

Genetic Testing in Insurance: Challenges and Opportunities

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Executive Summary

The successful sequencing of the human genome, completed just 13 years ago, has opened the door to a broad range of medical opportunities and challenges. The ability to gain health information from such tests and then apply it to diagnostics and therapeutics has already fostered enormous changes in clinical medicine, and has ushered in the era of precision medicine.

If the current pace of development in this area continues, genetic testing is likely to play an increasingly pivotal role in clinical medicine in the near future.

Genetic testing is also assuming a much higher profile in life and health insurance and could play a pivotal role here as well. Information from genetic tests has the potential to improve population mortality and morbidity experience, but there are many challenges for insurers in using such information. At this point, many countries do not permit genetic test results to be used in underwriting, even when the results are shared with an insurer. In addition, the widening ability of individuals to order their own genetic tests is generating a growing asymmetry of information which may create added challenges.

The impact of genetic testing on the insurance industry will continue to be the topic of actuarial research for some time, as insurers address this issue in their pricing and valuation. Insurance product development opportunities may also emerge to capitalize upon this medical trend in genetics that would benefit both the public and the insurance industry.



Genetic Testing: The Science, Validity, and Utility

Genetic information for each individual is contained within the 23 chromosome pairs that are in nearly every cell of the human body. Each parent contributes one of the two DNA chains comprising each chromosome, and every chromosome contains a total of three billion base pairs, or approximately 23,000 genes. These genes make up only 2% of our DNA. The rest of the noncoding DNA regulates gene expression.

Research has shown that all humans are about 99.5% the same genetically (Levy et al., 2007), and twin studies have shown that approximately 25% to 50% of morbidity and mortality differences from person to person are due to genetic factors (Christensen and Vaupel, 1996; Polderman et al., 2015). Mutations in human DNA can lead either to disease or to protection from disease, or might have little to no impact at all. The rest of the variance in disease rates is due to environmental and lifestyle factors.

There has been a rapid increase in public access to genetic testing either through doctors, employee health programs, or via direct-to-consumer genetic testing kits. Some countries have banned direct-to-consumer genetic testing, requiring genetic tests to be ordered by a physician who can then explain and interpret the test results for patients. Clinically, most genetic tests are done for patients whose families have a history of a particular disease.

Not all genetic tests are the same. Inexpensive genome wide association studies (GWAS) use microarray (gene chip) technology to examine a genome-wide set of genetic variants and produce genotypes. Genotyping then looks for single nucleotide polymorphisms (SNPs) in DNA that are associated with an increased predisposition to develop a disease or with side effect propensity for certain drugs.

Other sequencing methods include whole genome sequencing (WGS), which decodes every single base pair in the DNA strands, and whole exome sequencing (WES), which only decodes the protein-producing genes within a chromosome. If a person has symptoms or a family history of an illness, genetic tests can be ordered that look for specific mutations associated with that impairment without sequencing the entire genome. This can help the diagnosis and prognostication of a disease. The cost of commercially available genetic tests can range from US\$250 to US\$4,500, depending on testing methodology and completeness of the assay.



Genetic testing can also be done on genes in cancer cells. This has enabled the discovery of new targeted biological anti-cancer therapies, which have been shown to improve cancer survival in the approximately 10% to 15% of cancer patients who have advanced disease. A recent study reported that 91% of cancer patients had actionable mutations (that is, mutations with significant diagnostic, prognostic or therapeutic implications for cancer patients and their families) and that 10% of their treatment plans were altered as a result of genetic testing of their cancer genome done at the time of the cancer diagnosis (Uzilov, 2016). Unfortunately, these new targeted cancer medications are currently very expensive and usually only extend life expectancy marginally.

As with all medical tests, genetic tests are not perfect. There can be false positive and false negative results. Whether a genetic test is applicable in a given clinical situation depends on that test's analytical validity, clinical validity, and clinical utility. In terms of analytical and clinical



validity, genetic tests can reliably find mutations, but as genotyping panels do not test for all types of genetic mutations, the possibility of false negative results exists. Having a mutation also does not necessarily mean high penetrance (i.e., the chance the associated disease will develop). For example, genotyping results for multifactorial multi-gene disorders such as diabetes and cardiovascular disease are associated with a relatively small increase in the relative risk of developing these diseases.

Clinical utility, a major area of ongoing research, implies whether knowing a patient has a specific mutation might change how a doctor manages that patient, such as motivating him or her to change behaviors or instituting preventative medicine strategies that might materially improve clinical outcomes. For example, according to a 2013 study, approximately 3% of adults carry high-penetrance actionable pathogenic or likely pathogenic genetic mutations, where doctors can change patient care to prevent disease (Dorschner et al., 2013). Many critics of genetic testing argue that evidence is not yet strong enough to use genetic information in clinical care unless there is a strong adverse family history of a particular disease.

Genetics is also the backbone of the growing specialty of precision medicine and specifically of pharmacogenomics, which is the study of how genes affect a person's response to drugs, enabling the provision of the right drug, at the right dose, at the right time. Currently, 7% of all of the 1,200 medications ever approved by the FDA, and 13 of the 45 new drugs approved by FDA in 2015, are considered to be "personalized medicines" where drug-gene interaction plays an important role (Relling et al., 2015). As serious adverse reaction to medications is common in clinical medicine, increased use of pharmacogenomics to enable greater precision in prescribing and treatment could lead to significant decreases in drug side effects, improved disease outcomes, and ultimately, improved morbidity and mortality. This is extremely relevant, given that medical error has been reported as the third leading cause of death in the U.S. (Makary and Daniel, 2016).

Genetic tests are also being used to replace certain invasive diagnostic tests, which is affecting how insurers assess living benefit claims.

An exciting new tool in genetic research is CRISPR (clustered regularly interspaced short palindromic repeats) gene editing. This lets researchers slice a genome at a selected site. It is anticipated that this tool will enable not just the isolation of a specific section of a gene for study, but also the eventual possibility of treating a disease via gene editing; i.e., removing a disease-generating genetic mutation and replacing that section with healthy sequences.

Risks and Benefits of Genetic Testing for Insurers

Genetic testing is an emotionally charged and controversial topic for the public, for lawmakers, and for the insurance industry. For insurers, several possible risks and benefits exist in its use.

Regulations and Anti-Selection

Currently, no insurer anywhere in the world requires genetic tests to be ordered at the time of life or health insurance underwriting. Laws vary by country and product as to whether clinically obtained and disclosed genetic tests results can be used during the underwriting process and these laws are in constant evolution. Most countries, however, currently follow the general principle that applicants must tell their insurance companies what they know about all aspects of their health in order to keep the insurance contract equitable.

The U.K. as well as some European Union members have gone further, imposing moratoriums on genetic information and requiring underwriters to ignore any genetic test results – even if disclosed – if the sum assured being applied for is below a certain threshold. Other countries have imposed a complete ban on underwriting cases based on the results of any disclosed genetic test results. In the U.S., the Genetic Information Nondiscrimination Act of 2008 (GINA) is a federal law that prohibits genetic discrimination in health insurance and employment. Additionally, there are some other underwriting restrictions in individual U.S. states depending on insurance product.

As for anti-selection, it was demonstrated more than 10 years ago that there is a 5.7-fold increased tendency to buy more insurance if individuals know they carry genes associated with increased health risk (Zick, 2005). This impact could be magnified if regulators elect to ban insurers from using genetic test results in underwriting, or institute moratoriums on using genetic test results if the sum assured being applied for is less than a certain amount.

A ban on the use of genetic test results in insurance could also affect the industry's ability to adjudicate claims, as genetic tests are now an integral part of clinical diagnostics.

Impact on Product Pricing

The impact on product pricing due to information asymmetry that might stem from insurers' ability (or lack thereof) to access genetic testing information is currently unknown. Research conducted in 2011 found that the effect of restricting the use of genetic test results in underwriting would be minimal – about a 1% to 3% increase in premiums (MacDonald, 2011). However, a recent report from the Canadian Institute of Actuaries, which examined 13 impairments with a known genetic marker, found that banning the use of genetic test results in underwriting could yield an increase in average mortality rates of 35% in males and 60% in females (Howard, 2014). The same author, in a 2016 report, demonstrated that a ban on using genetic information in critical illness underwriting would result in a 26% increase in the average CI claims rate (+16% for males and +41% for females) (Howard, 2016), and could necessitate an increase in premium rates. The insurance industry in the U.S. is currently expanding research to verify and corroborate these findings.

Additionally, the impact of genetic testing on in-force lapse rates needs to be determined, as the results of a genetic test might have some impact on whether a policy stays in force or lapses.

Genetic testing can lead to increased earlier identification of disease risk and result in increased health care costs, as asymptomatic people will be more likely to use the information to seek specialized medical counsel and screening, and to access potential new treatments due to their genetic profile. Currently, most gene-based therapies are very expensive. Conversely, it is also possible that using preventative therapies guided by genetic tests could decrease the expense of healthcare costs associated with end-stage disease in the future.

Genetic testing can also lead to improved disease prognostication in clinical practice and better risk stratification for insurers underwriting those who have already developed a particular disease. It can also mitigate drug side effects and optimize medical therapies. Finally, there is hope that individuals, once informed about their genetic propensities, may be motivated to change lifestyle behaviors such as smoking, poor exercise habits, and overeating, and enter multi-faceted wellness programs. The literature, however, remains mixed on this.

It is conceivable that ultimately, more widespread use of genetics in clinical medicine and as part of insurance products could lead to improved morbidity and mortality experience, which might have favorable implications mitigating some of the above described insurance pricing concerns.

Risk of Promoting Genetic Testing Use

Insurers must be cautious when promoting the use of and access to genetic testing. Genetic test results are frequently complicated and clinicians may not yet have the education to interpret genetic test results and counsel patients. Also the clinical utility of this extra information is still yet to be proven in clinical studies. Additionally, insurers might be arming the public with genetic information that could be used to anti-select.

Insurers also have brand and reputational risk to consider. For an insurer, offering genetic testing to a policy owner could result in negative reputational impact and potential legal challenges if the insurer is perceived to be misusing test results or if insurers select genetic testing services that either cannot deliver or that produce inaccurate results. Insurers must also adhere to strict privacy and confidentiality policies with regard to genetic information or risk negative perceptions by the public and regulators.

Genetic Testing and Use in Underwriting and Claims

In general, the insurance industry has maintained that genetic tests should be viewed in the same fashion as any other confidential medical information obtained with consent from applicants in their declarations or from their treating physicians at underwriting. Along those lines, underwriters might be permitted to debit or credit a case based on disclosed genetic test results as long as it is legally allowable in each market and if actuarially and medically justified. The industry would also need to preserve the ability to use results of clinically obtained genetic tests to help adjudicate living benefits insurance claims.

Possible Product Concepts Involving Genetic Testing

There are many possibilities for insurance products to incorporate genetic testing as part of its design. A South African insurer, for example, has launched a product giving insureds subsidized access to genetic testing as part of its Wellness offering after the policy has been issued. Insurance companies in Asia have offered pharmacogenetic testing post-policy issue to their insured population. Genetic testing could also be incorporated into a product structure for use at time of claim to improve case fatality and avoid drug side effects.

If insurance products are developed that offer genetic testing in some manner, it will be important that the insured's privacy is maintained as to their results. The insured also needs to be reassured that any genetic test results found post-policy issue will not affect their current insurance policy that is in force. Also, the insurance industry needs to work with the clinical community to make sure that any genetic testing services offered to the insured have clinical utility giving a favorable material impact on the health and wellbeing of the insured.

Conclusions

- Genetics and precision medicine will play a rapidly increasing role in patient care and disease prognostication.
- Genetic testing should not be required for underwriting or claim adjudication
- It is advisable to promote the concept of equality of information between insurance applicant and insurance company to benefit both parties.
- It is too early to quantify the risk of anti-selection or the impact on population morbidity, mortality and lapse experience with any degree of certainty. The insurance industry needs to support and promote the development of research to gain a better understand of the impact.
- Access to genetic testing can improve patient care and could be incorporated into insurance products for policyholder benefit.

For more information, please contact your local RGA office.

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