

4th Annual Presidency Conference

Bibliothèque Solvay, Brussels

5-6 April, 2016



**European Alliance for
Personalised Medicine**

***'Taking Stock:
Where we are now and the
necessary next steps'***

Conference report

Put KNOWLEDGE together!

Now we have developed all these personal medicines...
What shall we do with it?

We have a bunch of very personal sick people over here...



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Taking stock: Where we are now and the necessary next steps

Foreword

The EAPM forum of 5-6 April 2016 was deliberately timed to take stock of where stakeholders should go next relating to the implementation of the Council conclusions on personalised medicine that was supported by all health ministers during the Luxembourg Presidency of the EU.

The aim was, and remains, to support the Member States, the European Commission, the European Parliament, and how the experts can support them in shaping an environment for personalised medicine.

Although it is happening slowly, genome sequencing is steadily being introduced into clinical care. Improving diagnosis and care of patients with rare genetic diseases is having a major impact on cancer diagnosis and therapies.

Test results must be delivered more quickly and data must be presented so as to allow relative simple decision-making by physicians.

Meanwhile, adapting sequencing to potentially lifesaving clinical work needs much higher levels of sensitivity and specificity than is currently required for research.

This area of science is fast developing and Europe's health systems needs to adapt quickly to allow health genomics to benefit patients. And the cost of genome sequencing has fallen substantially and this is clearly one area that can support personalised medicine.

The event was also an educational exercise built on the vision of mighty stakeholders supporting the development of the necessary frameworks.

One aim of the conference was to shape the landscape for the successful implementation of genomics. The meeting was not designed to find all the answers but to begin working and engaging with the necessary stakeholders.

Executive summary

Catching up with personalised medicine

Personalised medicine has never been more in the public eye than it is now, especially given US President Barack Obama's initiative on precision medicine, and the conference reflected this.

The Americans are moving quickly and have come to some obvious conclusions including that health equals wealth and that investment in research and innovation, alongside laws and

rules that are fit-for-purpose and reflect the swiftly changing world of medicine, are vital.

Europe needs to grasp these points at every level – not just the vision of an EU that creates a competitive environment that attracts investment, but also for the benefit of the millions of potential patients spread across 28 Member States.

At the conference, high-level speakers and attendees came from a wide range of stakeholder groups including patients, healthcare professionals, academics, industry representatives, politicians and legislators, the media and more.

The Luxembourg Presidency published its Council Conclusions on personalised medicine in December 2015. These featured heavily in the Alliance's conference.

Among other things, the Council document concluded that it is necessary to formulate a patient-centred strategy involving EU decision makers and regulators in the arena of public health, to enable the EU and Member States to contribute to integrating personalised medicine into clinical practice while enabling much-greater access for patients.

It also became clear that new approaches are needed in the following areas:

Research

In 2013, EAPM launched its **Integrated Research Policy Roadmap** to Embed Personalised Medicine in European Health Systems.

European researchers have been at the forefront of major scientific healthcare discoveries in areas such as cancer, cardiovascular disease, genetic disorders, and infectious disease.

The undeniable challenge is how best to translate this knowledge and expertise into medical advances that improve outcomes and enhance well-being for European patients.

The conference recognised that translational research is a key enabler of the European Union research effort and represents the conduit through which discovery science can be converted into new diagnostics, treatments, products and approaches that benefit European citizens and society.

All healthcare clinicians and patients are calling for a more personalised approach aimed as much at preventing disease as it is at tailoring treatment once it's there.

It quite clearly cannot be achieved without research and, of course, its effective translation.

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Regulation

The development of personalised medicine will require regulatory bodies to adopt new approaches to product approval.

There is no denying that science has led to major advances in the understanding of the role of genomics in diseases, in the discovery of biomarkers, in the development of new statistical methods and in the invention of dynamic tools for collecting real-world effectiveness and safety data.

The Brussels-based Alliance has worked hard to bring stakeholders together to find a way through the legislative labyrinth that surrounds these issues.

It is time that clear, harmonised rules are applied across the European Union, in all relevant sectors, imposing more rigorous review, but with standards of clinical evidence that balance the risk-benefit profile with the degree of innovation.

Incentives

New methods are required for calculating the benefit and risk factors when it comes to medicines.

Regulatory bodies, as well as payers, now need to approve drugs (and biomarkers) on the grounds of effectiveness and societal benefit.

Unfortunately, as it stands, there are not enough incentives for investing in developing of diagnostics, due to costly innovation - which includes generating clinical evidence.

Medicines and diagnostics work hand-in-hand. Without coordinated timing regarding reimbursement and approval of a companion diagnostic, this will mean potentially life-threatening delays for patient access.

Making better use of data

The Luxembourg Council Conclusions, which this conference reflected upon and reacted to, stated that, when it comes to Big Data, there are hurdles to overcome.

These include availability and for whom, security, safety and privacy.

There is clearly a need to bring stakeholders together to discuss the challenges and actions that can support and utilise health data for the benefit of patients and society.

In the meantime, taking urology as an example, there is a desperate need for urologists to have the ability to predict which



patient has a localised cancer that is going to metastasize and cause suffering and death, and which patient has a cancer that is destined to stay in the patient's prostate for the remainder of life.

The use of Big Data is the best method in this and many other cases.

Education

Personalised medicine is now at the centre of most, if not all, aspects of patient care. It is not limited to rare diseases or cancer, but spans all medical specialties. This exciting new way of treating patients is, however, based on specific concepts or biological pathways in a field which is continuously moving.

This means that all healthcare professionals (HCPs) in close contact with patients or their families need to possess a solid knowledge of the current aspects of personalised medicine and its latest breakthroughs, in order to better understand patients' concerns.

EAPM is firmly of the belief that HCPs cannot be expected to adapt to new ways of approaching patients and coping with new technology unless they are suitably trained.

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These HCPs are being asked to move beyond traditional reactive medicine towards proactive healthcare, interpreting information from across sources that blur the traditional boundaries of individual specialties.

Collaboration

To fulfil the promise of personalised medicine, greater collaboration is needed between all stakeholders, including for example pharmaceutical and diagnostic manufacturers.

Cross- and inter-disciplinary cooperation must see stakeholders in all sectors ditch the 'silo mentality' and work quickly towards, for example, deeper understanding of the differing development timelines and life-cycles, regulatory and reimbursement pathways, as well as markets and customers.



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Plenary Session I: Taking Stock – The Member States' Perspective, Commission and Stakeholder Perspectives

The conference brought together government representatives, health-care planners, scientists, industry players, members of parliament to discuss personalised medicine to improve citizens' quality of life and produce better patient outcomes.

In opening the event, Cristian Silviu Buşoi MEP (EPP, Romania) said that over the years, he and colleagues from the European Parliament Environment and Health Committee had focused their activity in the European Parliament to bring an added value to the European public health sector by contributing to finding solutions for a healthier Europe, which had meant fighting for patients to access the best possible treatment available and at the same time spending much less time in hospitals undergoing often expensive treatment regimes.

According to Buşoi, there is still unequal access to health services at EU level so we need to make sure that all patients have equal access to quality healthcare services at affordable prices.

Government representatives, academia, researchers, patient representatives, health-care planners, scientists, industry representatives, members of parliament, in attendance at the EAPM conference, were set to discuss how to put personalised medicine forward in an innovative way to improve citizens' quality of life and produce better patient outcomes using the best science available on the agenda of the European Union.

Yet, despite its many tangible advantages, the take-up of personalised medicine in Europe has been relatively slow because the competence and direction involved in bringing individual medicines and treatments to Europe's citizens are extremely complex, Buşoi added in his opening remarks.

Meanwhile, we should not focus our discussion only on health benefits, but also on the growth of jobs given by the development and research into new medicines where there will be, in research itself, education, design and the manufacture of individual products, all within the pharmaceutical industry..

Member states and stakeholders agree that such a focus will truly benefit society and, if Europe is in the precursor of developing new ways of keeping citizens healthy, it will also inevitably attract investment from outside of the EU.

However, there is a large requirement for networking and rethinking in many areas in order to bring the practice of medicine up-to-speed in a fast-changing world.

Much remains to be done to lower the barriers to give the right treatment to the right patient at the right time, thus ensuring



equal access to the best treatments available for all EU citizens across the 28 Member States.

So, the potential of personalised medicine presents us with many challenges. The conference was held as an educational exercise built on the vision of mighty stakeholders supporting the development of the necessary frameworks.

Delegates agreed that the conference was not designed to find all the answers but to begin working and engaging with the necessary stakeholders. The Alliance has already started working on Council conclusions on the ground in Italy, Bulgaria and Poland through its outreach programme, called 'SMART' (Smaller Member states and Regions Together).

Europe needs to promote the uptake and the alignment of existing agreed standards and also define those for interoperability of health information systems.

Also, there needs to be coordination and development of best practice for clinicians, researchers, industry, academics and policy makers, but the Alliance has also managed to have had personalised medicine recognised and included in recent and upcoming legislation. Strohmeier cited personalised medicine as being a patient-centred approach that carries the promise of

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making health care “smarter, better and more cost-efficient to the benefit of European societies and citizens”.

As research funder, the European Commission has focused on personalised medicine since the area started to gain interest in 2010, and has funded more than €1 billion of research in the Seventh Framework Programme, in areas that underpin the development of personalised medicine.

The Commission has also continued to focus on personalised medicine, plus personalised health and care through its current programme Horizon 2020 and in particular in democratic change, health and well-being. Also pivotal to personalised medicine research is the Innovative Medicines Initiative (IMI), the world’s largest public-run partnership in life sciences.

A constructive legal framework has also contributed to the development of personalised medicine. The regulatory framework for pharmaceuticals offers a number of tools and procedures to ensure that medicines placed on the market are of high quality, safety and efficacy.

These tools, complemented by scientific guidelines and expert evaluation, have already worked well for innovative products including therapies relevant to personalised medicine.

The ongoing revisions of important pieces of legislation address certain challenges identified in the development of these therapies.

The revision of the medical devices legislation will strengthen the legal framework of in vitro diagnostics and introduce a better consultation process for companion diagnostics to assess patient eligibility for treatment with a specific medicinal product. The revision of the Clinical Trials Directive is expected to simplify the conduct of clinical trials and consequently facilitate research in therapies using personalised medicine.

Taking Stock – The Presidency Perspective

Luxembourg Health Ministry First Government Counsellor Anne Calteux explained how the recent the Luxembourgish Presidency addressed the topic of personalised medicine: “We were asking ourselves, what is personalised medicine actually, and what do patients expect from it? What do they need in terms of personalised medicine, and how do to make it an integral part of our health-care systems?”

As a result of these questions, the Luxembourgish Presidency decided to trigger discussions on personalised medicine during the presidency that went beyond the current efforts in research, in order to disconnect personal medicines from purely economic considerations, to change the angle of perception by bringing

in a greater focus on the health dimension and on the central position of the patient.

The aim was to make personalised medicine a topic that unites, rather than a topic for the happy few.

“Bringing personalised medicine to the awareness and to the attention of politicians and decision-makers, in the field of public health, was the objective of the Luxembourgish Presidency,” Calteux continued.

Netherlands Health Minister Aldo Golja was next to speak, and he reiterated the fact that personalised medicine is all about the patient. He then spoke about affordability, access to innovation, sustainability of health-care systems, international cooperation and collaboration and some of the dilemmas that these pose, bringing long-term challenges in providing pharmaceutical care for patients in Europe.

The health-care system, Golja added, should be sustainable while providing the medicines for the patients who benefit from them.

The current system of research, development, market authorisation and reimbursement of pharmaceuticals and also of diagnostics poses challenges towards access and sustainability and there was a global challenge, he concluded, to offer patients with very little or no prospective care, an alternative to currently available treatments, but also to ensure long-term appropriate use of those three elements.

This will require an active dialogue between government and stakeholders, Golja said, promising that during the Dutch EU Presidency, measures will be proposed for a joint approach to the problem.

Finally, Permanent Representation of Slovakia First Secretary Dušan Šando took the floor – she said that Slovakia boasted leading researchers in the field of Alzheimer's, and that her country was very much looking forward to regulation concerning supervision of medical products for human and non-legislative activities concerning cross-border health.

Maltese Health Minister Christopher Hearne said that it was very important to “bring the two spheres of personalised medicine together”.

He went on: “There is a risk that we are now treating all patients with one disease the same. So the real world in the clinical sphere today is protocol driven, evidence based, best practice medicine which is good as it is causing standards to rise.

“On the other hand, we now have, and again this is a game changer, we now have next generation sequencing which has

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bought fast possibilities for research in this specialised industry. So we have two parallel universes which is the clinical world of best practices and protocols and the other universe of the research lab where now you can dig deep into the DNA of each individualised person."

Taking Stock – The Stakeholder Perspective

Peter Liese MEP (Christlich Demokratische Union Deutschlands, Germany) stressed the importance of having more targeted therapy, adding that there are "many diseases we will only be able to cure, if we focus much more on personalised medicine". Safety was crucial, he added, but warned against having too-rigid rules "because when they are too rigid, we block innovation, so it is not good for patients".

Liese said: "There are more and more mergers between devices and medicinal products, so some kind of medical devices administer a drug, or may be even remove a drug, and this kind of devices the Parliament asked for a special treatment.

"One of the most controversial parts of the regulation was the scrutiny and the provision proposal only for class 3 devices and the Parliament insisted that also class 2B devices are subject to a special surveillance. This is because we understand that there may be risks that need to be assessed in a specific way. This is what we did to address this problem and it is agreed now."

Founding Director and Full Professor of the Institute for Public Health Genomics Angela Brand concluded that personalised medicine needed to "move from innovation, creation and innovation management to something I would like to call innovation diplomacy".

She added: "Innovation diplomacy has very different meanings – gamechanging applications of new technologies and technics such as public diplomacy's through social media, to co-create and innovate to solve the shared problems and tackle the shared challenges of personalised medicine."

Conclusions

The panel agreed that personalised medicine is back to the true public-health approach, where through big data, analytics or smart phones, you may identify someone very early on and intercept them, and it may not be about medicines at all.

It's lifestyle change, and if it is about medicine, it is probably generic medicine that may be repurposed with the combined diagnostic. It is about the products that come and the investment decisions that have to be made – it is the budget impact.



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Plenary Session II: HTA, Payers, and Dialogue with National Medicine Agencies, National Health Technology Experts and Insurance

Hans Georg Eichler, of the European Medicine Agency, opened proceedings; he spoke about the interaction between different decision-makers, regulators, HTA bodies, payers, and the pharmaceutical products that were resulting from the interactions between these various decision-makers and potential points of friction.

"So, this is about the interaction between different decision-makers, regulators, HTA bodies, payers," Eichler said. "Do we have this going on for the time being? The answer is absolutely yes. And we have some very pertinent interactions between the regulatory camp and the HTA camp in Europe and we call those parallel scientific advice sessions – for those of you who don't know what it is, there is a developer, usually a pharmaceutical company, that is in the process of wanting to bring a specific drug to market.

"What we have to show, and in the past they would only come to us, the regulators, we tell them we would like to see this-and-that trial, but today we are doing this in parallel with a number of European Union Member States, HTA bodies."

Steve Shak, Co-Founder, Chief Scientific Officer, Genomic Health said that he believed that progress was being made in healthcare in the United States, with Barack Obama the first US president to have spoken about personalised medicine and precision medicine and also declared that access to care should be more broadly available.

In Shak's opinion, making data public in a responsible way, driven by the patient community, allowed to know better and to learn from what was being done in clinical practice in order to optimise what was being done. He also spoke about the opportunities arising in genomic health, with new models being developed in Europe.

There are new models for reimbursement, for example with regards to onco-type DX – Germany is now working through a new model, and France has come up with a new initiative in order for there to be access for multi-gene tests for the broad population of breast-cancer patients in France.

Hans Peter Dauben, head of the German Agency for Health Technology Assessment (DAHTA) and Medical Innovations spoke about how the handling of medical data has changed enormously in recent years; What is new today, Dauben said, is the excess of knowledge, and that it is becoming extremely difficult to handle all the data. The question is, he added, was how we can offer the knowledge to somebody else.



Dauben added that the most important bodies involved in HTA in Germany are the G-BA, the Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen [IQWiG]), and the DIMDI.

Others are the medical service of the head associations of the SHI (Medizinischer Dienst der Spitzenverbände [MDS]), the National Association of SHI Physicians (Kassenärztliche Bundesvereinigung [KBV]), and university-based institutes and others conducting HTAs in Germany.

The G-BA is the supreme decision-making body of the self-governing system in Germany. Physicians, dentists, hospitals, sickness funds, and patients are represented in the G-BA.

The G-BA issues directives and, thus, determines the benefit package of the SHI covering about 70 million people. Finally, the G-BA is responsible for reimbursement decisions. Like most other countries, in Germany, the parliament sets the legal framework for health-care provision and the G-BA issues standardised and binding directives to translate the legal framework into practice.

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The directives issued by the G-BA are legally binding for insured persons as well as for the providers and payers of health care: physicians, hospitals, and sickness funds.

The directives define the provision and reimbursement of pharmaceuticals, diagnostic and therapeutic procedures, medical devices, and non-medical treatment.

One important area of responsibility of the G-BA is the assessment of new diagnostic and treatment methods (including medical devices, if part of the respective method). In outpatient care, each new treatment method needs the explicit approval of the G-BA. In inpatient care, each new treatment method can be used as long as the G-BA has not excluded the treatment method from being used within the SHI.

The G-BA's assessment of medical treatments and procedures follows a standardised procedure which is founded on the principles of evidence-based medicine.

Based on the current state of medical knowledge, the effectiveness, quality, and economic viability of the treatment methods under examination are assessed. These assessments are pivotal for the development of the catalogue of benefits mainly in the area of diagnostics and medical treatment except pharmaceuticals.

Professional mobility is a hallmark of pan-European integration best understood as 'freedom per se' for the individual. In times of economic crisis, professional mobility offers a real alternative against unemployment and decreasing salaries.

Maarten J. Ijzerman, Professor of Clinical Epidemiology & HTA, University of Twente declared that he was "not stuck" to reimbursement entry, but also use of modelling methods and HTA approaches to inform decision-makers in a wider perspective.

As a previous chairman of the Pharmaceutical Economic Guidelines Committee, Ijzerman was asked to revise the guidelines for pharmaceutical economic evaluation in the Netherlands, which is quite close to the NICE process of single technology appraisal.

These guidelines were revised in terms of modelling approaches, where do we get the data from, how do we deal with uncertainty in the models – Ijzerman said that his concern with these guidelines was that they had just been handed over to the Ministry of Health Affairs in February this year, and his concern with these methods is that they are "pretty much based on the very rigorous theory that we have to look into procedures to put it into practice".

Concerning personalised medicine more specifically, Ijzerman

said that he considered there are three challenges in terms of HTA, that we didn't address in those guidelines and I think there is some more work to do, from a European perspective.

He said: "Current approaches in health technology systems define value in terms of quality, quality just at life years which is a very strong measure of health outcomes which can be used across countries.

"We actually do have some data: the Commission actively supported the comprehensive PromeTheus study. However, it does not fully cover the most recent events, for example the visible collapse of socially financed health care systems in countries suffering an overwhelming public debt.

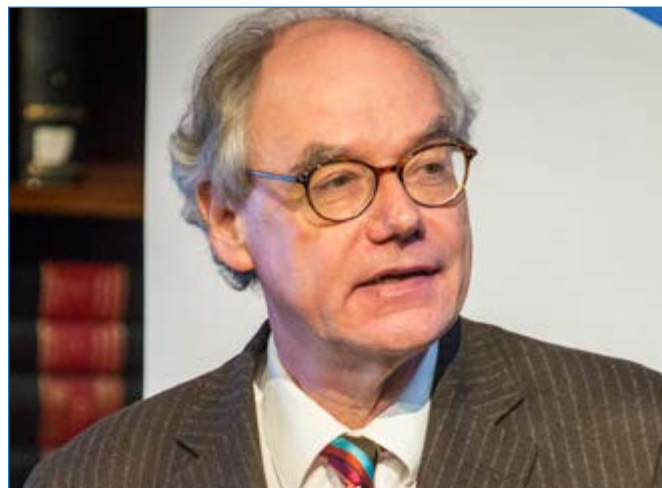
"Legally speaking, the EU is not responsible for the actual functioning of national care systems. I personally do not think that the EU, as such, is interested in matters beyond the scope of the implementation of the existing legislations. The shocking reality is that such conditions are no longer confined to traditional hot spots of poverty in the East.

"The brutal chain of events goes as follows: no economic growth, more public and private debts, no jobs and shrinking public benefits. As for accessibility of care, the differences within the EU are widening almost every month."

Conclusions

Concerning the flexibility of the innovative clinical trials, much rigour, and intellectual strength in what will be new ways of getting evidence is required.

We need to agree that there is a capacity for paying drugs or medical tools and so on in society. And this is a societal choice and we need to live with that, and it is impossible in the current system that we have prices that are the same.



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Roundtables

At the conference, there were 14 round tables with ten stakeholders representing the core groups of EAPM (patients, medical, healthcare planners, industry, scientists and researchers).

Each table discussed a particular issue based around thematic questions. At the end of the hour, the solutions proposed by each table were discussed and debated with the Commission, European Parliament and the EMA to get their feedback.

Based on this, a common approach was agreed with the institutions for actions to work on at the EU/national level to implement the council conclusions in years ahead.

Data privacy and consent

The development of personalised medicine can only occur if easier circulation of personal health data is allowed for scientific research purposes – with, of course, appropriate safeguards.

Understanding intricate health data is challenging, but when abundant health data is combined with innovative analysis strategies in a multidisciplinary setting, powerful models of complex diseases emerge.

This implies circulating and sharing personal health data with a wide range of data experts and medical specialists who can extend the work of each other and, together, can derive the most apt interpretation from the data and who can then extend the works of others.

This implies simplification of the current complex and inflexible regulatory procedures, a review of incentives for innovation, and greater regulatory predictability that would help reduce research costs. The current system of a unique approval moment should give way to progressive management and reduction of uncertainty, and access to new therapies based on a combination of data from randomised clinical trials and observational data.

Evaluation of clinical effectiveness and analyses of long-term treatment effects depend on availability of quality assured clinical registries for observational studies. No single entity has the depth of knowledge and financial resources to effectively collect and mine the biomedical data needed to enable personalised medicine.

New forms of collaboration are required between academic centres, the pharmaceutical industry, regulators and payers.



Diagnostics/medical devices and imaging

Diagnostics, both companion diagnostics and imaging, are crucial to personalised medicine – but they are often poorly understood, and incentives are often lacking for investing in their development.

Tests rarely enjoy market exclusivity, and although heavy investments are required to generate clinical evidence, the results can be reproduced without delay and at lower cost by 'fast follower' developers.

There are also wide divergences in national regulatory systems, and many countries do not require regulatory approval for reimbursement - thus disadvantaging or discouraging the search for clinical evidence.

Clear, harmonised rules should apply across the EU, imposing more rigorous review, but with standards of clinical evidence that balance the risk-benefit profile with the degree of innovation. Guidance from the EMA, setting standards for CDx review, would help clarify expectations and ensure that requirements remain realistic.

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Greater collaboration is needed between pharmaceutical and diagnostic manufacturers – based on deeper mutual understanding of the differing development timelines and lifecycles, regulatory and reimbursement pathways, and markets and customers.

To ensure effective introduction of imaging biomarkers into routine care, structured validation processes are needed to replace the current bottleneck of reliance on long and resource-intensive clinical trials - such as by a facilitated approach to allow their increased use in clinical trials.

Full interoperability is also needed between the '-omics' biobanks and imaging databases. And coordination of reimbursement approval of a CDx and its associated medicine would reduce delays for patient access.

ICT tools: Enabling patients

Personalised medicine depends on advanced technologies, particularly in relation to data generation and handling.

New solutions will be necessary to collect, integrate, and analyse this information - presupposing not only a massive data-handling capacity, but even more so, the use of these data to predict individual risk, disease course, treatment response, and the likelihood of adverse events.

Among the biggest challenges are interpreting different datasets and linking the findings to specific outcomes in individual citizens.

A linear approach is no longer enough: the functioning and cooperation of different sub-sets within the system in a dynamic manner has to be grasped - understanding the system in flux.

The data must be of sufficient quality, characterised, standardised, and compatible to allow integration from multiple sources.

Storage could also become a limiting factor without adequate action, as could re-use of personal data without adequate arrangements for consent of data originators, along with a range of other data-sharing considerations - including overcoming commercial barriers, and professionals must be trained to develop and implement technology solutions.

Progress will require new techniques for remote monitoring of the signals that will allow more sophisticated prediction and prevention – and that will in turn require wider patient and citizen acceptance of technology and of personalised medicine.

Personalised medicine offers the opportunity for patients to be seen not merely as passive recipients of care but as participants,



partners and even guides in their own health care. Involving patients in treatment-related decision making is in line with the increasing acknowledgement of patients' right to autonomy and self-determination.

Personalised medicines needs engaged and informed patients who are encouraged to discuss various treatment options, the possible consequences of those options, and then to arrive at an informed determination about the best action.

Clinical trials It is common knowledge that the present clinical drug development model is broken and in dire need of repairs.

There is no shortage of drug candidate discoveries, but unfortunately the vast majority of these fail to prove efficacy in the clinical setting. What's even more troubling is that many compounds in development are failing in later stages, which represents as much as 40 % of the entire clinical drug development budget.

Only one-in-ten compounds are approved for use; in the oncology space, the attrition rate is thought to be much higher.

The biggest inefficiencies of the traditional model are largely attributed to the improper selection of drug targets.

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With thin pipelines and blockbuster drugs coming off patent, pharmaceutical companies are seeing their profits being eroded by low-cost generic competitors.

These companies can no longer afford to sustain a drug development model that has become increasingly costly, unpredictable, and inefficient.

Researchers in Europe would benefit from research infrastructures able to support large screening platforms to identify the target population, as well as relevant IT tools such simulation or computer-assisted decisions.

New models of multidisciplinary collaboration between drugs developers, academia, regulatory agencies and payers should be developed allowing public-private partnerships and providing for appropriately trained professionals. And smart but robust clinical research methodologies need to be endorsed by regulators and payers.

At present, the legal framework in Europe is hampering international clinical research.

Legislation should be harmonised, and the related costs and administrative burden should be reduced. And public funding should be available for performing high-quality investigator-driven and academic international clinical trials.

Agreement on an appropriate final text for the proposed update of EU rules on clinical trials would boost the chances of successful development of personalised medicine.

Health technology assessment: Securing patient access to personalised medicine

Personalised medicine is all about the patient and innovation. It starts with the patient. It features big potential for improving the health of many patients and ensuring better outcomes of health systems' efficiency and transparency.

Moreover, in times of budgetary constraints, facilitating better-targeted and more cost-efficient treatment - to a potential 500 million patients in 28 EU Member States - is in line with the Europe 2020 strategy and the aims of the Juncker Commission.

The challenge to be addressed is to put into place a framework which allows to deliver the right treatment to the right patient at the right moment, in accordance with the principle of universal access to high quality health care and could be developed through guidelines on evidence requirements, scientific advice sessions, and assessments of relative efficacy and modelled relative effectiveness.



But ultimately, progress would require a commitment by payers to integrate these findings into their coverage policies. The process will be eased if regulators move away from a focus on short-term solutions to the broader concept of overall economic value, and acknowledge that coordination and standardisation are required in assessment.

Innovative payer models

A factor impeding the move towards more personalised treatment is a payment system that takes decisions based on limited knowledge about who the most likely to benefit patients are from a treatment.

Pricing and reimbursement levels are established through an evaluation of the average effect of a medicine, because it is rarely possible to identify in advance the patients who will benefit more than the average.

This homogeneous level for the value of a medicine is set at the time of launch, and paid for each dose prescribed, irrespective of the effect on specific patients.

But medical advance and the analysis of the molecular basis of diseases enable a stratification of patients, so that medicines can target narrower populations of patients which are more likely to respond to the treatment.

Payers are interested in driving the development of pricing and reimbursement models that allow them to pay only for those patients that respond positively to a treatment.

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But to make the shift, better collection of data on the effectiveness of treatments is needed, along with appropriate data assessment to determine the value of treatments. increased coordination of assessments, horizon-scanning projects, and more dialogue early in development and along the life-cycle of products, involving all decision-makers and the manufacturer.

Continuous assessment of added value by payers and benefit-risk by regulators should lead adapted prescribing, dosing and reimbursement conditions as new evidence emerges, in new forms of adaptive licensing.

Payers need to recognise their crucial role in incentivising and providing access to innovation.

Education and training of healthcare professionals in the personalised medicine era

The issue of education of health-care professionals (HCPs) is one of the major ones.

It is clear that a great degree of upskilling is already required and, to keep pace with the science, this must be ongoing. Stakeholders need to achieve this together - with agreed standards across the board so that no patient is denied a suitable, virtually tailor-made treatment due to a lack of knowledge or understanding on behalf of the HCP treating and diagnosing him or her.

New technologies will require new professional competences, and new levels of communication between healthcare professionals, scientists and biotechnologists. Health-care

professionals will also need to translate complex information into messages that the patient can understand, with the correct balance between saying too much and saying too little.

They will have to be alert to the ethical and data protection debate over personal data, too. Many educators have developed programs in personalised medicine/targeted therapy, but an overall structure is needed to achieve shared understanding among healthcare professionals, patients and the public.

Education and training that is high quality will be needed to translate personalised medicine into widespread clinical practice.

Plenary Session III: Value of Innovation, Access and Incentives

Agnes Mathieu of the European Commission's DG SANTE (Medical Products) began the debate, citing the crucial importance of pharmaceutical innovation, and how the European Commission was addressing the specificity of personalised medicine.

Tom Fowler, Director Public Health for Genomics England stressed his role as representing "the delivery body" for the UK hundred thousand genomes project, which he said "has a number of aims".

First and foremost, Fowler explained, is patient benefit. There was a big debate initially, he said, about whether or not what was being done was clinical transformation, or research, and this was battling back and forth between the different experts.

"Genomic medicine marks the beginning of creating a lasting legacy for patients and the NHS through the 100,000 Genomes Project. Health-care professionals and public health workers will be learning how to apply whole genome sequencing and helping to integrate genomic medicine into routine health care."

Agnes Mathieu then stressed how important personalised medicine was to the Commission. "Last year we were very pleased to see that the Luxembourg Presidency put a lot of emphasis and work on personalised medicine and they had a need to push the Member States to have the Conclusions.

"With the Council Conclusions we had a number of initiatives, especially for the Commission, and we are now very pleased and committed to move forward number of initiatives which will have great added-value to make personalised medicine a reality for the patients.

"So our objective is not to create brand new initiatives, but we have a number of initiatives with a positive impact on this medical approach that is personalised medicine."

4th Annual Presidency Conference

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Cancer and rare diseases

Concerning the Commission expert group on cancer and rare diseases, Mathieu stressed that personalised medicine is not only treatment, not only medicinal products, it is also the prevention of disease.

And experience shows that genomic, we spoke a little bit about genomic data, genomic information can be also very important for the prevention of disease, and how we will establish the screening of cancer for example.

So we would like also on how to integrate the genomic information into the current screening programmes. And the group on cancer will work on the position paper on public health genomic health In cancer.

Portugal MP Ricardo Baptista stressed that health systems were supposed to make people healthier, and the problem is that with the industrial revolution and over the whole 20th century "we have changed health from being a service into a product and we thought that using management models coming from Japanese car makers would be useful to make hospitals more productive and this has led us to be focused on administrative bureaucratic processes to our final goal as health care professionals, which is to make people healthier.

"Unfortunately the only reason why value has become an issue now is because of costs. It has been proven that health-care costs are going to rise in all systems and Europe is no exception.

"The OECD has shown that the average 6% GDP that we are spending today in 2060 if we do everything right we will be spending every right we will spending around 10%, if we do everything wrong we will be spending around 15% over GDP; which means that if we don't do everything right health care systems as we know them will be fully unsustainable.

"So once again it was the financial motive that has been pushing this forward. But it doesn't matter, at least we are having this discussion and the truth is that we have to shift now so that we can work on all of these issues of personalised medicine and creating value throughout our healthcare systems and we have to really change the way we look at our systems and the way we manage them.

"So we have to shift from these administrative hospitals where we are focused at the number of surgeries that the doctors are performing so that we can focus on the health outcomes that come out of that, so that is the only way we are going to lower the burden of disease.

"On the other hand, we have to create integrated models where we work as networks and not individual silos. And to do



all of this appropriately we will have to have a very strong information technology network established, that can use artificial intelligence to help us through cognitive processing, use big data, not only to help us select patients for clinical trials, but also for decision support when it comes to diagnostics and to treatment and using patients similarity to make those decisions better and better.

"You can actually use those to actually change the way we finance healthcare systems because that is a huge issue. If we really want to shift our health systems to be focused more on the creation of value then you have to finance the creation of value. It has been more than proven that paper performance is what works within the health sector, so artificial intelligence can help us with the reimbursement process."

Conclusions

"We need a society that is based on evidence, on human rights, on access, so we need innovation, we need access and we need to find the right incentives to get these two things.

"This a society moving, I don't think like democracy, there is no perfect democracy, but these are the terms that should be binding and probably as there are no guilties there are no innocents.

"We are not doing our work as citizens well enough. We are not enough part of the solution, only the problem, but these are the frameworks that we need to think, as citizens of Europe, that want to build something together.

"Otherwise we risk having a crumbling-down Europe."

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Plenary Session IV: Genetic Mapping & Ethics

Robert Johnstone, Board Member, European Patient Forum said: "It is getting to be a trendy subject. I was in an environment the other week, it wasn't a health-related environment at all but the topic came up, and three out of about 30 had already had their genes mapped, just out of interest.

One guy had been given it for his birthday, it is getting trendy, you know, it's like Facebook and things. But, you know my feeling about this is, you know, I am living with a chronic condition I've had all sorts of problems for 60 years. If knowledge of my body can help other people not to have to go through what I have gone through, I'm quite happy to share that knowledge in a properly controlled discreet environment.

"I would be quite happy to argue (that), it is a moral imperative. It's part of the social compact in society that we help each other in the health arena and every other arena, so I am quite open with this, I don't have any problems with it at all."

Agnes Mathieu, DG SANTE, European Commission said: "Having worked as a paediatrician, very early we try to find out all examinations from birth, pre-natally, then regularly then the child gets, the time between the examinations become bigger.

"And we try with other tools, with ultra-sound, or checking the eyes, the ears, the whole body to find out early signals of diseases. We ask about the family history etc. Now we have another tool in our hands."

Giovanni Martinelli, University of Bologna said: "In my opinion, what the immediate need for patients is, I think, for the majority, is more accessibility to diagnostics. There is nothing like this in Italy, no place we can apply next-generation secrecy to the sample of our patients.

"When we get that it takes a lot of time, we have to start the therapy before there is any acknowledgment of the disease. I think the majority of our information has to be for the patients, that is my opinion, and this is ethical, and represents a better quality of life."

Rob Hastings, a clinical geneticist, said: "We all have to accept the 100,000 Genome Model and we need to combine research, clinical practice, commercial and industry development in all that we are doing in the same systems."

Conference conclusions

Summing up the two-day conference in his conclusions, EAPM Executive Director Denis Horgan said: "More than 80 people spoke at the conference and we had 200 registrants. We tried to catch the right people in the different experts that were here.



"We had different experts from different Member States and they covered different issues. Whether it was on genomics, whether it was on education, whether it was on access, we had people from Portugal, Spain, France, Germany and these represent the different stakeholders that are in the Alliance.

"So we had experts and also lay persons to give the different types of perspective. We had different ambitions from the conference – some people were shooting for the moon, and other people were trying to keep their feet on earth, and trying to have a more practical point of view.

"What kind of people do we have to have involved and what kind of equipment do we need? We had people from the Brain Council, from the oncology sector and we had people who were smiling, serious and people who had different perspectives.

"The basis of the conference was 'Taking Stock' - where are we now and where do we want to go? It was a follow-on from the Council Conclusions on personalised medicine which was highlighted at various times through the conference. And you have people with different focus, different interest, that represents a perspective we were trying to take. What kind of data can be shared, what different kinds of clinical trials models can we have and what kind of education is needed?

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"We did this through various round tables and these are different perspectives that we had here today.

"We tried to ensure that this was an interactive conference so that we could identify the key messages from this. We tried to have a very personalised welcome in terms of interactivity between the different stakeholders to bring the two pieces together - the experts and also the issues.

"This brought together different knowledge from the different stakeholders and what we could do together. There's a lot of expertise and innovation in Europe and the key question is how can we realise all this innovation and have this diplomacy between different stakeholders? There's a lot of goodwill but how can we capitalise on the synergies between different types of stakeholders.

"And we had the Supermen coming here to save us...but, of course, we can't solve all the issues at one time so we need to have a focus on different issues.

"MEPs said we should have healthcare on the EU treaty, and other people said how can we modify different types of regulations. At the end of the day it comes down to what do the patients need? Patients want to get better access to treatment, they don't want to get over-treated, or under-treated, they want the right treatment for the right patient the first time. And this is what we are going to focus on at EU level - solutions, identify best practices, at EU level and at international level.

"A lot of the issues focussed on Big Data and how data can be shared between different stakeholders and who can access the different data – allowing data to be shared but in a safe way. We have to have a realistic discussion: we cannot be over-protective.

"There is no way to ensure that data is always kept safe, there needs to be proper safeguards in place to guarantee that data will be protected but utilised for the benefit of more research, to allow different treatments to be developed, to allow diagnostics to be developed and to allow rational use of resources and how they are allocated in different countries.

"There are different types of diseases and we need to understand how data is used. Personalised medicine and personalised medicine are very- much interconnected. To be able to understand the data you need to be able to know which patient this data belongs to and that is an important issue.

"We need more of an EU approach, or a common international approach on how data is utilised. And the EU has a role to play in how the Data Protection Regulation can be implemented at the national level, and different standards and guidelines at international level. Personalised medicine is all about patients, but how can we ensure that the patient is at the centre? We



need to involve patients more in the decision-making process. How can we ensure that putting patients at the centre really takes place?

"We need to integrate them into the decision-making process, not just talking about empowering them so that the patient is not only a stakeholder but also a shareholder in their own their own healthcare and an equal shareholder with the other stakeholders, whether that's medical professionals, industry... and we need a more common approach to this.

"And to use all this new knowledge we need an upscaling from the medical professionals and between different disciplines. We need more input from the experts to understand how regulators can facilitate change, so we can utilise this great science that's available.

"Personalised medicine has gained a lot of traction in the last years, we've tried to revise the legislation, not reactive - it's been pro-active. The Alliance is having it's SMART approach to health care, so we recently organised meetings in Italy, in Milan, and we're going to have more Outreach activity in Spain, France, Germany, UK, Ireland and bring the issues to the national level.

"Because a lot of decisions related to healthcare are decided at the national competence. Of course, while at EU level there is a common understanding of which direction we're going in, but we need more coherence in how this is done, identifying best practices and how we can have synergies between different regions and between all regions. This is a long-term objective."



European Alliance for Personalised Medicine

About EAPM

The European Alliance for Personalised Medicine (EAPM) , launched in March 2012, brings together European healthcare experts and patient advocates involved with major chronic diseases.

The aim is to improve patient care by accelerating the development, delivery and uptake of personalised medicine and diagnostics, through consensus.

As the European discussion on personalised medicine gathers pace. EAPM is a response to the need for wider understanding of priorities and a more integrated approach among distinct lay and professional stakeholders.

The mix of EAPM members provides extensive scientific, clinical, caring and training expertise in personalised medicine and diagnostics, across patient groups, academia, health professionals and industry. Relevant departments of the European Commission have observer status, as does the EMA.

EAPM is funded by its members.

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