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PERSPECTIVE

The collective nature of personalized medicine

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Summary

Precision medicine, incorporating personalized medicine, is an emerging medical model that holds great promise for improving the prevention, diagnosis and treatment of many diseases. The future success of precision medicine, however, depends on the establishment of large databases that collate diverse data, including family genealogies, disease histories, drug sensitivities and genomic data. Herein I raise some of the social and ethical challenges that such a system faces, specifically: the enrolment of volunteers into large genetic databases; the need for a change in mindset of clinicians, patients and the wider public; and the need for interdisciplinary ethics considering the emerging issues. Finally I argue that the future potential of 'personalized' medicine crucially depends on 'collective' participation of informed citizens.

Introduction

Precision, stratified or personalized medicine denotes emerging medical models that use molecular diagnostics, genetic sequencing, cellular analysis and pharmacogenomics to tailor individual healthcare treatment and prevention. By taking genetic, environmental and lifestyle factors into account, and by relying heavily on big data analysis, precision medicine aims to identify risk factors and biomarkers that predict health outcomes and help choose the best treatment for the patient. Recent advances in the speed and efficiency of genetic sequencing technologies mean that clinicians will very soon be able to quickly and cheaply obtain the full genomic sequence and transcriptome of their patients. Genomics is thus becoming central to the development of an effective system of 'personalized' medicine.

Herein, I raise three issues that need to be addressed in the development of personalized medical models: the need for large genomic databases; the need for a change in 'mindset' of clinicians, scientists, patients and the wider public; and a need for interdisciplinary ethics considering the emerging issues. I conclude that much of the potential efficacy of 'personalized' medicine actually depends on 'collective' participation.

Precision medicine

The recent technological advances in genomic sequencing power have precipitated significant precision medicine projects by major states. In 2012 the UK Prime Minister David Cameron launched a GB £300-million 5-year initiative to sequence 100 000 genomes from UK National Health Service patients with rare disorders, cancer and infectious diseases (Marx, 2015). Similarly, US President Barack Obama announced early in 2015 that he aims to launch a US$215 million effort that will couple patients' physiological and genetic data to improve the 'precision' of individual treatment (Reardon, 2015). Comparable projects are also under way in Australia, Japan, Canada, Singapore, Kuwait, Qatar, Israel, Thailand, Belgium, Luxembourg, Estonia and South Korea. The medical benefits entailed by these ventures could be great, but the impact on the way healthcare will be practiced in the 21st century has yet to be fully comprehended.

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Furthermore, 'precision medicine,' it has been argued, 'is much more than just genetics' (Lewis, 2015). While it is thought that precision medicine will also lead to the 'prevention' of many diseases, such data gathering efforts will also likely lead to new therapeutic strategies, entailing new ways of thinking about the role and experience of the patient. This will change the limits of disease experience, such as what counts as healthy or unhealthy, and at what point medical intervention is recommended. Likewise, the way disease categories are taxonomized will also change (National Academy of Sciences, 2011; European Science Foundation, 2012). For example, in the future, diseases might become taxonomized on the basis of the underlying genes or variants rather than on a similarity of symptoms.

Databases

The future success of precision medicine now depends less on technical and scientific advances than on ethical and socio-political developments. A prerequisite for meaningful and statistically significant genetic readings of patients, and the implementation of useful pharmacogenomics databases, is the voluntary participation of healthy populations. Large-scale genetic database projects are crucial to the bridging of individual molecular genetic readings with clinical diagnostics. This in turn will reveal how the diverse genetic makeup of populations relates to individuals' varying responses to treatments. This means that massive databases will need to be established, collating family genealogies, disease histories, drug sensitivities and genomic data in an integrated system. It is also becoming more common in cases when a family member is ill that healthy relations are also sequenced, or in some cases asked to act as treatment 'controls,' to help identify the pertinent genetic factors. However, to make the system of precision medicine work better, quality long-term medical records and oral family medical histories will be essential to meaningfully amalgamate clinical, historical and genetic data.

Mindset

The transformation of healthcare from treatment to prevention therefore necessitates a major change in the mindset on the part of clinicians, scientists, patients, close family members and the healthcare industry in general. Accordingly, in his recent editorial, '*Prioritizing personalized medicine*,' Noam Shomron (*Genetics Research*, Editor in Chief) reported Michael Hayden's (TEVA Pharmaceuticals) assertion that the major challenge facing personalized medicine is in fact the 'reversion of healthcare from treatment to prevention' (Shomron, 2014). Hayden pointed to the potential of next generation sequencing to be a major boost towards the development of personalized medicine, but emphasized that healthcare providers still need to embrace the 'idea' that genetic information is an important part of medical treatment.

The success of personalized medicine, and the building of large-scale databases with the collective and voluntary participation by both patients and healthy citizens, depends precisely on such a change in 'mindset.' Collaboration between clinicians, patients, scientists and the broader public on these matters could help bring about this change. Furthermore, wider public engagement in debate and decision-making could also help extend the range of stakeholders and decision makers involved, thereby improving what has been called good 'citizen science' (Prainsack, 2014 *a*). This, in turn, could help encourage voluntary enrolment in data collection and biobanking efforts.

While the benefits such databases will usher forward may still be unknown, and perhaps at this point inestimable, some of the problems that such collective projects raise are already very clear: genetic privacy; the ethics of data sharing; the impact on health insurance; the rise of medical 'risk' status; and the psychological effects on people and close kin, particularly if they are informed that they are carrying a pernicious risk factor.

Ethics

Genetic databases raise serious ethical dilemmas for clinicians and scientists. For example: What is the social nature of the 'individual' person in their community (Prainsack, 2014 *b*)? Who owns genetic data? What are the risks of sharing family data? What will be the negative impact of unearthing latent, but potentially negative, genetic data? Will the human genome be broken into regions or families of genes, weighted differentially and dynamically, according to their known significance? And, what are the legal or 'bioconstitutional' (Jasanoff, 2011) provisions for participants who may wish to withdraw their personal, or relatives', medical genetic data later on (Gurwitz, 2015)?

While personalized medicine certainly needs large databases to make sense of the complex workings of the human genome and proteome, to initiate large-scale data collection without sustained consideration of these social, legal and ethical issues would be irresponsible and possibly counterproductive. Clinicians and scientists must therefore also make collaborative efforts with bioethicists, social scientists and citizens, and forward a robust interdisciplinary research program on these important issues.

One way to tackle these kinds of ethical concerns is to make comparisons with historical precedents and to study the analogous consequences. There are many suitable comparisons, and perhaps even models, to

aid the design of genetic databases for personalized medicine. For example, a voluntary blood donation system has been established in Israel. Under this plan, individuals who elect to donate blood receive a government identity card assigning them priority to receive future emergency blood donations (https://www.mdais.org). There is also a similar system in place in Israel for organ donation (Mor & Boas, 2005; http://www.declarationofistanbul.org/resources/legislation/267-israel-transplant-law-organ-transplant-act-2008#), called the 'Adi card' (https://www.adi.gov.il). The signing of an Adi organ donor card expresses the willingness of the holder to donate their organs after death, so as to help save the lives of patients waiting for an organ transplant. The names of signatories to the Adi card system are deposited in a confidential database, and possession of a card grants priority to the holder on the transplant waiting list, and also to their close relatives, should they need a transplant.

Both these donor systems merge neoliberal market logics (foregrounding individual choice) with altruistic values and the participatory ethics and solidarity of a collectivist society. That is to say participants gain the option of personally benefitting from their contribution, but it nonetheless remains more likely that individual contributions will help others. These systems may be exemplars for designing personalized medical models, in which individuals could volunteer personal data in order to be accorded both direct benefits, by way of access to personal health assessment, and indirect benefits, by helping the wider community become healthier.

One way to spur genetic database enrolment could be the establishment of a similar democratic 'opt-in' membership modelled on the Israeli donor systems, whereby individuals can chose to share varying amounts of their genetic data. Allowing citizens to choose whether they participate empowers individuals, and may also cause more people to become more educated about the stakes (Sunstein, 2015). To encourage participation, staggered reciprocal benefits could be afforded to those members who chose to disclose varying degrees of their personal data.

The collective nature of personalized medicine

It becomes clear that much of the potential efficacy of 'personalized' medicine actually depends, paradoxically, on widespread 'collective' participation. If healthy individuals do not also collectively volunteer their genetic data, and likewise open their medical records and personal data for meaningful comparison, attempts to make robust statistical associations on an individual genetic level may be in vain, since there might not be sufficient data to make valid conclusions about the role of genetic markers in disease aetiology or optimal treatment.

On the other hand, individual patients and citizens may have objections against sharing their data, perhaps due to scepticism or fear of impending changes in the way medicine is practiced. With the advent of personal genomics and deep sequencing, we can only expect a rise in the number of identifiable 'risk factors' and prophylactic medication on that basis. One legitimate public concern is that the emerging logic of 'prevention by treatment' could go too far, and whole populations could become overmedicated for 'risk' (Rajan, 2006) with millions of people being put on multiple long-term prescriptions for life (Dumit, 2012). That said, personalized medicine still holds real promise, especially for rare genetic 'orphan' diseases, which have generally been neglected by the mainstream pharmaceutical industry, and which need and deserve more attention. Furthermore, as people are now living for longer, the impact of neurodegenerative and autoimmune diseases (diseases of ageing) will only become greater. In this regard, genetic predispositions for late-onset diseases will also become more important as we enter the age of risk and prevention.

Conclusion

Personalized medicine is on the horizon and it holds great potential, especially for the development of novel therapies for rare genetic disorders. The potential of personalized medicine depends, however, on secure databases and elective participation by large populations. One of the greatest challenges will be the human engineering of pulling citizens together and inculcating the informed interest and responsibility to volunteer their data to databases. The core challenges facing the development of an effective system of personalized medicine are thus neither technical nor scientific; rather they are now social, political and ethical. The future of personalized medicine depends, crucially, on collective participation.

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