2021 International Insurance Society RGA Leaders of Tomorrow: The Future of Insurance and Genomic Underwriting and Claims, Jade Baggs, AXA GIE

Contents

Introduction

For insurers to become world leaders in their field they must embrace advances in medicine and technology, including the current revolution in genetic testing and personalised medicine. This should not be seen as an emerging risk, but an opportunity. Since the completion of the Human Genome Project (HGP) the process of DNA and whole-genome sequencing has become quick, cheap, and effective. DNA sequencing can not only tell an individual if they are at risk of developing certain cancers but help tailor specific treatments to match the genetic makeup of the individual[1]. As insurers we have the possibility to not only provide insurance coverage to a wider

[1] A Crack in Creation: Jennifer A Doudna, Samuel H. Sternberg

market of previously uninsurable customers but also to empower our customers with the knowledge required to live healthier lives. DNA testing will help insurers to support advances in the diagnosis and treatment of disease and in the longer term, to support the cure of diseases which are today seen to be untreatable.

Historically it has not been conceivable that genetic information could or should be used for insurance purposes. However, DNA sequence analysis has entered the mainstream and is now commercialised direct to the consumer. For a few hundred euros individuals can send their saliva sample in the post and sequencing companies can make predictions about health, provide information regarding common traits, and offer clues of a person's ancestry[2]. This is a growing market, where more and more often potential health conditions are being included in tests. If companies like '23andme' operating with limited regulation can provide genetic testing, why not insurers?

A key concern is that of genetic discrimination which '…involves treating differently and negatively or unfairly profiling an individual relative to the rest of the population on the basis of actual or presumed genetic characteristics.'[3] However, are we already discriminating against our customers by using family history and are we forgetting the impact external factors have on an-individual's health. Also how do I feel about this on a personal level as someone who is potentially predisposed to Neuroendocrine tumours (NETs) on their maternal side and never knew their family history on their paternal side? The ethics behind the use of any sensitive information including genetics and the potential for this to be discriminatory is a risk which must be managed by insurers to ensure that genetic information is used to better the lives of customers, protect their premiums, and ensure our long-term profitability.

The Past and Present

Underwriting

For the last 150 years life insurers have asked for an individual's family history and used this information to determine if a customer is eligible for an insurance product and at what price.

[2] https://medlineplus.gov/genetics/understanding/dtcgenetictesting/directtoconsumer/
[3] Genetic Discrimination Observatory

In life insurance an insurer may ask "Have your parents, siblings or grandparents had any diseases of the nervous system, cardiac diseases, strokes, diabetes, cancer or hereditary diseases before the age of 55?"[4] For example, historically, if an individual had a family history of Huntington's chorea, they would be declined for cover. Huntington's is a rare disease that causes the progressive breakdown (degeneration) of nerve cells in the brain and is inherited from a parent[5]. However, if a parent has Huntington's, their offspring has a 1 in 2, or 50% chance of inheriting the mutated gene and developing the condition, meaning that individuals have potentially faced unfair discrimination from insurers in the past. Today, with advances in genetic testing an individual can find out if they will develop the condition and if the test is negative can be offered insurance coverage. But as insurers are we still being too risk adverse and missing an opportunity? If we look to the future, should we be offering customers who test positive long-term cover, such a life insurance, on the basis of a cure of Huntington's and other genetic diseases? Those diagnosed with sickle cell anaemia may struggle to obtain life insurance. However, CRISPR has recently been approved by the FDA for clinical trials as a curative treatment, and there are now ongoing studies reviewing the impact of gene editing on Huntington's.

Genetics has tremendous potential to impact on individuals' health, and the quality and longevity of lives; so why is the majority of the insurance industry regulated or steered against the use of genetic testing and information at inception of a policy? With the availability of testing at home, potential insurance customers are now able to determine a predisposition to a range of diseases, but this information does not have to be shared with insurers, leading to an anti-selection risk. Although a predisposition does not mean the customer will 100% contract a disease if they do, this could not only impact on the profitability of an insurer due to higher future claims, but also impact on other customers', as premiums increase to pay for those who knew they were likely to claim. Although in the case of underwriting insurers are mostly restricted from using genetic information, at claims stage there is an expectation from the customer and medical providers that genetic information should be used for treatments and both diagnostic tests and treatments should be covered.

[4] https://www.swissre.com/dam/jcr:2bccf1e2-eaa5-4ca2-a416-f6dedcebe9dc/Genetics_Seeing_the_future.pdf
[5] https://rarediseases.info.nih.gov/diseases/6677/huntington-disease, https://www.mayoclinic.org/diseases-conditions/huntingtons-disease/symptoms-causes/syc-20356117

In multiple interviews conducted with colleagues around the world, there was a high level of variability in opinion, regulation, and attitudes towards the use of genetic information for both underwriting and claims.

Examples of Current Regulation and Guidance for Genomic Underwriting[6]

Country/Region	Self-Regulation	Limitation by Law	Legal Ban	Current Legislation or Guidance
China	X			• No specific genetic test law but genetic information is considered as private and protected by laws. • Insurance companies are not restricted in asking for genetic test results and some health insurers are partnering with institutions that offer genetic tests by launching insurance packages that offer free tests, either via kits or in designated facilities. • No restrictions on the use of family history and is widely used. • Culturally the population is more adverse to the use of genetic information in case this is leaked and used in employment decisions/marriages.
France			X	• Illegal to use genetic tests or request genetic tests for underwriting purposes. • French ban on direct to consumer testing. • Genetic testing is only permitted in certain cases such as those ordered by a doctor, paternity tests ordered by a judge and DNA testing for use by the police or military.
Hong Kong	X			• The Hong Kong Federation of Insurers issued a code of practice for Genetic Testing and Insurance based on that issued in the UK. • Insurers must exercise care when relying on genetic information and discriminatory decisions are considered unlawful unless justifiable under the • No restrictions on the use of family history Disability Discrimination Ordinance.
Singapore	X			• Bioethics Advisory Committee has called on a moratorium on the use of genetic test results to calculate the risks and premiums of applicants. • The Life Insurance Association has agreed to the moratorium. • No restrictions on the use of family history
United Kingdom	X			• The Association of British Insurers (ABI) in agreement with the UK government must not request or require applicants to take predictive or diagnostic genetic test. • There is an exception for life insurance exceeding £500,000 and the applicant has had a predictive genetic test for Huntington's Disease • No restrictions on diagnostic genetic tests • No restrictions on the use of family history
United States		X		• The Genetics Information Non-discrimination Act (GINA) made it illegal for health insurance providers in the United States to use genetic information in decisions about a person's health insurance eligibility or coverage. • GINA does not apply to other forms of insurance, such as disability insurance, long-term care insurance, or life insurance. Companies that offer these policies have the right to request medical information, including the results of any genetic testing, when making decisions about coverage and rates.

It's not only insurance experts and regulators that have differing opinions, if we look to the general population, there are many ethical and cultural concerns raised by individuals and communities. Studies conducted in China and Japan highlighted a fear that the results of genetic tests could be leaked to employers and result in the loss of a job opportunity, or that they may even lose their job. There was also a concern that marriage proposals could be withdrawn should the families obtain genetic information showing a risk of genetic mutations being inherited by future generations. Another consideration raised by communities was that of racial and ethnic disparities; these are already evident in health among a range of diseases and health care services. New genetic technologies are likely to increase these disparities as access to expensive genetic tests further widens the gap. Wealthier individuals may have access to testing and follow up screening if they have a genetic mutation, whilst poorer individuals will not have the same access. Do insurers have a duty to help close this gap, and how?

[6] https://www.swissre.com/dam/jcr:2bccf1e2-eaa5-4ca2-a416-f6dedcebe9dc/Genetics_Seeing_the_future.pdf

Claims

Personalised treatments have the potential to transform the way we treat individuals, and any leading insurer should want to be part of this revolution. Investors and individuals are more likely to choose an insurance company, who is supporting emerging technologies, medical advances and partnering with them in their health care journey. Not only is this likely to result in better health and clinical outcomes for the customer, but in the long-run insurers should realise savings paying for more efficient treatment, although expensive upfront, this is likely cheaper than prolonged and costly treatments. For example, some customers require years of chemotherapy.

For example, Trastuzumab, approved by the FDA in 1998 for metastatic HER2-postive breast cancer, and later in 2006 for earlier stage HER2-postive breast cancer. Studies indicate that this treatment has improved survival rates by up to 30% for women found to be in stages 1-3 (often used in combination with chemotherapy drugs)[7]. In the past this type of cancer was considered by many to be a death sentence; but with pharmacogenomics (the study of how genes affect a person's response to drugs combining both pharmacology and genomics) safe medications and doses can be tailored to a person's genetic make-up and the use of Trastuzumab has revolutionised the treatment of HER2-positive breast cancer[8]. However, personalised, or targeted therapies are costly and although the cost of Trastuzumab has decreased, this can still cost up to $70,000 per year before paying for surgeries, hospitals admissions and chemotherapy drugs used in conjunction with this treatment.

If you focus on health insurance as an example, without ever speaking to customer, but from reviewing their claims and following them through their very personal healthcare journey, we all want the best outcome for the customer; a longer and higher quality of life. To hear a customer is having challenging and long-term treatment, or even worse that there is no longer a treatment option is heart breaking. Therefore, as leaders within the industry we must establish how we cover treatments that can prolong healthier lives without having long-term financial implications for us as a business, or our customers in the terms of premiums or excesses, such as moving towards partnerships with the pharmaceutical industry to reduce the cost of drugs and working with medical providers to ensure customers get the right treatment for the right price.

[7] https://www.cancer.gov/research/progress/discovery/her2
[8] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2910630/

Testing

Again, if you look to the health insurance market, prophylactic treatment including routine screening tends to be excluded from cover. On the one hand the insurer could argue that they should be able to make fact based underwriting decisions, requesting genetic information, and testing. However, the implications of this are that the insurer would use the information to potentially exclude a condition that a customer may be predisposed to or refuse insurance coverage altogether. Is this fair, or is not better to try and consider what coverage can be provided? Perhaps cover can be provided with an additional loading and a requirement for frequent screening to catch any disease early. As stated previously, predisposition does not guarantee disease will develop.

Let's look to one of the most publicised genetic tests in the world, the BRCA gene test;[9] apparently the 'Angelina affect'[10] (the actress Angelina Jolie famously had a double preventative mastectomy after testing positive for the mutated BRCA1 gene) has led to a two-fold increase in requests for the blood test to determine if an individual has mutations in their DNA that increase the risk of breast cancer. According to the 'national breast cancer foundation' it's estimated that 55 – 65% of women with the BRCA1 mutation will develop breast cancer before the age of 70 and approximately 45% of women with a BRCA2 mutation will develop breast cancer by the of age 70. However, less than 10% of women diagnosed with breast cancer are found to have a BRAC gene and the vast majority of treatments have a very high success rate. Surely as insurers we should encourage testing for the BRCA gene and partner with the women in our portfolio who are found to have the gene to make their own decision about potential preventative measures and support them living healthily through regular screening or even paying for a mastectomy in some cases. There may also be a need to develop pricing methodologies on a more accurate basis than the current assumptions made. The average cost of a mammogram in the UK is around £200; it would appear to make more sense financially to pay for screening as per guidelines rather than paying for claims, or our customers receiving later diagnosis and then enduring extensive cancer treatment.

[9] https://www.nationalbreastcancer.org/what-is-brca
[10] https://preventbreastcancer.org.uk/prevention-is-power/

However, there are still a number of risks for insurers to consider today. In 2019 the FDA approved the use of Zolgensma for Spinal Muscular Atrophy (SMA)[11]. The treatment is indicated for children less than two years of age; a one-time intravenous administration of Zolgensma results in expression of the SMN protein in a child's motor neurons, which improves muscle movement and function, and the survival of a child, at a cost of ~€2 million. Some insurers, including those interviewed, do not exclude, or have limits on congenital conditions or include newborn cover in their products. There is also a concern that SMA antenatal or neonatal screening leading to Zolgensma therapy is bypassing normal underwriting controls. This is a revolutionary and potentially curative treatment, but as an insurer, how are we meant to pay these claims? But if not, insurers who is responsible to pay; national health systems, individuals, or the pharmaceutical industry who are establishing the price of the treatments?

Another consideration is how reliable are genetic tests? The tests must be conducted by an accredited laboratory of course, but just because you receive a positive result for a genetic mutation, but are healthy, this does not always mean you will develop a disease. On the other hand, if you receive a negative result, this does not mean you will not develop a disease. Our lifestyle and external influences also impact on our health. For example, obesity, tobacco smoking and alcohol consumption might modify epigenetic patterns.

Insurers have tried in the past to offer support to customers to live a healthier lifestyle to try and mitigate risk factors, through the use of apps and services such as reducing the price for those who are physically active, without much success (excluding Vitality). However, if you look to the example of HIV, although not a disease caused by genetic variations, this disease was previously considered an uninsurable risk. Some studies of the HIV positive population in the west have found that individuals are living healthier and, in some cases, longer lives than those without HIV. As these individuals have the knowledge that they could be more susceptible to illness, they live a healthier lifestyle. Is this not an indication that if individuals have the knowledge of a potential predisposition to disease, they can and do make life prolonging decisions?

The Future

[11] https://www.policymed.com/2019/10/how-are-insurers-treating-the-2m-drug-zolgensma.html

The developments in genetics is unstoppable and unavoidable meaning that insurers should be looking to the future and consider what approach they will take in terms of the use of genetic information and how they should leverage this opportunity? Health insurers are already paying for Kymriah, a type of CAR T-cell therapy costing ~€500,000 per patient not considering all the other expenses to support the treatment which aggregated can exceed €1 million. Some insurers can still get stop-loss reinsurance, or some even exclude these treatments. But this does not seem sustainable, how are not only insurers but national health systems fund these revolutionary treatments?

Underwriting

If we look to life insurance, usually, underwriting leads to classification in three groups: standard, substandard, and uninsurable. Individuals in the first group have few problems getting insurance. Individuals in the second group must pay higher than average premiums, based on the risk they represent. Individuals in the third group are excluded because the cost of their coverage is unquantifiable or would exceed any reasonable premium.[12] Studies show the assessment of substandard risks due to genetic information is proved fair since the observed mortality is very close to what is expected meaning the use of this information will allow insurers to make a more precise calculation of which people are really in the same risk category or not, showing that the use of genetic testing at inception can lead to a fairer and more accurate risks assessment.[13]

Insurers who are going to use genetic information to make more accurate and fact based underwriting decisions should look to onboard an accredited network of testing facilities who can provide remote and convenient testing for prospective customers and there should be stringent governance processes in place to manage the network, customer data and ensure that all customer information is used devoid of genetic discrimination.

Insurers must not only focus on the benefits as an insurer as a result of more accurate risk pooling but the implications of genetic test results for customers even those who do not proceed to purchase an insurance product and genetic counselling should be provided to those found to have a predisposition to disease.

[12] https://www.nature.com/articles/5201117
[13] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3992580/

Products

Insurers should consider tailoring products to the needs of the customer and consider disease specific life and health products. Recent analysis conducted on data from ~17 AXA entities by diagnosis is reflective of the trends for common cancers globally meaning it would not be difficult to determine, in advance of genetic testing, which diseases you may want to focus on from a products perspective. In the case of cancer this would include breast, lung, colon, prostate and pancreas.

Cancer site	Relative risk ≥5.0	Relative risk ≥1.5 and <5.0	Relative risk ≥1.01 and <1.5
Lung	RB1, TP53		
Breast	BRCA1, BRCA2, TP53, PTEN, SK11, CHDH1	CHEK2, ATM, PALB2, BRIP1	CASP8, FGFR2, MAP3K1, TOX3, LSP1
Colon and rectum	APC, MLH1, MSH2, MSH6, PMS2	APC, BLM	MUTYH, CASP8, CRAC1, SMAD7
Prostate	BRCA2		NBS1, EHBP1, TVD2, CTBP2, JAZF1, MSMB, LMTK2, KLK3, SLC22A3
Pancreas	BRCA2, CDKN2A, STK11, TP53, PRSS1, SPINK1	BRCA1, MSH1, MLH1	

Figure 0.2: Genes Implicated in the Inheritance of Common Cancers[14]

These products can not only be priced more accurately based on the associated risk but can include the offer of mandatory relevant screening and services as part of the product conditions to ensure customers remain healthier for longer, ensuring earlier diagnosis leading to a better prognosis for the customer, and an opportunity for the insurer to better manage claims. These customers may be more receptive to making better lifestyle choices because of having additional knowledge regarding their health and insurers should use this as an opportunity to partner with customers on their healthcare journey.

Claims

Having a portfolio of customers better informed about their health and with access to services and screening may lead to a decrease in the severity and amount of claims. Insurance leaders of the future should consider how armed with genetic information they are able to develop disease

[14] Foulkes W (2008); N Engl J Med; 359:2143-2153

management programmes including structured treatment plans that aim to help people better manage their disease and to maintain and improve quality of life

Some customers will still need to claim as a result of the contracting the disease they were predisposed to. Insurers should consider how they will better manage these costs and should develop specialist networks for the most common types of cancers as detailed above ensuring that customers are provided the right treatment at the right price. Insurers must also consider how they will cover the costs of new and emerging treatments using genetic information, such as the emergence of personalised medicine, and should conduct robust portfolio monitoring along with sensitivity analysis as these treatments are approved to ensure they protect their profitability.

From a provider management perspective there is an opportunity for insurers to partner with those working to advance medicine such as medical trials at limited cost to support the development of these treatments and provide customers with a wider range of treatment options.

As an industry we continue to struggle with the cost of new treatments and insurers should look to work closer with pharmaceutical companies to control the price of these drugs. If you look to the case of Zolgensma detailed earlier in this paper, the pharma company is allowing some insurers to pay over a 4 year period, which in the case of health insurance would have less of a financial impact than paying €2 million in one go. Insurers should also take the opportunity to negotiate on the cost of new and emerging treatments but must also consider a greater risk.

The pharmaceutical industry has focused advances on less common disease so far. However, this is likely to extend to cure more common conditions in the future. Some health insurers cover chronic conditions such as diabetes type 1. Diabetes type 1 is already a costly condition to cover and there have been some successful disease management programmes implemented as well as pricing strategies to cover current treatment, but how do we plan to cover a new treatment or cure for diabetes should it arise through genetic editing (there is already some success in disease reversal in mice with the use of CRISPR)[15]? It would likely be a huge upfront cost, but again may save costs in the long run due to avoided claims for treatment of the disease and its many

[15] https://www.fiercebiotech.com/research/reversing-diabetes-by-applying-crispr-to-patient-derived-stem-cells

complications. Maybe if you have genetic information at inception, have priced accordingly and reduced claims due to screening and more effective disease management this is not such a problem. Maybe this really is an opportunity for insurers to support the customers who need is the most and transform their quality of life.

Conclusion

The use of genetic information is set to revolutionise how we approach product development, underwriting and claims and is an opportunity to manage financial exposure, providers, ensure clinical governance, and make sure customers get the best treatment possible, as well as emerge from a payer to a partner to our customers and stakeholders. This should not only lead to an improvement in customers quality of life and heath, protect the profitability of those insurers willing to embrace the future, but also ensure, by supporting innovation, the way the general population is treated receives treatment also continues to evolve. I personally have already booked my genetic test, as per the famous saying 'knowledge is power'.