

# Nature or nurture?

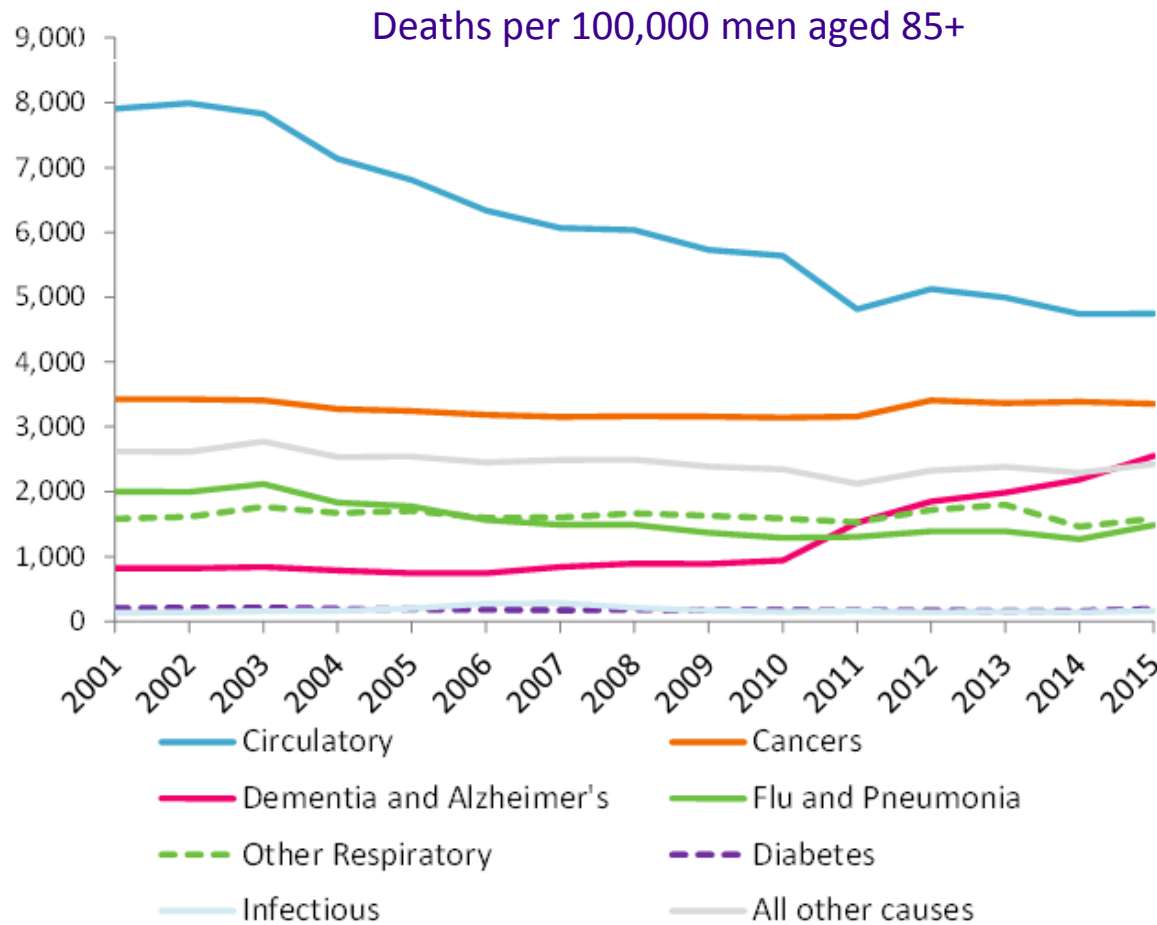
Douglas Anderson, Founder of Club Vita

Peter Joshi, Usher Institute, University of Edinburgh

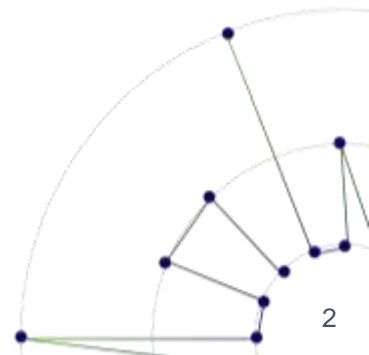
Nicola Oliver, Medical Intelligence

02 February 2018

# Causes of death



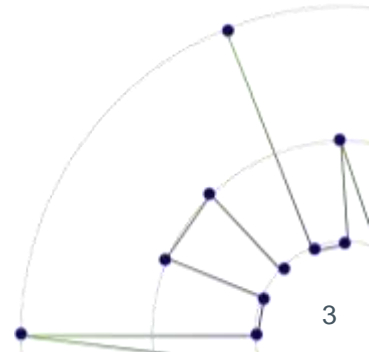
**CVD falling**  
**Cancer flatlining**  
**Dementia rising**






# Lifespan: Nature or Nurture?



Peter Joshi, Usher Institute,  
University of Edinburgh.

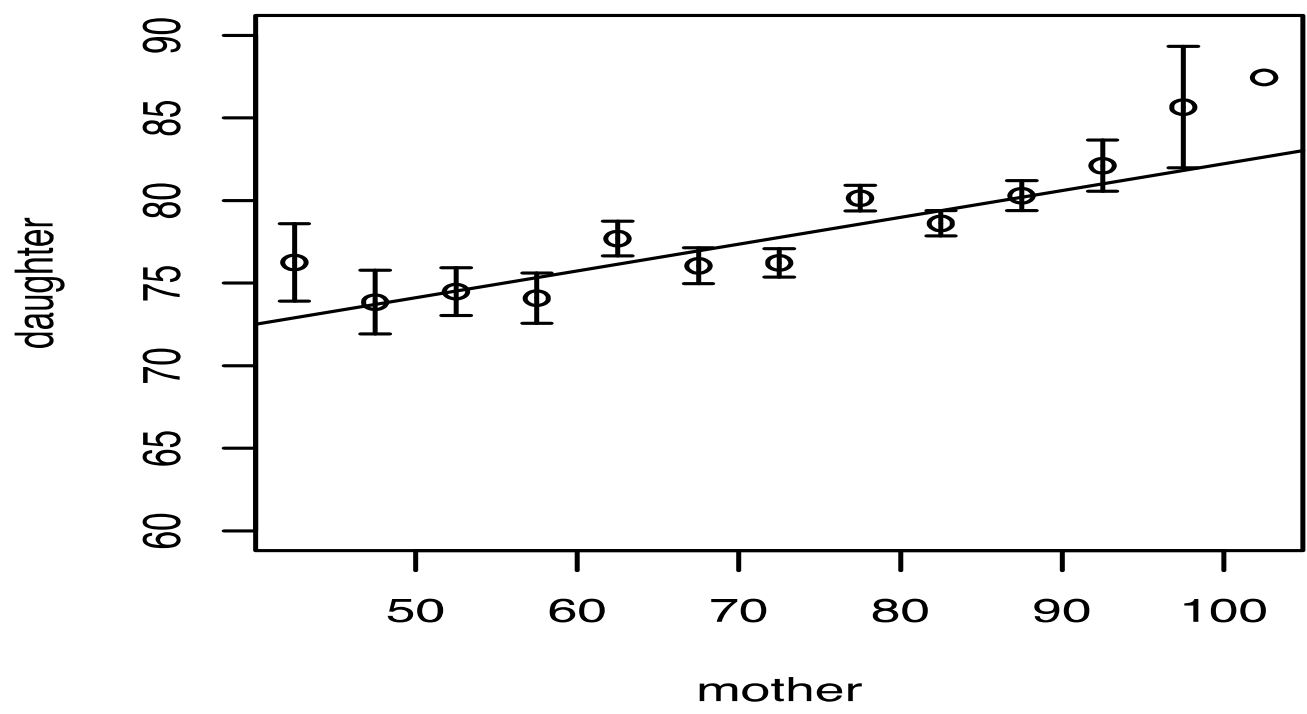


# Summary

- Your lifespan is determined by
  -  Your genes
    - Which impact your lifestyle choices
  -  Your lifestyle
  -  Chance



# Lifespan runs in families



*Long lived mothers have (slightly) long lived daughters*





# Genes or Environment?

	Genes	Environment	
Herskind et al., 1996	26%	74%	Danish twins
Ljungquist et al., 1998	33%	67%	Swedish twins
Gavrilova et al., 1998	18%	82%	Royal Families
Mitchell et al., 2001	25%	75%	Amish
Joshi et al (in prep)	16%	84%	Scottish nuclear fam

*Lifespan ~20% genetic: more nurture than nature*

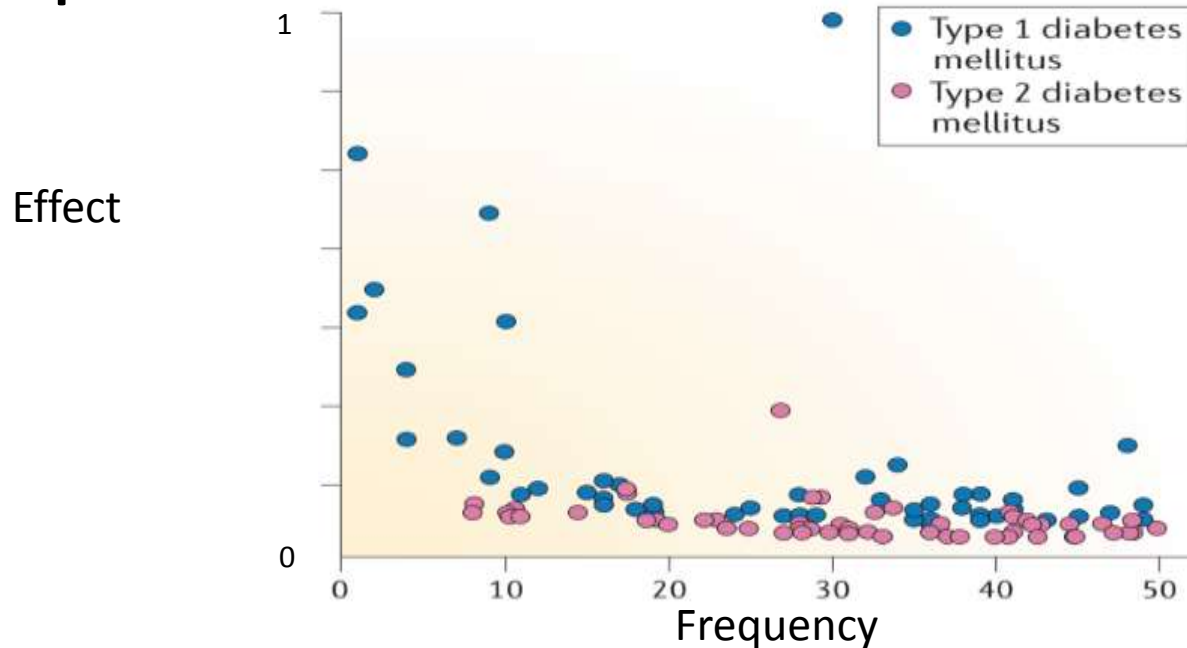




# GENETIC VARIANTS AFFECTING LIFESPAN



# Genetic variants affecting disease and lifespan are rare or small in effect



**nature**  
**REVIEWS** **GENETICS**

Genetic architecture: the shape of the genetic contribution to human traits and disease Nicholas J. Timpson<sup>1</sup>, Celia M. T. Greenwood<sup>2,3,4</sup>, Nicole Soranzo<sup>5,6</sup>, Daniel J. Lawson<sup>1</sup> and J. Brent Richards<sup>4,7,8</sup>  
124 | FEBRUARY 2018 | VOLUME 19





# Common Genes affecting lifespan

Gene	Proportion of population	Mean Years of life	Mechanism
<i>HLA-DQA1/DRB1</i>	17%	0.6	Immune Response
<i>LPA</i>	16%	-0.7	Blood Lipids
<i>CHRNA3/5</i>	59%	-0.4	Smoking
<i>APOE</i>	26%	-0.9	Alzheimer's Disease



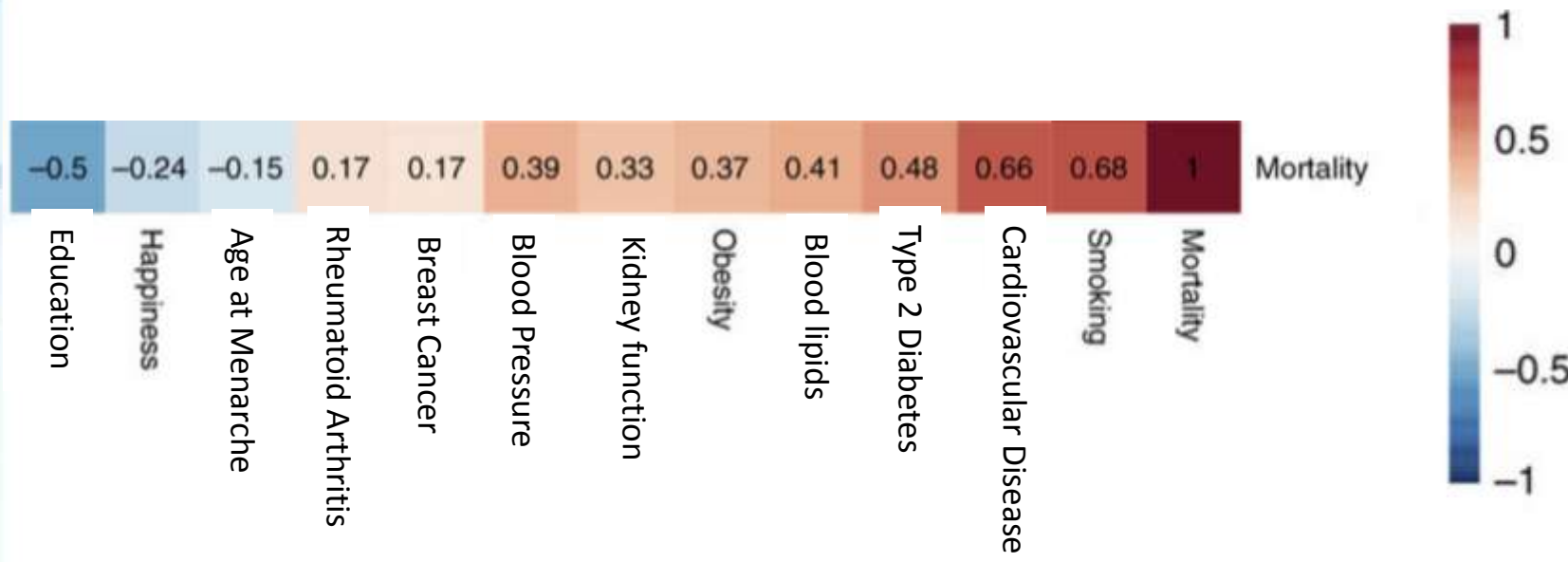
Article | OPEN

**Genome-wide meta-analysis associates HLA-DQA1/DRB1 and LPA and lifestyle factors with human longevity**

Peter K. Joshi, Nicola Pirastu, [...] James F. Wilson



# Genetic correlations with mortality



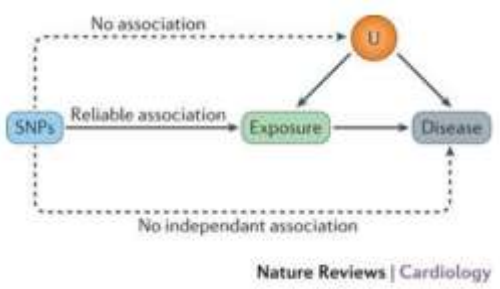
nature COMMUNICATIONS  
 Article 220 | October 1 | [View full article](#)  
 Genome-wide meta-analysis associates HLA-DQA1/DRB1 and LPA and lifestyle factors with human longevity  
 Peter K. Joshi, Susana Ferrel, ... James A. Wilson

*Nature influences nurture*

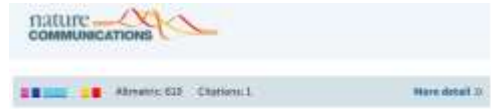
# Which affects lifespan more?

**Months**

- A. Smoking one cigarette every day      -4
- B. Spending a month in education      +1
- C. Carrying 1kg weight      -2



Nature Reviews | Cardiology



Genome-wide meta-analysis associates HLA-DQA1/DRB1 and LPA and lifestyle factors with human longevity

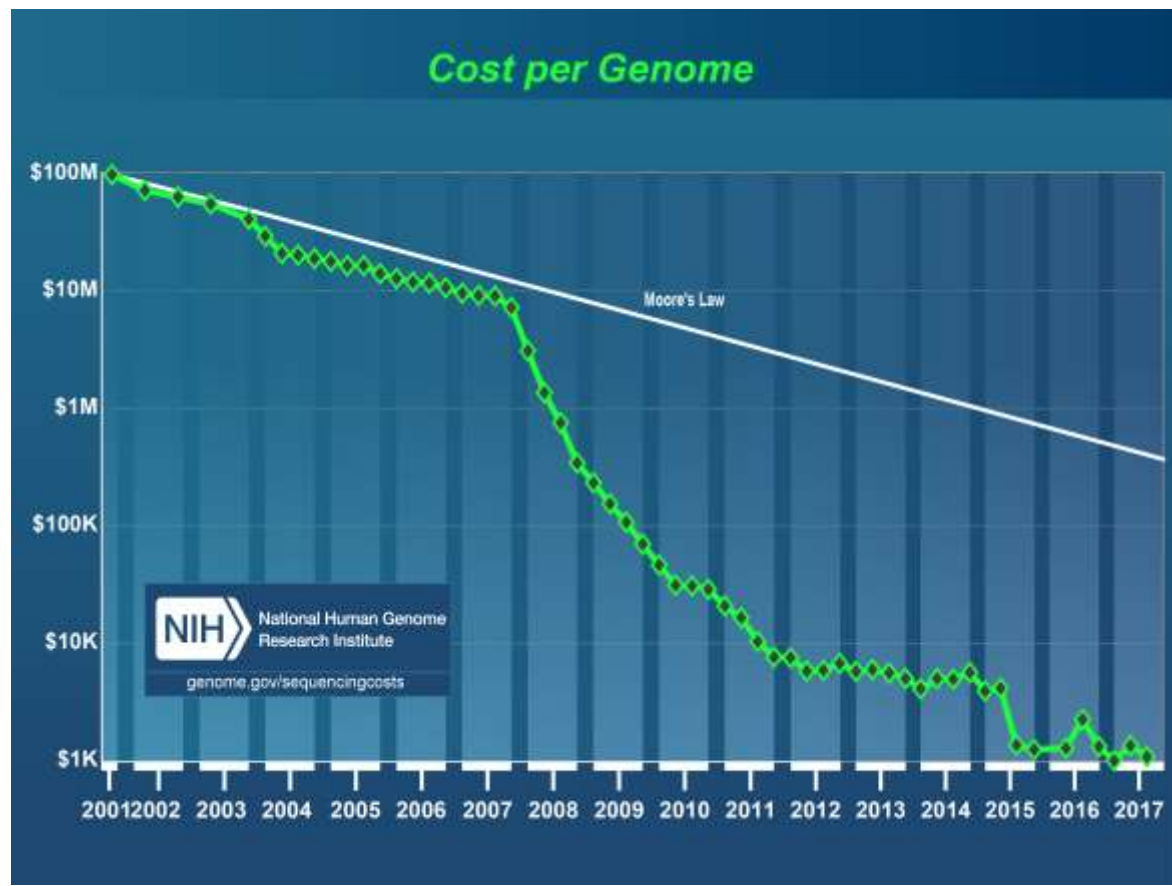
Peter K. Joshi, Nicola Pirastu, [...] James F. Wilson



# GENOMIC PREDICTION OF LONGEVITY



# Genomics and genetic testing





# Rare, genetic, devastating diseases

Condition	Prevalence	Penetrance
BRCA1 or 2	500	25%
HTCM	500	69%
DCM	2700	75%
ARVCM	1250	75%
Long QT	3000	50%
Brugada	2000	75%
Huntington	20000	90%
PKD	1000	100%
DM1 or 2	8000	75%
ADEO	2427	100%
HNPCC	500	50%
Marfan	5000	50%
CPVT	10000	75%



Report to  
CIA Research Committee

Genetic Testing Model for CI:  
If Underwriters of Individual Critical  
Illness Insurance Had No Access to  
Known Results of Genetic Tests

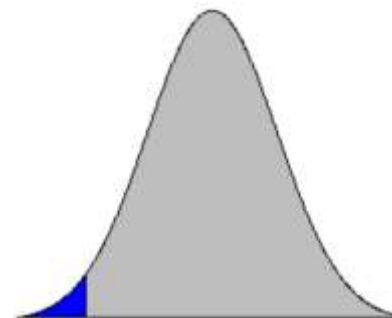
Prepared by  
Robert E. W. (Bob) Hawkins, FCA, FIA

*For a rare few nature exceeds nurture*

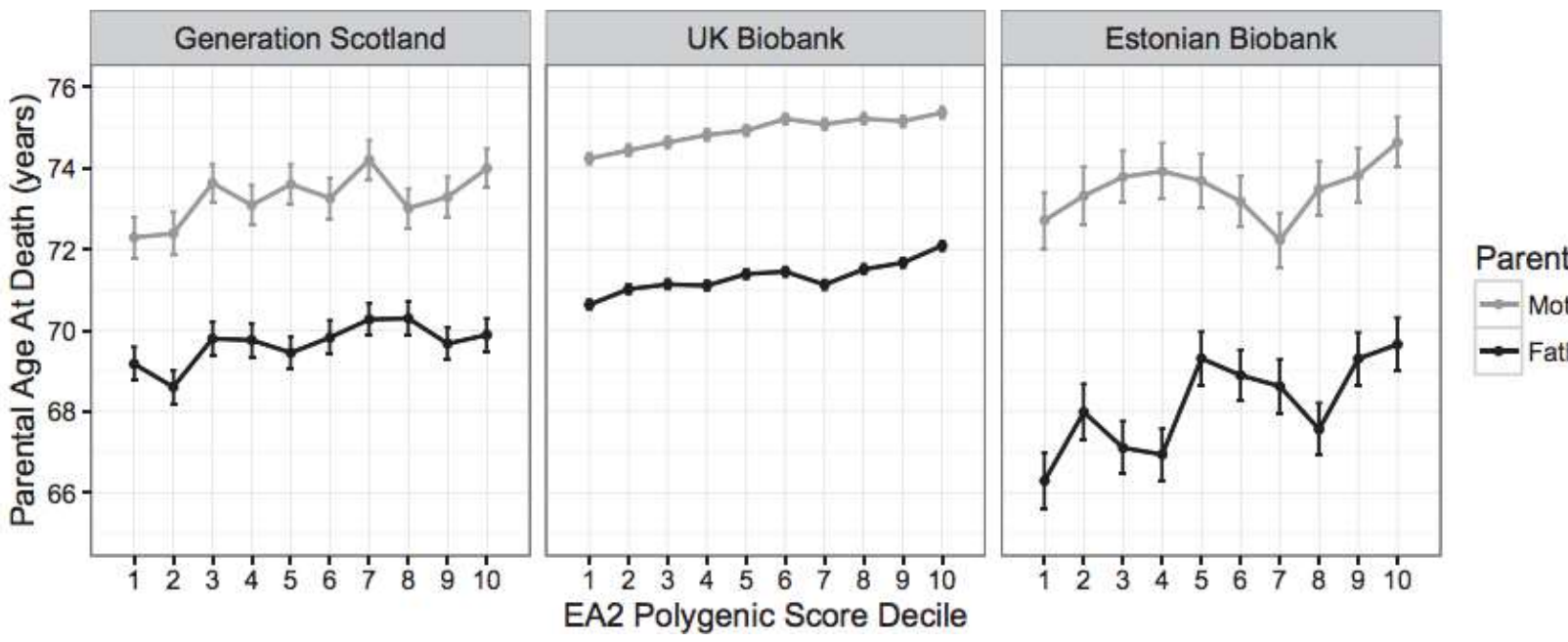


## Genomics and very early death: rare

- Genome sequencing may become routine
- Previous tests may become population wide
- Will discover many new mutations of unknown significance ??
- Not that significant at population level
  - Information asymmetry



# Whole Genomic prediction of longevity from Education genes



## Genetic variants linked to education predict longevity

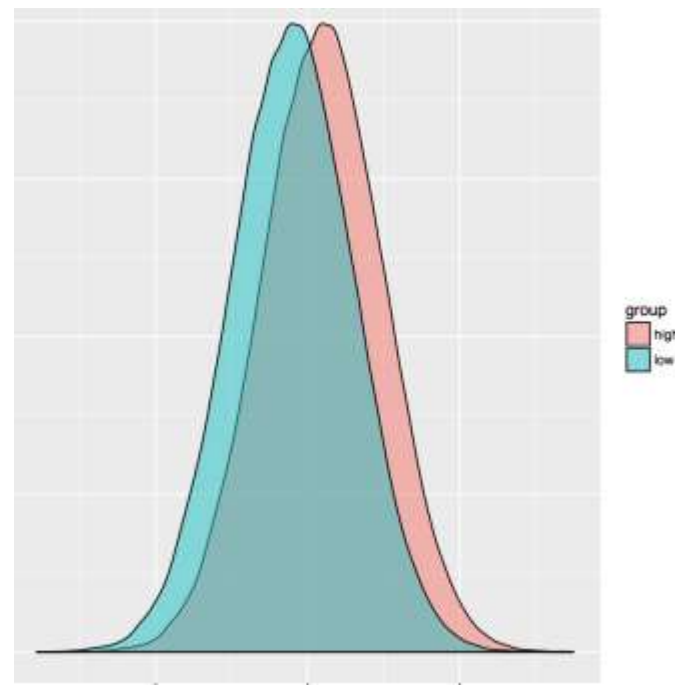
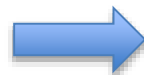
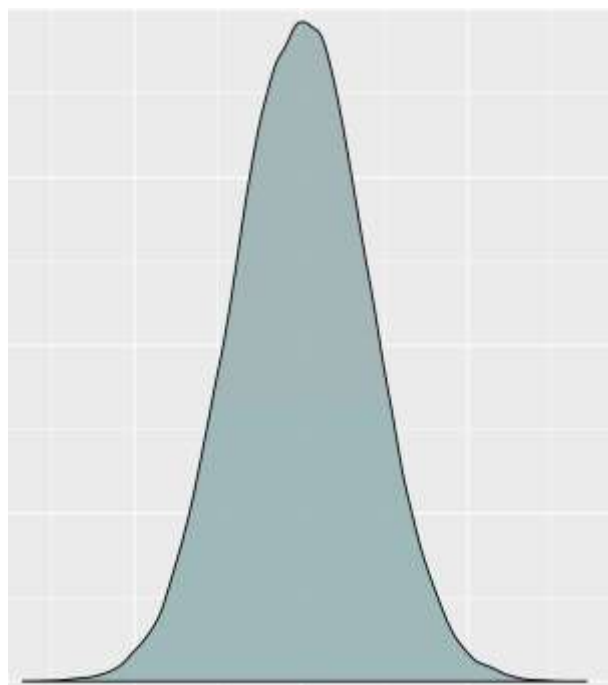
Riccardo E. Marioni<sup>a,b,c,d,e,f,g</sup>, Stuart J. Ritchie<sup>a,d,g</sup>, Peter K. Joshi<sup>h,i</sup>, Saskia P. Hagenaars<sup>h,d,f</sup>, Aysu Okbay<sup>h,i,j</sup>, Krista Fischer<sup>l</sup>, Mark J. Adams<sup>l</sup>, W. David Hill<sup>h,k</sup>, Gail Davies<sup>h,l</sup>, Social Science Genetic Association Consortium<sup>l</sup>, Reka Nagy<sup>h</sup>, Carmen Amador<sup>h</sup>, Kristi Läll<sup>h,l</sup>, Andres Metspalu<sup>h</sup>, David C. Liewald<sup>h,d</sup>, Archie Campbell<sup>h</sup>, James F. Wilson<sup>h,k</sup>, Caroline Hayward<sup>h</sup>, Tõnu Esko<sup>h,m,n</sup>, David J. Porteous<sup>h,i</sup>, Catharine R. Gale<sup>h,d,o,p</sup>, and Ian J. Deary<sup>h,d,q</sup>

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# Genomics and average life expectancy for large groups – modest effects



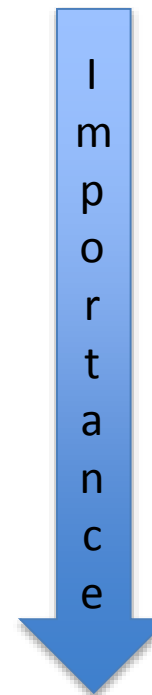
# Acknowledgements



# Summary

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  -  Chance

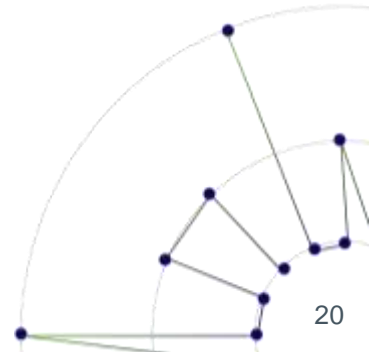
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# Genetic Testing & Insurance



Nicola Oliver,  
Medical Intelligence



**Current Regulatory Environment**

**Discrimination & Risk**

**Direct-to-Consumer Testing**

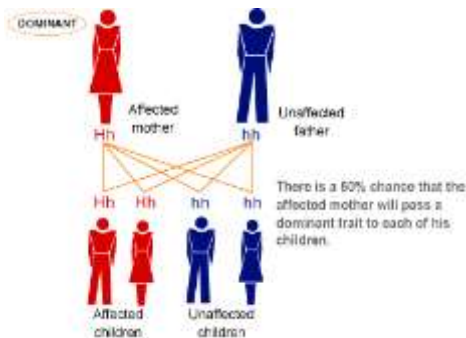
**Concluding Summary**



Single gene mutations are the result of a change to a single DNA nucleotide



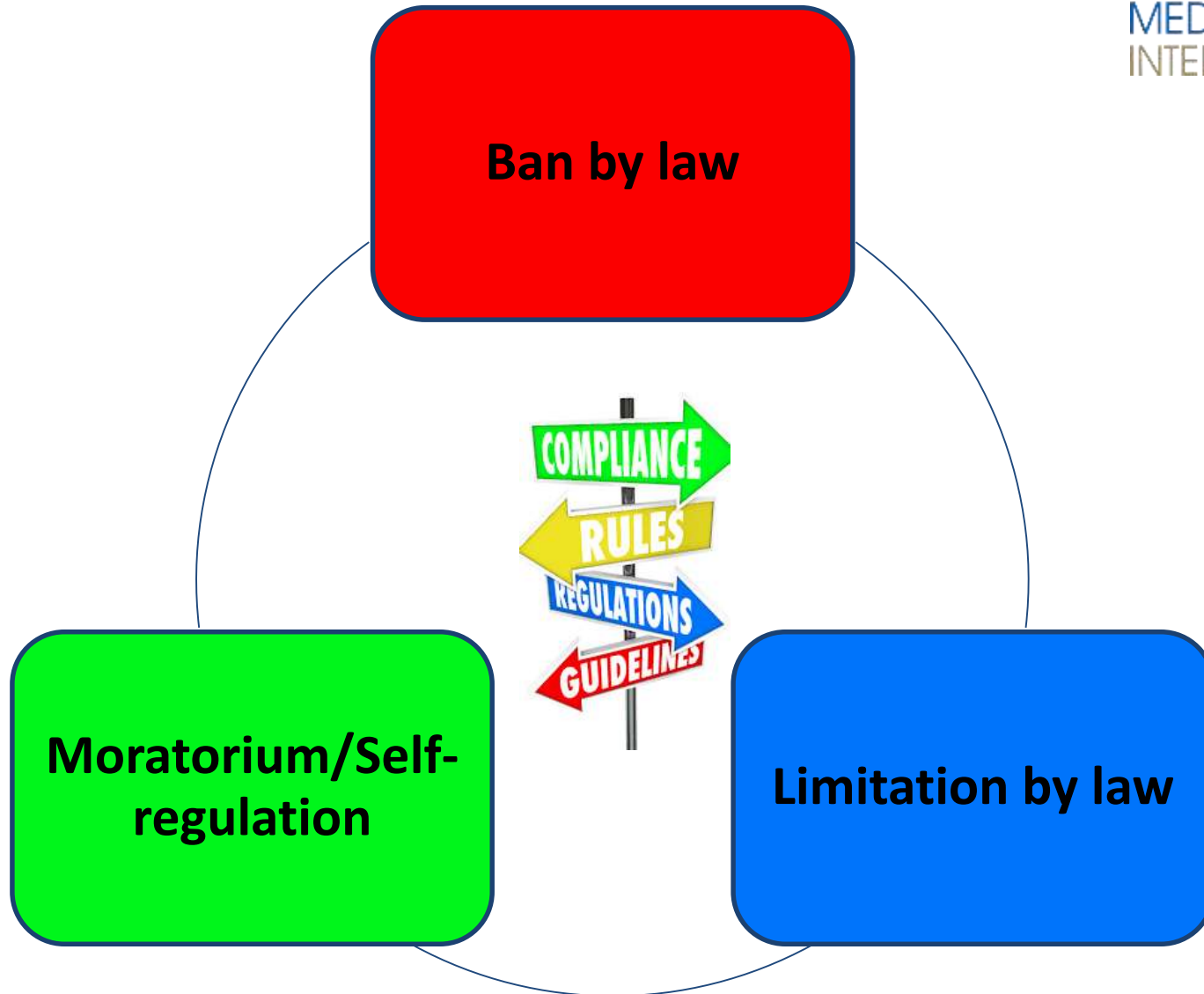
Chromosome structure mutations are the result of alterations to the structure of one or more whole chromosomes



**RESULTS ENCLOSED**  
**£500,000**  
**Huntington's Disease**



*Exceptionally Precise*  
 Medical Expertise





**Ban by law**



**Portugal  
Genetic Information  
Act (2005)**



**Poland  
Insurance Act  
(2015)**



**Canada  
Genetic Non-Discrimination  
Act (2016)**



# Limitation by law



## USA

**Genetic Information Non-discrimination  
Act (2008)**



## Netherlands

**The Act on Medical Examinations (1998)**



## Switzerland

**Genetic Investigations in Humans  
(2004)**



## Germany

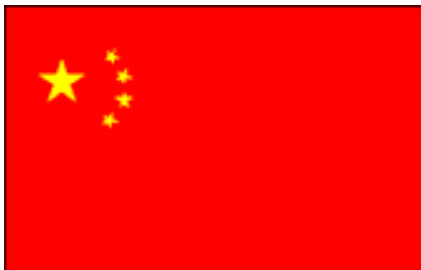
**Human Genetic Examination  
Act (2009)**

**Moratorium/  
Self-regulation**



Japan

Life insurers impose  
self-restrictions



China

No restrictions for insurance companies  
asking for genetic tests or results



UK

Concordat & Moratorium (2001)



Australia

Insurance companies are allowed to use  
genetic test results



*Am. J. Hum. Genet.* 50:476–482, 1992

## **Discrimination as a Consequence of Genetic Testing**

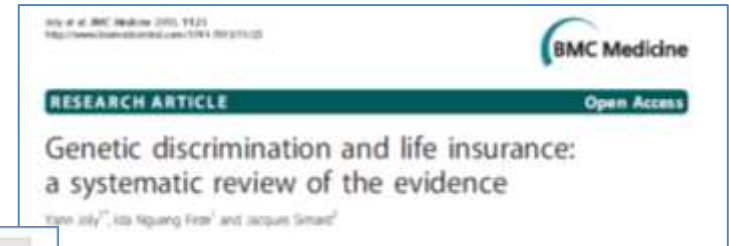
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***“Stigmatization, and denial of services or entitlements to individuals who have a genetic diagnosis but who are asymptomatic or who will never become significantly impaired, is noted.”***



**Avoidance of discrimination through refusing testing?**



**Low public awareness of legislation**  
**High levels of concern**  
**Limited physician awareness of legislation**



**Lack of evidence that discrimination occurs but fear exists**

**NIH Public Access**  
**Author Manuscript**

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**Genetic Testing for Alzheimer's Disease and its Impact on Insurance Purchasing Behavior**

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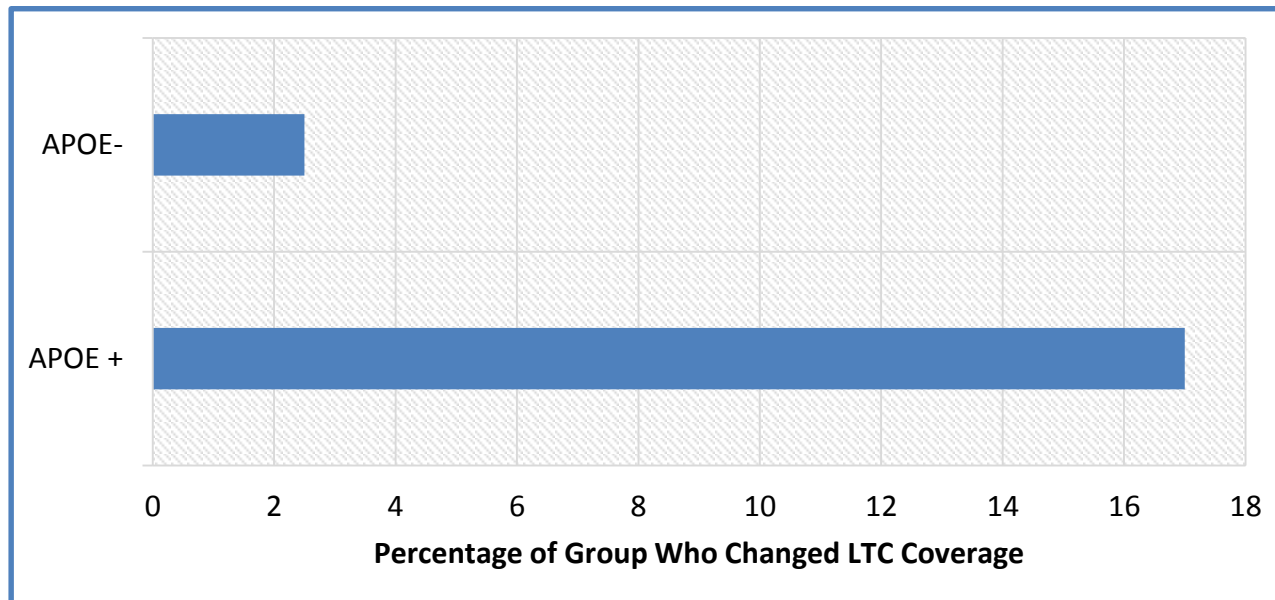
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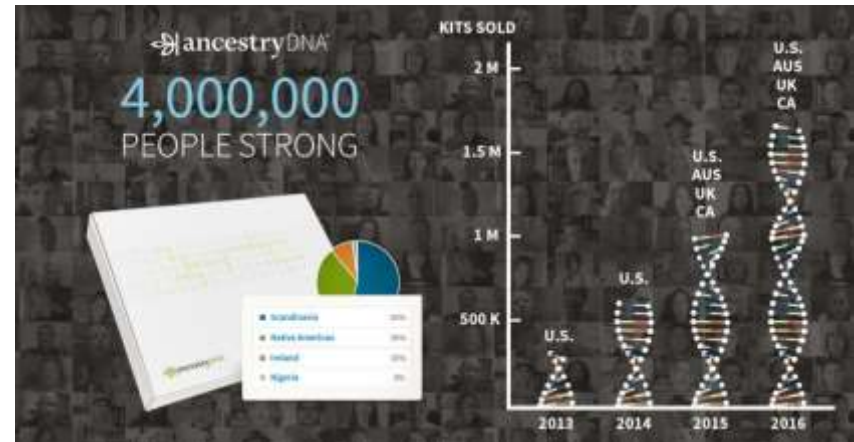
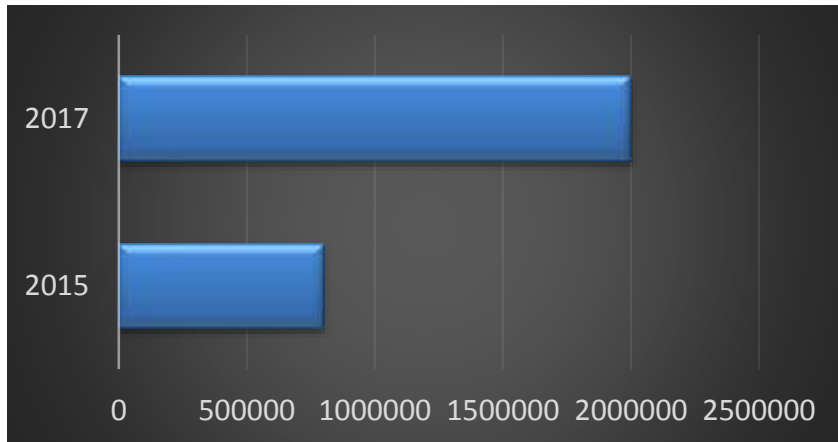
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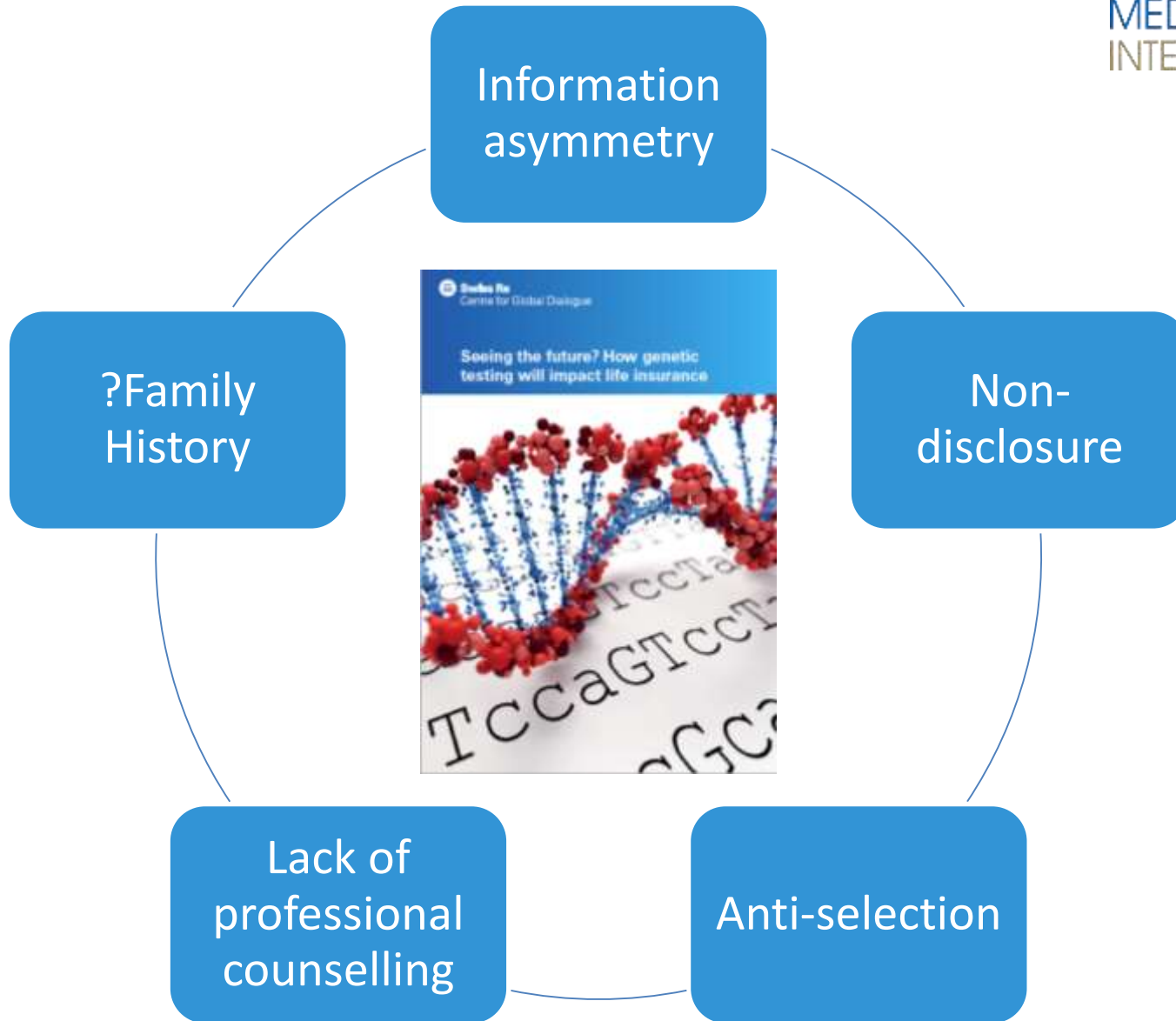
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for the REVEAL Study Group<sup>1</sup>

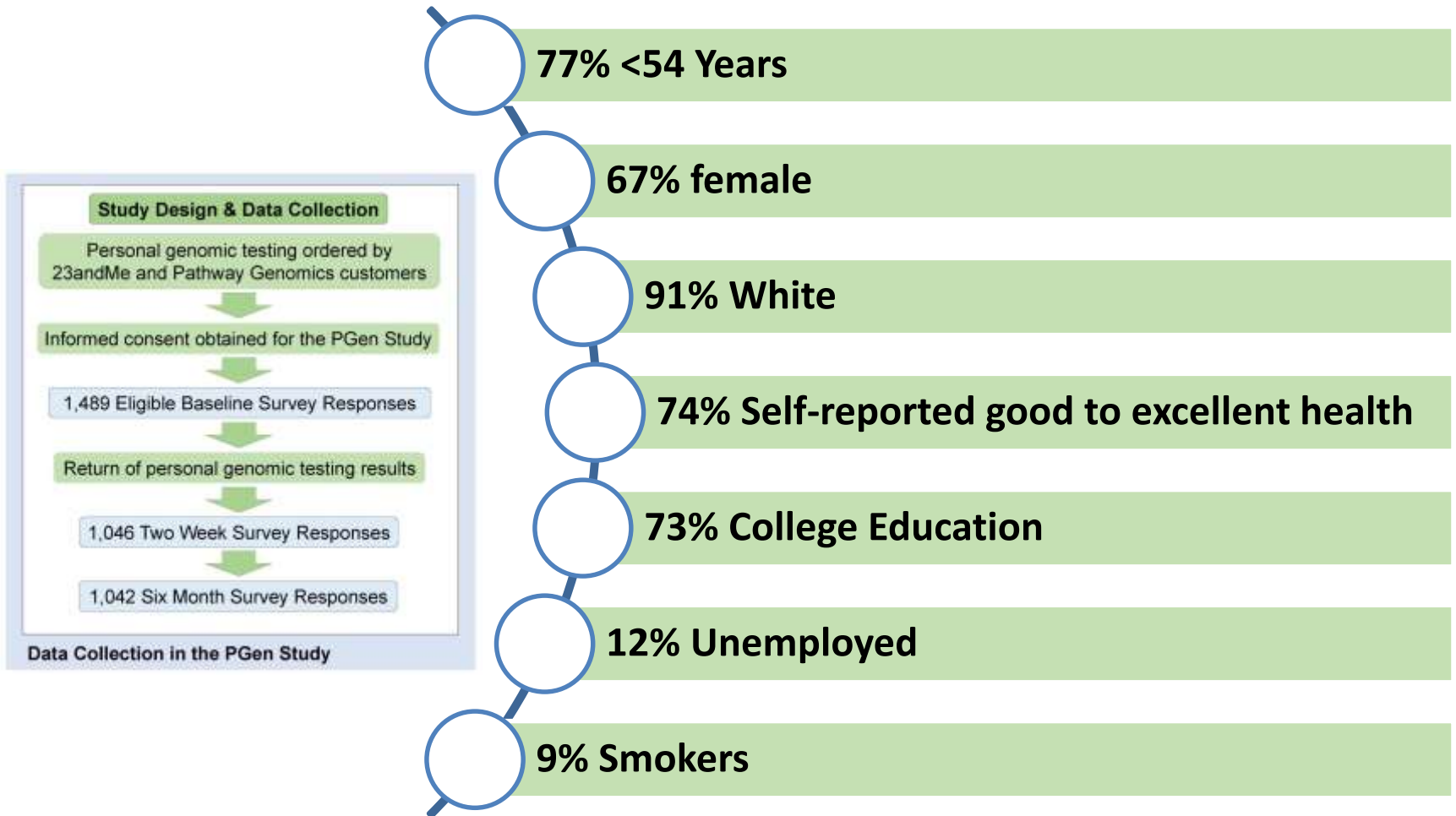




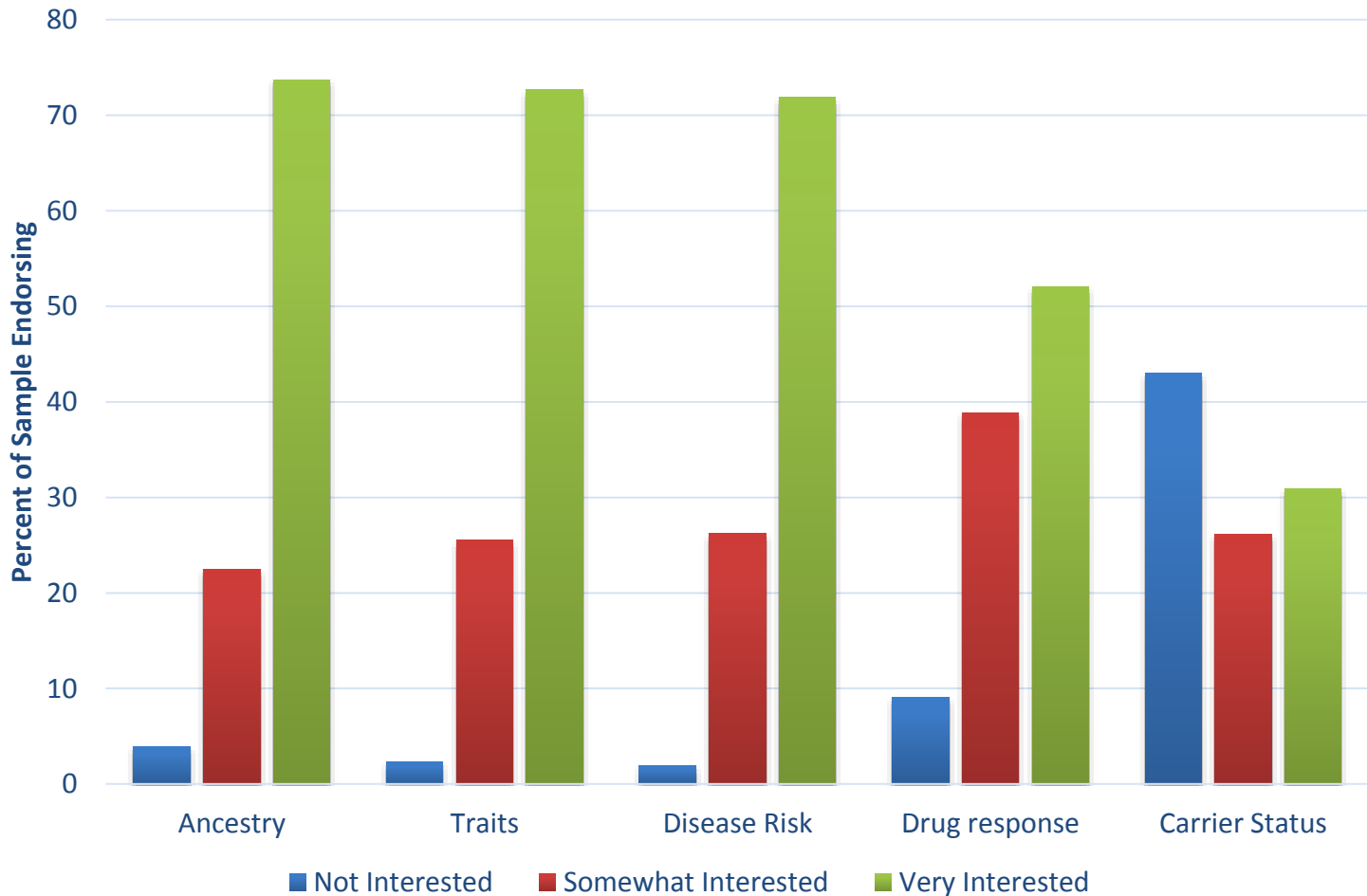
Exceptionally Precise  
Medical Expertise











Level of interest across types of personal genetic information

Report to  
CIA Research Committee

Genetic Testing Model for CI:  
If Underwriters of Individual Critical  
Illness Insurance Had No Access to  
Known Results of Genetic Tests

Prepared by:  
Robert C. W. (Bob) Howard, FCIA, FSA

January 2016

Report to  
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Genetic Testing Model:  
If Underwriters Had  
No Access to Known Results

Prepared by:  
Robert C. W. (Bob) Howard, FCIA, FSA

July 2014

Document 214082  
Ce document est disponible en français  
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***Material impact on insurer, average  
CI claim overall increase of 26% and  
concomitant increase in CI premium  
rates***

***Valuation strain (pricing loss) for the  
industry from those who test positive in a  
single year (based on the assumptions)  
would be about 12% of the total death  
claims for the year. There may be a  
concomitant increase in term insurance  
premium rates***



Thinking about  
life insurance  
through a genetic  
lens - Dr Damjan  
Vukcevic &  
Jessica Chen

## Potential lapse of in-force policies

## Potential increase in claim cost

More-tailored  
premiums, based on  
smaller pools

Much larger pools and  
restrictions on  
'tailorability'

Restrictions on factors  
that are allowed to be  
used for pricing  
premiums and setting  
exclusions

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Concluding  
Summary

**Little legislative or regulatory enforcement**

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**Insurers exposed to anti-selection and lapse risk**

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**Consumers fear, and face, discrimination**

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**Personal genomic testing adding to the debate**

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**New thinking required**

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