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Panel Sessions
Bioethics and Social Responsabilities

Bioethical challenges in personalised medicine*

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Resum. La gran majoria de les qüestions ètiques, legals i morals que es deriven del concepte de medicina personalitzada estan profundament relacionades amb les proves genètiques. En primer lloc, hi ha una creixent preocupació sobre la normalització, l'exactitud, la utilitat, i la interpretació dels resultats proporcionats per les proves genètiques directes al consumidor. En segon lloc, les proves genètiques haurien d'estar restringides per prescripció mèdica i per tant, hi ha una necessitat urgent de capacitar professionals de salut per a què siguin capaços de proporcionar assessorament genètic específic. En tercer lloc, les proves genètiques impliquen una nova dimensió de l'ètica de la privacitat, ja que els resultats obtinguts poden afectar als familiars i, en particular, a la descendència del pacient. D'altra banda, també poden donar lloc a noves formes de discriminació genètica o econòmica. Tots aquests factors s'han de tenir en compte per tal que les expectatives del públic en general respecte la medicina personalitzada siguin més realistes.

Paraules clau: medicina personalitzada · proves genètiques · factors de risc · assessorament genètic · discriminació genètica

Summary. Most of the ethical, legal and moral questions that result from the concept of personalised medicine are deeply related to genetic testing. Firstly, there is an increasing concern about the standardisation, accuracy, usefulness, and interpretation of the results provided by direct-to-consumer genetic testing. Secondly, genetic testing should be restricted by medical prescription and as such, there is an urgent need to train healthcare professionals so that they are also able to provide specific genetic counselling. Thirdly, genetic testing involves a new dimension of ethics of privacy, because the results obtained can affect your relatives and in particular your offspring. Furthermore, it can also lead to new forms of genetic or economic discrimination. All these factors should be taken into consideration so that the expectations created within the general public with regard to personalised medicine are more realistic.

Keywords: personalised medicine · genetic testing · risk factors · genetic counselling · genetic discrimination

Most of the ethical, legal and moral questions that result from the concept of personalised medicine are deeply related to genetic testing. On the other hands the greatest potential for medical advancements in personalised medicine is the development of new pharmaceutical drugs for people with a particular genetic makeup. When addressing the bioethical challenges in personalised medicine, we can draw a parallel and learn from the ethical debate on direct-to-consumer genetic testing.

Over the past ten years, since the completion of the sequencing of the human genome, there has been an explosion of websites offering direct-to-consumer genetic testing. As a result, there is an increasing concern about the usefulness of such tests in providing relevant clinical information for the general public. What about the accuracy of genetic testing? What standards do we have for their evaluation? Academic scientific research laboratories and professional healthcare providers only conduct a few, 30 to 35, standardised well-established genetic tests. However, we can find at least 2700 genetic tests available for purchase online [4]. Moreover, there is a huge variability between results from tests purchased online. Direct-to-consumer genetic testing has created unrealistic expectations that may induce to confusion and anxiety, because in addition to this huge variability between the websites or labs offering these services, there is a bigger problem related to the interpretation of the results of these tests based on the knowledge we have at the moment, and the absence of genetic counselling, which is not provided by the testing companies.

Most genetic risks claimed in direct-to-consumer genetic testing are very uncommon. So, there are genetic risk factors that are not relevant in the clinical setting. The products of even the most reputable companies (Navigenics, 23andMe,

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deCODE) can show marked differences in the calculated relative risk for individuals. Moreover, a genetic risk factor might not be the determinant for the development of a particular disease. We know that there are people with a particular genetic risk factor that will never develop the disease while others, without this genetic risk factor, may develop the disease due to other risk factors, such as environmental factors, occupational exposures, cholesterol, obesity, etc. If we wish to offer patient-tailored treatment planning, we should recognise that there is 'intelligent life' beyond the genetic tests.

Genetic testing should be restricted by medical prescription and as such, there is an urgent need to train healthcare professionals in genetics, so that they are able to provide specific genetic counselling. This is already the case in many European countries. For instance, in France, Germany, Portugal, and Switzerland direct-to-consumer genetic tests are illegal and only physicians can carry out genetic tests for medical purposes after providing adequate information to the patients about the implications of the finding and their limitations. France, in particular, foresees fines of up to 3000 or 4000 €. Still, the reality is another, because little can be done to stop European consumers from purchasing direct-to-consumer genetic testing through websites in the United States, for example, and then receiving the results at their own homes.

The third issue that comes out from direct-to-consumer genetic testing, particularly relevant in the case of personalised medicine, is related to the privacy and safeguarding of our personal and private information. When sending your biological samples to different online repositories, you run the risk of being identified. Genetic testing involves a new dimension of ethics of privacy, because the results of genetic testing can affect your relatives and in particular your offspring. And this is one of the biggest challenges to overcome in personalised medicine.

Personalised medicine can also lead to new forms of discrimination. For example, certain genotypes are much more prevalent in some ethnic groups. Imagine that to recover the development costs of a particular drug, pharmaceutical companies targeted the development of new drugs for the most prevalent genotypes, and the ones that best respond to treatment. Thus, a large fraction of the world's population might be left out in the development of new treatments, since companies will naturally favour those groups with genotypes that hold the potential for more profit. This is a very theoretical scenario, but it is something that we should consider. Similarly, insurers or employers could also use ethnic categories to lower healthcare costs by discriminating against patient groups who are labelled as difficult to treat, based on their pharmacogenomic profile. Again, this is a very theoretical scenario, but I think it is important to consider these possible new forms of genetic discrimination.

In addition, there is a real risk of economic discrimination. The potential profits resulting from genetically tailored drugs will probably be reduced because the market is much smaller, however, pharmaceutical companies will still need to make large investments to develop these drugs. Thus, we can predict that personalised drugs will be more, at least as expensive, if not more, as the standard ones. So who will be able to pay for them? Perhaps we should think of the consequences of a scenario where only the rich people or the rich countries, have the access and can afford the new personalised drugs. In my opinion the expectations regarding the clinical relevance of personalised medicine are excessive, have been greatly exaggerated and are highly unlikely to be accomplished in the short term.

There are several lobbies behind the topic of personalised medicine, scientists, pharmaceutical companies and genetic testing labs, which sometimes results in contradictory opinions about the future of personalised medicine. For example, some authors think that in contrast to the profusion of genetic testing companies, we should expect that the large pharmaceutical companies step up their development of personalised drugs very quickly. There are pharmaceutical companies that are reluctant to move to this other world where it would be more complicated to sell the pharmaceutical drugs to different national health services, compared to when they have a 'blockbuster,' a one-size-fits-all drug, where you can get a lot of revenues, independently of whether this drug works exactly the same in the different populations. This is why some authors think that the pharmaceutical industry will be reluctant to adapt immediately to this new world, because that would reduce the market size and the associated profits to the aforementioned one-size-fits-all drugs.

To finish, I would like to give you a brief review of state of personalised medicine in clinical practice. According to the Personalized Medicine Coalition website [2], there were "72 prominent examples of personalised medicine drugs, treatments and diagnostics products available in 2011." This is simply not true. The Food and Drug Administration (FDA) lists 78 different pharmacogenomic associations that are included in drug labels [1], however, more than 60 of these drug labels do not provide action-oriented information for physicians and patients, and these pharmacogenomic associations are for the most part research-based and with no clinical use at present.

As you know, we do not know how to appropriately interpret the results from genetic testing, and as such, many genetic tests are not relevant for the course of treatment. At present we have only a few very good examples in the field of oncology where, for instance, particular genetic tests can indicate the best course of treatment.

If we take all this into consideration, the expectations created within the general public will be more moderated, and we would also reduce the absurd consumption of genetic testing in websites that do nothing but can lead to confusion and anxiety. We should help people to better understand and better interpret what really is happening with the new developments and breakthroughs in science and how they really work.

In conclusion I think we should follow the conclusions of a 2005 report from the British Royal Society entitled Personalised medicines: hopes and realities [3]: "the clinical use of personalised medicines where patients are prescribed treatments based on their genetic make-up will not occur for at least another 15–20 years." Or even ten more! In any case, I think that personalised medicine is a very good endeavour

and that will help us to understand our lives. However, in practical terms, we should be very cautious regarding the expectations and promises of this new mantra.

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