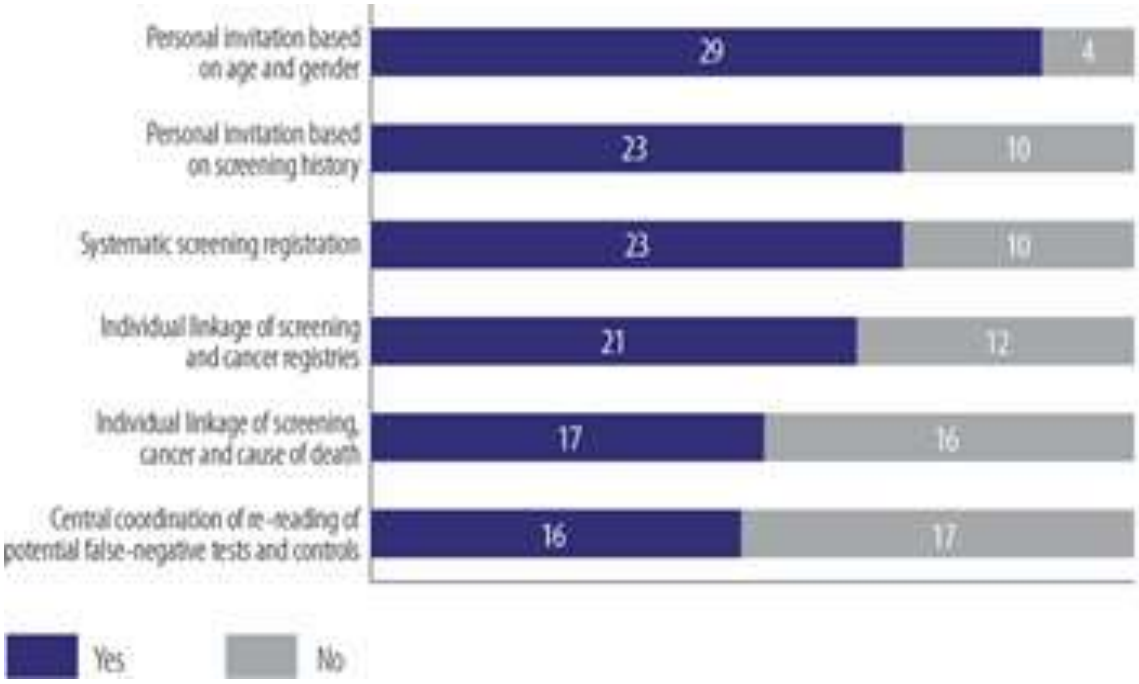

Figure 9: Legal frameworks for cervical cancer screening in 33 European countries (Anttila et al. 2019)

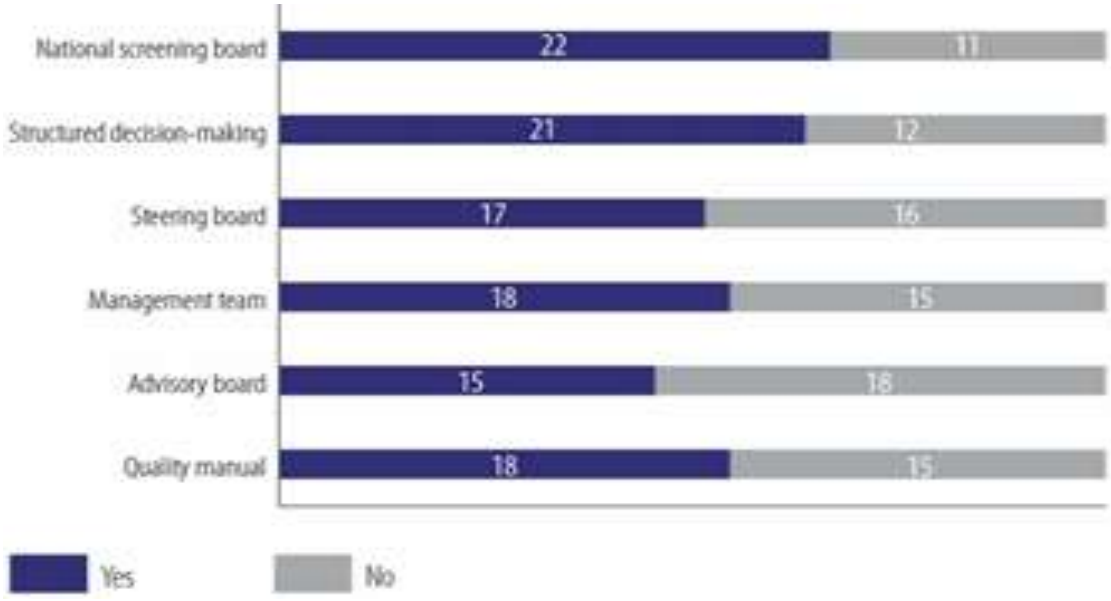

Figure 10: Governance of cervical cancer screening in Europe (Anttila et al. 2019).

2.7.5 Survival, cancer plans

Survival from cancer in Europe has increased steadily. Large collaborative studies like Eurocare-5 (24) with over 10 million patients and Concord-3 (Allemani et al. 2018) with 37,5 million patients report differences among European countries. These studies have also boosted developing cancer plans and learning from other countries. Eurocare-5 found that survival in eastern Europe was generally low and below the European mean, particularly for cancers with good or intermediate prognosis. Concord-3 reported that in Europe the 5-year net survival remained the highest in the Nordic countries with Denmark closing the survival gap with the other Nordic countries. The population-based studies are key indicators for systemic efficiency. They are drivers for countries to reach out for better outcomes. Concord-3 researches note that quality of data is a problem. Some countries could not report survival data at all because necessary linkages from registry database to regional or national death indexes were missing. “Governments must recognize population-based cancer registries as key policy tools that can be used to evaluate both the impact of cancer prevention strategies and effectiveness of health systems for all patients diagnosed with cancer.” Similar calls have been made by WHO and the leading global NGO, The Union for International Cancer Control (uicc.org), in its World Cancer Declaration.

Cancer plans have been developed as systematic tools to decrease inequalities. Joint action CANCON made a mapping on European cancer plans and its predecessor EPAAC introduced the elements of cancer planning (Jelenc et al. 2017; Albreht et al. 2014) and currently iPAAC Joint Action is examining cancer plans in Europe.

Survival differences also indicate that outcomes are not equal and access to innovation, new instruments and new drugs in the EU member states. Establishing an attractive environment for clinical research, commercial relationships, and drug development is necessary. The process should be balanced by an independent, non-commercial, and robust clinical research programme for the management of patients in clinical settings so as to be able to recommend access to therapeutic strategies based on solid foundations. 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. (Thierry et al. 2019)

2.7.6 Patient-centric cancer: quality of life, social cohesion and support

There are justified calls for including patient perspective in every level of cancer continuum. Disparities exist from access to medicines to surviving cancer.

Quality of life and late effects of treatments should be taken into account when discussing treatment options. Multidisciplinary teams (MDTs) are one example how to tackle different viewpoints. Patient voice is stronger than before with introduction of patient fora and advisory boards. Patient Reported Outcome Measures (PROMs) and feedback facilitated by Patient Reported Experience Measures (PREMs) are tools that can improve services. After treatments many patients report long-term effects. Long follow-up has impacted radiation doses of treatments to avoid secondary cancers.

Young patients, starting their family life, may experience fertility problems. These need to be planned in advance. In studies and working life, returning back is an important phase. Cancer patients have also right to be forgotten, when cured. There are still difficulties with insurances and other financial issues.

A survivorship care plan including secondary and tertiary prevention, rehabilitation and pain management has been developed on European level. The main messages were:

1. Cancer survivors’ follow-up, late effect management and tertiary prevention needs to be anticipated, personalized and implemented into care pathways, with active participation of survivors and relatives.
2. Improvement of early detection of patients’ needs and their access to rehabilitation, psychosocial and palliative care services is required.

3. An integrated and multiprofessional care approach with a coordination of community care providers and services are needed to implement a survivorship care plan that enhances patient's self-management and quality of life.
4. For children, adolescents and young adults survivors, late health and psychosocial effects of cancer and its treatments need to be anticipated and addressed.
5. More research in the area of survivorship is needed to provide data on late effects, as well as the impact and cost-effectiveness of supportive care, rehabilitation, palliative and psychosocial care interventions. (Albreht et al. 2017)

Global cancer information service group ICISG shares online best practices from its members from 40 countries and over 70 cancer information services (icisg.org). In Europe, the patient support working group is convening regularly and sharing experiences from the members of the Association of the European Cancer Leagues. Hospitals have developed support networks and communication channels for interaction. European Cancer Patients Coalition and other patient groups follow closely health policies advocating patient perspectives. The importance of communications is reflected in the work of International Psycho-Oncology Society (ipos.org). There are special aspects into communication and quality of life issues, for example geriatric psycho-oncology or adolescents and young adults (AYA). Multiple channels make peer to peer support services easy.

Tailored communications are possible for special groups and require service design methods for the patient needs to be met. Confidentiality and privacy issues are challenges in digital environments, yet digital interventions offer solutions (Bradbury et al. 2019).

The European Cancer Patient´s Bill of Rights includes 3 principles: 1) the right of every European citizen to receive the most accurate information and to be proactively involved in his/her care. 2) the right of every European citizen to optimal and timely access to a diagnosis and to appropriate specialised care, underpinned by research and innovation. 3) the right of every European citizen to receive care in health systems that ensure the best possible cancer prevention, the earliest possible diagnosis of their cancer, improved outcomes, patient rehabilitation, best quality of life and affordable health care (Lawler et al. 2016).

Trust in science and evidence-based therapies are competing with false information and rumour society. Developing patient-centric services and engagement is one way to build trust in the future.

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ANNEX II - TWO SCENARIOS WITH FOCUS ON THE FUTURE OF FIGHTING CANCER WITH REGARD TO PREVENTION, DIAGNOSTICS AND TREATMENT, AND SURVIVORSHIP

Experts:

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Satu Lipponen
Thyra de Jongh
Kerstin Cuhls
Dana Wasserbacher

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INTRODUCTION

This report summarises the work done to adapt two future health scenarios with the aim of tailoring them specifically to possible futures in the fight against cancer. The two future health scenarios were developed in an earlier EU-funded project entitled "FRESHER - FoResight and Modelling for European HEalth Policy and Regulation", which aimed to identify future research policies to effectively address the burden of noncommunicable diseases (NCD) using emerging health scenarios with a time horizon up to 2050.

Within a scenario workshop with members from the Mission Board on ‘Fighting Cancer’ and members from the European Commission, the two FRESHER scenarios were discussed and feedback for desirable futures with regard to fighting cancer was collected.

The specific objectives of the workshop were to

- produce sketches based on the Fresher scenarios with focus on the future of cancer (prevention, diagnostics & treatment, survivorship)
- outline desirable futures with regard to cancer (prevention, diagnostics & treatment, survivorship)

in order to support the Mission Board to identify future-oriented topics from multiple perspectives for their mission.

In a final step, the gathered ideas and future outlooks were discussed with experts of the project team and the scenarios were further developed with a special focus on the fight against cancer. The resulting final scenarios are presented in the following.

SCENARIO “WE WILL HEALTH YOU”

The scenario workshop took place on 30th March 2020, from 13:45 to 15:45 (CEST) in a virtual online meeting room. Eight participants discussed the plausibility and consistency of future trends summarised in the basis scenario “We will health you” and provided input to possible futures of cancer and on desirable future developments. Kerstin Cuhls moderated the discussion and editing of a shared online document. Experts from the project team were present and supported the workshop.

Table 1: Participants of the online workshop

First Name	Name
Anne Lise	Ryel
Fiona	Godfre
Konrad	Rydzynski
Pedro	Pita Barros
Ruth Lydia	Ladenstein
Marcis	Leija
Walter	Ricciardi
Regina	Beets-Tan

General Picture: Economy, Politics, Society

We celebrate the year 2050. Today’s priority is to guarantee access to adequate health care for all European citizens in a timely manner in a growth-oriented society. Governments and the private sector collaborate closely to maintain a healthy workforce and to keep Non-Communicable Diseases (NCDs) under control, with the aim of ensuring the continuation of economic productivity as well as the sustainability of the healthcare systems. Thanks to big data, pattern recognition, public and private investments effectively influence citizens’ behaviour towards healthy lifestyles. When meeting the „general standards“ of a healthy lifestyle, you get a reward and your insurance is kept at stable costs. By offering healthy working environments and care services, employers compete to attract talented, motivated and well-educated people. Employers are increasingly held accountable for providing working conditions that are optimal for health.

On the other hand, thanks to fair labour legislation, employees increasingly have the means, including money, time and knowledge, to take better care of their own health and there are high expectations to do this. This top-down approach is accompanied by ambient 24/7 surveillance measures and a high degree of regulation and control of individual behaviours through personal implanted chips. Before the Covid-19 crisis in 2020, nobody in Europe would have expected that such chips would be accepted - but now, renouncing privacy is considered to be a low price to be paid for the advantages offered by the guarantee of a treatment, non-infectious tele-medicine or tailor-made diagnostics and treatment. The Covid-19 crisis paved the way for new measures in surveillance and devices that are widely accepted by the population that had and keep a self-image of suffering during the crisis even though a small percentage of the population was really confronted with covid-19 directly. If Covid-19 may cause cancer, is still unclear as only 30 years have passed since the ”crisis”. There are many other virus candidates assumed to cause cancer.

All this was a silent and unnoticed development that the rather paternalistic measures and additional surveillance (mutually and by the state) are accepted. And the young do not know a world with a „freedom“ of choice or without being under surveillance.

Innovations for “Healthing you”

In healthcare and for fighting cancer, this means, it is easy and normal to screen, monitor, gain data, or process data - or have them processed automatically. Huge databases are available, AI scans and

summarizes them. AI is used to identify tumours, scan skin or organ images and give a warning if someone in the usual and mandatory screening is positive. It predicts from genome data bases who is at a risk of becoming ill and warns quite early in lifetime so that people under any risk of getting cancer are under specific monitoring.

Monitoring also takes place at the workplace. Europe is a dynamic and innovative economy competing with emerging economies' cost advantage by delivering high-quality goods and services. The introduction of ICT in workplaces led to a situation where surveillance devices do not only monitor health for workers' private use. Many companies also monitor if their employees have healthy lifestyles. This had an additional effect: ambient surveillance creates stress because even though the technology for monitoring is invisible, people know that every move is observed - they cannot escape and behave accordingly, they get under permanent stress. Stress puts pressure on the immune system and can indirectly cause cancer. But economy comes first, and EU countries enjoy a new era of economic growth and social progress founded on education, innovation and full employment, thanks to important government action, and the "European model", which stands out in an increasingly competitive world. Tracking Apps are not only to monitor economic activities but also sports, visiting a hospital, using prevention measures etc. Mobile phone operators can be asked for data, for example on the question when people leave their homes. All these are normal activities and tracking apps are always switched on - nobody cares because it is for the personal benefit and security. In former times, people thought that this is only true for payments and in cancer research or for patients it would be different. But it is not - people are used to this way of being tracked and being transparent.

Innovation in medicine supported the policy measures. There were promising breakthroughs for example in personalised medicine. Thanks to government-managed big data, implanted chips and gene scans personalised prevention and treatment, including organ or tissue regeneration, are now accessible and paid by insurances. New treatments are largely affordable because the drug pricing framework has been reformed to reflect a fair balance between intellectual property and public health rights. A strong governmental top-down policy on data and on drug pricing affected the fight against cancer dramatically. We now have a fair distribution of drugs, common affordable pricing. Big Data and AI introduced new ways for research and insights, and hence accelerated better and more cures. Cancer is not the predominant worry of our societies, anymore, but just another chronic disease. It has been replaced by the fight against dementia.

Part of the success story was that the EU guided on the IP protection in academic centres and universities to stimulate research and spin-offs from the universities, in particular in countries were strict regulations were not in place. This was directly linked to specific funding and fostered an exchange of knowledge among the member states in cancer research. The formerly uneven distribution of knowing what to do was overcome. Knowledge spread quickly in cancer-related open networks. In our paternalistic states, the public money is used for new ways of intervention also by regulators or authorities along the whole innovation process. Altogether, more public money is available for the health sector and research in cancer or for fighting dementia.

Migration

Yes, migration is still an issue with two facets. Europeans are old but healthy and work longer to sustain themselves and to be part of the work-oriented society. The number of people who want to move to another country rises but the EU accepts only those who can match the qualification needed in the EU economy. People from non-EU countries have restrictions when they want to enter Europe - very restrictive migration policies exist that take into consideration the migrants' skills and their possible contributions to the EU economy's growth. The state policy allows exactly the number of rather young people from the south to enter the country that is needed to keep the economy in a stable state, but in the long run, this is not enough to compensate for the costs that have already risen because of the many very old people (older than 100) and the very old people with unavoidable and uncurable cancer. The cases of cancer related to age are still increasing.

Between Citizen Empowerment and Big Brother

People who live in Europe are the lucky ones. In a competitive world, equity is reached in the EU by ensuring that economic growth leads to (some) social progress. In Europe, equity is improved thanks to the new wave of economic growth and targeted redistribution policies. Equity, economic growth and redistribution lead to a relatively stable situation, in which most people can afford a healthy lifestyle and have equal access to tests for illnesses (like cancer), diagnosis and treatment. But it took a long time and a lot of cultural change for people to accept cancer screenings and tests. Thanks to a broad European change management programme in respective cultures the new „culture“ of prevention and screening normality was successfully installed. A lot of nudging and a bit of direct pressure was necessary for this.

In our uniform society, online information is strictly controlled to avoid dilution or manipulation of information. A new order is set in the digital world, now governed by an alliance of governments, industries and citizens' representatives to serve public policy goals and the common good. But there are some problems: The control of data and information often enhances bureaucracy and hampers creativity, e.g. with regard to patient empowerment. But what does citizen empowerment mean if we are all in a good state? We accept the situation as it is good for us - and as a patient, I get the treatment I need.

Some people ask strange questions: Can we trust governments in general or our own governments? Can we trust in reporting? Can we trust the information in the open networks? Are we manipulated? For example, with statistics? Do we need more independent data sources? But in fact, who cares... the situation is fine, why worry.

The role of Urbanisation, Climate Change and Environmental Issues in Fighting Cancer

Cities are the engines of ongoing growth and first and foremost places to work. Urban planning aims at offering the optimal conditions to work in cities (housing, transport and health services), especially as it is much easier to control employment and movements of people. Cities are a good environment to provide technical as well as social innovations in order to nudge people to a healthier lifestyle (physical exercise, neighborhood communities for urban gardening, social care, etc.). Societal pressure is enough, and it is fashionable to live in cities. The countryside is outdated - an image also propagated by the official media.

But the concentration on cities has also disadvantages and disregards everything that is not related to productivity, including environmental issues. For example, air pollution, soil and other pollution have their effects anywhere, but the negative effects are visible especially in the cities with smog, where lung diseases including lung cancer are spreading tremendously. And to stress it once more: we do not know which of these lung cancers can be traced back to one of the viruses of the last three pandemics.

People are stressed because of the mass of people living in small flats or apartments - even in Europe. Stress develops - often unnoticable - at many different levels, by being tracked, by being observed by neighbours to obey all rules of state and society, by being exposed to new and ever more substances, by the lack of personal time, or by just living in small spaces. We sometimes wonder if this is still „species-appropriate keeping“ (which is highly regulated for animals). Human beings have less and less physical education or training and their „city lifestyle“ is based on consumption, also consumption of fast food (of course ”bio”), „healthy convenient bio food“ and the availability of everything at the moment it is desired. Food of high quality is available, but not all people want it - and even though it is tracked what we buy and eat, here many people still try to escape the strict rules. ”Junk food” is forbidden, but still eaten and it is difficult to prove who does not obey the rules. Of course, since 2025, smoking is forbidden, and since 2028 tobacco can only be sold in drug stores and for medical reasons. But that was long, long time ago.

Environmental sustainability is the principle in the background as efforts are focused on producing and delivering more to everyone, without any paradigmatic change in production and consumption, which had been expected in 2020, but was never realised. This led to the continuous outbreak of environmental emergencies (floods, cyclones, heat waves), the exacerbation of pandemics from time to time when a new virus or bacteria occur, and the increase in economic and environmental migration of people.

The ongoing and consumptive lifestyle has other impacts. At one point in time, the system was not able to compensate the deficits of the carbon society, anymore, and the effects on people's health were more severe than ever before. When the Paris Agreement was not signed or de-signed by more and more countries, there were only a few countries left trying to take measures for decarbonisation. They were not very successful - the earth is no island but an interwoven space. And the effects of climate change let the cancer rates increase in an unknown way when governments moved beyond the environmental limits. The few people who tried to stabilize their immune system by staying outside in the sun, evoked many more skin cancer cases, especially because of the huge ozone holes in nearly every zone of the Earth.

Growth and increases in production and consumption are the general receipe for economic cures - this did not change for decades. And although there were a lot of warnings that this cannot go on forever and also economic growth might lead to a kind of ”economic cancer”, the principles in the state-lead capitalist system did not change as it is the principle of the European Union, which struggled but also survived. In the whole EU? No, there is a small community in Belgium and some other spots all over Europe living a kind of ”postgrowth society”. They are not mainstream, they are ”outsiders” but they survive in their small environments. For them, economic growth is not in the forefront. The Covid-19 crisis gave them the impetus to experiment with new ways of living with (real) sharing, time banks, no use of money, sufficiency in some respects, being makers of their own needs (clothes, some old machines etc.), growing most of their own food and keeping away from tracking apps where possible. They are still part of the digital world to a certain extent but learnt to switch off what they do not need. The consequence is that they are not part of the full medical system, anymore, but rely on the standard functions, only. Insurance companies often refuse to take them as members - and of course the cancer detection functions do not work that well if they are not part of the screening mechanisms. But because of their way of living, the members of these ”communities” live in a good health even in older ages and they do not develop more cancers than other inhabitants of the countries they are living in. As they do not cause costs for state, the state lets them live their lives in the niche.

In the major parts of Europe, increases in production and consumption put a huge pressure on the ecosystems. Green investments were only undertaken if they were economically profitable in a rather short time. The direct impact was that the risk factors for cancer changed dramatically - not to the positive, so the cases of diagnosing cancer are still on the rise in numbers, but more can be cured. The governments tried to get hold of this by generally tracing whatever is possible (e.g. specific cancer-related substances) and for the individual by tracing the exposures of individuals in the environment, e.g. on workplaces to provide early treatments if necessary. On the other hand, the exposures of the individual are related to the life style habits that is highly related to the economic status. This means, the rich are not better off.

SCENARIO “THE RICH GET HEALTHIER”

The scenario workshop took place on 30th March 2020, from 13:45 to 15:45 (CEST) in a virtual online meeting room. Eight participants discussed the plausibility and consistency of future trends summarised in the basis scenario “We will health you” and provided input to possible futures of cancer and on desirable future developments. Susanne Giesecke moderated the discussion and editing of a shared online document. Experts from the project team were present and supported the workshop.

Table 2: Participants of the online workshop

First Name	Name
Andres	Metspalu
Bettina	Ryll
Christine	Chomienne
Elisabete	Weiderpass
Martine	Piccart
Regina	Beets-Tan
Serban	Ghiorghiu
Tomi	Mäkelä

General Picture: Economy, Politics, Society

The Europe of 2050 presents a very fragmented picture. It is fragmented in terms of equity as large income gaps exist across and within European countries and the distribution of wealth has been ever more uneven since 2020. It is also fragmented in terms of health and well-being, which parallel the social stratification of wealth and income. What is even more crucial is the changing structure of what was called the European Union (EU) many years ago. Today, the EU consists of 16 core member states that are considerably wealthy and claim to share the same values. These are: green growth, technological progress, roll back of the state and the democratic principle of separation of powers. During the last 30 years about half of the former 31 Member States have left or had to leave the EU. Some left because they could not comply with the fiscal criteria of green growth. Others left because of because they were infringing peoples’ right to vote in a democratic manner or suppressed the freedom of the press and thus impeded the principle of separation of powers.

Apart from the 16 EU core members, there is a de facto second layer of some former EU members as well as some other European countries, including Switzerland and Norway, Catalonia, Scotland that have either mutual agreements with the EU or bilateral agreements with some of the core members. These agreements insure free trade, close scientific collaboration and trans-border health care. Thus, citizens of countries that are part of the agreements have the choice of health/ cancer treatment in an associated country if their private insurance scheme is offering it.

Innovation in Medicine and the Health Care System

After the COVID-19 crisis in 2020, a window of opportunity had opened for strong governmental measures to be taken in order to prioritize health over economic measures. These measures, though subsided after a few years, have also affected the approach to fight cancer in the long run. Public hospitals and GPs have become part of a much tighter and efficient network governance by state health authorities. The basic supply for medication, hygiene etc. was improved. Most of these basic supplies incl. medication and medical appliances are produced within the country or in another EU core country. Besides, more expert occupations have emerged within the health sector, thus improving the overall health provision in the EU, or what remained of it. Innovator networks committed to the health sector provide the resources for rapid production of new appliances, e.g. through 3D and 4D printing. Better provision is also the case for diagnostic and screening facilities. Though this is generally not affordable for the poorer part of society, patients with private insurance schemes profit

from the progress. Such provisions account for the fact that more cancer screenings among the better-off are done.

When it comes to rare cancer diseases national health systems are short of capacities. Access to the newest and most expensive medicines are limited to those who are employed or have an additional health plan or special insurances. Older precision medicines are available and in use once their patents have expired or cheaper biosimilars are available. Out of pocket payments are burdening the poorest part of the population.

Private health plans over the last years are offered by multi-national companies with mixed services and goods (conglomerates). People and organisations can buy shares to participate in the profits and to share the risk burden of high investments in personalized and the latest diagnostic services. Many cancers have become chronic and the most expensive medicines and diagnostics are prolonging life with fighting against metastatic tumours. These multi-national companies (MNCs) are joint ventures of former insurance companies, pharmaceutical companies, hospital providers, IT companies and miscellaneous investment companies. The unlimited provision of services within the core EU countries and agreements with some of the associated countries have fostered economies of scale for the MNCs. With their shares, shareholders have the opportunity for advanced and personalized medication and treatment if the company is investing in such directions or if one of their partner companies is. The breadth and depth of the provision for each patient depends on his/her health plan or the collective health plan their employer has bought for them. Wealthy people are exposed to over-treatments as a follow-up of development of diagnostic services.

Environmental Change and Urban Development

The EU wide campaigning to put a halt on carcinogenic emissions has improved the general health of the people and reduced the rate of cancer incidents among younger people. There are less dangerous emissions from traffic, heating, industry and agriculture. Most importantly, healthy lifestyles are fashionable and wealthy people are sportive, do not smoke or use alcohol. Smoking is concentrated in the poorest section of population coupled with many addictions (games, drugs...). Nonetheless, there is still an increase in the total number of cancer patients due to the fact that the people keep getting older. Younger people are less confronted with cancer.

The green growth orientation has relieved some stress from the bigger EU cities and promoted the attractiveness of small cities and the rural area. Thanks to ubiquitous technologies, the importance of location for doing business has subsided over the years. More and more families and alternative household units have moved to energy neutral housing, improving also the overall public health. E-health and m-health facilities help to monitor patients if necessary and to communicate with doctors far away. People who cannot afford private insurance plans may at least profit from the strong social networks in smaller cities and villages, showing a strong neighborhood spirit.

Equity

It is obvious that this system of health provision has improved access to medical care only for the most basic treatments. Profit-driven health systems produce inequity instead of health outcomes. Looking at the system in more detail will display that a large part of the citizens cannot afford shares in private health plans or do not have additional health plans through their employers. Especially economically marginalized people, unemployed, one-person start-ups, the major part of the low-tech service sector, but also single person companies and those in precarious employment etc. are dependent on the basic provision for general care. Parallel to the rudimentary public health care system, the private health care system is growing. In addition, there are also private philanthropists and charities that raise money from profitable companies and private donors to support patients in need for special care.

Low income for many citizens means also that their personal health is not on top of their daily agenda and that they cannot afford spending a lot of time to a healthy life style. Accordingly, many determinants that promote cancer such as unhealthy, industrialized food, tobacco and alcohol, sedentary behavior etc. are on the rise, accompanied by co-morbidities from life-style diseases such

as diabetes. Insurance systems may cause also situations, in which wealthy people get unnecessary treatments or too invasive care.

Digitalisation

In the aftermath of the COVID-19 crisis, digitalization in the health sector experienced an unprecedented boost. Critics of private data collection were silenced by the argument that this is done in the name of public health. Health data can now be combined with population data and are the basis for modelling future projections of health incidences related to certain basic assumptions. Health data are not only collected by professionals but also by individual citizens and patients. The quantified-self movement inspires a lot of people to monitor, collect and provide their personal health data – and treat it in return for the promise of special health services. Thus, personalized medicine is able to make a big advancement in terms of diagnostics and recommending to some cohorts applying more suitable treatments for many more indications than ever before. The bottleneck, however, is, that some treatments are more expensive than others and most people cannot afford the more expensive ones. The digital hype is spurred by many individuals who “donate” their data to health companies and get the option of reimbursement for treatment – if necessary - in return. People who donate their data can become stakeholders of such companies and in some cases get the option of a paid treatment.

New data medical scientists have emerged as a profession to advise clinicians and patients on how to interpret the data and find feasible therapies.

The definition of rich and poor is changing. It does not run along material wealth alone but also depends on digital savvy, non-digital savvy; health literacy vs. health illiteracy. digital pathology, deep learning etc. Computational approaches can aid oncological practice by predicting drug response, improving cancer diagnostics and treatment, or engaging patients into care. Patients are shopping high-tech and best treatments across borders.

Citizen Empowerment

A gene scan at childbirth and big data give a statistical estimation of a person’s likelihood to develop cancer or other non-communicable diseases, if parents want it and can afford it.

People are empowered in a way that they seemingly have more transparency about their propensity to become ill. But therapies etc. are not always available and even if, not affordable to everyone.

There is also a plethora of information on cancer related issues and other diseases available in scientific and social media. It is impossible for anybody to keep an overview on the latest breakthroughs, prevention and diagnostic measures or treatments. Patients have to rely on medical experts but often have difficulties to find the best specialist for their needs and often get contradictory information. The urgent demand to find reliable and understandable information often makes them get in touch with social media where there is an uncontrollable abundance of information. But for lay persons it is almost impossible to make a judgement on the quality. Affordable medical care is often offered by pseudo-healers and uncertified self-announced therapists which creates a lot of confusion and even despair among cancer patients and their families.

Especially with the advancement of personalized medicine coupled with an increasing economization of the health sector the responsibility for health more and more has become a person’s own business and less a matter of a national health system. The public health sector is not providing any basic safety net such as vaccination programmes for the whole population but concentrates on expensive technologies to treat the healthiest and the wealthiest part of the population. This development favours people who have more sensitivity and resources to take care of themselves – and their family. People with little material and knowledge resources are disadvantaged.

Well to do people with a high level of (health) literacy, sometimes with practitioners in their family, have a more sensible approach to interpret the relevant information concerning their health, do testing at the right timing, consult experts and take preventive or treatment measures. They have the means

to cope with their own health in a more responsible way than the health illiterate people. The use of digital technologies for the monitoring of one's own health contributes to the increase of information and at the same time can be understood as the empowerment of citizens and patients to engage in 'communities of practice' with peers and specialist. These 'communities' are dedicated to certain indications and develop new approaches to tackle cancer diseases, increase the survival rate and improve the quality of life of patients and survivors.

Generations of citizens growing up with innovative technologies and societal enactment contribute also to a better scientific basis for the understanding of what and how treatments work for people at different age, thus slowly increasing the propensity of people to live with cancer for a long time during their life.

Demographic Change and Migration

As citizens get older and older, one in three persons will be diagnosed with cancer over the course of their lifetime. Even personalized treatment cannot make a relevant statistical change for the cohort above 90 years of age. In this age group, there are personalized treatments including geriatric oncology. Certain expensive new medicines can prolong life by an average of three months, though not necessarily improve the quality of life. This development has ignited a public debate over the value of life prolongation and health investments.

Through migration measures within the core EU countries and the associated ones, and through voluntary services, governments have attempted to ease the need for care for the elderly. However, the system is at the edge of the abyss, as the number of the very old and sick who are in need for care keeps growing and the resources are limited. Here again, equity is the crucial factor if a person may grow old and die with dignity or not. There is a trend of middle-class families transferring their old and sick family member to less expensive care homes and medical treatments in some of the associated countries.

Another challenge for the health systems, especially the public ones, is the increase of aging migrants, whose lives often have been rugged, painful and full of privation, thus increasing the prevalence of certain cancers and co-morbidities. The literacy problem is one factor why they do not have equal access to the health system, but there are cultural issues too that increase the propensity of premature death from cancer.

ANNEX: AGENDA ONLINE SCOPING WORKSHOP

Virtual Scoping Workshop on Trends & Drivers in Cancer for the EU Cancer Mission Board

Date: 23.3.2020 - 7.4. 2020
Tools: go to meeting, google docs
Location: online life and remote

Objectives:

- Produce 2 sketches based on the 2 characteristic FRESHER scenarios with focus on the future of cancer (prevention, diagnostics & treatment, survivorship)
- Outline desirable futures with regard to cancer (prevention, diagnostics & treatment, survivorship)
- Think long-term, think from the future, consider measures that have to be taken today to reach future objectives
- Open up different perspectives for more innovative ideas, avoid biases

All this in order to support the Mission Board to identify future-oriented topics from multiple perspectives for their mission.

The virtual workshop consists of five parts or blocks. It will take place during a time span of approximately two weeks. In order to substitute the envisaged on-site workshop, we will use online tools which every member can use easily by invitation. During this time, we will ask the Mission Board Members to provide inputs remote in block 1 and 4 and gather all together in online meetings in block 2 and block 3. Block 5 will be provided by the FOD Cancer team only.

Block 1: Mission Board members are asked to comment and add the list of trends & drivers base on the long paper sent in January.
Block 2: The sketches will be revised versions of the two of the four FRESHER scenarios with a focus on “What does this mean for cancer?”
The two FRESHER scenarios we will use are “The Rich get Healthier”, “We will Health you”.
Block 3: We will design “desirable futures" from different actor perspectives, outlining what desirable events and milestones would be to reach a desirable future and to avoid undesirable ones.
Block 4: Access to the documents of all groups and possibility for all participants to make additional written contributions or ask questions.
Blocks 2 and 3 will be done online and live. All other blocks will be done remote. Net time (remote and live) will be approx. 125 min per person overall.

AGENDA

March 23 to March 26 Remote google docs	**Presentation of Trends & Drivers** **Presentation of Scenarios** Block 1 **Additional Drivers** Get acquainted with the 1st scenario and nominate of additional drivers/trends/ developments for the scenario if necessary	FOD will provide and introduction in combination with the short version in written form. (will last approx. 10 min. per participant)
Until March 26	**Preparation for Group Work** For scenario work: split Board Members into 2 group (mix the members of the 4 working groups, mix nationalities/regions) For small stakeholder perspective group: split Board Members into 5 group à 3	MB leaders will assign members to groups
Until March 29	Mission Board Members get acquainted with their framework scenario (for March 30th workshop) and their stakeholder group (for March 31st workshop)	FOD team will send out appropriate links to the google docs and to the go to meeting room

Date: 30.3.2020 **Time: 14:00 – 15:45** **Location: online** *Will last 1 hour and 15 minutes for each group* *Google docs* *Go to meeting*	Block 2 **Future Focus: Cancer** **Welcome & Introduction** to the Workshop Discuss in the group about the question of how the trends, drivers and developments **in cancer** may unfold in the future if the 1st scenario comes true. *What are the future developments (from the trends & driver analysis and others) in cancer/ cancer research that directly fit into this scenario? What are underlying tensions between imaginable developments? What are contradictions between some developments, actors, policies etc.?* You may also sketch a new title for the developments in cancer (as a "new scenario" or picture of the future)	Online meeting: the 2 groups meet in separate "virtual meeting rooms" where we can listen to each other, see each other and share written inputs (screen). The two groups will meet in parallel. The scenarios we will refine are separated into sections. Each moderator gives instructions, participants write via online tool (visible for everybody) and explain their thoughts. Note taker of FOD team takes notes of discussion. One participant after the other will give inputs. This document will be a collection of thought! The moderator and note taker will work out a coherent text offline. With this option, we will do only one scenario per group.
Date: 31.3.2020 **Time: 13:00 – 13:45** **Location: online** *Will take approx. 30 min for each group* *Google docs* *Go to meeting*	Block 3 **designing "desirable futures":** On the basis of the scenario sketch participants in group of three take different actor perspectives *(1) patient organization,* *(2) survivor,* *(3) MEP,* *(4) pharmaceutical company,* *(5) physicians' organization.* What would you like to see happen in the development of (… any other?) Write desirable future events/ milestones in the online tool on a prepared timescale and discuss them in your group: when should this event/ milestone realistically happen? What does the event/ milestone imply? • Cancer prevention? • Cancer diagnosis and treatment? • Cancer survivorship?	The participants will form 5 groups of 3 plus one moderator. FOD Cancer has 5 moderators; each will host 1 group. The groups will take place in parallel. Each participant will get a link to their document and a link to participate in the video meeting. The participants will write their thoughts (key words, entire sentences) into the document. The Moderator will take care that all participants are integrated and that there will be inputs for all 3 questions.
Until 2 days after the work shop	Block 4 **Wrap up & final** remarks	FOD will distribute access links all results and ask for feedback/ concluding remarks. This can be done remote. (will last approx. 10 to 20 min. per participant)
Until 7 days after the work shop	Block 5 **Harvesting of results**	FOD team will distribute an overview and short interpretation of the results from the previous 4 elements and prepare Phase 3 of the support contract: Backcasting: Possible pathways how to reach desirable futures from the basis of the 2 scenarios.

ANNEX III - ROADMAP OF EVENTS AND MILESTONES IN THE FUTURE OF FIGHTING CANCER FROM DIFFERENT STAKEHOLDER PERSPECTIVES

Experts:

Susanne Giesecke (Project Lead)
Satu Lipponen
Thyra de Jongh
Kerstin Cuhls
Dana Wasserbacher

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INTRODUCTION

The roadmap of events and milestones were formulated and discussed by Members of the Mission Board on Cancer in a virtual workshop that took place on 31st March 2020. The workshop was part of an interactive Foresight exercise on behalf of the "Foresight on Demand" (FoD) study in support of the Mission Board's work. It was organised and hosted in five parallel sessions by the FoD team. There were three to four participants in each session, some supported by experts from the European Commission who accompanied the work of the Mission Board. In the sessions, the participants were asked to assume the role of certain stakeholders such as cancer survivors, a patient organisation, Members of the European Parliament group against cancer, a large pharmaceutical company, and general practitioners. From these perspectives, the participants formulated crucial events and milestones to take place in the future on the pathway to fight cancer in the European Union.[40]

This document presents such events and milestones in form of three graphical roadmaps, each summarising what needs to happen on a successful pathway in terms of prevention (roadmap 1), diagnostics and treatments (roadmap 2), and survivorship (roadmap 3). The stories behind the events and milestones are provided in the second part as separate texts of each stakeholder perspective. They contrast the two scenarios presented in Annex II, in which future societies are depicted in rather contrasting and controversial features.

The project team would like to thank all participants of the Mission Board and the European Commission for their valuable inputs and commitments, as these were

Mission Board Members

First Name	**Last Name**
Regina	Beets-Tan
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First Name	**Last Name**
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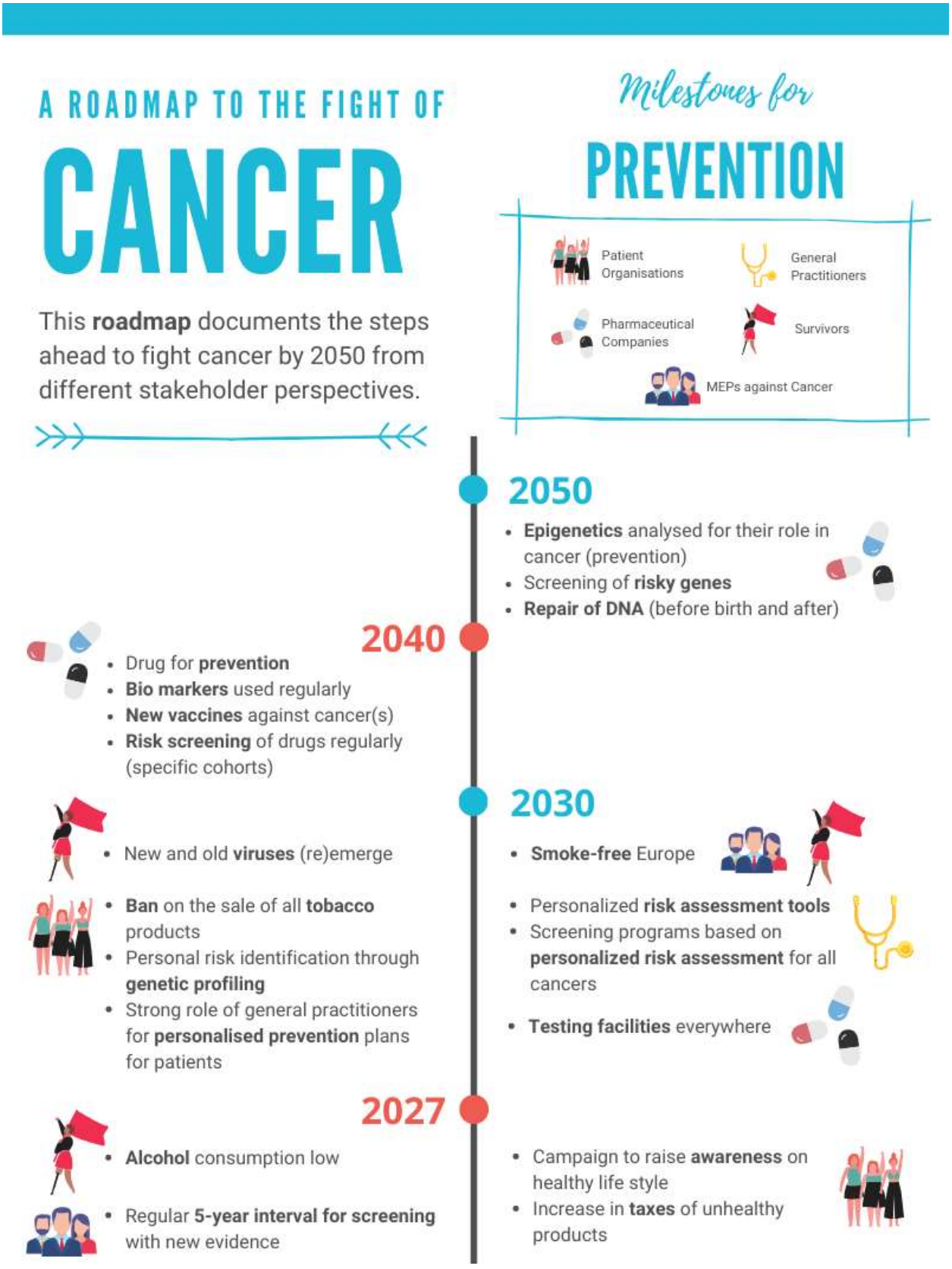
Nikolaos	Kastrinos
Barbara	Kerstiens
Katja	Neubauer
Annika	Nowak
Jan-Willem	Van de Loo
Ioannis	Vouldis

[40] **Disclaimer:**
The results reported are the output of a creative and interactive role play exercise as part of a larger foresight approach. The participants assumed the role of stakeholders but did not represent stakeholders. The statements and projections do not represent any official stakeholder group.
Neither the European Commission nor any person acting on behalf of the Commission is responsible for the use that might be made of this information.

ROADMAP 1: PREVENTION



2025

- Automatic **screening** for everybody
- **PRS**
- Central **registry**

- New low-cost, non-invasive **screening tests** (e.g. liquid biopsy) routinly performed by general practitioners

- Full implementation of the WHO Framework Convention on **Tobacco Control** (FCTC)

- **New technologies** for early detection (microbiota, polygenic risk scores) combined with **AI**

- Solutions to **prevent ageing** and cancer

2024

- **HPV vaccinaction** for all girls and boys

- Compulsory **vaccination** in Europe performed by general practitioners

2022

- Coordinated **databases** for quality control of **screening** in EU

- School-based **health literacy** programmes

2021

- Nutrition, life style, and medication **guidelines**

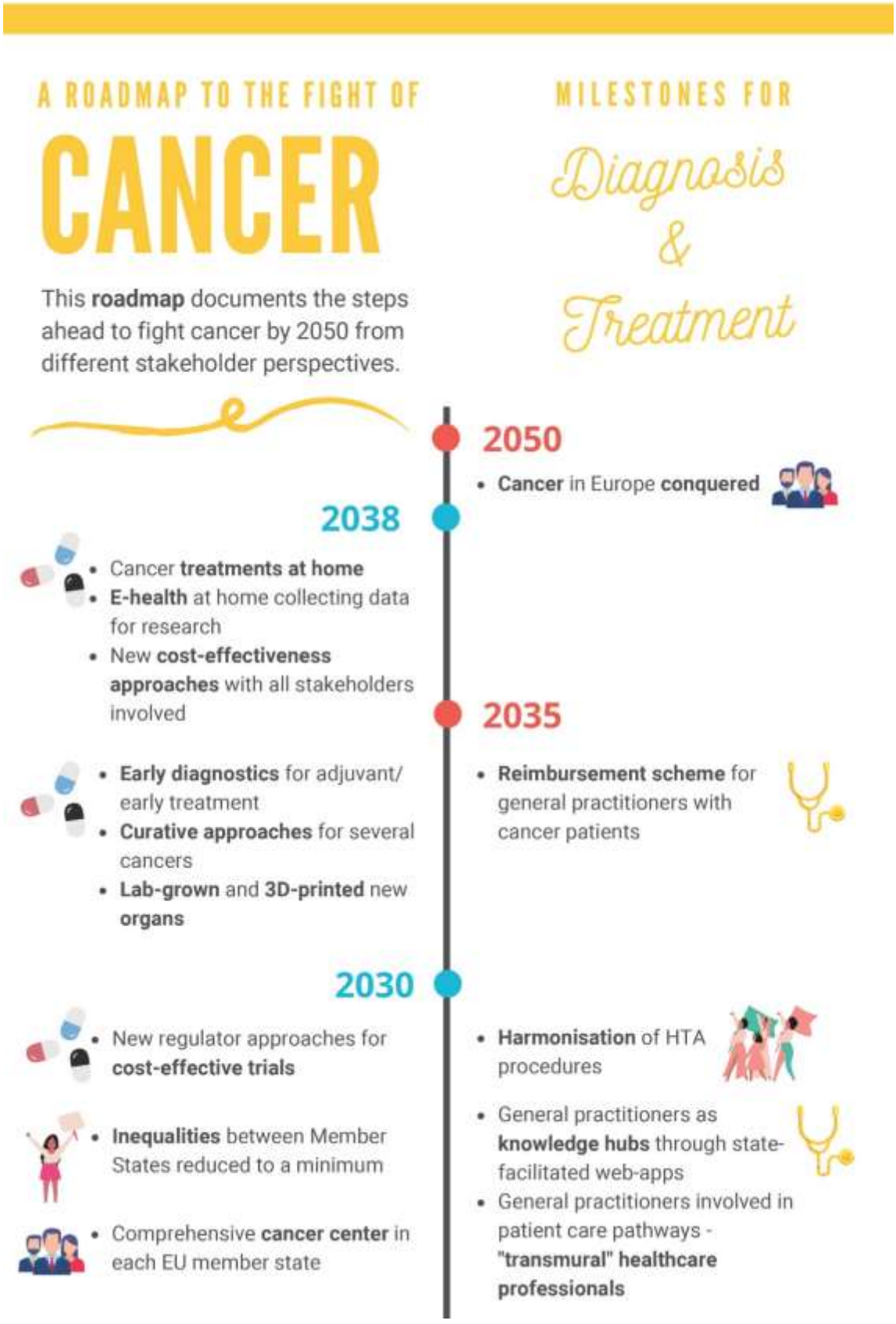
- Strong **healthy environments** regulation in EU cities

- National governement authorities are important players in determining how to **test** (structured, centralized)

2020

- Survivor **passport**
- Large scale **sreening**
- Updated **EU guidelines** for risk-based sreening for all types whenever applicable

ROADMAP 2: DIAGNOSIS & TREATMENT



2028

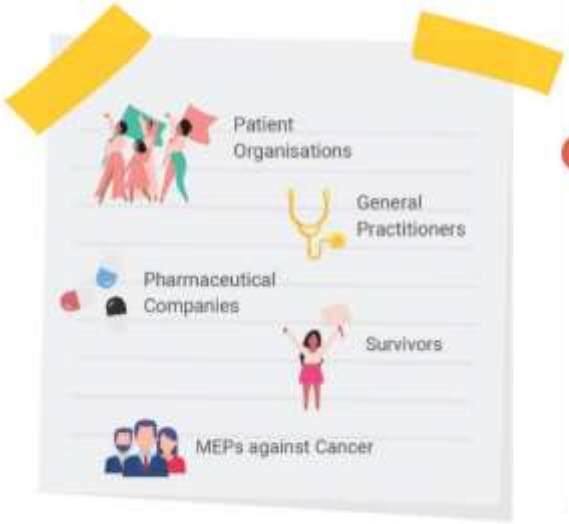
- **Personalised medicine** becomes standardised
- **Tests** for the "best" treatment

- **Ban** on parallel **export** for (cancer) medicines
- **No discrimination** of survivors

2025

- Each European has **true ownership** of own **health data** providing it to an integrated European (digital) cancer center
- **Biobank networks**

- **Cancer centres** across Europe at a density of one centre for every 5 million citizens
- **Drive-in blood tests** for specific cancer types
- Treatments **without side effects**



2022

- Screening for **early diagnosis**
- Incorporating early detection in **EU recommendations** on cancer screening

ROADMAP 3: SURVIVORSHIP

A ROADMAP TO THE FIGHT OF CANCER

This **roadmap** documents the steps ahead to fight cancer by 2050 from different stakeholder perspectives.

Milestones for SURVIVORSHIP

2035

- **Test kits** for cancer survivors to be used at home
- **Data collection** of cancer survivors in a non-invasive manner
- **Monitoring** the quality of life of survivors

2030

- Cancer a **chronic disease**, patients know how to live with it
- **Personalised treatment** is commonplace
- Cancer **survivors large part of the population**, which is considered in all aspects of society
- **New health policy targets**, when survival rates double every two years

2025

- Establishment of long-term **follow-up clinics**

- Stimulation of **innovation and co-creation** in the area of data protection (MyData) - **Cancer passport** for all Europeans

- **Inclusivity: remove** all associated **stigma** with being a cancer survivor - **allow to be forgotten** concept
- Adress **discrimination**

- **Use of databases** but strict control and stop after some time to protect privacy of survivors

- General practitioners play a crucial, **educational role** in **avoiding stigma** and **social discrimination** of cancer patients
- General practitioners have improved **knowledge** on **long term toxicities** (stigma, fertility problems, etc.)
- Full **e-health approach** is implemented that allows general practitioners to monitor cancer survivors and **self-monitoring**

- Increased number of cancer survivors supports **awareness raising campaigns** with "carriers of emotions"

2020

- **Safeguarding** vulnerable cancer patients from pandemics

A PATIENT ORGANISATION'S PERSPECTIVE

Author/Moderator: Thyra de Jongh

Prevention

Prevention of cancer is aimed by addressing the underlying determinants and risk factors that are associated with cancer. Whilst these may differ from type to type, certain risk factors are directly associated with multiple forms of cancer, in particular the use of tobacco and other unhealthy lifestyle behaviours. Therefore, an important step on the road towards tackling cancer in Europe is the full implementation of the WHO Framework Convention on Tobacco Control (FCTC) by 2025, which has been in force already since 2005. This implementation paves the way for a complete ban on the sale of all tobacco products by 2030. Whilst the general public is already largely aware of the increased cancer risk associated with traditional tobacco products, further measures highlight the risks of newer, smoke-free tobacco products (e-cigarettes or 'vaping'). Similarly, the cancer risks of alcohol use are now much better known than before, thanks to the efforts of the European Commission to engage all Member States and multiple media outlets in a large-scale campaign to raise awareness among the general public about such risks and to promote healthier lifestyle choices.

Education and sensitisation tend to have the highest impact on people who are not yet engaging in the harmful behaviours such campaigns seek to address. Key, therefore, is to focus in particular on young people (under the age of 25), through for instance school-based programmes. Promotion of healthy eating, simultaneously tackling the increased cancer risks associated with obesity and other health risks, starts already at school. This is made possible through commitment from and cooperation between ministries of health and education in the Member States. The EU is supporting them by preparing educational materials and tools.

Reducing the use of harmful products is achieved not only by informing and encouraging healthier behaviours but also by dis-incentivising the use of these products by decreasing access to them. One way to do this is by increasing the price of such products by levying higher taxes on them across the EU. Likewise, health taxes should be enacted on foods high in sugars, saturated fats and salt and sugar-sweetened beverages. To do this, the EU has been granted the necessary regulatory powers.

Another area of attention for the roadmap to tackling cancer relates to personalised prevention, including personal risk identification through genetic profiling. Although the diagnostic tools for genetic screening and risk identification have existed several years before, with rapid progress in next generation sequencing (NGS) and discovery of new genetic markers, the effective use of such tools has been lagging for some time. Both, patients and their treating physicians require support in interpreting the results of tests and the consequences thereof for their own personal prevention activities. The EU, therefore, started supporting the development of guidance materials to increase health and risk literacy in both these groups. General practitioners especially play a crucial role in prevention and are thus provided with tools that enable them to proactively prepare personalised prevention plans for their patients, on the basis of specific patient characteristics.

Diagnosis and treatment

In comparing not only the rates of cancer prevalence but also available diagnosis and treatment options across Europe, a main area of concern has been for many years the persistent inequality. To provide more equal access to patients, cancer centres across Europe have been established at a density of one centre for every 5 million citizens.

By 2025, a higher degree of implementation and adherence to existing guidelines for screening and best practice recommendations coming out of every research project is achieved, in order to improved and equal access to high quality diagnosis and treatment.

Access to new cancer treatments was in the past delayed by bottlenecks in the regulatory processes, at the level of the EMA/FDA, or by national public agencies such as those involved in Health Technology Assessment (HTA). There is now a much stronger collaboration between such stakeholders, and improved harmonisation of HTA procedures, to accelerate access to innovations. This, however, is not done at the cost of patients in terms of safety and effectiveness of new products. Instead, there is a distinction between products that offer true value to patients, and for which the path to market should be accelerated as much as possible, and those that do not.

Finally, parallel trading has been eliminated, pointing to the former practice whereby products were exported to markets where they were be sold at a higher price, leaving countries with lower purchasing power to deal with medicine shortages.

Survivorship

For patients, their battle with cancer does not end the moment they are declared ‘cured’. The effects of the disease, both mental and physical, can be felt long after the cancerous cells have been driven away. Even those who have been cared for by family or friends can remain affected for a long time thereafter, possibly having had to give up jobs. Dealing with cancer survivorship in an appropriate way now means considering both the health and social long-term implications of the disease. Employers, for instance, understand that those who return to work after having overcome cancer may not be able to resume their responsibilities in the same way as they have done before. Supporting a return to the workplace requires a sensitivity to the survivor’s needs and possibly a redesign of the role and expectations. The need to invest in trials to evaluate active interventions to support cancer survivors, is acknowledged by using patient-relevant outcome measures.

In general, across Europe there follow-up clinics and medical specialisation in long-term follow-up care for cancer patients.

One way to support young survivors of paediatric cancers is through the ‘Survivorship Passport’ (Sur-Pass), consisting of electronic documents that summarise their clinical history. This initiative is rolled out to cover every paediatric cancer survivor in the European Union by 2025. For adult cancers, similar initiatives are initiated for some of the most prevalent forms of cancer.

A SURVIVOR'S PERSPECTIVE

Author/Moderator: Kerstin Cuhls

Prevention

Very soon from now, in 2021, a large proportion of the population benefits from screening and early detection of cancer in general, but also secondary cancers. This still needs a lot of convincing people because in countries, in which screening is not mandatory, people often do not use these preventive measures. There will also be an update of the EU Guidelines for breast, cervical and colorectal cancer screening. Guidelines for lung cancer screening are added and the discussion about risk-based screening for prostate cancer is on its way. The aim is to provide a risk-based screening for all types whenever applicable.

For survivors, this is important as cancer may come back. It is also important for the family members of survivors - in case they have the same high risk of becoming ill. Nutrition, lifestyle, medications etc. for survivors are taken into account by the public health care system and specific guidelines for surviving people are developed.

To improve the screenings, more coordinated approaches are necessary and from the year 2022 onwards, there are coordinated databases for quality control and comparison of screening information across the European countries. A EU survivorship passport (Sur-Pass survivorship passport, which was originally established for childhood cancer survivors by FP7 ENCCA and PANCARESURFUP; being rolled out in IT and AT) is available for all survivors. First attempts are made to find out high risk people and groups of people who are at the risk of developing cancer and focus the screening on them. The passport helps documenting it.

But also, education on health literacy brings fruitful results: The awareness for early symptoms of cancer increased across Europeans by 2023. Europeans start to know what cancer is, what are the risk factors and how to prevent them.

Whereas the HPV vaccination is already voluntarily available in some EU countries, starting in 2024, it is ruled out across Europe for girls; whenever possible also for boys to gain sufficient immunisation.

Screening is further enhanced by automatic screening in 2025. Similar to new born screening, everybody is tested for the sake of the whole society. A population based polygenic risk score (PRS) assessment has started for certain groups of the population, later for all. The question remains if people use the information from the screening, and how they use it - even if they know they bear some risk many people might do not react. In the focus of screening activities are survivors and higher age groups in several countries for at least for breast ca, prostate ca, melanoma, CRC etc. The EU Survivorship passport collects and stores the data for a limited number of cancer indications in a central registry. With this, research can collect and analyse real-world data to serve tertiary prevention.

A huge step in fighting cancer marks the year 2030 when Europe is a smoking free continent. Tobacco smoking is below 5 % of adult population in all European countries (from 2020 to 2027 prevalence of smoking decreases stepwise, taxation of smoking increased, restrictions for selling tobacco were reinforced. The price of a packet of cigarettes increased stepwise to 20 Euro (as in Australia today, 2020) from 10 Euro, which is currently the price in France. Tobacco use in any form is banned from Europe. The same is starting with alcohol in the same year. In 2027, alcohol consumption already decreased in all EU countries considerably. Europeans know well that alcohol is carcinogenic, they are not only well informed, but their behaviour also changes. Selling alcohol drops drastically because the retailers support the campaigns.

But, we see new threats ahead. In 2030, new viruses are emerging more and more, and old ones are re-emerging, they all can cause cancer. Especially because of the changing climate and higher temperatures, viruses can survive much better - and the immune systems of people are more and more vulnerable. The expectation of a further increase is high - not only in Europe but all over the world.

Diagnosis and treatment
We learned from the Covid-19 crisis that testing and screening on a large scale is accepted much more if it is quick. So starting in 2024, we see the first drive-in blood tests for specific cancer types. With the widespread use of the liquid biopsy and the quick whole genome sequencing for early detection of cancer, the screening will be cheap and anonymous which is important for cancer survivors - they need certainty and they do not want to be stigmatized. The full roll-out of large screening and immediate treatment takes time. From 2020 onwards, we see a better timeliness of therapies: everything is offered in time. Patients do not have to wait for therapies, they can start as soon as they got their diagnosis. The health systems are prepared (until 2020, delays were too often observed).

Starting in 2025, Europeans are less and less exposed to environmental poisoning, anymore. Air, soil, water and food are getting save step by step - cancer evoking material, molecules etc. are banned. Those who still develop cancers, can hope for very good and effective treatments without side effects.

In 2027, early diagnosis and (minimal list of) treatment of high quality are available in real time to all Europeans. The quality is assured and high. Treatments are affordable and Europeans do not face financial disasters when they are affected by cancer.

Less invasive cancer diagnostic tools are available in this time. Patients have full access to their cancer diagnosis and treatment data (e.g. via the EU survivorship passport). Patients are able to understand the information given by the tools, which is translated to a non-technical language comprehensible for them and their families. Chemotherapies are less toxic. Immunotherapies have been further developed. All treatments and better, more specific drugs that are less expensive start to be available to all so that by 2030 the inequalities between the Member States of the still existing EU are reduced to a minimum (at least within an agreed list of interventions).

Survivorship
The year 2022 will see a use of data bases in the EU under strict control. The databases are deleted after some time, and the surveillance of survivors stops after some time to keep the privacy of the survivors. Soon from today, in 2023, the first possibilities are offered to relatives of former patient that they can be tested for germline mutations, which means if there is a kind of inherited cancer risk, they may know early. The reason to offer it is that it is cheaper and better for the society if they are tested and treated early enough instead of late with expensive, high tech treatments. But it is a sensitive issue and not all cancer survivors will tell their relatives that they had cancer. As first cases occur, in which the survivors are under pressure to tell their relatives, and the relatives are under pressure to have tests, soon after that, in the year 2025, the EU addresses stigma and discrimination which survivors suffer from.

In 2027, it is hoped that cancers (in general) have become more of a chronic than a lethal disease. Patients know how to live with it. They are aware of how they should continue their lives with appropriate medication and its follow up. They have access to quality supportive care as needed.

A PHARMACEUTICAL COMPANY'S PERSPECTIVE

Author/Moderator: Susanne Giesecke

Prevention

By the year 2030, there is the political will to fight cancer and there are dedicated policy measures to achieve this goal, e.g. by national prevention policies for cancer testing with accessibility of cancer testing facilities everywhere. These policies are big incentives for the pharmaceutical companies that provide these test kits. Consequently, the pharma companies engage in mass production for such test kits. They profit from the large margins, the mass testing and mass treatment.

Pharma companies acknowledge that national government authorities are important players to determine what way to test. This structured and centralized approach starts in 2021 and requires heavy investments by the state in medical facilities and underlines the important role of regulators for testing guidelines and products. By 2025, former differences between FDA and EMA approval are solve and harmonized, which is a relive for R&D departments of pharma companies.

By 2040, Pharma companies find a test that directs patients early enough, to use a drug for preventive purposes (recurrently). Bio markers are used regularly in order to achieve results early enough for treatment. New vaccines for virus-induced cancers, e.g. cervical cancer, are available and provided by pharma companies.

As a cancer prevention measure, more generally, some drugs are used routinely in some patients after the risks were identified by screenings. Screening activities are designed for specific cohorts and patient groups and more targeted than general screening since 2040.

By 2050, after new screening technologies have identified risky genes, specific genomic technologies are applied that enable the repair of damaged DNA to prevent cancers of genomic origin before birth, but also perform later-life DNA repair (pre-natal repair).

By the same year, the role of epigenetics in carcinogenesis has been sufficiently analysed including potential influence of nutrition- nutraceuticals (eating the right nutrition and influence genetic health).

Already in 2025, international and national associations of pharma companies engage in partnerships with regulatory authorities identifying risks, speed up approval in pre-cancerous disease treatments.

Diagnosis and treatment

In 2035, pharmaceutical companies develop early diagnostics for adjuvant/ early treatment such as potentially curative approaches for several cancers. This is in part realized through combination therapies, including different treatment modalities. Personalised medicine approaches concentrating on smaller patient groups, histology-agnostics drugs, are essential for better and more effective cancer treatment.

Also, in the same year, pharma companies introduce regenerative medicine: through extraction of cancerous organs and replacement by healthier lab-grown versions patients can be cured. Organs are not only lab-grown but also produced in 3D printing.

Where it is still needed, in 2038, chemotherapy is possible at the bedside of the patient at home. People do not have to go to particular facilities for treatment.

The home becomes a central place for treatment in general, e.g. for collecting home based data, from wearables etc. stick-based test for different parameters. Clinical studies monitor patients at home and thus they are less invaded in their normal life.

The close partnership of pharma companies with regulatory authorities is continued in the field of diagnostics and therapeutics along the innovation path of cancer medicine. Personalized medicine

requires the involvement of state authorities, insurances and several other players to develop a cost-effectiveness approach. In the field of personalized medicine pharma companies face more difficulties to run randomized studies. Thus, in 2028, they start to define different procedures for different medication and groups of patients. At the same time, there is the chance to tests for the “best” treatment. There is now also greater use of real-world evidence, that was not efficient in the past. New procedures account for the safety and efficacy of drugs.

Together with state and regulatory authorities at national and international level in 2030, significant change in institutional settings made it possible to deal with the approval of personalised medicine. This made it possible to deal with the requirement of random trials and with cost-effectiveness approaches.

Survivorship
Some pharmaceutical companies develop test kits for cancer survivors to be used at home for routine checks in 2035. Pharma companies now also collect long term care data of cancer survivors in a non-invasive manner, that point out how efficient a treatment is or not. This also includes the monitoring of behavioral elements of people, e.g. nutrition supplements. This is a promising market for pharma companies. A prerequisite for this, already happening in 2030, is that such companies merge with e-health and m-health companies to monitor quality of life of survivors, going far beyond the pure medical aspects. Instead, they take a life cycle approach where the individuum and their personal situation is at center.

MEPS AGAINST CANCER PERSPECTIVE

Author/Moderator: Satu Lipponen

Prevention

One top priority is to put decades of research and evidence into action and primary prevention high on the Parliament´s agenda. Calls for eradication of HPV virus linked to cervical cancer are getting stronger after COVID-19 pandemic. Across Europe, the vaccination programmes are interesting and cost-effective ways for primary prevention.

Early detection, if organized effectively, is reducing cost of care and inequalities. MEPs (Members of the European Parliament) support measures to implement fully the Council recommendation of cancer screening (2003/878/EC) and therefore are backing updating the recommendation. This is done 2 December 2022, on the date of recommendation adopted at the Council of the European Union 19 years earlier. MEP group lobbies successfully for updating the guidelines of the screening programmes in 2022 and 2027 for quality assurance. It is agreed that the screening guidelines would be updated after every 5 years for new evidence. This is a success and many countries are linking the databases to most important sources and develop legislation to support the screening programmes. In cervical cancer, incidence rate of less than 4 cases per 100,000 women is the goal in many Member States. This is one of the best achievements in prevention during 2022-2027. Also, breast and colorectal cancer screening made big improvements in implementation by 2022. New pilots are on their way to organized screening programmes.

Another success are tobacco control and anti-pollution measures. In 2021 MEPs manage to get through strong healthy environment regulation at the Parliament with the focus on EU cities and population exposure to air pollution. This, together with Smoke-free Europe in 2030, reduces lung cancer incidence in Member States.

As a result of COVID-19 pandemic, science and research of prevention get necessary funding starting from 2021. Public activities to fight against cancer are strong during the 2021. MEP cancer group is one of the biggest specialized groups of the Parliament. Research programmes produce several milestones in 2025. New technologies for early detection/screening gain ground - such as polygenic risk scores, circulating tumour DNA and microbiota. Combined with artificial intelligence these technologies are leading the way to enhancing prevention. Another research investment is done to understand cellular ageing mechanisms with the goal to provide solutions of preventing ageing and thereby cancer.

Diagnosis and treatment

Early diagnosis and detection are becoming more organised due to improvement of data management systems in Member States. In 2021 large scale national screening programmes for early diagnosis are initiated after the Parliament resolution. MEPs also call for personalized diagnostics and access to equal treatments for all Europeans. Several advocacy groups are active during this period, because cancer patients have gained political power as voters. Four years later, in 2025 MEPs reach an agreement of support and partnerships with hi-tech EU industry to develop new cancer detection and treatment tools. This is welcomed as a necessary step towards improving competitive status of EU. There is effective networking of cancer biobanks throughout Europe. The Parliament works hard to provide each European a true ownership of his/her own health data and samples. This makes it possible to build an integrated digital cancer centre in Europe. MEPs against Cancer are working in several Parliamentary committees to foster digitalization.

By 2030 there is at least one Accredited Comprehensive Cancer Centre in each EU member state. They are networking throughout EU and beyond. There are some important steps made in rare cancers. The cancer MEPs organize a 10-year anniversary of *Rare Cancer Agenda 2030.*
*The Parliament has a special session in December 2030, announcing a new initiative "*Conquer cancer in Europe by 2050". It has specific targets. Cancer has become a chronic disease in many cancer types.

Survivorship
Cancer survivors are working with co-creational methods with governments and enterprises in securing that patients can own and access their own data. My Data is introduced in 2030 with European cancer passports. Digitalization and follow-up mechanisms are useful when climate changes and new pandemics make patients in treatments vulnerable.

In 2025 French MEPs against Cancer introduce a re-invented concept of the right to be forgotten in a digital world. There is a strong debate of survivor rights and insurances where these concepts are tested. After a long discussion, the Parliament regulates the right to be forgotten after 10 years from cancer diagnosis. By 2030 cancer patients and survivors represent an increasingly large part of the population.

Returning to normal life after disease is easier, because precision medicine is by 2030 producing solutions to long term side effects of many cancer treatments. Hospitals are following up patients to give accurate information about late effects. The new Morse Law means double survival rates for every cancer type every 2 years so new health policy targets are needed. These targets show that by 2050 cancer can be conquered. Genetic testing is widely used to make sure that precision medicine is are suitable.

Survivors are very active in the Parliament, which is preparing to evaluate “Conquer cancer in Europe by 2050” initiative. Patient coalitions and survivor activists call for pan- European efforts and more funding in Member States and at the European level when the resolution is accepted.

A GENERAL PRACTITIONER'S PERSPECTIVE

Author/Moderator: Dana Wasserbacher

Prevention

By 2022, the spread of the Corona virus in 2020 starts to show impact on society: the anti-vaccination movement comes to a halt globally, which stimulates the implementation of a series of health measures to prevent cancer. Compulsory vaccination, primarily for children, is put into place on a European level, and general practitioners play a crucial role in supporting this measure.

In 2025, a reward- respectively fine-system is implemented, accompanied by a wide-ranging information campaign. In the context of these awareness raising efforts, general practitioners are supported by (evidence-based) communication tools, to inform patients, why they should get vaccinated. Therefore, (state) reimbursed coachings and trainings for school children are introduced to foster behavioural changes and to reinforce appropriate attitudes towards drugs, tobacco, nutrition, and HPV vaccination.

Regarding existing differences in national situations, there is a strong necessity for European harmonization, foremost with regard to a coordinated introduction of trainings (i.e. standardized and evidence-based communication tools in lay language to be distributed to patients respectively parents of school kids), but also in terms of additional reimbursement of general practitioners for their awareness-raising and educational efforts.

Low- cost non-invasive tools, i.e. new technologies like fluid biopsy (for ctDNA, gene risk profiling, PSA detection), for cancer screening are used routinely by general practitioners.

In contrast to outdated screening methods based on gender and age, screening programmes based on individualized risk assessment for breast, lung, and prostate cancers are now in place. This also heavily depends on the necessity of EU harmonization.

Screening programmes based on individualized risk assessment are available for all cancers, including rare cancer types by 2030. Furthermore, general practitioners refer patients with a high suspicion of cancer of the breast (palpable lump), of the lung (symptoms) and of the prostate (PSA elevation) directly to a diagnostic unit for mammography and breast ultrasound, for CT chest and for MR prostate, respectively biopsy. This reduces costs related to intramural care.

Diagnosis and treatment

Cancer diagnosis and treatment shows an increase in the use of artificial intelligence tools and software by general practitioners for more cost efficient, time efficient and more accurate diagnosis by 2025.

In 2030, general practitioners act as knowledge hubs in cancer diagnosis and treatment, i.e. they know about the existing dedicated pathways for diagnosis and treatment for each cancer at their national level and they know where to send their patients and how to guide them during the treatment (e.g. through web applications facilitated by the state, through principles of national cancer plans or national cancer programmes). Hence, general practitioners are more involved with patient care pathways and have a more prominent role as "transmural" healthcare professionals. This includes the ability to directly refer patients to a diagnostic unit and - based on the diagnosis - triage for intra- or extramural care. The general practitioners play a prominent role in the follow up of patients after treatment, i.e. in palliative care.

In 2030 and beyond, general practitioners are reimbursed at a higher level for the time (or the number of patients they have with cancer), either by state or private insurance. The reimbursement scheme is not fully developed yet. First ideas point towards a mode, that enables general practitioners to declare the proportion of cancer patients, e.g. 10%, and based on this share, to claim reimbursement for additional time efforts.

Survivorship

Although initial efforts to strengthen the legal and social framework to protect the rights and well-being of patients, survivors, their families and carers were already visible in national Cancer Control Plans, these efforts are fully implemented in 2025 and contribute to avoid social discrimination and stigma. This applies in particular to insurance issues, avoiding discrimination that may result from not granting bank loans to cancer patients. Also, in this matter, general practitioners play a crucial, educational role by informing patients on these issues.

To support cancer survivorship, the provision of improved knowledge for general practitioners on long term toxicities (of cancer and cancer treatment, e.g. negative impacts, like stigma, fertility problems arising from cancer) and further challenges, that patients should be aware of, is in place also in 2025, enabling GPs to inform and support cancer survivors accordingly.

A full “e-health” approach is implemented, that allows general practitioners to monitor cancer survivors respectively that allows self-monitoring by patients with the help of online tools and apps.

Since the number of cancer survivors increases, there are now more possibilities to introduce them as important actors in public awareness raising, e.g. for campaigns with “carriers of emotions”.

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For access to legal information from the EU, including all EU law since 1952 in all the official language versions, go to EUR-Lex at: http://eur-lex.europa.eu

OPEN DATA FROM THE EU
The EU Open Data Portal (http://data.europa.eu/euodp/en) provides access to datasets from the EU. Data can be downloaded and reused for free, for both commercial and non-commercial purposes.

The European Union introduced missions as a new instrument in Horizon Europe. Mission Boards were appointed to elaborate visions for the future in five Areas: Adaptation to Climate Change, Including Societal Transformation; Cancer; Healthy Oceans, Seas, and Coastal and Inland Waters; Climate-Neutral and Smart Cities; Soil Health and Food. Starting in autumn 2019, five Foresight on Demand projects supported them with foresight expertise and methodology.

This report provides the work in support of the Mission Board on Cancer. In interaction with the Mission Board members and responsible Commission services, the project team scanned trends and drivers for cancer, developed two future health scenarios targeted at fighting cancer and roadmaps of events and milestones in the future of fighting cancer.

Studies and reports

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