



**2018 SOA Asia-Pacific
Annual Symposium**

**Session 4A, The Wave on Shore: Genetic Testing & the Impact on
Insurance**

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The Wave on the Shore - Genetic Testing & Impact on Insurance



The Wave on the Shore Genetic Testing & Impact on Insurance

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Agenda

1. Overview
2. Evolving Regulations
3. Application in Insurance
4. Implication for Insurance
5. Attempt in quantifying the impact
6. Reflection

Overview

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

Pharmacogenomics 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

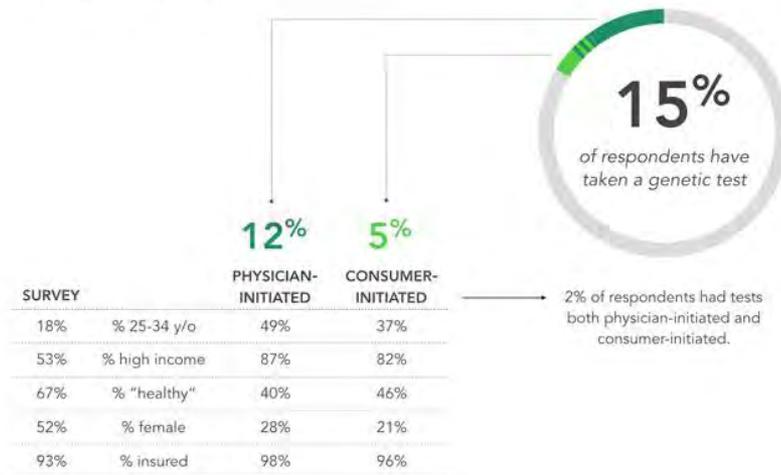
Studies the effect of genetic variations in relation to the interaction between diet/nutrition and health

Liquid biopsy testing

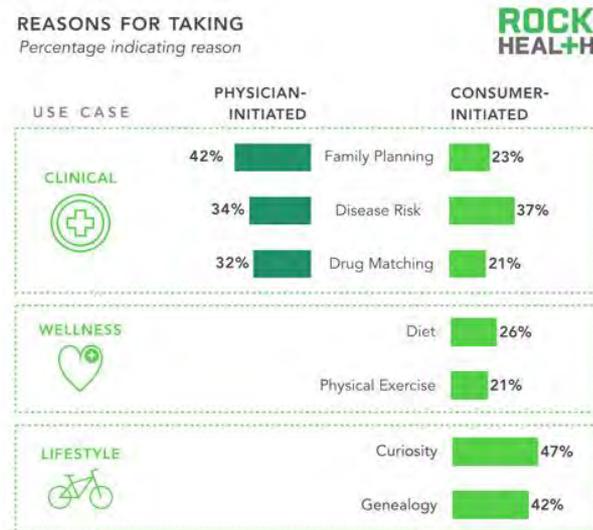
Detects molecular biomarkers in blood & other body fluids for diagnosis, prognosis and treatment

Higher than expected US genetic testing consumer adaption rates of 15% observed in 2016

GENOMICS ADOPTION
Percentage of adoption by channel



REASONS FOR TAKING
Percentage indicating reason

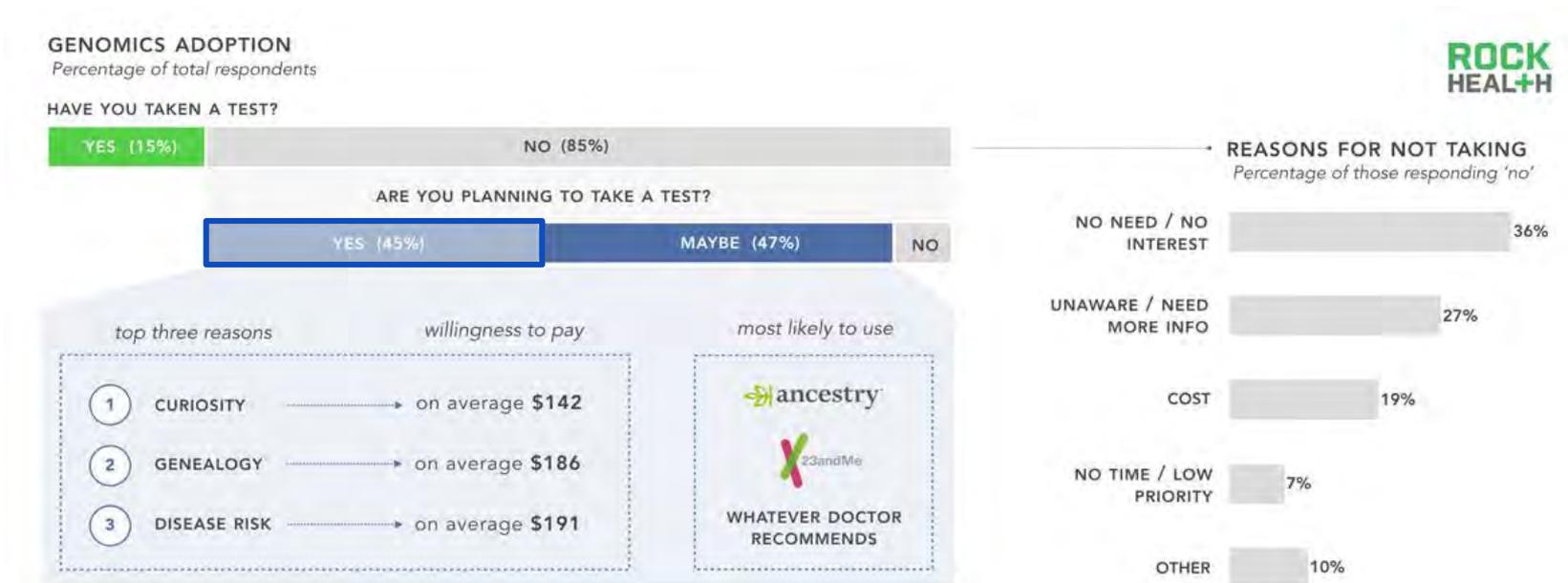


Source: <https://rockhealth.com/reports/the-genomics-inflection-point-implications-for-healthcare/#consumer-sentiments>, 2016, n=1060

Other studies

% taken a genetic test	#Participants	Year	Source
6%	1'489	2016	STAT-Harvard Poll on Genetic Editing, Testing, and Therapy
3%	694	2016	Attitudes to return of incidental findings
18%	1'588	2011	Nature readers flirt with personal genomics
14.8%	890	2010	Science after the sequence

Additional 45% of consumers considering to get tested as prices for testing drop



Source: <https://rockhealth.com/reports/the-genomics-inflection-point-implications-for-healthcare/#consumer-sentiments>, 2016, n=1060

At least half of consumers open to taking a genetic test in the future; most to satisfy personal curiosity but half wants to know more about potential disease risk

Growing Market for DTC Genetic Testing in Asia



China's Example

- Market size five folded from RMB 1.2b in 2012 to RMB 6b in 2016.¹
- Genetic testing industry listed as important force in the new momentum of China's economic development by National Development and Reform Commission¹.
- Over 400 genetic testing suppliers by 2017.
- Cancer and prenatal tests are the top 2 most popular sectors

华大基因
BGI

61.6bn
CNY²

BerryGenomics
贝瑞和康

21.7bn
CNY²

GRAIL

?

1. Genetic testing industry boost China's economic development, datenna, Nov 8, 2017

2. Market CAP, Bloomberg, 24 April 2018 (Estimation only)

Liquid Biopsy

- Blood contains two types of cancer-derived materials that are susceptible to detailed molecular analysis:
 - intact circulating tumour cells (CTCs)
 - cell-free circulating tumour DNA (cfDNA; also referred to as circulating tumour DNA, or ctDNA)
- The evolution of sensitive CTC and cfDNA detection technologies has enabled the development of liquid biopsies with many clinical applications, including:
 - screening for presence of disease (yet to mature);
 - patient stratification and therapy selection (companion diagnostics);
 - monitoring treatment response and drug resistance;
 - detection of minimal residual disease after surgery/recurrence.



Liquid Biopsy – Holy Grail

Liquid biopsy for NPC screening proves effective in large-scale study



Table 2. Sensitivity and Specificity of the Two-Stage Screening Protocol for the Detection of Nasopharyngeal Carcinoma.*

Finding	Screen-Positive (N=308) [†]	Screen-Negative (N=19,865)
Confirmed nasopharyngeal carcinoma by the screening protocol or nasopharyngeal carcinoma reported to have developed within 1 yr — no.	34	1
No nasopharyngeal carcinoma within 1 yr after screening — no.	274	19,864
Sensitivity — % (95% CI)	97.1 (95.5–98.7)	
Specificity — % (95% CI)	98.6 (98.6–98.7)	
Positive predictive value — % (95% CI)	11.0 (10.7–11.3)	
Negative predictive value — % (95% CI)	99.995 (99.99–100.00)	
Proportion of stage I/II disease in the 34 cases of nasopharyngeal carcinoma identified by screening — % (95% CI)	70.6 (69.6–72.5)	

* Screen-positive is defined as persistently positive for plasma EBV DNA at baseline and at follow-up. Screen-negative is defined as negative for plasma EBV DNA either at baseline or at follow-up.
[†] The participant who had declined further investigation but in whom advanced nasopharyngeal carcinoma developed 32 months after screening is not included in this number.

Single Blood Test Screens for Eight Cancer Types



The test was evaluated on 1,005 patients with nonmetastatic, stages I to III cancers of the ovary, liver, stomach, pancreas, esophagus, colorectum, lung or breast. The median overall sensitivity, or the ability to find cancer, was 70 percent and ranged from a high of 98 percent for ovarian cancer to a low of 33 percent for breast cancer. For the five cancers that have no screening tests—ovarian, liver, stomach, pancreatic and esophageal cancers—sensitivity ranged from 69 percent to 98 percent.

1. Analysis of Plasma Epstein–Barr Virus DNA to Screen for Nasopharyngeal Cancer, NEJM, K.C. Allen Chan, Nov 10, 2017
2. Single Blood Test Screens for Eight Cancer Types, Press Release, James Hopkins Medicine, Jan 18, 2018

Evolving Regulations

Genetic testing regulation

- Regulation acts between the poles of avoiding anti-selection and the fear of denied insurance for people with adverse test results

No genetic test disclosure

Policyholders who have more information about their health than the insurer might anti-select

Full genetic test disclosure

Potential policyholders might be discriminated against or cancel/postpone planned genetic tests out of fear of being denied insurance based on the results

- Regulatory restrictions typically apply to
 - **predictive testing** . 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
- Regulation is still developing in many countries

Restrictions on use of genetic data for insurers

Last updated: Jan 2018. For reference only.



No regulation/code of conduct	Code of conduct from insurance industry	Prohibited to require genetic test, but can use existing test	Prohibited to use tests below given SA	Prohibition/ moratoria to use genetic tests at all
China	Greece	Australia	Germany	Austria
Finland	Hong Kong		Netherlands	Belgium
India	Japan		Switzerland	Canada
Spain			United Kingdom ²	Denmark
US (Life, DI, LTC) ¹				France
				Ireland
				South Korea
				Poland
				Portugal
				Singapore
				US (Medical)
<i>Legislator might still be working to pass regulation</i>			<i>Certain level of life insurance/DI deemed basic right</i>	<i>Wait-and-see approach</i>

¹Legislation varies at state level. Approx. 1/3 of states have regulation restricting the use of genetic information in life insurance

²Only for list of approved tests. Currently only Huntington's disease

Regulation in Canada



Last updated: Jan 2018. For reference only.

- Bill S-201 *"An Act to prohibit and prevent genetic discrimination"* passed in March 2017 prohibits an insurer from:
 - requiring a person to take a genetic test
 - requiring a person to disclose the results of a genetic test
 - discriminating against a person because they did not take a genetic test
- An earlier version allowed insurers to ask for prior test results for life insurance with SA \geq 1 Million CAD or DI with annual payments \geq 75'000 CAD.
- However, Federal Government is on record to seek clarity from the Supreme Court of Canada on the constitutionality of the law.

see <https://openparliament.ca/bills/42-1/S-201/>

Regulation in Australia



Last updated: Jan 2018. For reference only.

- Self-imposed industry standard
 - Life insurers will not initiate a request for a new genetic test or in any way coerce an applicant for insurance to undertake a new genetic test.
 - Where an applicant has already undertaken a genetic test, the results are required to be provided if that is requested by an insurer
 - The insurer will take account of the benefits of special medical monitoring, early medical treatment, compliance with treatment and the likelihood of successful medical treatment when assessing overall risk.
 - The insurer will provide reasons for any adjustment to premiums or policy conditions imposed after their assessment of the application
- Recommendation by the Australian genetic non-discrimination working group (December 2016)
 - For the Australian government to enact legislation to regulate the use of genetic information.
 - Until such legislation is in place, the Australian government to enact a ban or moratorium on the use of genetic data by life insurers.

Regulation in South Korea



Last updated: Jan 2018. For reference only.

- Act on bioethics and bio-securities:
 - *No discrimination in social activities such as education, promotion, employment or insurance is allowed because of genetic test information.*
 - *Nobody can force the other person to have the genetic tests nor to submit the genetic test results.*
- There is no specific legislation on family history or questions on any specific diseases. However, FSS (financial supervisory services) allowed questions on family history of some diseases related to CI cover for CI application form.

Regulation in China



Last updated: Jan 2018. For reference only.

- Regulator is reviewing the regulation around the use of genetic testing information for insurers. The direction is geared towards disallowing any usage.
- Genetic testing information and family medical history are considered as sensitive personal data under the Chinese law. The data subjects' informed consent is required for any collection, use and further sharing of sensitive personal data for legitimate business purposes.
- The collection, research, sale and cross-border transfer of genetic information of Chinese population is subjected to administration of the PRC Ministry of Science and Technology ("MST").
- Clinical use of genetic testing is not allowed without prior approval of the China Food and Drug Administration ("CFDA") and the Commission of Health and Family Planning ("CHFP").

Application in Insurance

Application by Insurers in Asia

Value-added-services (Common)



Nutrigenomic testing

Studies the effect of genetic variations in relation to the interaction between diet/nutrition and health



Pharmacogenomics testing

Guides individual drug dosage, selection and response

Value-added-services (Some Attempt)



Predictive and pre-symptomatic genetic testing

Estimates the risk of developing adult-onset disease or predicting future disease onset

Most offered to customers with family history but some attempted to extend beyond (unconditional)

Integrated with Product (Withdrawn)



Bundled Insurance Product

Insurance providing DTC predictive genetic testing for certain diseases and coverage varies by the genetic testing result – ranging from lump sum coverage to provision for cancer screening.

Insurers to offer genetic testing to clients/applicants

Human Longevity, Inc. and MassMutual Sign Groundbreaking Agreement to Offer HLIQ™ Whole Genome Sequencing to MassMutual's Customers, Financial Professionals and Employees

...HLIQ Whole Genome, to eligible MassMutual customers, employees and financial professionals at a reduced price. The initiative should help enable HLI's goal of providing up to 200,000 HLIQ Whole Genome reports.

HLIQ Whole Genome, which is ordered by a client's physician, includes comprehensive sequencing and analysis of the individual's whole genome. The report may give insight into health status and risk for disease, details on which pharmaceuticals may work better for individuals, carrier status for family planning decisions, along with ancestry and personal traits.

Source: MassMutual Press Release, 15 March 2017, <https://www.massmutual.com/about-us/news-and-press-releases/press-releases/2017/03/15/14/55/human-longevity-inc-and-massmutual-sign-groundbreaking-agreement>

Implication for Insurance



Cancer Predictive Testing

How “predictive” is cancer predictive testing?

- Inherited (germline) mutations are thought to play a role in about **5%-10%** of all cancers.¹
- >100 germline mutations identified conferring high or moderate risk of cancer (>2 fold relative risk, at least 5% develop cancer)².
- Most cancers (~80%) are sporadic (not due to inherited gene mutation).³

How should results be interpreted?

- **Genetic counselling** is required to properly explain the result as inappropriate interpretation may lead to **unneeded anxiety, false assurance or important decisions about medical treatment.** ¹
- Interpretation of results is complex (not straight yes or no). Follow up actions advised require careful considerations. For example, regulator in US advised caution towards nutrition advice by DTC companies.⁴

Who should take it?

- Most publications advise for person having **personal or family history** to take it.

Positive result interpretation¹:

- *Confirm diagnosis of a hereditary cancer syndrome.*
- *Indicate an increased risk for developing certain cancer.*
- *Indicate as carrier of a gene mutation without increased risk, but that might affect offspring.*

Negative result interpretation¹:

For person with strong family history / known genetic causing gene alteration in the family:

- ***True negative:*** *absence of specific known gene mutation; no increased genetic risk of developing cancer.*
- ***Uninformative negative:*** *absence of a known mutation associated with hereditary cancer.*

More generally:

- ***False negative:*** *Absence of tested gene mutation associated with cancer but is inconclusive of whether the person has higher or lower risk.*
- ***Variant of unknown significance:*** *Unknown variant today but might have significance in the future.*

1. National Cancer Institute, the Genetics of Cancer, <https://www.cancer.gov/about-cancer/causes-prevention/genetics>

2. Realising the Promise of Cancer Predisposition Genes, Nazneen Rahman, MD PhD, *Nature*. 2014 Jan 16; 505(7483): 302–308.

3. Force, Hereditary Cancer & Genetics, <http://www.facingourrisk.org/understanding-brca-and-hboc/information/hereditary-cancer/hereditary-genetics/basics/hereditary-vs-sporadic-cancer.php#text>

4. Federal Trade Commission, customer information, Direct to Consumer Genetic Tests, <https://www.consumer.ftc.gov/articles/0166-direct-consumer-genetic-tests>

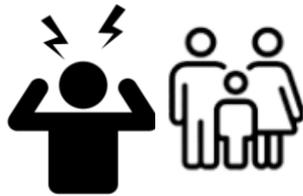
Predictive Testing: Possible Responses & Insurance Risk



Improvement in mortality and morbidity risk:
Extent depending how modifiable is the risk



Anti-selection:
Additional purchase depending on effectiveness of UW, selective lapse



Counselling, Reputational



Impact on risk:
Uncertain about Critical Illnesses depending on definitions and structure.
Improvement in Mortality.



False Assurance:
Lapse, relaxed guard for screening / lifestyle modifications

An illustration



Liquid Biopsy as Screening - Considerations



Maturity of Technology:
Sensitivity, Specificity,
Tested subjects

The test was evaluated on 1,005 patients with nonmetastatic, stages I to III cancers of the ovary, liver, stomach, pancreas, esophagus, colorectum, lung or breast. The median overall sensitivity, or the ability to find cancer, was 70 percent and ranged from a high of 98 percent for ovarian cancer to a low of 33 percent for breast cancer. For the five cancers that have no screening tests—ovarian, liver, stomach, pancreatic and esophageal cancers—sensitivity ranged from 69 percent to 98 percent.



Acceptance of Medical Community

Despite the limited sample size, our data show very low congruence for same patient-paired samples in 2 CLIA-certified commercially available tests with self-reported high accuracy, specificity, and sensitivity to specifically detect and quantify tumor-specific alterations. These data cannot determine which test is more accurate but suggest that reported gene alterations will not be the same across different platforms, raising the specter that patients could potentially receive different treatments depending on the cfDNA platform. Insufficient genetic profiling congruence could jeopardize the clinical benefit of personalized medicine.^{1,6}



Underwriting:
1. Duty to disclose
2. Classification of test
3. Credible underwriting decision



Claims & Definition:
What is Cancer?
Impact for long term guarantee?



Anti-selection:
1. Extent
2. Impact of DTC testing



Over-diagnosis and/or over-treatment

Sources:

- (1) Single Blood Test Screens for Eight Cancer Types, Press Release, James Hopkins Medicine, Jan 18, 2018
- (2) Patient-Paired Sample Congruence Between 2 Commercial Liquid Biopsy Tests, SOA Onc Pacific Annual Symposium, 2017 24 May 2018
- (3) A blood test that can detect cancer?, Swiss Re

Risk Considerations for Insurers



Regulations around use of genetic testing information in underwriting



Healthcare cost may increase due to more screening, counselling, etc.



Anti-selection risk through additional insurance purchase / persistence.



Genetic counselling available and use of genetic testing result



Over-diagnosis and overtreatment risk



Legal risk – regulation, potential law suite



Reputational Risk, ethical concern



The future unknown

Sources:

(1) Genetic testing and implications for life insurers, Swiss Re

Attempt in quantifying the impact

Modelling around the world

Institute	Year of Publish	Risk	Estimated impact
Canadian Institute of Actuaries ¹	2014	Mortality	Average 44 % (35 % male, 60 % female)
Canadian Institute of Actuaries ²	2016	Critical Illnesses	Average 26 % (16 % male, 41 % female)
Institute of Actuaries of Australia ³	2017	Critical Illnesses	1.8 % (assuming 0.5 % population) 17.5 % (assuming 5 % population)

Sources:

(1) Genetic Testing Model: If Underwriters Had No Access to Known Results, Canadian Institute of Actuaries, Robert C. W. (Bob) Howard, July 2014

(2) Genetic Testing Model for CI: If Underwriters of Individual Critical Illness Insurance Had No Access to Known Results of Genetic Tests, Canadian Institute of Actuaries, Robert C. W. (Bob) Howard, January 2016

(3) Thinking about life insurance through a genetic lens, Damjan Vukcevic & Jessica Chen, May 2017

Key & Sensitive Assumptions

1. Impact of genetic factor to the claim
2. Proportion of claim due to those diseases under the study
3. Proportion of population taking the genetic test
4. Proportion of policies that may lapse if known to have lower genetic risk
5. Proportion of new application if known to have higher genetic risk
6. Effect of Underwriting (e.g. family history)
7. Anti-selection: How much higher face amount is bought, relative to the average person?



Reflection

Reflection



“Equality” for insurance entitlement? Discrimination?
Genetics, family history and beyond?



Known unknown – complexity of interactions of genes, linkage of
diseases is just at the beginning.
Beyond genetics? (e.g. epi-genetics, microbiomes)



Medical advancement, innovation & customer protection
Embracing changes with prudence







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