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IFoA Genetics Working Party

What next for the Concordat and Moratorium?

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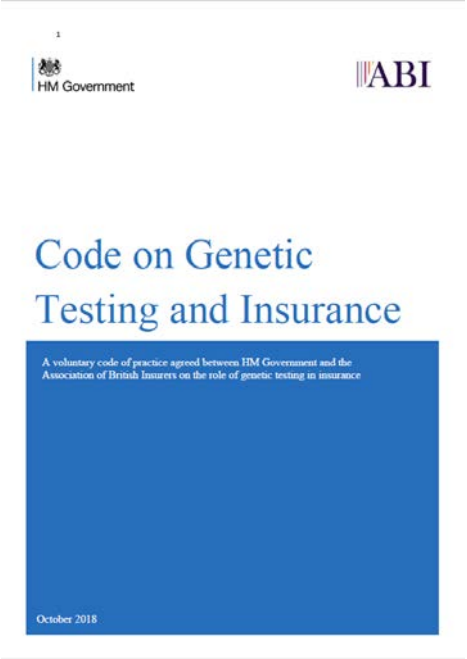
23 November 2018

The Concordat is dead! Long live the code.



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Core principles

- An insurer will not require or pressure an applicant to undertake a predictive or diagnostic genetic test in order to obtain insurance.

- The results of a predictive genetic test may be considered in an application for insurance only when both of the following conditions are met:
  - This Code states that the specific predictive genetic test may be considered and;
  - The sum assured exceeds the financial limits set out in this Code.

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Current predictive tests that may be considered

Type of insurance	Financial limits above which predictive genetic tests may become relevant	Medical conditions for which insurers may ask for and take account of predictive test results, for policies above the financial limits
Life Insurance	£500,000 (per person)	Huntington's disease
Critical Illness Insurance	£300,000 (per person)	None
Income Protection Insurance	£30,000 per annum (per person)	None
All other types of insurance	Predictive genetic test results will not be asked for, or taken into account, whatever the level of cover.	

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What does the future hold?

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Where are we at the moment?

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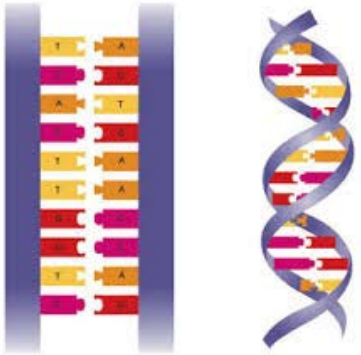
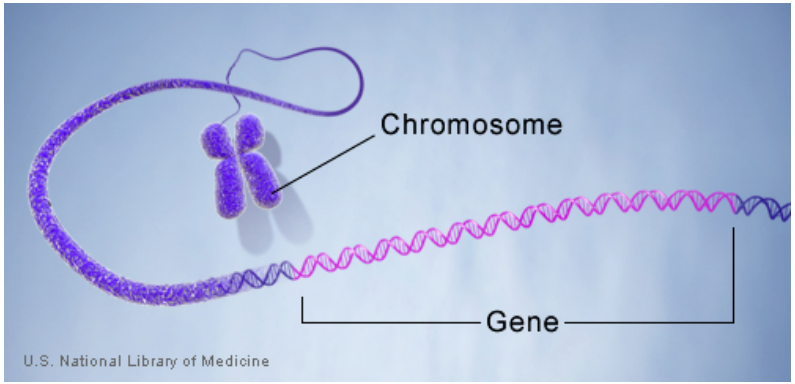
Genetic Testing – the landscape

Genes and Mutations

- A gene is a collection of bases (or letters) which can either act as instructions to make proteins or influence the production of other proteins (by forcing genes that make proteins to be repressed or activated).





- A ‘spelling mistake’ in the code of a gene (known as a mutation) mean that the gene may perform at a sub-optimal level, potentially not performing at all.

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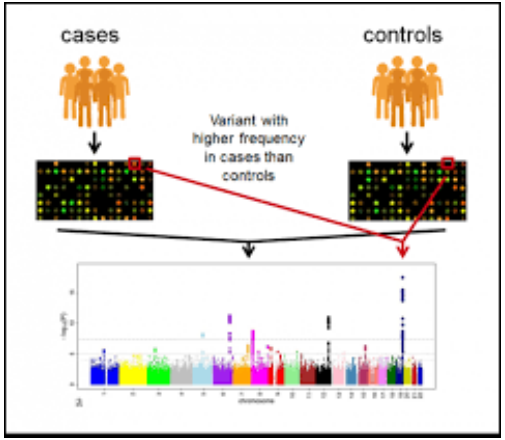
Identifying and testing for mutations

- Specific mutations are linked with a disease by using either genome wide association studies (GWAS) or gene-specific candidate-driven studies



- Identifying a definitive causative relationship between a gene and a disease can be difficult
  - Polygenetic expression – more than one gene involved (polygenic risk score – regression analysis)
  - Genotype vs Phenotype
  - Epigenetics - Non-sequence alterations to DNA
  - Environmental factors influencing disease expression

Uses of Genetic tests

Purpose	Description	Relevant Insurance/Actuarial and why
Predictive Medicine	Predictive genetic testing determines the chances that a healthy individual with or without a family history of a certain disease might develop that disease.	Life/CI: Probability to present with a specific disease is determined by the genetic make-up of an individual – this could lead to an invalidation of actuarial models via anti-selection.
Diagnosis (and prognosis)	Diagnostic testing is used to identify or confirm the diagnosis of a disease or condition in a person or a family. Diagnostic testing gives a "yes" or "no" answer in most cases. It is sometimes helpful in determining the prognosis in addition to any treatment.	CI: Diagnosis of specific conditions leading to a pay-out.
Pharmacogenetics	The ability of an Individual to metabolise specific drugs might impact dosage or side effects. Targeted treatments that are specific to the DNA of a Cancer might improve treatment outcomes.	Health/PMI: payment for ineffective drugs; New targeted therapies costing much more money
Lifestyle/Traits	Testing of non-clinical genes that might impact lifestyle, including nutrition and exercise.	All – indirectly. Improvements in lifestyle leading to lower incidence of disease and lower severity/quicker recovery if occurs.
Ancestry	Ancestry/Genealogy testing lets you know where your family came from and which genetic markers you have.	Not currently applicable – although certain diseases are more or less prevalent in certain Ancestral profiles.

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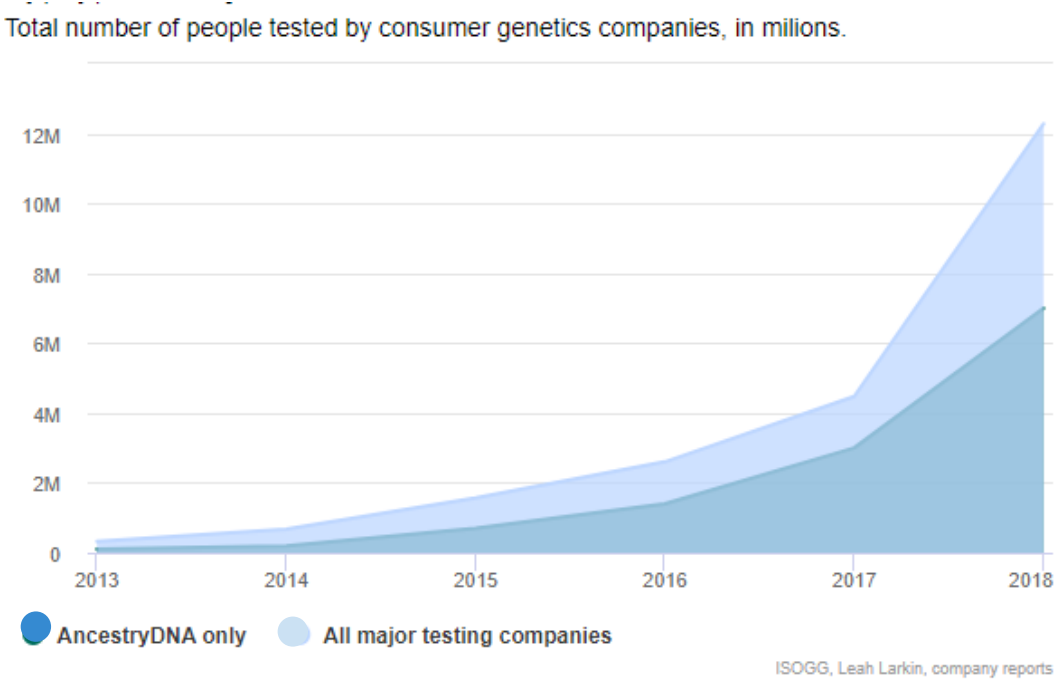
Factors influencing Penetration

Take-up rates of testing and how this has ramped over time



Source: MIT Technology Review

https://www.technologyreview.com/s/610233/2017-was-the-year-consumer-dna-testing-blew-up/

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D2C

Pharmacogenetics	Human Longevity, Inc. · GeneAccount · MYOGENES Personalising Your Health · invivo · gknowmix genetic knowledge integration
Diagnosis	CeGaT Center for Genomics and Transcriptomics · genepeeks
Predictive medicine	23andMe · color · Helix · Human Longevity, Inc. · MYOGENES Personalising Your Health · 24 genetics · gknowmix genetic knowledge integration · BaseHealth Precisely.
Lifestyle/Traits	ome · VITAGENE · MYOGENES Personalising Your Health · Helix · 24 genetics · Human Longevity, Inc. · newtopia · DNAFit · 23andMe · Arivale Your scientific path to wellness · gknowmix genetic knowledge integration
Ancestry	23andMe · Human Longevity, Inc. · MYOGENES Personalising Your Health · MyHeritage DNA · ancestryDNA

B2B

Roche · NHS

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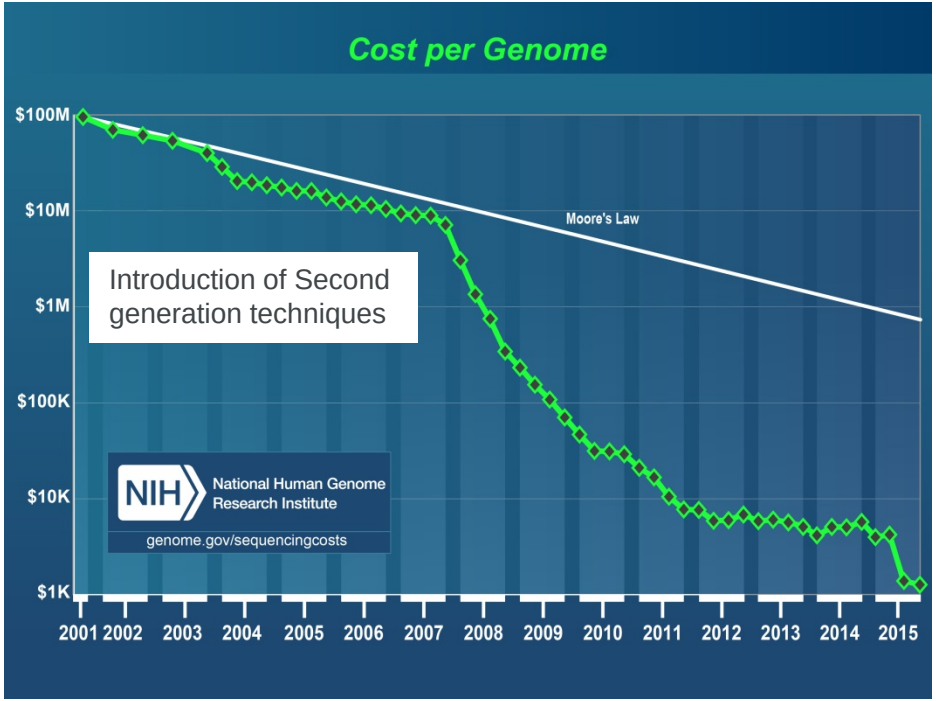
Cost of Genetic Testing

- The National Human Genome Research Institute (NHRI) estimates that it cost between c.$500m-$1bn to complete the first whole genome sequence in 2003 as part of The Human Genome Project. This process took more about 13 years in total.

- In 2006 the average cost had reduced to c.$20-25m.

- In 2016 this would have cost below $1,000.



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How useful are genetic tests in predicting future illness?

12 June 2024

Case study – 23andme

Age-Related Macular Degeneration	Slightly increased risk
Alpha-1 Antitrypsin Deficiency	Variant detected, not likely at risk
Late-Onset Alzheimer's Disease	Slightly increased risk
BRCA1/BRCA2 (Selected Variants)	Variants not detected
Celiac Disease	Variants not detected
G6PD Deficiency	Variant not detected
Hereditary Hemochromatosis (HFE-Related)	Variants not detected
Hereditary Thrombophilia	Variants not detected
Parkinson's Disease	Variants not detected

What does slightly increased risk mean?

A "slightly increased risk" means that, based on your genetic result for this test, your chances of developing late-onset Alzheimer's disease are slightly higher than average. Studies estimate that, on average, a man of European descent with your genetic result has a 4-7% chance of developing Alzheimer's disease by age 75, compared to a 3% chance for the general population. By age 85, that risk is 20-23% for people with your genetic result, compared to 11-14% for the general population. See Scientific Details for more information.

Non-genetic factors may also influence your risk of developing late-onset Alzheimer's disease. Learn more about other factors.

Is this answer helpful? Yes No

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How Predictive are Current Genetic Tests?

23andMe's DTC tests include:

- Parkinson's Disease
  - Variants in just two of the genes known to be associated with PD are included; LRRK2 and GBA
- Late-onset Alzheimer's Disease
  - The test focuses on APOE, a gene involved in cholesterol metabolism
  - Carrying two APOE4 variants is thought to increase risk 11-fold but many individuals with one of two copies of APOE4 never develop the disease, and many with no copies get AD
- Celiac disease
  - 23andMe test for 2 variants
  - 15-30% of the population have one of these, however only 3% of these will develop the disease

But not:

- Coronary Artery Disease
  - A heritable component accounts for approximately 40-50% of risk, with over 60 known genetic variants accounting for only half of this

These genetic tests can tell an individual they have an increased risk of developing a disease, but not whether the individual will or will not get the disorder. In fact, most individuals with one of these risk variants will in fact never develop the disease.

How Predictive are Current Genetic Tests? - Cancer

Cancer is caused by uncontrolled cell division. Mutations in genes associated with increased cell division are linked with an elevated risk for cancer.

- Breast Cancer
  - Most incidences of breast cancer are not hereditary.
  - For those with a genetic component, mutations in BRCA1 or 2 (the “Angelina Jolie gene”) account for 20% of the increased risk.
  - 23andMe only test for 3 out of thousands of possible mutations in the BRCA genes and these 3 are only present in individuals of Ashkenazi Jewish ancestry.

- Prostate Cancer
  - The primary risk factor (apart from sex!) is age, but those with a family history are twice as likely to develop the disease.
  - BRCA genes are implicated.
  - It is only possible to identify high risk individuals by combining tests for many variants of a large number of genes. Alone, each of these would confer only a slightly greater risk.

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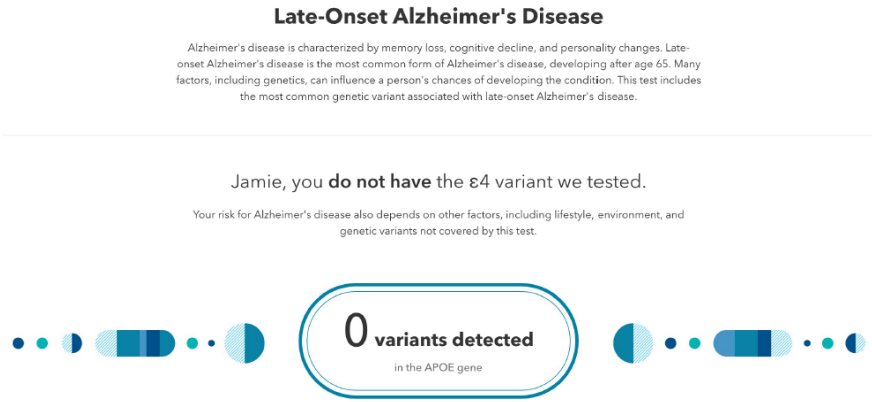
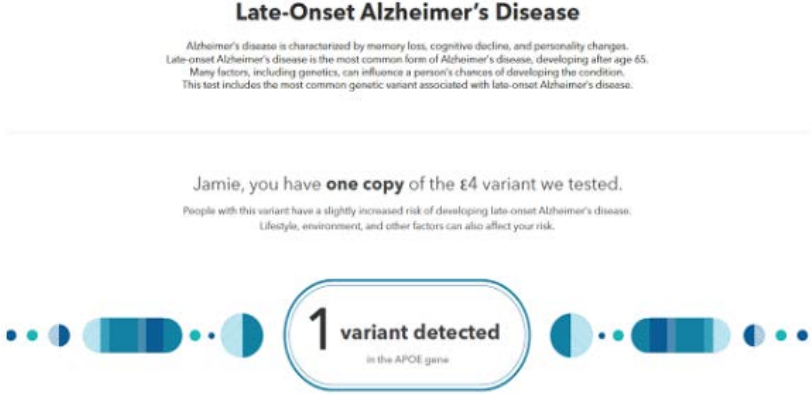
How Predictive are Current Genetic Tests?

- Genetic risk factors depend on ancestry.
- Some genetic variants may correlate with the disease rather than being a causal factor.
- For most disorders, only a certain variant is tested for while there may be many more risk factors.
- Most genetic variants confer only a small increase in risk, and the best predictive power for a meaningful result comes from combining many variants.





Source: Example Reports from 23andMe

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How Useful is the Prediction?

- Most disorders are multi-causal in nature, either multi-genic or caused by the interaction between genes and the environment/lifestyle.
    - E.g. Parkinson's, Alzheimer's, cancers and cardiovascular disease.

- Often lifestyle risk or protection factors play as much – or more – of a role in disease prediction than genetics, e.g. stroke.

- The risk result for an individual can change over the course of their lifetime and lifestyle can often counteract genetic risk.

- One individual may get contrasting risk reports from different companies through their alternate selection of genetic variants and assumptions in their risk models.

- Risk reports by companies such as 23andMe can be updated with new knowledge, but new tests will not be run. One might question the validity of a risk report that is subject to change.

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Impact on Insurance

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Impact of Genetic testing on Insurance

- Various academic papers have reviewed the odds ratio change in likelihood to increase insurance coverage with a positive genetic test result.

Genetic disease (Gene)	Year study	Insurance product	Odds ratio of change behaviour after positive test
Breast cancer (BRCA1/2)	2003	Life insurance	**5.1x** more likely to increase coverage
Huntington's disease (HD)	2010	Long-term care insurance	**5x** more likely to buy insurance
Colorectal cancer (HNPCC)	2001	Life insurance	**1.3x** more likely to buy insurance

- A 2016 meta-analysis published in The BMJ suggests that communicating DNA based disease risk estimates has little or no effect on risk-reducing health behaviour.

- A 'Genetic lens' paper analysed the impact of genetic testing on trauma cover if widely adopted for breast and prostate cancer and coronary heart disease.
  - There is little or no impact on lapse rates
  - A four fold increase in genetic test take-up rates could lead to a claim cost increase of 7%

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Conclusion

Conclusion

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Questions?