EAPM: a unique bridge in EU health policy

Innovation, Public Trust and Evidence: Generating Alignment to facilitate personalized Innovation in Health Care Systems

July 1st, 2021

European Alliance for Personalised Medicine

From the discussions at this conference, a number of recommendations

...on national and European alignment

- Coordinating, building and linking alliances
- Developing a common understanding of the role of RWE
- Promoting interoperability of data and infrastructure
- Maximising the use of EU guidance and initiatives aimed at collaboration - and ensuring national implementation
- Profiting from the lessons of the coronavirus pandemic
- Overcoming fragmentation and variations in approach while remaining sensitive to accept regional and cultural perceptions and sensitivities
- Staging a cancer conference under the Slovenian presidency to discuss common key issues

...on integrating advanced and comprehensive molecular diagnostic

- Establishing (and co-financing) networks of accredited centres
- Establishing networks of oncological genetic clinics
- Establishing guidelines / standards according to which pathologists will commission tests for specific types of cancer, matched with a guaranteed benefits package
- Raising physician awareness of the benefits of multi-biomarker testing and developing guidelines for the stage of neoplastic disease, diagnostics and therapy, at which molecular diagnostic tests should be performed
- Providing for upfront capital investment in infrastructure
- Generating frameworks for demonstrating the value of multi-biomarker testing

...on promoting trust in a learning healthcare system

- Maximising secure access to and controlled use of patient level data
- Leveraging new knowledge and best practices
- Refining risk stratification
- Balancing the multiple interests of multiple stakeholders
- Recruiting, training and sustaining a skilled workforce
- Promoting adaptations among regulators and payers
- Communicating clearly and sensitively among all stakeholders, including healthcare professionals, hard-to-reach populations or senior policymakers.
- Benefiting from the expertise of patients associations

Report

Foreword

In line with what is now an established EAPM tradition, its conference on 1 July 2021 reliably provided that necessary bridge to ensure smooth continuation of reflections on its priority health issues across the shifts in leadership of the EU Council of Ministers. Coming immediately after the eventful Portuguese Presidency, and right at the start of the Slovenian Presidency, the meeting reviewed recent advances in personalised healthcare innovation, in prostate and lung cancer and in securing patient access to advanced molecular diagnostics. And it offered clear perspectives on progress in the use of real world evidence, and on the importance of ensuring public trust and promoting health literacy to guarantee better patient well-being in Europe.

Its title of "Innovation, Public Trust and Evidence: Generating Alignment to facilitate personalized Innovation in Health Care Systems" also indicated EAPM's other role as a bridge – in bringing together stakeholders from across the widest spectrum of health care, to seek common ground and consensus, and to candidly identify persisting divergences and challenges still to be overcome in implementing personalised care in Europe and beyond. Consequently, its panel of distinguished speakers from the research community, regulatory agencies, public health decision makers, clinicians, patients and industry attracted more than 150 delegates from an even wider range of disciplines. The meeting took place against a background in which the need for Europe to coordinate more closely on health policy is increasingly recognised, and just as Slovenia has signalled its intention to make health a priority of its presidency to aid Europe in its recovery from the disruption of the coronavirus pandemic.

Coordination and collaboration were themes that received strong endorsement during the conference, relating to winning an informed acceptance among regulators of the merits of RWE, or to maximising EU-level learnings from different national programmes on screening, or pursuing interoperability of infrastructure or data or procedures, or to profiting from the synergies of public-private partnerships. So too was the concept of learning from the pandemic experience, and the agility and acceleration seen in data-sharing and in regulatory processes. A learning healthcare system also emerged as a lei motif in the discussions, both as a paradigm for intelligently leveraging new knowledge and best practices, and as a light-touch alternative to an imposed and potential inflexible regulatory framework. Appropriate communication was constantly referenced, in relation to developing health literacy or to training of healthcare professionals or to boosting screening recruitment among hard-

to-reach populations or to improving the links between the healthcare community and senior policymakers. And amid the determined optimism about the potential for improvements, unmistakable notes of disappointment were repeatedly sounded at failures to take advantage of the opportunities. A flavour of the discussions is offered in the following account, and a summary of recommendations appears at the end.

Dr. Denis Horgan, PhD, LLM, MSc, BCL
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Session 1: Generating alignment in the regulation of Personalized Medicine: Real World Evidence and Citizen Trust

“Trust is central to the entire precision medicine process

Denis Horgan, *Executive Director, European Alliance for Personalised Medicine*, outlined the underlying dilemma in exploiting the new possibilities opened up by real world evidence (RWE) and new diagnostic options. The concept of trust is central to the entire precision medicine process, from the collection and analysis of data right through to the provision of health and medical care, and each actor or process in the system must be trustworthy for what it aims to deliver. “RWE has generated a lot of evidence of innovation, but we need to work out how to bring this evidence into use in society,” he said. The development of trust has taken different pathways in different contexts and countries, and promoting collaboration among the many actors is therefore a necessary precondition to seeing precision medicine deliver on its full potential, he commented.

The new public prominence that the pandemic has given to health data and to diagnosis may offer useful opportunities for increasing citizens’ understanding and appreciation of the value of data and its role in healthcare. The upcoming European health data space offers further possibilities, as do some of the projects envisaged in the European Beating Cancer Plan and other current EU initiatives. Earlier identification of disease to permit better treatment is now more widely perceived as being dependent on integrating novel medical diagnostics into healthcare systems – which is a question not just of technology but of resources and resource allocation. And the common experience of the pandemic has drawn attention to the divergent responses of different countries, and demonstrated that deriving benefit from innovation for all citizens of Europe will need a new level of agreement across different healthcare systems, which in turn requires a new balance among the different stakeholders – patients, researchers, medical societies, payers, industry, regulators and policymakers – and an appropriate policy framework to

support this evolution.

This session explored the issues of innovation and trust from the distinct perspectives of regulation, public health, genomics, rare diseases, and distinct countries, and looked at potential solutions, including the role of public private cooperation.

Ralf Herold, *Senior scientific officer, Task Force Regulatory Science and Innovation, Research and Innovation at the European Medicines Agency*, provided a regulatory perspective. Speaking in a personal capacity, he observed that real-world evidence is no more or no less acceptable than any other source of data, and could help address specific questions after a benefit risk assessment has been conducted, and help to focus on real patient outcomes. But because regulators have little experience so far of its use, RWE would need to be qualified as a new methodology, with an evaluation "like a new drug, prospectively, with well controlled studies and according to a plan that has been discussed by stakeholders. " To realise its full benefits, "we need to think of developing a learning healthcare system with all stakeholders, to optimize clinical practice, to invest in processes and data infrastructure, and in building up methodologies prospectively," he said, insisting that regulators alone cannot do this, and that it needs multi-stakeholder collaboration and understanding and trust within society. He also pointed out that regulators' powers do not extend beyond pharmaceutical companies and medicine developers: "We do not regulate health care." And he offered a note of caution on requests for the imposition of a regulatory framework. "Rather, I would suggest reflecting on the overarching model of a learning healthcare system where all stakeholders can engage and make their inputs".

From a public health perspective, there was also strong support expressed for the potential merits of real world evidence. **Daria Julkowska**, *Assistant Director of the Thematic Institute of Genetics, Genomics & Bioinformatics at INSERM, who is also EJP RD Coordinator and a member of the IRDiRC Scientific Secretariat*, said RWE could not only help provide evidence of the potential benefits or risk of a medical product, but was also valuable in minimizing hurdles in collection of sufficient evidence in the rare diseases context. It could also contribute to research, regulatory approval and decision making on pricing and reimbursement. But she stressed the central importance of the citizen and the patient, and how they see their own data that lies at the heart of RWE. For patients to share their data requires trust and confidence about reciprocal benefits to patients and society, and about control against data misuse. These factors must be taken into account in the building of healthcare data systems – not just robust national systems, but in their connections and interoperability at European and international level. National health data hubs can be linked with mechanisms providing secured

access where researchers can work within platforms without removing any data – along lines now envisaged for federated access at European scale. Success will depend, suggested Julkowska, on cooperation among all the stakeholders, including with the private sector in dialogue. For her, a clear regulatory framework is essential in exploiting RWE, so as to establish a common understanding and common standards, and to ensure trust and acceptance across all stakeholders, at the European and the national level.

Giving a German perspective, **Jan Korbel**, *Head of Data Science at the European Molecular Biology Laboratory in Heidelberg* noted that the rapid growth in biomedical data makes it vital to find trusted solutions for the data sharing, covering quality standards and providing an ethical legal framework for data access. Several national initiatives in Europe have established large scale resources in omics research, in ways that can create a better evidence framework in precision medicine. But, he said, Germany's infrastructure remains fragmented, without an integrated resource to overcome data silos and research bottlenecks, or to take advantage of innovations in machine learning and artificial intelligence. Even on consent, Germany's federal constitution is complicating the search for a single solution. Some progress has been registered in setting up the German Human Genome Phenome Archive, which aims to establish a national infrastructure for human omics data, providing a platform for long term d ata archival and connected to major omics centres in Germany and interfacing with international genome initiatives. And he cited the example of EMBL's unified approach to data science, embracing the entire biodata lifecycle from data generation and analysis methods to hypothesis, interpretation, data reuse, publication and archiving. He depicted a Europe that would enable genomic medicine, with secondary use of clinical omics data in research, using biological discovery and replication of findings to show validity, and operating in a federated infrastructure that integrates genome research and healthcare data.

Speaking of public private cooperation from her industry standpoint, **Martina von Meyenn**, *Global Medical Chapter Lead for Real World Evidence at Roche*, considered it insufficient to rely on data from just one institution or one particular market. "We're looking at a scalability here that is currently difficult, and compounded by lack of interoperability, and by access largely to data that is aggregated, and only rarely individual patient level data – a combination that makes insights very challenging." For her the year of Covid demonstrated that with the right sense of urgency, data can be generated and shared, and efforts can be quickly aligned across borders. The pandemic also highlighted the importance of a digital infrastructure to enable rapid decision making. What is needed, she said, is to unlock fuller

access to patient level data - something that the healthcare community, and notably patients, collectively need to drive. An appropriate regulatory framework could then define clinically meaningful data points that actually impact on care – with valuable outcomes for patients and for informed research and development. We require clear evidence frameworks that guide and appreciate the current learning healthcare ecosystem until RWD is able to live up to its promise."

For **Mark Caulfield**, providing a genomics perspective as *Chief Scientist at Genomics England*, "Above all, making use of genomics in health demands creating and maintaining trust with public and patients." His recommendations were for continued research into whole genomes, linked with life-course clinical data in trusted research environments. Echoing calls for federated data access, he saw data sources as 'reading libraries' rather than 'lending libraries', with patients deriving benefit from global research access. Using the example of the 100,000 genomes project to demonstrate the possibilities for scaling up genome sequencing for healthcare gain, he reported on its ability to deliver a 25% uplift in diagnostic yield across areas of unmet diagnostic need. "The governing paradigm is systematic engagement of public and patients within an ongoing dialogue," he pointed out, suggesting that this might provide a model for the future for Europe. However, any overarching approach must aim to gain that trust in a regional and national basis, to account for local differences. "It is harder to secure it in a pan European way." This sort of approach needs light touch regulation, reliant more on voluntary agreements than imposed rules, he observed.

A patient perspective was provided by **Birgit Bauer**, *a journalist* who suffers from Multiple Sclerosis. She said that patients and citizens do not have high levels of information about personalized medicine, and tend to express concerns over its cost and the data sharing it depends on. "Innovation needs motivation and trust. This needs information. And empowerment. We have to talk with the patients and public at eye level", she urged. "Do we know how much patients and citizens know, and did we ask them what they need to know, and are we communicating with them in their language to provide trustworthy information?" Bauer questioned. "If people don't have trust they will not accept novel approaches and innovation will be hampered," she concluded.

Session 2: Beating Prostate Cancer and Lung Cancer – The Role of the EU Beating Cancer Plan: Updating EU Council Conclusions on Screening

“It’s clearly more than good enough

Horgan reminded the audience of the long history of European debate over the implementation of prostate and lung cancer screening, in the scientific community and with politicians at the national and European level. To move the discussions along, EAPM has recently focused attention on widened use of diagnostics and related themes of access, with particular attention to the potential of screening for reducing mortality from lung and prostate cancer. Now the question is whether policymakers at European level will support this – and the approach to be adopted by Slovenia, which developed the first council conclusions on cancer back in 2008 and led the way towards screening guidelines for breast and colorectal cancer. The needs are not only for an assessment of the potential economic impact of implementation, but also for guidelines to assure effective and safe implementation of lung cancer screening in Europe, he said. The session reviewed country perspectives and how to bring innovation into healthcare systems.

Giorgio Scagliotti, *Professor of Oncology at the University of Torino*, insisted that the time for European action on lung cancer screening is now, given the high costs of the disease and the persistent low survival rates, despite the improvements resulting from targeted therapies and immunotherapy. His work with academic and industrial partners in the Lung Ambition Alliance was making it possible to identify needs more precisely, and the depth of resources was helping to amplify impact, he said. To tackle the challenges arising from late presentation, earlier diagnosis could cut mortality rates – but the necessary screening protocols have not been universally incorporated into lung cancer care. Despite Italy’s multidisciplinary lung cancer care pathways, there are continuing delays in identifying high-risk individuals, and efforts to raise awareness of the merits of screening have not yet been successful among national politicians and primary care physicians. He urged that lessons of risk stratification should be built into the design of future lung cancer screening programs, including high-quality multidisciplinary lung cancer care pathways, reliable means of identifying

people at highest risk, and securing attendance, particularly among vulnerable groups. Other key factors are recognising the essential role of primary care professionals, building cancer screening into overall prevention messages and personalized screening to minimize potential harms from screening.

Step-wise implementation of lung cancer screening could bring immediate benefits in prevention of 22,000 lung cancer deaths each year in Europe, said **Harry De Koning**, *Professor of Public Health & Screening Evaluation at Erasmus Medical School in the Netherlands*. A risk-stratified patient-centred approach in recruitment and in screening intervals can reduce the burden for citizens and lead to sustainable programmes for governments and health care, he contended, citing the 6-country 4IN The Lung Run project, which he described as the first large-scale multi-centered implementation trial on volume computerised tomography lung cancer screening, aiming to develop and investigate the most optimally personalized ("patient-centered") CT lung cancer screening programme for high-risk populations. Refining eligibility criteria on a risk basis while ensuring safety could make major savings in the costs of screening programmes. Volume CT scans may be the most effective approach (apart from smoking cessation), and is now probably the most personalised innovative, trustworthy and evidence-based preventive measure possible for European citizens, he said. A patient-centred and personalised approach in recruitment will be illustrative for many other personalised screening and prevention strategies in the near future (including biomarker initiatives), he suggested.

Sebastian Schmidt *of Siemens Healthcare* was unequivocal in his view that lung cancer screening is a proven way to reduce cancer mortality. In addition, technology is ready for it to be implemented immediately, he said, offering reassurance on the safety of the radiation dose, the low level of false positives, and the "very favorable incremental cost". There is now some momentum among a few EU member states to move ahead, with regional lung screening programmes in UK, Slovakia and Poland, a national programme in Croatia, a pilot programme in Hungary, and a recommendation for a programme expected imminently in Germany. But it needs an official recommendation in an updated guideline from the EU if there is to be real impact, pointing to the Europe Beating Cancer plan's aim of an update to the decades-old cancer screening recommendations in 2022. "The position of the EU Commission on lung cancer screening is an important sign whether they take the cancer plan seriously or not," he said. Concerns over the safety and efficiency of the current methods is mis-placed, he argued, urging immediate action to deliver updated EU guidance, and rapid take-up by all member states. "It's clearly more than good enough," he said.

Witold Rzyman *of the Department of Thoracic Surgery in the Medical University of Gdansk* recounted progress with the first phase of the lung cancer screening program in Poland, and expectations following recent health ministry promises for an official programme starting in 2023. Improvements had been made already in the methods of reaching the target population, "which has a key role in a population program": some success was achieved with national level leaflets distributed in family doctor centres and through advertisements in newspapers and on TV and radio, but a crucial element had been the follow-up with direct visits of members of screening teams to the family doctor centres. The initial level engagement from family doctors, and from radiologists, had, however, been low, and this remains one of the practical difficulties to be overcome.

Richard Booton, *Clinical Senior Lecturer and Honorary Consultant Respiratory Physician at the University of Manchester and North West Lung Centre, Wythenshawe Hospital Manchester*, noted the importance of involving primary care in the community-based screening program he has been leading in the UK. He underlined that success requires a multi-step process. "Screening is not just a matter of conducting a scan and reporting it. It is the whole journey, from how we engage with primary care, how we get their patients into a program, scan them, report them, diagnose them, operate on them and then follow them up and look at the quality of what we do," he said. This requires not only working closely with family doctors, but also providing the necessary infrastructure, with a sufficient workforce of pulmonologists, radiologists, pathologists and other workers – and shortages are 'the element in the room' in managing the outflow of a screening program in a quality-assured way, he added.

Lung cancer risk should become an eligibility criteria in reaching the right population with screening, Booton urged, since these target populations are typically in areas of social deprivation, economically disadvantaged and with high levels of health inequality, and often hard to reach with health messages. Methods used by his teams to overcome these barriers included adopting a terminology of 'lung health checks' rather than 'cancer screening', education and engagement at the community level, and locating pop-up screening facilities in local football grounds and supermarket car parks, to avoid requiring travel to a hospital. More investment is still needed in infrastructure to keep pace with the development of technology in imaging and diagnostics, but it can be highly cost effective as long as there is planning for follow-up on higher diagnosis levels, and "there's a real commitment and political drive to get this done in the UK."

Discussion among panellists focused on the need to derive synergy through collaboration amongst the current national screening programs and pilots, with the Netherlands healthy ministry recently approving an implementation

trial, Italy starting work across 13 centers , and the UK expanding its sites for community screening. Collaboration could provide a bottom-up approach to complement pressure exerted at a more political European level for an update to guidance. But the beneficial influence of EU guidance was repeatedly remarked on as an important driver of national activity, reinforcing peer comparison and promoting the use of best practices. It could reinforce national initiatives – such as a consensus statement on lung cancer screening recently reached among all stakeholders in Poland as a policy input. It would also open up access to EU funding, vital for many smaller member states. As Horgan summarised the situation, there is discernible movement in EU policymaking circles towards updating the cancer screening guidance, and efforts are underway to obtain stakeholder input – but there is at present still no guarantee that an update will appear.

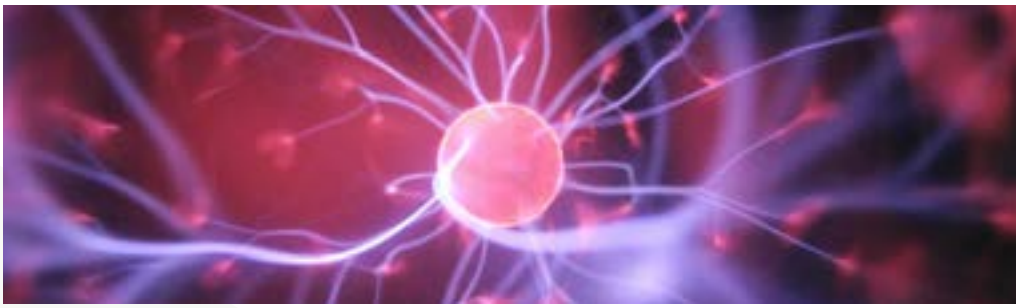
Hendrik Van Poppel, *Adjunct Secretary General of the European Association of Urology set the scene on prostate cancer*, insisting that early detection of prostate cancer should be a priority for Europe's Beating Cancer plan. He outlined the gravity of the threat from this leading killer of men in Europe, recalling the capacity of screening to decrease mortality by more than 50 % over 20 years, even with a recognised cost of over diagnosis and overtreatment. But he cautioned that it has to be right kind of screening: opportunistic, wild, non-organized screening does not decrease mortality and does not avoid over diagnosis and overtreatment. Hower, the exaggerated propaganda from opponents of PSA testing had led to late diagnoses and increased mortality, and he argued for efficient early detection through risk stratification. Correct use of PSA testing should focus on well-informed men from the age of 45-50 until life expectancy decreased below ten years, and deploy risk calculators, restriking biopsy to those at risk of significant cancer, and active treatment to those at risk of dying. Managing low and intermediate risk with active surveillance would decrease the costs of prostate cancer, decrease mortality and improve quality of life, he argued. **André Deschamps**, *chairman of Europa Uomo*, reinforced the message about quality of life, pointing to outcome studies showing chemotherapy-induced fatigue in more than a third of treated patients, and discomfort, insomnia, depression and anxiety in men treated with radiotherapy and androgen deprivation therapy. "Early detection is the key," he concluded.

Peter Albers, *Chairman of the Department of Urology of Düsseldorf University Hospital*, reported on the PROBASE trial, which is studying risk-adapted screening in prostate cancer on a "baseline" PSA value in young men. The findings urge caution over indiscriminate screening, which – the study suggests - saves no lives and means that around 20 men will be diagnosed with cancers that would not have caused any harm. But with individualised early detection, in age-adapted risk groups with hereditary

risk and through risk calculation and a combination of risk calculators, better outcomes can be achieved. This prospective multicentre randomized trial revealed in a first screening round that prevalence of prostate cancers at age 45 is very low (0.19%), prevalence of unfavourable prostate cancers is even lower (0.05%), and the prevalence of DRE - detected PCA is extremely low. Its initial conclusion is that risk stratification (using MRI) avoids more than 50% of biopsies and radical surgery interventions. Population-based screening with PSA alone is obsolete, said Albers. But risk-adapted screening is possible and effective, and more than 50% of biopsies and over-treatment can be avoided. Again discussion focused on how to ensure that these issues receive adequate attention in the European Beating Cancer plan, and how to take advantage of new technologies and approaches. “The key issue how to convince policymakers to improve and to support the implementation of these screening propositions,” said Horgan. But delivery of the message on prostate cancer screening requires careful presentation, it was agreed. While simple population-based screening with PSA alone is agreed to be obsolete among experts, that could be misinterpreted by politicians as an indication that prostate screening should be abandoned.

Session 3: Availability, Accessibility & Affordability: Understanding Ownership and Privacy of Genetic Data

“Health literacy is a neglected public health challenge



This session reflected on how the power of digitalized health data and the growing public engagement with personal choices have created new appetites for information about individuals’ data and how they can benefit from its exploitation. For this to provide a universal benefit, it was argued that all stakeholders need the digital literacy and capacity to value, contribute, use and benefit from health data responsibly, ethically and sustainably. The coronavirus crisis has provided an opportunity to stimulate societal participation through citizens’ involvement and broad stakeholder engagement by engaging society in a co-management strategy where citizens play a proactive role. At the same time, effective information provision to the public – about the pandemic and about the uses their data can be put to - can also benefit frontline health professionals and policy makers and help in promptly communicating crucial findings to the international scientific community. This can contribute to building a scientifically literate patient community and supporting public involvement in science and technological development, and provide a more constructive approach to the conflicts that surround the issue of data ownership and use.

Tanja Spanic, *President of Europa Donna*, recounted her organisation’s efforts to develop education – “education of patient advocates all around Europe not just to listen, but well-trained patient representatives who are familiar with research and scientific aspects and the procedures of policy making.” Education is crucial, she argued, to pursue Europa Donna’s priorities of the implementation of breast cancer registries, prevention and survivorship, and the unmet needs of women living with metastatic breast cancer. Collaboration is needed to advance this agenda, but that is easier for patient associations to achieve with healthcare professionals and policymakers in a smaller country such as her native Slovenia, it is more of a challenge in decision-making processes at European level. She lamented the

failure to follow through on important EU promises – such as recent supportive European Parliament written declarations, which "unfortunately are still not a reality in many EU countries". Writing guidelines and recommendations about European standards doesn't help if they are not applied at the national level, she remarked, adding that the same is true with patient representation. "Just having it on the agenda is not always very efficient. In some cases we get the feeling that on the EU level and even at national level a random patient representative is invited just to put a tick in the box, without caring about whether it will bring any input."

Kristine Sorensen *of the Global Health Literacy Academy* described health literacy as "a neglected public health challenge in Europe that has a high impact on the effectiveness and quality of care." In her calculations, one in three people face health literacy challenges - difficulties in finding information and understanding what is provided to them and also then to judge and participate in shared decision-making and finally apply the advice given or the decisions taken. Without the knowledge and motivation and competence to access and understand and appraise and apply information regarding health care and prevention and promotion, it is difficult for people to take decisions in everyday life to improve their quality of life. She urged a shift towards clear language and timely communication, in a spirit of dialogue that respects and accommodates people's distinct situations and enables a fulfilling life. But this, she argued, requires a transformation at all levels - among healthcare staff and managers, and among decision-makers and politicians.

For **Natacha Bolaños**, *Global Alliances Manager of the Lymphoma Coalition*, the central issue is for patients is to accelerate society's ability to translate research into better healthcare. She counselled against viewing patient data through the prism of regulation, and urged exploration of different partnerships that use data, analytics and real life insights to create a care experience that more precisely meets the needs of patients. "Rather than speak of data ownership, of the data belonging to the patient, it is more constructive to see the data as about the patient - and equally about families, communities, diseases, and health systems. Flexible models can then reconnect patients and communities with their clinical data. Conscious of the role of genetics to better understand diagnosis, prognosis and treatments of lymphoma, we put the focus on building the genetic literacy capacity of our community," she said. Anecdotal evidence from her member organizations indicates that testing is not widely available, especially the most sophisticated genetic tests. For patients to have the best diagnosis and prognosis and to enable their health care team to recommend the most appropriate treatment, access to testing must be increased.

From an industry perspective, **Emanuele Ostuni**, *Head of Cell and Gene Therapy at Novartis Oncology Region Europe*, offered ideas on how to bring innovaton into healthcare systems, and stressed the importance of collaborating with stakeholders to foster an environment conducive to dialogue and to effecting change that benefits patients and health systems. This could mean leveraging some of the learnings from the pandemic – such as rapid reorganisation of health service components or accelerated development and acquisition of medicines – or capitalising on the evolving attitudes towards data to gain the trust of citizens on the role of data sharing to realize the potential of personalized medicine. Data-driven healthcare that is fit for the 21st century requires everybody to break out of the default ways of working, starting with health literacy, he said. Standing in the way is the hesitation of systems to respond to the opportunities, but "If we don't collaborate, we don't win," he said.

Stefan Gijssels, *Chair of the Belgian Patient Expert Center*, provided a harrowing personal account of prolonged misdiagnosis of his metastatic colorectal cancer as the rationale for every country to make progress and overcome uneven performance in early cancer diagnosis. There is a lack of a systems approach, he said, and of systematic health policies linking patient, doctor and regulatory and reimbursement authorities. He emphasised the need for up-to-date data: "In the European Commission's information system on cancer, the latest survival data are from 2014. How can you base policy on that? How is it possible to provide 7-year-old data?" And he argued that patient organisations are seriously undervalued in healthcare systems, and can often guide patients and give them comfort and contact with other patients with a deep understanding that cannot always be found in the medical establishment. He welcomed the idea of European initiatives to provide recommendations and guidelines and plans, but "If we don't get them into the system, if they don't become a reality, it really doesn't help."

Discussion among panellists ranged across how much information to give a patient after diagnosis (a step-by-step approach at the speed dictated by the patient was the tentative consensus), and how far the pandemic had been a change factor in demonstrating how slow siloed healthcare systems had traditionally been in adapting to innovation and how fast they could change as politicians recognised the new urgency and the wider healthcare community adopted new levels of collaboration and public-private partnership. It also explored how mindsets within healthcare systems might be shifted to overcome silos and to recognise the need for multi-year budgeting on healthcare programmes that by their nature require time to deliver results.

Session 4: Securing Patient Access to Advanced Molecular Diagnostics

> **Comprehensive genomic profiling for all advanced non-small cell lung cancer because it works**

This session reviewed how different countries and regions are responding to the increased molecular understanding that could transform the prospects for health care, and to the new pathways for molecular diagnostics to a shift in healthcare strategy. Molecular testing has informed some major preventative public health strategies, such as the significant reduction in cancer mortality, and could mark the threshold of a new future in which emphasis will shift away from treating illness and move toward maintaining the health of the individual. Early diagnosis and personalised healthcare will have a central part to play in this scenario, particularly in the cancer arena – but only if opportunities are seized.

Lars Bullinger MD, *Professor of Hematology and Oncology, Medical Director of the Department of Hematology, Oncology and Tumorimmunology at Charité University Medicine Berlin*, provided a view of a multistakeholder approach to bring next generation sequencing into healthcare systems. His account of the Harmony Alliance – a European-level public-private partnership for big data in haematology – suggested how Big Data analytics could accelerate better and faster treatment for blood-cancer patients. Its platform will soon contain over 100,000 datasets bringing together data from all stakeholder groups, public and private, to help identify and define outcomes relevant to patients. It aims to speed up drug development, access pathways, and bench-to-bedside process, and to enable data driven decisions for payers and regulators, based on artificial Intelligence techniques. Harmony is an attempt to ensure that all valid datasets generated, including from commercial tests, are stored centrally and can be made publicly available to generate further benefit. “There is a need to work together so that valuable raw data are not lost,” said Bullinger. It could also have a local benefit in that reimbursement of diagnostics is still

subject to debate in Germany over accreditation of diagnostic approaches, he pointed out.

According to **Piotr Rutkowski**, *Professor of Surgical Oncology at the Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw*, NGS in oncology is routine practice in comprehensive cancer centres in Poland. He depicted laboratories integrated into a pathomorphological and molecular diagnostic unit to ensure close cooperation between surgeon, pathologist, molecular biologist and clinical oncologist. But there is a need for more such centres to increase access and availability of personalised medicine, and alternatives for financing genomic diagnostics – and overcoming the challenge that reimbursement represents - have been identified by advocates of personalised medicine. They include simplifying the financing of genomic testing and developing greater consistency over decision-making, as well as allowing the pharmaceutical industry to help fund genomic testing. Arrangements should be made, however, to ensure that raw data from commercial tests is also made available for storage. "We really have to work together," he said.

For **John Longshore**, *Head of Scientific Affairs at AstraZeneca*, access to NGS is critical to enable selection of optimal therapy for every cancer patient – but at present practical challenges for its implementation have led to variation in access to multi-biomarker testing across Europe, with high availability in Germany and Scandinavia, low in much of central and eastern Europe, and significant regional variations in Italy and Spain. Lessons must be learned from the experience of countries taking steps to support access to the technology, he said, suggesting that Belgium and France provide interesting models of reimbursement and investment in infrastructure. NGS has an increasing number of applications in oncology, but challenges remain to improve patient access, he said. To drive improvements across Europe in cancer care and outcomes, particularly as the number of targeted treatments increases, "We need a collaborative environment and input from stakeholders' different perspectives and expertise."

From beyond the EU, the session provided examples of best practice in Canada and Israel. **Étienne Richer, PhD**, *Associate Scientific Director at the CIHR Institute of Genetics in Canada*, noted that the falling cost of sequencing a human genome now offered the prospect of 60 million within five years, by 2026, opening up new prospects of integrated this wealth of data into clinical care. This made it all the more important to maximize the value for human health by common sets of standards to ensure interoperability and effective management of access to data that addresses ethical and legal aspects, as well as managing the necessary data infrastructure and computing power. Canada has established a federal approach to combining its provincial data, providing a single entry-point for

all Canadian genomes (clinical and research), and spearheading the adoption and use of a pan-Canadian genomic consent. Responding to the historical neglect of its indigenous population, it has also initiated a specific program to reduce the genomic divide and potential bias caused by a paucity of genomes other than those of European descent. His view is of genomics in a true learning healthcare system, in which a critical mass of genomes will help develop and train algorithms using AI and computational biology.

Gilad W. Vainer, MD PhD, *of the Onco-proteomics lab and Head of Department of Pathology at Hadassah Hebrew-University Medical Center in Jerusalem*, reflected on early use of advanced diagnostics. Since the start of 2020, Israel has provided "comprehensive genomic profiling CGP to all advanced NSCLC – because it works", he said, with results in longer overall survival and better quality of life. This nation-wide early adoption of comprehensive molecular profiling was medically needed and is proving economically efficient, he added. CGP may result in savings, since the additional costs might be offset by healthcare system cost-effectiveness. It holds out the prospect of eliminating unnecessary molecular tests and biopsies and optimizing approved targeted and immuno-oncology therapy utilization, and reducing cytotoxic chemotherapy use, hospitalisations and emergency department visits. In addition, pricing parity with single gene testing is becoming a reality, with CGP not costing much more than a handful of old generation tests. "We pay the same as for four and we get hundreds for free."

Discussion among panellists focused on the prospects of further cost reductions in technology and equipment facilitating even wider use of NGS, and on the further challenges this will bring for integration into health systems. There will be a need for regulatory agencies and reimbursement payers to adapt, and a wider range of questions of an ethical nature will be raised about management of generalised genome information and its impact on individuals. A concomitant need for training for wise use of this wider information was also emphasised. Other opportunities for the use of NGS beyond diagnosis and screening may emerge, such as monitoring patients over the course of their therapy, using markers that can measure residual disease or detect resistance mechanisms in patients on maintenance therapy. But the existence of another type of resistance – within the medical establishment – was also commented on: how soon will oncologists be ready to accept evidence of progression of a tumour prior to the classic radiographic evidence. "We have quite a bit of evidence generation to do," commented one panellist.

Conclusions

The potential of personalised healthcare has been increasingly recognised over the last decade, and its scope is almost unlimited for exploiting new understanding of medicine through innovative technologies. Despite all the recognised possibilities that personal healthcare can offer, it has not yet delivered the benefits it could, largely because of hesitation within health-care systems to take up the opportunities. Now, as the recovery from COVID 19 gets underway, with novel technologies widening the opportunities still further, and with complex changes taking place in European society and governance, the time is right to review how change can be leveraged to develop a policy framework that will permit maximisation of the potential of personalised healthcare.

…on national and European alignment

- Coordinating, building and linking alliances
- Developing a common understanding of the role of RWE
- Promoting interoperability of data and infrastructure
- Maximising the use of EU guidance and initiatives aimed at collaboration - and ensuring national implementation
- Profiting from the lessons of the coronavirus pandemic
- Overcoming fragmentation and variations in approach while remaining sensitive to accept regional and cultural perceptions and sensitivities
- Staging a cancer conference under the Slovenian presidency to discuss common key issues

…on integrating advanced and comprehensive molecular diagnostic tests into care:

- Establishing (and co-financing) networks of accredited centres
- Establishing networks of oncological genetic clinics
- Establishing guidelines / standards according to which pathologists will commission tests for specific types of cancer, matched with a guaranteed benefits package
- Raising physician awareness of the benefits of multi-biomarker testing and developing guidelines for the stage of neoplastic disease, diagnostics and therapy, at which molecular diagnostic tests should be performed
- Providing for upfront capital investment in infrastructure
- Generating frameworks for demonstrating the value of multi-biomarker testing

Conclusions

...on promoting trust in a learning healthcare system

- Maximising secure access to and controlled use of patient level data
- Leveraging new knowledge and best practices
- Refining risk stratification
- Balancing the multiple interests of multiple stakeholders
- Recruiting, training and sustaining a skilled workforce
- Promoting adaptations among regulators and payers
- Communicating clearly and sensitively among all stakeholders, including healthcare professionals, hard-to-reach populations or senior policymakers.
- Benefiting from the expertise of patients associations

Next steps

- Publication on RWE and Public Trust, Q3/4, 2021
- Publication on NGS integration in healthcare systems
- Event planned for **Sept 17th, 2021** entitled "The need for change – and how to make it happen: Defining the healthcare ecosystem to determine value".
- Event in November during Personalised Medicine Month, **Nov 4th, 2021**
- Various policy engagement Q3/Q4, 2021

From the discussions at this conference, a number of recommendations emerged summarised in the following (non-exclusive) list...

For more information

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About EAPM
The European Alliance for Personalised Medicine brings together Europe's leading healthcare experts and patient advocates to improve patient care by accelerating the development, delivery and uptake of personalised medicine and diagnostics.