Genetics and Insurance: Hypertrophic Cardiomyopathy (HCM)

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Introduction

Since the DNA-based testing became available in the 1990s, the use of genetic information by insurers has been disputed:

- Individuals were concerned about genetic discrimination.
- Insurers were concerned about adverse selection.

Motivation

Macdonald & Yu (2011) Model:

- Six major single-gene disorders (rare and dominantly inherited).
- The highest increases in life insurance premium rates were 0.6% if genetic test results were undisclosed to insurers.

Howard (2014) Model by Canadian Institute of Actuaries:

- Thirteen genetic disorders, mainly cardiomyopathies different than Macdonald & Yu (2011).
- The life insurance premium increases were as high as 12% if genetic test results were undisclosed to insurers.

Cardiomyopathies

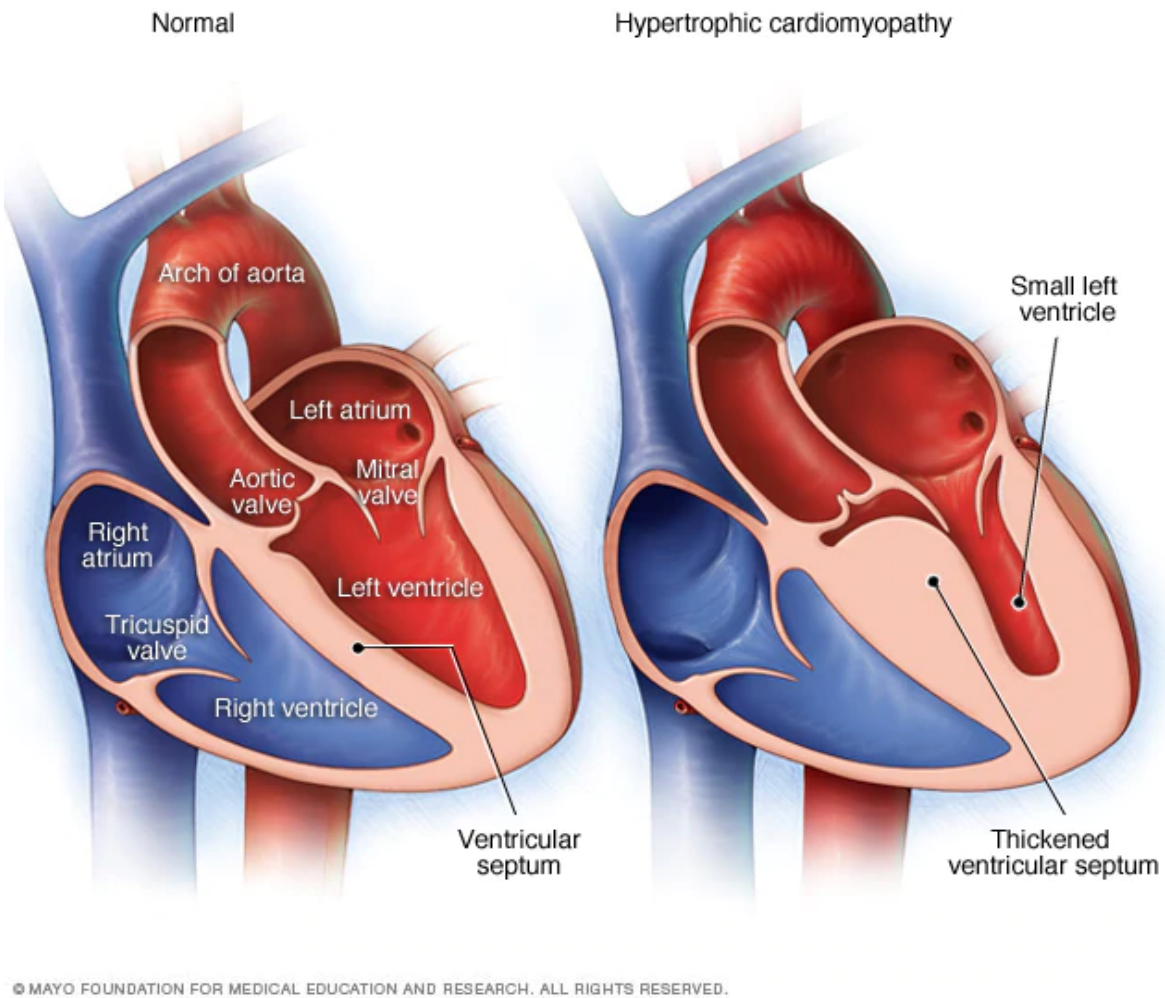
They are...

- inherited heart muscle disorders.
- similar in that single-gene disorders, dominantly inherited.

They differ in that...

- Sudden Cardiac Arrest (SCA), usually at early adulthood.
- Clinically group into many genetic heart muscle disorders.
  - Hypertrophic Cardiomyopathy (HCM) (most prevalent),
  - Dilated Cardiomyopathy (DCM),
  - Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC),
  - Long QT Syndrome (LQTS),
  - Brugada Syndrome,
  - Catecholaminergic Polymophic Ventricular Tachycardia (CPVT),

Hypertrophic Cardiomyopathy (HCM)



SOURCE: MAYO CLINIC FOUNDATION

Hypertrophic Cardiomyopathy (HCM)

Prevalence: 0.2% in the general population.

Onset: Left Ventricular Wall Thickness (LWVT)$\geq$15 mm.

Diagnosis: Echocardiography & Cardiac Magnetic Resonance.

Symptoms: Chest pain, shortness of breath, syncope.

Genetics: Autosomal dominant mutations in over 8 genes.

HCM-Related Mortality: SCA, Heart Failure (HF), Stroke.

HCM-Related Annual Mortality Rates (AMRs)

In the earliest studies of HCM (1960-1990):

- The AMRs of HCM were 3-6%.
- They were based on severely symptomatic individuals.

Later studies of HCM (after 1990):

- Unbiased sample $\rightarrow$ the AMRs of HCM were about 1%.
- They were also explained by modern diagnosis and treatment.

HCM-Related Annual Mortality Rates (AMRs)

Fatal HCM Endpoint:

- *The following endpoints were used in the survival analysis: (1) sudden cardiac death — witnessed sudden death with or ..., and successfully resuscitated cardiac arrest; (2) ...*" (Elliott et al. 2006).

Recent studies (Maron et al. 2016, 2015, 2013):

Ages	HCM-related AMR
7-29	0.00535
30-59	0.00556
60-91	0.00483

Modelling Genetic Testing in HCM for Life Insurance

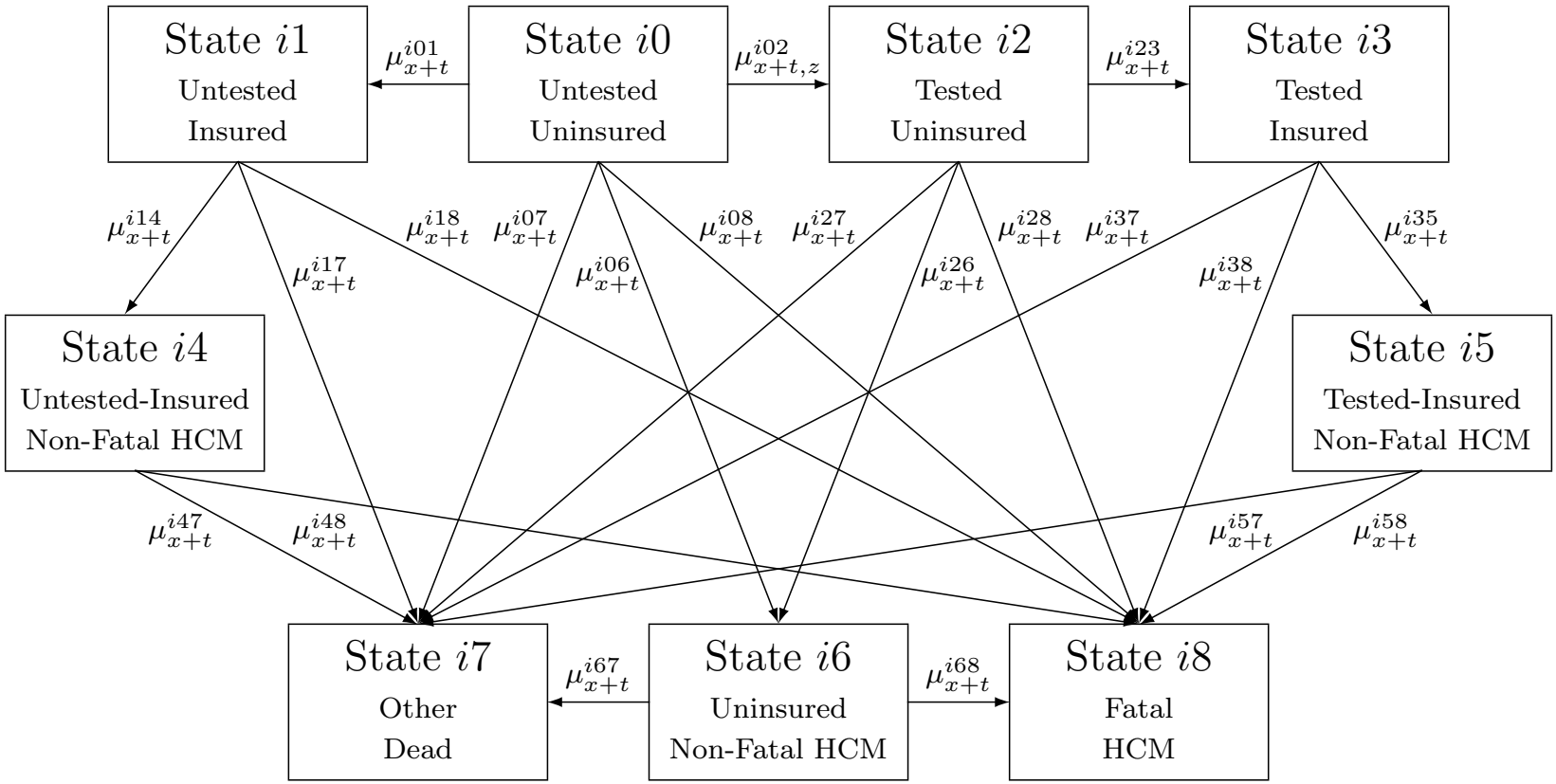
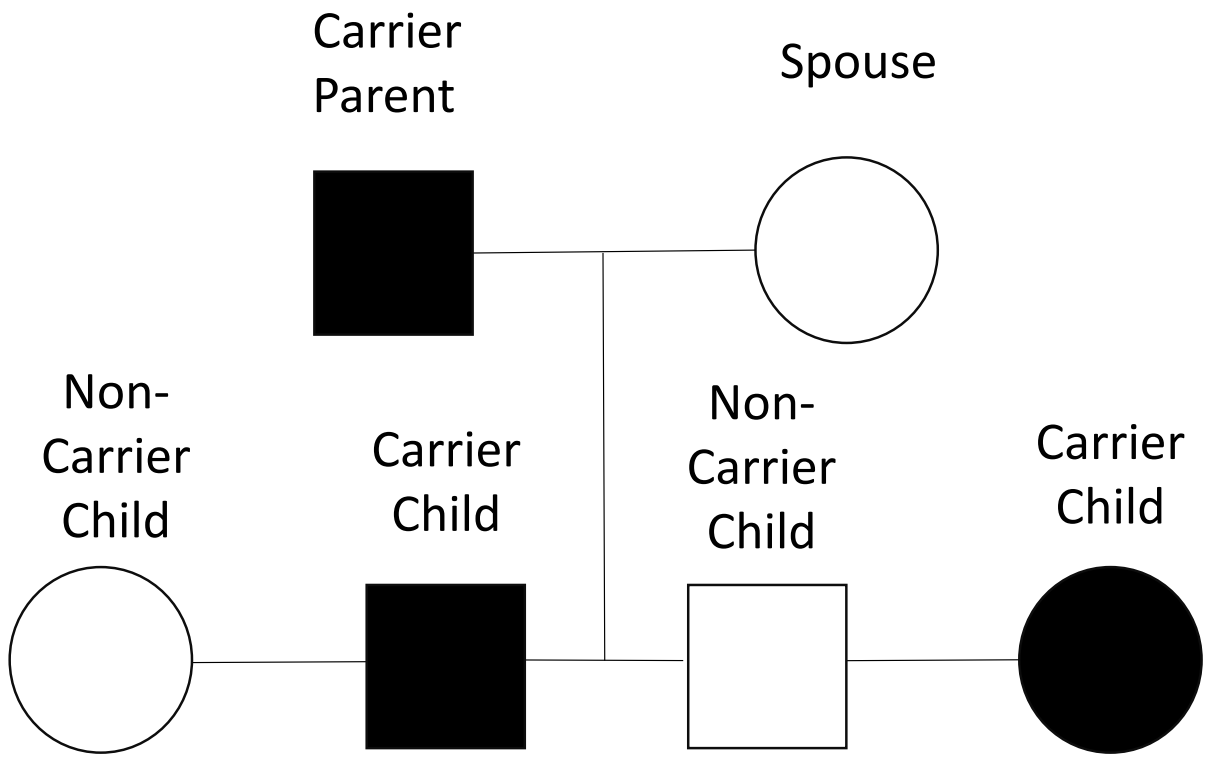


Figure 1: A mathematical model of adverse selection in HCM for a person after age $x + t$ in the ith of several sub-populations defined by HCM genotype in a life insurance market.

Modelling Genetic Testing in HCM for Life Insurance

- i is a sub-population by HCM genotype, $i = 0, 1, 2, ..., 8$.
- μ_{x+t}^{ijk} is the transition intensity depending on the state currently occupied and the family history at age $x + t$.
- A key piece of family history information is whether or not a proband exists in the family.
- A proband, generally the first clinically affected person in family, triggers genetic testing through all family members (Cascade Genetic Testing).

A Hypothetical Nuclear HCM Family with No Proband



Modelling Genetic Testing in HCM for Life Insurance — No Proband Exists

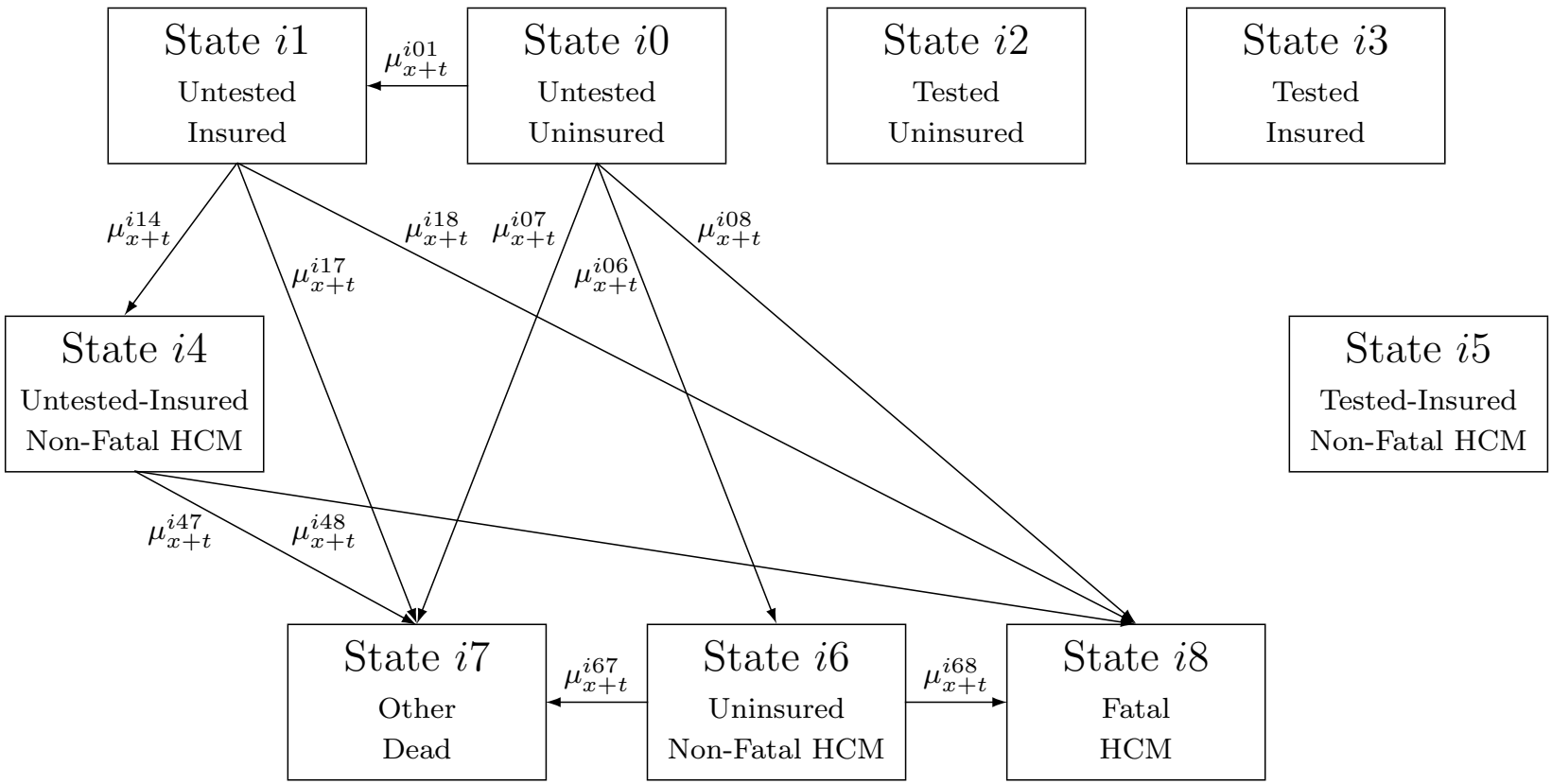
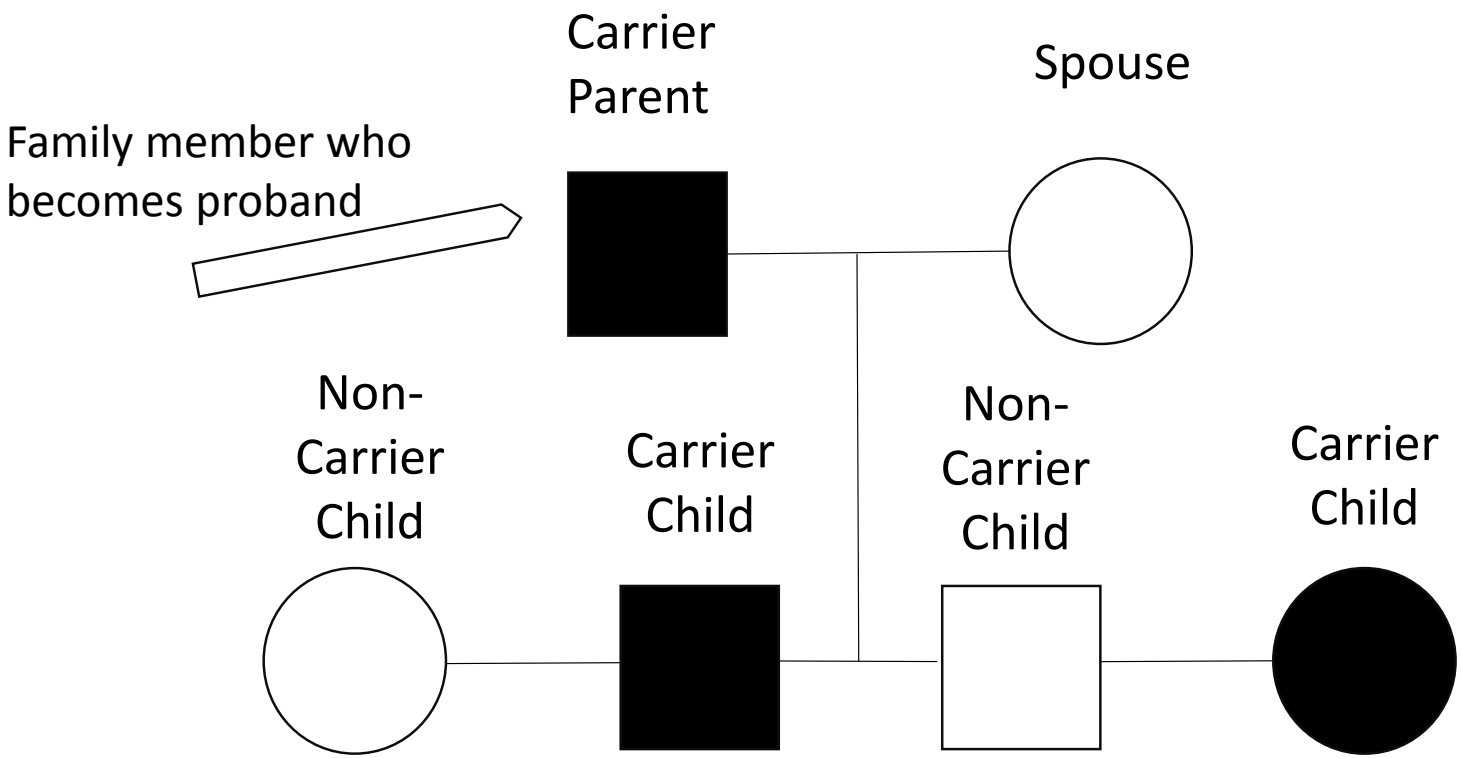


Figure 2: A mathematical model of adverse selection in HCM for a person after age $x + t$ in the ith of several sub-populations defined by HCM genotype in a life insurance market.

A Hypothetical Nuclear HCM Family with A Proband



Modelling Genetic Testing in HCM for Life Insurance — A Proband Exists

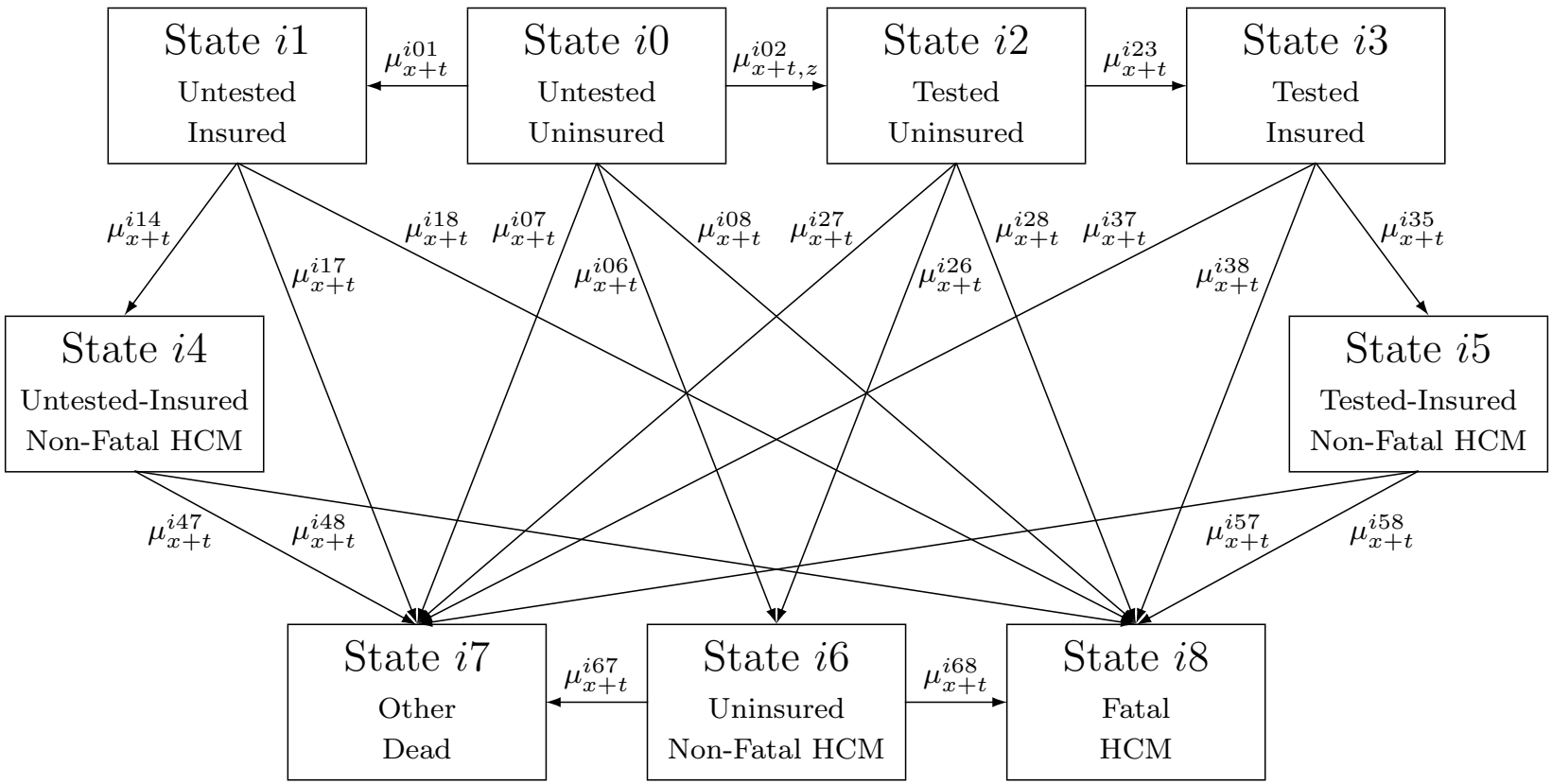


Figure 3: A mathematical model of adverse selection in HCM for a person after age $x + t$ in the ith of several sub-populations defined by HCM genotype in a life insurance market.

Simulation — Creation of HCM Families

- A family has one parent carrying an HCM mutation.
- The other parent does not carry the HCM mutation.
- If both parents alive at age 30:
  - The family has random number of children $\sim$ Poisson(λ).
  - Each child inherits the HCM mutation with 0.5 probability.
- We simulate 10,000 independent HCM families.

Simulation — Life Histories of HCM Families

- Suppose the family has m members.
- Loop through the m family members one by one.
- Suppose eth member ($e = 1, 2, ..., m$) in state ij at age x.
- If $\sum_k \mu_x^{ijk} dt < 1$, simulate $\mathcal{U} \sim U(0, 1)$.
- If $\sum_{l=0}^{k-1} \mu_x^{ijl} dt < \mathcal{U} \leq \sum_{l=0}^{k} \mu_x^{ijl} dt$ $(k = \{1, 2, ..., 8\})$,
  - transits from state ij to state ik during time dt;
  - stays in state ij, otherwise.

Simulation — Behaviour under Adverse Selection

What is Adverse Selection?

- Asymmetry of information between 'insurer' and 'insured'.

How Insurers Behave under Adverse Selection?

- Assumptions of prevalence, onset, mortality of disorders.
- Calculation of premiums assuming all purchasing 'normal'.

How Individuals Behave under Adverse Selection?

- 'At-risk of HCM' persons purchasing 'more than normal'.
- Then, adverse selection gives rises to insurance losses.

Simulation — Individual Insurance Losses

Individual loss between time t and $t + dt$:

$$dL_{r;e}(t) = A^{ad}_{r;e}(t)dN^{ad}_{r;e}(t) - a^{a}_{r;e}(t)I^{a}_{r;e}(t)dt. \qquad (1)$$

label r: an insured person label e: a random experiment
label a: insured alive state label d: insured dead state

- $A^{ad}_{r;e}(t)$: Sum assured if the rth person is dead at time t.
- $dN^{ad}_{r;e}(t)$: Counts the jumps of the rth person to state d:

$$dN^{ad}_{r;e}(t) = \lim_{dt \to 0} \left[N^{ad}_{r;e}(t) - N^{ad}_{r;e}(t - dt) \right]. \qquad (2)$$

- $a^{a}_{r;e}(t)$: Annual payment by the rth person alive at time t.
- $I^{a}_{r;e}(t)$: 1 if the rth person alive at time t^{-}; 0, otherwise.

Simulation — Individual Adverse Selection Costs

1. Present value of total losses from N persons at time 0:

$$L_e = \sum_{r=1}^{N} \int_0^{\infty} e^{-\delta t} dL_{r;e}(t). \tag{3}$$

2. Present value of total income from N persons at time 0:

$$I_e = \sum_{r=1}^{N} \int_0^{\infty} e^{-\delta t} a^a_{r;e}(t) I^a_{r;e}(t) dt. \tag{4}$$

3. The mean individual costs from W random experiments:

$$\frac{1}{W} \left(\sum_{e=1}^{W} \frac{L_e}{I_e} \right). \tag{5}$$

Results

Individual premium increases in the life insurance market in which the annual purchase rate of 'at-risk of HCM' individuals, adverse purchase rate, is 'more than normal'.

Market Size	Adverse Purchase Rate (per annum)	Sum Assured	Fatal HCM Rate (per annum)	Family History	Premium Increases %Mean (CI,95%)
Large	5xNormal	£1	0.0055	✓	0.0189 (-0.0041,0.0421)
				✗	0.0518 (0.0284,0.0751)
Large	5xNormal	£1	0.01	✓	0.0210 (-0.0036,0.0493)
				✗	0.0646 (0.0392,0.0939)
Large	5xNormal	£10	0.0055	✓	0.1852 (0.0658,0.3079)
				✗	0.5107 (0.3957,0.6354)
Small	25xNormal	£1	0.0055	✓	0.1054 (0.0518,0.1641)
				✗	0.2998 (0.2448,0.3598)
Small	25xNormal	£10	0.01	✓	1.1767 (0.7681,1.6619)
				✗	3.8307 (3.3934,4.3614)

Comparison with Howard (2014)

- Key Assumptions:

Sum assured at-risk of HCM individuals.	\$1M
Fatal HCM per annum.	0.01
Lapse rate of at-risk individuals per annum.	0.5%
Lapse rate of not-at-risk individuals per annum.	3%

- Result:

3% of the 12% costs explained by HCM.

Discussion

Conclusion: Pricing assumptions have much more impact to the costs than that of epidemiological assumptions.

Further Work: Including lapse state(s) into our model and calculate the impact of the lapse rate to the costs.

Thank you!

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