Session 59: The Impact of Genetics on the Life Insurance Industry

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2019 LIFE & ANNUITY SYMPOSIUM

The Impact of Genetics on the Life Insurance Industry

Thomas Ashley, MD, FACP and Jean-Marc Fix, FSA, MAAA

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Agenda

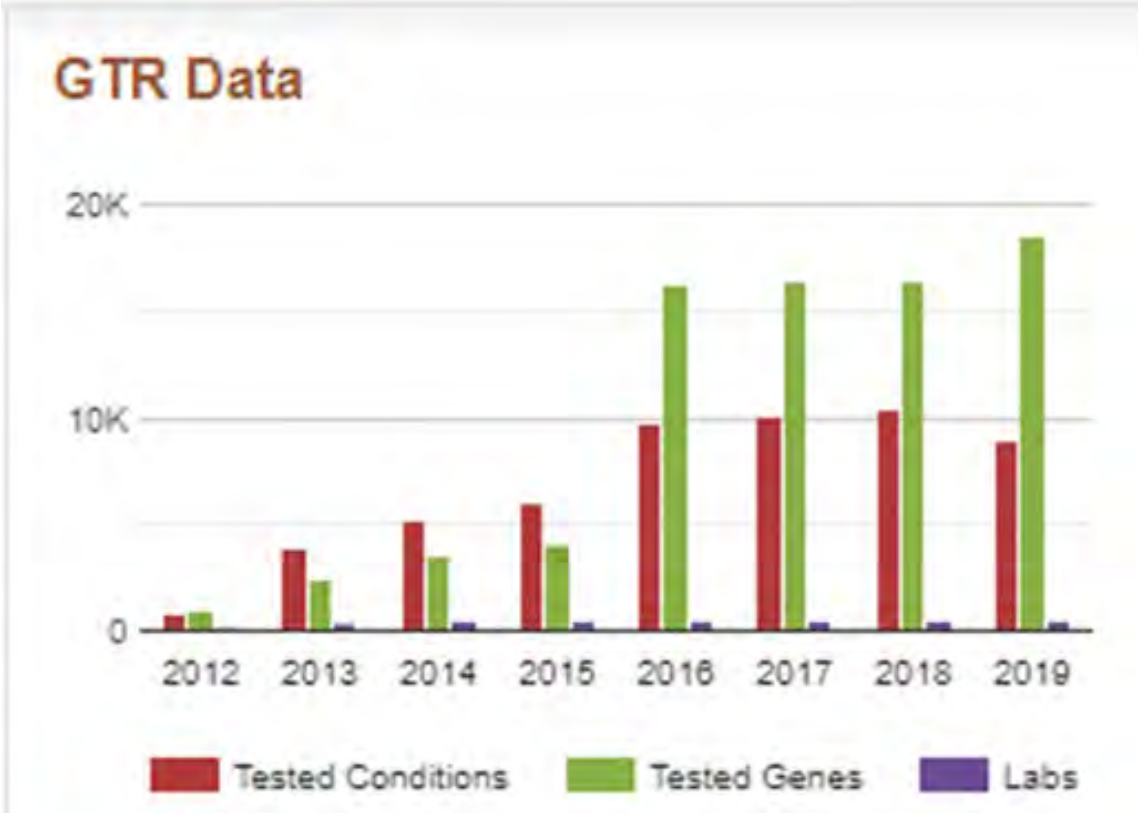
- Why is genetics prominent?
- Biology
- Genetic information in practice, clinical and DTC
- Issues and regulations
- SOA model

Why is genetics prominent?

- Cost = Speed and Volume

About GTR®

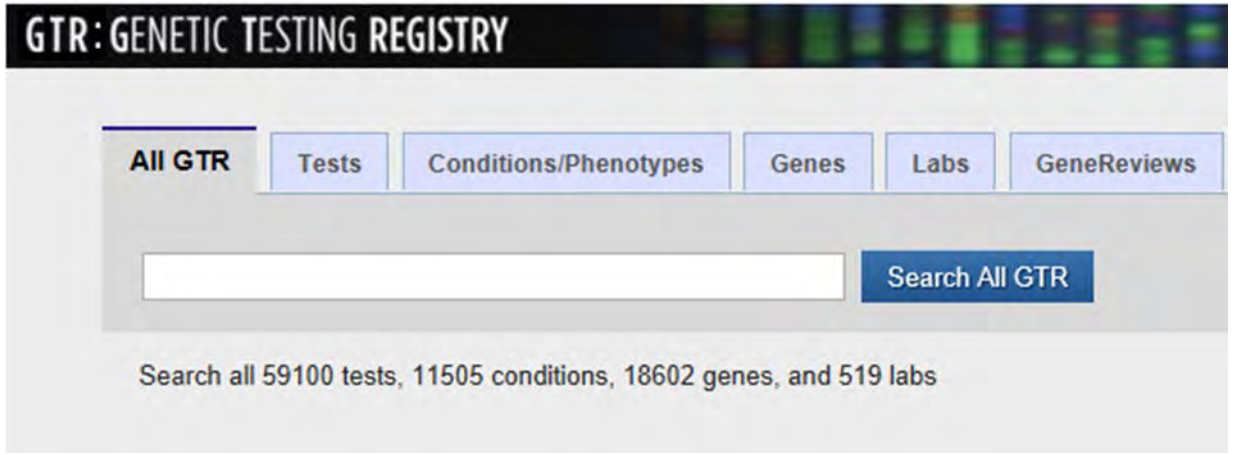
The Genetic Testing Registry (GTR®) provides a central location for voluntary submission of genetic test information by providers. The scope includes the test's purpose, methodology, validity, evidence of the test's usefulness, and laboratory contacts and credentials. The overarching goal of the GTR is to advance the public health and research into the genetic basis of health and disease



https://www.ncbi.nlm.nih.gov/gtr/

Applied Science

- Precision medicine
- Cancer classification
- Consumer products

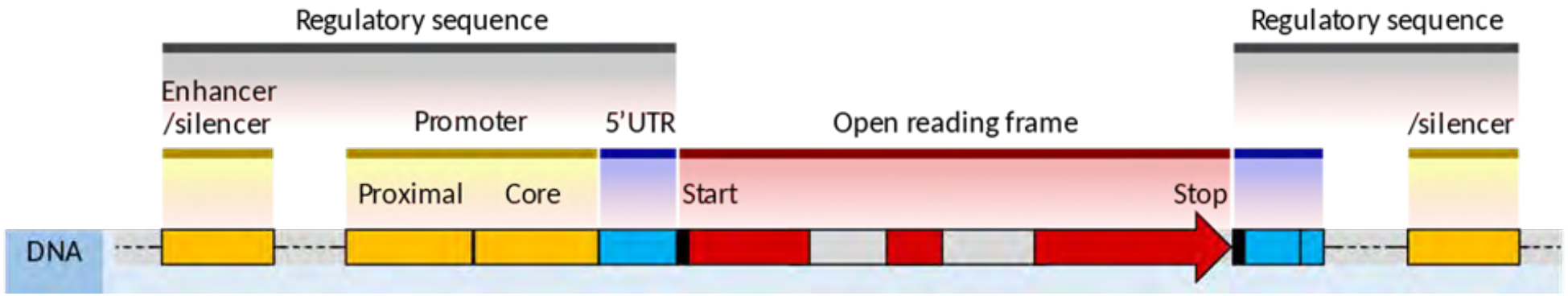


https://www.ncbi.nlm.nih.gov/gtr/

Biology (and Vocabulary)

- Genome
  - Chromosome pairs
  - Genes
    - Base sequence/allele
    - Transcription/mRNA
    - Translation/protein

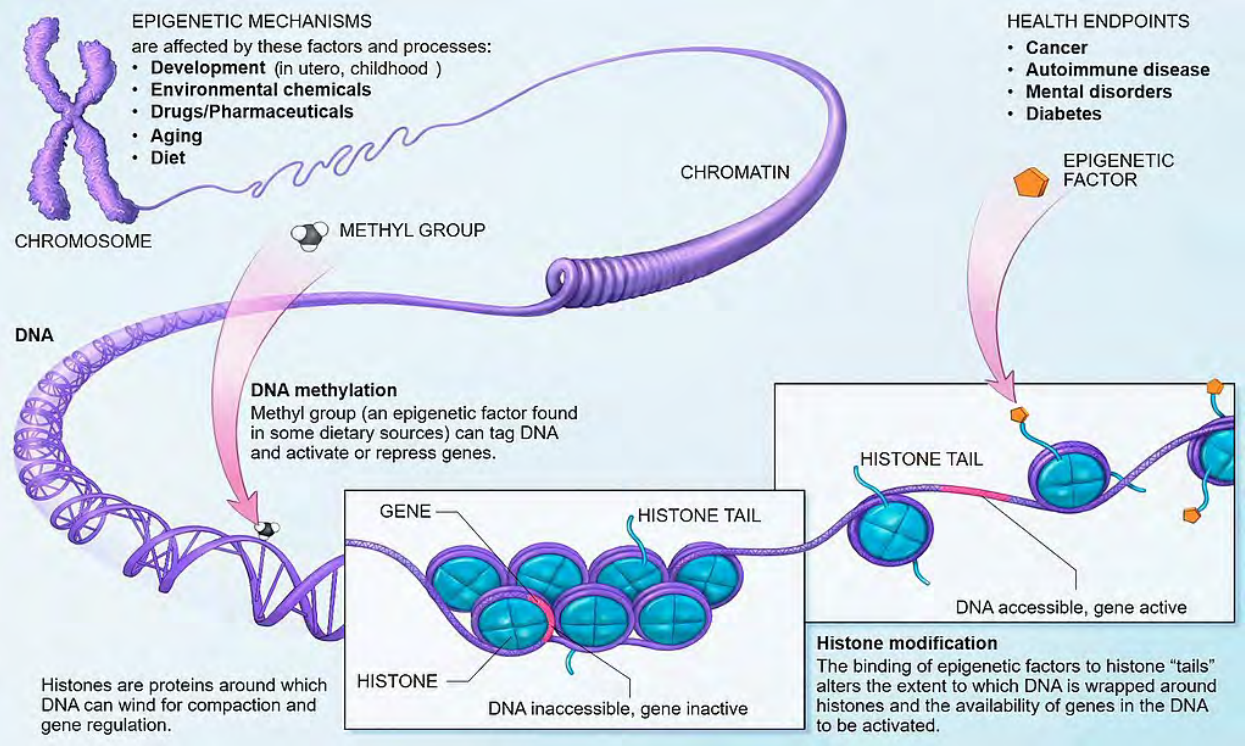
Genes



- Exome
- Control elements

Source: Shafee T, Lowe R (2017). "*Eukaryotic and prokaryotic gene structure*". *WikiJournal of Medicine* **4** (1). DOI:10.15347/wjm/2017.002. ISSN 20024436.

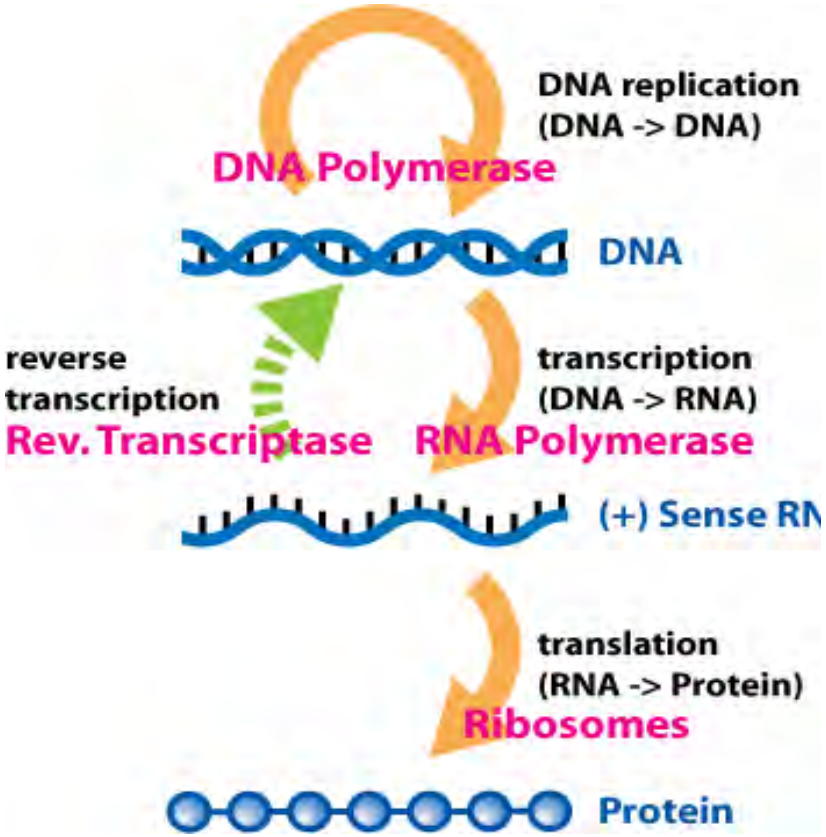
Beyond Genes



https://en.wikipedia.org/wiki/Epigenetics

- Epigenetic modification – environment and inherited
- Gene expression/ penetrance

After the Genome



Transcription (transcriptome)

Translation (proteome)

http://creativecommons.org/licenses/by-sa/3.0) or GFDL (http://www.gnu.org/copyleft/fdl.html)], via Wikimedia Commons

What is a Genetic Test?

- Heritable or not?
- Easy: examination of information content of DNA
- Harder
  - Family history
  - Gene expression
    - Protein example: hemoglobin electrophoresis for sickle cell anemia
    - Metabolites example: sweat chloride for cystic fibrosis
    - Cholesterol

What is a Genetic Test?

- Information content of DNA always/strictly genetic
  - Others are not always genetic and have environmental influences
  - Phenotype/genotype

DNA Technology

- SNP (“snip”)
  - Single nucleotide polymorphism
  - Correlates with a gene mutation
- Gene or exome sequence
  - Entire gene
  - Specific allele
- Outcomes
  - Normal
  - Pathological mutation
  - Variant of undetermined significance (VUS)

SNP Compared to Sequence

Single nucleotide polymorphism

- Presence of a particular nucleotide base at specific location in the genome
- Associated with a gene but not necessarily in the gene itself
- Basis for GWAS (genome-wide association studies)
- Statistical exercise in risk classification

Sequence

- Delineation of long segments or all of the genome sequence
- Still requires assessment of correlation between variant sequence and disease

Clinical Practice

Diagnostic

- Hemochromatosis (abnormal iron metabolism)
- Test for two known pathologic mutation
- Autosomal recessive requires mutation in both alleles
- Definitive determination of presence/absence of hemochromatosis

Predictive

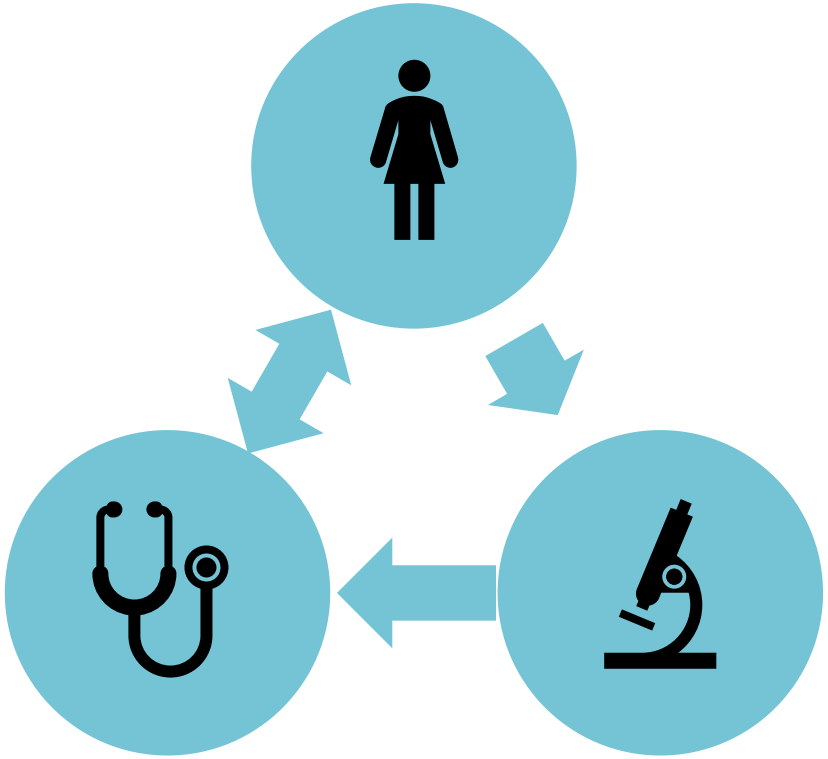
- BRCA
- Many different pathologic mutations in BRCA genes
- Establishes risk of breast or ovarian cancer, not diagnosis
- Penetrance complicates interpretation

Clinical Practice

Cancer

- Acquired genetic disease
- Change from cancer of <organ> to cancer of <gene mutation> in <organ>
- Specific drug to address gene product

Clinical Lab Process



Doctor initiates test	Purchase from commercial vendor
Medical advice as to reason for test	Medical advice on interpretation of test

Direct to Consumer -DTC

Consumer initiates test	Purchase from commercial vendor
No medical advice as to reason for test	No medical advice on interpretation of test

What is Available via DTC?

	Ancestry	23andMe	Helix
Technology	SNP	SNP	Partial sequence
Medical	None	Carrier screen: dozens of conditions BRCA1 / BRCA2 (Selected Variants) Late-Onset Alzheimer's Disease Parkinson's Disease	Carrier screen: 65 autosomal recessive Medication response APOE MODY Familial hypercholesterolemia
		FDA approved	Physician interpretation*
Genealogy / Ancestry	Kinship Geographic	Neanderthal Kinship Geographic	Geographic
Wellness			Nutrition Fitness
Cost	$99	$99–$199	$99–$1000+

Sequence Data

Possession of genome sequence allows another form of DTC gene analysis: Promethease.

- Upload your sequence and Promethease tells you what you might have
- Many variants (not the “usual” sequence) are not known to cause disease
- VUS (variant of undetermined significance) will someday divide between normal and disease

Implications and Consequences of DTC

False reassurance

- Many mutations can have the same consequences
- No screening test can assess all
  - 23andMe tests a few common BRCA mutations
  - Some people with “negative” results still have BRCA mutation

Overreaction

- VUS (variant of uncertain significance) anxiety
- Potential increased health care utilization?
- Psychological distress?

Observations on Consequences of DTC

- No significant psychological harm
- No change in healthcare utilization

One study shows that knowledge of APOE status (Alzheimer) results in higher prevalence of LTCI purchase.

Testing Regulations

- From 2008 launch to 2013, 23andMe assessed health and disease risks
- In 2013 FDA issued a warning letter
  - Health and disease assessment is a medical device
  - Medical devices require FDA review and approval
- 23andMe suspended the medical tests and applied for approval
- In 2015 FDA authorized the tests
- First clinical test was Bloom syndrome, later added selective BRCA

Testing Regulations *(continued)*

- Helix restricted clinical tests with requirement for physician authorization
- States sometimes differ
  - MD Physician order required
  - NY Only licensed laboratory can offer test without physician order

Why Now from the Insurance Regulatory Front?

- Availability of direct to consumer testing (DTC)
- Public's awareness of the perceived dangers of genetic information
- Interest groups pressure
- International movement to regulate
- Regulatory push and "easy wins"

Why is it an Issue for Us?

- No healthcare footprint
- Antiselection
- Genetic exceptionalism
- Erodes underwriting
- May sweep in family history

Genetic Information Nondiscrimination Act 2008

- Genetic information: “ The genetic information protected by the law includes family health history, the results of genetic tests, the use of genetic counseling and other genetic services, and participation in genetic research” (1)
- Only applies to (most) health insurance and employment

(1) www.GINAHelp.org

What is “Genetic Information” in Proposed Laws?

- Result of “genetic test”
- “Genetic test, a test of human DNA, RNA, mitochondrial DNA, chromosomes or proteins for the purpose of identifying genes, inherited or acquired genetic abnormalities, or the presence or absence of inherited or acquired characteristics in genetic material, which are associated with a predisposition to disease, illness, impairment or other disease processes” MA Gen L ch 175 § 120°
- Number of exceptions like diagnostic tests, HIV, cholesterol…

What is Prohibited?

- Requiring a genetic test
- Asking if an insured has undergone a genetic test
- Using the results of a test (on the applicant and in some versions on the family of the applicant)
- Unfair discrimination
- Some allow actuarial principles safe harbor

What is “Unfair Discrimination”?

- “… unfair discrimination means cancellation, refusing to issue or renew, charging any increased rate, restricting any length of coverage or in any way practicing discrimination against persons unless such action is taken pursuant to reliable information relating to the insured’s mortality or morbidity, based on sound actuarial principles…” MA ibid
- What about NY’s DFS Circ. 1 “definition”?

Lots of Legal Activity

- Laws in MA and VT
- Bills in CT, DE, FL, IL, ME, NC and NY

Genesis of the SOA project

ACLI

- Created a Genetic Testing Task Force
- The Task Force's work led to an SOA research project

SOA

- Volunteer driven research function
- The Reinsurance Section Research Team undertook a project to measure the impact of genetic testing on the life insurance industry

Goal

Measure the potential impact of one-sided genetic testing information on life insurance claims.

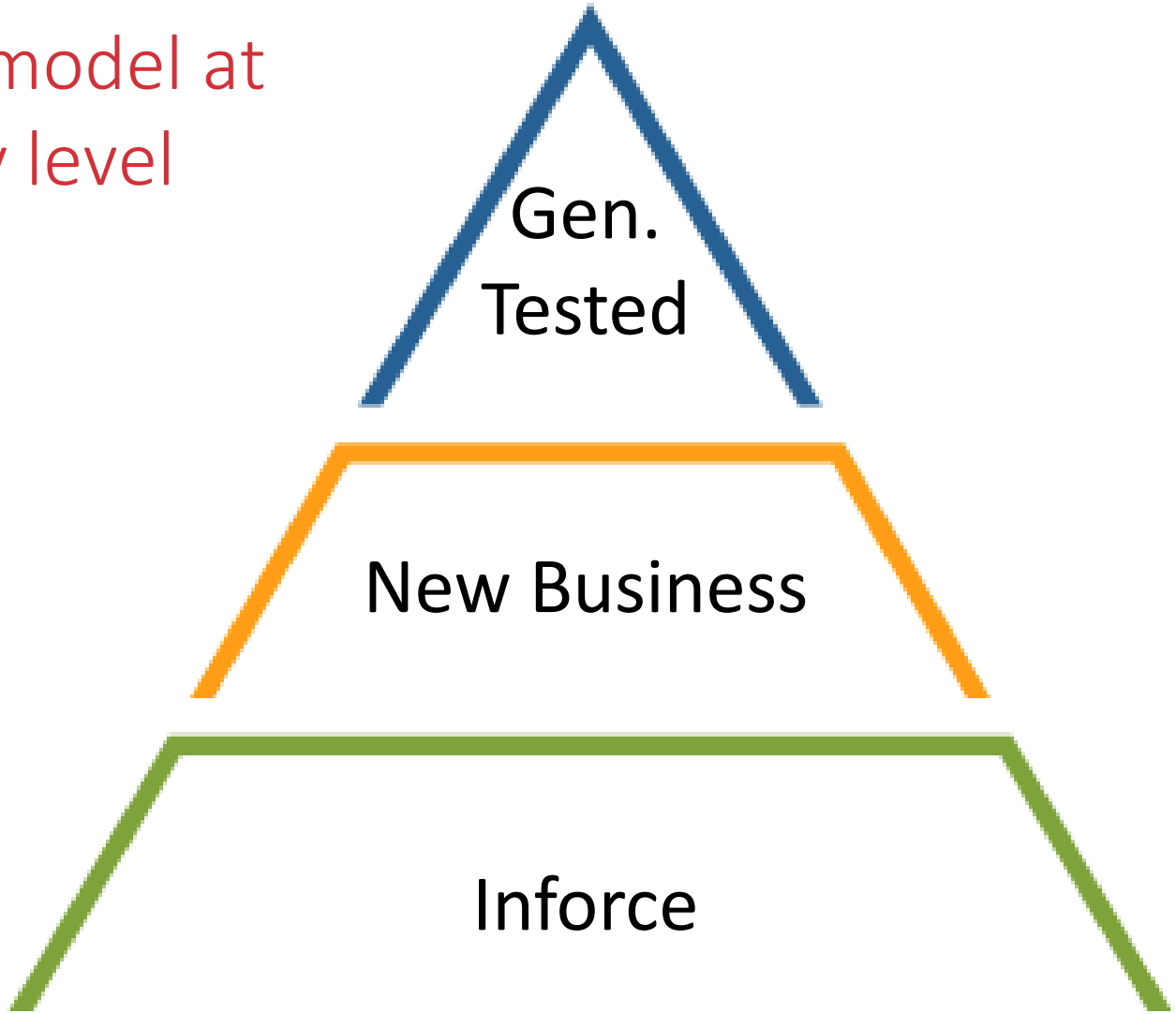
- Look at genetic testing only
- Look at genetic testing and family history

One-sided:

- Potential client has the results
- But life insurance company does not have the results

Modeling Approach

Deterministic model at whole industry level



Covered Conditions

Monogenic diseases with significant mortality impact

13 conditions, about 20,000 cases, reflected in the model in one year

1. Breast Cancer
2. Hypertrophic Cardiomyopathy
3. Dilated Cardiomyopathy
4. Arrhythmogenic Right Ventricular Cardiomyopathy
5. Long QT Syndrome
6. Brugada Syndrome
7. Huntington's Disease
8. Polycystic Kidney Disease
9. Myotonic Dystrophy
10. Early Onset Alzheimer
11. Hereditary Nonpolyposis Colorectal Cancer
12. Marfan's Syndrome
13. Catecholaminergic Polymorphic Ventricular Tachycardia

Covered Conditions Caveat

- Not all genetic diseases
- Not all single gene genetic diseases: “over 10,000 human diseases are known to be monogenic” (1)
- Not gene or gene interactions creating a higher risk profile

(1) www.who.int/genomics/public/geneticdiseases/en/index2.html

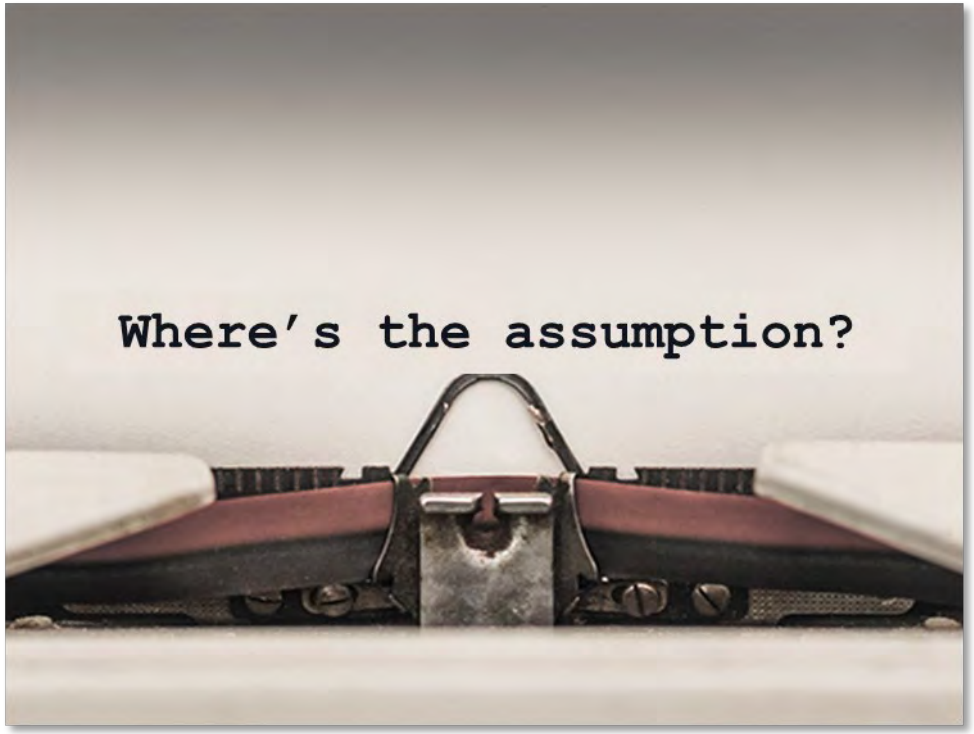
Model Assumptions

For the industry: Type of plans, average face value, number of policies?

For testing: How many tests will be done?

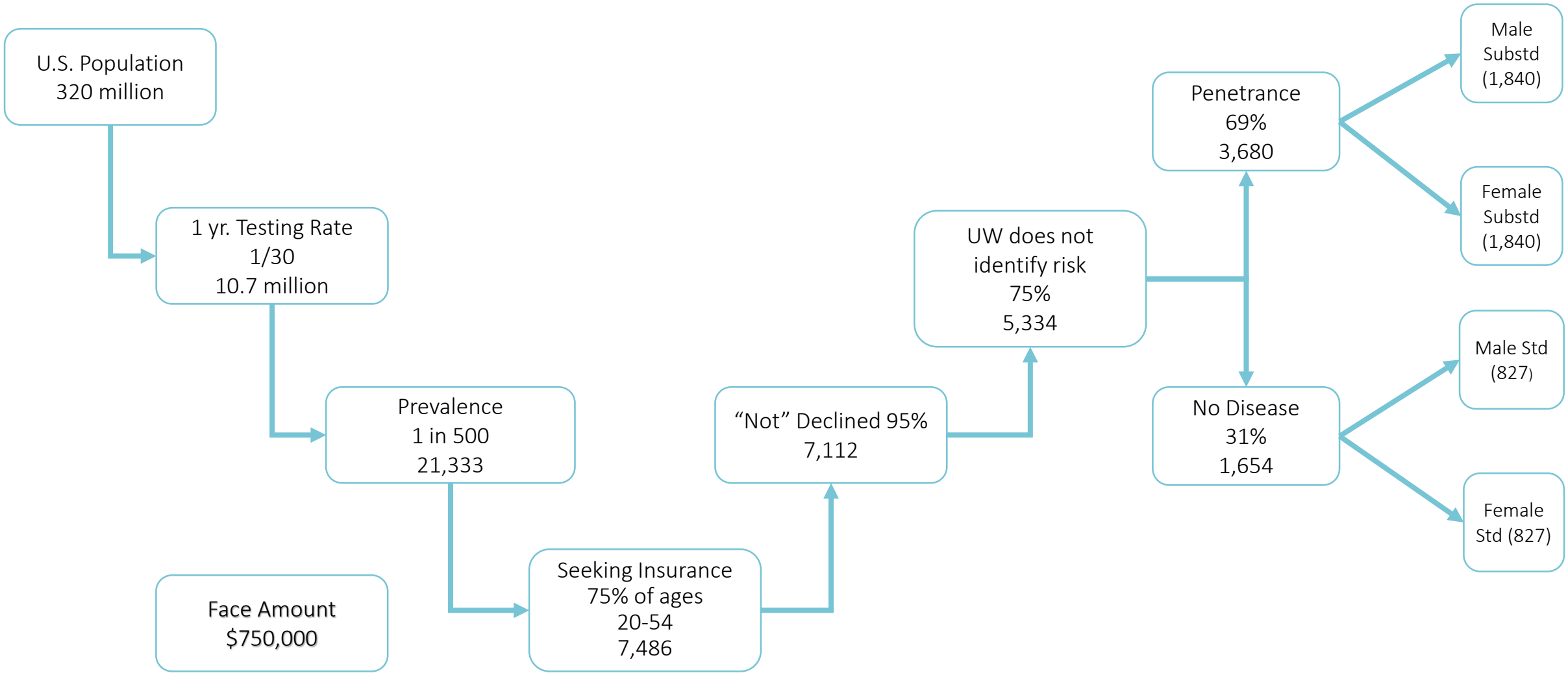
For issuing:

- How many antiselect?
- How much extra coverage is bought?
- How many are detected by the current underwriting process?
- How many are declined for other reasons?



For each condition: prevalence, penetrance, mortality pattern?

Modeling Flow Example: Hypertrophic Cardiomyopathy



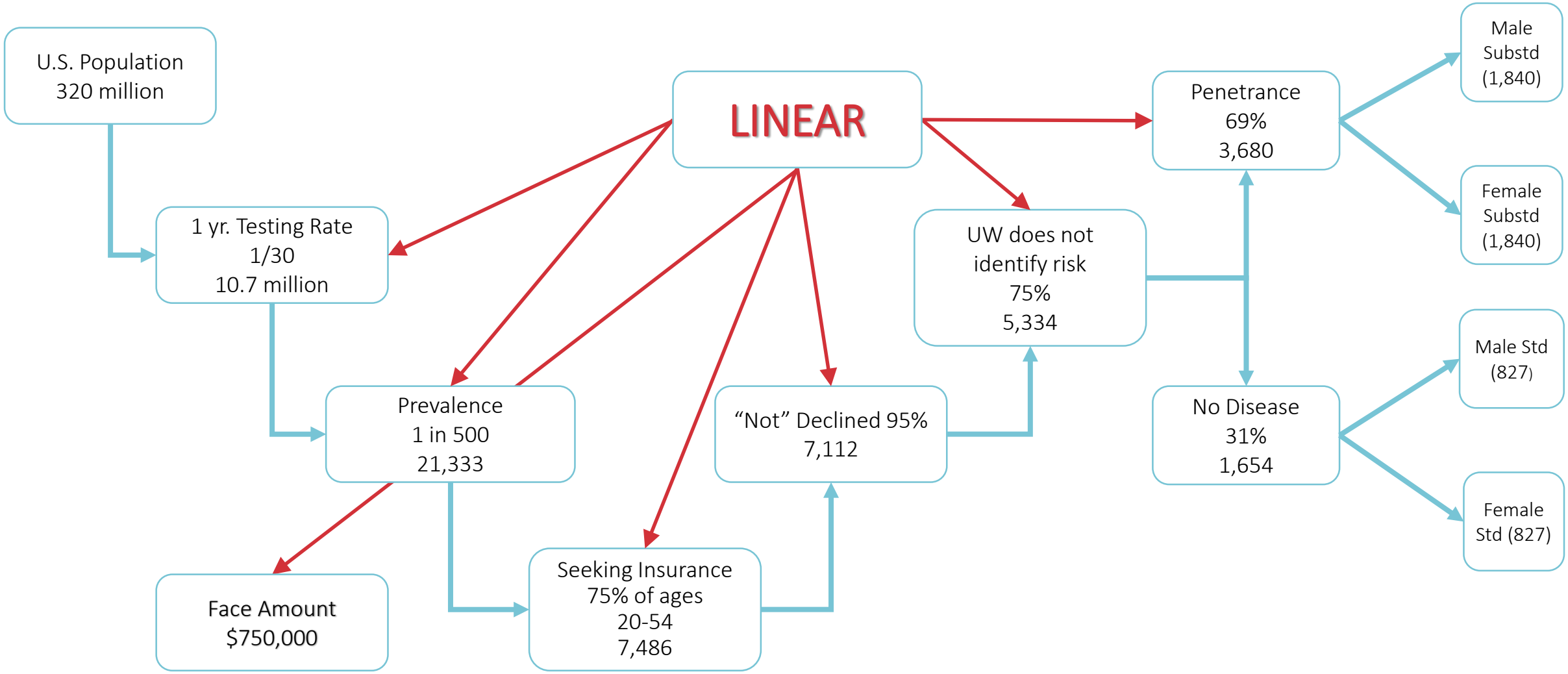
Results

Claim Impact	GT Positive New Business / Baseline Blocks % Increase in PV of Claims @ 4% – All Projected Years			
	FHx Included in Underwriting		FHx Excluded in Underwriting	
	Low	High	Low	High
New Business Claims (Overall)	4.4%	7.4%	5.7%	9.5%
New Business Claims (M)	2.7%	4.5%	3.7%	6.1%
New Business Claims (F)	8.6%	14.6%	10.7%	18.2%

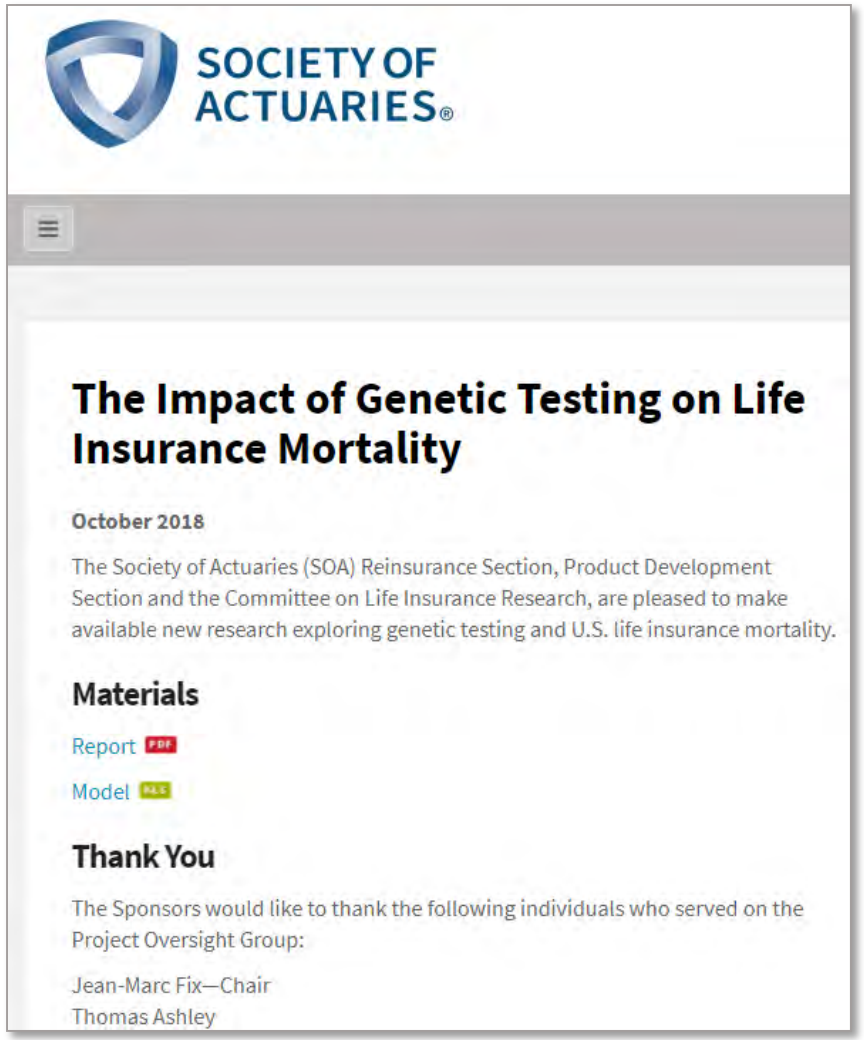
Low: portfolio is based on whole life
High: based on 20-year term

Source: The Impact of Genetic Testing on Life Insurance Mortality

Sensitivity Testing



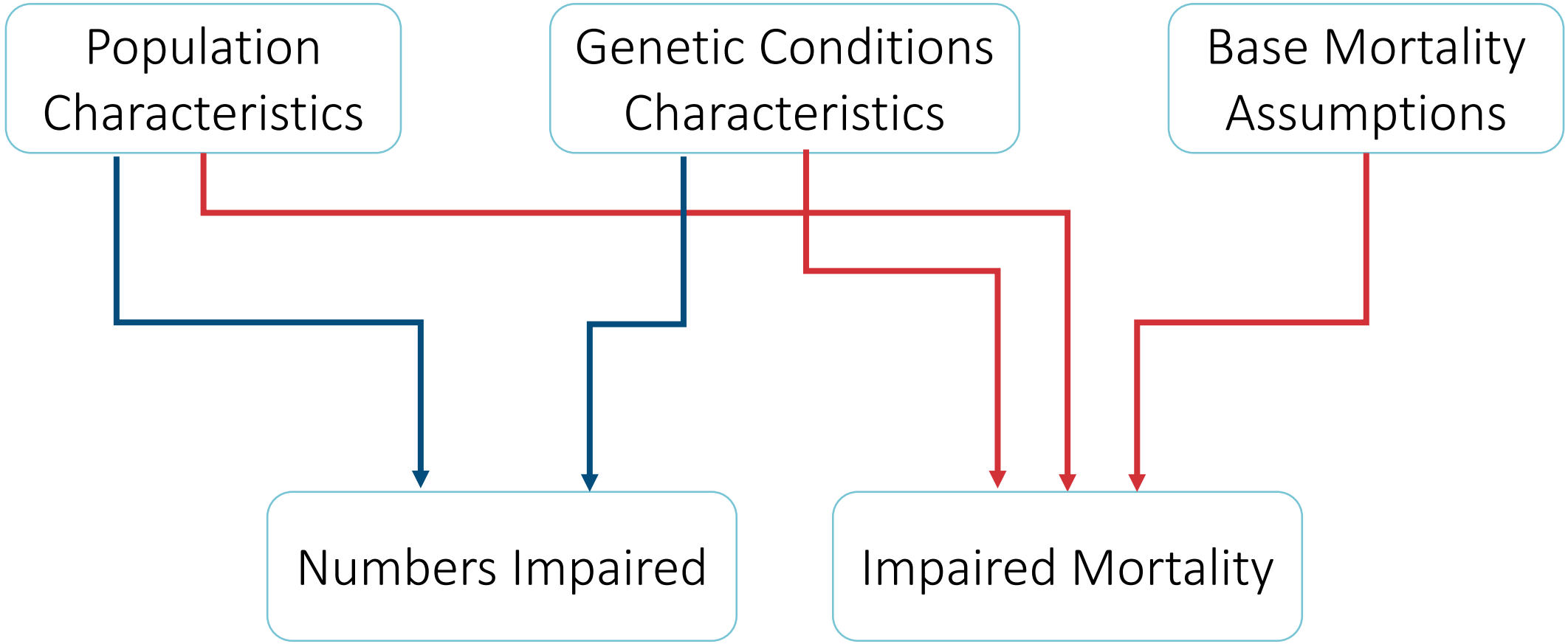
Build Your Own Model



The spreadsheet that is part of the report allows you to build your own models!

https://www.soa.org/resources/research-reports/2018/impact-genetic-testing/

Using the Spreadsheet to Create Your Model



Population Characteristics

Results Dashboard

POPULATION ASSUMPTIONS	
Population	320,000,000
Genetic Testing Rate	1/30
Percentage Seeking Insurance	75%
Policies Declined	5%
FA of Tested in 2016	700,000

	Start	End
Tested Age	20	54
% Population in age group	46.8%	

GENETIC CONDITION RELATED ASSUMPTIONS

Condition	Prevalence of gene mutation (1 in X)	Penetrance of clinincal expression given mutation positive	Multiple Rating	Flat Extra	Predicted
Hypertrophic Cardiomyopathy	500	69%		10.00	25%

Is Family History Available to Underwriting?
Yes

Genetic Conditions Characteristics

	A	B	C	D	E	F	G	H	I	J	K
1	**Assumption Set by Genetic Condition**										
2											
3											
4											
5	**Condition**	**Prevalence of gene mutation (1 in X)**	**Penetrance of clinincal expression given mutation positive**	**Rating**	**Predicted with FHx Included**	**Predicted with FHx Excluded**	**Tested**	**Male**	**Standard Period (years)**	**Grading Period (years)**	**Study Reference**
6	**USER INPUT - New Condition (s)**										
7	Breast Cancer (BRCA 1 or 2)	900	75%	350%	25%		30	0%	-	5	https://www.ncbi.n h.gov/books/NBK1
8	Hypertrophic Cardiomyopathy (HTCM)	500	69%	0.0100	25%		25	50%	5	15	- http://www.ncbi.nl .gov/books/NBK17
9	Dilated Cardiomyopathy (DCM)	2,700	75%	0.0400	0%		35	50%	-	30	- http://www.ncbi.nl .gov/books/NBK13
10	Arrythmogenic right ventricular cardiomyopathy (ARVCM)	2,500	75%	0.0230	0%		25	50%	-	-	- http://www.ncbi.nl .gov/books/NBK11

Genetic Conditions Mortality Grading

Grading Patterns

This is the number of years over which mortality is assumed to increase from standard to the full rating. The grading is linear over this period. For example, if

		Grading Patterns										
Grading Period	Lookup	1	2	3	4	5	6	7	8	9	10	11
0	2	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%
5	3	10%	30%	50%	70%	90%	100%	100%	100%	100%	100%	100%
10	4	5%	15%	25%	35%	45%	55%	65%	75			
15	5	3%	10%	17%	23%	30%	37%	43%	50			
30	6	1.7%	5.0%	8.3%	11.7%	15.0%	18.3%	21.7%	25.0			

DCM Grading Pattern Special 30 year grading pattern starting at age 30

Year\Age	0	1	2	3	4	5	6				
1	0%	0%	0%	0%	0%	0%	0%	0			
2	0%	0%	0%	0%	0%	0%	0%	0			
3	0%	0%	0%	0%	0%	0%	0%	0			
4	0%	0%	0%	0%	0%	0%	0%	0			
5	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
6	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
7	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
8	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
9	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
10	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
11	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
12	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
13	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
14	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
15	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%

Other Assumptions

Special assumptions for some conditions

Alzheimer's disease early onset - autosomal dominance (ADEO)

Alzheimer Conversion Rate (Standard)	50%
Alzheimer Conversion Rate (Substandard)	100%

Long QT Syndrome (Long QT)

Lapse Long QT Lapse >= 40	100%	40	As Long QT syndrome is assumed to apply on

Dilated Cardiomyopathy (DCM)

Special grading pattern table that is age specific.

Base Mortality Assumptions

	A	B	C	D	E
1	**Mortality Improvement Table**				
2					
3	**Attained Age**	**Males**	**Females**		
4	-	0.0185	0.0150		
5	1	0.0185	0.0150		
6	2	0.0185	0.0150		
7	3	0.0185	0.0150		
8	4	0.0185	0.0150		
9	5	0.0185	0.0150		
10	6	0.0185	0.0150		
11	7	0.0185	0.0150		
12	8	0.0185	0.0150		
13	9	0.0185	0.0150		
14	10	0.0185	0.0150		
15	11	0.0185	0.0150		
16	12	0.0185	0.0150		
17	13	0.0174	0.0142		
18	14	0.0163	0.0133		
19	15	0.0153	0.0125		
20	16	0.0142	0.0117		

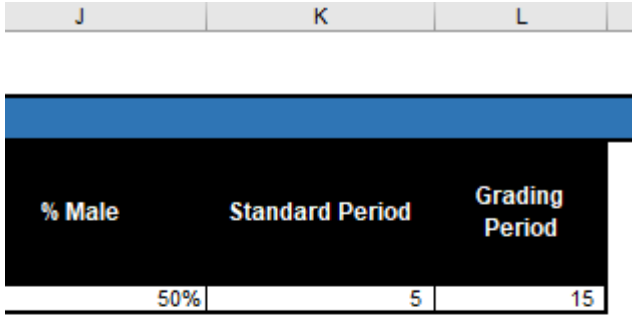
	A	B	C	D	E	F
1	**Base Mortality Assumption**					
2	**Base Female Mortality Table**					
3	1	2	3	4	5	6
4		Issue Age				
5	**Female**	**0**	**1**	**2**	**3**	**4**
6	1	0.2200	0.1200	0.0800	0.0700	0.0700
7	2	0.1200	0.0800	0.0700	0.0700	0.0700
8	3	0.0800	0.0700	0.0700	0.0700	0.0700
9	4	0.0700	0.0700	0.0700	0.0700	0.0700
10	5	0.0700	0.0700	0.0700	0.0700	0.0700
11	6	0.0700	0.0700	0.0700	0.0700	0.0700
12	7	0.0700	0.0700	0.0700	0.0700	0.0800
13	8	0.0700	0.0700	0.0700	0.0800	0.0800
14	9	0.0700	0.0700	0.0800	0.0800	0.0700
15	10	0.0700	0.0800	0.0800	0.0700	0.0800
16	11	0.0800	0.0800	0.0700	0.0800	0.1200
17	12	0.0800	0.0700	0.0800	0.1200	0.1900
18	13	0.0700	0.0800	0.1200	0.1900	0.2400
19	14	0.0800	0.1200	0.1900	0.2400	0.2700
20	15	0.1200	0.1900	0.2400	0.2700	0.2700
21	16	0.1900	0.2400	0.2700	0.2700	0.2700
22	17	0.2400	0.2700	0.2700	0.2700	0.2600
23	18	0.2700	0.2700	0.2700	0.2600	0.2700
24	19	0.2700	0.2700	0.2600	0.2700	0.2700
25	20	0.2700	0.2600	0.2700	0.2700	0.2700
26	21	0.2600	0.2700	0.2700	0.2700	0.2600
27	22	0.2700	0.2700	0.2700	0.2600	0.2600
28	23	0.2700	0.2700	0.2600	0.2600	0.2700
29	24	0.2700	0.2600	0.2600	0.2700	0.2800
30	25	0.2600	0.2600	0.2700	0.2800	0.3000
31	26	0.2600	0.2700	0.2800	0.3000	0.3200
32						
33	**Attained Age**	**Ult**				
34	0	0.2200				
35	1	0.1200				
36	2	0.0800				
37	3	0.0700				
38	4	0.0700				
39	5	0.0700				
40	6	0.0700				

Output: Impaired Mortality and Counts

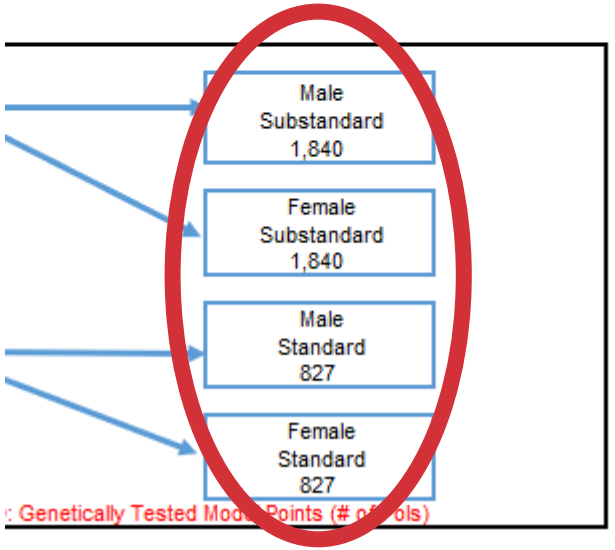
	A	B	C	D	E	F	G	H	I	J
4	**Genetic Condition Specific Assumptions**									
5	**Condition**	**Prevalence of gene mutation (1 in X)**	**Penetrance of clinincal expression given mutation positive**	**Multiple Rating**	**FE Rating ($ per 1000)**	**Predicted**	**Male**	**Standard**	**Grading**	
6	Hypertrophic Cardiomyopathy (HTCM)	500	69%		10.00	25%	50%	5	15	
7										
8	**Illustration Assumptions**	**Illustration Inputs**								
9	**Underlying Mortality**	**Insured**		**UW Assessment**				**Qx Assumptions**		
10	**Base:** 2015 VBT RR100 NS ALB	Sex	M	Multiple Rating		Standard Period	5	Application of Multiple	Apply to Ultimate Rates	
11	**Improvement:** Mortality Improvement Rates for AG-38 for Year-End 2016	Issue Age (x)	20	Flat Extra/k	10	Grading Period	15			
12		Smoke Status	Non-Smoker	Flat Extra Yrs	120	Improvement	Yes			
13										
14	**Attained Age**	**Duration (t)**	**Standard Qx (sel/ult)**	**Stnd Qx (ult)**	**Qx Impr**	**Grading Pattern**	**Added Qx from Multiple**	**Added Qx from Flat Extra/k**	**Stnd Qx (sel/ult improved**	**Substnd Qx (improved)**
15	20	1	0.510	0.260	0.9880	0%	-	-	0.5	0.504
16	21	2	0.570	0.270	0.9761	0%	-	-	0.5	0.556
17	22	3	0.570	0.270	0.9644	0%	-	-	0.5	0.550
18	23	4	0.550	0.270	0.9529	0%	-	-	0.5	0.524
19	24	5	0.530	0.260	0.9414	0%	-	-	0.49	0.499
20	25	6	0.520	0.260	0.9301	3%	-	0.33	0.484	0.794
21	26	7	0.510	0.270	0.9190	10%	-	1.00	0.469	1.388
22	27	8	0.470	0.280	0.9079	17%	-	1.67	0.427	1.940

Output: Impaired Mortality and Counts

In Results Dashboard



J	K	L
% Male	Standard Period	Grading Period
50%	5	15



The mortality and counts can also be found in sheet Extra Claim Cost Illustration

2019 LIFE & ANNUITY SYMPOSIUM

QUESTIONS?

Contact Jean-Marc Fix jean-marc.fix@genre.com

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