



The Impact of Personalised Medicine and Genomics on the Insurance Industry

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What is Personalised Medicine?

Personalised medicine tailors medical treatment to the individual characteristics of each patient. This has long been an ideal in different forms and paradigms of medicine – to focus not only on the disease but also on the person. But new technological developments are now making it possible to make treatment far more personalised than it has ever been. This approach is dependent on understanding how a person’s molecular and genetic profile makes them susceptible to certain diseases. Genomics enables doctors to better understand why some people get sick from certain infections, environmental factors and behaviours, while others do not.

The National Human Genome Research Institute described genomics as follows¹:

Virtually every human ailment has some basis in our genes. Until recently, doctors were able to take the study of genes, or genetics, into consideration only in cases of birth defects and a limited set of other diseases. These were conditions which have very simple, predictable inheritance patterns because each is caused by a change in a single gene. ... (now) scientists and clinicians have more powerful tools to study the role that multiple genetic factors acting together and with the environment play in much more complex diseases. These diseases, such as cancer, diabetes, and cardiovascular disease constitute the majority of health problems in the United States. Genome-based research is already enabling medical researchers to develop improved diagnostics, more effective therapeutic strategies, evidence-based approaches for demonstrating clinical efficacy, and better decision-making tools for patients and providers. Ultimately, it appears inevitable that treatments will be tailored to a patient's particular genomic makeup. Thus, the role of genetics in health care is starting to change profoundly and the first examples of the era of genomic medicine are upon us.

Equipped with advanced, more precise and affordable technology, doctors can now treat patients based on their unique molecular profile while minimising harmful side effects. Personalised medicine also enables early detection of the onset of disease and pre-empts the progression of disease. Personalised medicine thus has the capacity to improve health outcomes and reduce costs compared to the traditional “trial-and-error, one-size-fits-all” prescription. The efficiency and efficacy of the healthcare system as a whole will be enhanced as the quality and affordability of care is improved.

An example of the application of personalised medicine is in respect of breast cancer. Identification of BRAC I and II genes improved early detection of breast cancer. Further, certain patients have a form of breast cancer that over-expresses a particular protein which is not responsive to standard therapy. A treatment has been tailored to specifically treat these patients, significantly improving health outcomes.

¹ <https://www.genome.gov/18016863>

However, personalised medicine is not only about genomics. Personalised medicine should also in theory incorporate any information about the patient that would be relevant to their health status. For example, personalised medicine should integrate data on health behaviours and choices such as data from fitness devices, home monitoring devices for chronic conditions, data from electronic health records, and so on.

Personalised Medicine is attracting serious attention at many levels internationally. For instance, the NHS in the United Kingdom is developing a strategy on Personalised Medicine, and has released some information on their thinking².

The Future of Genomics

The evolution of personalised medicine has been mainly driven by advances in genomics, and in particular the advances in genome sequencing, the process used to map the human genome. Potential application areas of genomics, and particularly genome sequencing, include:

- Clinical diagnostics – for example, non-invasive prenatal screening to detect Down Syndrome and other defects
- Drug discovery – understanding disease pathways and the potential of targeting genes greatly improves the speed of new drug discovery, and the efficacy and side effects of the potential drugs
- Biomarkers – used to identify the prevalence of particular diseases
- Pharmacogenomics – personalised drug treatment protocols

The dramatic decrease in the cost of genome sequencing for an individual, falling from \$2.7 billion in 2003 to less than \$1000 today, has exponentially increased access to genetic testing. Experts predict that this cost will drop even further to a few cents by 2020, with the potential of completely revolutionising healthcare.

One of the big challenges until now has been the cost of the computing power required to handle the raw data generated from genome sequencing. This cost continues to decrease significantly, and advances in cost-effectively analysing very large datasets results in advances in Personalised Medicine. Once the cost of sequencing and analysing this genetic data becomes marginal, radical changes will truly begin, with a shift from reactive retrospective medicine to predictive prospective medicine. Recent advances in data science and computing power have enabled more powerful data handling capacity and analyses, and this will continue.

Advances in the field of genomics will also accelerate the practice of predictive medicine, enabling the screening of people in advance (perhaps on the day that they are born), to determine any genetic susceptibilities to diseases, vulnerabilities to cancer, expected longevity and the most effective and ineffective medications for a given patient. Further, new target therapies will pass clinical trials giving doctors greater confidence to administer personalised medicine.

² See, for instance, <https://www.gov.uk/government/publications/personalised-health-and-care-2020>

It is expected that mammograms and colonoscopies will be replaced by blood tests able to identify microscopic tumours, well before the development of cancer. Together with genome analysis, doctors can then determine the most effective form of treatment, with some patients no longer having to endure long and agonising battles against cancer.

Personalised medicine is therefore expected to have a profound impact on the future of healthcare. Genomics promises to deliver healthcare in a proactive, personalised and precise manner, leading to improvement in longevity and higher quality of life.

Challenges of Genomics in Medicine Today

Cost of Genetic Testing

Although the cost of whole genome sequencing has fallen considerably, these tests remain costly and inaccessible to most. However, cost effective alternatives are becoming more and more available, such as restricted screening for specific purposes at different stages of life e.g. at pregnancy or at the onset of cancer. The cost is also likely to decrease rapidly as the technologies develop.

In addition, there is a growing list of companies worldwide offering genetic testing directly to consumers, such as the well-known American company *23andMe*. While such companies may give consumers direct access to genetic testing, some of these tests have been criticised for lack of accuracy as the testing methods adopted utilise limited information, giving consumers an incomplete view of their risk to a particular disease. Further, with this direct access to testing, consumers are able to side step their doctors completely, increasing the risk of misinterpreting results and seeking inappropriate care thereafter. *Genomic Literacy*

In addition to the cost constraints there are other significant constraints that hamper the widespread adoption of genomic testing. Given that this is a relatively new field, doctors may be unfamiliar with how to interpret genomic data. Moreover, the role of most of the genes in the human genome is still unknown or incompletely understood, and much of the information found in a human genome sequence is unusable at present. Doctors may also be hesitant to administer personalised treatment protocols and may prefer to treat based on the results of large existing studies. Further, customised treatments such as personalised chemotherapy remain costly. With high volumes of genomic data included in clinical trials in the near future, this situation will however change rapidly, and doctors may well adapt treatment to the latest findings as and when they emerge.

Ethics

Despite the advancements and proven advantages of genomic testing, there remains a large degree of controversy around the ethics of genetic testing. An individual's genome may contain information that they would prefer not to know. For example, during the process of genome sequencing to identify the most effective treatment plan for diabetes for a particular individual, an unrelated allele may be discovered that indicates a high probability of a terminal disease with no effective treatment, thereby creating psychological distress. On the other hand, people with

family histories of genetic disease already live with similar knowledge, and it is arguable that genetic testing would really fundamentally change the outlook for such people.

Discrimination

Genomic testing could also cultivate a practice of discrimination, particularly in employment and insurance. This applies particularly to predictive genetic tests which are offered to *asymptomatic* individuals to predict risk of disease. Usage of these tests in underwriting is therefore often restricted. This is different than diagnostic genetic testing used to confirm or rule out a known or suspected genetic disorder in a *symptomatic* individual. These tests generally have no restriction when used in underwriting.

While legislation such as the United State's GINA (Genetic Information Non-discrimination Act) passed into law in 2008 provides some protection against such discrimination, the law and regulation will probably have to develop to keep up with emerging science and practice. The way in which such laws develop are likely to have profound consequences for the Life and Health insurance industries.

Privacy and Security

Before institutions or healthcare providers employ genetic testing, precautionary measures must be implemented to curtail the risk of infringements of patient's privacy, given the potential degree of harm (such as financial loss, reputational damage, stigmatisation, psychological distress etc.). Given the vast volume of information contained in a genome sequence, policies and security measures to maintain the privacy and safety of this information are still at early stages. In addition, institutions collecting this data must carefully balance the trade-offs between privacy and the utility of data (for research, administration, commercial exploitation), to ensure individual and collective rights are protected.

Big Data

Given the magnitude of data generated, genomics will be highly reliant on Big Data to store, retain analyse and interpret the data. Big Data systems must ensure data is adequately and safely stored, whilst enabling easy retrieval and access to data. Security measures must be in place to ensure the protection of individuals, companies and societies at large, from criminal activities such as piracy. Further, as advancements in genomics are made, Big Data systems must evolve to handle the increasing complexity of the data, and be able to combine genomics data with structured and unstructured data from other sources. Lastly, physical processes of Big Data systems must be refined to ensure data errors are eliminated, as errors could be life-threatening.

The Impact of Genomics on the Insurance Industry

Anti-selection against insurers

Developments in genetic testing are expected to give people profound insight into their future health status and expected longevity, enabling them to purchase insurance accordingly. This

may expose insurers to a new and potentially detrimental source of anti-selection, which, if not adequately contained, could lead the industry into an actuarial death spiral; where the healthy opt out and the sick opt in, spinning premiums out of control.

This risk could be mitigated in health insurance markets governed by strong social solidarity principles of mandatory membership, open enrolment and community rating. However, in voluntary health insurance markets, and in those which rely on underwriting and risk rating, there are many challenges, particularly if insurers may not insist on disclosure of genetic testing results.

However, in other protection insurance markets, such as Life, Disability, Critical Illness and Long-Term Care, where cover is perceived to be more commercial and optional, this risk of anti-selection could be particularly harmful to insurers. Arguments could be made that family history is already routinely used in underwriting in many markets, and there is no reason why genomes should be treated differently, but it remains to be seen what regulators would allow, and how people's behaviour may change once they have the insights arising from genetic testing.

A report prepared for the Canadian Institute of Actuaries Research Committee³ assesses the impact of this anti-selection on life insurance companies should life insurance companies be prohibited from accessing the results of genetic tests for the purposes of underwriting. The report found that the impact on insurance companies can be substantial, resulting in pricing losses, increased mortality rates and a concomitant increase in premium rates.

On the other hand, in a statement by the Canadian Institute⁴ it is noted that for the time being, habits such as smoking and lifestyle remain far more useful and reliable in predicting an individual's health and lifespan than his/her specific genetic testing. Further, much of the information that could be provided by today's genetic testing is available through conventional questions about medical and family history, and is already being factored into traditional underwriting. Traditional underwriting methods will therefore remain an effective tool in identifying anti-selection, with genetic testing likely to complement current underwriting methods

Some insurance companies today request a disclosure stating whether the policyholder has undergone any form of genetic testing, or is aware of any genetic diseases other than what has been disclosed. Such disclosures may provide a solution to insurers in the short term, but stakeholders in the insurance industry must keep abreast of developments in genomics to evaluate how the risk of anti-selection affects their market, given the regulatory context in which they operate. The American Academy of Actuaries⁵ suggest reinsurance pools could be developed for to mitigate against such risks arising from genetic testing. In this model, companies would have the right to reinsure genetic risk into a pool and would be required to participate in the pools according to their market share. This would socialise the cost among all market participants.

³ <http://www.cia-ica.ca/docs/default-source/2014/214082e.pdf>

⁴ <http://www.cia-ica.ca/docs/default-source/2014/214073e.pdf>

⁵ http://www.actuary.org/files/publications/genetic_25apr02.pdf

Discrimination against policyholders

In some markets, insurers may use genetic testing as a form of underwriting for a more precise assessment of the underlying risk profile of new applicants. Insurers may then be legally entitled to risk rate premiums accordingly, discriminating against the sick. To the extent that genetic testing is employed in underwriting and pricing, premiums may become unaffordable for high risk individuals, who need the cover the most. Also, those insurers choosing not to employ genetic testing, will face such anti-selection that, if the first insurer in the market does it, others will have no choice but to follow.

However, both the Canadian Institute of Actuaries⁶ and the American Academy of Actuaries⁷ feel that this risk is not extremely significant to policyholders given that over 90 percent of life insurance applicants receive cover at standard rates. While additional genetic information may be of some assistance to insurers in deciding whether to offer or decline insurance coverage for an individual, it is expected that the vast majority of applicants would still be accepted as standard risks and pay standard premiums. Despite all of the medical advancements over the last 50 years, the percentage of people applying for life insurance accepted as standard risks has remained fairly stable and the presence of genetic testing is not expected to change this.

The American Academy lists possible options available to individuals who are denied standard coverage such as; coverage with an extra premium, guaranteed issue insurance, limited underwriting coverage, automatic group insurance coverage, purchasing cover prior taking a genetic test and buying life insurance options that guarantee the right to purchase defined amounts of insurance.

The consequences of increasing longevity

It is possible that personalised medicine improves the prognosis and clinical outcomes of many diseases in future, and that this has a significant impact on longevity. The consequences of increasing life expectancy on some forms of insurance and on social security systems are well researched, but personalised medicine has the potential of resulting in a step change in longevity with potential far-reaching negative consequences for certain books of insurance business, such as annuity business. On the other hand, many other classes of Life and Health insurance may benefit greatly from lower morbidity and mortality arising from the successful implementation of Personalised Medicine, provided of course that there aren't adverse changes in lapse experience.

Earlier identification of disease

The earlier identification of disease through genetic testing could result in a significant impact on critical illness business. Disease which may otherwise have gone unnoticed for several years, during which time many other risk events may have occurred, will now be identified earlier, and

⁶ <http://www.cia-ica.ca/docs/default-source/2014/214073e.pdf>

⁷ <http://www.actuary.org/files/genet.4.pdf/genet.4.pdf>

treatment is likely to commence earlier. The timing and incidence of risk events may therefore be significantly higher than what was priced for in these products.

For indemnity health insurance, the main consequences of earlier identification of disease will also be a higher incidence of diagnosed disease in the insured population, as well as longer treatment of disease per patient. Both of these effects are likely to increase costs and premiums, which may further lead to demographic deterioration in voluntary markets.

Higher cost of treatment?

As medication will be designed and prescribed for particular genetic profiles, it is likely that the cost of treatment per patient will increase. Cheaper generic alternatives may no longer be indicated for people with particular genetic profiles. Further imperfect genomics processes may lead to erroneous results, resulting in medical malpractice with the unintended consequence of higher costs. This has clear consequences for indemnity health insurance and social or national health insurance.

On the other hand, because there will be less “trial and error” in prescription, and because patients are likely to recover at a higher rate, or have better health outcomes, the cost savings inherent in this may well offset the potentially higher cost of treatment.

Recommendations for actuaries

Learn from past experience

A similar set of issues was raised the 1990s with the onset of the HIV/AIDS epidemic. Despite legitimate concerns, HIV/AIDS did not bankrupt the insurance industry, and insurance companies in many jurisdictions are now legally entitled to test for HIV/AIDS and price accordingly.

It is of course very hard to predict the impact and outcome of personalised medicine at this early stage, but it is likely to have both positive and negative implications for the industry, and careful consideration and planning would be required.

Be aware of developments in personalised medicine

Actuaries should keep abreast of developments in personalised medicine, and continuously evaluate risks arising from significant changes in treatment and clinical outcomes. Also, the regulatory context in which genetic testing operates, and the risks arising from this context, should form part of the assessment, including those risks relating to anti-selection, earlier identification of disease and longevity.

Consider ethics and privacy

Personalised medicine may give rise to many complex ethical issues, and to serious privacy concerns. The complex terrain of ethics and privacy will be influenced by the regulatory framework and how the technologies develop, but actuaries would have to consider how to

manage the risks posed by personalised medicine in this broader context, given the type(s) of business they are advising on.

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