



The Actuarial Profession

making financial sense of the future

Greg Becker
Prof Michael Patton



Science non-fiction: Genetics and Insurance

November 2011

**We always
overestimate the
change that will occur
in the next two years
and underestimate
the change that will
occur in the next ten.
Don't let yourself be
lulled into inaction.**



Greg Becker
Prof Michael Patton



Science non-fiction: Genetics and Insurance



November 2021

A tale of two disciplines: our talk will try to link the two

Genetics

- Brief science lesson
- Recent scientific developments
- The road from science to medicine
 - Diagnostics
 - Treatment

Implications for Insurance

- Consider various products
 - Life
 - Critical Illness
 - Longevity
- Consider various types of impact
 - Selection
 - Anti-selection
 - Claim rates

Ethical questions
Outstanding questions

Starting with a quiz

Raise your hand if you:

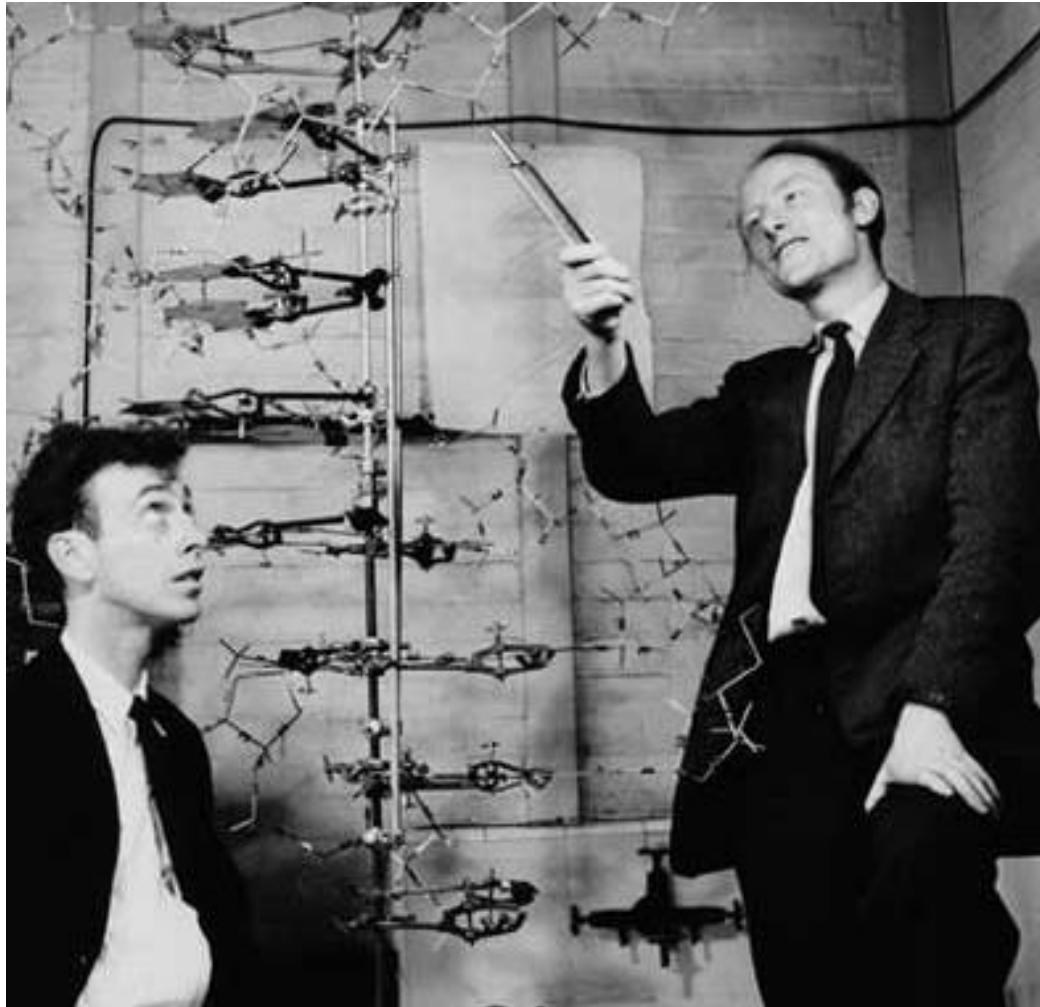
1. have had a genetic test?
2. know someone who has had a genetic test?
3. know that there is moratorium on the use of genetic test results?
4. know what a single nucleotide polymorphism is?
5. know what whole genome sequencing is?
6. have heard of www.23andme.com?

If you raised your hand 6 times, we recommend you quickly head for another venue...



Prof Michael Patton

Genetics

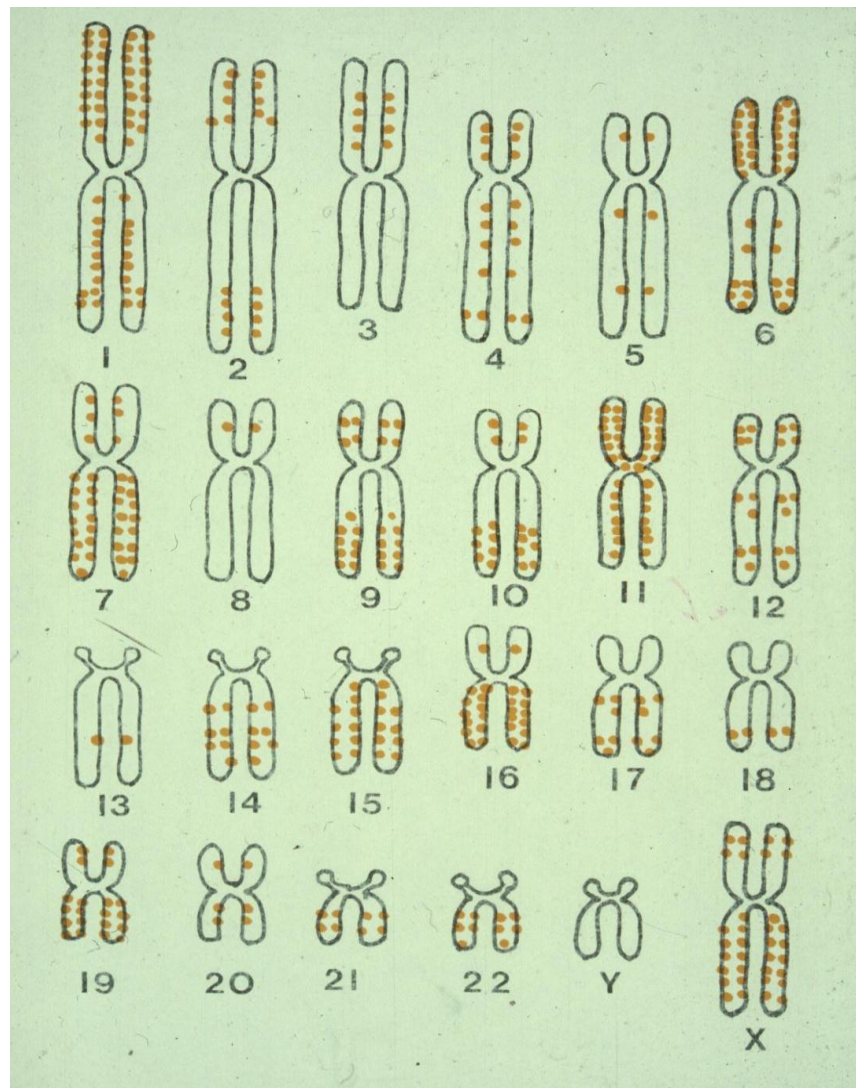
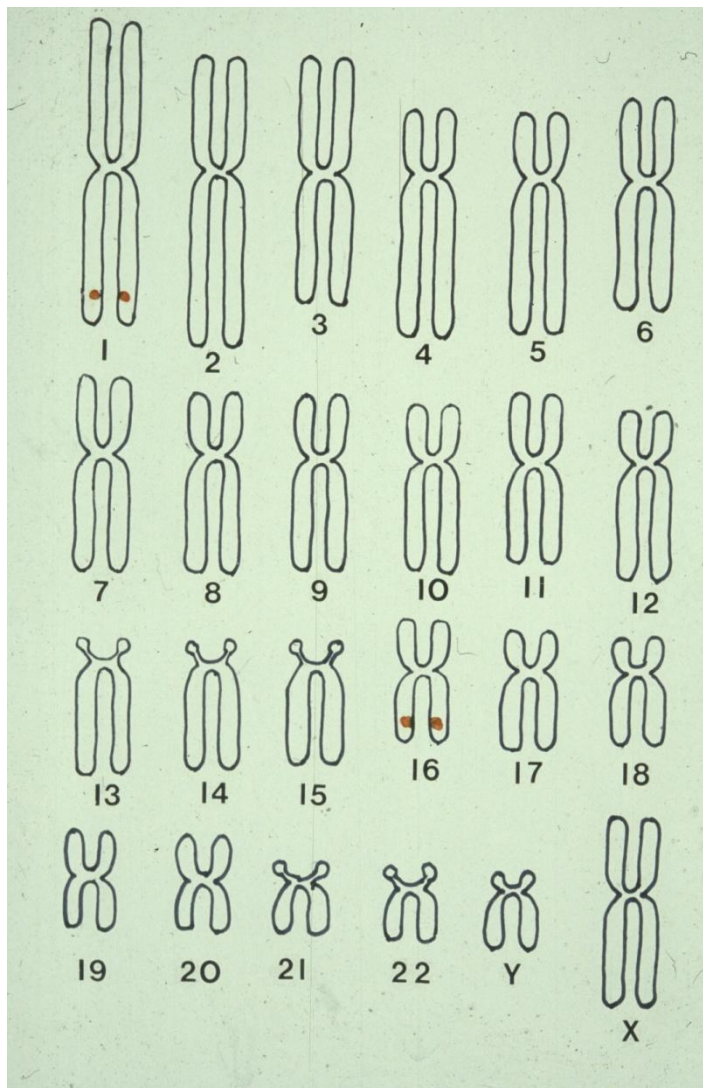


James Watson

Francis Crick

**“Genetics will be the most
important part of medicine”**

Francis Crick 1968



Human Gene Mapping Project

- US & UK
- Preliminary draft published
- 10 years ahead of schedule
- International collaboration
- In own department: 25 genes



Regional Genetic Service

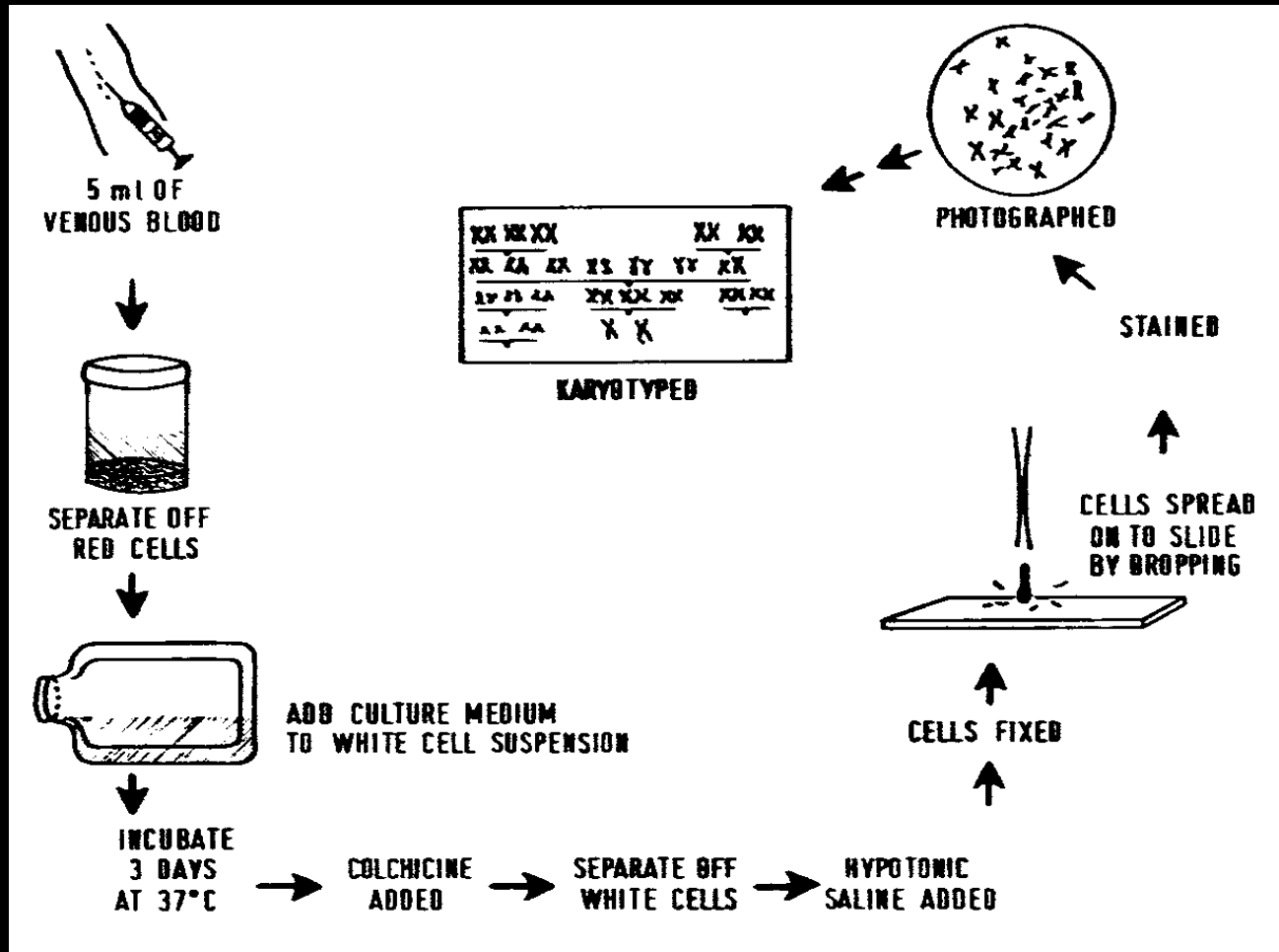
- Providing clinical and laboratory services for patients and families with inherited disease
- SW Thames Regional Genetics Centre
70,000 families seen in the population of c3 million over 25 years
 - approximately 2% of the population



Genetic disease

- Chromosomal
- Single gene
- Multifactorial

Chromosome preparation





1



2



3



4



5



6



7



8



9



10



11



12



13



14



15



16



17



18



19



20



21



22



X

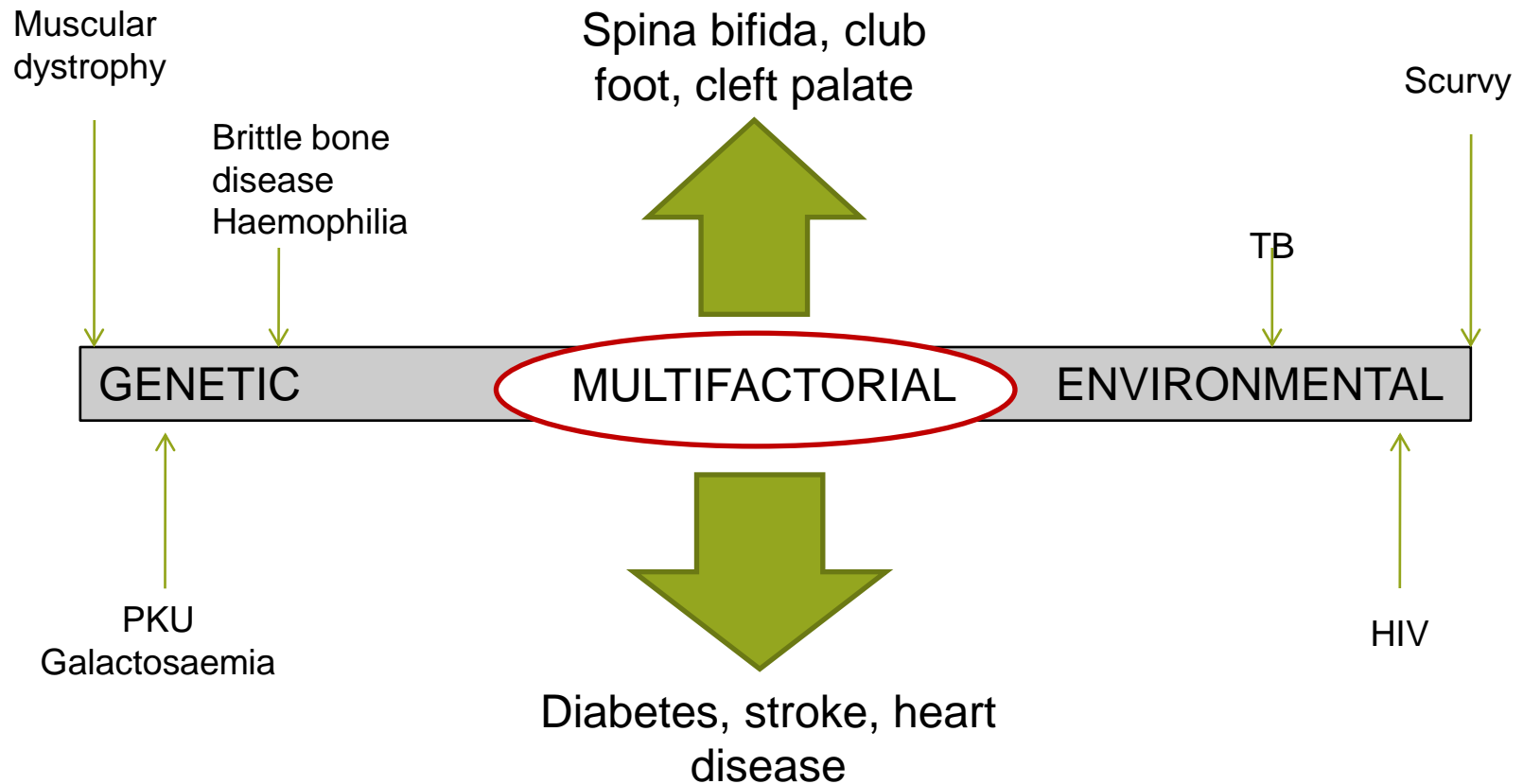


X

Single Gene disease

- Autosomal dominant
 - e.g. Huntingtons disease or breast cancer
- Autosomal recessive
 - e.g. Cystic fibrosis
- X linked
 - e.g. Haemophilia

Multi-factorial disease



Molecular Genetic Testing

1 Diseases with specific mutations

- Sickle cell disease, haemochromatosis, Huntington's disease.
- Test will give clear unequivocal answer
- Unfortunately still relatively few can be used to 100% exclude

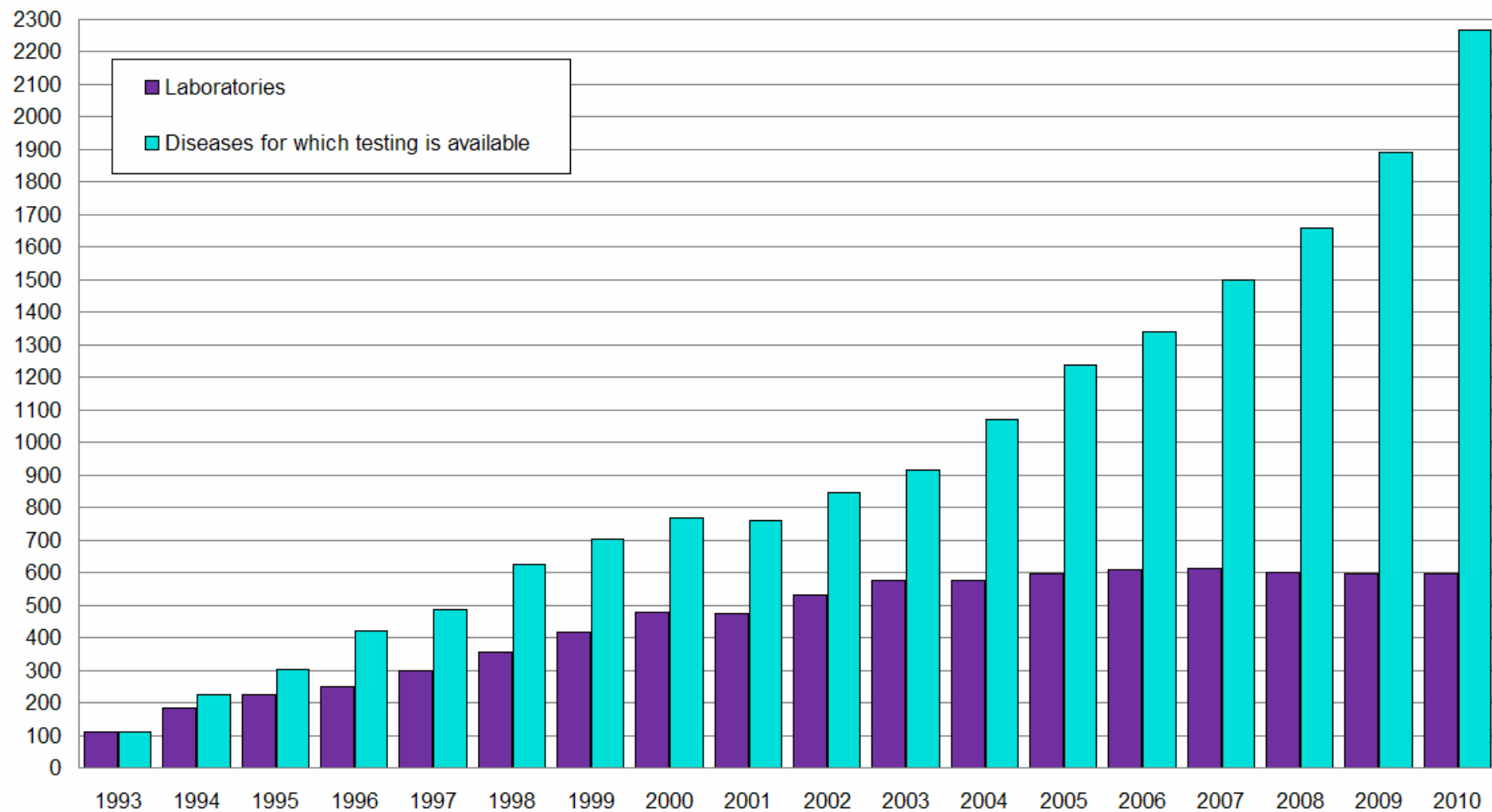
2 Confirm but not exclude

- Cystic fibrosis has >400 mutations in gene. If a mutation is found diagnosis confirmed but if no mutation cannot 100% exclude
- By screening for 30 mutations we exclude 90% of risk
- Many other examples are like this

3 Currently too difficult

- We do not know clinical diagnosis
- We do not know causative gene
- Too many genes e.g. Retinitis pigmentosa has 53 different genes and mental handicap may have many hundreds

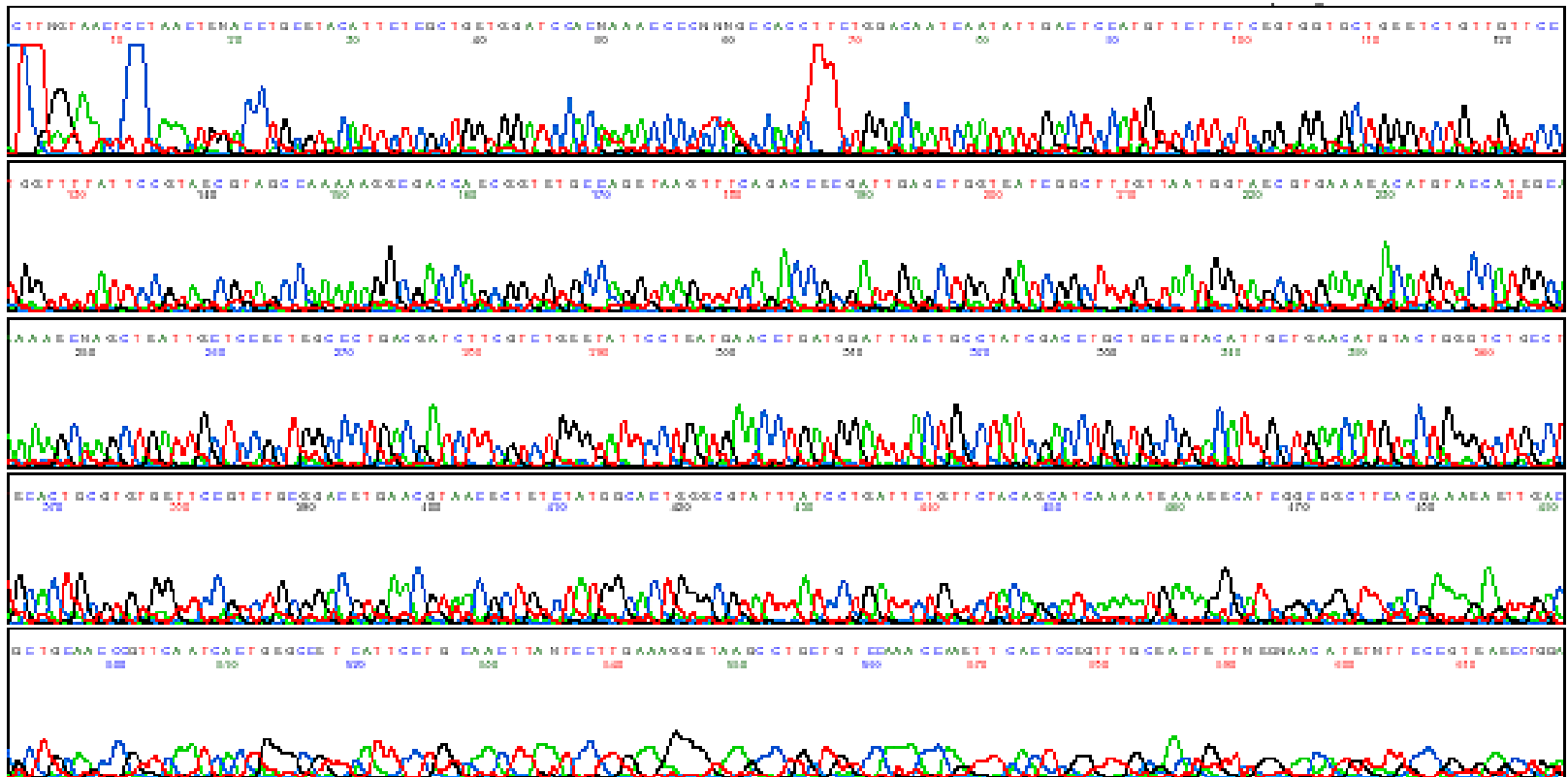
GeneTests: Growth of Laboratory Directory



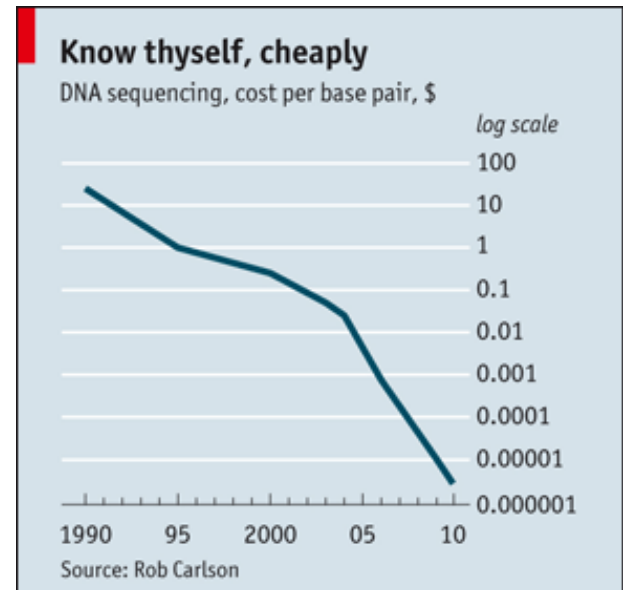
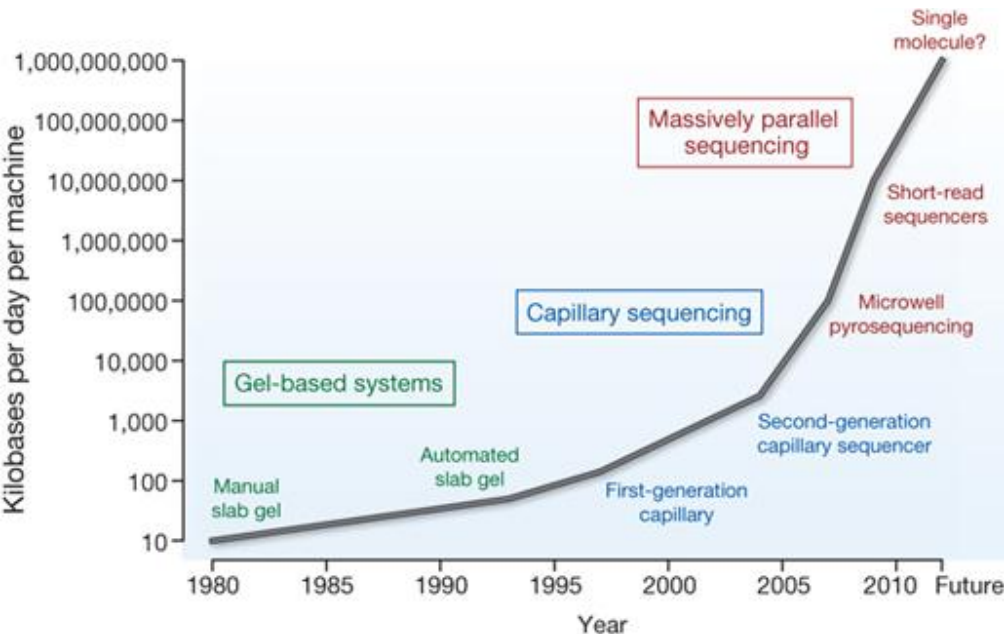
Data source: GeneTests database (2010)/ www.genetests.org

Molecular Genetic Testing

Currently most specialised molecular tests cost about £600 and take 2-3 months for results



Power is increasing, Costs are falling fast



“In 2007 Knome charged \$350,000 to sequence a human genome. Today it charges \$40,000. Mr Conde predicts that by 2015 the price will have fallen below \$1,000. Complete Genomics charges about \$10,000 to sequence more than 90% of a genome. It too predicts that the cost will drop below \$1,000 within five years.”

Exponential increase in speed and cost

Next and *Next Next* sequencing

- Many new techniques - proven and unproven
- Multiple parallel sequencing
- Nanopore technology
- Industrialisation of genomics
 - e.g. Beijing Genomics Institute



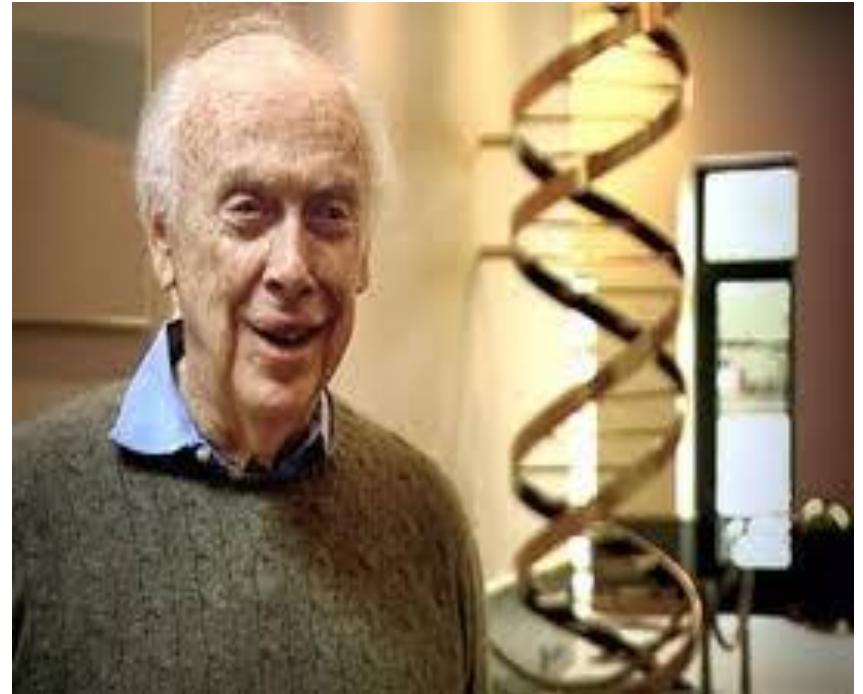
Whole genome sequencing

- Craig Venter
- Biotech pioneer and founder of Celera
- Co discoverer of Human Genome
- Cost of first whole genome sequence = US\$ 17 million



Whole genome sequencing

- James Watson
- Nobel prize winner for discovery of DNA structure
- Cost of second whole genome sequence = US\$ 1 million



Whole genome sequencing

- Just celebrities or big egos?
- 1000 genome study UK
- Human Variation Study different populations
- Personal Genome Project at University of Harvard up to 100,000 people
- Up to end of 2011 around 30,000 people have had full genome sequences



**Personal Genome
Project**

www.personalgenomes.org

Current problems of the US\$ 1,000 whole genome scan

- Volume of data
 - 3 billion nucleotides per person (can sequence coding genes only which is 1% - exome sequencing)
- Accuracy of sequencing
 - at present need to confirm results on Sanger sequence
- Bioinformatic screening of data
 - software to sieve out normal variation or polymorphism and to predict important changes
- Clinical interpretation of results

**Pandora's box effect
unwanted results leading to
psychological distress**



How might we use whole genome scans?

1. Probably not to look at everything, but rather to answer clinical questions
2. Diagnostic testing for deafness, blindness and mental handicap
3. Specific diagnosis of causes (e.g. epilepsy or hypertension) leading to focused treatment
4. Pharmacogenetic screen to avoid drug reactions

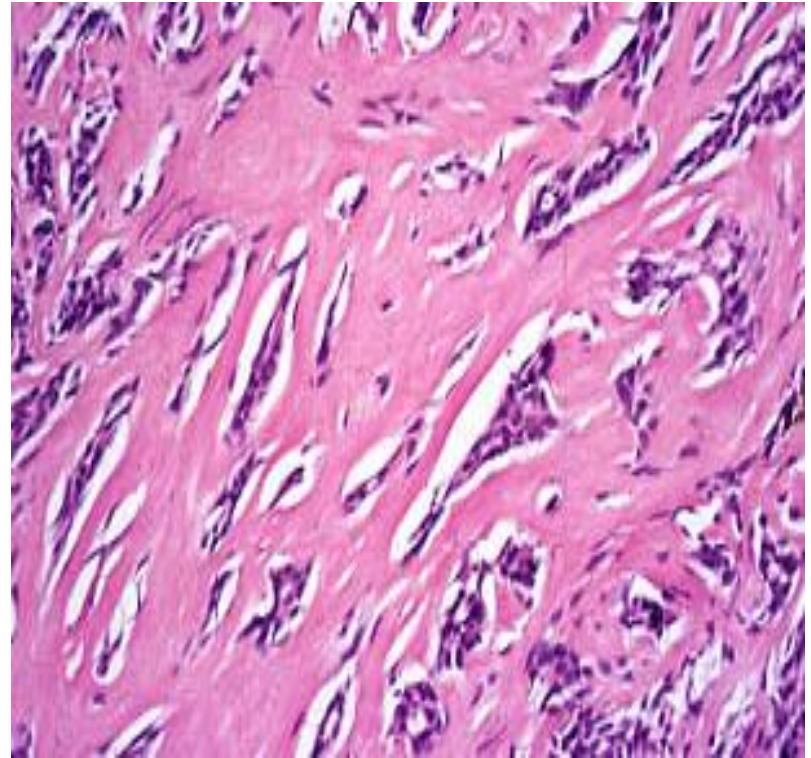
We will be able to look for everything all of the time

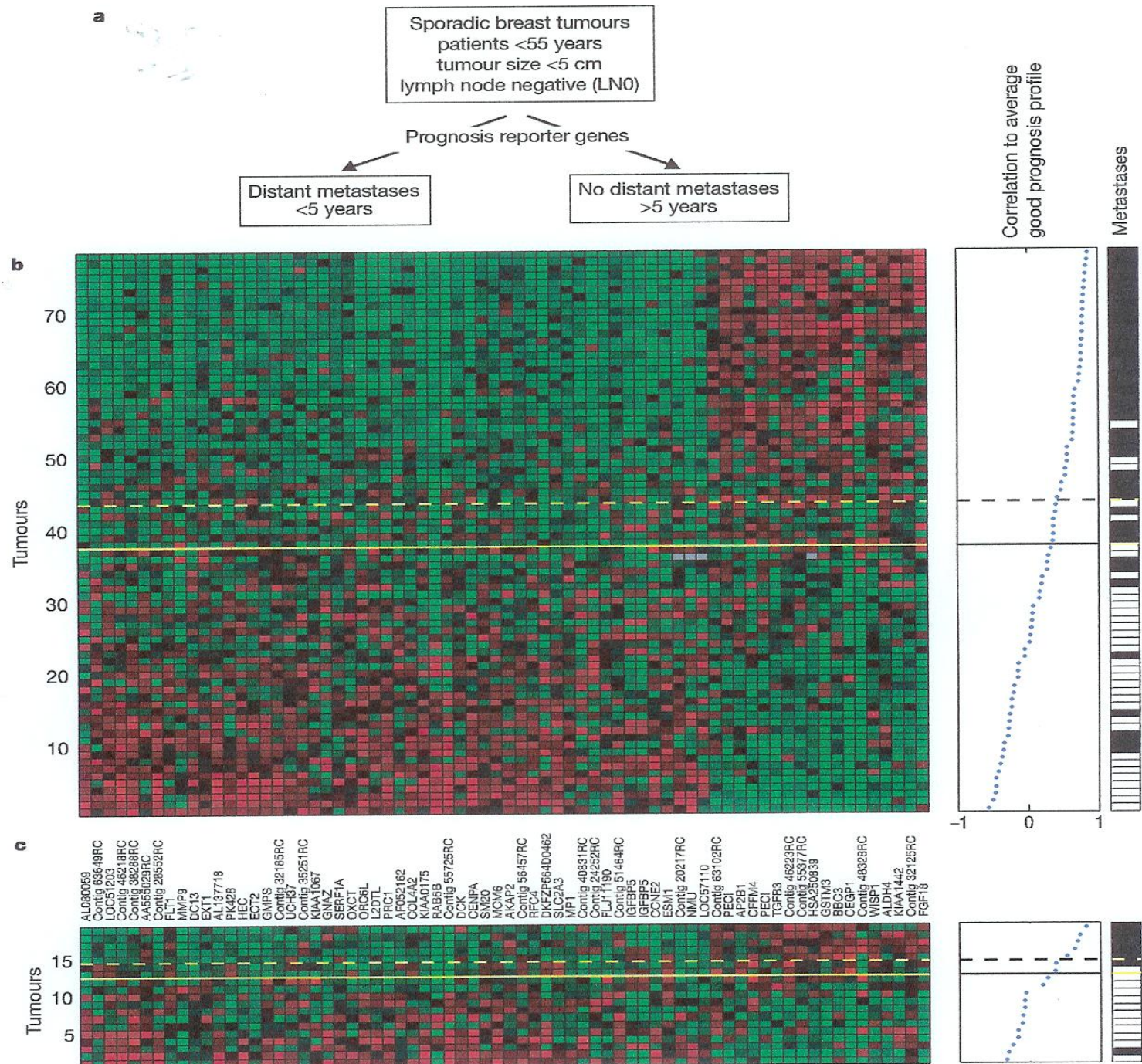
But do we want to?

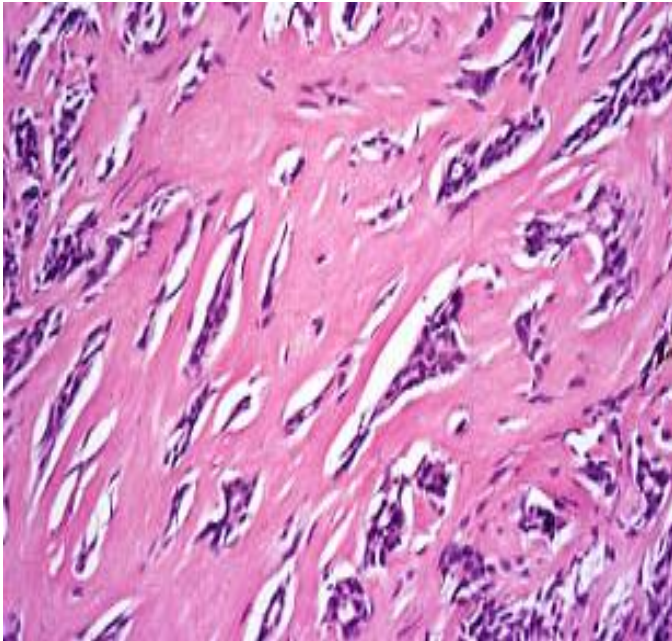
How might we be using whole gene scans?

Profiling cancers

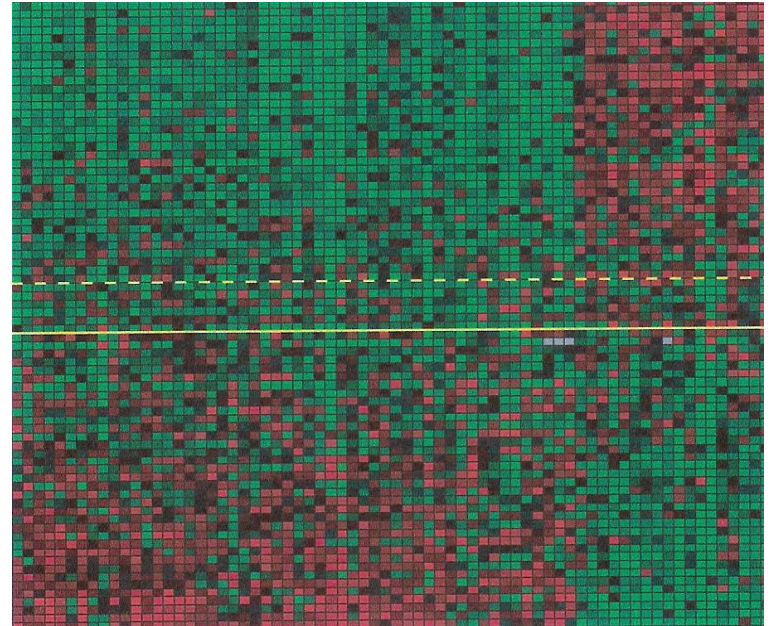
- Pathologists have used histology to determine the grade or prognosis of a tumour
- Gene expression profiles may come to be used in same way







Histopathology



Genomic pathology

Direct Consumer Gene Testing ?

Two approaches: a) SNP

SNP (Single nucleotide polymorphism) analysis

- 1) 23 and me
- 2) Decode
- 3) Navigen



Sergey Brin and Anne Wojcicki

23andMe genetics just got personal.

Search 23andMe Go Log in Register Your Kit Blog Help Cart

welcome ancestry health how it works store

Start filling in the gaps with your DNA

"Because I had given my doctor information from 23andme, he got to a diagnosis much faster. 23andme saved my life." Kirk C.

\$99* Our new low price for all! Was \$199

Order Now »

*Requires a 1-year commitment to the Personal Genome Service® at \$9/mo. Order for \$399 without commitment.

1 Get Your Kit 2 Provide Saliva 3 Learn About Yourself 4 Get Monthly DNA Discoveries

Type 2 Diabetes

AS LOW AS 8 % AS HIGH AS 52 % What's your genetic risk? see more

Gain insight into your traits, from baldness to muscle performance. Discover risk factors for 97 diseases. Know your predicted response to drugs, from blood thinners to coffee. And uncover your ancestral origins. [start tour »](#)

Overview Discover Health & Ancestry Keep Your Doctor Informed Participate In Research

global similarity



Uncover the heritage in your genes.

Map your global origins with the most complete coverage of your DNA.

23andMe Personal Genome Service also includes:

- Your [Relative Finder](#): Find people who share DNA with you.
- Your [Ancestral Lineages](#): Mitochondrial and Y-DNA.



Your DNA reflects the complexity of human history.



Where in Africa or Europe did your ancestors live?

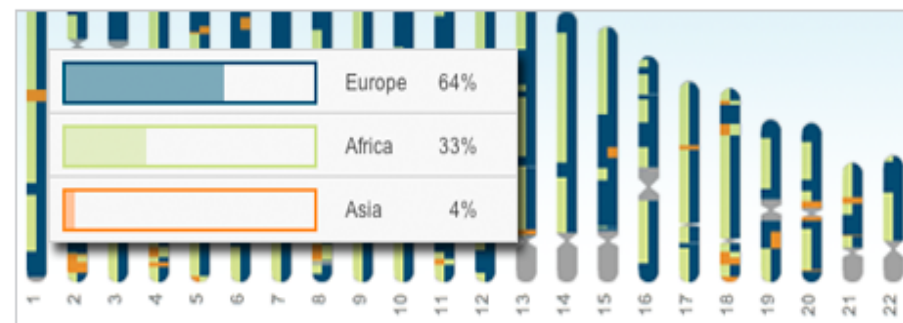
If you're African-American, 23andMe can tell you approximately what fraction of your ancestors were African, and what fraction were European. If you're of European descent, we can pinpoint what populations your DNA is most similar to.

Does your DNA show Native American ancestry?

Using a technique called Ancestry Painting, 23andMe can determine whether you have any Native American ancestors within the past five generations.



Your continental origins revealed.



Your unique Ancestry Painting reveals where your ancestors lived hundreds of years ago. See your history reflected in each piece of your chromosomes.

Compare your DNA to populations around the world.



23andMe genetics just got personal.

[Log in](#)[Register Your Kit](#)[Blog](#)[Help ▾](#)[Cart](#)[welcome](#)[ancestry](#)[health](#)[how it works](#)[store](#)

Personal Genome Service™

Get to know your DNA. All it takes is a little bit of spit.

Here's what you do:

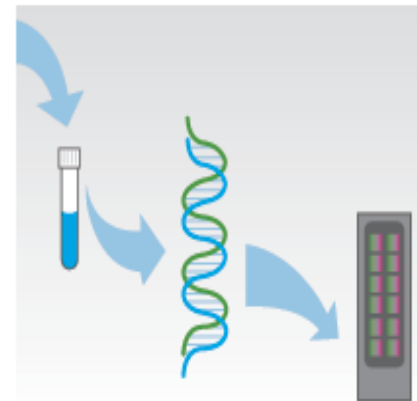
PGS™



1. Order a kit from our [online store](#).



2. [Register your kit](#), spit into the tube, and send it to the lab.



3. Our CLIA-certified lab analyzes your DNA in 6-8 weeks.



4. [Log in](#) and start exploring your genome.

Frequently Asked Questions

- How does 23andMe genotype my DNA?
- Why can't 23andMe diagnose me?

<https://www.23andme.com/howitworks/>

[visit the store](#)[try a demo](#)

A temporary password has been sent to your email. Please check your email for instructions. Order your [Personal Genome Service](#) now.

[My Home](#)
[Inbox](#)

health overview

[Print my health overview](#)

My Health

[Disease Risk](#)

[Carrier Status](#)

[Drug Response](#)

[Traits](#)

[Health Labs](#)

My Ancestry

[Maternal Line](#)

[Paternal Line](#)

[Relative Finder](#)

[Ancestry Painting](#)

[Global Similarity](#)

[Ancestry Labs](#)

Sharing & Community

[Compare Genes](#)

[Family Inheritance](#)

[23andMe Community](#)

[Genome Sharing](#)

23andWe

[Research Surveys \(31\)](#)

[Research Snippets](#)

[Research Initiatives](#)

Show results for

 ▾

[See new and recently updated reports »](#)

 23andMe Discoveries were made possible by 23andMe members who took [surveys](#).

Disease Risks (115) ?

↑ Elevated Risks

	Your Risk	Average Risk
Atrial Fibrillation	33.9%	27.2%
Prostate Cancer ♂	29.3%	17.8%
Alzheimer's Disease	14.2%	7.2%
Colorectal Cancer	7.8%	5.6%
Restless Legs Syndrome	2.5%	2.0%

[See all 115 risk reports...](#)

Carrier Status (28) ?

Hemochromatosis	Variant Present
Alpha-1 Antitrypsin Deficiency	Variant Absent
Bloom's Syndrome	Variant Absent
BRCA Cancer Mutations (Selected)	Variant Absent
Canavan Disease	Variant Absent
Cystic Fibrosis	Variant Absent
Familial Dysautonomia	Variant Absent
Factor XI Deficiency	Variant Absent

[See all 28 carrier status...](#)

Traits (52) ?

Alcohol Flush Reaction	Does Not Flush
Bitter Taste Perception	Unlikely to Taste
Earwax Type	Wet
Eye Color	Likely Blue

Drug Response (20) ?

Clopidogrel (Plavix®) Efficacy	Reduced
Warfarin (Coumadin®) Sensitivity	Increased
Abacavir Hypersensitivity	Typical
Alcohol Consumption, Smoking and Risk of Esophageal Cancer	Typical

Example Genetic Data

Information for **Greg Mendel (Dad)** assuming ethnicity and an age range of

[Where's mine?](#)



Greg Mendel (Dad)

46.3 out of 100

men of European ethnicity who share Greg Mendel (Dad)'s genotype will get Coronary Heart Disease between the ages of 45 and 79.



Average

46.8 out of 100

men of European ethnicity will get Coronary Heart Disease between the ages of 45 and 79.

What does the **Odds Calculator** show me?

Use the ethnicity and age range selectors above to see the estimated incidence of Coronary Heart Disease due to genetics for men with **Greg Mendel (Dad)**'s genotype. The 23andMe Odds Calculator assumes that a person is free of the condition at the lower age in the range. You can use the name selector above to see the estimated incidence of Coronary Heart Disease for the genotypes of other people in your account.

The 23andMe Odds Calculator only takes into account effects of markers with known associations that are also on our genotyping chip. Keep in mind that aside from genetics, environment and lifestyle may also contribute to one's chances of having coronary heart disease.

Genes vs. Environment

39-56 %
Attributable to
Genetics

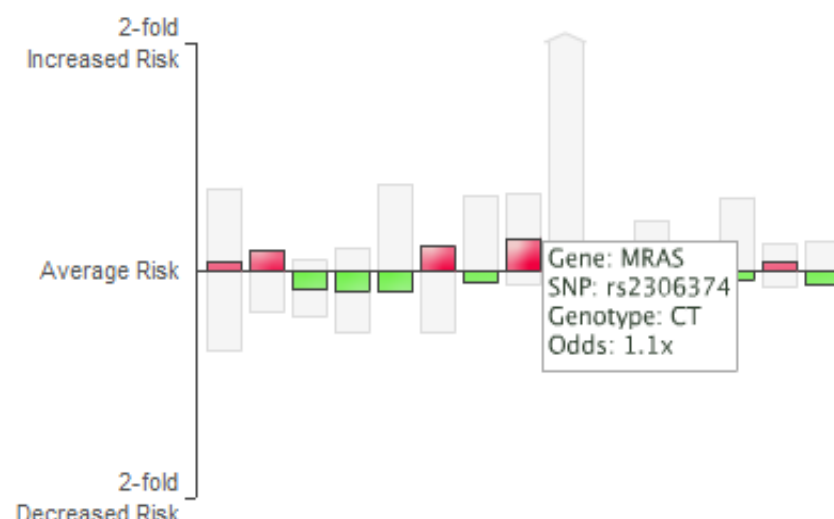
Heritability for coronary heart disease ranges from 39% to 56%, depending on the exact subtype of heart disease. This means that genetic factors and **environmental factors** contribute about equally to risk for coronary heart disease. There is also evidence that genetic factors may contribute slightly more to risk of death from coronary heart disease in men than they do in women. Genetic factors that play a role in coronary heart disease include both unknown factors and known factors such as the SNPs we describe here. Other factors that increase your risk include being older, being male, being African-American, smoking, having high blood cholesterol or high blood pressure, physical inactivity, being overweight, having diabetes, alcohol use, and stress. ([sources](#))

Genes vs. Environment

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Marker Effects



What does this chart show?

The chart shows the approximate effects of the selected person's genotype at the 15 reported markers. Higher, **red bars** indicate **increased risk** from the average, while lower, **green bars** indicate **decreased risk** from the average. The light gray bars show the maximum possible effects for the possible genotypes at the marker.

Mouse over individual bars to view additional information about each marker. Click on a bar to view detailed information about that marker below. You can read more about all markers in the [technical report](#).

9p21 region

Marker: [rs10757278](#)

Numerous SNPs associated with coronary heart disease risk have been identified in a region on chromosome 9 known as 9p21. 23andMe reports your results for a **SNP** that is one of the most strongly associated SNPs in this region. The reported SNP is not in a known

Citations

[Broadbent HM et al. \(2008\)](#) . "Susceptibility to coronary artery disease and diabetes is encoded by distinct, tightly linked SNPs in the ANRIL locus on chromosome 9p." *Hum. Mol. Genet.* 17(6):806-14.

[Preuss M et al. \(2010\)](#) . "Design of the Coronary Artery Disease Genome-Wide Replication And Meta-Analysis (CARDIoGRAM) Study: A Genome-wide association meta-analysis involving more than 22

Gene or region: MRAS

SNP: rs2306374

	SNP used	Genotype	Adjusted Odds Ratio*
Greg Mendel (Dad)	rs2306374	CT	European: 1.1
* Odds ratios are reported for all available ethnicities.			

This SNP is equivalent to rs9818870, which is located near the MRAS gene. It is not currently known how this SNP or this gene is involved in CHD.

Multiple studies have shown this SNP to be associated with CHD in populations of European ancestry. The association has not been studied in Asian or African populations.

Citations

[Erdmann J et al. \(2009\)](#) . "New susceptibility locus for coronary artery disease on chromosome 3q22.3." *Nat. Genet.* 41(3):280-2.

Coronary Heart Disease - Sample Report

[» view all sample reports](#)

Established Research report on 15 reported markers,

Example Data

How It Works

Timeline

MD's Perspective

Technical Report

About Coronary Heart Disease

Coronary heart disease (CHD), also called coronary [artery](#) disease, is a condition characterized by blockage of the arteries that supply the heart with blood. CHD can result in shortness of breath, chest pain (angina) and heart attack. It is a leading cause of death in both men and women worldwide. In the United States, about 1.2 million people will have a heart attack each year, and many of those heart attacks will be fatal. Healthy lifestyle choices play a major role in preventing CHD. If a heart attack does strike, prompt medical attention is vital.

[Learn more about the biology of Coronary Heart Disease...](#)

[Major discoveries in Coronary Heart Disease...](#)



1 of 4. Over a lifetime, the average human heart will beat about 3 billion times and pump a total of 60 million gallons of blood.



[visit the store](#)

[try a demo](#)



You answer questions.



Other 23andMe members
answer questions.



23andMe scientists
work their magic.



And make discoveries!

23andWe community contributions

You haven't taken the surveys that led to these discoveries (yet!).



Allergies of a Feather Flock Together — Sometimes

This report is based on "Allergies and Asthma".

[View this report](#)

[get involved!](#)



Asparagus in Your Pee? There's a SNP For That

This report is based on "Ten Things About You".

[View this report](#)

[get involved!](#)



The Backstory on Hair

This report is based on "Physical Features".

[View this report](#)

[get involved!](#)

How do the SNP predictions compare with other clinical data?*

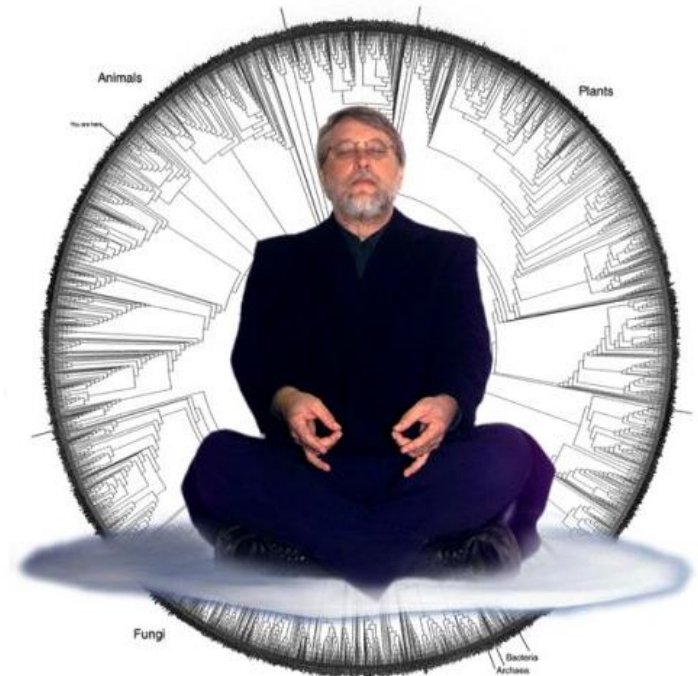
- Will pick up 10% of people with >1.4 relative risk
- In this 10% average relative risk is 1.6
- Raised **LDL** Cholesterol gives 1.3 RR
- 23andMe plan to include other environmental and ethnic parameters
- Therefore SNP + **LDL** Cholesterol + age =?

*Helgason & Stefansson 2010

Disorder /Test	Relative risk
LDL Cholesterol	1.3 x
SNP coronary heart disease	1.6 x
SNP / Cholesterol / BMI	???
BRCA1 /BRACA2 Breast cancer	5 x

“Lifestyle / Risk Guru”

- New role for advising on risk and supporting life changes
- New Age GP
- Mentor
- E-Coach
- Ying Yang balance



...it is about balance

“Other types of Guru”



Direct Consumer Gene Testing ?

Two approaches: b) Whole Gene Sequencing

Two potential companies

- 1) Knome \$100,000
- 2) Complete Genomics \$ 5,000
(but only research samples at present)



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END-TO-END OUTSOURCED SOLUTION

We offer an end-to-end, outsourced solution delivering research-ready genomic data and analysis for complete human genomes.



Human Genome Sequencing & Analysis Service

Dedicated to complete human genome sequencing and analysis provided as an innovative, end-to-end, outsourced service model, Complete Genomics enables researchers to conduct large-scale complete human

Applications of Whole
Human Genome Sequencing

**Fall Seminar
Series 2011**



Comments on DNA sequencing technology and the coming era of genomic medicine

letting the **GENOME**
out of the bottle  [Visit Blog](#)

News

[Complete Genomics Schedules Third](#)

Whole Gene Sequencing

- Whole gene sequencing will do all that SNPs do but with more data
- Most of population is a slightly greater or lesser risk of disease unless predicted to have a single gene disorder from their family history

➡ therefore most will remain around average risk

➡ but some may find unexpected major disease risk

Medical Conclusions Actuarial Questions

1. New genetic testing will continue to increase in power and reduce in cost
2. Technical problems of accuracy and interpretation can be resolved
3. This will lead to improved medical diagnosis and treatment
4. This could reduce the cost and improve the effectiveness of healthcare - health providers will encourage it's use
5. Good for health and longevity
6. Life style improvements have already helped to increase life expectancy but newer preventive therapies will be developed
7. How much could this improve life expectancy in next 40 years?
8. Direct consumer testing by Google is a disruptor in innovation and users will increase exponentially outside any national control
9. If the customer has risk information that the insurance company does not have or cannot use – will selective insurance survive, or how will it adapt?



Making Medicine Personal





Greg Becker

Implications for Insurance

Current Status: Moratorium until 2017, to be reviewed in 2014

- Moratorium is the starting point
 - In 2014 we'll be making decisions relating to 2017+
- European law can trump local initiatives
 - There are already wide differences across Europe

Gender directive take 2...

ABI News Release

Tuesday, 05 April 2011 Ref: 17/11

Insurance Genetics Moratorium extended to 2017

The ABI has today announced that the long-standing *Concordat and Moratorium on Genetics*, agreed with the Department of Health has been extended to 2017.

Nick Starling, the ABI's Director of General Insurance and Health, said:

"The Concordat and Moratorium on the use of predictive genetic test results works well for consumers. It means people can insure themselves and their families, even if they have had an adverse result from a predictive genetic test. The moratorium has proved effective since its introduction in 2001 and has now been extended to 2017."

The moratorium means the results of a predictive genetic test will not affect a consumer's ability to take out any type of insurance other than life insurance over £500,000. Above this amount, insurers will not use adverse predictive genetic test results unless the test has been specifically approved by the Government. Only around 3% of all policies sold are above these limits. The only test that is approved is for Huntington's Disease.

Health Minister Anne Milton said:

"This is an excellent agreement that has benefitted both patients and consumers. The extension of the moratorium will ensure that the public continue to have confidence in using predictive genetic tests and being insured."

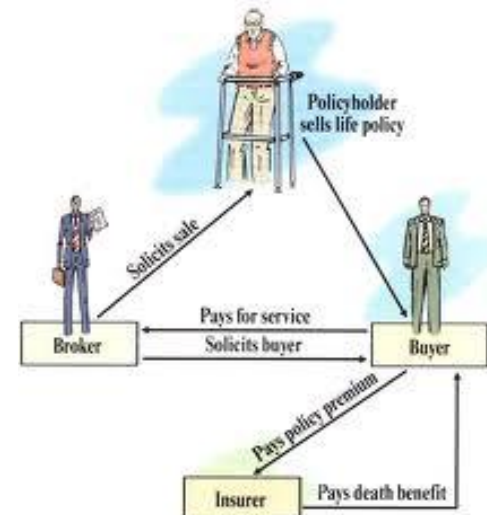
To provide ongoing certainty for consumers, the ABI and the Department of Health undertake planned reviews three years before the end of each extension. This announcement follows the 2011 review; the next review will take place in 2014.

Life Insurance

- Anti-selection
 - impact on 'quality of business' - people get tests and if the tests say they're sub-standard, they'll take out policies
 - selective lapses
- Reducing Medical Errors
- Life settlements and viaticals



Could 23andME help to reduce the 100,000 prescription drug related deaths each year in the US?



Critical Illness

- What is a diagnosis?
 - Can it be based on genetic analysis?
- When is a payout due?
 - Symptomatic?
 - If it is in your genes, is it from birth?
- Is an illness with genetic causes a pre-existing condition?
- What does earlier diagnosis on a policy with a limited term do to
 - Claim rates
 - Anti-selection rates
- Anti-selection of those who know their genetic future

Annuity/longevity products

- Impaired annuities
 - genetic 'readout': could it be used to demonstrate ill-health
- Standard annuity
 - anti-selection where only 'high quality' lives take out the product
- All annuities
 - medical advances and improved life expectancy due to early diagnosis and improved treatment

Random clinical trial of those who had a genetics test to see if insurance product purchasing behaviour was *special*: for LTC products it was!

MARKET WATCH

MARKET WATCH

Genetic Testing For Alzheimer's Disease And Its Impact On Insurance Purchasing Behavior

Widespread genetic testing for Alzheimer's susceptibility could present dilemmas for long-term care insurance.

by Cathleen D. Zick, Charles J. Mathews, J. Scott Roberts, Robert Cook-Deegan, Robert J. Pokorski, and Robert C. Green

ABSTRACT: New genetic tests for adult-onset diseases raise concerns about possible adverse selection in insurance markets. To test for this behavior, we followed 148 cognitively normal people participating in a randomized clinical trial of genetic testing for Alzheimer's disease for one year after risk assessment and Apolipoprotein E (APOE) genotype disclosure. Although no significant differences were found in health, life, or disability insurance purchases, those who tested positive were 5.76 times more likely to have altered their long-term care insurance than those who did not receive APOE genotype disclosure. If genetic testing for Alzheimer's risk assessment becomes common, it could trigger adverse selection in long-term care insurance.

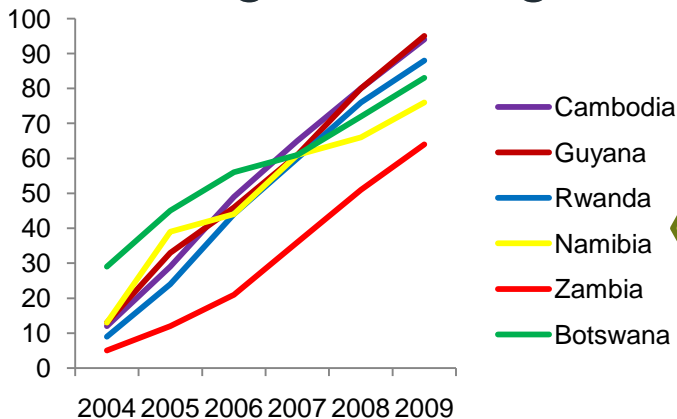
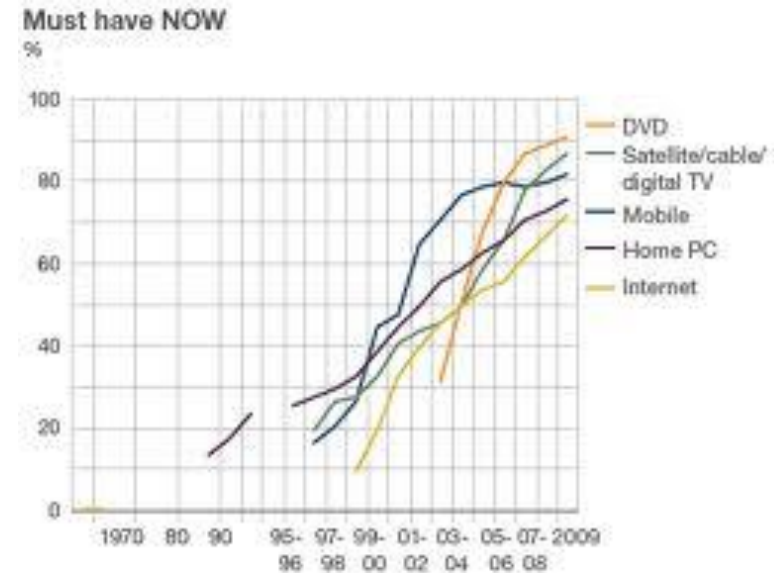
PROGRESS IN UNDERSTANDING the human genome and the recent development of genetic tests for susceptibility to adult-onset diseases have sparked debate in the public policy community regarding who should have access to genetic test results. Insurers argue that if they do not have access to such information, people who learn that their test results indicate an increased risk for serious adult-onset diseases would purchase more insurance coverage at prices that are below an actuarially fair rate. That is, genetic testing has the potential to create adverse selection in an insurance market.

The Actuarial Standards Board defines adverse selection as "the actions of individuals, acting for themselves or for others, who are motivated directly or indirectly to take financial advantage of the risk classification system."¹ For example, if people know that they are at higher risk of dying from cancer at an early age, then they might be inclined to purchase life insurance to preserve wealth for surviving family members. If insurers are unaware of who might be engaging in this behavior, they would be unable to adjust their actuarial calculations and could face economic losses.²

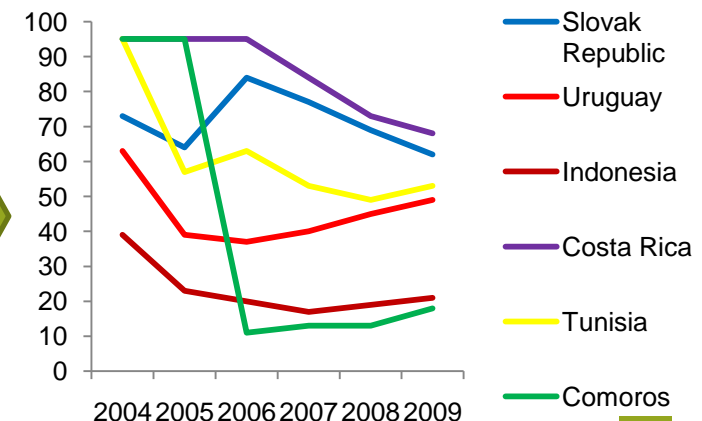
Consumers and proponents of anti-genetic

Factors that can have a big effect

- Take-up within society
 - Can be quick or slow
 - Influenced by cost, reputation, benefits
- Differ by socio-economic groups
- Incremental changes; Seismic shift
 - e.g. Smoking, ARVs, Viagra



Changing levels of ARV availability for different countries





You, the audience

Ethical questions

Closing comments

Outstanding questions

Outstanding questions, outstanding because they're *good* or *unanswered*?

- What is a pre-existing condition?
- Information asymmetry: when is it good/bad - because the use of the information means that someone will get a higher price for their life insurance/annuity
 - but what if the higher price is the more accurate price?
 - if you have a test, should the information be made available?
 - if you have not had a test, could having a test be mandatory?
- What is the accuracy of these tests: if they are inaccurate, is their use like that of a 'generalisation'?
- Proactive use of the data by individuals - should this to be encouraged?
 - e.g. people presenting at ill-health annuity application
 - is there a difference in mandatory or optional use?



Outstanding questions, outstanding because they're *good* or *unanswered*?

- Should/will companies take advantage of the genetic information and the asymmetry?
- What does this mean for the cost of underwriting when each has many complex predictors of disease and each is different?
- What would it mean if the predictors of early death or longevity were comprehensive and more accurate than existing processes and calculations?
- Will clients ever go to a PGA (*a Personal Genetic Advisor*) to get an estimate of their longevity, and plan savings according to this, or even bet against the insurance providers?
 - Will a traded life settlements market emerge to take the bets?
- Should pension schemes ask those predicted to be centenarians to retire later and encourage the members to build up a large enough pot to cover their predicted life span?
- What will 2020 look like?

Could, would, should ...

Starting with a quiz

Raise your hand if you:

1. know what a single nucleotide polymorphism is?
2. know what whole genome sequencing is?
3. have you heard of www.23andme.com?
4. should we extend the moratorium?
5. when reviewing the moratorium, should the scope be amended?
6. will laws in Europe trump those made in the UK?

Questions or comments?

Expressions of individual views by members of The Actuarial Profession and its staff are encouraged.

The views expressed in this presentation are those of the presenter.

