Drug Discovery Today: Therapeutic Strategies
Vol. 10, No. 4 2013

Personalized medicine

Ethical issues in personalized medicine

Ruth Chadwick

Cesagen, Cardiff University, 6 Museum Place, CARDIFF, CF10 3BG Wales, UK

The search for personalized medicine is not a new phenomenon, but it is only with developments in genetic knowledge – and pharmacogenomics in particular – that the 'personalization project' stands a realistic chance of improving health on a wide scale. Despite recent advances, the risk of hype is still present, as can be seen by expectations and claims surrounding direct-to-consumer genetic testing. The move towards personalized medicine may disadvantage some patients in some social contexts, by shifting the allocation of resources in the health care system. Risks also surround the increasing accumulation of health data that goes hand in hand with personalized medicine: a study has been able to identify individual research participants from stored genetic data.

Section editor:
Steve Holgate – Faculty of Medicine Clinical and Experimental Sciences, Southampton General Hospital, Southampton, UK
Barbara Prainsack – Department of Social Science, Health and Medicine, King's College London, London, UK

Introduction

Thinking about the ethical issues associated with the objectives and practice of personalized medicine requires us to think clearly about what is meant by 'personalization'. Close inspection of this term reveals multiple possible meanings, although there is arguably a core meaning which appears to have arisen alongside the development of pharmacogenomics. The very concept of 'personalization' seems to be already imbued with ethical associations, appearing to reinforce an individualist paradigm in ethics, although it may emerge that the choice of terminology between 'personalization' and 'individualisation' is significant. It will also become clear, however, that 'personalization' is related in interesting and different ways to concepts of responsibility. On the one hand personalization may be perceived as a 'project' which increases responsibility for the individual [1] and personalized medicine fits into that. By contrast, personalization, in so far as it requires 'big data', puts responsibilities on those who curate the data.

In addition there is a host of other ethical issues raised by personalized medicine, relating to: problems of hype; allocation of health care resources, both intra- and internationally; issues related with perceptions of different social groups; issues of implementation; issues related to control of data.

What is personalization?

Although the concept of personalization in medicine has to a considerable extent become associated with genomics, it may be helpful to remember that there is a longer history in which debates over personalization in a wider sense have taken place. For example, the debates over treating the patient *as* a person with beliefs and wishes, and respecting patient autonomy; the difference between treating 'symptoms' and treating the patient as a whole person; the perception of medical practice as the application of professional judgment to the individual case – all these could be interpreted as aspects of personalization [2].

Personalization really came into its own in a technical sense, however, as interest increased in pharmacogenomics. Although the latter had been implemented to some extent since the mid-twentieth century, it became high profile as an issue from the late 1990s onwards. The central idea of pharmacogenomics, of prescription being informed by

E-mail address: (ChadwickR1@cardiff.ac.uk)

 http://dx.doi.org/10.1016/j.ddstr.2013.05.001

information about the variation in genetic make-up between individuals, introduced a specific sense to personalization: in effect, personalization became 'geneticized'. The purported ethical imperative driving this was underpinned by an argument about the need to reduce the incidence of mortality and morbidity resulting from adverse drug responses (ADRs). It should be noted that although personalization may suggest avoiding harm to and increasing benefit for the individual, there is a clear public health argument here. Personalized prescribing could be genetically informed not only in relation to the choice of drug, but also as regards dosage. As has been pointed out in the literature, however, it might be more accurate to call such a strategy 'stratification' rather than 'personalization' [3] – dividing the population into different groups such as good and poor responders.

While such patient stratification may be important and desirable from an ethical point of view, in so far as it is likely to produce less harm and more benefit as a result of medical intervention, it seems a somewhat awkward account of what it means to 'personalize'.

With the advent of whole genome sequencing (WGS) the possibility of 'tailoring' medical advice and treatment to the individual throughout a lifetime becomes at least an in principle possibility, although the term 'tailoring' was used by the UK Department of Health in 2003, before WGS was on the horizon [4]. Under this vision all the multiple variations between individuals could be taken into account. The use of the tailoring metaphor is interesting. In the clothing industry there is of course a distinction between clothes tailored for the individual, and those ready to wear for the mass market, and it might be tempting to think that this mirrors the distinction between personalized and blockbuster approaches to pharmaceuticals. However, within tailored clothing there is also a distinction between 'bespoke' and 'made to measure'. Whereas 'bespoke' clothes are created without the use of a pre-existing pattern, 'made to measure' alters a standard-sized pattern to fit the customer. The move from genetic testing to WGS arguably suggests a move from 'made to measure' to 'bespoke'. There is a caveat here, however, and that is that the word 'bespoke' comes from 'bespeak' which suggests that the individual is in control of the process. This may be where the analogy between personalized medicine and tailoring breaks down, as we shall see when we come to discuss implementation.

It is important not to overlook the fact that although the ethical argument for personalized medicine was initially to prevent ADRs, and thus the argument for it deemed non-controversial from that point of view, once a richer version of tailoring comes on stream attention also inevitably turns to benefits. The issues then include not only 'how can we prevent harm to this person,' but 'how can we maximise the benefit?' And that becomes increasingly complex when allocation decisions have to be made [5•].

More recently a new form of personalization has emerged, relating not so much to the variation in the genetic information of the patient *per se* affecting drug response, but regarding the *disease-type* of the patient. Accessing the particular genetic factors at work within tumours, for example, shows us that 'cancer', of the breast or otherwise, is not just one disease: there are many subtypes. So analysing the genetic make-up of the tumour of a patient also divides the patient population into different types, but according to their condition rather than by factors affecting predisposition or response.

The difference between personalization according to genetic factors affecting response to particular drugs and factors informing the specific disease type may not always be clear, as can be seen from research in the variation in response to asthma medication [6]. One in seven asthma sufferers has a genetic variant – the arginine-16 genotype of the beta-2 receptor. In a study carried out by researchers in Brighton and Dundee in children, all of whom had this variant; half were given salmeterol and the other half montelukast. Those on the latter responded better. Although the report stated that more research was needed before a genetic test for Arg16 should be implemented, this is suggestive of a personalized medicine approach for children with asthma. The Department of Health commented, however, that asthma itself is increasingly being thought of as a group of conditions rather than a single disease:

> By looking at specific genes in people and finding out their specific genotype, patients may, in the future, be able to use medicines that are precisely targeted to their own type of asthma [7].

Problems of hype

The history of developments in genetics offers precedents in which new developments appeared to promise much, only to disappoint, at least in the early stages. The troubles faced by gene therapy provide a good example. Similarly, there is a worry that it may not be possible to fulfil the promises for personalization, at least not for a long time. The possible pathways to personalization appear to have more twists and turns than was originally anticipated.

It has become increasingly clear that there are multiple gaps in our understanding of the factors affecting gene expression. Research in epigenetics and metabolomics is producing information about how an individual's genome interacts with diet, lifestyle and other environmental triggers [8]. Speaking of reconstruction model of the human metabolome, co-author Pedro Mendes commented:

> 'The results provide a framework that will lead to a better understanding of how an individual's lifestyle, such as diet, or a particular drug they may require is likely to affect them according to their specific genetic characteristics. The model takes us an important step closer to what is termed 'personalized medicine', where treatments are tailored according to the