

pharmacogenomic-related variants may be larger and clinically relevant. The recently launched Clarification of Optimal Anticoagulation through Genetics (COAG) double-blind, randomized controlled trial² will ascertain whether adapting the dose of warfarin therapy based on genetic variants located within the *CYP2C9* and *VKORC1* genes may improve patient care as compared with a clinically-guided dosing algorithm. Designing such a trial is particularly challenging because the power to detect a pre-specified between-group difference will depend on the genetic makeup of the participants. The challenge comes from the fact that allele frequencies may vary substantially across ethnic groups. To recommend genetic testing, investigators will need to demonstrate that drug dosing based on genetic information significantly reduces costs and morbidity.³

Focusing on a single disease or on a single trait does not allow understanding the full range of phenotypes associated with many genes, for which pleiotropic effects have been described (i.e. one gene may be involved in both cancer and cardiovascular disease). Hence, an additional challenge for epidemiologists is collecting extensive phenotypic data, not only at a single point in time, but longitudinally, again. The collection of high quality phenotypes and more comprehensive phenomes are therefore of utmost importance and will be key to better account for the underlying biological complexity of human organisms living in selected environmental conditions.^{4,5} The digitalization of patient's records and imaging technologies, as well as web-based testing, should allow accumulating and linking massive amounts of information for each person. The availability of entire genomes and phenomes may revolutionize the way we classify diseases. There is little doubt that data-gathering technology has dramatically changed and will

continue to largely influence the way epidemiologists conduct research. Making best use of all the available information, without harming study participants (i.e. discrimination by insurance companies or employers, undue access to the data by third parties, etc), will be a challenging task in the years to come.

In conclusion, recent advances in genomics have highlighted the polygenic nature of most common disorders. The effects of these genetic variants also need to be studied taking into account time-dependent environmental and behavioural factors.⁵ As a consequence, any single genetic variant has little impact in terms of disease risk prediction. Yet, polygenic risk scores in relation to continuous traits (i.e. BMI, blood lipid, blood pressure, etc) should stimulate public health researchers to change paradigms and consider integration of multilayer biological data, dynamic designs, agnostic approaches, as well as using quantitative measures in assessing both exposures and outcomes (i.e. continuum of affectedness). Such quantitative thinking leads to a public health model that focuses on prevention on a continuous scale rather than just treating cases. Looking at multivariate continuous dimensions rather than clinical diagnoses using arbitrary cut-offs represent more powerful approaches to decipher the complex etiological mechanisms leading to human diseases.

Large inter-disciplinary teams are needed to properly design studies and collect, store and analyse high-throughput data. Whereas the prices of 'omics' data production have dramatically come down, the costs of data storage and analysis are very high and often tend to be underestimated. Unless studies are not well funded, epidemiology will not be able to assume the challenges mentioned above. High-quality and continuously updated education programmes are needed to ensure that researchers and health-care

professionals are able to critically appraise research findings in the 'omics' fields, including 'epi-omics'.

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A European view on the future of personalised medicine in the EU

At the European Health Forum Gastein in October 2010, personalized medicine was presented as a new paradigm for health care in Europe. I had the opportunity to participate in this session and to listen to the views of my esteemed co-participants on what can be done at the European level to achieve implementation of personalized medicine

approaches and other emerging technologies.

Personalized medicine is becoming an ever more important area for the application of genome-based information and technologies identified under public health genomics. The scope and vision of public health genomics, according to the 2005 Bellagio

Conference¹ is 'the responsible and effective translation of genome-based knowledge and technologies for the benefit of population health'.

This concept encompasses both population and individual health. It covers prevention, treatment and care.

Genomics is clearly an area of innovative research that seeks to close the

evidence gap of today's biomedical and health research. This is an important area of potential innovation in Europe. As the Commission has set out in the Europe 2020 strategy and its related initiatives, it is essential for Europe to build on our strengths to develop innovations to promote growth and benefit European citizens. Genomics has the potential to be a key sector contributing to this in the future.

Future epidemiological studies may begin by grouping participants according to their genomic patterns, then according to environmental factors like exposure levels e.g. by life styles. The relationship between environmental factors and genetics is an area that needs more exploration. This will enable us to pin down and predict disease patterns and susceptibility in individuals. Genomics not only has potential for epidemiological research but also for individual prediction and prevention of health risks as well as for personalized treatment and care. This involves developing tailor-made treatments.

In the treatment of cancer, for example, the concept of pharmacogenomics is gaining ground due to the fact that there are so many different types of cancers.

This kind of medicine is already making its mark. It is taken into account in pharmaceutical companies' business strategies, the design of clinical trials and the way medicines are prescribed.

Although personalized medicinal products are expensive, their efficacy and safety could actually make them more cost effective in the long run than traditional medicines. Their potential is therefore huge. If the specific quality, safety and efficacy of individual personalized medicines can be assured, they will respond to patient needs in a much more targeted manner.

There is currently an assumption that personalized treatment options would put a strain on public healthcare budgets. An alternative viewpoint is that they would in fact reduce health spending in the long run, through greater effectiveness and the avoidance of unwanted side-effects. Indeed, being able to immediately select and offer patients the medicine that is effective for them will be a bonus, as trial and error can be avoided. However, we need to ensure

that equity and access are also taken into account. The progress offered by emerging technologies and therapies needs to be analysed by the Commission over the coming years in order to keep the EU regulatory framework up to date. We need to constantly look at better ways to address medical needs and one way to do this is by encouraging the development of innovative technologies.

The concept of personalized medicine is an important driver for innovation. It is clear to all that 'pharmaceutical innovation' is a crucial component of this concept. It is of key importance in addressing unmet medical needs within society. The lack of adequate treatment for many diseases requires continuous innovative efforts to find new medicines. This equally entails the engineering of innovative *in vitro* diagnostic medical devices.

But we need collaboration and co-operation. The Innovative Medicines Initiative (IMI) is an excellent example of how collaboration between industry and the Commission can deliver concrete results. We are determined to take this agenda forward.

Our ambition must be to continue our strong support for fundamental pharmaceutical research in Europe to improve chances of translating research results into successful products on the market.

With regard to the regulatory framework for pharmaceuticals, we have a comprehensive EU legal framework coupled with detailed scientific guidance documents, enabling economic operators to foster public health by bringing safe, efficacious and quality medicines to the market.

The Commission has in place several mechanisms to support innovation. The Internal Market framework provides various incentives for innovation. In addition to the Community Code relating to medicinal products, there is the Regulation on orphan medicinal products. This seeks to encourage research and development of medicines for patients suffering from rare diseases. This has proved to be a great success over the past 10 years.

Another example is the Regulation on Advanced Therapy Medicinal Products, adopted in 2007. This legislation aims to speed up the development of

regenerative medicine products and promote industry's competitiveness, while respecting national prerogatives on ethics. This initiative is also starting to yield results.

The Commission funded, Public Health Genomics European Network (PHGEN) has mapped the foreseeable impacts of the evolving genome-based information and technologies in all areas of public health, health care and health systems and is developing the 1st edition of European guidelines for quality assurance, provision and use of genome-based information and technologies due in 2012. Furthermore, we continue with interest to follow developments in science, product development and public discussions on this subject.

In this context, I should also mention that the European Medicines Agency (EMA), together with its network of expertise in the Member States, is an excellent pool of knowledge. At the Commission, we are working across different departments, from Research to Public Health, to share information.

I am convinced that the area of personalized medicine, and its fascinating emerging technologies such as pharmacogenomics, patient-specific modelling and disease simulators, has enormous potential for our citizens. It will lead to Europeans ageing in better health and receiving better health care when necessary.

Reference

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