Genetic testing anti-selection risk and implications for insurers

Florian Rechfeld
Senior Research Analyst, Life & Health R&D, Swiss Re

CRO Assembly, 31\textsuperscript{th} May 2018
Trends and prospects in genetic testing
What is Genetic Testing?

“Genetic testing looks for alterations in a person's genes or chromosomes to identify heritable or acquired mutations related to disease and health”

- **Diagnostic / confirmatory genetic testing**: Identifies or confirms a specific genetic condition in a symptomatic individual.
- **Pharmacogenomic testing**: Guides individual drug dosage, selection and response.
- **Direct-to-consumer (DTC) genetic testing**: Genetic tests marketed directly to consumers without involving healthcare professionals.
- **New-born screening**: Identifies highly penetrant genetic disorders that can be treated early in life.
- **Predictive and pre-symptomatic genetic testing**: Estimates the risk of developing adult-onset disease or predicting future disease onset.
- **Nutrigenomic testing**: Studies the effect of genetic variations in relation to the interaction between diet/nutrition and health.
- **Liquid biopsy testing**: Detects molecular biomarkers in blood & other body fluids for diagnosis, prognosis and treatment.
Declining sequencing costs and rapid growth of genetic tests

Plummeting genome sequencing costs and advances in human genetics increases the availability for different types of genetic testing


Genetic Testing Registry (GTR)
- 54,538 Tests
- 11,169 Disorders
- 16,415 Genes
- 506 Laboratories

May 24, 2018
Genetic testing in the clinical practice has grown more than 20% annually in recent years.

Trend in UK clinical genetic testing activity

Advances in the understanding of human genetics increases the availability and uptake of genetic testing in the clinical practice.

Source: ACGS audits
23and Me & Co: A booming Direct-To-Consumer market

23andMe customer development

- Starting a family: find out if you are a carrier for certain inherited conditions.
- Learn how your genetics influence your risk for certain diseases.
- Discover where your DNA is from out of 31 populations worldwide.
- Learn how your DNA influences your facial features, taste, smell and other traits.
- Learn how your genes play a role in your well-being and lifestyle choices.

40+ reports including:
- Polycystic Kidney Disease
- Cystic Fibrosis
- Hereditary Hearing Loss

5 reports including:
- BRCA1/2 (selected variants) NEW!
- Late-Onset Alzheimer's Disease
- Parkinson's Disease

5 reports including:
- Ancestry Composition
- Your DNA Family
- DNA Relative Finder tool

5 reports including:
- Hair loss
- Sweet vs. salty
- Unibrow, freckles...

21 reports including:
- Deep sleep
- Lactose intolerance
- Genetic weight
At least half of consumers open to taking a genetic test in the future as prices drop; most to satisfy personal curiosity but half wants to know more about potential disease risk!
Use of genetic testing information in L&H insurance underwriting
Key markets under regulatory pressure from banning genetic testing information for insurance underwriting

Current regulatory approaches to insurers’ access and use of genetic data fall into 3 major categories:

- **Legal ban**
  - Austria
  - Belgium
  - Canada
  - France
  - Ireland
  - Korea
  - Poland
  - Portugal
  - USA (Health)
  - Tendency towards increased regulations or complete ban!

- **Limitations by law**
  - Germany
  - Netherlands
  - Switzerland
  - UK

- **No / Self-regulation**
  - Australia
  - China
  - Hong Kong
  - India
  - Japan
  - Singapore
  - South Africa
  - USA (Life, DI, LTC)

Regulatory restrictions typically apply to:
- **Predictive genetic tests**
  - The use of diagnostic genetic information to confirm the presence of a disease is generally allowed for underwriting purposes as long as actuarially justifiable;
- **Life insurance/disability income/long-term care** as most developed countries offer public healthcare or mandate the purchase of health insurance

1 Legislation varies at state level. Approx. 1/3 of states have regulation restricting the use of genetic information in life insurance
2 Only for list of approved tests. Currently only Huntington’s disease for life insurance
Predictive value of genetic tests and risk assessment
Insurance underwriting and risk classification

Many factors that influence the risks of ill health or death may be used in insurance underwriting, based on statistical evidence. Such risk factors may include:

• **Non-medical factors:**
  - Financials: occupation, income, sum assured, ...
  - Habits: sport, travelling, alcohol, drugs, ...

• **Medical factors:**
  - age, (gender), medical records, family history, smoking status, blood pressure, lipid levels, .....  
  - **Genotype** as a valid risk factor candidate in insurance pricing?
The risk for disease is multi-factorial and depends on genetic and environmental components.

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Environment</th>
<th>Spectrum of Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Huntington’s</td>
<td>Non - Genetic</td>
<td>Thrombosis, Schizophrenia, Fam. breast cancer, Colon cancer syndrome, Cystic Fibrosis, Huntingdon’s</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td></td>
<td>Alzheimer, Diabetes, Asthma, Lung cancer, Car accident</td>
</tr>
<tr>
<td>Colon cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>syndrome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fam. breast cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombosis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Genetic contribution to disease
ACMG reporting of “secondary” findings from genome/exome-sequencing

ACMG POLICY STATEMENT

ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing

Robert C. Green, MD, MPH1,2, Jonathan S. Berg, MD, PhD3, Wayne W. Grody, MD, PhD4–6, Sarah S. Kalia, ScM, CGC1, Bruce R. Korf, MD, PhD7, Christa L. Martin, PhD, FACMG8, Amy L. McGuire, JD, PhD8, Robert L. Nussbaum, MD9,10, Julienne M. O’Daniel, MS, CGC3, Kelly E. Ormond, MS, CGC11, Heidi L. Rehm, PhD, FACMG2,12, Michael S. Watson, PhD, FACMG13, Marc S. Williams, MD, FACMG14 and Leslie G. Biesecker, MD15

• Minimum list of 59 genes and variants for 27 conditions to be returned whenever clinical exome sequencing is performed for any medical reason.

• Medically "actionable" pathogenic variants with strong evidence for clinical validity and utility.
Genetic testing and anti-selection risk for insurers
Future trends in genetic testing and insurance risk considerations

- Genome sequencing costs will continue to decline
- Genetic testing rates in the general population will continue to increase
- Associating future disease risk to specific gene characteristics will improve
- Regulatory restrictions on access and use of genetic information for insurers will increase
- Growing asymmetry of risk relevant genetic health information will expose life insurers to increased adverse-selection
### Studies on genetic testing and its impact on insurance purchasing behaviour

<table>
<thead>
<tr>
<th>Genetic disease (Gene)</th>
<th>Insurance product</th>
<th>Odds ratio of over - insuring after positive test</th>
<th>Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast cancer (BRCA1/2)</td>
<td>Life</td>
<td>5.1x more likely to increase coverage</td>
<td>Armstrong et al.; 2003 (USA)</td>
</tr>
<tr>
<td>Alzheimer's disease (APOE4)</td>
<td>LTC</td>
<td>5.7x more likely to change coverage</td>
<td>Taylor et al.; 2005 (USA)</td>
</tr>
<tr>
<td>Alzheimer's disease (APOE4)</td>
<td>LTC</td>
<td>2.3x more likely to increase coverage</td>
<td>Zick et al.; 2010 (USA)</td>
</tr>
<tr>
<td>Alzheimer's disease (APOE4)</td>
<td>LTC</td>
<td>4x more likely to change coverage</td>
<td>Christensen et al.; 2015 (USA)</td>
</tr>
<tr>
<td>Huntington's disease (HD)</td>
<td>LTC</td>
<td>5x more likely to purchase insurance</td>
<td>Oster et al.; 2010 (USA &amp; Canada)</td>
</tr>
<tr>
<td>Colorectal cancer (HNPCC)</td>
<td>Life</td>
<td>1.3x more likely to purchase insurance</td>
<td>Aktan-Collan et al.; 2001 (Finland)</td>
</tr>
</tbody>
</table>

Understanding of consumers behaviour is key to investigate the potential impact on insurance purchasing behaviour and level of adverse selection against insurers.
Important model assumptions

- Proportion of population at risk for genetic conditions under study
- Proportion of population taking a genetic test each year
- Proportion of new applications if known to have higher genetic risk
- Proportion of policies that may lapse if known to have lower genetic risk
- Effectiveness of UW (e.g. family history)
- Anti-selection: How much higher face amount is bought, relative to the average person?

Sources:
(1) Genetic Testing Model: If Underwriters Had No Access to Known Results, Canadian Institute of Actuaries, Robert C. W. (Bob) Howard, July 2014
(3) Thinking about life insurance through a genetic lens, Damjan Vukcevic & Jessica Chen, May 2017
(4) Genetic Testing & the Threat of Anti-selection, Mark Lombardo, ACLI Symposium on Genetics & Insurance, April 2018
Additional risk considerations for insurers

**Disease incidence & over-diagnosis**

Genetic tests used for screening (e.g. liquid biopsy) may lead to increase in disease incidence & over-diagnosis.

Over-diagnosis: Identification of "disease" that may never have caused symptoms or premature death

**Health-care costs**

- Increased medical treatment costs: additional screening, medical counselling, preventive or therapeutic interventions
- Reimbursement cost of genetic testing

**Legal risk**

- Request & use of genetic information in underwriting is highly regulated in an increasing number of markets
- Insurers’ medical risk selection process is further limited

**Insurance non-disclosure and/or access restrictions to risk-relevant genetic information**

**Adverse selection** through selective purchase or lapse

**Adverse selection**

Consumer’s knowledge of their genetic information and future health

**Reputational risk**

Debate on potential discrimination in employment, insurance and privacy & security of personal genetic information

**Insurers voluntarily limit the use of genetic testing data for risk selection**
Reflections

• Scientific advances
  – clinical and over-the-counter genetic testing will continue its rapid growth

• Regulations
  – increasing regulatory pressure restricting request and use of genetic tests and family history for insurance UW

• Anti-selection
  – growing availability of predictive health information from genetic testing leads to increased exposure to anti-selection

• Additional risks
  – enhanced screening leading to early disease detection/over-diagnosis of indolent disease and increased medical treatment costs
Further information and client material on genetic testing

• Publications:
  - Seeing the future? How genetic testing will impact life insurance
  - Genomic Medicine
  - Personalised genetic testing and its impact to insurance
©2018 Swiss Re. All rights reserved. You are not permitted to create any modifications or derivative works of this presentation or to use it for commercial or other public purposes without the prior written permission of Swiss Re.

The information and opinions contained in the presentation are provided as at the date of the presentation and are subject to change without notice. Although the information used was taken from reliable sources, Swiss Re does not accept any responsibility for the accuracy or comprehensiveness of the details given. All liability for the accuracy and completeness thereof or for any damage or loss resulting from the use of the information contained in this presentation is expressly excluded. Under no circumstances shall Swiss Re or its Group companies be liable for any financial or consequential loss relating to this presentation.