



Care for Cancer

Conclusions from Uppsala Health Summit
14–15 June 2018



About Uppsala Health Summit

We all know that healthcare today is faced with ever greater challenges. We are faced with both economic and ethical dilemmas, and while advances in research and innovations may open new possibilities for better health and improved care, they do not always reach those who need them.

Uppsala Health Summit is an international arena for frank and challenging dialogue, exploring possibilities and dilemmas associated with advancement in medicine. Uppsala Health Summit stimulates dialogue from various perspectives, such as medical, economic and ethical.

We are an enabler for change, and an arena laying the foundation for long-term relationships and insights that can help you in your work to improve health outcome in your part of the world.

Uppsala Health Summit is arranged in Uppsala, Sweden, by partners with long experience of developing health and healthcare from different perspectives, and who see the potential for improving health and healthcare globally.

The effort is run as a collaboration between Uppsala University, the Swedish University of Agricultural Sciences, Uppsala Region, the City of Uppsala, the Swedish Medical Products Agency, The National Food Administration, The National Veterinary Institute, Uppsala Monitoring Centre, the Swedish Research Council for Health, Working Life and Welfare, and the network World Class Uppsala. This year, we are also proud to have the Swedish Childhood Foundation as a partner to Uppsala Health Summit

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Professor Klas Kärre, of the Swedish Cancer Society's research committee, gives an overview of research funding in the field of tumour localisation.

Photo: Danish Saroee

Care for Cancer

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Science and innovations have laid the ground for fantastic steps forward in cancer diagnostics and treatments. Many cancers that previously were death sentences are today treatable, or even curable.

However, access to these advancements is far from a reality to all due to lack of resources, a frail infrastructure for healthcare, or absence of planning and coordination of healthcare on

a national level. The possibilities to help the individual cancer patient is growing faster than available resources. Thus, the gap between a care that is medically possible, and the care that is actually feasible to provide is widening. In some areas of cancer care, there are also gaps between the available scientific evidence and the understanding how to implement new practices in routine care.

In 2012, the Globocan report estimated the number of new cancer cases to 14 million globally. Approximately 6,8 million, or 48 %, occurred in low- and middle-income countries. According to the same source, the number of new cancer cases is projected to have reached 24 million in 2035. 54 % of these, or almost 13 million, will occur in low- and middle-income countries. The major increase in cancer incidence and prevalence will thus take place in

One of the challenges in terms of cost effectiveness, and the assessment of that, is about the fact that we typically get registration in late stage disease.

Dr. Susan Galbraith, Head of Oncology, iMed, Innovative Medicines, AstraZeneca



Photo: Danish Saroee

countries where universal healthcare is rarely available and which with few exceptions lack a national cancer strategy. In many of these countries not only access to the most modern and costly diagnostics and treatments are lacking, but even basic surgery, radiation equipment and palliative care may be scarcely available.

Therefore, the resolution adopted by the World Health Assembly, WHA, in May 2017 requiring all member countries to develop national cancer plans, including diagnostics and treatments, was an important health policy step forward. As a corollary, you would think that the global increase in cancer incidence and prevalence is well known, a matter of urgency for health actors all over the world or to anyone interested in how we invest in our common future. But the cancer burden still has an inconspicuous role in the global health dialogue, despite the SDG 3 target: *By 2030, reduce by one third premature mortality from non-communicable diseases through prevention and treatment and promote mental health and well-being.* Also, the global cancer dialogue is dominated by life-style prevention. But two-thirds of all cancers are not life-style related, notably most childhood cancers; some important life-style factors are not directly amenable to interventions such as women's age at first pregnancy.

These are the reasons why much more attention must be brought to how we can make advancements in cancer diagnostics and care accessible globally and why we need to talk about how to more rapidly and universally implement the possibilities that science has provided to enable treatment and cure.

We convened policy-makers, academic researchers, industry, patients and funders to Uppsala Castle and Uppsala Health Summit in June 2018. While most cancer meetings present and discuss advancements in science and innovations for care, we wanted Uppsala Health Summit to focus on how to open up these opportunities for a growing number of patients, by making better use of data and technologies and on how such use can pave way for a more equitable access to the best possible treatment and diagnostics within any given context. The suggestions developed were in general valid for the majority of cancers and patient groups. In several workshops, special thought was given to children, as they have unique needs and are, in many contexts, surrounded by special medico-legal regulations and ethical considerations.

Shared themes and suggestions from the workshops

The conclusions and suggestions from the eight workshops are presented in the following chapters, but some salient themes and suggestions are common, despite the different areas treated.

Share and facilitate access to data

A lot of data exists that can be used to develop, prioritise and optimise use of diagnostics and treatments, rehabilitation programs, support to survivors and palliative care. Development and implementation of molecular and genetically based diagnoses and treatments, e.g. the development and use of biomarkers and precision medicine, depend on the availability of huge amounts of data from biobanks coupled to clinical information. However, data is scattered, often difficult to access or to combine and compare.

Several workshops pointed out the need for:

- standardisation of collection of data and samples to enable global collaborations.
- flexible, transparent and easy-to-understand consent agreements allowing the use of data whether in academia, in industry or for health policy.
- assuring access to data in a way that doesn't compromise patient integrity but still are detailed enough to allow research to understand individually tailored interventions whether these may be diagnostics, treatments, rehabilitation or palliation
- collection of patients' own observations using user-friendly new techniques such as wearables and apps, e.g. to better understand the clinical value of new treatments.

Some workshops touched upon the issue of ownership of data, and it was suggested that patients should own their own data.

My question is: Why shouldn't the patient, who is the guy, or the girl, who has the most to win, or to lose in healthcare, not own their own data?

Marie Ennis O'Connor, Patient Empowerment Foundation and Health Care Social Media.

National initiatives were deemed not to be enough to make better use of data: some cancer types are too rare (e.g. childhood cancers) to assemble the amount of data needed in one country; advanced research demand collaborations between different actors and different scientific fields from all over the world. International policy initiatives in this area was therefore called for. Can the International Association for Research on Cancer (IARC) and the World Health Organization (WHO) take up the baton? The European Union? And are national legislators, regulators, health technology assessors, industry, research and funders prepared to lift the issues to an international level?

Patients and their kin must be at the centre of all efforts

Consider the patient as the main resource in cancer care, was a message from both plenum and workshops. Patients and their kin have a central role in providing key information making cancer diagnostics, care and rehabilitation more efficient. Many delegates pointed to the need to organise care around the patient rather than around the health professionals.

I don't treat prostate cancer, I treat men with prostate cancer.

Dr. Ingela Franck Lissbrant, MD, PhD, Sahlgrenska University Hospital and the Swedish National Prostate Cancer Registry

In plenum, the summit discussed the relation between the doctor and the individual patients and kin. A better understanding of how the informed patient best works together with the doctor as a guide – not as an indisputable authority – can achieve substantial advancements in cancer care. However, in many parts of the world, the level of health literacy is still low and must be improved, as an investment in prevention, early diagnosis and improvement of cancer care.

And as mentioned above, if collected systematically, real-life data in the form of patients' own observations, will be important for evaluation care and treatments and for driving its development further. Three workshops pointed to the need to collect such data in a timely manner

to capture side-effects early, to rapidly identify candidates for drug-repositioning, and to inform ongoing or planned clinical trials.

Cancer is a global health challenge

The need to increase awareness on cancer as a global health challenge was brought up in plenum as well as in several workshops. Childhood cancers are to 80 % curable in Europe, but still a major killer for the majority of children of the world. This is to a large extent a question of health literacy among parents and access to care, since many treatments for childhood cancers have a cost that is affordable also in low- and middle-income countries.

Our ignorance, our poor healthcare system is the thing around our neck, that makes it a little bit challenging to have our patients in the driver's seat.

Kelechi Eguzo, MD, MPH, Nigerian Christian Hospital; Chairman Marjorie Bash Foundation, Nigeria

A reliable mapping of cancer incidence and prevalence with high coverage is key to make priorities, national cancer plans and take strategic, rational long-term decisions. For this, stable investments in managing world-wide cancer registries will be necessary.

Less than five percent of global investments in cancer research is spent on matters of direct relevance to low- and middle-income countries. Discussions during the conference made it clear that more investments from high-income countries in such research would gain all. There

The two main segments are research on basic cause and treatments, so very little on practicalities of cancer control, cancer care and cancer prevention.

Professor Max Parkin, Nuffield Dept. of Population Health, Oxford University

are several areas all the way from health policy making to aspects of genetic variation where there could be significant knowledge-transfer also from low- and middle-income countries to high income countries. To many, the experience now developed by Tata Trust in Assam, one of India's poorest regions, setting up a centre for advanced, distributed care was an eye-opener and something to learn from, not only in other low resource settings.

Wake up!

On several occasions, delegates pointed out the need to make "wake up-calls" to policy makers, development organisations and funders. Awareness of the growing cancer burden was in general deemed to be low. Pointing more directly to development organisations and funders, the sense was that it is high time to realize that global health issues is no longer a matter only of infectious diseases, and pointing out the urgency to develop cancer care in all parts of the world.

Many delegates voiced a feeling that there is now an opportunity to form new types of very fruitful partnerships between all stake-holders, always including the patient perspective, to propose solutions to pressing problems. Greg Simon from the Biden Cancer Initiative expressed this in a call to "collaborate with a capacity you never worked with before and do something new". Several work-shops pointed to the necessity to form new collaborations, e.g. to integrate effective biobanking in healthcare structures, to make the patient journey from care to rehabilitation to palliation smooth without gaps, or to find better and faster solutions how to reposition drugs.

The proposals developed in the workshops are an important result from the two intensive days at Uppsala Health Summit 2018. We hope that this post-conference report will inspire all types of actors sharing an interest in improving global health to see new perspectives, find new collaborations, and take actions. With global access to data and access to modern technologies, we should be able to do much more and much better with the science and the resources we have.



Workshop Conclusions and Suggestions

Workshops

- Precision Medicine in Cancer Care
- Global Biobanking
- Clinical Value and Price-setting for New Cancer Drugs
- Long Term Care for Cancer Survivors – Striving for the Best Quality of Life Possible
- Towards Useful Cancer Biomarkers to Improve Care for Cancer
- Using Data for Better Cancer Treatments
- Implementing Physical Exercise in Cancer Care
- Drug Repositioning – An Underused Strategy for Cancer Drug Development and Access to Next-line Cancer Treatment?



Precision Medicine in Cancer Care

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Aim

The focus of this workshop was on how precision medicine can be implemented within modern cancer care systems. The discussion assumed access to the most recent state-of-the-art technology, primarily that which is built around the analysis of patient genomes but also around protein- or metabolite-based features of human tumours. Thus, the workshop aimed at:

- Identifying new ways to **implement large data sharing** for further translation to an improved decision making system.
- Defining the **requirements** and necessities that are applied to the **molecular data**, so that they can be used to formulate best possible treatment alternatives for patients.
- **Pinpointing** a set of **limitations** that currently slow down the realisation of individualised cancer care in existing healthcare systems.

Main conclusions

Inter-disciplinary collaborations

To bring precision medicine to the clinic and improve patients' cancer care, clinicians and scientists must be given the possibility to collaborate and translate the technology to the clinic. It was suggested that "molecular tumour boards" be set up, around which clinicians and scientists from different disciplines, e.g. chemists, biologists and IT-specialists, can collaborate. Cancer Core Europe and Genomic Medicine Sweden were mentioned as good examples. These collaborations can be initiated by clinicians or technology-oriented researchers, but will always need support from policy makers.

Data standards

Minimal data standards are needed on an international level to be able to efficiently accumulate and share data. In addition, we need to develop policies for access to these data in such ways that the patients' integrity is protected. The recently adopted European data protection rules (GDPR) can provide a starting point. The process must involve clinicians and policy makers, as changes in legislation will be necessary. However, the process should be initiated by IT-specialists who can build and curate the new digital infrastructure that supports precision medicine.

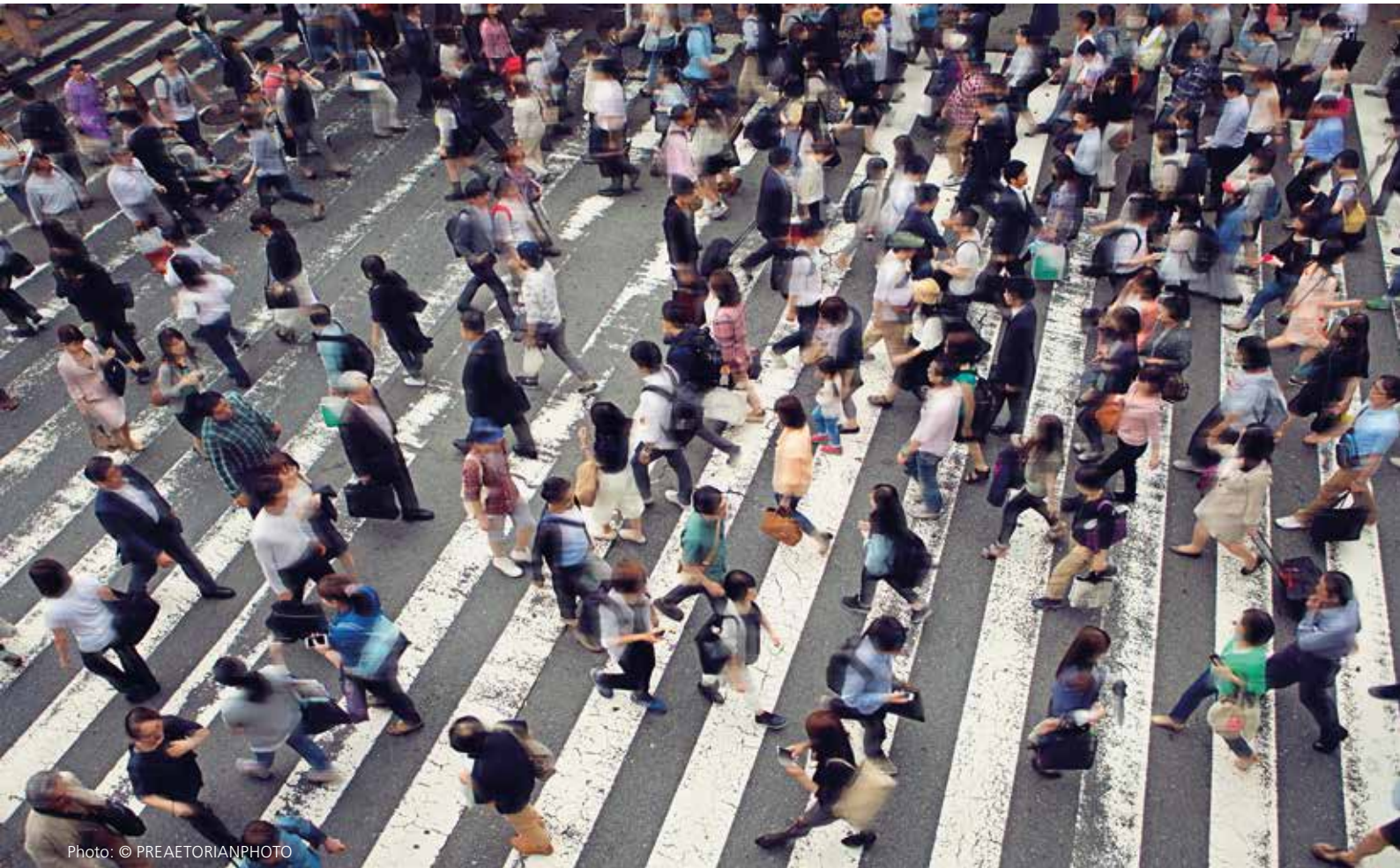


Photo: © PREAETORIANPHOTO

New improved consent handling

Transparent data sharing is dependent on patients' and/or their kin's understanding of what data is stored and shared, and their clear consent. A dynamic consent process is called for, which can be initiated by policy makers (legislation), IT-scientists or ethicists. In the end, all three professional groups, as well as clinicians, must be involved.

Background

Implementing personalised medicine in the clinical setting will need and lead to accumulation of large amounts of data with information that can be associated with individual, identifiable patients. This new reality of clinical work requires careful standardisation and the building of data infrastructures that are flexible but interconnected into robust networks within single countries and internationally. The aim should be enhanced and automated communication that facilitates data sharing and the coupling of care units, their clinicians and collaborating researchers and technology or therapy providers. Currently, precision medicine in cancer care is

building a new infrastructure based on a secure and legal organisation around the protection of patient data. Furthermore, implementation of appropriate ethical regulations that not only centre on the patient, but also permit rapid communication between data collectors and care providers, is gradually being achieved. Existing organisations such as the Global Alliance for Genomics and Health are generating the necessary norms to deal with the above demands and implementation into the national healthcare systems is a major responsibility for the future.

Precision medicine generates data upon analysis of the genomes of individual tumours sampled prior to or after therapy, and applies informatics so that classification and comparative analysis can be implemented based on unified standards. This technology depends on the curation and rapid expansion of databases of DNA and phenotypic (image-based or drug sensitivity-based) variation. Application of robotic handling of data processing guarantees speed and ability to work with very large sample numbers, necessitating a substantial IT-infrastructure coupled to

the oncology ward. Such IT-based interconnection between all players involved in the treatment, sample collection and the analysis of data from cancer patients, aims at generating a new type of clinic that handles large data sets with the same ease as a traditional stethoscope.

In the end, precision medicine aims at contributing to saving more lives with fewer side effects and being able to treat more cancer diseases than today. There is also an inherent willingness to share and collaborate that hopefully will aid in realising those goals in the future.

The workshop and its participants

The workshop on precision medicine included delegates from the private sector, including leading pharmaceutical companies, academic scientists from different disciplines, representatives from regulatory agencies, journalists, clinicians and IT specialists representing fourteen countries from Europe, Africa and the Americas. The workshop was run along a small, group-based, highly interactive format that encouraged intense discussion, brain storming and sharing of ideas.

We are not yet at a point of releasing data's power in healthcare because the vast majority of information remains proprietary and fragmented.

Marie Ennis O'Connor, Patient Empowerment Foundation and Health Care Social Media

The field of precision medicine faces a number of challenges and the workshop started by identifying some concrete *obstacles* and potential *bottle-necks* to full clinical application, namely:

- The biology is complex, involving tumour microenvironment heterogeneity and the microbiome
- Clinicians are not enough involved in the development of precision medicine
- Fear of misuse – Further work on consent needs to be done

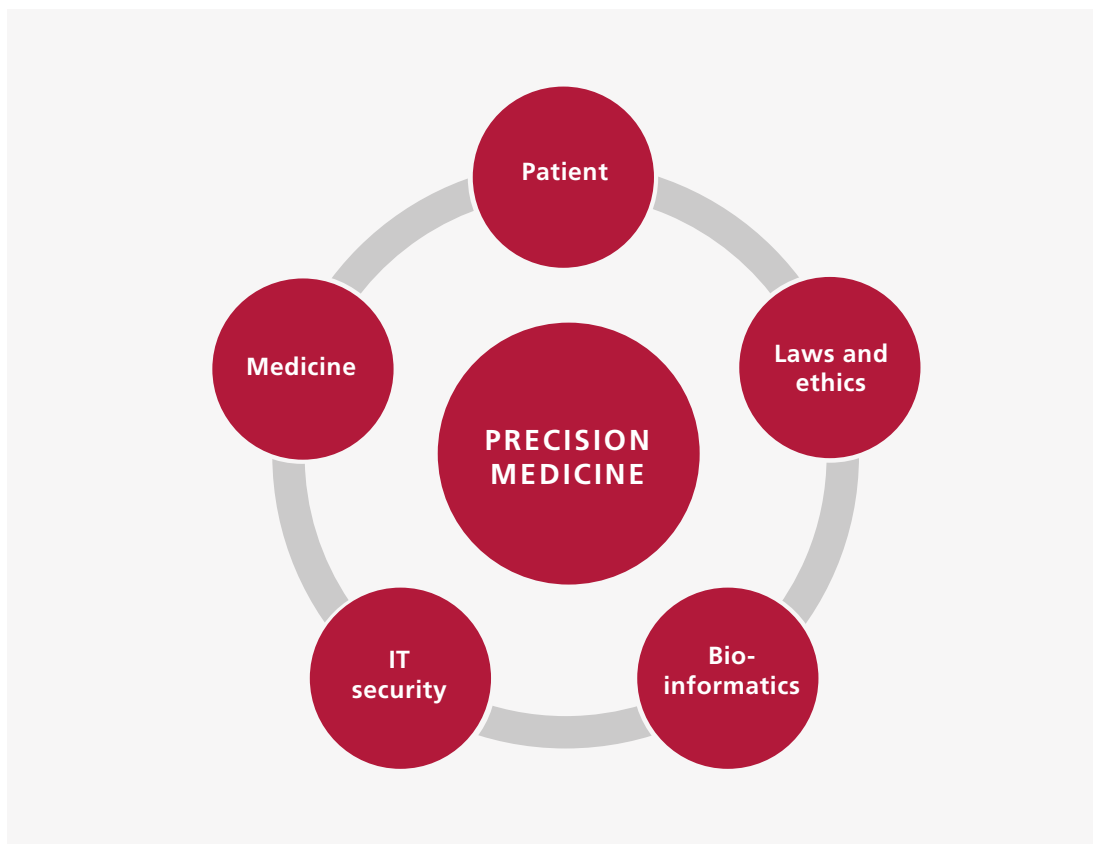
- Fear of abuse by insurance companies (access to genomic data must be controlled and not exploited against individuals)
- But...regulations can make it harder to maximise the impact of scientific advances

Conclusions and suggestions from the workshop

Given the recent advances in technology, the large volumes of data run the risk of becoming “data silos” if the proper infrastructure and meta-data framework for structuring and sharing is not rapidly addressed. The technology is good and it is here – but we need to understand the biology associated with data of strict genetic nature, for example. Solutions across both national and international platforms need to be generated that will allow for better exchange in a controlled and evidence-based way. Education is another pressing need. This includes educating not only medical personnel, geneticists and scientists but also patients and their relatives. Since cross-disciplinary communication and collaboration is crucial in the field of precision medicine, this issue will be of primary importance in order for the field to move forward. Moving away from the “business as usual” culture was highly recommended by many delegates.

Develop a more effective inter-disciplinary collaboration
Since precision medicine involves technologies that range from traditional medical examination to molecular analysis all the way to information technology and therapy development, inter-disciplinary exchange is needed to move the field of precision medicine forward. This action involves clinicians, scientists and policy makers and can be initiated as concerted action from all groups. The main aim is to deliver more comprehensive results on patient stratification and patient responsiveness to existing or novel therapies in a more efficient manner. The workshop emphasised that, whereas the technology is mature in generating and delivering large sets of molecular data on cancer, the mere collection of large sets of data does not automatically translate to precision medicine. This realisation is often referred to as the precision oncology illu-

To implement precision medicine, we need a more effective collaboration between disciplines and sectors.



sion and points toward the rapid development of a precision science that evaluates not only DNA sequence variation but also considers the functional features of tumours, their response to existing therapy and what is known as systems medicine. Such technological advances leave one major caveat: what is the best way to translate the technology in a realistic manner to patients? Some concrete steps in addressing this pressing issue occupied a fair portion of the workshop's discussions. A prime example is the generation of new organisations, such as the *Genomic Medicine Sweden initiative*, that aims to bring together all the university hospitals in order to build a new type of infrastructure within Swedish healthcare to implement precision medicine on a national level through seven regional *Genomic Medicine Centres*. These centres will not only in-

volve the physicians and patients, but actually recruit molecular scientists, information technology specialists and generate interfaces with the new drug developers in academia or the pharmaceutical industry. This example is already programmed to explore its potential to connect with additional international centres, including *Cancer Core Europe*, thus sowing the seeds for the new and necessary system of healthcare.

A need for consensus on international data standards

The development of common standards requires the involvement of clinicians together with scientists, primarily IT specialists, and policy makers developing the legal system both nationally and at the European, or even better the global, level. The action should be initiated by scientists in information technology.



Photo: Danish Saroee

Delegates at Uppsala Health Summit exchanged thoughts on how to implement precision medicine.

By setting common rules and fostering a smoother interoperability, new standards can promote better implementation of precision medicine. When offered improved access to their own health data, cancer patients may experience better life quality and improve their capacity to be involved in decision-making during the process of care and therapy.

Intimately coupled to the issues of standardisation is the need for clear ethical and legal standards for how to collect and use data, as the aim is that it should be translated to the clinic for the benefit of individual patients. However, regulatory processes that govern the application of precision medicine today are time-consuming and complicated. For this reason, the workshop clearly *underlined the need for improved processes that can retain the integrity of patients while the research community benefits from the data produced in the best possible way.* Recent regulations (such as the EU

General Data Protection Regulation, GDPR) on personal data handling provide a framework that aims at preservation of individual integrity and guides the legal aspects of ownership of medical data. However, this promising activity on the legal front was also criticised by delegates as being rather slow.

The necessity for a new and improved consent handling Consent issues need to be handled in a multi-disciplinary team with clinicians, IT-specialists, ethicists and the legal system, whereas ethicists and IT-specialists should take the lead in initiating the action. This action aims at providing transparent data sharing to increase efficiency in cancer care, and should support the individual patients and increase their power when taking the decision to share data or not. The action will have an impact on future generations of patients and their kin. Ethical issues involve constructing a framework for handling the overload of data

that is created and defining how the information available should be handled and by whom. A lot of information is gathered at patient level and needs to be secured to avoid misuse. Also informing parents of very young patients in a transparent way is of great importance to make sure they are aware of how the personal data is used. The workshop also took a stand on the global aspect of this new evolution and debated views around the best practice for internationalised standardisation when considered from an ethical and legal side. Concrete suggestions on this critical issue remain open for formulation in the future.

Consequences for cancer care, patients and their kin

The implementation of precision medicine holds in itself some important promises for more efficient and equal cancer care, if the technology can be implemented on a broad scale, selecting which patient will benefit from which treatment.

Common standards for data collection and sharing is a development which is expected to reduce costs and open up precision medicine technology for more patients. This in turn will contribute more to improved cancer care based on accurate data on the patient's profile and needs, thus reducing possible socio-economic biases.

Equal care on a global scale though would also demand access to precision medicine technology, on site or via other solutions, in regions where healthcare today has very few resources and access to an oncologist is limited or not even possible. The workshop agreed that this is an open-ended question that needs to be addressed in the future.

Improved consent processes and informed understanding of the treatment options can benefit patients' and their kin's understanding of their disease, its prognosis and which healthcare decisions they may take. A more active involvement in decision making is expected to generate trust between healthcare providers and the patient, and to contribute positively to the patients' quality of life.

Further Reading

Moscow JA, Fojo T, Schilsky RL. *The evidence framework for precision cancer medicine*. *Nat Rev Clin Oncol*. 2018; 15(3):183–192.

Korngiebel DM, Thummel KE, Burke W. *Implementing Precision Medicine: The Ethical Challenges*. *Trends Pharmacol Sci*. 2017; 38(1):8–14.

Sutton LA, Ljungström V, Mansouri L, Young E, Cortese D, Navrkalova V, Malcikova J, Muggen AF, Trbusek M, Panagiotidis P, Davi F, Belessi C, Langerak AW, Ghia P, Pospisilova S, Stamatopoulos K, Rosenquist R. *Targeted next-generation sequencing in chronic lymphocytic leukemia: a high-throughput yet tailored approach will facilitate implementation in a clinical setting*. *Haematologica*. 2015;100(3):370–6.

Prasad V. *Perspective: The precision-oncology illusion*. *Nature* 2016;537(7619):S63.



Biobanking for Global Cancer Care

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Aim

Several studies reveal substantial genetic differences between population groups of importance for healthcare strategies, including both prevention and treatment.

To understand these differences, and to develop efficient healthcare strategies, biobanks fulfil an important role on a national as well as on a global level.

This workshop was convened to identify which measures to take to **support the development of biobanks for global cancer care**. More precisely the aims were to:

- Develop ideas on how to embed biobanking within the landscape of clinical services and encourage collaboration across disciplines.
- Identify long-term funding opportunities to bring biobanks in low- and middle-income countries, into international collaborations.
- Find mechanisms for strengthening local control over samples and data while encouraging international collaboration.

Main conclusions

- Identify the stakeholders needed to create sustainable global biobanks, and then initiate a dialogue between them to align their visions and address norms, regulations and laws.
- Integrate biobanks as a part of existing healthcare infrastructures.
 - Identify norms, regulations, laws and other issues that hamper the introduction and management of biobanks in the healthcare

infrastructure, including the sharing and analysis of personal information about donors.

- Secure long-term funding for biobanks in low- and middle-income countries (LMIC) and associated data analysis capacity to avoid genetic exploitation.
- Identify and promote successful examples of biobanks in different settings.

Background

As people live longer and better, there is an increasing need for new tools that support the prevention, diagnosis or treatment of cancer. In high-income countries, efforts for cancer care are becoming increasingly targeted using precision, or even, personalised medicine to find optimal treatment profiles of patients.

In low- and middle-income countries (LMICs), the burden of cancer is expected to increase and decision-makers face difficult dilemmas when prioritising between immediate care and building domestic life science capacity. So far however, many governments have been unable or unwilling to do either, leading to an increased risk of genetic exploitation as research funding remains reliant on short-term projects decided by external stakeholders rather than domestic funding based on national strategies and needs.

To gain acceptance for investing in biobanks as an integrated part of any country's healthcare budget, biobanks must show that they generate knowledge directly applicable in national health-



Photo: Danish Saroee

Dr. Maimuna Mendy, International Agency for Research on Cancer, IARC, summarises the table discussion in the workshop on Global Biobanking.

care strategies. The Gambia Hepatitis Intervention Study carried out by the Medical Research Council – The Gambia is one such example. The study has been carried out for more than 30 years, monitoring the impact of hepatitis B vaccination on the incidence of Hepatocellular Carcinoma (HCC) and other liver diseases.

Projects such as this have revealed several significant examples on disparities in incidence rate and treatment outcomes based on gender, ethnicity and the environment of the surveyed population(s). It is, for example, now known that the incidence rate of HCC in some ethnic groups in the Gambia may be over 50 % higher than in the largest population group, the Mandinkas, even when adjusting for geographic location and lifestyle factors*.

* Sighoko et al., 2011

The differences in ability to metabolise drugs also mean that treatment strategies should be adjusted to produce more equal cancer care. It is, for example, well known that many populations in Africa metabolise drugs differently than most Europeans due to the prevalence of genetic differences in the CYP P450 genes necessary for metabolising the majority of clinically administered drugs**. Biobanks here serve an important role as an infrastructure which can support long-term surveillance projects, provide a baseline for epidemiological studies and provide more fine-grained knowledge about population genetics which may influence treatment decisions.

Global biobanking as well as global sharing of data and material is also critical to the development within the area of childhood cancer due to the intrinsic problems with statistical power in research concerning rare diseases in small patient groups.

The workshop and its participants

Participants from Africa, Asia and Europe attended the workshop and included biobank experts as well as professionals from medical research, healthcare, ethics & law, IT & bioinformatics and other fields. They represented a wide selection of countries with conditions for healthcare and research varying substantially: from high-income countries with a developed and well-funded universal healthcare system to low-income countries with very limited access to healthcare and where national funding strategies are lacking.

Speakers were invited from the Bridging Biobanking and Biomedical Research across Europe and Africa (B3Africa) and the Medical Research Council, the Gambia to highlight the advances in information technology and how it can be integrated with biobanks to support cancer care and genomics research.

** Bains, 2013



Photo: Danish Saroee

Conclusions and suggestions from the workshop

Identify and convene stakeholders

There was general consensus that the biobanking ecosystem is a complex one as it comprises a plethora of stakeholders. During group discussions on different topics, it also became clear that stakeholder groups and their priorities can be dramatically different depending on whether stakeholders are discussed on a macro level, when talking about national research strategies and needs, or on a micro level concerning day-to-day operations at a university or company. Researchers may, for example, in general favour a national research strategy supporting biobanks but be unwilling or slow to utilise the biobanks currently available to them. This may be due to practical concerns such as ownership concerns regarding stored samples, costs or due to practical issues such as an inability or delay in getting biobank-based work funded. Stakeholder groups may also show disparate behaviour based on who is interested on different levels. The public, when represented by patient organisations are, for example, often a strong partner supporting biobanks and research in healthcare.

At a macro level where the debate concerns broader topics such as “personal data” rather than “personal *health* data”, other groups such as privacy advocates may have a greater interest and influence on public discourse, meaning that it is important for biobank advocates to analyse stakeholders and their interests on several levels. Especially on high level issues, such as data protection and benefit sharing, this is important to recognise as stakeholders may not recognise themselves as such until late in the process when the expected impact is becoming more readily.

The workshop developed an extensive list of presumable stakeholders that could be part of any biobank effort that aims to become a stable, well integrated and long-term part of the healthcare infrastructure. See Box 1, page 19.

The workshop also underlined the importance of convening the identified stakeholder at an early stage in the process, to involve them actively in the identification of barriers such as norms, legislation and regulations, and in developing solutions to these barriers.

Integrate biobanks in existing healthcare infrastructures

A biobank must find a place within established local healthcare infrastructures, which may require significant formal and informal adjustments. In addition, existing IT-systems are often poorly constructed for large-scale data integration or have been developed in such a way that it is hard for healthcare providers to share their data in a harmonised manner.

The complexity of operations and the need to integrate biobanks within structures, norms and laws means that establishing new biobanks remains a challenging task. The challenges will vary between different countries and their stages of development, but will largely relate to current legislations and prevailing norms.

It says in the cancer atlas, that only about 2,7 % of global cancer investment is research directly relevant to low- and middle-income countries. That includes the simple basics of data collection.

Professor Max Parkin, Nuffield Dept. of Population Health, Oxford University

In some high-income countries, the lack of trust between the population, the government and the research community are often reflected in legislation which prohibits the storage, reuse or sharing of samples, which will in turn limit the impact of the biobanks on research, development and healthcare. In others, Sweden being one such example, trust between patients, researchers and the healthcare system is high which makes it easy to gain public approval for large-scale studies using personal information. Nevertheless, numerous regulations restrict sharing of data, or of samples, and establishing biobanks is a complex and often challenging process as evidenced by the regulatory issues surrounding landmark projects such as the Swedish Life-Gene project. Recently, a draft for a new more comprehensive law on biobanks was also presented to the Swedish government.

Collaborate internationally on legislation and management

The transfer of lessons learned by biobank stakeholders in establishing a legislative framework allowing the biobank's integration into current systems, is of great importance, and the workshop delegates called for improved and global transfer of information regarding biobank operations on these issues. Questions suggested for such exchanges were e.g. "How have others developed a cost/ownership model for their biobanks?"; "How do we organise international collaboration?" and variations on the theme of "how does my speciality/research fit into the wider research community surrounding biobanks?".

The workshop delegates also called for a more coordinated international collaboration to guide development of national biobank regulations, hopefully improving conditions for collaboration between biobanks and their stakeholders, while protecting donors.

Even within established networks between biobanks, such as B3Africa, BCNet, H3Africa, European BBMRIs, the workshop delegates identified a substantial need for improved communications and knowledge transfer between their respective stakeholders.

Secure long-term funding of biobanks in low- and middle-income countries (LMICs)

Long-term and sustainable funding is a critical issue for all biobanks, though the issue is of course a greater problem in LMICs, where basic healthcare is still largely under-financed.

In addition, there is an urgent need to increase the analytical capacity in many LMICs to ensure that the benefits from research can be implemented in national healthcare strategies and support a nascent life science industry capable of turning raw data into refined products benefiting the local economy. The workshop suggested increased investments in LMICs' capacity to analyse and drive indigenous research based on specimens and data from biobanks in these countries.

Capacity building through information, training and funding, as provided by networks such as H3Africa and BCNet, is important for the dissemination of knowledge regarding biobanking, but cannot remedy the substantial lack of funding.

The workshop did not identify new sources for funding, but it was suggested that evaluations of research funding applications should favour proposals which can leverage existing infrastructures to generate research results.

Concern was raised though that if we cannot adjust the largely unequal conditions for research and analysis of biobank samples, we still risk perpetuating the situation with LMICs exporting low-priced resources – the samples or their corresponding data – but having to import expensive refined products created from the very same resources they exported. Samples are only of value if they can be turned into relevant data which is analysed using bioinformatics, requiring both expensive hardware and skilled professionals.

The workshop suggested that regulations covering the sharing of biospecimens and derived data should be developed to secure a stable R&D landscape in LMICs. Delegates also suggested the development of extensive benefit sharing agreements between countries of different income levels and commercial stakeholders.

Some of these concerns are being handled in networks such as H3Africa and support networks through projects such as BCNet and H3Abionet but there is a lack of available funding to move from capacity building to direct collaboration in cohorts.

Restrictions on access and sharing, to stemming the loss of data, must be combined with measures to *enable* sharing of data. Incidental findings and *ad hoc* collaborations are of great importance to scientific developments. Too rigid regulations would isolate LMIC researchers from the international community. It is therefore very important that a biobank is not only organised to host samples for time-limited projects but that there is a realistic data management plan which provides a long-term capacity for data analysis and translational medicine.

Consequences for cancer care

Biobanks provide the basis for population-based genetics and make possible long-term epidemiological studies which enable evidence-based national healthcare strategies for the prevention, diagnosis and treatment of cancer. Especially in LMICs, it is important that biobank studies are oriented towards applications that can contribute to the development of efficient national healthcare plans. **A sustainable global biobank program will enable national governments to monitor the development of cancer and accurately assess how cancer incidence and mortality change over time as nations develop, thus leading to more efficient and equal cancer care.**

References and further Reading

Bains, R. K. (2013); *African variation at Cytochrome P450 genes*, Evolution, Medicine, and Public Health, vol. 2013, no. 1, pp. 118–134 [Online]. DOI: 10.1093/emph/eot010

Bongcam-Rudloff E., Klingström T. (2018); *Global Biobanking in Uppsala Health Summit Pre-Conference Report 2018*, <http://www.uppsalahealthsummit.se/summit-2018/pre-conference-report-/global-biobanking/>

The Gambia Hepatitis Study Group; *The Gambia Hepatitis Intervention Study*, Cancer Res November 1 1987 (47) (21) 5782–5787

Kirk, G.D., Olufunmilayo A.L., Mendy, M., et al. (2004); *The Gambia Liver Cancer Study: Infection with Hepatitis B and C and the Risk of Hepatocellular Carcinoma in West Africa*; Hepatology Vol 39, issue 1, 2004 DOI:10.1002/hep.20027

Munung, N.S., Mayosi B.M., de Vries, J (2018).; *Genomics research in Africa and its impact on global health: Insights from African researchers*, *Global Health, Epidemiology and Genomics* (2018), 3, e12, page 1 of 8. doi:10.1017/ghg.2018.3

Sighoko, D., Curado, M. P., Bourgeois, D., Mendy, M., Hainaut, P. and Bah, E. (2011) *Increase in Female Liver Cancer in The Gambia, West Africa: Evidence from 19 Years of Population-Based Cancer Registration (1988–2006)*, PLoS ONE, vol. 6, no. 4 [Online]. DOI: 10.1371/journal.pone.0018415

Box 1

Biobank stakeholders

Governments must provide stable frameworks for biobank operations. A biobank is a long-term commitment and which must be accounted for in regards both to the legal process and funding. In low- and middle-income countries, governments often accede the responsibility to foreign aid projects and in high-income countries, governments may often accede responsibility to individual researchers by providing funding for biobank structures on a short-term project basis just like for other research projects, making it a responsibility of a principal investigator or coordinator to obtain future funding.

Academic researchers and their institutions must adjust to the changing demands of science. High-throughput omics research requires extensive sampling and annotation of samples and it is hard, if not impossible, to justify that access, replicability and reusability is limited to further the career goals of individual researchers. Innovative study designs and application of new molecular techniques or bioinformatics applied on a shared pool of samples is more cost-efficient and enables small and innovative groups to better test and validate their ideas to improve cancer care.

Industry research must be more intimately connected to the academic process. Pharmaceutical companies often already possess considerable biobanks for pre-clinical and clinical trials. Precompetitive collaboration is a major trend in the pharmaceutical industry and biobanks are one of many cases where we may see significant benefits from this.

Healthcare providers are the first line of contact with patients and are an important stakeholder both for collecting information and turning the generated knowledge into practical applications.

Healthcare authorities set the terms for the relationship between local healthcare providers and other stakeholders. Investing in sample collections is a cost in time, effort and equipment which may not immediately pay for itself but can contribute significant value over time. Providing access to samples, and just as importantly, relevant data is therefore highly important.

Comprehensive cancer centre are centres that have a well-established combination of fundamental and translational cancer research and can provide or coordinate care along the whole process of cancer treatment. As such, they form a key stakeholder to provide ideas, samples and data based on their extensive work with cancer patients.

E-Health infrastructures providers create the infrastructures necessary to collect data in local journal systems and national registries or the archives of pharmaceutical companies. Combined with biospecimen from the biobanks, E-health infrastructures can provide a wealth of information in a cost-efficient and timely manner.

Local biobanks collect samples and may in some cases also handle data associated with the samples. In many cases, local biobanks are members of international or international networks that coordinate methods and support the sharing of samples to support larger-scale studies.

Research funding organisations have an important role to ensure that funding is used appropriately.

International research consortia and infrastructures have driven much of the harmonisation of biobanking. Especially in research for rare diseases, international collaborations have played an important role in enabling the sharing of samples between countries to reach sufficient sample sizes for studies. International organisations, such as the International Society for Biological and Environmental Repositories, the European and Middle Eastern Society for Bio-preservation and Biobanking, as well as funded infrastructures, such as The Human Heredity and Health in Africa (H3Africa) Initiative and BBMRI-ERIC, also play an important role in harmonising sample collection and serve an important role to influence in shaping how conflicting interests such as personal data protection versus legitimate use of samples for research on human health may be balanced.

Ethical review committees and policy makers are not only gatekeepers against illegitimate research, but can also drive development towards stable, fair and predictable systems for data collection and sharing. Revealing information about the human nature and what makes individuals different will always be the key towards precision medicine and improved cancer care. The sharing of personal information will therefore always be a sensitive and potentially dangerous issue in research. Building stable, fair and predictable systems for evaluation is therefore important to ensure appropriate handling, transparency towards society and accountability for those involved.

Civil society (patients, donor organisation and others) is a broad group, but perhaps the most important stakeholder of all as research cannot persist without support. In many countries, patient organisations are the most vocal proponents of research and improved care. As cancer in children and adults are very different diseases, and this needs to be considered when developing biobanks for the future, childhood cancer advocate groups play a specific stakeholder role. With the development of E-Health systems, individualised records keeping and monitoring of patients are possible throughout the daily life of a patient and not only during times of direct contact with the healthcare system. Patients are therefore no longer only champions of research but also partners who can generate the data and knowledge necessary for improving the care of future patients. In this context, it is important to consider children's need of age-specific information on data ownership, generation and sharing.



Clinical Value and Price-setting for New Cancer Drugs

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Aim

The workshop “Clinical value and price-setting for new cancer drugs” was convened to suggest feasible strategies for establishing models for monitoring the healthcare outcomes of new cancer drugs once they have been approved for marketing. The discussions started from the context of an imaginary country (e.g. an OECD-country) with established authorities for prioritisation, health-economy evaluations, and price-setting and covered:

- the possibilities to implement a lifecycle perspective on new cancer drugs, for a more comprehensive, dynamic and knowledge-based foundation for continuous evaluation of the clinical value as a base for prioritisation, health-economy evaluations, and price-setting at any time post marketing approval.
- the potential implications of a lifecycle perspective for the formal decisions and communication (“information package”) of marketing approvals by regulatory authorities as well as for other stakeholders.
- sustainable models for price-setting which reward continuous monitoring and gathering of knowledge.

Main conclusions

The top three suggestions from the workshop were:

- Develop central price setting models, both in Europe as well as globally, with evidence-based standards for reimbursements. This action would need the active involvement of national regulatory authorities, health technology assessment authorities (HTA), pharma industry, the European Commission, payers and governments but would need to be initiated by the European Commission and/or the European Parliament.
- Develop an international infrastructure and standards for collecting post-marketing data of relevance for all stakeholders. This action would need the active involvement of healthcare, governments, academia, companies, patients and the European Medicines Agency (EMA) but would need to be initiated by the European Commission and/or the European Parliament in cooperation with healthcare providers.
- Develop international standards for analysing and sharing post-marketing collection of knowledge from the data systems in healthcare (“real-life data”). This action would need the active involvement of healthcare providers, governments, academy, pharma industry, patients and the EMA, but would need to be initiated by the European Commission and/or the European Parliament.



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Background

In recent years, as a consequence of considerable research activity, science has made rapid progress in the field of cancer research. This has resulted in many newly approved treatment options along with other products which are currently in development.

The new cancer drugs are often initially developed to target specific cellular mechanisms which characterise a subpopulation of patients within a certain type of cancer (personalised). If they show promise, it is not unusual for them to be put on a “fast track” authorisation process and receive rapid marketing approval. However, the knowledge of the clinical value, e.g. overall survival, quality of life and possible side effects, is usually rather uncertain at this time.

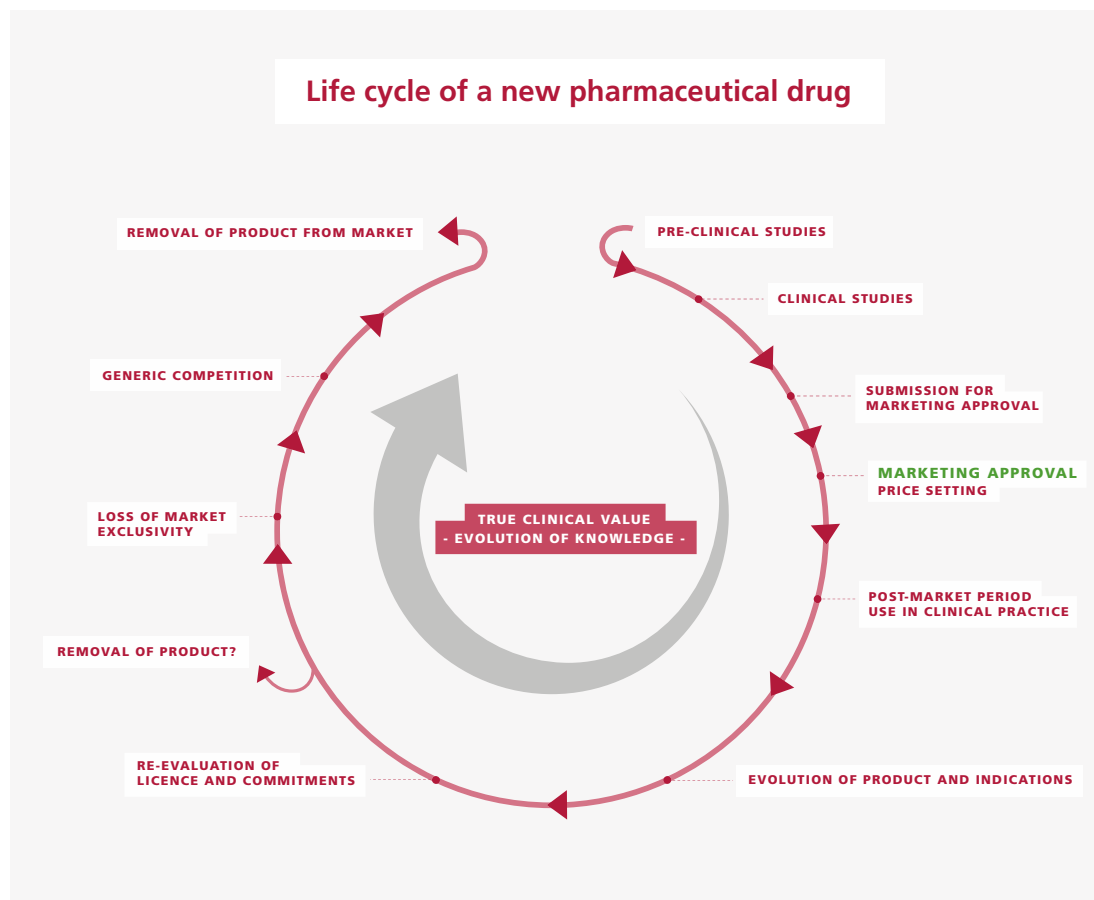
Some of these new products can provide significant clinical improvements to the available alternative, others perhaps offer only limited additional value. The true additional clinical benefits of a new drug, however, can be difficult to judge from early clinical trials and may not be established until after years on the market. This process will require long-term follow-up including patient-reported outcomes. One basic challenge is that price negotiations are done at a point when we know very little about the true value of the new drug. It seems reasonable that re-evaluation should be carried out based on

longer follow-up of pivotal studies and real-world data to ensure a price that reflects the clinical value. However, there are only weak incentives for this today. Another problem is the system of separate price negotiations in different countries.

The cost of new treatments is often substantial and the bodies responsible for approving payment and reimbursement have to make difficult choices that restrict patients’ access to these new drugs. This raises important questions for all stakeholders. How can new, improved therapeutic options become available and affordable to all those who would benefit? Can new options be created that enable continuous collection of evidence after marketing approval?

The workshop and its participants

In an overview of the regulatory perspective on the determination of the clinical value of cancer drugs, Dr. Filip Josephson, Clinical Assessor at the Swedish Medical Products Agency and member of EMA’s Committee for Medicinal Products for Human Use (CHMP), reflected upon the interplay between the regulatory perspective and Health Technology Assessment (HTA) functions. A marketing authorisation can be granted if data demonstrate that benefits outweigh risks with the proposed use. However, important information for determining an appropriate price may be missing at the time of approval, e.g. a precise estimate of the impact



on overall survival. The approval of a drug impacts the equipoise for its further study in the approved indication. Therefore, the need to provide timely access to therapies with a demonstrated positive benefit/risk for patients may adversely affect the ability to generate precise estimates of relative efficacy versus other therapies. It cannot be ascertained that bias is controlled in non-randomised comparisons of outcomes (e.g. real-world data).

Dr. Deepak Khanna, Senior Vice President and Regional President for Europe, Middle East, Africa and Canada (EMEA), MSD Oncology, underlined the need to rethink authorisation, pricing and reimbursement. The increasing complexity of new medicines (multiple indications, combinations) requires new access models based on collaboration with payers and other stakeholders to ensure timely and affordable patient access. He also mentioned a few national access initiatives. Dr Khanna concluded that current access processes have to be adapted to the reality of more complex treatments. An open exchange and collaboration between innovative

industry, payers and policy makers is needed. Timely patient access is a joint effort in a world of rapidly evolving science.

The workshop gathered about forty delegates representing regulatory agencies, health technology assessing functions, politicians, patient associations, clinically active oncologists and the pharmaceutical industry.

Two major blocks of discussions took place, before prioritising suggestions of measures to take.

During the first block of the workshop, participants were invited to successively take four different stakeholder perspectives, discussing pertinent questions laying the ground for a holistic understanding of the complex issue of how to assess the clinical value of new cancer drugs.

The second discussion session was organized as a “World café” with four tables covering different phases of a new cancer drug’s lifecycle. Each table considered the perspectives of different stakeholders when discussing possible implications of a lifecycle perspective on new cancer drugs.

Conclusions and suggestions from the workshop

Stakeholder perspectives to consider when implementing a lifecycle perspective on new cancer drugs.

The patient perspective:

A patient perspective includes a discussion on the influence of age-specific factors of life quality and the safety of new cancer drugs. Thought also needs to be given to how well patients actually understand market access decisions.

Patients and the general public demand a higher degree of transparency and information/knowledge, thus becoming more involved in processes for bringing new medicines to the market.

Patients need information and education to improve their capacity to navigate the healthcare system. This can be achieved through direct interaction with stakeholders, but also as a result of policy decisions taken to strengthen health navigation capacity. Systems for education and knowledge-transfer to patients will become more important as patient empowerment, and thus their capacity to influence development and access to medicine, increases.

The medicines that sit on the shelf in the warehouse, because it's unaffordable, is useless for patients, and it's also useless for the manufacturer. We need to have a better partnership!

Dr. Mariângela Simão, WHO, Assistant Director General

The socio-economic impact on patient needs to be considered, and patient advocacy organisations have a role to play pushing and addressing these needs.

The workshop noted that with a lifecycle perspective on new cancer drugs, the value of a successful treatment of childhood cancers can have a substantial impact on the full clinical value of the drug, provided that future costs for treatment and late effects decrease.

We need to improve methodologies for measuring quality of life, including how to validate

patient-related outcome measurements. Patients need to be included in decision making at every step.

The pharmaceutical industry (producer-vendor perspective):

The workshop discussed what could become basic principles to make promising cancer drugs both available and affordable, considering the need for a sustainable relation between healthcare, producers and vendors.

Multi-stakeholder discussion and interaction and collaboration should be initiated as early as possible in the development, in order to influence decisions on access and funding.

Such new approach must cater for sharing the financial risks between the industry and the healthcare/national authorities. Risk-sharing between producer/vendor and buyer/payers was considered an attractive approach that can become part of the trend in pharma industry to deliver a “full care cycle” including diagnosis and treatment.

However, predictability of costs, financing, risk, access, etc., is a major success factor. A lifecycle perspective needs to balance early access, based on little data, with the needs to collect data post market access. This can be achieved by iterative assessments of new medicines.

With a lifecycle perspective, it is reasonable to expect a lower price upfront. A true outcome price can be developed, based on the iterative assessments and confirmed benefits of the drug, which implies a dynamic pricing over the drug's lifecycle.

Healthcare/national authorities (buyer/payers):

Equally important for a life cycle is to have sustainable and transparent principles for how the healthcare authorities evaluate treatments.

We must always strive for a high quality of evidence, but we also need a holistic approach to evaluations, considering the overall impact on society of new cancer drugs (e.g. in relation to already existing treatments for cancer and prioritisations between different areas in healthcare, affordability, etc.).

Risk-sharing is possible and acceptable, if constructed as value-based pricing based on clinical evidence. It was suggested that new drugs should be introduced at a low price and then re-evaluated after 2–3 years to achieve a fair price based on overall survival and quality of life data.

The workshop also suggested EU-based negotiations, value- and evidence-based price setting, while considering the overall impact on society and health systems.

Regulatory authorities:

The workshop further discussed what the implementation of a life style perspective would mean to the regulatory authorities, notably how to establish principles according to which they can stimulate and support the evaluation of new cancer drugs, also after marketing approval. This would cover effect data when used in clinical routines, evaluation with respect to already existing therapies as well as the effect and tolerance in different age groups, thus providing a patient perspective.

It is no doubt that we as industry need to do better and we need to do more. Affordability is one of the ways of doing better and more.

Thomas B. Cueni, Director General, International Federation of Pharmaceutical Manufacturers & Associations (IFPMA)

Regulatory authorities can and should cooperate to ensure availability of and access to registry data. Which clinical endpoints to use should be agreed upon between regulatory authorities and health and technology assessment (HTA) bodies. Risk-sharing agreements are important in order to provide good incentives to generate data needed.

In conclusion, we need a closer coordination between the developers of HTA dossiers, clinical health and medical products assessors and HTA bodies in different countries, together with a mechanism to support such coordination.

Other perspectives mentioned in the discussions:

A Pan-European price negotiation collaboration should be established and could be initiated by the European Commission.

For a lifecycle perspective to work, early dialogue needs to be established between producers, HTA bodies and regulatory agencies, already in the clinical trial phase of drug development.

Healthcare and sponsors can influence trials to focus on relevant areas that are more important for a wider scope, a lifecycle approach, than “only” the risk/benefit model used today.

It was also suggested that it would be worthwhile to start looking into developing pricing frameworks for combinations of medicines, treatments, and diagnostics. Affordability and willingness to pay are factors that need to be reckoned with.

Potential issues relating to privacy and sharing of data need to be addressed to be able to accumulate relevant data. This needs to be done in close collaboration with data protection agencies and international counterparts. A re-think of incentives for innovation is called for!

Implications of a lifecycle perspective on new cancer drugs, on the different phases of drug development

Clinical studies phase and marketing approval phase

In the following discussion, the possibilities and consequences of including a lifecycle perspective already in the early clinical studies phase were considered, as well as the perspective to move from a sole focus on market approval, to a situation where we continue to accumulate knowledge of a drug for the next phases.

More emphasis is needed on the pre-clinical and early clinical phase of development relating to e.g. research and evaluation of bio-markers and similar tools that can potentially be used for detection of specific sub-types of cancer for which the new drug is specifically designed.

Further work is also needed on harmonisation of requirements for different markets and countries. The need for a closer collaboration between regulatory and HTA authorities was reiterated.



Photo: Danish Saroee

The workshop on clinical value gathered expertise from pharma industry, patient organisations, healthcare and regulatory authorities in creative discussions.

It was suggested that we should consider *conditional approvals*, requiring real-world data.

Price setting phase and post-market period phase

The prerequisites for monitoring new cancer drugs after their introduction into healthcare routines need to be identified, particularly as regards the capturing and validation of real-life data.

The question for pharma is: What is a sustainable return on investment that actually leads to affordable access?

Dr. Mariângela Simão, WHO, Assistant Director General

Capturing reliable data of effects is a challenge, and a universal, internationally standardised system for collecting and reporting these data is something worth striving for. Payers, i.e. healthcare systems, are the most appropriate actors to drive the development of infrastructures and collection of data. Relevant data need to be accumulated over the whole lifecycle of a drug.

This needs to be driven in close collaboration with regulatory agencies, HTA authorities, payers and producers.

Timely patient access is important in an environment where science is evolving rapidly. Thought needs to be given to how, in the future, a controlled introduction of a new, potentially effective drug might be managed. This would include access, use and follow-up in order to assess the true clinical value of the drug.

The current systems and methodologies for monitoring and measuring quality of life need to be improved. How can we assure data collection by means of “wearables”, “apps”, and other new tools? And how can these data be made useful? The capacity to process very large amounts of (big) data will influence our knowledge of a drug’s effect over its lifecycle. Artificial intelligence and machine learning will also open up new possibilities to consider, and we should be able to capture more patient-relevant data from registers. However, new systems for accumulating and collecting data need to be compatible and we need international harmonization of standards for capturing and accumulating data.

Table 1. Summary of consequences of suggestions for cancer care and patients.

	Suggestion 1	Suggestion 2	Suggestion 3
	Develop central price setting models in Europe as well as globally, with evidence-based standards for reimbursements.	Develop an international infrastructure and standards for collecting post-marketing data of relevance for all stakeholders.	Develop international standards for analysing and sharing post-marketing collection of knowledge from the data systems in healthcare (“real life data”).
How will this contribute to more efficient* care?	Creates evidence-based price setting and knowledge clinical value	Creates evidence-based price setting and knowledge clinical value	Creates evidence-based price setting and knowledge clinical value
How will this contribute to more equal** cancer care?	Stronger evidence-base for equal and fair use	Stronger evidence-base for equal and fair use	Stronger evidence-base for equal and fair use
How will this improve the individual patient’s quality of life?	Improve affordability and access	Creates possibilities for collecting patient generated data	Creates possibilities for collecting patient generated data
How will this influence which health decisions the patient and her kin have to make?			Decision to accept collection/ sharing of data from medical records within legal restrictions.

Consequences for cancer care, patients and kin

The top three suggestions from the workshop are presented below, including presumed consequences for cancer care efficiency, equity, patients’ quality of life and the health decisions the patient and her kin can make.

The workshop’s three top suggestions were expected to contribute to more evidence-based price setting and a knowledge-based clinical value, which together with a stronger evidence base for which patients will benefit from the treatment in case, will contribute to more efficient* care, as well as to a more equal** and fairer use of new treatments.

* **efficient** = optimal value for available resources in a wider sense

** **equal** = independent of socioeconomic status, gender, age, race etc.

Central price setting models in Europe, as well as globally, with evidence-based standards for reimbursements, are expected to improve both affordability and access.

An international infrastructure and standards for collecting post-marketing data of relevance for all stakeholders, together with standards for how to analyse the same, will improve our possibilities for collecting patient-generated data in a secure manner.

However, collecting and sharing post-marketing data will always require the consent from the individual patient, who thus will need to actively take a health decision concerning the own situation.



Deepak Khanna, Senior Vice President and Regional President, EMEAC Oncology at MSD, one of the workshop speakers, advocated new perspectives on the clinical value of cancer treatments.

Photo: Danish Saroee

Further reading


Mathers C, Rebelo M, Parkin DM, Forman D, Bray, F. *GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide*: IARC CancerBase No. 11: International Agency for Research on Cancer; 2013.

International Agency for Research on Cancer, Stewart, B.W. and Wild, C.P. (editors) *World Cancer Report 2014*.

Jönsson, B., Persson, U., Wilking, N., *Innovative treatments for cancer in Europe-value, cost, and access*. IHE Report. 2016:2, 2016.

World Health Organization, *Cancer, Fact sheet*, Feb. 2017.

World Health Organization, *Towards Access 2030: WHO Essential Medicines and Health Products Strategic Framework 2016–2030*, (WHO/EMP/2017.01), 2017.



Long-Term Care for Cancer Survivors

Striving for the Best Quality of Life Possible

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Aim

The workshop aim was to give guidance globally regarding the long-term follow-up of cancer. Objectives were to incorporate such guidance into the creation of national cancer plans, building on existing experiences from mainly young cancer survivors and to give guidance on the development of sustainable post-cancer knowledge centres or systems, adaptable to local contexts, defining the minimum elements required for their establishment. Prioritisation, good patient engagement practices, the need for effective methods for detection of late or rare side-effects of treatment and the variable health literacy among patients were aspects to consider. The workshop examined the problem from three major perspectives: the clinical and organisational, the societal and a patient-centric perspective.

Main conclusions

Systems for systematic long term follow up of growing populations of cancer survivors are rapidly developing but still almost exclusively in high-income countries, and is not included in the WHO guidelines based on the World Health Assembly's resolutions, a blind spot between treatment and palliative care. It was concluded that such guidelines could deliver substantial benefit for both individual survivors and society

both more generally and monetarily. For low- and middle-income countries in particular, developing cancer care, it would be an advantage to plan holistically, i.e. to already now take into account the need for systematic, long-term follow-up of survivors.

Clinical and organisational healthcare systems perspectives

- Establish common global definitions of terms surrounding cancer survivorship.
- Develop international guidelines for support to cancer survivors that can be adapted locally.
 - Sustainability, equality and equity should be the hallmark of the guidelines and the real-world implementations thereof.
- Risk-based planning should be used when conducting follow-up of individual patients in order to improve predictions and relevance of long-term health prioritizations.
- Build up organisational structures in healthcare systems and between stakeholders that bridge the gaps between units, avoiding “silo-structures”.
 - Incorporation of lessons learnt and technologies developed in long-term follow-up in other medical specialities and from non-healthcare contexts into cancer patient management,



Photo: Danish Saroee

Dr. Françoise Meunier, EORTC, a strong voice for holistic approaches to cancer survivors' needs. Here in conversation with Dr. Bella Jaboma, Hope for Cancer Kids, Kenya, and Ms Ingrid Kössler, patient representative, RCC West, Sweden.

- An iterative, needs-driven approach should be used to meet and manage long-term needs of patients. Societal stakeholders should be consistently included in this process.
- Create three-way communication systems (patient-to-patient, patient-to-physician, physician-to-physician) to share knowledge, experiences, data and information.
- Create a supportive legislative framework around individual patient data globally and address issues such as access and accessibility, ownership, personal integrity and cyber safety.
 - Improve the patient's access to medical records across the healthcare chain to stimulate patient health literacy and empowerment.
 - Establish global standardisation for data collection on survivorship to facilitate global collaboration.
- Establish medical registries with alert systems to enable detection of signals of rare and/or late post-cancer treatment effects paired with the already existing global systems for detecting new adverse drug reactions.

Societal perspectives

- Increase and encourage evidence-based research on legal and societal aspects of cancer survival to support rational decision making by legislators and other stakeholders.
- Measure cost-effectiveness of long-term, post-cancer treatment interventions.

Patient-centric perspectives

- Guidelines for long-term, post-cancer care should be age-adapted and adapted to the specific cancer diagnosis.
- Continuity and coordination within health-care systems to manage patients' post-cancer treatment is important. A “survivorship passport” was suggested.
- Patients and survivors should own their health data.

Background*

Issues of long-term or late side-effects of cancer diseases and their treatment are increasingly becoming a reality for long-term cancer survivors worldwide, with steady improvements regarding

* See also Grundmark et al. “Long term care for Cancer survivors” in Uppsala Health Summit Pre-Conference Report 2018, www.uppsalahealthsummit.se/digitalAssets/692/c_692758-l_1-k_uhs-preconf-2018-web_180518.pdf

novel cancer treatment methods and healthcare in general. Clinical-organisational, societal and patient perspectives need to be considered when solutions to long term survivors' issues are sought.

It is only by a common understanding of the real needs and the existing possibilities only then, we can ask the right questions and find the meaningful answers. This, we have to do together with the patient, for the future.

Dr. Ingela Franck Lissbrant, MD, PhD, Sahlgrenska University Hospital and Swedish National Prostate Cancer Registry

Long-term adverse health consequences for cancer survivors are dependent on the specific cancer diagnosis, the type of treatment delivered as well as treatment intensity. Examples of such side-effects from classic treatment modalities include secondary tumours, infertility, cardiac and neuropsychiatric toxicity, accelerated aging post cancer treatment including premature menopause. Late side effects of novel effective treatment modalities, e.g. targeted therapies and cell therapy, remain to be thoroughly described. Improvements in methods for detecting and managing late onset side-effects are clearly needed, both for classic and more modern treatment modalities. In addition to the late health effects directly related to cancer treatment, societal problems also often arise, e.g. related to education, employment, personal economy and position in society post cancer.

The workshop and its participants

The workshop gathered expertise from a wide selection of backgrounds and countries with a considerable variety in healthcare systems. Several participants came from Sweden, a high-

income country with a highly developed and well-funded universal healthcare system where systems for clinical, individual, long-term, follow-up of cancer still are in the process of being built up. Several other participants on the other hand represented low- and medium-income countries with, in some cases, limited access to healthcare in general, let alone cancer care, and currently completely without resources for long-term follow-up of cancer.

Three invited speakers shared their thoughts in relation to the three perspectives: Professor Françoise Meunier from the European Organization for Research and Treatment of Cancer, EORTC, talked about societal aspects giving examples of late, negative, socio-economic discrimination of cancer survivors and potential solutions to such issues. Dr Marianne Jarfelt, Sweden, presented the success story of building up a long-term follow-up system for young cancer survivors in Gothenburg, Sweden and cancer survivor Maria Weimer, Sweden, shared valuable insights from the patient perspective e.g. suggesting improvements on post-cancer fertility issues.

Many of the participants had limited personal experience from long-term follow up of cancer and the lively and intense discussions mirrored this often ending in more general cancer care issues such as the availability of and development of cancer care globally and hence were not limited to the pre-specified intended aims of the workshop. Participants however agreed that, even with such varied representation as regards healthcare and cancer systems, the discussions were applicable to most settings. Countries or systems still in the phase of building up cancer care in general may benefit from important lessons learned from countries who have come further and possibly incorporate long-term follow-up early on in their development of cancer care.

Conclusions and suggestions from the workshop

Clinical and organizational healthcare systems perspective

Common definitions and global guidelines

To expand the debate to include various healthcare systems around the world in addressing already known, as well as rising, challenges of long-term care for cancer survivors, the adoption of common definitions and using a joint language defining the cancer survivor must be established. In practice, different approaches and definitions of cancer care might result in fragmentation of its management: Who qualifies as a cancer survivor as compared to a patient?; How do we define palliative care?; What is cancer-related care or a late consequence of cancer?

Moreover, the socioeconomic situation and the infrastructure status varies in different contexts and may have implications regarding who to include as stakeholders when developing the area. Not only cancer survivors, but also their families and their communities may need to be eligible to access adequate support and information.

Looking at the problem from a healthcare systems perspective, there is a call for adaptable local guidelines based on international ones. They should include strategies for long-time follow-up of childhood cancers. Such action plans should be global, but flexible enough for different countries to be able to use different criteria from the same guidelines, and implement them depending on what works in the national scenario as systems of care for cancer will vary significantly in different regions.

Inspiration from other disease models

Long-term cancer care development in general should be able to extrapolate best-practices and experiences gained from childhood cancers as well as incorporate lessons learnt from other medical specialities. Certain elements and concepts in managing of other diseases could also serve as models for rehabilitation efforts in post-cancer treatment and follow-up, such as existing examples of schemes for rehabilitation after stroke or in rheumatoid arthritis. Similarly, technology that works in other contexts could be borrowed and adapted for the needs of cancer patients. Numerous modern technological solutions exist to monitor performance of athletes

– would it be possible to use the same tools to monitor cancer patients? An example from the Netherlands was brought up in the discussions, where athletes can log on to a website and receive psychosocial prompts and ratings that they can then bring to their doctor – similar systems could be implemented for healthcare including cancer care. Patients and doctors could use such systems for self-monitoring of potential late side effects and other individual disease and post-disease care management.

Organizational structure of the post-cancer team and communication

The organizational structures of healthcare systems were generally viewed by participants as being in need of reshaping in order to support individual patients to more effectively make use of their experiences and expressed needs. An iterative approach would be needed in order to identify the non-medical and medical specialties which should constitute the care team surrounding a cancer patient and adjusted according to needs-driven principles and priorities. Other stakeholders who could enhance the quality of life of patients by facilitating management of inevitable long-term consequences could also be involved in the planning and could be alerted of the long-term effects of cancer, e.g. insurance companies, religious leaders or trade unions in societies where this would be culturally relevant. In discussing the formatting of a care plan, it was evident that the delegates of the workshop called for a needs-driven care plan enabling the patient to also express personal worries or topics of discussion as relevant.

A cross-cutting issue mentioned alongside patient management and cancer care organisation was that of a three-way system of communicating: patient-to-patient, patient-to-physician, physician-to-physician; of knowledge and experiences and access to information and sharing data. The term “physician” should here be understood as not being limited to that person or title per se, but rather to include a multidisciplinary team of healthcare professionals. Patient representatives in the discussions underlined the need for a coordinated access to safe and effective systems for exchange and sharing of clinical and non-clinical data and experiences, whether it be

in form of a staff focal point or other method for coordinated access to care and health data. This would benefit both the individual patient and local healthcare at the point of care. It should be structured in ways and formats which allow and sustain a global learning system. The scope of such systems would entail a post-treatment contact point for all patients, new technologies or making use of available technologies to improve patient-to-patient, patient-to-physician, physician-to-physician communication. Conceptually it was identified that all these challenges could potentially be addressed through joint communication platforms or through possibilities of sharing electronic records or the data therein in a controlled way.

Health data registries to detect rare or late effects

The importance of establishing and keeping high quality registries with, if possible, automated alert systems that could detect and recognise signals of new, rare and/or late effects of post-cancer treatment for both different patient populations and individual patients, was emphasised. Experiences from existing, global, spontaneous, adverse drug reaction reporting systems, which are effective in detecting early side effects as well as signal detection methods, should be taken into account. Using risk-based planning when conducting follow-up of patients was also pointed out as important to individualise follow-up and conserve resources. Tools should be developed to promote the systematic and automatic identification of problems from these registries and a concrete suggestion from the workshop was to use a system of flagging in medical records, to alert different specialists who may later meet cancer survivors. Another idea presented was the compilation of a list of the most common symptoms or complications experienced by cancer survivors, and address those as 'cancer-rehabilitation' needs for the use of non-oncology physicians and other healthcare personnel who are treating the patient.

Data repositories and digitalisation in the long-term care of cancer were mentioned as a success factor in countries where they are already in place. These could furthermore provide a live learning system for patients as well as the healthcare systems when continuously updated according to the latest scientific evidence. Integrated

cancer databases could evolve into repositories composed of evidence-based information and emerging knowledge from patients and individual healthcare staff on a national and international level. This would again need the establishment of standardised data collection on cancer data to facilitate global collaboration. Technology will play an important role in linking medical records between different care parties, and the infrastructure for this development should be needs-driven, rather than technology-driven as was unfortunately felt to be all too often the case. A key success factor to increase detection, understanding and management of late side-effects from post-cancer treatments is to prioritise the establishment of good, high quality registries globally, integrating them and making use of data.

Societal perspective on long-term cancer survival

Budget constraints and resource allocation differences in healthcare systems globally were discussed as a limiting factor to advancements surrounding the management of long-term cancer survivors and limiting the implementation of existing guidelines and thus constraining their realisation in healthcare.

The impact of evidence-based research on health budget allocation was identified as a potential driver for change but also a research gap that could prove the value of certain global interventions that were mentioned. Other areas where additional research is needed are the legal and societal aspects of cancer survival and their implications for individual patients and a better understanding of social aspects of cancer survivorship including delayed effects on work productivity and employment, healthy lifestyle efforts. The workshop also called for research aiming at improved healthcare management and how policy making in a broad sense could influence patients and long-term cancer care. Research and development to address these gaps would facilitate the measuring of the cost-effectiveness of long-term post-cancer treatment interventions and thus influence policy changes and enhance decision-making in this area.

The participants in the workshop suggested that national care plans should be more detailed. For



Photo: Danish Saroee

Dr. Kelechi Eguzo, University of Saskatchewan, Canada and Dr Uwemedimbuk Ekanamen, Uyo Teaching Hospital, Nigeria, find a moment to network during the coffee break.

example, they should systematically include and address the different known social and medical side effects and the management of them. The view was that they should also include a coordination effort to solve potential, non-clinical challenges arising in the various walks of life of a cancer survivor, such as socio-economic implications and issues surrounding employment and insurance policies thus preventing discriminatory, cancer-related restrictions which can affect the lives of survivors. Where relevant, the need for education and information on cancer was emphasised to overcome or reduce the serious stigma of having a cancer diagnosis that patients face in some societies.

Global, culturally flexible solutions to societal issues may be difficult to achieve but a desire was expressed for increased cross-border collaborations within the field of cancer survivorship research and policy-making. These societal change movements would ideally involve globally-based patient organisations or unions, in addition to national organisations, to include post-cancer survival care in the global agenda and in high-level fora.

Patient perspectives on long-term care for cancer survivors

Cancer affects people from all walks of life and at all ages. A long-term care plan should therefore have a format allowing to take individual differences into account. It is essential to start from the patients' perspective and start acting locally. What are the patients' expectations for follow-up cancer plans? How are patients expected to benefit from them? What would patients want to be included into such plans?

Priorities for the long-term care plan should be impacted by patient age, fertility status, level of fatigue, level of cognitive impairment e.g. during childhood, adolescence, education, treatment given as well as other medical and psychological conditions. Participants further stressed that global guidelines should be both age-adapted and based on the cancer diagnosis. The importance of involving patients representing different age groups with varying needs and life priorities, such as reproductive age, sexuality and body image issues, projected future cognitive functions, in a stage of (re-)entry to working life was stressed. Solutions must respect principles

of equity and equality, regarding long-term support, and this for as long as possible. That support should include educational and social support: children affected by cancer might perform poorly in school compared to their peers and will need extra attention.

Another patient perspective voiced during the workshop was the importance of continuity and coordination within the healthcare system to manage patients post-cancer treatment, with available systems of support and communication also where contextually and culturally relevant, extended to both close and extended family and other partners, stakeholders and medical specialties and non-medical staff as needed. To establish continuity over the years, contact points, connectors or guides could be established between healthcare and patients in a manner that patients would know how to reach a relevant contact point even long after their treatment.

Representatives of the patient perspective expressed a wish for continued ownership of their health data, and to take steps in bridging the gap between healthcare and patients. A suggestion raised was that healthcare professionals should draw up a summary of all treatments patients received, with recommendations on how to best follow up on them (long) after they have

been declared cancer-free. Just as desired when initiating treatment, patients should receive personal and detailed information at the end of their treatment. The information should be flexible, adapted to the patient's needs, and could be either on paper or in electronic/online format. In several countries this has been carried out in practice through introducing a "survivor passport"* summarizing his or her cancer treatment history, containing individualised follow-up recommendations for screening of potential late effects, educational materials, and a notebook to create and store information.

On the topic of patient empowerment and needs-based care for cancer survivors, emphasis was made on the importance of improving accessibility of one's own medical records and across the healthcare chain in general, with IT system functionalities supporting the detection of late side-effects that might arise over time e.g. treatment-related ADRs such as cardiac and neuropsychiatric toxicity to mention a few. This also brought out the need to have a supportive legislative framework around this type of data and addressing related issues to access and accessibility, ownership, personal integrity and cyber safety surrounding such databases and systems.

* <https://cancersurvivor.passportforcare.org>



Photo: © ISTOCK/OLASER



Towards Useful Cancer Biomarkers to Improve Care for Cancer

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Aim

Each year, thousands of papers on biomarker discovery are published, but almost none of these lead to markers being approved by regulatory agencies. Improving and facilitating the biomarker discovery process was therefore the focus of the workshop.

The workshop aimed to discuss and suggest measures to enhance and accelerate biomarker discovery and validation to improve effective translation into clinical use. The following questions were asked:

- Which forms of cancer are most in need of diagnostic biomarkers? And which have a greater need for prognostic or predictive biomarkers?
- How should we improve the design of academic and industrial biomarker discovery programmes to better address the criteria for regulatory approval?
- How can we most effectively build a sound, best-practice platform for biomarker development?
- What are the benefits of comparative oncology for accelerated biomarker discovery and application?

- How can comparative models (non-rodent mammals) enhance biomarker discovery and validation?

Background

The definition of a biomarker is for all practical purposes made by the regulatory agencies that approve their use. For example, the FDA has the following criteria for a biomarker: effectiveness (sensitivity vs. specificity), safety and benefit-to-risk ratio. According to these recommendations, a new marker should only be introduced in the market if it is at least as good as already existing ones. The different types of markers address different questions about the patient's health. Diagnostic biomarkers, like prostate-specific antigen (PSA), clarify whether a tumour of a specific type is present or not. Prognostic markers help to decide if the treatment should be given at this point in time due to high risk of recurrence or progression (circulating tumour DNA, CA-125). Finally, predictive markers, like genetic mutations or gene expression, determine if a specific treatment will be beneficial to the patient.



Photo: Danish Saroee

Dr. Christian Ntizimira, Rwanda Palliative Care and Hospice Organisation.

Main conclusions

One of the major pre-requisites for successful and effective biomarker development is biobanks with rich sample collections, with, for example, correct information on diagnosis and outcome and already established structure and guidelines. Both academia and industry need clear criteria and guidelines for biomarker performance, that can be addressed by, among others, regulatory agencies like the FDA and the EMA.

Guidelines for the biomarker research and development process in academia are needed as well. Research funding agencies can initiate the process. The workshop urged everybody to make use of the consultative services provided by regulatory authorities (EMA, FDA) and to contact them as early as possible to ensure an efficient approval process.

Data-sharing policies need to be developed and formalised structures for this should be created so that results from biomarker discovery studies can be accessed by researchers globally. That will save money and time.

The discovery of predictive biomarkers should be incentivised, and a business model for biomarkers as a product should be developed. Healthcare payers and health technology assessors (HTA) must be involved in this, while patient advocacy groups, pharma industry or funders could initiate the process.

Biomarker discovery needs a mechanism to prioritise which biomarker needs to meet first. Such prioritisations can be handled by research funders, while academia and patient groups should be involved in developing such policies.

The workshop and its participants

The workshop had a broad mix of delegates: scientists performing image-based validation of biomarkers or clinical studies on markers; physicians; veterinarians; representatives from biobanks; regulatory agencies; and companies producing biomarker panels, medical devices or drugs.

The workshop was kicked off by three presentations to inspire and inform the discussions in the workshop.



Dr. Jimmy Lin, Chief Scientific Officer at Natera Ltd, introduced the workshop with perspectives on using circulating free DNA as a biomarker.

Dr. Cheng-Ho Jimmy Lin, Chief Scientific Officer, Natera Ltd, discussed the utility of circulating free DNA as a cancer biomarker. Tumour recurrence remains a major clinical problem. For example, the five-year survival for ovarian cancer patients diagnosed at stage I is 92% but at stage IV is 17%. Early detection is therefore a key to curing cancer. Existing technologies have important limitations: medical procedures are invasive and require sophisticated infrastructure, medical imaging exposes patients to radiation and is unavailable in low-income settings, and protein biomarkers have low specificity and high false positive rates. Going forward, we need biomarkers which are minimally invasive, do not require complicated infrastructure, have high specificity and low false positive rates, do not involve radiation and are universally applicable. Circulating tumour DNA (ctDNA) that is shed from the tumour might be an answer.

Dr. Chand Kanna, Chief Scientific Officer, Ethos Veterinary Health, discussed the benefits of comparative oncology using naturally occurring cancers in animals. Comparisons of gene expression patterns between primary canine and human osteosarcoma tumours revealed no segregation of samples based on species suggesting that the osteosarcoma expression phenotype was indistinguishable between dogs and humans. Dogs are good cancer models because they are large outbred animals, have genetic similarities to humans, have naturally occurring cancers, are immune competent and syngeneic,

have relevant tumour histology and genetics, receive relevant response chemotherapy, have compressed progression times, display heterogeneity and recurrence/resistance, and enable the study of metastasis biology. Dogs can be used in pre-clinical studies, prospective clinical trials (phase I and II), ADME studies, prognostic and predictive biomarker development. Due to shorter period of tumour development and time to relapse, it is also easier to study biomarkers in longitudinal studies, as well as monitor ctDNA with time in dogs.

Dr. Didier Meulendijks, Clinical Assessor Oncology/Haematology, Dutch Medicines Evaluation Board focused on predictive biomarkers and how we can unlock their full potential. Studies show that treatment chosen based on a predictive biomarker gives better response and longer cancer-free survival. However, not all targeted therapies have a predictive marker. Currently, 57 % of cancer drugs do not have any markers stated in their indications. For example, use of checkpoint inhibitor anti-PD-L1 therapy does not require a biomarker in many cancer types, even if PD-L1 expression has been shown to enhance the response. To couple the indications of targeted therapies with specific biomarkers, there is a need for better evidence, which can be provided by examining tissue samples and matched clinical data from randomised clinical trials. Therefore, we must also discuss how to stimulate biomarker discovery/validation efforts in the post-authorisation phase.

Conclusions and suggestions from the workshop

Promote and use biobanks as a resource for biomarker discovery and development

Population-based, favourably longitudinal, biobanks have a strong potential in the discovery phase. Collections of samples from healthy individuals as well as longitudinal sampling of different specimens from patients provide researchers with an enormous source of data. DNA, RNA, proteins and metabolites specific for cancer patients can be studied. Here, general signatures revealed in oncological patients are more important than individual data. Simultaneous discovery efforts in multiple tumour types will help to address high specificity. Genome and transcriptome sequencing data from the tumour samples will aid interpretation of plasma biomarker data. For early discovery biomarkers, we should collect different non- or minimally invasive samples in biobanks. We may need to exploit different biological fluids, analysis methods or combinations (blood, urine, exhaled air, imaging, stool, and clinical stratification). With the high prevalence of certain tumours, especially in dogs, companion animal cancer biobanks also serve as an excellent tool to test candidate biomarkers in a clinically relevant environment. This enables information to be transferred to parallel projects on the same tumour entities in man.

What I think is really exciting now is the potential to use circulating tumour DNA to actually detect patients the might benefit from additional treatments in the adjuvant setting following initial surgery, chemo and radiotherapy.

Dr. Susan Galbraith, Head of Oncology, iMed, Innovative Medicines, AstraZeneca

Develop clear guidelines for biomarker performance and biomarker discovery

It is important to have clear guidelines from the regulatory bodies and agencies on what will be considered a good marker in the early stages of discovery and/or development processes.

The FDA and the EMA have issued principles for collaboration on scientific advice on human

medicinal products and decided to share scientific perspectives and advice on biomarker regulation, thus facilitating applicants' regulatory burden*. Researchers can get consultations with regulatory agencies for free from e.g. the EMA. The workshop delegates strongly recommended prompt interaction with the regulatory agencies early in the discovery and development of biomarkers, independently of whether the biomarker is developed in academia, in industry or in collaboration between the two.

Despite the current possibilities for scientific advice, coordinated between the FDA and the EMA, **the workshop called for clear guidelines on the quality for different types of biomarkers, and for the process leading up to developing them.** This action needs to be firmly embraced by EMA, FDA and national regulatory agencies, but will also need the involvement of academia and industry.

The definition of an effective biomarker will depend on its purpose.

A *diagnostic cancer* biomarker should be usable at General Practitioners' level and relatively cheap to use. Biomarkers that require extremely sophisticated technologies for detection will not be affordable in low-income settings. Not missing the true cases is important for a diagnostic marker, but it needs to have high specificity to be used as a screening test. Biomarkers with high false positive rates cause a number of unnecessary extra diagnostic tests and are therefore too costly for the healthcare system.

Regarding *predictive biomarkers*, it was proposed that new cancer drugs should come with a biomarker in their indications. Comprehensive validation of such biomarkers should take place in samples from healthy individuals using population-based collections from biobanks. Such efforts may be initiated by academic researchers,

* www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000049.jsp&mid=WC0b01ac05800229b9
www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000319.jsp&mid=WC0b01ac0580022bb0

supported by the pharmaceutical industry and patients' associations. For evaluating treatment results achieved by biomarker-directed drug use, prospective clinical trials should be performed, where industry, clinicians and scientists should collaborate.

If the same target is identified in an animal model, comparative studies can be performed with same type of methodology as in human oncology. With its shorter lead times, typically shorter survival times and high tumour prevalence, this could be an important model at an early stage to either promote or detect concerns about the pathway/marker selected for the drug used. A successful biomarker discovery process should help us to identify high-risk patients at an early stage. Therefore, samples from these patient groups must be collected in biobanks and studied prospectively. Here healthcare authorities will be a key player, while insurance companies will influence the decisions. And, of course, there is a need to enhance awareness about cancer risks, so that these high-risk patients will actually be examined in the future. This comparative approach will of course even benefit the optimisation of cancer diagnostics and treatment in the species used itself (normally dogs or cats) and contribute to improved animal health and welfare.

Biomarker discovery should follow a systematic, integrative approach, in which machine learning can potentially play an important role. Multidisciplinary approaches will be of great importance. A new marker should meet the objectives of the study and pre-defined performance criteria. Obviously, to validate and create evidence, there is a need for prospective clinical trials. The biomarker should be at least as effective as already existing markers with regulatory approval. Safety of the marker can be an issue in potentially infectious settings – invasive tests or even minimally invasive ones might cause complications.

Scientifically there are questions to address, for example: whether the tissue expression should be consistent with the blood protein markers; to what extent should we rely on liquid biopsies (not very sensitive so far and quite expensive time- and moneywise, but obviously that will be

tremendously improved); how can we get more studies with investigation of the tissue samples. Even though those questions are not primarily addressing the issue of effective biomarker development, they are still extremely valid for the researchers.

Developing evidence in biomarker development is of course crucial. It was therefore proposed to identify patient and healthcare needs in this evidence. By promotion and implementation of long-term “phase 4” studies, sharing and pooling data from these studies, more and more evidence will be provided. The action would involve all previously mentioned stakeholders from the very start. It was even suggested that funding bodies could drive this kind of joint action.

Develop clear guidelines for access to and sharing of data collected in biobanks and healthcare

A successful biomarker “from discovery-to-use” process will need clear regulations on data-sharing and data ownership. The fact that there are still no common worldwide agreements and regulations in the scientific community in this area creates a situation where each and every study starts with sample collection and their own data generation. The result is inadequate sample sizes and poor statistical strength of the study. Sharing data may increase the statistical power, save research money, and give new answers. Several changes were suggested.

Biological data should be combined with clinical records. A collaboration between biobanks with data-sharing should be established with the help of academia, industry and regulators together with funding agencies and philanthropies. There is a need for international regulations on data-sharing and biobanking policy, which can be developed by regulatory agencies with the help of researchers, where scientific and ethical aspects are covered. It was also proposed that patients should have control over their data and be allowed to access it.

Incentivise biomarker discovery in industry

It was also suggested to promote biomarker development via specific incentives to industry. Authorities should play a key role in the initiation of this process, with industry and patients influencing the process. Instead of identifying



How should prevention measures be deployed? Via policy and governance or via behavioural changes? Dr. Barbro Westerholm, Member of Swedish Parliament; Dr. Vinyak Prasad, WHO's Tobacco Control programme and Dr. Folke Tersman, Professor of practical philosophy at Uppsala University, agreed that policy is important to create the necessary conditions for behavioural changes.

predictive biomarkers during post-marketing clinical trial drug development, companies should rather discover them simultaneously with the compound and provide this information in the indications. Even though targeted therapies are developed based on the knowledge of specific tumour mutations, other biomarkers that play important role in the sensitivity to the drug are not always taken into account. Addressing this gap might help in further personalisation of effective therapies.

It was also suggested that an investigation should be made into how a sustainable business model for biomarkers could be developed on a societal level. An effective biomarker should bring benefits to the patients, healthcare system and society at large by revealing the disease early or suggesting a treatment with the best possible effect thus saving money from fewer periods of sick leave, fewer unnecessary treatments and a better

quality of life for the patient. It was suggested that national healthcare systems supported by governments take the lead. Today, if no marker is developed ahead of clinical trials, there is little financial incentive for industry to develop companion diagnostic biomarkers after completion of clinical studies and regulatory approval of a new drug.

In companion animal oncology, the driver should be quality of life and animal welfare. As good biomarkers can guide therapy to more precise and effective responses, this will reduce unnecessary or futile treatment with expensive drugs that could potentially reduce quality of life. As the owners pay for this treatment, it will be more cost-effective and a strong incentive for owners, insurance companies and animal welfare organisations to also promote development of effective biomarkers in veterinary oncology.

Dogs are suitable as model animals as they are biologically similar to humans, and are immunocompetent animals. Even if there are species- and breed-specific mutations in dogs, no differences in treatment outcomes depending on the breed have been observed, but rather depending on the tumour biology, which is positive. There are also high-risk breeds that one can sample and follow.

However, to make more out of the comparative studies for biomarker discovery, there is a need for more samples in the studies to provide better statistics, more prospective studies in dogs. The Comparative Oncology Trial Consortium can serve as a good example, and create a business model for the biomarker discovery in dogs that does not yet exist.

Mechanisms to prioritise by need

To select the cancer types most in need of biomarkers, several aspects were considered: incidence and mortality rates, course and heterogeneity of the disease, treatment landscape together with a societal perspective (ex. childhood cancers). An important suggestion was raised that funding agencies can influence this process of prioritisation moneywise and shift a need in a particular direction.

Diagnostic biomarkers should enable early detection in pre-symptomatic individuals. Cancers considered to have the biggest diagnostic biomarker need were ovarian, pancreatic, lung, gastric, prostate, multiple myeloma and paediatric cancers.

For development of *predictive markers*, it was strongly suggested to focus on cancers with existing effective treatments. Also, if there are many therapeutic options, predictive markers are more needed than when options are limited. Markers for immunotherapy in general are also urgently needed.

For *prognostic* biomarkers, the imminent needs are in lung, prostate, urothelial, thyroid, breast, colorectal, ovarian, pancreatic cancers and melanomas. Prostate cancer needs prognostic markers to improve decision making, as patients are currently stratified based on pathology examination and there is a lack of pathologists. Breast cancer has various therapeutic approaches, so proper risk stratification is needed. As there are no targeted treatments to ovarian or pancreatic cancers, regulators could incentivise the pharmaceutical companies to develop predictive markers for new drugs.

Thus, there are many issues in the biomarker discovery and development field that are in need of prompt and effective solutions. Good communication between all the sides and result orientation should help us address these problems.

Further reading

Glimelius B., Melin, B., et al. *U-CAN: a prospective longitudinal collection of biomaterials and clinical information from adult cancer patients in Sweden*, Acta Oncologica, 57:2, 187–194, DOI: 10.1080/0284186X.2017.1337926

Paoloni M, Khanna C., *Translation of new cancer treatments from pet dogs to humans*, Nat Rev Cancer. 2008 Feb;8(2):147–56. doi: 10.1038/nrc2273

Paoloni M et al., *Prospective molecular profiling of canine cancers provides a clinically relevant comparative model for evaluating personalized medicine (PMed) trials*, PLoS One. 2014 Mar 17;9(3):e90028. doi: 10.1371/journal.pone.0090028. eCollection 2014.



Photo: Evan Duggan



Using Data for Better Cancer Treatments

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Aim

During the workshop “Using data for better cancer treatments”, groups of participants developed visions for the future for each of the following stakeholder groups: physician, nurse, patient and researcher. The visions aim to describe how data, as well as knowledge banks built from data, can be utilised more effectively and in a more integrated way to inform cancer diagnosis and treatment in the year 2050.

Main conclusions

Barriers to efficient data usage:

- Lack of infrastructure, mainly in low- and middle-income countries
- Data lacking structure
- Fragmented data
- Unclear rules for consent and usage

Enablers for efficient data usage identified:

- Improved access to mobile phones and networks
- Improved possibilities to store data
- Artificial intelligence

Actions needed to establish efficient data usage and to close the circle of knowledge:

- Standards for interoperability
- Infrastructure for secure and powerful data transfer on a global scale.
- Legal changes to clarify issues related to access, sharing, and ownership of data on a global scale.

- Allow patient contributions, for example with notes and self-measurements.
- Dynamic patient consent needs to be developed.

The workshop and its participants

Before developing the scenarios, several barriers and enablers related to data usage on a global scale, were identified, inspired by three critical incidents where knowledge building and access to data had played an influential role. The three incidents described were: *Dr Marije Wolvers, Helen Dowling Institute*: experience from an ambulant activity feedback intervention (AAF) for chronic cancer-related fatigue; *Dr. Kelechi Eguzos, Nigerian Christian Hospital and the University of Saskatchewan*: experience as a young physician of how a night of unexpected adverse effects from chemotherapy caused a revision of treatment protocols; and *Dr. Isabella Scandurra, Örebro University*: experience as a cancer patient of medication with side effects.

The participants in the workshop, almost 70 experts and decision makers from healthcare, academia, patient organizations, industry and healthcare related authorities, were organised in stakeholder labelled groups, and from the barriers and enablers identified, developed scenarios, *Visions for the future*, for their different “roles”: physicians, nurses, patients and researchers.

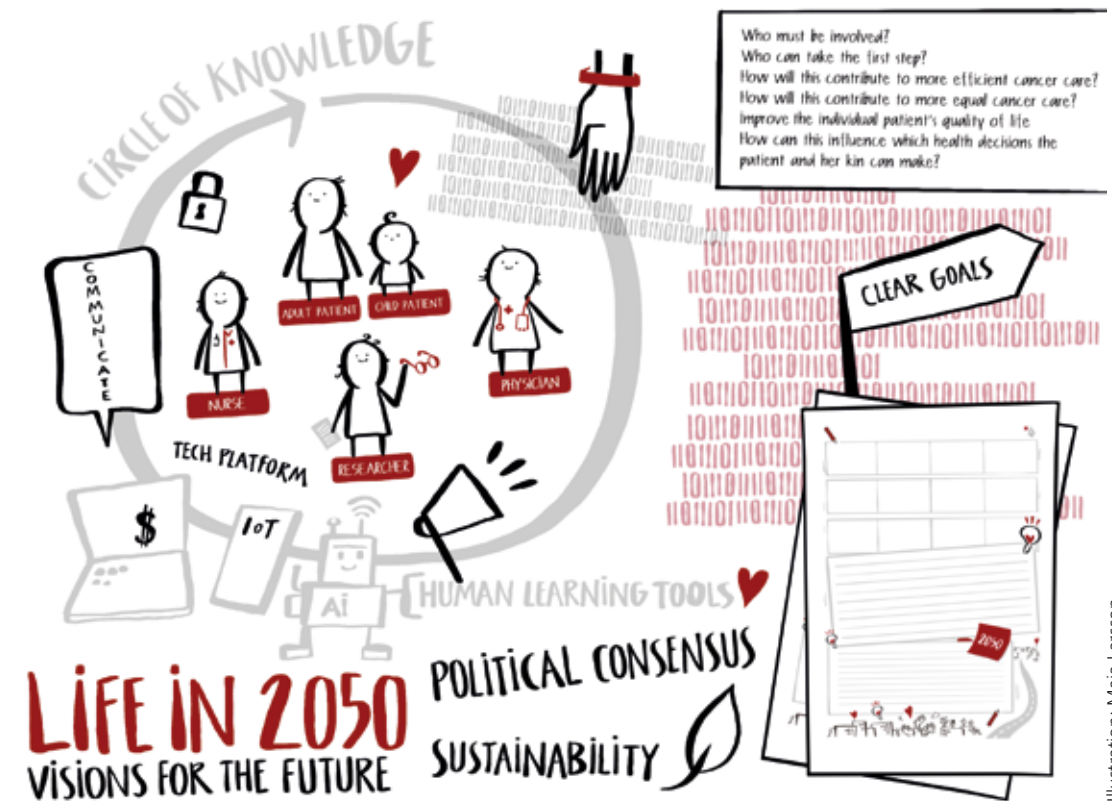
The workshop finally established a list of prioritised actions to reach the visions.

Barriers and enablers

The most commonly mentioned barriers were a lack of infrastructure in low- and middle-income countries, overwhelming amounts of data lacking a clear structure, fragmentation of data caused by lack of integration between systems and unclear rules for consent and ownership of data. Commonly mentioned enablers were con-

stantly increasing access to mobile phones and mobile networks all over the world, increasing possibilities to store vast amounts of data and artificial intelligence. In the remainder of this section, one scenario each for the different roles physician, nurse, patient and researcher will be presented, all taking these barriers and enablers into account.

Visions for the future



Physicians

In 2050, the circle of knowledge, which includes everything the physicians need to make the best possible decision, will finally be closed. This circle is a new concept which is now central to all healthcare stakeholders. It acknowledges that we need to store and use data that is not only generated from researchers and healthcare professionals, but also from patients collected through self-reported data as well as e.g. sensors. A central component is also that physicians use systems that are compatible not only on a national but also on a global scale, in order for up-to-date knowledge to be transmitted within and across healthcare systems. Thus, the circle of knowledge is a global concept. Through the circle of knowledge, all stakeholders work together to build global human learning tools, which every-

one can access and benefit from – a sustainable system for global cancer care.

Artificial intelligence, AI, now plays a central role in supporting physicians in making the best possible decisions. The AI solutions are mainly used to indicate possible treatments or to alert the physician if the available data in the knowledge base indicate that a patient, who uploads data automatically through sensors, can be in danger.

Also, in the future the software is made based on a modular, usable design where data is presented using different visualisations of overviews. Moreover, care processes in the system are automatically changed when updated.

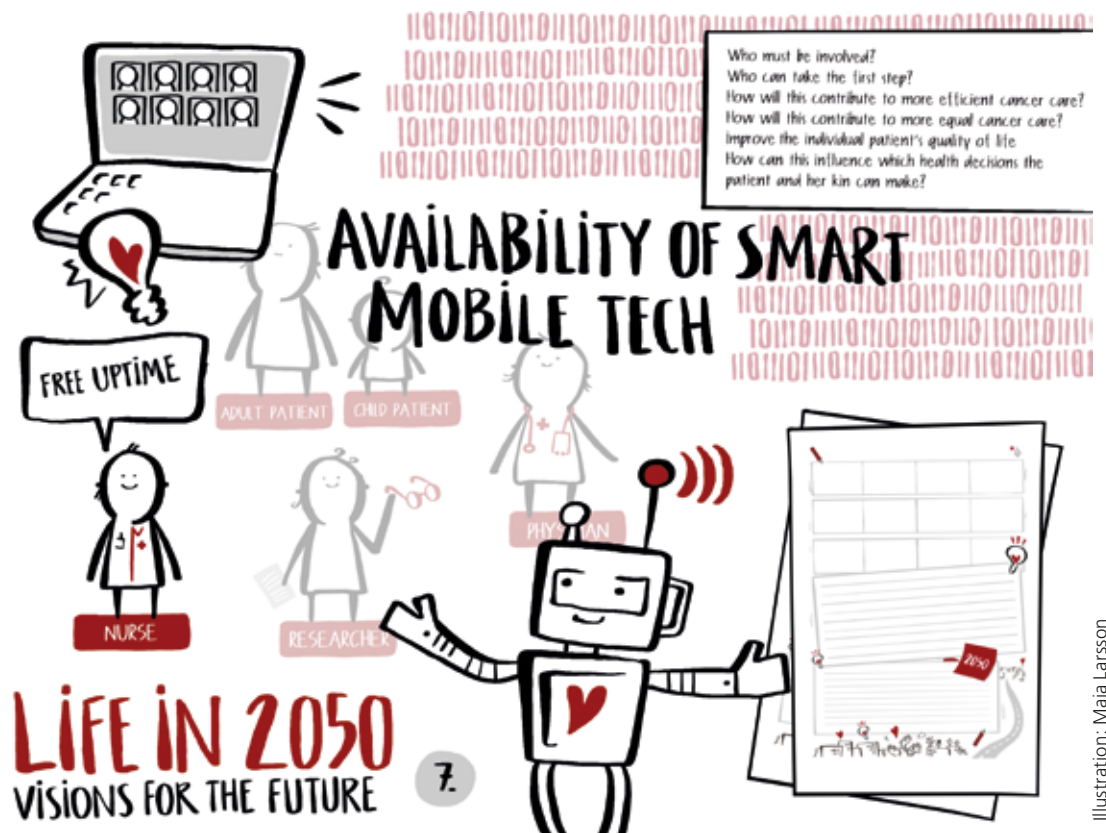


Illustration: Maja Larsson

Nurses

In 2050, there will be many more nurses and they are going to be even more skilled than today's nurses thanks to e-learning. This, together with the introduction of automated care technology, like care robots and machines for drawing and analysing blood samples, into patients' homes, will reduce nurses' workloads and enable them to dedicate time to patient outreach, increasing the effectiveness of preventive interventions. Although a higher number of nurses will be working locally, they will all be connected to a broader, virtual network of healthcare professionals.

Telemedicine and virtual meetings with patients are at the core of our vision of what nurses' working life will be like in 30 years. Facilitating

patient group meetings via a virtual meeting room accessible from anywhere will become one of nurses' central tasks. These patient meetings will bring together 30–50 patients suffering from a similar condition and enable participants to both 1) communicate their health status in a standardised way to the nurse through the system and 2) share their stories with the other participants. Regular meetings with her/his patient groups enables the nurse to monitor their symptoms and act in time when the condition of one of the patients seems to worsen. In those cases, nurses will be able to simply have their patients draw their own blood samples at home, thanks to the help of care robots. Drones will ensure the transportation of the samples between the patients' homes and the lab.

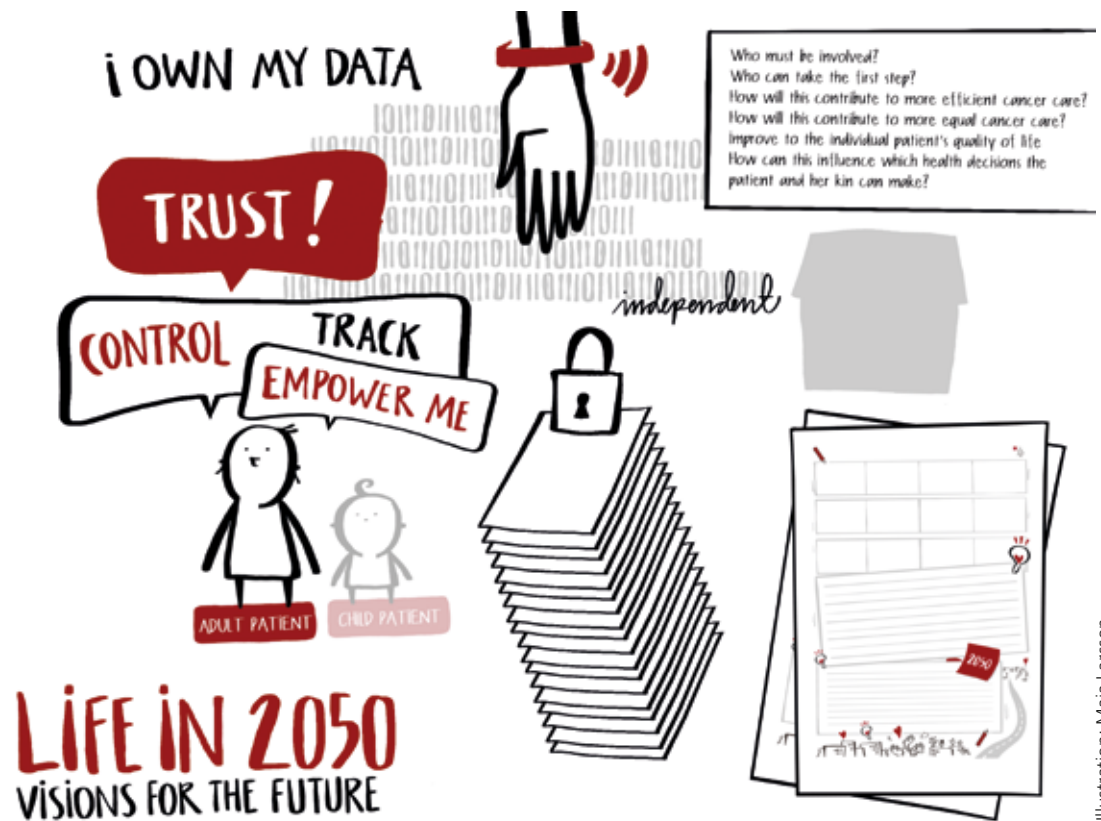


Illustration: Maja Larsson

Patients

In 2050, healthcare is centred on preventive measures and early flagging of potential issues based on continuous monitoring of an individual's metrics through non-invasive measurements. It will no doubt be easy to perform the necessary measurements through an implanted chip, but to also cater for the patient's need for control, a bracelet-based device is the preferred choice.

Data regarding the individual's health will be divided into several streams depending on how the data will be used. To enable early warning of potential health concerns, and for patients undergoing treatment, there will be a stream of data that is connected to the patient's healthcare records. The patient's healthcare provider is granted access to this data by the patient's express consent and is able to perform analysis on and interpret the data. The result is then communicated back through whatever channel is most suitable to the patient. A second stream of data is used for research and for tracking health trends in the general population and is thus anonymised and used in aggregated form for data analysis. This use of the patient's data

is also contingent on express consent by the patient.

Given the sensitivity of the data, it is imperative that the patient can trust the institution managing the patient's data. The data will also remain patient-owned and, as mentioned above, the patient is in control of the data and must consent to any and all uses of it. If dissatisfied with the service provided by one institution, the patient will have the ability to easily switch to another such institution.

The traditional processes in healthcare may have changed by 2050 in that patients only visit the hospital or local health centre when absolutely necessary. Technological innovations related to data collection and telemedicine help to provide professional expertise on demand and over long distances, making it obsolete for patients to wait for several hours in a waiting room. Instead, if a consultation is needed, patients can see their doctor using telemedicine technology or be scheduled for a face-to-face consultation with the required specialist.



Illustration: Maja Larsson

Researchers

In 2050, the cancer treatment will be carried out also outside of the hospital, for example at home or at work. Tele-medication will have advanced even further, and a patient from anywhere in the world could be treated by an expert in, for example, Nigeria.

The possibilities for early diagnosis to prevent cancer will be developed. The changes in the immune system for a particular patient will be possible to compare to a large dataset collected in a universal registry. In this way, the development of cancer can be identified a long time before symptoms appear. The registry is also to be used as a control arm in studies, giving cheaper and faster clinical tests.

To be able to share the data from all different healthcare records and collect the data in one registry, a standard way to transfer and store data is needed. This will be solved by an international agreement on data storage and access. The patients own their data and are the ones

that take the decisions on how it can be used. The sharing of patient data will be possible by allowing the patient to give a broad consent for using their data, and with an easy possibility to opt out of a particular study at any moment. Artificial Intelligence, AI, will be used to analyse the increasing amount of data collected. We, therefore, need a shared international agreement on how AI is going to be utilised in accordance with ethical standards.

Problems that hinder efficient use of data today are e.g. very fragmented registers and data bases, different and unclear data structures and definitions, too much free text documentation, unclear ownership of data and bad usability. Systems for entering data are complex and inefficient. Organisations and work processes are not developed to support better use of data. Documentation does not support individualised care or reflects the patient's own situation and preferences.

Summarising the perspectives

In the future, information systems must have the basic goal to support efficient translation of information into knowledge for the benefit of patients. This requires a number of major changes in organisation, work processes, information systems and competencies. Patients must be empowered and caregivers will have to change their attitudes towards patients who are now far better informed. Better use of data requires new competencies and skills that must be provided in education and training. Future cancer care will face new requirements. Information systems, e.g. patient record systems, and databases must be harmonised and build on common definitions and structures. Systems must be modular and communicate via standardised interfaces. Entering data must be facilitated and partially automated. New data types supporting individualisation and equal care must be documented. Patients must be allowed to document their own experiences, status and preferences in an agreed-upon format enabling the data validation necessary for efficient and reliable care. Information retrieval must be flexible and allow all stakeholders to access data that support their needs. Even though efficient access will be enabled for all stakeholders, patients included, the data as well as the access to it must be protected and regulated. Decisions must be checked in relation to best available medical knowledge and evidence-based medicine and support shared decision making between caregivers and patients.

Actions needed to reach the visions

The circle of knowledge comprises all the stakeholders involved in the care process (i.e. nurses, researchers, patients, caregivers, physicians, industry and other healthcare professionals) who are engaged in healthcare. For this circle to be closed, everyone needs to be able to contribute with data as well as having access to it. In the future, even more data will be collected from diverse sources, e.g. patient-generated data from sensors, medical devices, or self-reported data on their experience. Healthcare professionals will also continue to collect and record data for documentation, some of which will occur manually (e.g., written, typed or even spoken), and some will be automatically recorded.

A problem that may arise is that we thirst for knowledge, but ultimately drown in data. Already today a lot of data is collected that is never used. Algorithms or AI may help to analyse these “big data” and to communicate knowledge back to healthcare professionals and patients to support decision making and help to close the circle of knowledge. This being said, it will become more and more critical, as data repositories are growing in size, that we collect data that is likely to be used.

Opportunities for telemedicine (e.g., having a quick consultation with an expert via video calls) are expected to become more popular. Increasing data collection and storage also involve risks in terms of data security and privacy.

The patient was seen as the owner of the data who needs to consent to what data is collected, how it is used and with whom it is shared.

- **Implement standards for interoperability.** The important premise to the “Visions of the Future” was the development of standards to ensure interoperability.
- **Infrastructure for secure and powerful data transfer.** Data need to be accessed and submitted securely and efficiently through infrastructure solutions that work on a global scale.
- **Legal changes.** Regulatory aspects have to be solved not only on the national level but internationally. These changes relate to e.g. sharing, data accessibility and ownership of data on a global scale.
- **Allow patient contributions.** For the circle of knowledge to be complete, patients will not only need an access point, but also possibilities to contribute with their own notes and data from self-measurements.
- **Dynamic patient consent needs to be developed.** Regulations regarding patient consent have to be developed in light of new possibilities enabled by Big Data analysis so that old data can be used for new purposes as long as the patient consents to it.
- **Patients own their data.** It is especially important that all stakeholders recognise patients as owners of their own health data. Patients should have access to their data and decide how it should be used, for research and sharing purposes, and by whom.
- **Children** should have the right to obtain age-specific information concerning ownership of data and consent to share their data.



Implementing Physical Exercise in Cancer Care

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Aim

The workshop aimed to target implementation barriers and incentives for promotion and organisation of physical exercise among cancer survivors* during and after treatment both within and outside the healthcare system. Societal, organisational and individual aspects were addressed.

Background

Physical exercise not only decreases the risk of developing cancer; it also relieves the toxicity of cancer treatment and diminishes the negative, long-term consequences of both the disease and the treatment. However, despite the solid evidence base and international guideline recommendations about physical exercise, they are far from being implemented within cancer care. Considering the growing number of cancer survivors, it will not be possible for healthcare services in many countries to provide exercise support and facilities to all of them.

Main conclusions

The implementation of physical exercise in cancer care can only be realised if several actors collaborate. Patients, healthcare professionals, researchers, policy makers and the private sector may all take the initiative. However, none of these actors can perform a successful implementation on their own.

Knowledge and attitudes to physical exercise in cancer care must change

- Implementation of physical exercise is complex and guidelines must be developed for how to prescribe individualised exercise.
- Additional research is needed to optimise prescription of exercise.
- Physical exercise in cancer care should be included in the educational programs for physicians, nurses and physiotherapists.
- Special training for gym instructors should be provided.
- Patients and their kin shall be active partners in the entire process.

Marketing and PR

- Changing attitudes will need well designed lobbying aimed at policy and healthcare decision makers.

Collaboration

- Implementation of physical exercise demands cross-disciplinary teamwork.
- New partnerships between healthcare and wellcare need new infrastructures to enable a smooth transition for cancer survivors between organisations.
- A common understanding among professionals and patients regarding the importance of physical exercise in cancer care is imperative for implementation.

* A person is considered to be a cancer survivor from the time of diagnosis until the end of life.



Photo: Danish Saroee

Professor Karin Nordin, Uppsala University, introduces the workshop discussion on physical exercise to Dr. Peter Daneryd, CEO at the Joint Commission of County Councils for Advanced Radiotherapy, Sweden and Dr. Micheal Newell, Clinical Science Institute, National University of Ireland.

All patients are different

- Exercise programs should be individualised according to e.g. preferences, previous exercise habits and the trajectory of the cancer disease and treatment
- Structured exercise programs must allow for a variety of modes – group exercise, individual exercise, on-line, etc.
- Plan for physical exercise from the beginning of the cancer therapy.
- Different ages need different interventions.

Contexts are also different

- Deciding who to involve and influence is highly different in high-income countries with extensive public healthcare compared to low- and middle-income countries.
- Where can we seek finance for this intervention?

The workshop and its participants

Inspirational speakers

Dr. Martijn M Stuijver, Associate Professor, Amsterdam University of Applied Sciences and Researcher, Netherlands Cancer Institute gave an example from the Netherlands where a physiotherapist network has been established. It covers more than 500 locations where cancer survivors have access to specially trained physiotherapists. Another example from Northern Ireland was a MacMillan initiative whereby 700 local physical exercise providers outside healthcare received a brief course on exercise and cancer. Both these examples show that it is possible to integrate exercise into treatment at a population level. Dr Stuijver pointed out challenges such as sustainability and uptake of such programs.



Photo: Danish Saroee

Catrin Forsberg, from the Swedish well-care NGO Friskis & Svettis discusses implementation of physical exercise with Dr. Henrik Lindman, Uppsala University Hospital; Ingrid Kössler, RCC West; Arun Gupta, Win over Cancer and Dr. Tsetsegsaikhan Batmunkh, National Cancer Council of Mongolia.

Šarūnas Narbutas, cancer patient, and president of Lithuanian Cancer Patient Coalition (POLA), Lithuania talked about the importance of empowering patients and increasing their awareness of the importance of physical exercise. He gave examples on how non-governmental organisations (NGOs) who arranged cancer rehabilitation activities such as walking with peers and collaboration with local gyms. He emphasised small-scale initiatives to get started immediately rather than waiting for big funding before taking action.

Professor Mike Kelly, Senior Visiting Fellow, Department of Public Health and Primary Care, Institute of Public Health, University of Cambridge, UK, stressed the importance of broadening the focus of both policy and decision makers to include other aspects of cancer care rather than solely the medical-pharmacological. He also pointed out the necessity of increasing

awareness of the complexity of implementation of interventions such as physical exercise in cancer care. He argued that the efforts to support physical exercise for cancer survivors must be evidence-based and adapted to each individual patient.

Workshop participants and format

The workshop gathered 30 delegates with a background from NGOs such as patient organisations and research funding bodies, healthcare, wellcare, academia and the business sector. Both high, middle and low-income countries were represented. The workshop focussed on facilitators, barriers and solutions on policy, organisational (healthcare and wellcare) and individual (staff and patients) levels. Discussions about specified themes were held in mixed groups according to a pre-set agenda. All groups summarised their discussions and suggested action points.

Conclusions and suggestions from the workshop

Knowledge and attitudes

Increased knowledge about the evidence base regarding the benefits of physical exercise for cancer survivors is needed at all levels. Also, it is of utmost importance that policy makers and leaders in cancer care are aware of the complexity with regard to the implementation of exercise and other non-medical treatments in cancer care. Thus, detailed guidelines for how to write an individualised exercise prescription to cancer survivors and how to support survivors to adhere to such prescriptions need to be developed and anchored at all levels in the healthcare organisation and among policy makers.

Additional research is needed to gain more knowledge about how physical exercise interacts with cancer treatment and to optimise prescription of exercise for different groups of cancer survivors. It is important that cancer survivors are regarded as active partners in care with their own resources and abilities to promote health and as partakers in the development of cancer care, within and outside the healthcare organisation. The misapprehension that physical exercise may be harmful during cancer treatment needs to be altered to an understanding that exercise is an important way to promote wellbeing and diminish morbidity for cancer survivors as well as for persons without lived experience of cancer. Social media is an important resource to spread knowledge and change attitudes regarding exercise in cancer care.

Physical exercise in cancer care should be included in education programs for physicians, nurses and physiotherapists, on basic and advanced levels, and training should also be arranged for exercise instructors in public gyms to facilitate long term support of exercise for cancer survivors.

Collaboration

One main challenge for implementing physical exercise is the suboptimal collaboration between different healthcare professions. Focus is often solely on the medical treatment and other rehabilitation needs are frequently left aside. The need for multi-professional teamwork has to be highlighted and the complexity of creat-

ing teams has to be recognised. Furthermore, collaboration between healthcare and well-care actors (e.g. public gyms and NGOs) need to be developed in order to facilitate a smooth transition for cancer survivors between organizations. There is a need to create new infrastructures for such collaborations, as well as a structure to allow for partnership. For example, staff may have joint positions in healthcare and wellcare, and agreements between them about the possibilities for healthcare to use gym facilities may be needed. It is also necessary that stakeholders have an agreed understanding about the importance of implementing physical exercise and how it should be carried through. Cancer survivors, their family and friends are to be included in the team, being experts in their own lives and needs.

Structured programs for different cancer survivors

Another challenge for implementation is the great variety of patient needs, resources and preferences when it comes to physical exercise. How can one provide individualized options? Some patients are already physically active at a high level, others may need support to start taking walks as a daily routine. One model is to create structured programs with a variety of modes: group exercise, online exercise modules, personal instructors, home-based exercise and already existing facilities such as gyms. Even if healthcare cannot provide all the exercise facilities, it has to develop an infrastructure that supports routines for information, referrals, follow-up and collaboration with other providers. The programs also have to take into account accessibility regarding location, logistics and costs. For children, even more options may be relevant, such as gaming and playing activities. In some cases, social media may be used to create groups, and physical exercise may be added as an extra feature. Also, adjustments need to be made with regard to the age of the cancer survivors. Children, adults and the elderly do definitely need different kinds of exercise interventions to make adherence to exercise prescriptions realistic. To enable such programs, participation should be planned already from the start of treatment.

Marketing and campaigns

The awareness that a sedentary life style has negative consequences for cancer survivors and that physical exercise may improve wellbeing during and after cancer treatment needs to be spread among policy makers and in the society as a whole. Patient coalitions, cancer specialists (e.g. nurses, physicians and physiotherapists) and researchers are well situated to lobby for the implementation of physical exercise in cancer care. It is important to “knock on doors” and take part in forums for policy and decision makers and argue that actions are needed on a society level.

Public health campaigns promoting a healthy lifestyle including physical exercise for all, including cancer survivors, are one example of relevant actions. Traditional media along with social media should be used. Influencers and celebrities e.g. well-known athletes can serve as inspiring role models and ambassadors.

Adapt to context

All actions taken to implement physical exercise for cancer survivors as a part of treatment of cancer care need to be adapted to the context in which these actions are taken. It needs to be recognised that the conditions for implementation differ depending on a country’s level of prosperity e.g. between high-income economies, economies in transition and low-income economies. The differences with regard to financing, legislation, personnel resources and infrastructure should not be underestimated.

Governmental funding is definitely a realistic option in high-income economies with an extensive public sector since improved health among cancer survivors unquestionably will be beneficial for the public finances. Insurance companies are in some contexts another partner option to consider. In low-income countries, reliance on non-governmental organisations, corporate

social responsibility companies and charities is a more realistic alternative. Large companies or other employers, in the private; semi-private or public sectors, were also mentioned as possible partners and initiators of physical exercise programs for their employees. In the Netherlands, the national police force provides such programs for employees in cancer treatment.

Differences due to socio-economic conditions, level of education and other differences between groups of citizens within countries are also important factors to consider to adapt the implementation of physical exercise in cancer care to all individual’s needs. The workshop also advocated a “just do it” approach, suggesting small local initiatives to be taken immediately rather than waiting for big money and decisions that may never appear.

We have to start starting things that put the patient at the centre. And if people think they have to have a five-year plan, a ten-year plan, they are mistaken. You need a now-plan, a today-plan.

Gregory C. Simon J.D., President, Biden Cancer Initiative

Consequences for cancer care, patients and kin

The implementation of physical exercise in cancer care will contribute to a more efficient and equal care by improving treatment efficacy and cancer outcomes. In addition, it is a cheap and low-tech intervention that may be adapted to different economic and local prerequisites. Patients’ quality of life will improve with less symptom burden, improved participation in activities and social life, probably less sick leave and thereby an improved economic situation. The implementation of physical exercise also appeals to the person’s healthy side and may well include activities together with kin.



Photo: Danish Saroee

Ms Rebecca Ritzel, freelance journalist, contributing to the discussions in plenum.

Further reading

Bourke L, et al. *Interventions for promoting habitual exercise in people living with and beyond cancer*. Cochrane Database of Systematic Reviews. 2013. Doi:10.1002/14651858.CD10192.pub2.

Flottorp S. et al. *A checklist for identifying determinants of practice: a systematic review and synthesis of frameworks and taxonomies of factors that prevent or enable improvements in healthcare professional practice*. Implementation Science. 2013; 8:35.

Samdal GB, et al. *Effective behavior change techniques for physical activity and healthy eating in overweight and obese adults: systematic review and meta-regression analyses*. International Journal of Behavioral Nutrition and Physical Activity. 2017; 14:42.

Segal R, et al. *Exercise for people with cancer: A clinical practice guideline*. Curr Oncol. 2017; 24(1), 40–46. doi:10.3747/co.24.3376

Sweegers, M. G. et al. *Which exercise prescriptions improve quality of life and physical function in patients with cancer during and following treatment? A systematic review and meta-analysis of randomised controlled trials*. Br J Sports Med. 2017 doi:10.1136/bjsports-2017-097891



Drug Repositioning

An Underused Strategy for Cancer Drug Development and Access to Next-line Cancer Treatment?

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Aim

The overall aim of the workshop was to raise the awareness about drug repositioning, the potential it offers and the challenges it brings. More specifically, prior to the workshop, the organisers identified the following issues to be of potential importance for discussion:

- Can clinical trials for drugs earmarked for repositioning be simplified but still give the necessary scientific evidence?
- What would make it more attractive to increase investments in drug repositioning?
- Is 'innovative practice' with repositioning candidates an acceptable approach in healthcare and, if so, how can the knowledge obtained from such practice be collected and made public?
- What are the ethical considerations involved in drug repositioning?

Main conclusions

- Drug repositioning is a promising approach to improving drug treatment of cancer.
- Adverse drug reactions registries can be used as a source for identifying drug candidates for repositioning and the planning of clinical trials.

- Paediatric oncology would benefit from drug approval by mode of action, rather than by diagnosis. Development in paediatric oncology is already today partly dependent on drug repositioning.
 - EU-wide studies should be initiated in paediatric oncology in order to enrol sufficient number of patients.
- Improve incentives for companies to engage in drug repositioning, e.g. via extended IP-rights or data exclusivity.
- Consider setting up social enterprises and/or patient-driven structures when commercially driven interests fail.
- Set up a working group to develop registry-based randomized clinical trials (R-RCT) methods for drug repositioning in cancer.
- Develop awareness among policy makers on the rising costs for cancer care, and the possibilities with drug repositioning.
- Off-label use in innovative practice should be possible provided there is a scientific rationale, informed consent and if standard care is not withheld.
- Global, public registries with off-label data should be set up.



Photo: Danish Saroee

Workshop group deeply engaged in concrete discussions on drug-repositioning as a tool in cancer strategies.

Background

Several new and also very expensive drugs are currently being introduced for treatment of cancer. These drugs will hardly be affordable for most patients in low and middle-income countries and they also put pressure on the healthcare systems in high-income countries, especially considering the growing number of cancer patients as a result of an aging population. Another problem is that most of the new and expensive drugs provide very limited benefit in terms of survival prolongation and quality of life.

To manage these problems, we need cheaper, yet efficient, alternatives to complement the development of new and expensive drugs. Drug repositioning is the use of an existing licensed drug for a new indication, and this strategy has been proven to have great potential to be a valid, safe and much cheaper way to develop new treatments. An example is propranolol that originally was approved for treatment of hypertension, but now is used for several other indications, e.g. infantile hemangioma.

Drug repositioning can be divided into ‘soft’ drug repositioning, where a drug approved for one cancer indication is used in another cancer indication, and ‘hard’ drug repositioning where a drug approved for a non-cancer indication is developed for treatment of cancer. There are, however, challenges connected to the development and possibilities to use repositioned drugs in healthcare.

Today, patients receive treatment according to clinical guidelines, starting out with 1st line then 2nd line etc treatment, with a number of lines available depending on the cancer type and setting. When there are no more treatment options in the guidelines, patients are in principle left with the following options:

- Best supportive care, which is often not adequate for patients who are still in good general condition.
- Enrolment in a clinical trial provided that there is a trial with appropriate inclusion criteria available in the geographical area.

- Off-label treatment within established healthcare, provided that the treating physician has knowledge of off-label treatments with a scientific basis and the healthcare provider allows such treatment.
- Alternative treatment options outside of established healthcare.

Drug repositioning, within a clinical trial setting or as ‘innovative practice’, i.e. treatment of an individual patient with a drug that on scientific grounds is a candidate for repositioning but outside of a formal clinical trial, offers an alternative to these patients. However, in the same way as for cancer drugs developed ‘de novo’, robust clinical evidence is necessary for repositioned drugs to be included in clinical practice guidelines for use in an efficient and safe way. Thus, the drug to be repositioned needs to go through high-quality clinical testing to establish its benefit/risk ratio. Given the considerable costs and resources needed for such testing and the expected difficulties to get funding for drug repositioning, *one* option that was suggested for discussion by the workshop was the concept of registry-based randomized clinical trials (R-RCT). This offers a possibility to simplify the necessary clinical trials in drug repositioning and, thus, to make such trials cheaper and within reach for drug repositioning projects. However, all other aspects of drug repositioning which aim to make progress in the field were also open for discussions.

The workshop and its participants

The workshop gathered a group of delegates from the fields of clinical oncology, registry-based research, industry, patient organizations and regulatory authorities. It was based on the “Open space” format, i.e. the specific questions to be discussed were identified and detailed

by the participants themselves, following an introduction along the lines indicated above. “Open space” is a format which aims to ensure that the discussions are focused on the themes that are relevant and interesting for the workshop participants.

The themes suggested by the workshop participants for further elaboration were:

- Identification of candidate drugs for repositioning based on rare side-effects reported globally.
- The role of non-governmental organizations (NGOs) and pharmaceutical companies in drug repositioning.
- Who will/can take the lead in drug repositioning: Companies? Healthcare? NGOs? Funding agencies? Patients? Anyone else?
- Should ‘innovative practice’ with repositioning candidates be allowed in established healthcare?
- How can off-label data from such ‘innovative practice’ be shared and made easily accessible?
- How can trials in the oncology arena be more streamlined and made more cost-effective?
- Can R-RCTs be useful for drug repositioning in oncology?
- How can biomarkers be used in drug repositioning?
- In paediatric oncology there is experience from both ‘soft’ and ‘hard’ drug repositioning. Is drug repositioning in paediatric oncology following, or leading, the development?

There were overlaps between some of the themes while others were clustered or not considered possible to cover, which resulted in five themes that were discussed in depth during the workshop and that are reported from below.

Conclusions and suggestions from the workshop

The overall workshop conclusion was that drug repositioning is a promising approach to improving drug treatment for cancer and that it could contribute to solving some of the issues related to cancer drug development and use indicated above.

Identification of candidates for repositioning based on rare side effects

It was concluded that there are already examples of drugs used in a certain indication which result in adverse drug reactions that have been turned into a clinical advantage for another indication and subsequently been approved for that indication. An example is sildenafil (Viagra) that was developed for cardiovascular disorders and where erection was reported as an adverse drug reaction. Later it got approval for treatment of erectile dysfunction. Could this approach also be used for finding drugs that could be repositioned for cancer treatment? A ‘cancer cure’ is not likely to be found in this way but hints of new indications could probably be identified by systemic signal detection based on adverse effects.

Moreover, for drugs already planned for repositioning studies, the adverse drug reaction registries could be a source of information useful for design and planning of trials. Thus, there might be reports where the drug has been used in patients with the proposed new indication or information on effects in off-label use at higher dose or longer treatment time. The challenge with using these registries is that data is ‘patchy’ and often in the case report format. The advantage is that data is global and it was concluded that it might be used as one among several other ways to identify repositioning candidates and plan drug repositioning trials.

Drug repositioning in paediatric oncology

Drug repositioning and off-label use is common in paediatric oncology, since many cancer drugs have not been tested and approved for use in children. However, the need for clinical studies in children is large, since, for many reasons, it is not possible to merely extrapolate results from

clinical studies in adults to children. In paediatric oncology, it would be beneficial if drugs could be approved by mode-of-action (i.e. biomarker-based) instead of diagnosis-based. The reason is that there are usually very few patients for a certain indication and thus clinical studies in children become very expensive and difficult to perform.

Related to this, it was discussed whether R-RCT could be a solution to the trial issue in children and thus lead the way for this concept in oncology. It was also considered important to perform EU-wide clinical studies to enrol a sufficient number of patients to obtain clinical evidence for repositioned drugs in children. Furthermore, the participants called for increased ear-marked funding from governments, patient organisations, funding agencies and charities for clinical studies based on drug repositioning in paediatric oncology. Finally, in order to get companies interested in performing the difficult and expensive clinical trials in paediatric oncology, there must be more incentives, e.g. extended patent protection and data exclusivity.

Registry-based randomized clinical trials (R-RCT) in drug repurposing

It was concluded that the concept of R-RCT is very interesting and attempts should be made to apply it for drug repositioning in cancer. There are challenges though, and just copying the R-RCT concept directly from how it has been very successfully applied in e.g. cardiology will be difficult. To elaborate on this issue, it was suggested that a working group with an interest in developing the R-RCT concept for oncology should be formed.

Who can take the lead in drug repositioning?

Many drugs approved for non-cancer indications but which have the potential to be repositioned for cancer, are drugs that have been used for a long time and that are now off-patent and marketed by generic drug companies. Thus, there is often no real financial incentive for the



Photo: Danish Saroee

WHO Assistant Director General, Mariângela Simão, in dialogue with Dr. Alessandro Di Capua, Union for International Cancer Control (UICC).

WHO Essential Medicines model has a cancer working group, which noted that close to 75 % of the drugs approved in the last 15–20 years, lacked evidence of substantial clinical benefits for patients at registration.

Dr. Mariângela Simão, WHO, Assistant Director General

companies to perform or fund drug repositioning clinical trials. Are there still ways where companies can take the lead? One option would be to extend patent and data protection times for companies.

Furthermore, drug repositioning clinical trials and applications for intellectual property rights for new indications could be done by social enterprises that, at least in some countries, can receive a tax reduction. There are also examples of organisational structures driven by patient engagement.

For example, parents of children with cancer have founded a social, virtual enterprise – the charity aPODD* – focusing on repurposing of approved drugs to develop new cancer treatments, suitable for children. An investigator-initiated study could then be performed to get clinical evidence of effect of the drug in children. There have also been attempts to let governments take responsibility for new indications for existing drugs and to get the clinical evidence necessary to prove their effects in new indications. However, these attempts have not yet been successful. To convince politicians about the need for this kind of governmental support, we need a greater awareness about the economic burden of today's cancer care and more attention paid to the promising potential of drug repositioning.

Should off-label use of repositioning candidate drugs be allowed within 'innovative practice' and how can off-label data be shared and made accessible?

The participants concluded that off-label use in 'innovative practice' should be possible if there is a scientific rationale for the treatment, the patient provides informed consent and standard care is not withheld from the patient. Thus, it should not be an alternative to standard care but rather a possibility when standard care is no longer an option and a formal clinical trial is not available. There is clearly a need for registries where off-label data are collected, e.g. as an add-on to existing data collection within healthcare quality registries. This would provide support to physicians globally for off-label use and be a more robust and widespread way to collect and report data than case reports in scientific journals. This system needs to be global and the data made public.

* <https://apoddfoundation.org/>



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Further reading

Cohen D., *Cancer drugs: High price, uncertain value*.
Br Med J 359:4543, 2017

Pantziarka P., *Scientific advice – is drug repurposing missing a trick*. Nature Rev Clin Oncol 14:455–456, 2017

Sleire L, Forde HL, Netland IA, et al., *Drug repurposing in cancer*. Pharmacol Res 124: 74, 2017

Workman P, Guilio F, Schellens J, et al., *How much longer will we put up with 100.000 dollar cancer drugs?*
Cell 9:579–583, 2017

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Uppsala Health Summit 2019

Healthy Urban Childhoods

Uppsala Castle, 8–9 October 2019

In 2050, around 70 per cent of the world's children will live in urban areas. This means that many children will not only have better access to services but also have a greater range of choices of activities and options for going to school than their peers in rural areas. But already today, and for most children, growing up in a city also means inadequate access to green space for physical exercise, play or rest as well as exposure to harmful air, overheated cities and dangerous traffic. Many children are isolated in high-rise buildings, in sprawling cities without freedom of movement, and in neighbourhoods with little sense of community and social cohesion.

In short – the way we plan, build and develop our cities includes a multitude of challenges to children's physical and mental health. We could manage these challenges so much better if we used insights from science, innovations and the experiences of those working with and for children.

With rapidly growing global urbanisation, our ability to manage life in cities will define our ability to achieve the UN Sustainable Develop-

ment Goals. In 2016, UN member states adopted the New Urban Agenda to guide governments in their development of national implementation plans for sustainable urban growth.

Uppsala Health Summit 2019 will convene on the theme "Healthy Urban Childhoods" and provide an arena for discussions on solutions and their implementation. At the meeting, researchers, practitioners and decision-makers will come together to discuss intersectoral action for children's mental and physical health through innovation, improved policy instruments and methods.

Central questions for the meeting are how scientific disciplines and different stakeholders can collaborate to implement solutions to the challenges in the physical planning and management of urban areas, for greater equality, participation and accessibility.

How can we ensure that when cities grow, they develop on foundations of social, economic and environmental sustainability, with future generations in mind?

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