Final Statement on The Revolution of Personalised Medicine

Concept

During our workshop on Personalized Medicine, three conceptualizations of the term emerged. The first fits the NIH's definition: "A form of medicine that uses information about a person's genes, proteins, and environment to prevent, diagnose, and treat disease". This wording relies on ordinary notions of "disease", "treatment", "patients" and "research".

However, even within this gradualist framework of increased precision in medical science, we see some reshuffling of established nosologies. One example is the titles "coma", "vegetative state" and "minimally conscious state". New neuroimaging techniques have exposed huge variations in brain functioning among seemingly similar patients. Hence, personalization is about uses and processing of biological signals from individuals in order to redefine and classify states of health and disease.

The second conceptualization of personalized medicine is a new approach to "people", not necessarily "patients", who undergo comprehensive and continuous collection of genomic, proteomic, omics, microbiome and lifestyle related data in order to optimize "wellness" by means of early detection of "abnormalities" that may cause or lead to disease. The biochemical, genomic and lifestyle measurements empower the individual to optimize his or her wellness by acting upon "actionable possibilities" originating from the analysis of the collected data.

Because everybody is invited to participate in continuous monitoring, this new approach to people breaks away from the traditional notions of “disease”, “patient”, “treatment” and “participant in research”. It also adds new terms and roles, such as “quantitative wellness” and “wellness coaches”. This second conceptualization relies on identified actionable possibilities derived from established scientific publications and those that emerge from the integration of different data types. This form of personalized medicine is especially pertinent to people coping with a serious health crisis, such as cancer, and need organization of relevant information to reduce the gap between their personal life and the vast ocean of medical knowledge.

Many action items are quite cheap, such physical training and food supplements. Reliance on coaching by lay healthcare workers, who receive basic training, is a well-established practice in primary care and public health (e.g. “barefoot doctors”).

Because biomedical knowledge is exponentially growing, artificial intelligence is key to optimizing the benefits of biomedical knowledge by indicating the action items relevant to every individual. Additionally, “deep machine learning” (non-symbolic artificial intelligence) analyses the large sets of data to create novel hypotheses that can be tested experimentally. Many of these experiments will have to be “one patient trials”, that compare the biometrics of the relevant patient with an intervention (e.g. a special diet for a few months) and without it.

According to the third conceptualization, ongoing bio-tracking and collection of data from a growing number of participants and for longer periods of time – perhaps the whole life-cycle – will gradually reveal a new dimension of knowledge that is independent of clinical trials and laboratory work. This “knowledge” emerges from the correlations produced by artificial intelligence between input (i.e. data) and output (i.e. predictions and action items), even without understanding the links. Such an achievement depends on near universal and equal participation (everybody yields to the same kind of comprehensive monitoring) to come up with personalized predictions and advices. Even though enterprises at this level do not take place yet, many healthcare services and research practices already collect, store, trade and process data (often following “anonymization”) in preparation for such a future.

Science

Personalized medicine promises to transform medicine. There are three caveats to this claim. The first pertains to feasibility. Whereas the treatment of some diseases has indeed been revolutionized by targeted treatments (e.g. lung cancer and melanoma), most chronic diseases (e.g. atherosclerosis, schizophrenia, obesity, osteoarthrosis) are complex and will require multimodal therapies.

The Human Genome Project had led to a vast range of scientific discoveries, including identifying the genes responsible for more than 7,000 single-gene diseases and far more than 100,000

genetic loci that contribute to thousands of common polygenic diseases and traits. However, it remains frustratingly challenging to convert such discoveries to cures. Though cumulatively quite common, each individual single gene disease affects a sliver of humanity (generally less than 1%), and the miniscule contribution of every genetic locus to human afflictions sets limits on our capacity to infer cures from the genetic code and to estimate their ultimate impact (size effect).

The second set of caveats points to many sources of bias, especially in relation to population selection and gender. Research has demonstrated that “learning machines” often “learn” human prejudices and incorporate them in their outputs. Understanding human “wellness” calls for attention to vulnerable phases of the life cycle, such as pregnancy, childhood, ageing and disability. The proposed moratorium on human germ-line editing embodies lack of knowledge about the long-term impact and procreative effects of personalized genetic interventions on future generations. Limiting research to animal germ-line manipulation, seems an appropriate interim step at least until regulation of biotechnology matures at the levels of international and national law.

Physicians’ wisdom, fidelity and interpersonal skills are key to integrating patients’ words, culture, and behavior in clinical care. There is a huge gap between Artificial Intelligence’s powers to compute biological data and its capacity to integrate the humane dimensions of health and healthcare. Because blood samples or even behavioral data via digital sensors are easy to obtain, store and process, there might be a tendency towards this venue of analysis and conceptualization, at the expense of more demanding methods of study and less quantifiable data and concepts.

Lastly, we do not know yet when information technology can provide the desirable data protection, and service stratification. Beyond the technological challenge, this issue depends much on the regulatory environment and on the courses of justice open to participants from low and middle-income countries.

Overall, better understanding of relevant regulatory levers and their intersection is required to facilitate the translation of personalized medicine to the clinic safely, efficiently and for the benefit of patients and their families and communities. Currently, the law relating to these matters ranges across the full gamut, from outright prohibition to more permissive approaches. Countries must decide, collectively and individually, what approach to adopt.

Ethics

The survey of ethical issues will develop from concerns that are less specific, to issues that pertain to personalized medicine as such.

Among the less specific but more pressing issues is the governance of biomedical data in relation

to privacy and property rights. The more technology-intensive a medical service becomes, the more susceptible it is to monopolies, licensure of intellectual property and market failures. Contemporary medical research is ever more dependent on government grants and contracts as well as on the solicitation of high-risk capital. The ensuing burden to turn a profit boosts the prices of drugs in niche markets. The inflationary language and unbridled optimism of entrepreneurship may not square well with clinical reality.

Socio-economic gaps, in which gender, ethnicity and political helplessness play major roles, are the fundamental and universal causes of morbidity and mortality. In this respect too, personalized medicine initiatives, whose information technology is not open-source code, pose serious scientific, epidemiological and regulatory challenges. Moreover, retention of intellectual property might bar healthcare providers, the academy and the biomedical industry from essential access to data culled by *omics* operations, with the risk of aggravating social inequalities even further. Considerations of “cost effectiveness” depend much on the regulation within which “costs” are set and against what criteria “effectiveness” are evaluated. In order to build itself on-top of public health, personalized medicine and its public sector spearheads should strive to rely on building blocks from the public domain and to preserve people’s power over their own data.

Personalized medicine’s explicit goal of sparing side-effects from patients who are unlikely to respond to treatment must not be accompanied by exclusion of patients who are less likely to respond. The decisions on which chances merit effort are moral and political. Statistical scores must not be the only factor determining the right to receive care.

Digitized medicine may help physicians concentrate on the humane aspects of care by saving much labor and time. However, clinicians need to catch up with medical knowledge, the intricacies of statistics, and skills of interacting with “thinking machines”. There is an urgent need for new approaches in healthcare education and in improved literacy of computer mediated decision-making. Without this education, scientists, physicians and patients alike will not be able to participate in the development, governance and proper use of personalized medicine.

The promissory power of prediction might label people by the medical conditions they are at risk of developing. Hence, not only do patients need education in relation to their own healthcare, but the public at large also needs education about the meaning of “predictive risk”, lest it turns into an oracle of exclusion and stigmatization. Prediction should empower people to act in promotion of their own health and in the benefit of the vulnerable, allowing patients suffering from rare conditions to extract themselves from clinical and political isolation.

Lack of education and deep participation may deteriorate into alienation at four fronts. The first is erosion of doctor-patient trust. The more personalized medicine develops in the direction of its third conceptualization, the higher is the risk of weakening “clinical judgment”, “second opinions”, “differential diagnosis” and similar key elements of care. Today, clinicians evaluate lab results in

light of the patient's story, physical exams, and imaging studies. When clinicians receive prescriptions from one gigantic and all-inclusive algorithm, they might be less skeptical, less attentive to clinical hunches and less cautious in their decisions. This and other considerations support a stratified approach that grants legitimacy to people who prefer to live a life of lower intensities of surveillance, digitization and medicalization, without affecting the quality of standard care.

The second alienation is internal. The digitization of life and the medicalization of data may alienate persons from their experience of life, parenting, illness, handicap and dying. It is about alienation of the autonomous agent from the experience of self-care and of being in command of one's body. People may "share" data and interact with healthcare with no apparent symptoms and signs. They may adhere to computerized goals of "wellness", feeling neither need nor opportunity to reflect on the nature of health and good life. Chronic patients are already having difficulties with adherence to medication and basic action items (e.g. diet). The addition of monitoring and action items might be beyond the capacity of many people to juggle.

The third alienation might develop between people and the human institutions that own, design and run "personalized" health programs. From Genome Wide Association Studies, we have learnt that in order to capture disease-relevant mutations, very large number of participants must be studied. The boundaries of the "system" in focus (e.g. the body, family, societies, economies) and the scientific lenses scrutinizing it are value-laden choices. Developers of personalized medicine must reflect on the values involved, not allowing medical science to be locked in a kind of "engineering mindset" and to be drifted wherever the winds of the market blow.

The fourth alienation may develop between disadvantaged people, whose data contribute to the common healthcare cloud, and their lack of resources to act upon the advice personalized medicine would give them. Moreover, many people, whose data is needed for the databases, live outside the jurisdictions where personalized medicine's information technology centers operate, thus having limited power in terms of participation in democratic regulation.

These alienations are exacerbated by a reconfiguration of fundamental concepts of health and health care that have been with us for a long time. First and foremost, personalized medicine caters to the healthy as much as to the sick; it also blurs the distinction among clinical standards, experimental care ("off-label"), experiments on healthy volunteers, and clinical trials. If every "participant" is a "patient" with a personalized set of risks and advises, we might lose our commitment to prioritize the sick as a special category of needy people. Instead, every person will be preoccupied with his or her own unique set of risks and promises. Personalized medicine might inform every person (and all those who access the data) about the level of relative risk this person carries to every disease and outcome, thus blurring further the distinction between the healthy and the sick, and between conditions people have, and things that might happen to them. People will know more about themselves but will be less confident about the practical meaning of that

knowledge. Put in other words, having more information may not entail knowing more. For a better integration of personalized medicine in human cultures, the concept of “wellness” had better develop in relation to WHO’s definition of health, and to moral traditions.

Genuine participation includes the capacity to engage with others in the shaping of society, its governance, its values and its most ambitious enterprises, such as personalized medicine. It is about personal responsibility for the common good, especially for the needy. Personalized medicine’s vision is about optimizing the health of each and every single individual. The “personal” always includes interpersonal relationships. This capacity to act responsibly for others is essential for human wellness. Personalized medicine’s focus on the human genome highlights the capacity of every human to create family relationships with every other human, and the capacity to offer personalized care for every other human on the basis of shared public goods, communal webs of support, and personal responsibilities.