The evolution of genetic testing

The pace of discovery in human genetics has accelerated exponentially within the last two decades. Since the completion of the Human Genome Project (HGP) in 2003, genome-sequencing costs have fallen dramatically (see figure 1). At the same time, the number of available genetic tests has grown substantially. In recent years, many of these tests have moved rapidly into clinical practice providing patients and physicians with access to personal genetic information. This progress has the potential to revolutionise the approach to patients and to health care in the prevention, diagnosis, and treatment of disease, realising the ultimate goal of truly personalised medicine.

Figure 1: Cost per genome

Source: National Human Genome Research Institute
https://www.genome.gov/sequencingcosts/

Clinical genetic testing

Genetic testing in patients has become increasingly sophisticated. With the exponential increase in genetic data, scientific progress has established relationships between genetic variants and diseases. Such variants, also referred to as single nucleotide polymorphisms or SNPs, can act as biological markers to locate genes that are associated with disease. So far, over 10 million different SNPs have been discovered and more than 21,000 SNPs have been associated with over 800 diseases and traits.1,2

Over recent years there has been significant growth in our ability to test for genetic conditions accompanied by exponential falls in the cost of genetic testing. The implications for modern medical practice are substantial, and the insurance industry is supportive of the many advantages genetic testing has to offer in the prevention, diagnosis and treatment of disease. Nonetheless, there is concern that policy holders may not always share risk-relevant genetic information, thereby increasing insurer’s exposure to adverse-selection.

About the author

Dr Florian Rechfeld is a medical biochemist in the Swiss Re Life & Health R&D department. His research interests span many areas including advances in human genome sequencing and genetic testing and the future impact of personalised medicine on healthcare. Prior to joining Swiss Re, Dr Rechfeld was a postdoctoral fellow at the Institute of Infectious Diseases and Oncology at the University Children’s Hospital in Zurich. He also received a PhD from the Institute of Medical Biochemistry at the Innsbruck Medical University in Austria.
Previously, clinical genetic testing was carried out gene by gene. Today, large-scale genome-wide SNP genotyping offers a single, cost-efficient platform to assess risk of multiple common genetic disorders with variably documented associations in one test. Advances in sequencing technology have also made multigene testing, or “panel testing,” a practical option when looking for multiple genes that may be associated with a disease. Moreover, the number of test available in the clinical practice has rapidly grown in recent years. As of August 2016, the National Institutes of Health’s (NIH) Genetic Testing Registry (GTR) lists over 35,000 tests related to over 9,000 medical conditions and 4,000 genes.

Although single-gene testing, SNP genotyping and gene panels are still often used, whole-genome sequencing (WGS) is increasingly being utilised in clinical diagnostics. WGS allows simultaneous detection of all genetic variants with different pathogenic effects within an individual’s genome. This will help to better understand underlying mechanisms of many diseases and will ultimately improve disease diagnosis and aid in guiding personalised treatment and prevention plans.

Direct-to-consumer (DTC) genetic testing

The rapid growth of the DTC genetic testing market is the result of the fast evolution in testing technology, as well as the dramatic increase in the discovery of information related to the genetic risk of disease. Private companies are attempting to capitalise on these advances by providing genetic testing that estimates the risk of a disease, gives advice on nutrition, lifestyle changes and medication or informs about potential medical care and prevention for a customer, given their genotype. DTC providers claim that insights into personal genetic information could encourage consumers to take a more proactive role in their health care.

Because these tests make claims about (future) medical conditions, they have come under scrutiny by regulatory agencies. Although based on robust and accurate SNP microarray platforms to screen for genetic variants associated with disease, most of these variations, however, only account for a small fraction of a specific disease risk. Compared to clinical genetic testing, the majority of DTC services are offered without the involvement of health professionals, are interpreted without personal medical and family history or lifestyle choices and do not require pre- or post-test counselling. Hence, at current state, the predictive value from DTC genetic tests for future disease risk is poor and any medical benefit or clinical utility gained through a DTC service is modest at best (see table 1).

<table>
<thead>
<tr>
<th>Technology</th>
<th>Rare diseases</th>
<th>Common diseases</th>
<th># of genes tested</th>
<th>Turn-around time</th>
<th>Approx. cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNP microarrays</td>
<td>Moderate</td>
<td>Poor</td>
<td>Thousands</td>
<td>Days to weeks</td>
<td>$100s</td>
</tr>
<tr>
<td>Single-gene sequencing</td>
<td>Good</td>
<td>Poor</td>
<td>One</td>
<td>Weeks</td>
<td>$100s – $1000s</td>
</tr>
<tr>
<td>Panel sequencing</td>
<td>Moderate</td>
<td>Good</td>
<td>Few – Hundreds</td>
<td>Weeks to months</td>
<td>$100s – $1000s</td>
</tr>
<tr>
<td>Whole genome sequencing</td>
<td>Good</td>
<td>Good</td>
<td>All</td>
<td>Weeks to months</td>
<td>$1000s</td>
</tr>
</tbody>
</table>

Source: Swiss Re

There are four main platforms of genetic testing services available: SNP microarrays typically run on high throughput platforms and have been the genetic testing service most frequently offered by DTC genetic testing providers. Single gene sequencing has been to date the main choice to analyse certain known disease causing genes. Disease-targeted (e.g. breast cancer) gene panels use next generation sequencing technology to simultaneously assess variations in multiple well-defined disease-causative gene. WGS has the potential to capture all classes of genetic variation associated to diseases and is going to change current clinical and public health practice. Categorical assignments for validity and utility in the columns are subjective and vary according to context of the tests being ordered. The ‘poor’, ‘moderate’ and ‘good’ categories are presented to simplify and to compare platforms generally.
Regulating access to genetic information

Worldwide, the reaction to the use of genetic testing information for life and health insurance purposes varies from legislation or total moratoria banning any use of genetic test results by insurers to a status quo approach letting the industry regulate itself.

North America

In the United States, the Genetic Information Non-discrimination Act (GINA) 2008 prohibits insurance companies from using genetic information to make underwriting decisions with respect to health insurance. However, GINA does not cover life insurance, disability insurance or long-term care insurance. Most American states have similar laws.

In Canada there is presently no law or regulation in place that specifically address the use of genetic information by insurance companies. Under the Canadian Life and Health Insurance Association (CLHIA) Code on Genetic Testing, insurers agree that they will not initiate or require any person to undergo genetic testing. They may, however, use or request available information from existing genetic test for classifying risk. In 2013, Bill S-201 was proposed, aimed at prohibiting life insurance companies from accessing the results of genetic tests for the purpose of underwriting.

Europe

Europe has more regulation governing genetic testing than any other markets. Several European countries have prohibited or introduced moratoria on the request and use of genetic test results by insurance companies. In the UK, the Association of British Insurers (ABI) and the federal government have agreed on a voluntary moratorium covering the use of predictive genetic test results for life insurance policies under £500,000, or critical illness policies under £300,000. Similarly, in Germany, insurers can use genetic tests only for life insurance paying more than €300,000 or disability insurance paying more than €30,000 annually.

However, in many European countries (e.g. Austria, Belgium, Denmark, France, Norway and Portugal) any use of predictive genetic test results for insurance purposes is not permitted.

Asia

In Asia, with the exception of South Korea, who bans genetic testing for insurance purposes, no specific regulations have been enacted. In Australia, life insurers comply with the FSC Genetic Testing Policy No.11 (2001/2005), which allows insurers to use existing genetic test results, where appropriate.

Implications for the insurance industry

The rapid developments in genomics combined with greater affordability and accessibility to genetic testing hold great potential for more accurate future risk prediction of a variety of diseases. From an underwriter’s perspective, meaningful predictive genetic information, which reveals an applicant’s likelihood to suffer a critical disease, may be a crucial piece of information for a more granular risk classification.

Recent studies published by the Canadian Institute of Actuaries concluded that non-disclosure and/or restriction in access and use of existing predictive genetic information will have a substantial financial impact on insurers offering life and critical illness insurance. At the same time, information from genetic tests has been shown to significantly alter decisions regarding the purchase or alterations of insurance cover.
Insurers broadly welcome the increased use of genetic testing in the clinical practice, as it will aid in the identification of disease and facilitate effective personalised therapies. In addition, genetic testing may cause individuals to change their lifestyle or health management, thereby increasing life expectancy or decreasing morbidity.

However, the growing availability of reliable and predictive health information from genetic testing will increase the threats of anti-selection for insurers. Genetic information, including family history, may or may not be relevant when underwriting an individual applicant. Insurers do not initiate or require an applicant to undergo genetic testing as part of the process of applying for insurance. However, if relevant genetic information is available and known by the applicant, this information should be shared with the insurer to preserve the balance between viable insurance markets and fair premium rates for consumers.

References
4. Genetic Testing Model: If Underwriters Had No Access to Known Results, Report to Canadian Insurance Actuaries Research Committee, Robert C.W. Howard (FCIA, FSA), July 2014

Additional reading
Seeing the future? How genetic testing will impact life insurance

23andMe consumer genetic testing – a challenge to the insurance industry?