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Advances in genetics and their impact on life insurance

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Abstract

As genetic research continues to advance, we see regulators around the world placing bans on the life insurance industry from using predictive genetic information. In this paper, we provide a framework for assessing the extent to which these trends may lead to adverse selection on the life insurance industry.

We begin with the state of global life insurance regulation on the use of predictive genetic tests. By summarising the latest genetic research relevant to life insurance, we highlight how much progress has been made in a single year. We then describe how new emerging predictive genetic tests differ to those currently available. Finally, we suggest how the life insurance industry might respond to any adverse selection and assess the difficulty of implementing those responses and their chances of success.

Keywords: genetics, life insurance, regulation, predictive genetic tests, genetic variants, polygenic risk scores, underwriting, product design, ethics

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Dr Damjan Vukcevic is employed by The University of Melbourne. Jessica Chen is employed by BT Financial Group. The opinions outlined in this paper are their own and do not necessarily represent the views of their employers.

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1. Executive summary

Changing landscape of genetic research and life insurance regulation

Rapidly advancing technology and scientific progress are hallmarks of the modern era. These have led to a substantial increase in information about many aspects of our lives. A recent example is the development of predictive genetic testing, prompting business and community concerns about how it may influence the life insurance industry.

In March 2018, the Australian Parliamentary Joint Committee on Corporations and Financial Services recommended a **moratorium** on the use of predictive genetic information by insurers. Once this is implemented, individuals will not need to disclose their genetic information when obtaining life insurance cover, even if it informed their decision to apply.

In this paper, we present a framework for assessing the likelihood for an individual to act on genetic information. We find that:

- **Currently available** genetic tests are **highly predictive** but **only for a small minority of individuals**. Therefore, while the test results may provide a strong impetus for individuals to act, the overall impact to the insurance industry is expected to be **minor**.
- **A new generation** of predictive genetic tests is being developed by the scientific community. These tests are still immature and **not currently available** to the public. The emerging tests are less predictive but provide results that will be relevant and likely actionable for a substantial proportion of individuals. Therefore, if they become available and widely used, we expect a **more substantial impact** on the life insurance industry.

Assessment criteria	Current generation of tests	New generation of tests
Predictive strength	High	Low – Medium
Test coverage	Low	High
Availability	By medical referral	Not currently available, but expected in the future
Cost	$100 – $1000	$100 – $1000 (current lab costs)
Overall assessment **i. Likelihood to act** **ii. Impact on insurers**	 **i. High** **ii. Low**	(Once available and in a mature state) **i. Low – Medium** **ii. Medium – High**

The predictive strength of the new generation of tests is developing rapidly. At the Actuaries Summit last year, we presented a report that assessed their current capabilities and modelled the potential future impact on life insurance. Here, we review the latest research and show that **substantial improvements** in the predictive strength of genetic tests have been made for **three of the top five diseases** that affect life insurance: coronary artery disease, prostate cancer and depression.

Challenges to life insurance industry business model

Over time, as medical information and treatments become more personalised, the life insurance industry may need to reconsider its approach to risk pooling. The following illustrates the gap between current strategies and future responses:

- **Family history**, information available to insurers, does **not provide a substitute** to predictive genetic information. Their differences are summarised below:

	Family history	Predictive genetic tests
Measured genetic variation	Yes (imprecise)	Yes
Unmeasured genetic variation	Yes (imprecise)	No
Shared environment	Yes	No

  As such, a prohibition on the use of predictive genetic information will dampen the insurer's ability to fully assess an individual's disease risk.

- **Lifestyle choices** can offset a degree of genetic risk. This is particularly effective against certain diseases and improving life expectancy. Here we show an illustrative model for coronary artery disease where for every low genetic risk policy that is replaced with a high genetic risk policy, one unhealthy lifestyle policy will need to be converted to having a healthy lifestyle to offset the risk.

  How such conversion might happen is unclear. To date, the encouragement by life insurers for healthy lifestyles has been mainly to improve customer retention and reduce insurance claims. These 'wellness' programs have not been designed specifically to target genetic adverse selection risk. Ultimately, making lasting lifestyle changes is difficult for individuals; insurers might only have a limited influence in this domain.

Shaping the agenda

Although insurers can choose to respond by increasing prices or limiting insurance cover, this is likely to have a negative social impact by reducing the affordability and effectiveness of their policies. The scale of social impact will depend on the magnitude of any adverse selection.

Genetic information asymmetry may therefore become a significant disruptor to the existing structure of the industry. We encourage the industry to set clear principles and frameworks to steer the direction of discussion. An overarching principle may be 'accepting that everyone has some level of health risks and ensuring that the Australian population has access to an affordable basic level of cover'.

The industry should continue to monitor the impacts of the prohibition on the use of genetic information by insurers and get involved in shaping the use of genetic testing. We suggest several possible actions centred around the governance and monitoring of genetic testing.

In this paper we have reported on rapid recent progress in predictive genetic tests. The governance of this technology, including its impacts on life insurance, will be a global issue. Any policies should account for the current and expected future advances and their likely use in medicine and other applications.

2. Introduction: A framework for assessing adverse selection

Imagine a world where genetic testing is routine, helping to inform us of our risk of developing common diseases such as cancer, Alzheimer's and heart disease, before the onset of any symptoms. Armed with this information we can tailor our lifestyle, financial decisions and insurance needs to maximise our longevity and quality of life. Rapid advances in genetic research make this scenario plausible in the future.

A fundamental principle of insurance is the concept of risk pooling across a group of individuals. The equilibrium between individuals and insurance companies is reached when the products offered meet societal needs and are at a fair price that is sustainable for the industry.

Around the world, the trend in regulation has been to disallow the use of genetic information in underwriting life insurance. Australia is set to follow suit soon (see Section 3). At the same time, research into genetic risk prediction continues to progress rapidly (see Section 4). The introduction of a moratorium on the use of genetic information raises the prospect that customers who are at higher risk of disease or mortality could preferentially apply for life insurance, leading to adverse selection.

To explore this potential scenario and assess its extent, many factors need to be considered. We suggest the following framework to outline the key aspects:

1) **Factors influencing individuals' actions**

   a) Types of genetic tests and the information they provide
   b) Strength and coverage of genetic information as it relates to future health
   c) Availability and cost of genetic tests
   d) Societal perceptions and attitudes to obtaining genetic information
   e) The likelihood for an individual to change lifestyle based on their genetic information
   f) The likelihood for an individual to make insurance decisions based on their genetic information

2) **The ability for the life insurance industry to respond to any adverse selection**

   a) Understanding the degree of substitution between family history and genetic information
   b) Potential to influence lifestyle factors to offset genetic risk
   c) Changes to products to ameliorate the impact of adverse selection
   d) Structural changes to the whole industry to cope with adverse selection

To help understand the factors influencing individuals' actions, in Section 5 we describe what current genetic tests are capable of, as well as a new generation of tests being developed in research labs. This covers 1a to 1c from the above framework; we do not evaluate the other factors here.

In Section 6 we then describe four potential responses by the life insurance industry, giving a brief assessment of the challenges and prospects of success for each one.

3. Life insurance regulatory developments

3.1 PJC report

In March 2018, the Parliamentary Joint Committee on Corporations and Financial Services (PJC) released its report on the Australian life insurance industry (Commonwealth of Australia, 2018). The report made several recommendations about the life insurance industry. Here we outline their rationale and findings in relation to genetic information (Chapter 9 of the report).

In summary, the PJC's main recommendations were:

- Life insurers to be **prohibited** from using the outcomes of predictive genetic tests, at least in the medium term, **as a matter of urgency**. The exception is in the circumstance whereby genetic information can be provided to life insurers to demonstrate that an individual is not at risk of developing an inherited condition.
- The moratorium to be **reviewed** five years after being imposed, with the review to account for the impacts of this change on customers.
- If life insurers fail to implement or abide by the prohibition, the government should instigate legislation to the same effect.

The arguments put forward to the PJC supporting the prohibition were centred on protecting customers against genetic discrimination, which occurs when people are treated differently based on which genetic variants they have present in their genomes. Genetic discrimination is generally considered to be undesirable because people have no control over the composition of their genomes, just like they have no control of their sex and ethnicity, and therefore such discriminated would be unfair.

The PJC did however acknowledge the existence of the adverse selection phenomenon in insurance. That said, the PJC felt that life insurers did not provide strong enough evidence that not having access to predictive genetic testing results would make the life insurance industry unsustainable.

Further, whilst information asymmetry between insurers and customers may result in insurers increasing premiums to compensate, on balance, the PJC believed the benefits to customers in preventing duty of disclosure is greater.

3.2 Regulations in different countries

The PJC's recommendations in Australia have followed similar global trends whereby rapid genetic advances have prompted countries to enact agreements to restrict or fully ban the use of genetic information in life insurance.

The table below summarises the life insurance regulations on the use of genetic information for several countries (as reported by Klein, 2017). Australia is shown as before and after the PJC's recommendations.

Regulation category	Name of countries
No regulation	China, Finland, India, Spain, United States
No regulation with written or unwritten codes of conduct from insurance industry groups	Greece, Japan
Prohibitions on insurers requiring applicants to take a genetic test and prohibitions on discrimination if the applicant refuses to take a test	**Australia (before PJC)**
Prohibitions or moratoriums on using results from existing tests when policies are below certain limits	Germany, Netherlands, Switzerland, United Kingdom
Prohibitions or moratoriums on using results from existing tests at all, sometimes including use of family history information	Austria, Belgium, Canada, Denmark, France, Ireland, Poland, Portugal, Singapore, **Australia (after PJC)**

4. Genetic research over the last year

In our report presented at the Actuaries Summit last year (Vukcevic and Chen, 2017), we gave a brief historical account of genetic research, particularly as it related to risk prediction, and presented a detailed assessment of the current state of genetic research for the top 5 diseases that lead to life insurance claims (in particular, for trauma and income protection insurance): coronary artery disease, breast cancer, prostate cancer, stroke and depression.

To illustrate the rapid progress of genetic research, here we summarise the latest research for each of these diseases and contrast it to the information we presented last year. In addition, we provide an informative summary of genetic research into lifespan/longevity. This is particularly of interest for death cover, which we did not discuss in our previous report.

Our description here refers to the concept of a **polygenic risk score** (PRS). This is a single-number summary of the disease risk for an individual as quantified by a statistical model, based on a set of measured genetic variants. Higher scores represent greater risk. For more details, see our previous report (Vukcevic and Chen, 2017).

4.1 Top diseases

The table below compares the predictive performance of PRSs developed for each disease as reported by various recent studies. We considered any study published or available as a preprint since the start of 2017.

The numbers in the table each represent a comparison of two groups of people, as indicated at the start of each row. For example, for coronary artery disease, last year we reported PRSs that gave approximately a 2-fold increase in risk when comparing individuals in the top 20% of risk (as judged by the PRS) with those in the

bottom 20% of risk. Each number is a ratio of the risk for the two groups, measured on a scale that can vary by disease (e.g. hazard ratios, lifetime risk) but is comparable within each disease.

In just a single year, substantial advances have been made for **three of the five diseases** being coronary artery disease, prostate cancer and depression.

	Reported last year	Newer studies
Coronary artery disease		
Top 20% vs bottom 20%	**~2** (Khera and Kathiresan, 2017)	**~4.2** (Inouye et al., 2018)
Breast cancer		
Top 1% vs population average	**3.4** (Mavaddat et al., 2015)	**3.5** (Michailidou et al., 2017)
Top 20% vs bottom 20%	**3.2** without family history **2.7** with family history (Mavaddat et al., 2015)	**3.2** (Li et al., 2017)
Prostate cancer		
Top 1% vs population average	**4.2** (Olama et al., 2015)	**5.7** (Olama et al., 2018)
Top 10% vs population average	**2.3** (Olama et al., 2015)	**2.7** (Olama et al., 2018)
Stroke		
Top 10% vs bottom 20%	**1.2 – 2** (Hachiya et al., 2017; Malik et al., 2014; Tada et al., 2014)	*No recent studies found*
Depression		
Top 10% vs bottom 10%	*No studies found*	**2.4** (Wray et al., 2017)

4.2 Lifespan/Longevity

Extensive research has been done on the genetics of human lifespan (also referred to as human longevity). It has been known for a while that there is a genetic component, with heritability[1] estimated to be about 25% (Eline Slagboom et al., 2017).

A few of the recent studies have been very large, using cohorts with 100k–600k individuals, and finding approximately 10–20 genetic variants with strong evidence of association (Joshi et al., 2017; McDaid et al., 2017; Pilling et al., 2017).

Although most of these studies developed a PRS, they used it only as a means to validate their results and did not directly assess its predictive performance. We only found two studies that quoted such a performance measure:

- Top third vs bottom third: **0.55 years longer lifespan** (Marioni et al., 2016)
- About 0.3% of Europeans are carriers of risk variants at both of two specific genes (*APOE* and *CHRNA3/5*) and are predicted to have **3.3–3.7 years shorter lifespan** (Joshi et al., 2016)

[1] **Heritability** is the proportion of the variation (in the population) of a trait that is attributable to genetic factors. It is a common way of quantifying the contribution of genetic as compared to non-genetic factors (the latter are usually referred to as **environmental** factors). For a more detailed introduction to relevant genetic concepts, see our previous paper (Vukcevic and Chen, 2017).

In addition, a number of interesting facts have emerged about the genetics of lifespan:

- **Differences between males and females.** The genetic factors that influence lifespan for males differ from those that matter for females.
- **Differences between young and old**. Certain genetic factors influence variation in lifespan amongst people who die younger, but this changes with age and a different set of factors are more influential for such variation amongst people who live to a much later age.
- **Relationships with several other traits**. For example, the genetic factors that predispose individuals to develop coronary artery disease or to smoke are also associated with shorter lifespans. Conversely, individuals with a genetic propensity for attaining a higher level of education were also predisposed to have longer lifespans.

The substantial number of genetic variants highlighted from these studies, and the relationship with other traits, suggest that a powerful prediction tool could be developed that simultaneously considers lifespan and diseases (i.e. mortality and morbidity) based on genetics, coupled together with relevant lifestyle variables.

5. Genetic testing and its influence on individuals' actions

The PJC's recommendation to prohibit the use of predictive genetic information by insurers would mean that only individuals would be able to use this information when obtaining life insurance cover. How likely will customers use it to influence the type and amount of insurance obtained?

Genetic information is obtained from genetic testing. There are many different purposes for testing, including medical (e.g. diagnosing a genetic disease or predicting disease risk) and non-medical (e.g. confirming parentage or forensic investigation). More details are available, for example, from the National Library of Medicine (2018) or in ALRC Report 96 (Commonwealth of Australia, 2003: 10). The use of interest to our discussion here is the prediction of disease risk or longevity, which are relevant to life insurance.

There is a marked contrast between genetic tests that are currently available on the market and tests that are being developed in research labs. Current tests typically measure a small number of genetic variants, often only one. We will therefore refer to them as **monogenic tests**. In contrast, the tests being developed can survey a very large number of variants across the whole genome; we refer to these as **polygenic tests**.

The key differences between the two types of tests are as follows:

- Monogenic tests typically measure genetic variants of **large effect**, which also tend to be **rare** and lead mostly to **rare diseases**.
- Polygenic tests survey a **greater number** of variants, which are typically **common** but each having a **minimal effect** on its own.

Many common diseases have a genetic architecture that is particularly suited to a polygenic test. For that reason, although they are not currently available, polygenic

tests show promise in being useful as generic risk predictors that could form a standard part of medical care and preventative health programs.

In Appendix A we describe both types of tests in more detail. The table below summarises the main points and provides our assessment of the likelihood for an individual to act on their results and the potential impact on the life insurance industry.

Assessment criteria	Monogenic tests	Polygenic tests
Predictive strength	High	Low – Medium
Test coverage	Low	High
Availability	By medical referral	Not currently available, but expected in the future
Cost	$100 – $1000	$100 – $1000 (current lab costs)
Overall assessment **i. Likelihood to act** **ii. Impact on insurers**	 **i. High** **ii. Low**	(Once available and in a mature state) **i. Low – Medium** **ii. Medium – High**

Our overall assessments are indicative only and depend on many factors that are still poorly understood and are the subject of current research. This is especially the case for polygenic tests, given they are not yet publicly available.

Understanding in more detail why individuals decide to get a genetic test, how they interpret the results, and what they subsequently do in response, are important to better assess their likelihood to act. We have not attempted to summarise the current knowledge here; we leave this as important future work. However, for now we use the predictive strength of the genetic tests as a proxy: it is plausible to assume that an individual is more likely to act on a result they are told is more highly predictive.

Determining how all of this translates into an impact on life insurance companies, especially for a future scenario where polygenic tests are commonplace, is therefore somewhat of a speculative exercise. For monogenic tests, we are not aware of any evidence that suggests that they are currently having a material impact. For future polygenic tests, our modelling from last year suggested potential material impacts once around 2-5% of people got tested (Vukcevic and Chen, 2017).

With the predictive strength of polygenic tests improving rapidly over time (see Section 4.1), assessing their impact is somewhat of a moving target, but clearly the direction is towards higher potential impact in the absence of any other actions taking place.

6. Potential responses by the life insurance industry

The degree of any genetic adverse selection on the life insurance industry is a combination of the potential for an individual to act, together with the ability and speed in which the life insurance industry can respond to any behavioural changes.

In this section we discuss the risks to the industry and some potential responses. Specifically, we explore the following fundamental questions:

- Can family history be used as a substitute for genetic information?
- Can insurers encourage positive lifestyle changes to offset genetic risk, without the need for prices increases?
- What are the societal implications if the industry response was to increase prices and/or limit cover to diseases with high genetic influences?
- How can the insurance industry influence structural changes in an environment of genetic information asymmetry?

6.1 No action, using family history as a substitute for genetics

Customers already routinely provide their family history when applying for life insurance. Does this convey much or all the information that a genetic test might reveal? If the two are substitutable (for the purpose of underwriting), then genetic information asymmetry does not pose a risk to the insurance industry.

To explore this question, the following is an assessment of family history and genetic information in the development of coronary artery disease (CAD); a leading cause of death as well as insurance claims. Figure 1 shows the cumulative likelihood of developing CAD over a 15-year period for combinations of different degrees of genetic risk and family history, taken from a recent study (only the results for older people are shown here; similar conclusions were reached for younger people).

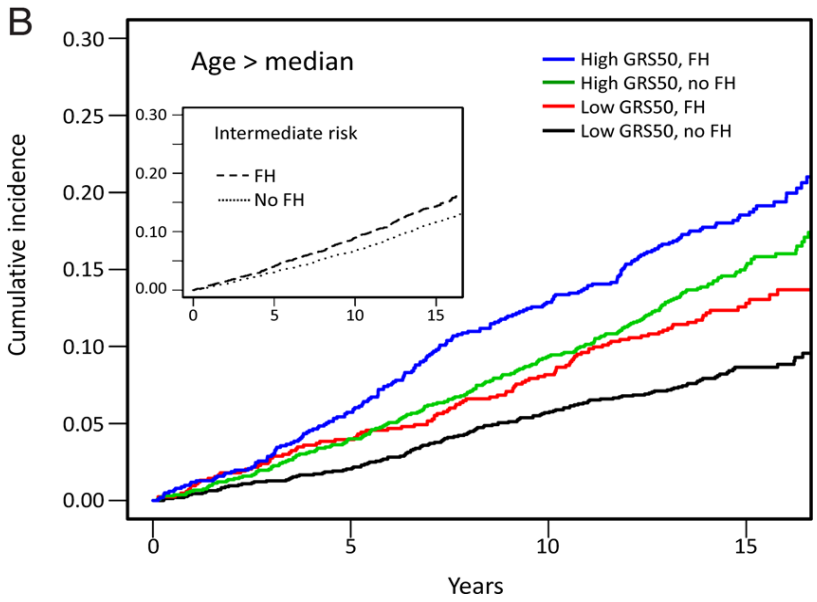


Figure 1. Taken from Tada et al. (2016, Figure 1B), licensed under CC BY-NC 4.0. The lines show the cumulative incidence of coronary heart disease events amongst study participants older than the median age (57.6 years), split according to family history (FH) and genetic risk category (GRS50). Blue and green: those with high genetic risk and with (blue) or without (green) a family history. Red and black: those with low genetic risk and with (red) or without (black) a family history. Inset: those with intermediate genetic risk and with (dashed) or without (dotted) a family history.

The research shows that, in this case, the genetic risk category and family history **provide complementary information** for assessing the risk of developing CAD and the two are **not substitutable**. While it is possible that for other choices of assessing

both types of information the conclusion may differ, there are reasons to think that this is a more general phenomenon:

- An individual's genome is determined by a combination of the genomes from both parents. Since only a portion of each parent's genome is inherited, family history will not precisely represent the actual genetic composition of the children.
- Genetic tests will measure the actual variants present in an individual. However, they are limited to only those that are measured as part of the test. They might therefore miss important variants that influence disease risk. Family history can capture these, albeit imprecisely.
- Family history combines information about shared genetics (inherited genetic variation) and shared environmental factors (e.g. lifestyle choices, socio-economic factors, living conditions). A genetic test only captures genetic information.

The information captured by each of the two sources can be summarised as follows:

	Family history	Predictive genetic tests
Measured genetic variation	Yes (imprecise)	Yes
Unmeasured genetic variation	Yes (imprecise)	No
Shared environment	Yes	No

To conclude, we see that predictive genetic tests can provide additional information to family history. Furthermore, the reverse is also true. Therefore, it is useful to know both to obtain a more comprehensive understanding of overall disease risk for an individual. As such, a strategy of using only family history will likely leave insurers susceptible to potential adverse selection.

It should be noted that the industry's underwriting methods are evolving. The recent trend has been to reduce the number of questions but make them more targeted.

6.2 Actively influence lifestyle to offset genetic risk, with no price increase

Disease risk is combination of genetics and lifestyle factors. In this section we provide:

- Scientific research showing that lifestyle changes can offset genetic risk (partially or completely)
- Illustrative modelling on the degree of lifestyle change required to offset against CAD genetic risk, if only lifestyle and not genetic information is known
- Considerations on the ability of insurers to influence lifestyle changes.

Scientific evidence

As we reported in Section 4.2, genetic factors are estimated to only account for about 25% of the variation in lifespan. Therefore, we might expect that significant improvements in mortality can be obtained by adopting a healthier lifestyle.

Indeed, a recent large study in the US showed that substantial increases in life expectancy are possible when adopting up to five specific healthy lifestyle

behaviours (Li et al., 2018). The five behaviours were: never smoking, regular exercise, high quality diet, moderate alcohol intake and maintaining a 'normal' weight. At the age of 50, the incremental benefit of each additional behaviour was approximately 2 years of extra life expectancy.

Further, for morbidity, the potential impact of lifestyle varies by disease. The following table shows a summary of the estimated overall contribution of genetic factors to the risk of several common diseases (data from Do et al. (2012), rounded to the nearest 5%).

Disease	**Heritability (approx.)** Variance explained by genetic factors
Type 1 diabetes	85%
Alzheimer's disease	80%
Coronary artery disease (CAD)	50%
Prostate cancer	40%
Parkinson's disease	25%
Breast cancer	25%
Stroke	15%

Diseases that have low heritability (e.g. stroke) are more likely to be influenced by lifestyle factors. However, even those with substantial heritability, such as CAD, can be influenced by lifestyle, as we show below.

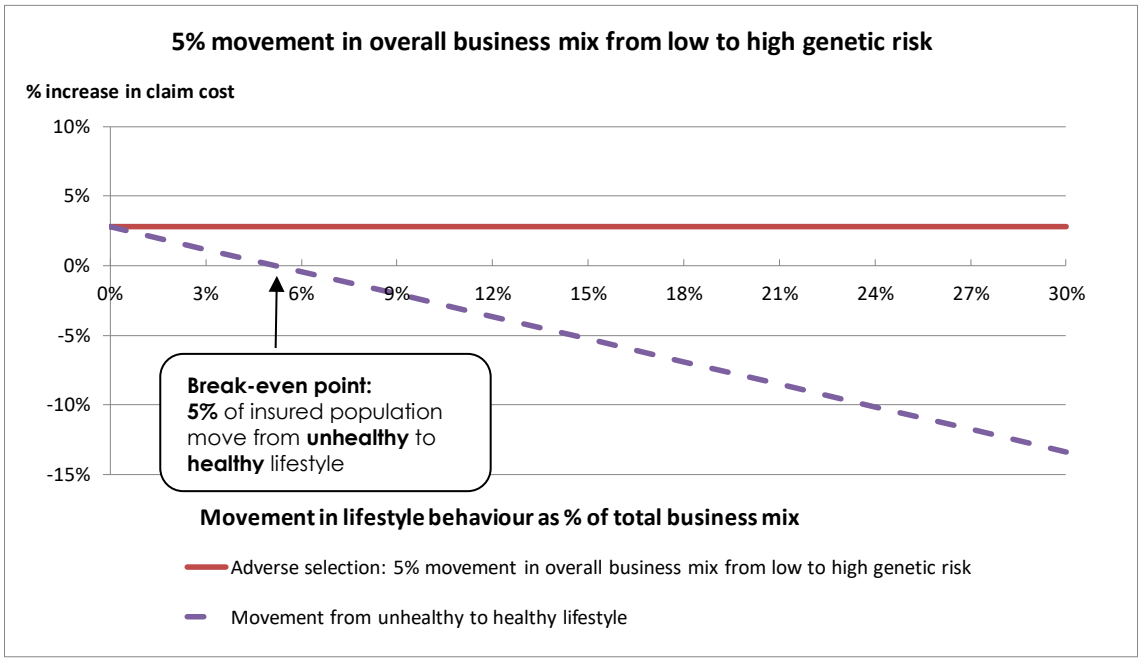
Illustrative model (based on scientific literature)

Using the results from a recent study of CAD, we developed a simple model to assess the extent to which initiatives to shift lifestyle across a pool of customers could affect overall risk, and whether this could offset the impact of adverse selection. The basic assumptions and details of the model are shown in Appendix B and more detailed results are shown below.

Result 1: Adverse selection based on genetics only

We consider an adverse selection impact where **5%** of policies lapse, all of which are assumed to have **low genetic risk**, and that they are **replaced** by policies with **high genetic risk**. This change is assumed to happen proportionately across all lifestyle categories.

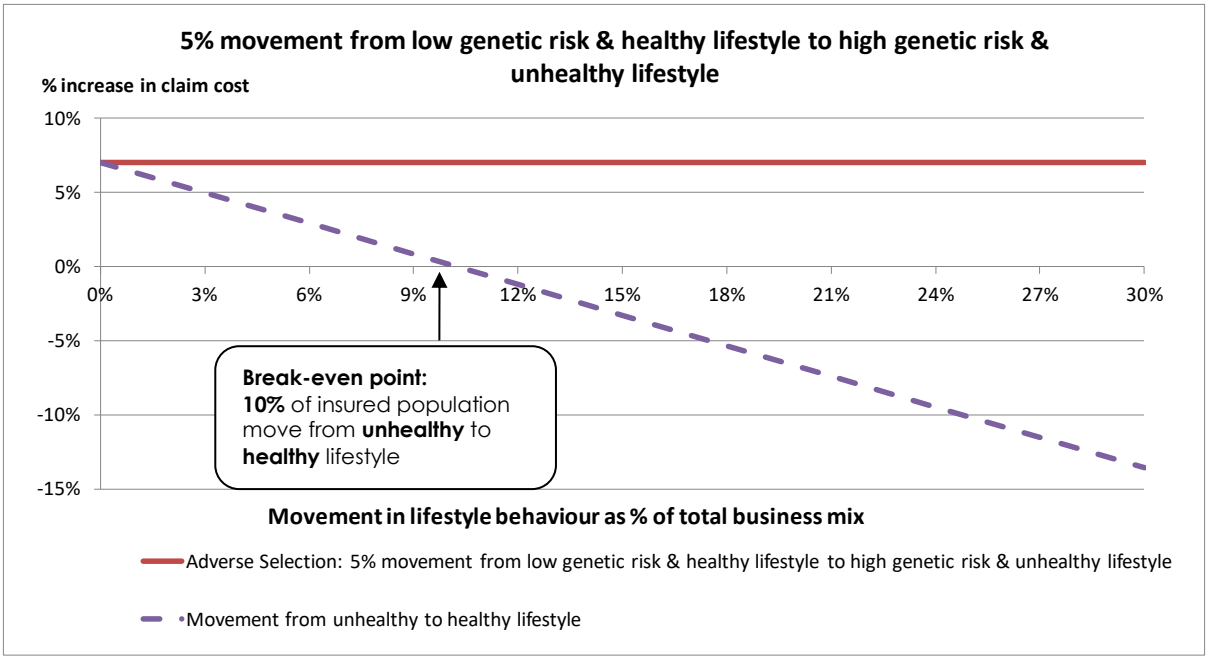
The change in claim costs in response to a subsequent shift in the lifestyle of customers is shown in the following figure. We see that we need a 5% shift in lifestyle to completely offset our assumed 5% change in genetic risk.



This conclusion is consistent with what we know about CAD: genetic and environmental factors each contribute roughly equally to risk, and the environmental factors largely consist of modifiable lifestyle variables. For other diseases the relative impacts may differ depending on the relative influence of genetics and lifestyle.

Result 2: Adverse selection based on genetics and lifestyle

We now consider a similar but more extreme adverse selection impact where **5%** of policies change from **low genetic risk and healthy lifestyle** to **high genetic risk and unhealthy lifestyle**. The impact on claim costs of any subsequent lifestyle changes is shown in the figure below. We see that we now need a 10% shift in lifestyle to completely offset the change in risk. In other words, the results show if adverse selection were more targeted, the amount of lifestyle risk required to offset it would need to increase compared to Result 1.



It is important to note that the results shown here specific to CAD and our assumptions. They will likely vary for other diseases.

The ability of insurers in influencing lifestyle change

Theoretically, lifestyle changes can offset a degree of genetic risk depending on the disease. However, what is the role of insurers in managing or encouraging lifestyle change and is it feasible?

A recent trend in life insurance products is a move towards encouraging healthier lifestyles. Examples of these include discounts on premiums for customers with a 'normal' weight or discounts for gym memberships. The intent of these products is typically to:

- Improve customer engagement through more frequent and meaningful interactions. This is hoped to improve customer retention.
- Improve the overall awareness of the benefit of leading a healthy life. This is hoped to reduce the number of claims.

Insurers will typically return some of the financial benefits to the customer in the form of reduced premiums or discounts to products and services. Therefore, if genetic information asymmetry causes adverse selection, insurers would need to either improve the effectiveness of their wellness programs or perform them at lower cost.

Ultimately, lifestyle changes require high motivation from individuals since the benefits only arise over time and through persistent action. This is complex to manage, with many factors affecting an individual's motivation. Therefore, the ability for insurers to influence lifestyle changes may be somewhat limited.

6.3 Increase prices or limit cover for diseases with high genetic influence

In the event of strong genetic information asymmetry, insurers could respond by changing the price or cover available for diseases that might be driving any adverse selection. Possible actions may include:

- Increasing prices to offset any increase in claims costs
- For specific diseases, limiting the maximum amount of sum insured
- Setting and monitoring limits on the desired exposure to high versus low genetic risk claims. Sales and pricing changes may be modified to stay within the set limits.

Any response in this manner is likely to have societal impact. For example, reducing the affordability of insurance or its effectiveness in helping people cope with disease and disability. To extent of such a response that would be required depends on the magnitude of any adverse selection (taking into account the effect of any other interventions, such as lifestyle-based initiatives as discussed above). Therefore, care should be taken to balance the societal impact while ensuring industry sustainability.

The PJC's recommendation to review the customer impacts five years after the change in disclosure rules will help to assess whether the right balance is being struck.

6.4 Structural changes to the life insurance industry

Genetic information asymmetry is yet to pose a threat to the life insurance industry. As predictive genetic tests improve over time and become more widely adopted, the way in which life insurance is delivered may need to adapt. In particular, the increasing ability to differentiate individuals by risk may require us to change how we pool this risk.

Potential changes could take the form of:

- More tailored premiums, based on smaller risk pools, whereby individuals may differentiate themselves by providing updated lifestyle data.
- Establishing a pooled industry fund to support claims for diseases that are high in genetic risk.
- Move towards a community rating structure where claim costs are shared amongst all policies and insurers.
- A government subsidy for the provision of life insurance to ensure societal needs are being met. This may be in the form of tax incentives, rebates or a government fund.

To shape the future structure of insurance, in our previous paper we suggested that the life insurance industry set clear principles and frameworks to steer the industry towards a desired long-term state (Vukcevic and Chen, 2017). Our proposed overarching principle of 'accepting that everyone has some level of health risks and ensuring that the Australian population has access to an affordable basic level of cover' remains relevant.

Continual monitoring of customer and industry impacts will become increasingly important. Possible actions by genetics experts and the life insurance industry to aid in shaping and monitoring the future may include:

- Establishing guidelines for the interpretation of genetic results, particularly for polygenic tests

- Ensuring there are sufficient genetic skilled personnel in society to support any medical, research and social changes
- Establishing a life insurance industry database of claims decisions and analysis of claim trends with respect to genetic risks
- Benchmarking the cover and affordability of insurance across countries with prohibition on the use of genetic information
- Establishing a genetic testing monitoring committee with wide representation, including from the government, insurance industry, medical profession, researchers and the public.

7. Conclusions

Australia is set to prohibit the use of predictive genetic information in life insurance, following a global regulatory trend.

Earlier this year, the Parliamentary Joint Committee on Corporations and Financial Services recommended such a prohibition, to protect customers against genetic discrimination. Once implemented, insurance applicants would not be required to disclose genetic test results, even if it informed their decision to apply. Similar regulations have been put in place in other countries around the world.

Genetic research continues to progress rapidly. The new generation of genetic tests differs substantially to those currently available. Widespread testing is more likely with the new tests.

Tests of the future will be 'polygenic', simultaneously assessing a large number of genetic variants to predict the risk of common diseases such as cancer and heart disease. This makes them applicable for routine and potentially widespread use.

Such tests differ to current, 'monogenic', tests which only consider a small number of high-impact variants. These variants tend to be rare and widespread testing is generally unhelpful and avoided.

Polygenic tests are not yet publicly available, but current genetic research is rapidly improving their feasibility. Of the five top diseases affecting life insurance claims, substantial improvements in predictive power have been achieved for three of them in just the past year.

A future with widespread genetic testing will challenge the existing structure of the life insurance industry.

If genetic research delivers useful polygenic tests that get extensive adoption, we enter a world where we can stratify individuals by risk more finely than ever before. This will stretch the current way we pool risk within life insurance.

It is unclearly how the industry should respond. Using family history alone does not capture a sufficient amount of the genetic information as compared to a genetic test. Promoting lifestyle improvements is complex and unproven, especially by life insurers.

More fundamental changes may be required in the future. For example, setting up a pooled industry fund to support claims for diseases with a high genetic influence.

A key next step is to monitor how genetic tests are developed and implemented.

The state of the future is unknown but with clear signs pointing to likely change, a prudent step would be to closely monitor the progress of genetic research and initiatives around adoption of the technology (e.g. medical screening).

Furthermore, there will be a need for many parties, including life insurers, to be involved in shaping the governance and oversight of such technologies and their use.

The same developments are happening around the world, as illustrated by the common trends in regulation. This will therefore become a global issue, providing the opportunity to collaborate internationally to find workable ideas and solutions. Policy proposals should account for the rapid progress in genetics research and anticipate the likely future uses of genetic testing in medicine and other applications.

Appendix A. Genetic tests

In Section 5 we briefly introduced monogenic and polygenic tests. Here we provide more detail to help you understand how the differ.

A.1 Monogenic tests

Existing genetic tests typically measure a single gene or genetic variant. Many of these are well known, for example the *BRCA1* and *BRCA2* genes which affect breast cancer risk and variants of the Huntington gene which cause Huntington's disease.

Apart from simply the number of genetic variants being measured, two other features distinguish these from polygenic tests. The genetic variants they measure:

- Are known to either **cause** the disease of interest or otherwise be **highly predictive**.

  A 'positive' result leads to a moderate to high certainty of developing a specific disease. A 'negative' result may either mean the individual will not develop the disease (where the specific variants tested are the cause, as in Huntington's disease) or otherwise excludes the possibility of them being at elevated risk due to specific variants but are still at a general population-level of risk (e.g. breast cancer not caused by *BRCA1*).

- Tend to be **rare** in the population (although they might not be rare in certain groups of people or subpopulations).

  While the information provided can be strongly predictive, most of the variants tested are rare in the population. Moreover, the prevalence of the diseases caused by these variants is also generally low. Thus, they have limited coverage, in that they affect very few individuals.

Since many monogenic tests measure variants that are **causal**, their predictive power can be very high and are therefore able to be used as a **diagnostic** test. This is where the patient is already ill and our aim is to **confirm** a specific cause for the illness.

They might also be used as a **predictive** test. This is where an individual is healthy but wishes to **assess their risk** of developing a disease. Since the specific genetic variants being measured are typically rare, such predictive usage is only informative if you already suspect the presence of the risk variant (e.g. if carried by a family member or if you already have the disease), rather than as a generic risk predictor for healthy individuals.

Monogenic tests are available for some common diseases as well (e.g. breast cancer). However, they only test for specific high-risk genetic variants which tend to be rare and only account for a relatively small proportion of the incidence of such diseases (e.g. *BRCA1* for breast cancer). Therefore, they do not provide a 'broad spectrum' risk predictor for such diseases and can still be considered as a test for a rarer disease (more precisely, a rare subtype of the common disease).

A note on nomenclature: while we use the term 'monogenic' to refer broadly to existing tests, we do so mainly for convenience. The tests do not necessarily all target only a single gene. For example, a test for Down syndrome might look for an extra copy of a whole chromosome, which is a large part of the genome. Also, some tests would measure more than one gene, but generally not a substantial number. Although neither of these examples are strictly monogenic, the key features discussed above still apply and serve to distinguish them from polygenic tests.

Regarding availability, in Australia the standard situation is that a medical referral is required to obtain a genetic test. These tests are conducted by accredited laboratories, and the results returned to the referring medical specialist who can discuss the results with their patients and advise them accordingly.

The accreditation scheme is operated by the National Association of Testing Authorities, Australia (NATA). More details about the governance of this process can be found in ALRC Report 96 (Commonwealth of Australia, 2003: 11).

The Royal College of Pathologists of Australia keeps a register of accredited laboratories in Australia and the tests they provide (Royal College of Pathologists of Australasia, 2017). At the time of writing they listed 31 labs, collectively offering 1700 tests which covered 1138 genes.

The cost of tests can range from less than $100 to more than $1000, depending on various factors (Commonwealth of Australia, 2003: 10). Medicare rebates are available for some tests, often only under certain criteria, but many tests are not covered at all.

A.2 Polygenic tests

Recent scientific advances have led to the discovery of thousands of genetic variants each of which confer small increases in disease risk. While the effect of any specific variant might be negligible, in combination it is possible for them to explain a sizeable proportion of the risk. Determining which variants to measure and how to optimally combine their effects into a polygenic risk score (PRS) is an important strand of contemporary genetics research.

A polygenic test would involve measuring a large number of genetic variants for a given individual and calculating a PRS. This can be compared against a reference range to determine whether the individual is at a high or low risk compared to the

rest of the population and could even be calibrated to give an actual prediction of risk (e.g. '10% lifetime risk of breast cancer'). A separate PRS is necessary for each disease of interest and will typically use a distinct set of genetic variants.

We can therefore summarise the key features that distinguish them from monogenic tests. The genetic variants they measure:

- Can be **common or rare** in the population.
- Each contribute a **small amount** to the overall disease risk.

The latest research suggests that the genetic component of risk for many common diseases (e.g. heart disease, diabetes, various cancers) is spread across many variants, each contributing a small amount to the overall risk. This makes a polygenic test perfectly suited to assessing such risks.

Even for common diseases that have high-risk genetic variants (e.g. *BRCA1* for breast cancer), most of the genetic risk is typically attributable to a large number of lower-risk variants. Thus, these tests are expected to be mainly of interest for common diseases, which are not well 'serviced' by monogenic tests.

In contrast to monogenic tests, the predictive power of the polygenic tests is lower. Partly this is due to the fact that common diseases are only partly attributable to genetic factors, and partly to the fact that these tests are still under active development. As research has progressed, so has the predictive strength for many diseases.

These tests are **not** suitable for use as diagnostic tests. The diseases of interest will typically not be solely caused by a genetic mutation, so these tests will generally not be capable of determining the presence of disease.

Moreover, their predictive power varies greatly by disease, the target population and other factors. In fact, the current best-performing PRS for a given disease will typically not cover all of the underlying causal variants. Rather, it will measure genetic 'markers' that are correlated with the causal variants, and often cover only a subset of them. This leads to reduced predictive power. Therefore, for many diseases these tests are not necessarily suitable for use as predictive tests at this stage. However, this is changing rapidly as research progresses, through the discovery of new genetic variants and refinement of the respective PRSs.

Since polygenic tests survey common genetic variants, and aim to predict the risk of common diseases, they are **potentially useful as a generic risk predictor for all individuals**. The key aspect is whether they are predictive enough to allow useful clinical/lifestyle decisions to be made, especially when combined with other relevant information such as family history and lifestyle factors.

It is important to note that, whilst polygenic tests are still to mature, their predictive power is developing rapidly, as we showed in Section 4.1. As a further example, Figure 2 illustrates how breast cancer risk prediction has improved historically over the space of six years.

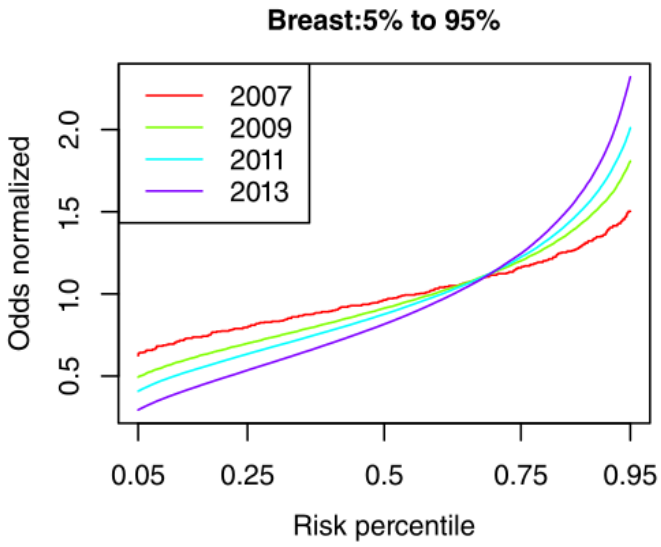


Figure 2. Taken from Krier et al. (2016, Figure 3), licensed under CC BY 4.0. The y-axis shows the odds ratio of developing breast cancer relative to the population mean, where individuals are ranked in order (along the x-axis) of their predicted genetic risk. Steeper gradients indicate a greater ability to differentiate individuals based on genetic risk. In 2013, individuals predicted to be in the top 5% of genetic risk (95th percentile) were predicted to have more than 4 times greater odds of developing breast cancer than those in the bottom 5% (5th percentile). In 2007, the same comparison was only about a 2-fold greater odds.

As the technology advances, so could the **interpretation** of a given test result be **updated over time** to incorporate new research findings. This leads to many ethical issues. For example, will the test facility have the obligation to inform the patient of updated results? When a person takes one genetic test, have they pre-emptively consented to all future genetic tests?

Despite ethical considerations, in principle, polygenic tests could subsume monogenic tests since any variants of interest in the latter could be included in the former, as long as the measurement technologies used allow that. Many such technologies are now relatively mature and cheap to run. Furthermore, they allow a large proportion of the genome to be measured, meaning that a single measurement run could produce data that could be used for many different polygenic tests, even ones that are not developed yet but will be produced in the future as a result of new research.

One important caveat to note is that the strength of any polygenic tests is likely to depend on the ancestry of the individual. Most of the currently completed research has only been done with individuals of European ancestry and the predictive power is likely to vary for other populations (Martin et al., 2017). Therefore, further work will be required before the results can be generalised and used for all individuals.

To the best of our knowledge, polygenic tests (in the form described above) are currently not offered to the public. They are still under active development and have not been validated to the extent required to be acceptable for use. Furthermore, there is debate on exactly how such tests should be used, how predictive they need to be, and what kind of regulation and oversight is required.

Several companies have attempted to sell polygenic tests through a direct-to-customer (DTC) business model, usually via the internet. Many of these have

discontinued. The most prominent such company that still exists is 23andMe. From 2007, they offered predictive disease reports for an ever-increasing number of diseases, tracking the latest scientific discoveries. However, in 2013 the US Food and Drug Administration (FDA) ordered them to stop due a failure to get FDA pre-approval and the lack of medical oversight. In 2017, the FDA approved a small number of tests for specific diseases for 23andMe, allowing them to once again report on disease risk, however now the tests are essentially monogenic tests. (For a brief recent history of DTC offerings and related discussion, see Metcalfe (2017).)

Technically savvy customers can download their raw genetic data from services such as 23andMe and then calculate their own risk scores based on current research. However, this is beyond the abilities of most people.

Despite their current unavailability, there is a widespread expectation that polygenic tests will be commonplace in the future and actively used. For example, to:

- Inform which medical treatments are most effective for a given individual based on their genetic profile ('personalised medicine').
- More effectively target public health interventions and screening programs, by prioritising those at highest genetic risk.

As an example of the latter, currently many screening programs such as mammograms are offered to people once they reach a certain age (since risk increases with age). In the future, we might screen those with high genetic risk at an earlier age and those with low risk at a later age. This would be a more targeted deployment of medical resources.

Figure 3 illustrates this with an example taken from a study of heart disease risk. Suppose we have a health program that we wish to target to people who have at least 10% risk of developing heart disease. By splitting the men in this cohort into three classes of genetic risk (low, medium, high), we see that we should start contacting the men who are at high risk soon after 50 years of age, but can delay contacting any who are at low risk until they are at least age 70.

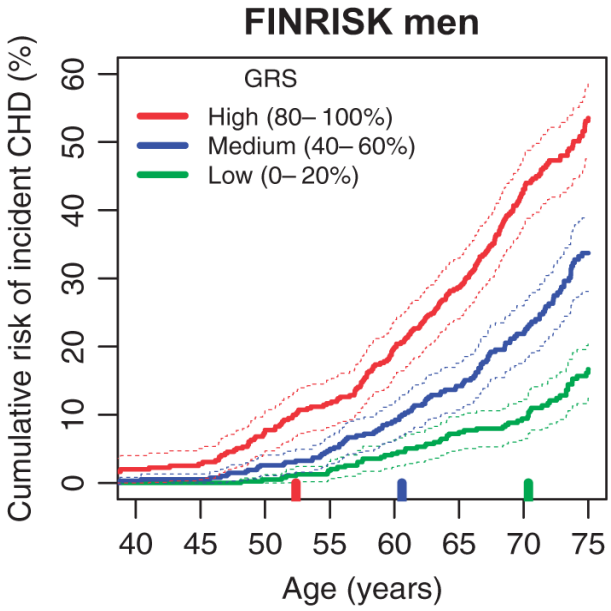


Figure 3. Taken from Abraham et al. (2016, Figure 3), licensed under CC BY-NC 4.0. Estimates of the cumulative risk of heart disease events amongst men in the FINRISK cohort, split by genetic risk group (as indicated). The vertical bars along the x-axis indicate the age at which each risk group attains a cumulative risk of 10%. Dashed lines indicate 95% confidence intervals of the estimates.

Initiatives of this form could lead to many people getting a polygenic test. Indeed, a public health program like this would only be effective if testing were widespread.

One possibility is to offer standardised genetic testing to everyone early in life, to help inform both preventative and clinical care throughout each individual's life.

A single comprehensive polygenic test could be done once and would provide information relevant to many or all of the above uses. The laboratory costs for such tests are relatively low ($100–$1000 per individual, depending on how much coverage of the genome is required), although it would be a substantial cost in total if rolled out on a large scale. Therefore, initiatives such as those above will need to demonstrate a clear benefit to justify this cost.

We expect to reach this tipping point eventually, as technological improvements drive the cost down and advances in research to lead to more effective ability to use the genetic information.

A new company, Genome.One, offers an example of how medical care informed by polygenic testing might look like in future. They combine a standard medical check together with results from whole-genome sequencing to present customised medical advice. Crucially, a referral by a medical doctor is required and the service only offers genetic testing for conditions with known, effective treatments or preventive interventions. This addresses the issue that has plagued many DTC offerings. The cost of this service is more than $6000 and is not covered by Medicare (Scott, 2017).

Appendix B. Illustrative model details

B.1 Modelling assumptions

B.1.1 Impact of genetics and lifestyle on disease risk

The table below shows the 10-year cumulative incidence rate for developing coronary artery disease based on distinct categories of lifestyle and genetic risk.

The statistics are taken from a recent study of the degree to which genetics and lifestyle contribute to an individual's risk of coronary artery disease (Khera et al., 2016). We used the estimates from the Atherosclerosis Risk in Communities cohort (one of three that were featured in the study), which included 7814 participants between the ages of 45 to 64 years, enrolled from1987 onwards.

10-year cumulative incidence rate (%)		Lifestyle		
		Healthy	Intermediate	Unhealthy
Genetic risk	Low	3.1	4.3	5.8
	Medium	4.8	5.0	7.3
	High	5.1	7.3	10.7

Lifestyle categories were defined as:

a) **Healthy** lifestyle is **3 or 4** healthy lifestyle factors
b) **Intermediate** lifestyle is **2** healthy lifestyle factors
c) **Unhealthy** lifestyle is **0 or 1** healthy lifestyle factor.

The four healthy lifestyle factors considered were: no current smoking, no obesity, regular physical exercise and a healthy diet.

Genetic risk categories were defined as:

a) **High** genetic risk is a polygenic risk score in the **top 20%** of the distribution
b) **Medium** genetic risk is a polygenic risk score in the **middle 60%** of the distribution
c) **Low** genetic risk is a polygenic risk score in the **bottom 20%** of the distribution.

B.1.2 Distribution of risk factors

The proportion of people in each risk category, using data from the same study as above, is shown in the following table. We assumed that in the absence of any adverse selection, the insurance customer profile also followed this distribution.

		Lifestyle			
		Healthy	Intermediate	Unhealthy	
Genetic risk	Low	6%	8%	6%	**20%**
	Medium	19%	24%	17%	**60%**
	High	6%	8%	6%	**20%**
		32%	**40%**	**28%**	**100%**

B.1.3 Base case adverse selection

For the base case adverse selection, we assumed that the overall customer profile will shift towards higher risk, with 5% of people moving from low genetic risk to high genetic risk, spread proportionately across the lifestyle categories:

		Lifestyle			
		Healthy	**Intermediate**	**Unhealthy**	
Genetic risk	**Low**	5%	6%	4%	**15%**
	Medium	19%	24%	17%	**60%**
	High	8%	10%	7%	**25%**
		32%	**40%**	**28%**	**100%**

B.1.4 Base case lifestyle intervention

For the base case lifestyle intervention in response to (the base case) adverse selection, we assumed that the insurer successfully shifts their now riskier customer profile towards a lower risk, with a 5% move from unhealthy to healthy lifestyle, spread proportionately across the genetic risk categories:

		Lifestyle			
		Healthy	**Intermediate**	**Unhealthy**	
Genetic risk	**Low**	6%	6%	3%	**15%**
	Medium	22%	24%	14%	**60%**
	High	9%	10%	6%	**25%**
		37%	**40%**	**23%**	**100%**

B.1.5 Further assumptions

For simplicity, we use the overall incidence rate across our customer pool as a proxy for the total costs of claims. We quantify the change in incidence rate under different scenarios and assume this is representative of the change in claim costs.

This simplification ignores any details regarding the age of customers and when they experience a disease event, effectively assuming that all customers are always eligible to make a claim. It also ignores any large changes to the **number** of customers, effectively assuming a fixed number across different scenarios.

B.2 Base case results

No adverse selection. The expected overall (10-year cumulative) incidence rate amongst customers, assuming no adverse selection, is **5.7%.** This is calculated as the weighted mean of the incidence rates across the 9 risk categories (assumptions 1 and 2, above).

Adverse selection (5% shift to high genetic risk). Using the customer profile assuming the presence of adverse selection (assumption 3, above), the expected overall incidence rate is **5.9%**, which is a **3% increase in total claim costs** compared to no adverse selection.

Lifestyle intervention (5% shift to healthier lifestyle). Using the customer profile assuming a successful lifestyle intervention to reduce risk (assumption 4, above), the expected overall incidence rate is **5.7%**, which effectively **offsets adverse selection.**

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