Best Practices on Genetic Testing – The way forward

Session 2: Get ready for a genetic moratorium (era)

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Moderator:

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Agenda

01 Key Principles of the HK Best Practice

02 Risk Assessment and Selection

03 Operational Considerations

04 RGA Global Client Survey

05 RGA Impact Model

06 RGA Support

07 Q & A

Key Principles of the HK Best Practice

RGA

Key Principles

No pressure
- Insurers will not require applicants to undertake genetic testing for underwriting purposes

Scientific Research
- Insurers will not ask for the results of any genetic test for the purpose of underwriting if the genetic testing was conducted in the context of scientific research or the Hong Kong Genome Project

Test Results
- Insurers may request for the results of Diagnostic Genetic Tests for the purposes of underwriting

Three Criteria
- Certain Predictive Genetic tests can be asked for dependent upon defined limits and products

Family/ Relatives
- Insurers will not ask or use the results of any genetic tests of a relative or a family member of a proposed or existing insured for the purpose of underwriting.

Exception
- Insurers may use the results of a Predictive Genetic Test if the applicant voluntarily provides such information and the information will result in a more favourable decision to the applicant.

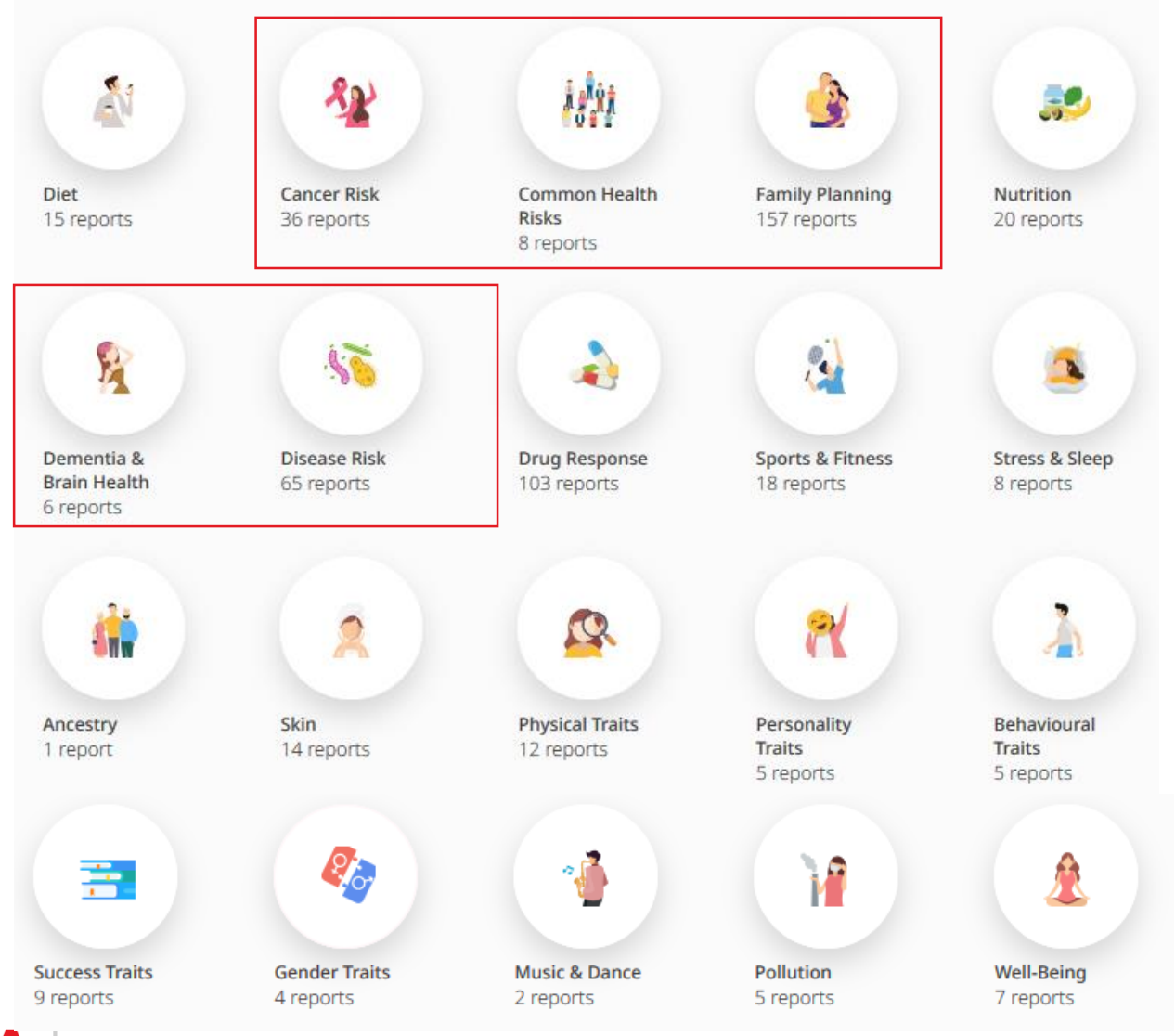
Overview

<table>
<tr><th>Type of insurance</th><th>Threshold of sum insured in the insurance policy above which Predictive Genetic Tests results may be requested</th><th>Medical conditions for which Member Companies may ask for and take into account the Predictive Genetic Test results</th></tr>
<tr><td>Life insurance</td><td>HKD 5,000,000</td><td rowspan="2">• Early-onset autosomal dominant Alzheimer disease (EOAD)
• Hereditary breast and ovarian cancer syndrome
• Lynch syndrome/Hereditary non-polyposis colorectal cancer
• Autosomal dominant polycystic kidney disease (ADPKD)
• Huntington’s Disease (HD)
• Hypertrophic cardiomyopathy (HOCM)</td></tr>
<tr><td>Critical Illness</td><td>HKD 1,000,000</td></tr>
<tr><td>VHIS</td><td colspan="2" rowspan="2">Predictive Genetic Test results will not be asked for, or taken into account, regardless of level of cover</td></tr>
<tr><td>All other types of insurance</td></tr>
</table>

Genetics: Risk Assessment & Selection considerations

RGA

Prenetics Test Report – Premium Package



- 20 categories
- 500+ reports, including **identification of risk** for:
  - 36 cancers
  - 80 common diseases such as stroke, and heart diseases,
  - 150+ hereditary diseases; and
  - Others such as diet
- Complementary 30-minute phone consultation with a Genetic Counsellor (Advance booking required)

Prenetics Test Report – Premium Package

Your **Cancer Risk** Results Summary

Breast Cancer 14 gene(s) tested	A cancer-causing variant was detected in BRCA1 gene(s)
Ovarian Cancer 12 gene(s) tested	A cancer-causing variant was detected in BRCA1 gene(s)
Pancreatic Cancer 17 gene(s) tested	A cancer-causing variant was detected in BRCA1 gene(s)
Prostate Cancer 16 gene(s) tested	A clinically significant variant detected in RNASEL gene(s)
Bladder Cancer 1 gene(s) tested	No cancer-causing variant detected
Brain Cancer 15 gene(s) tested	No cancer-causing variant detected

Your **Family Planning** Results Summary

Alpha Thalassemia Due to HBA1/HBA2 variant	Carrier
Achondrogenesis Due to SLC26A2 variant	Negative
Achromatopsia Due to ATF6 variant	Negative

WeGene Genetic Test Sample Report

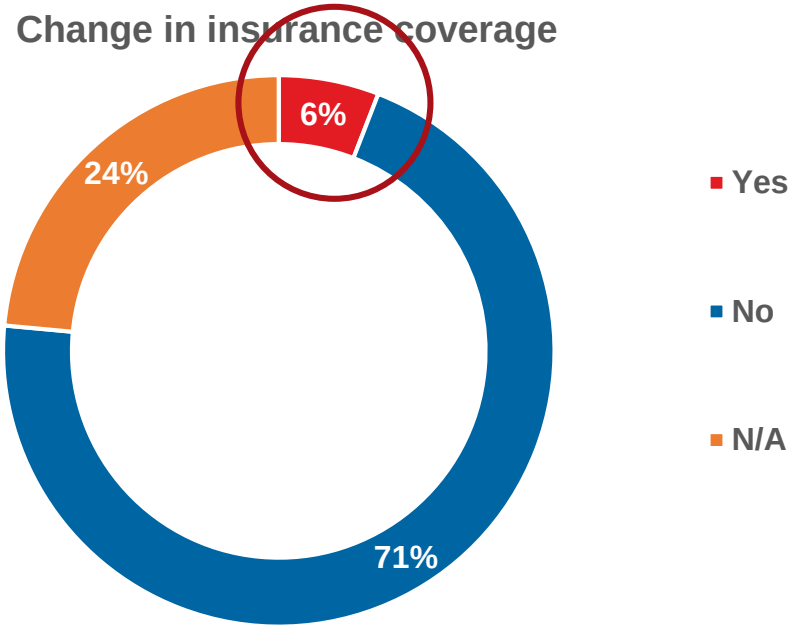
Lung Cancer

Result presented for each condition, with research reference

Recommendations, e.g. vaccination, dietary requirements

A risk score (versus an average sample) is provided for each condition.

Did you change your insurance coverage?



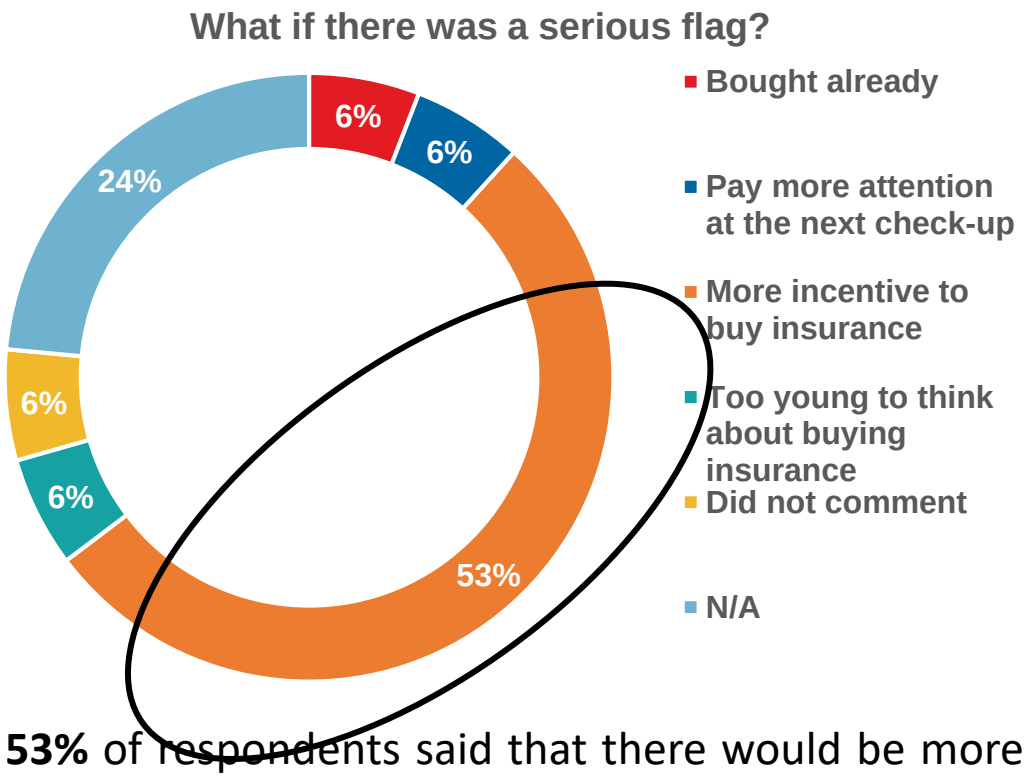
- 6% of respondents increased **insurance coverage before** the test due to concerns on potential disclosure requirement in future insurance application

- Individual 1: *"I'm a carrier for one of the hereditary gene mutation that may impact my children, and also have a few "Elevated Risks". I'm not sure how bad these are. Will do more study before thinking about insurance."*

- Individual 2: *"I didn't have insurance coverage in mind. Will read through group coverage from my employer first"*

- Individual 3: *"There was no alarm in the reports and I do not plan to change insurance coverage, but cancer report is an obvious one that could change people's behaviour"*

Will you change your insurance coverage if there was a serious result?

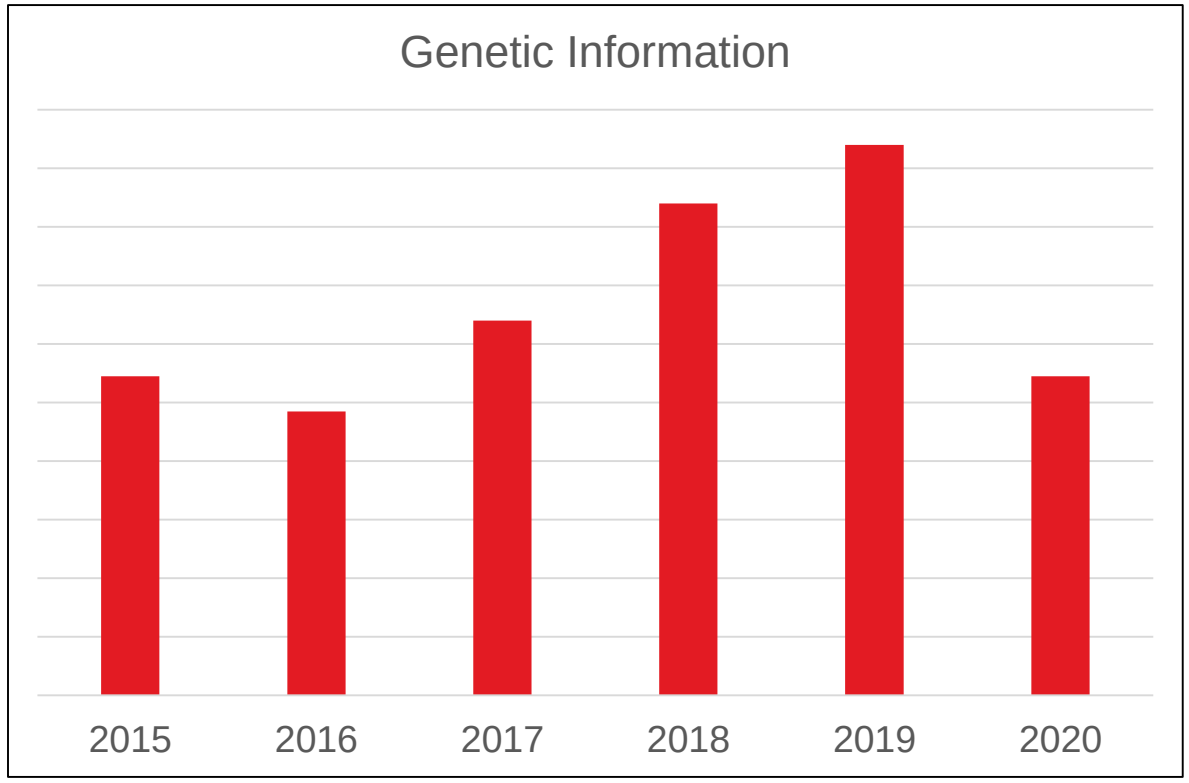


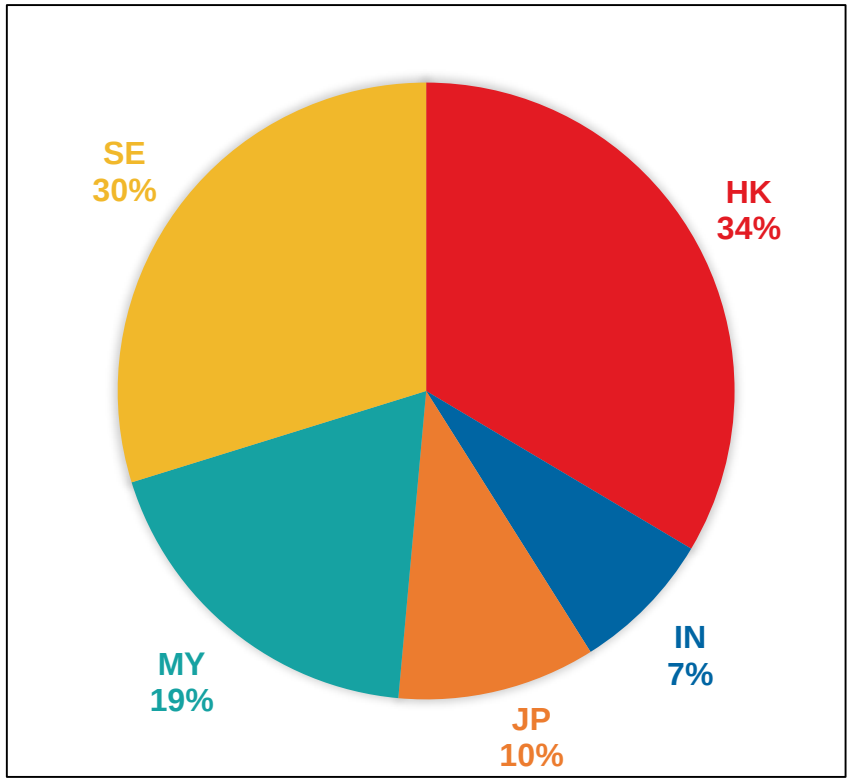
- **53%** of respondents said that there would be more incentive to buy **insurance coverage** if there was a red flag, e.g. cancer marker
- This could be for themselves or for family

- Individual 1: *"if there was anything hereditary, I may consider buying for my kids"*
- Individual 2: *"I do not consider these tests to be diagnostic. I will seek advice from a genetic counsellor first but I will consider buying insurance"*
- Individual 3: *"I will consider buying Cancer only type of YRT products such as mutual insurance and Million Dollar medical product"*
- Individual 4: *"I may consider upgrading my CI coverage"*

Genetics: Operational Considerations

RGA Asia Data





UK Market – Legal & General

Instructions to Applicant

Product Information

Genetic Testing

The only genetic test result which you will need to tell Legal & General about is one for Huntington's disease, and you will only need to tell them about this when the total life insurance you have or are buying is over £500,000.

Application Form – Health Questions Section

Genetic Testing.
The Association of British Insurers (ABI) have a policy on genetics and insurance. Currently, you only need to tell Legal & General about any genetic test results concerning Huntington's disease, for life insurance over £500,000 in total. This is because the Government has approved this test for insurers to use. The total is for any life insurance application being made now together with any life insurance you have already. You don't need to tell Legal & General about any other genetic test result. However, you must tell Legal & General if you are experiencing symptoms of, or are having treatment for, a medical condition including any genetically inherited condition. You must also tell Legal & General of any family history of a medical condition as asked for in the relevant question in this application. If you want to tell Legal & General about a negative genetic test result, we'll be willing to consider this when setting your premium. A copy of the Concordat and Moratorium on Genetics and Insurance is available from Legal & General on request or from the ABI website abi.org.uk

UK Market – AVIVA

Instructions to Applicant

Application Form

Section 5 – Lifestyle

IMPORTANT: You must answer all questions fully, truthfully and accurately. Failure to do so may result in your policy being amended or cancelled, may reduce the amount payable in the event of a claim, or may result in the non-payment of a claim. You do not need to tell us about any predictive genetic test results unless this application, together with any existing cover, will total over £500,000 of life insurance. If your cover is over this limit, we only need to know about predictive genetic tests for Huntington's disease. You can tell us about any negative predictive genetic tests results, because it may help your application.

Family History Question

Have you had or been offered screening for any other condition that runs in your family?

☐ Yes ☐ No

Australian Market - TAL

- Included as part of Family History
- Specific and detailed Questions

- Code allows results of all genetic tests above a Threshold
- No distinction between Diagnostic & Predictive

15. FAMILY HISTORY (continued)

Information about genetic tests

If you have had a genetic test, you only need to disclose this to us if your total insurance cover will be more than:

- $500,000 Life cover,
- $500,000 Total and Permanent Disability (or TPD) cover,
- $200,000 Critical Illness (also known as trauma) cover, or
- $4,000 per month Income Protection cover, salary continuance or business expenses cover.

These amounts apply to all insurance held by you (including held through a superannuation fund) or other life insurance companies, not just under this application.

If you have a favourable (negative) genetic test result, you can provide this information to us , if you wish, regardless of the cover amount.

You are only required to complete question 3 if your cover amount is more than any of the cover amounts specified in the box above. You may choose to disclose any favourable genetic test result (irrespective of the cover amount) if you wish.

3. Have you ever had a genetic test where you received or are awaiting an individual result, or are you planning to have a genetic test (excluding prenatal genetic screening)?

☐ No → Go to Section 16. ☐ Yes →Please complete the following.

a) What was the reason for undertaking or planning to have the genetic test?

☐ Due to my family history

☐ Pregnancy / Fertility / IVF purposes → Go to Section 16

☐ To investigate symptoms → Please specify below

☐ Other → Please specify below

b) What potential condition(s) was being investigated?

☐ Breast cancer ☐ Ovarian cancer ☐ Bowel cancer ☐ Cystic fibrosis

☐ Haemochromatosis ☐ Heart disease ☐ Huntington's disease ☐ Coeliac disease

☐ Muscular dystrophy ☐ Dementia ☐ Thalassaemia ☐ Other → Please specify

c) What was the result of the test? Please select the appropriate statement

☐ Negative – I don't have the gene being tested for

☐ Positive – I have the gene being tested for

☐ I am still waiting for the result /I have not had the test yet

https://adviser.tal.com.au/tools-and-resources/documents-and-forms

HK Risk Selection Considerations

- Proactive Approach
  - Explain exactly what information is required
  - Ask direct questions

- Define Diagnostic and PredictiveTests
- Define the 6 Predictive Tests

- Informative Approach
  - Confirm that genetic test results should be disclosed
  - Maintain existing questions

- Passive Approach
  - No reference to genetic tests
  - Maintain existing questions

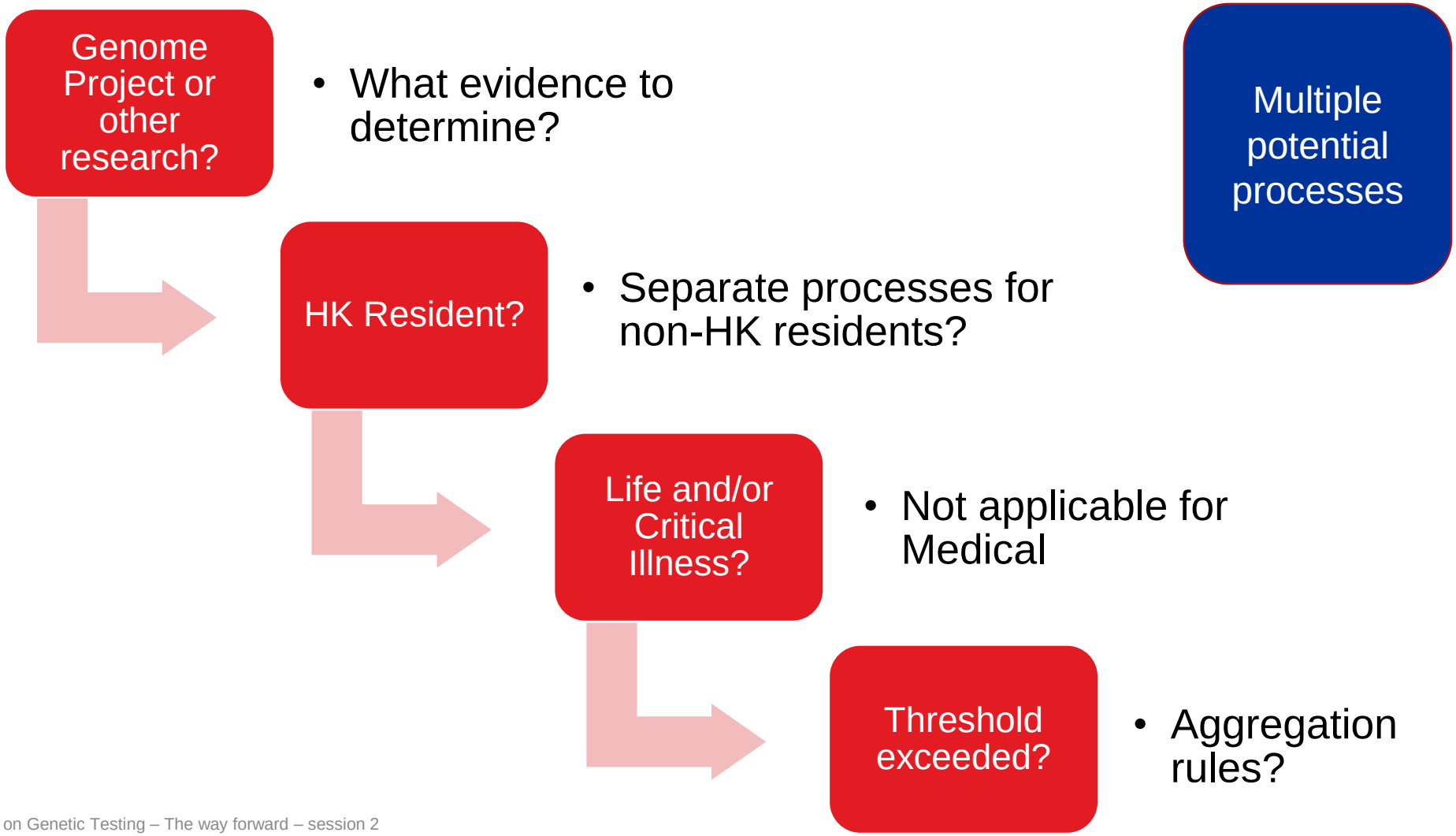
- Impact of VHIS and the Standardized Underwriting Questionnaire (SUQ)?

VHIS SUQ Q13

13.	In the last <<*insert a period of not more than 5 years*>>, have <<*you*>> ever had or been advised to undergo investigations (such as blood or urine test, ECG, X-ray, ultrasound, CT scan, MRI, PET scan, HIV test, Hepatitis B test, Hepatitis C test)? 在過去<<*填入不超過五年的時間*>>內，<<*您*>>是否曾接受或曾被建議接受檢查（例如驗血、驗尿、心電圖、X 光、超聲波、電腦掃描、磁力共振、正電子掃描、愛滋病測試、乙型肝炎測試、丙型肝炎測試）？ If the answer is "Yes", do <<*your*>> investigation result(s) include the followings? 如果答案屬「是」，<<*您的*>>檢查結果是否包括下列情況？ <<*Insurer can ask fewer criteria from the following list*>> <<*保險公司可按需要刪減下列詢問的準則*>>	☐	☐
(a)	Normal test result is advised 檢驗結果正常	☐	☐
(b)	Abnormal test result is advised 檢驗結果異常	☐	☐
(c)	<<*you*>> are still awaiting test / test result <<*您*>>正等候檢驗或檢驗結果	☐	☐
(d)	Test result is inconclusive or uncertain (retesting or follow up test is required) 檢驗結果為無定論或不確定（需要重新或進一步檢驗）	☐	☐
(e)	Medical advice has been sought or treatment is required for the test result (such as liver cyst / brain cyst / joint degeneration or calcification / lung or breast or thyroid calcification discovered on imaging test, that may not require immediate treatment) 就檢驗結果已尋求醫療意見或需要接受治療（例如一些未必需要即時治療的情況如肝囊腫 / 腦囊腫 / 關節退化或鈣化 / 於成像檢測中發現肺部或乳房或甲狀腺出現鈣化）	☐	☐

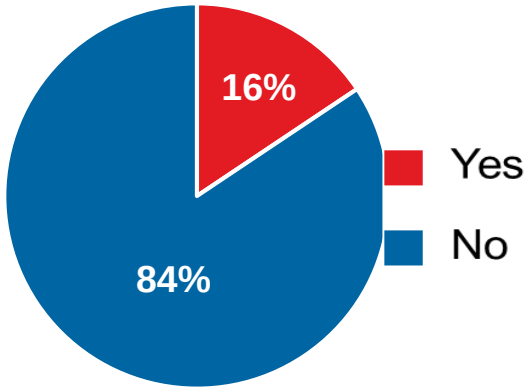
Other Decision Points for Implementing the Best Practice

Underwriting & Claims



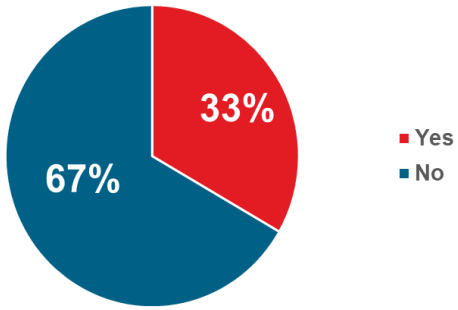
Voice of RGA Underwriters - Challenges for handling genetic information

- **Consistent methodology used**

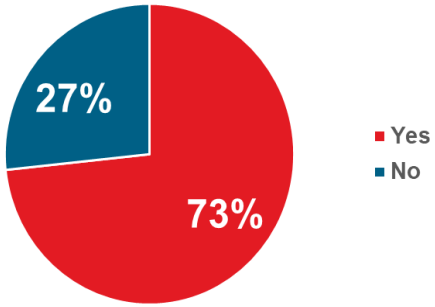


- **Decisions on genetic cases being challenged**

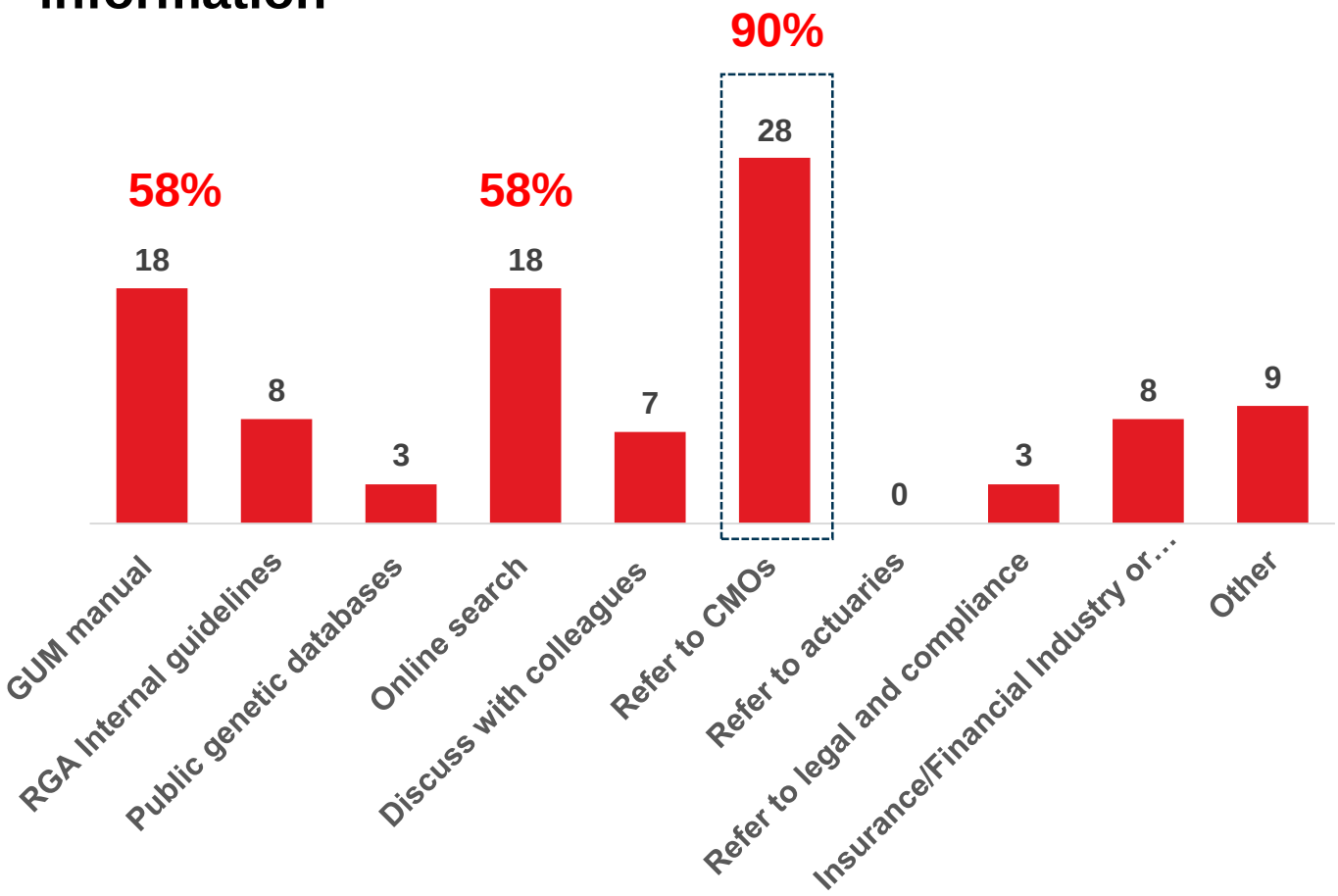
Current status



Future Likelihood



- **Limited resources when assessing a case with genetic information**



Genetic Test Best Practice

Operational Impact

Focus areas

- Assessment methodology
- Dedicated Resources
- Increased appeal or complaints
- Database

Key Considerations

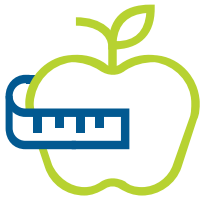
- Impact on processes and efficiencies — EUW Systems
- Clear guidelines for assessing genetic-related disorders — UW & Claims
- Development of a Knowledge Centre
- Training

RGA Global Client Survey

RGA

RGA/X Global Client Surveys 2020

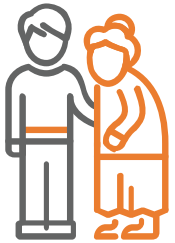
Wellness



Mental health and wellbeing, & financial wellness

- Support customer engagement, as a source of UW evidence
- Chronic disease management

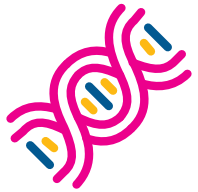
Eldercare



Meeting the needs of seniors

- Live well (live/health) e.g., access to medicine, care at home or at a nursing home.
- Financial health needs.

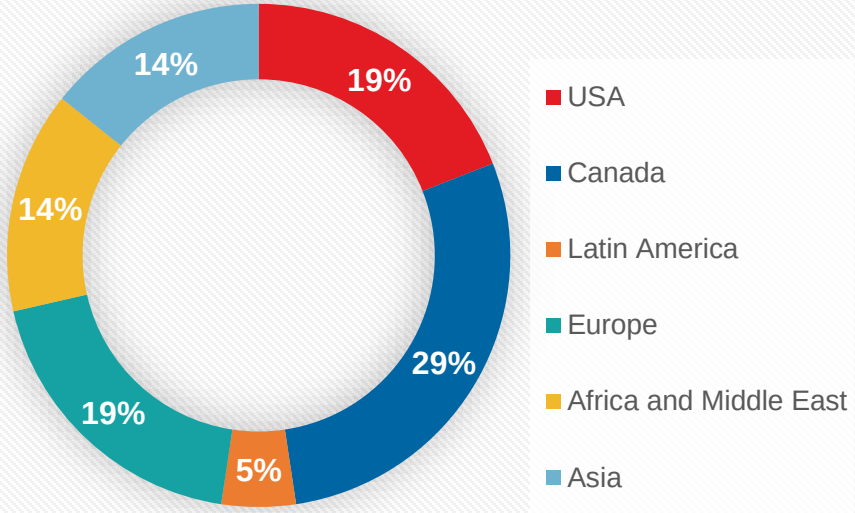
Genetics



Genetics and insurance

- An UW source (depending on market specific regulatory constraints)
- Improve IFM
- Increase customer engagement
- Chronic disease prediction/preventative approaches

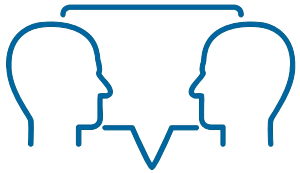
Countries represented



Survey results will provide industry insights and support RGAX/RGA Thought Leadership

Underwriting and Medical

Factors to Consider Regarding Genetic Test Results



Analytical validity

Is the test accurate in detecting a particular genetic variant or abnormality?

Clinical validity

What is the ability of a test to distinguish whether someone has, will, or will not develop a condition?

Clinical utility

What is the likelihood that the test will significantly improve patient outcomes? Is the result “actionable”?

Analytic and Clinical Validity are among the top 3 factors for insurers to evaluate third-party vendors per RGA survey

Top ranked metric for partnerships

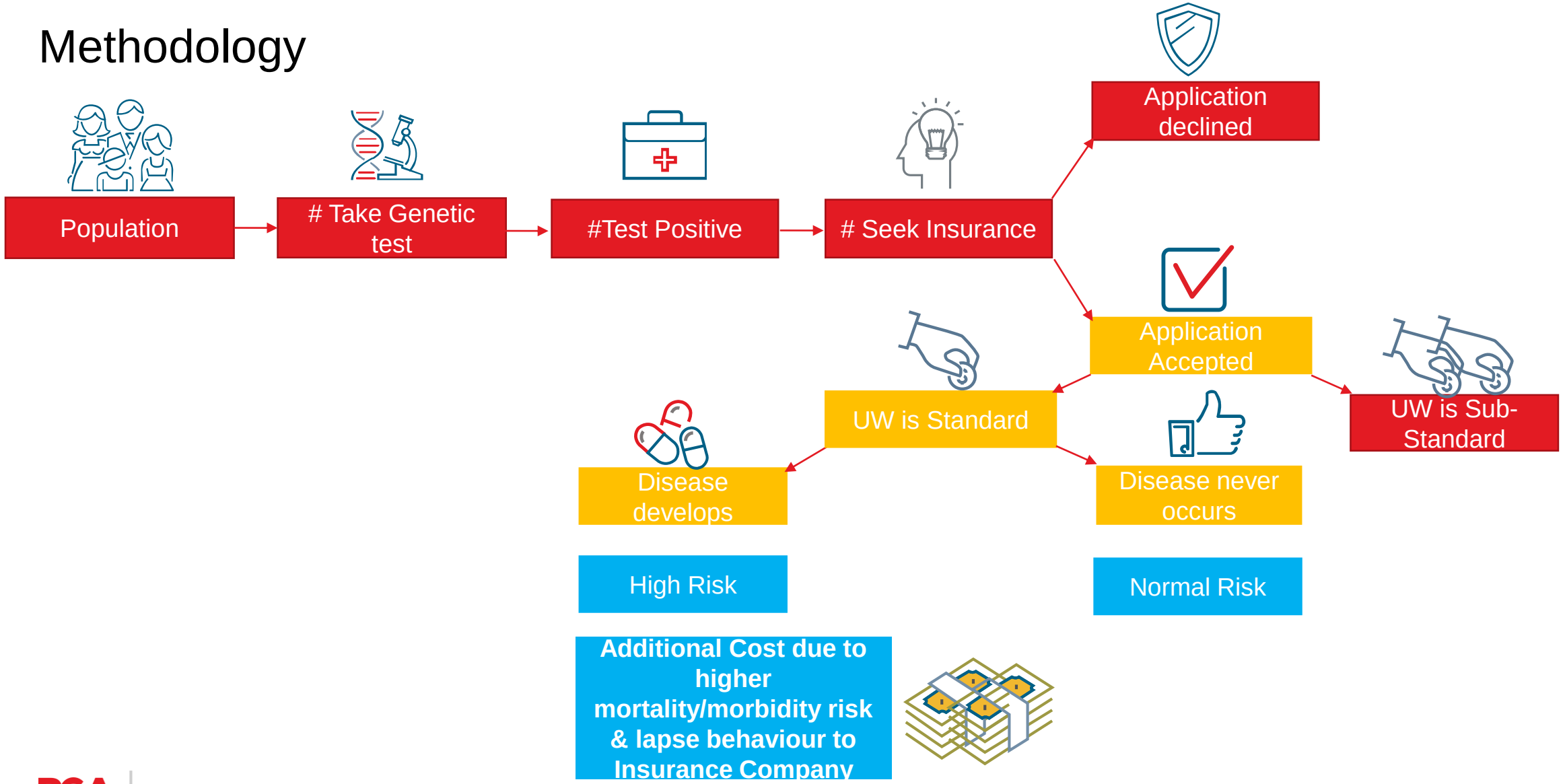
1. Analytic Validity
2. Ethical, Legal and Social Implications
3. Clinical Validity
4. Consumer Engagement

Insurers need to take these factors into account when assessing any genetic testing!

RGA Asia Impact Model

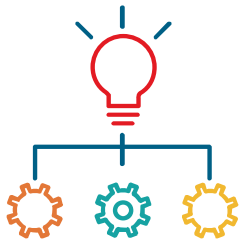
The RGA Model

Methodology



The RGA Model

Conditions included



Selection Criteria

1. Strong evidence plus reliable testing to confirm genotype-phenotype correlations
2. High prevalence
3. High penetrance (the net risk in the absence of any competing risks);
4. Long asymptomatic period during adulthood

Genes/Conditions Selected

1. BRCA
2. Lynch (Hereditary nonpolyposis colorectal cancer)
3. HD (Huntington Disease)
4. PKD (Polycystic Kidney Disease)
5. HCM (Hypertrophic Cardiomyopathy)
6. EOAD (Alzheimer's Disease – Early onset)
7. LOAD (Alzheimer's Disease – Late onset)
8. Other Conditions Group 1
9. Other Conditions Group 2
10. Other Conditions Group 3

Medical and Underwriting Expertise

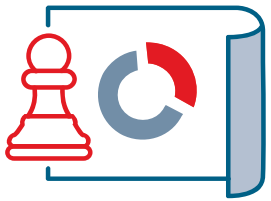
Highly Predictive Genes

Including LOAD due to strategic importance and increasing prevalence of Dementia

Adding Condition Groups 1-3

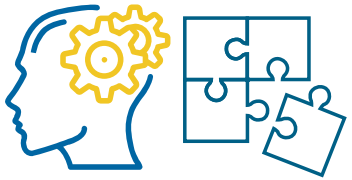
The RGA Model

Key Assumptions



Gene Specific A number of assumptions set for each gene included

- Prevalence Rate
- Penetrance Rate
- Additional risk on Mortality and Morbidity rates
- % Predicted by Underwriting taking into account existing UW processes
- …



Behavioral How customers may react to genetic test pertaining to insurance purchase

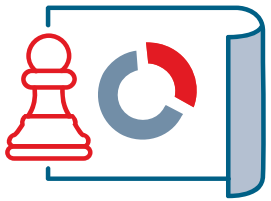
- % Taking genetic test
- % Buying insurance after tested positive
- Extra insurance coverage
- Lapse rate
- …

Market Specific Consider the type of product, and insurance penetration in the market

- Population size
- Size of new business volume
- Product split
- …

The RGA Model

Key Assumptions



Gene Specific A number of assumptions set for each gene considered

- Prevalence Rate
- Penetrance Rate
- Relative Risk
- % Predicted by Underwriting taking into existing UW process
- …

We have used:

Research based on Asia population, where available and credible.

The studies from other Actuarial bodies (SOA and CIA) were based on research mostly on Caucasian population.

Examples of research

1) SUMMARY OF ALLELE AND GENOTYPE DISTRIBUTION OF ALL PUBLISHED ASSOCIATION STUDIES (BY ETHNIC GROUP)

			Alleles			Genotypes					
	# Case-Control Samples		2-Allele (frequency)	3-Allele (frequency)	4-Allele (frequency)	2/2 (frequency)	2/3 (frequency)	3/3 (frequency)	2/4 (frequency)	3/4 (frequency)	4/4 (frequency)
Caucasian	28	AD	0.04	0.59	0.38	7 (0.003)	132 (0.047)	969 (0.346)	75 (0.027)	1210 (0.432)	407 (0.145)
		CTR	0.08	0.78	0.14	44 (0.009)	602 (0.120)	3039 (0.606)	106 (0.021)	1122 (0.224)	99 (0.020)
African Descent	2	AD	0.09	0.56	0.35	2 (0.028)	8 (0.111)	23 (0.319)	1 (0.014)	26 (0.361)	12 (0.167)
		CTR	0.05	0.76	0.19	1 (0.009)	10 (0.090)	62 (0.559)	0 (0.000)	34 (0.306)	4 (0.036)
Asian	4	AD	0.02	0.70	0.28	0 (0.000)	9 (0.044)	101 (0.490)	1 (0.005)	76 (0.369)	19 (0.092)
		CTR	0.05	0.86	0.09	1 (0.001)	113 (0.085)	986 (0.739)	16 (0.012)	210 (0.157)	9 (0.007)
Hispanic	1	AD	0.06	0.71	0.24	1 (0.016)	2 (0.033)	33 (0.541)	3 (0.049)	18 (0.295)	4 (0.066)
		CTR	0.03	0.85	0.12	0 (0.000)	5 (0.056)	65 (0.722)	0 (0.000)	18 (0.200)	2 (0.022)

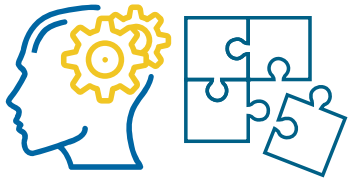
Source: AlzGene - Meta-Analysis of All Published AD Association Studies (Case-Control Only) APOE_e2/3/4

Breast and ovarian cancer penetrance of *BRCA1/2* mutations among Hong Kong women

LingJiao Zhang,[#1] Vivian Y. Shin,[#2] Xinglei Chai,[1] Alan Zhang,[3] Tsun L. Chan,[4,5] Edmond S. Ma,[4,5] Timothy R. Rebbeck,[6] Jinbo Chen,[1] and Ava Kwong[2,5,7]

The RGA Model

Key Assumptions



Behavioral How customers may react to genetic test when it comes to insurance purchase

- % Taking genetic test
- % Buying insurance after tested positive
- Extra insurance coverage
- Lapse rate
- …

We have considered:

1. Business projections from **test providers in Asia**
2. **Behavioral Science** + Research
3. **Moratorium limits +** SEC status
4. **Product Types**, Protection or Savings Products

Example

% Buying Insurance after tested positive

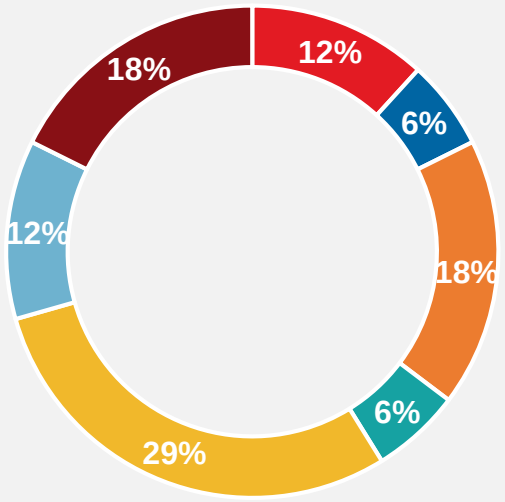
Consumers behave differently to different user cases:

1. **Medical Genetic Test – Relatively high** due to strong clinical and analytical validity, underlying reason for the test
2. **DTC Genetic Test – Relatively low** as customers may feel the tests lack medical relevance compared to medical genetic test, purpose might be not medical related e.g. ancestry
3. **Tests provided within insurance context – Relatively high** due to significant insurance marketing from agents

RGA's Internal Survey

Do consumers change their behavior after genetic test

Lifestyle Change

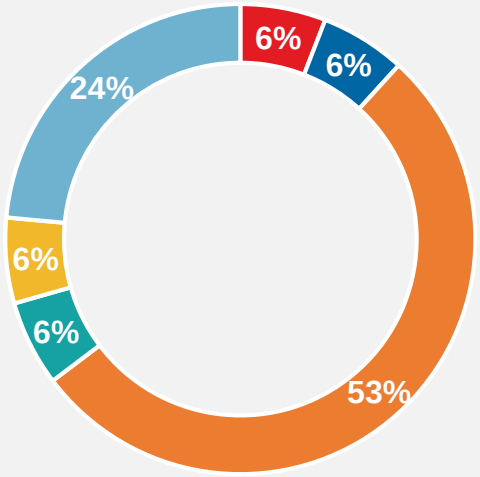


- Dietary changes/less smoking /less drinking
- Increase vitamin intakes
- More health conscioius
- Change fitness plan
- Do nothing
- No comment
- N/A

42%

Either made lifestyle changes or became more health conscious after getting the results

Would you buy insurance if there was a serious flag?



- Bought already
- Pay more attention at the next check-up
- More incentive to buy insurance
- Too young to think about buying insurance
- Did not comment
- N/A

59%

Either had more incentive to buy insurance or bought insurance after they saw alarming disease risk from genetic test results

The RGA Model

Key Assumptions

Market Specific Consider the type of product, and insurance penetration in the market

- Population size
- Size of new business volume
- Product split
- …

We have considered:

Market specific statistics from **regulatory bodies,** as well as RGA's **market insights**

香港保險業聯會
The Hong Kong Federation of Insurers

ACTUARIAL SOCIETY of HONG KONG 香港精算學會

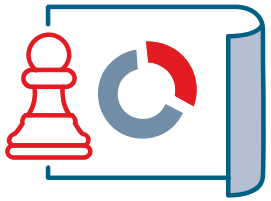
Example

Size of new business volume

Key considerations include:

1. % of policies issued to HK residents and PRC lives
2. Type of products issued
3. Industry wide new business volume per year

Why the RGA Impact Model is important

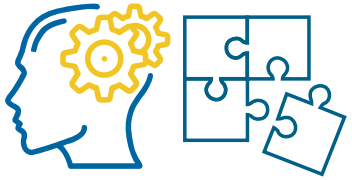


Research and Medical Insights

We have gone through intensive research and gained a much better understanding of the impact of genes on mortality and morbidity risks.

This strengthens our core risk framework:

- Expands our UW capabilities
- Medical case underwriting
- Claims assessment



View on Customer Behavior

By utilizing and expanding our behavior scientist, market and industry research and expertise, we have a much better view of:

- How consumers' insurance purchase behavior
- How behavior could change under different scenarios

Flexible Impact Model

Most importantly, we now have a tool to assess and better understand possible outcomes under a range of different scenarios:

- strengthens our core pricing and product development capability
- Understand the impact of different business use cases
- Able to assess a range of possible cost impact from genetic tests
- Enables us to better support client initiatives

Genetics and Insurance: RGA Support

RGA

What's Next – RGA Support

	Focus areas	RGA support
	Effective Information design and provision	• Distribution • Sales • Customers
	Application form design	• Information provision • Question design ○ Behavioral aspectS
	Underwriting	• Guideline • Training • Case review & sharing
	Claims assessment	• Training • Case review & sharing
	Product and pricing	• Knowledge sharing

Q & A

RGA

Best Practices on Genetic Testing – The way forward

Session 2: Get ready for a genetic moratorium (era)

Presenter:
- **John Cardus**
- **Neill Muller**

Moderator:
- **Dipali Jawalkar**

27.10.2020