ACTUARIAL SOCIETY OF SOUTH AFRICA

Science Non-Fiction: Genetics and Insurance

Greg Becker

Noelene Kinsley

2012 CONVENTION 16 – 17 OCTOBER

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.

ACTUARIAL SOCIETY OF SOUTH AFRICA

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2022 CONVENTION 16 – 17 OCTOBER

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

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Genetics

- Brief science lesson
- Recent scientific developments
- The road from science to medicine
  - Cause
  - Diagnosis
  - 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
Please raise your hand if you:

1. have had a genetic test?
2. know someone who has had a genetic test?
3. think you can use the results of genetic test results to underwrite?
4. know what whole genome sequencing is?
5. know what a gene variant is?
6. have heard of www.23andme.com?

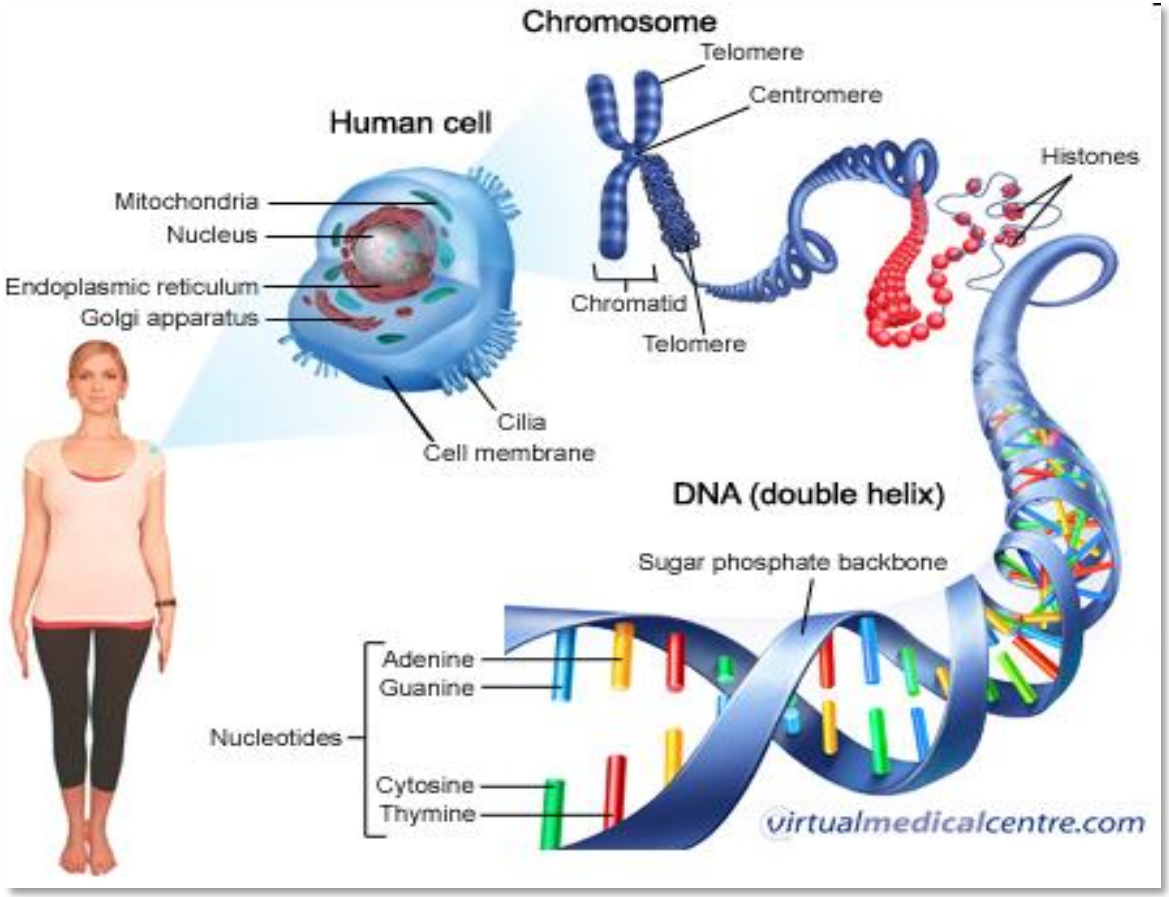
We're not looking forward to questions from those who put their hand up every time!

'For decades knowledge of genetics has had a large role in the healthcare of a few patients and a small role in the healthcare of many. We have recently entered a transition period in which specific genetic knowledge is becoming critical to the delivery of health care for everyone.'

Guttmacher and Collins (2002)

New Engl J Med 347: 1512-1520

Why Genetics?



Identify differences in the genome that alter who we are, how we function and our risk for disease

One Gene – One Protein

Genetics in a Century - A link with technology

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Microscope and dyes	**1886**	Chromosomes
Chemical analysis	**1956**	Role of DNA DNA Double Helix
Chromosome Banding	**1973**	Chromosomes carry genes Human chromosome abnormality
Gene cloning	**1977**	Study gene
Sequence the DNA Code	**1983**	DNA sequence
Polymerase Chain Reaction (PCR)	**1987**	Automated DNA Sequences

Genetic Disorders

- Chromosomal
- Biochemical
- Mendelian (single gene)

Chromosomal Disorders

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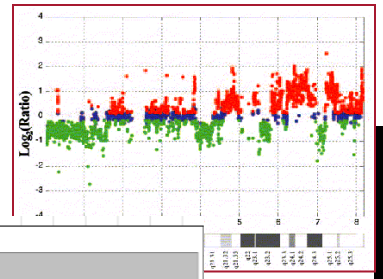
46 chromosomes
+/- 1,000 genes per chromosome

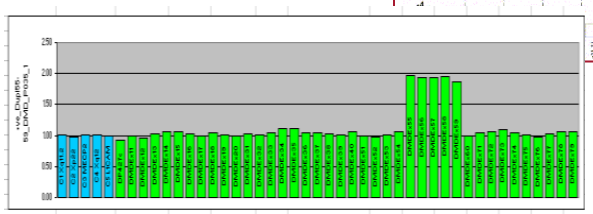
DNA Sequencing | MLPA | CGH | FISH | Chromosome Banding

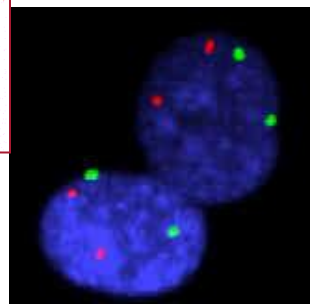
High Resolution — Low Resolution

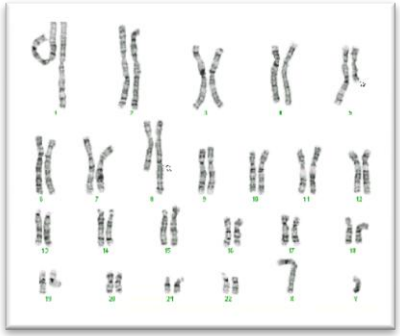
1 bp — 3-5Mbp

DNA Sequence — Chromosome number/structure









TIME

72 hours — 2 weeks

Single Gene Disorders

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- Clinical features
- Inheritance (population and family)
  - Autosomal dominant
    - e.g. Huntington disease or breast cancer
  - Autosomal recessive
    - e.g. Cystic fibrosis, sickle cell anaemia, albinism
  - X linked
    - e.g. Haemophilia
- Molecular diagnosis (DNA sequencing)

Single Gene Disorders

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Albinism	Haemophilia	Huntington Disease	Retinitis Pigmentosa	Cystic Fibrosis
Population specific	Biochemical specificity	Population specific	Inheritance	Common population specificity
OCA2 and TYR	F8 and F9	HD1 and HD2	>53 genes	CFTR
100% detection	?	100% confirmation	30% Detection	Common (90%) Unique
DNA Sequence	DNA Sequence and RNA Sequence	DNA Sequence	DNA Sequence Microarray NGS	DNA Sequence Microarray NGS

Genetic Disorders

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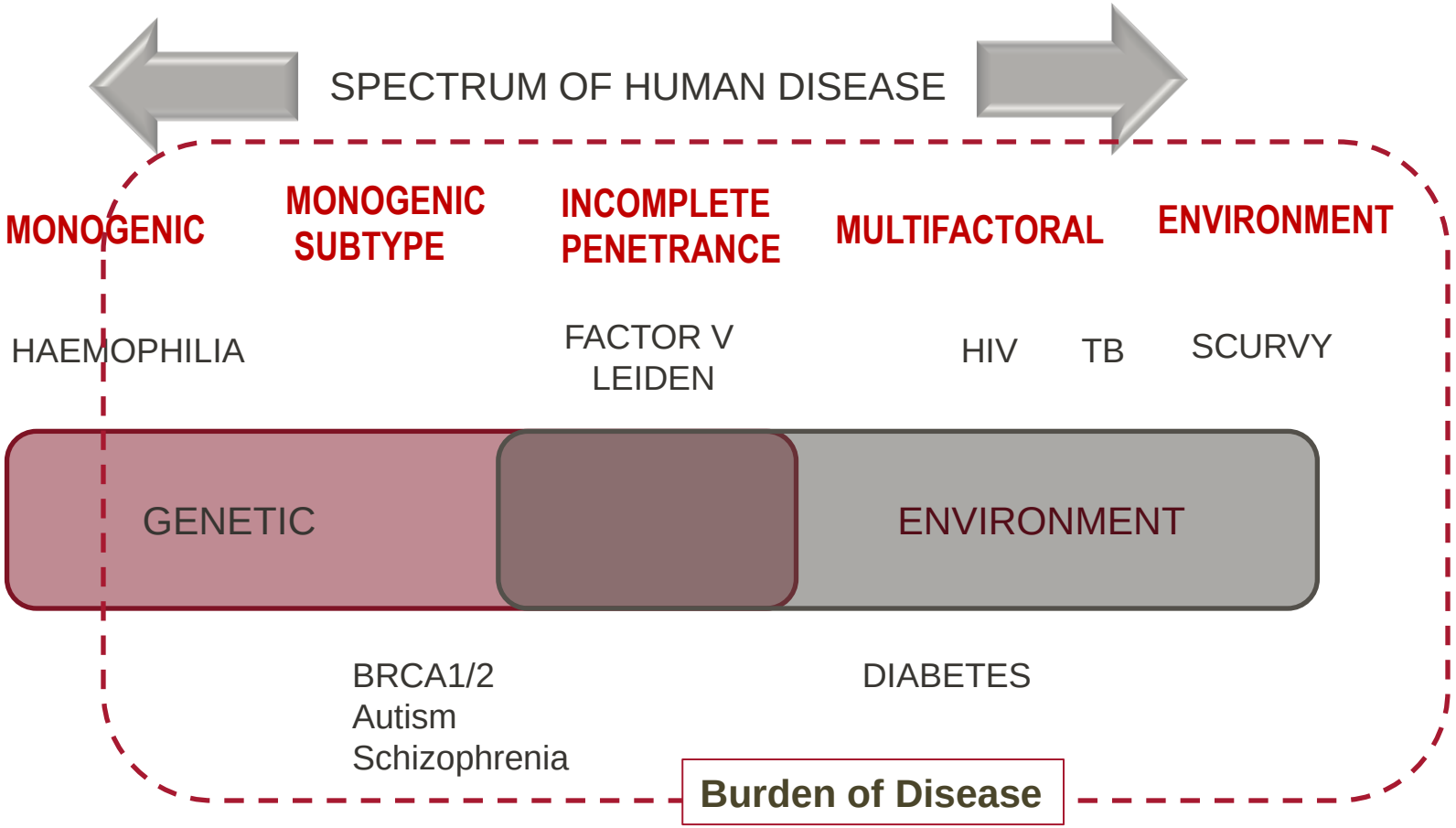
"How many genetic disorders are there?"



Human Genome Project

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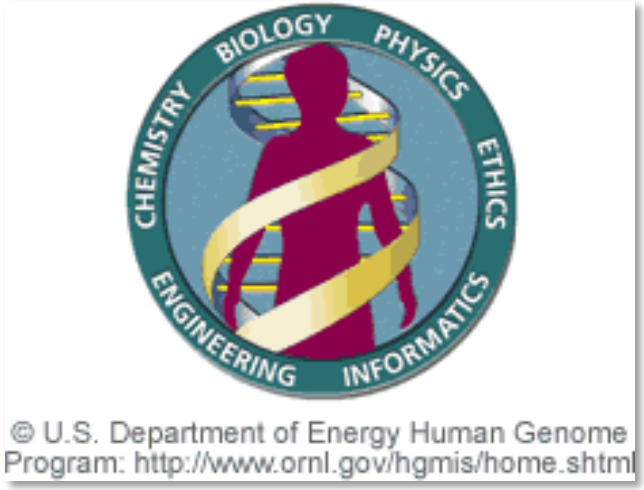
Decode all 3 billion DNA base-pairs in a human cell

- Understanding *cause and process* of disease
- Reveal *genetic predisposition* to disease
- New *diagnostic* tools
- New *therapy* options
- *Personalised medicine*



CARE → INTERVENTION → PREVENTION

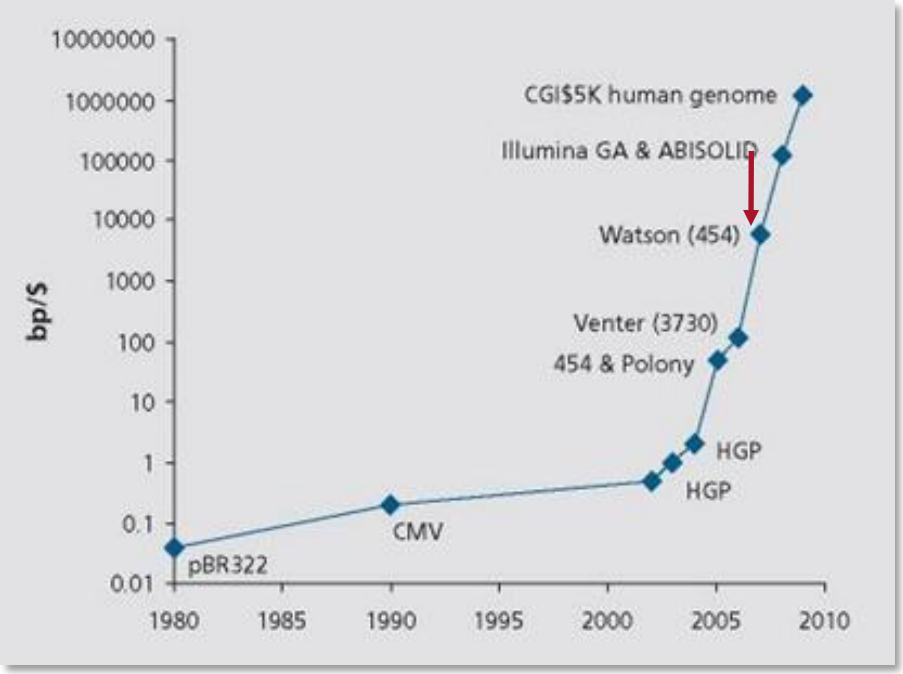
Human Genome Project

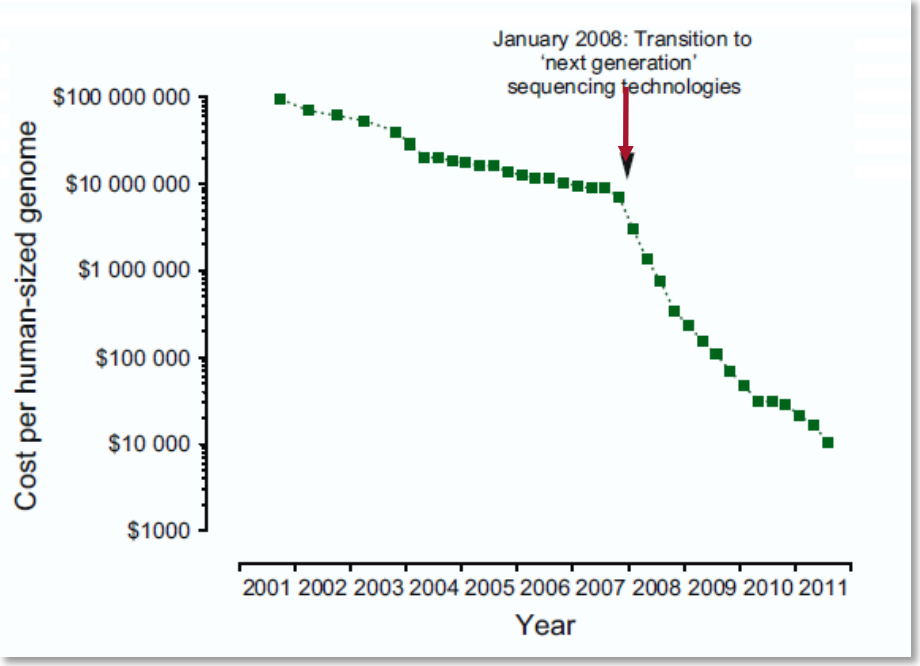
"Humankind is on the verge of gaining immense, new power to heal... It will revolutionize the diagnostic, prevention, and treatment of most, if not all, human disease"…

"We'll go from knowing almost nothing about how our genes work to enlisting genes in the struggle to prevent and cure illness. This will be the scientific breakthrough of the century, perhaps of all time."

Bill Clinton, 2000

Whole Genome Sequencing

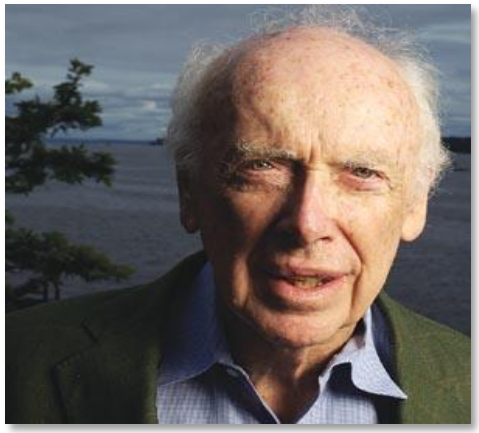


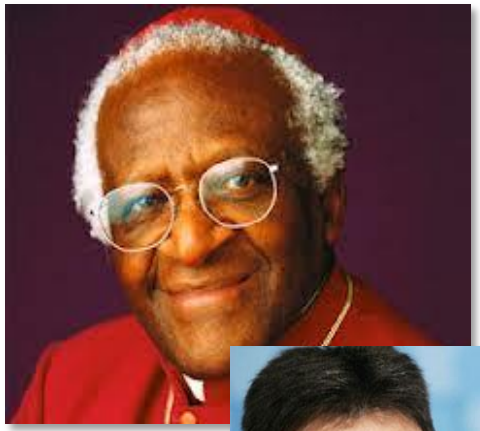


ARCHON GENOMICS X PRIZE
PRESENTED BY EXPRESS SCRIPTS®

	2011
Knome	$39,500
Complete Genomics	$10,000
Illumina	$ 5,000

Whole Genome Sequencing





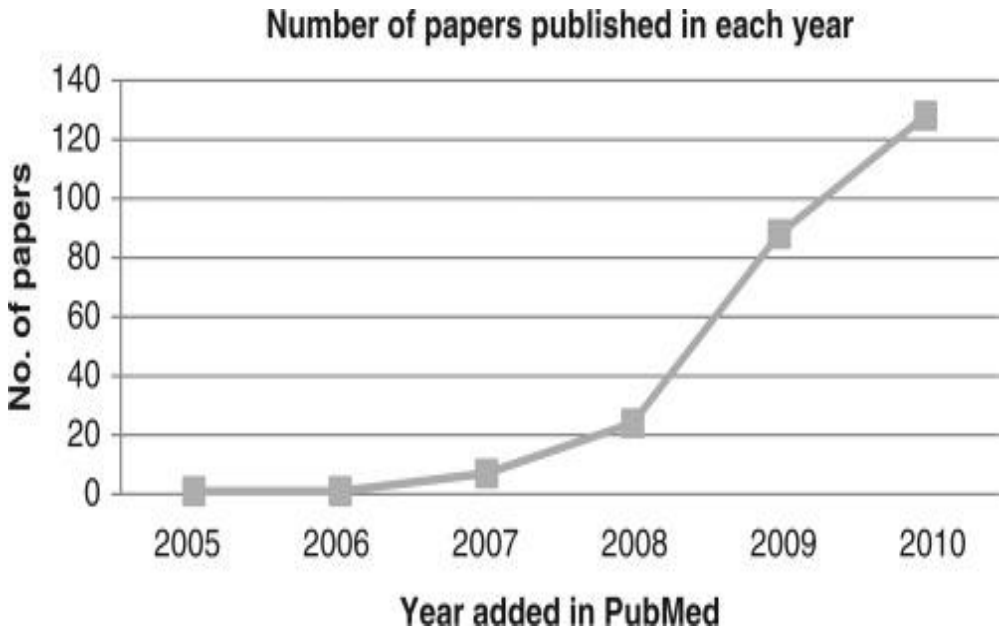
- Craig Venter
- 2004
- Capillary sequencing
- 10 years
- US$ 17 million

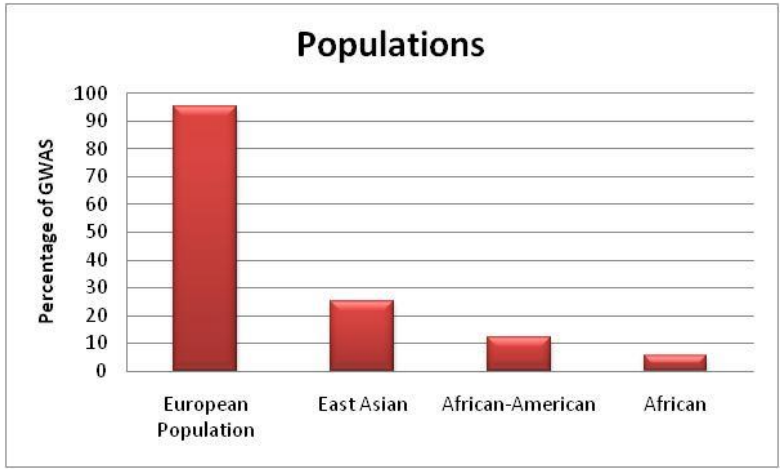
- James Watson
- 2008
- Next Generation sequencing
- 4 months
- US$ 1,5 million

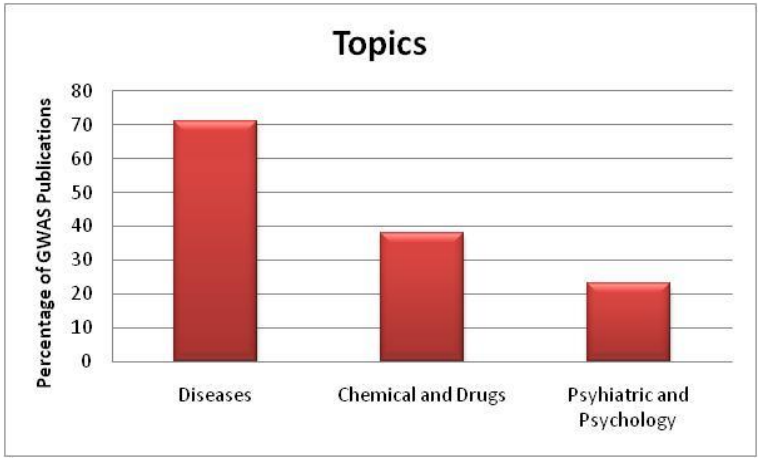
Knome | The Human Genome Interpretation Company™

$4,998

Genome Wide Association Studies







1300 Loci and ~200 diseases or traits
Variant disease effects 1.2x
Unknown: Rare causal and heredity

Limitation to Whole Genome Studies

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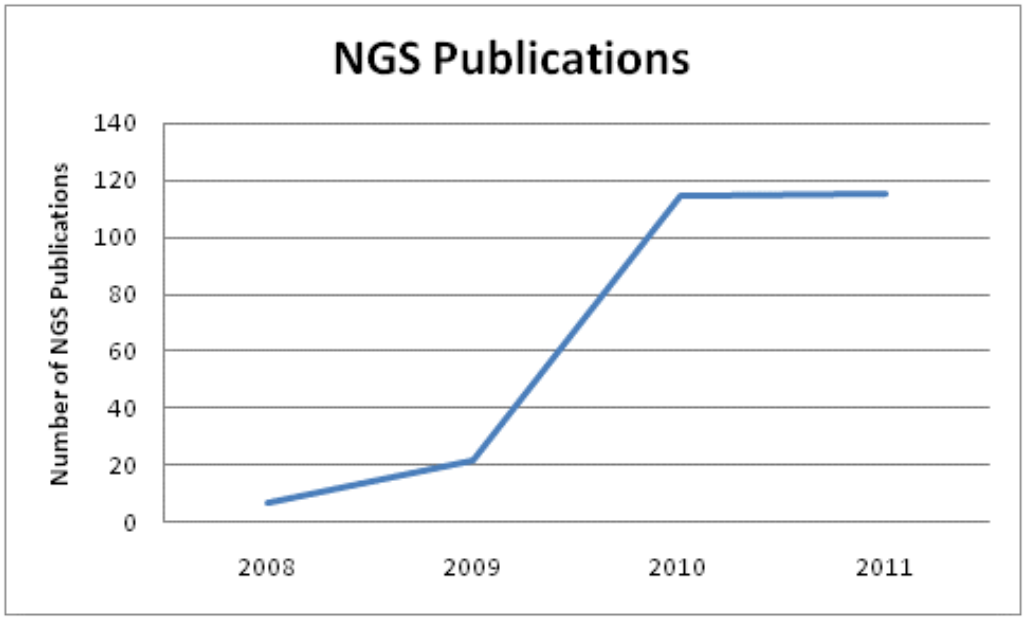
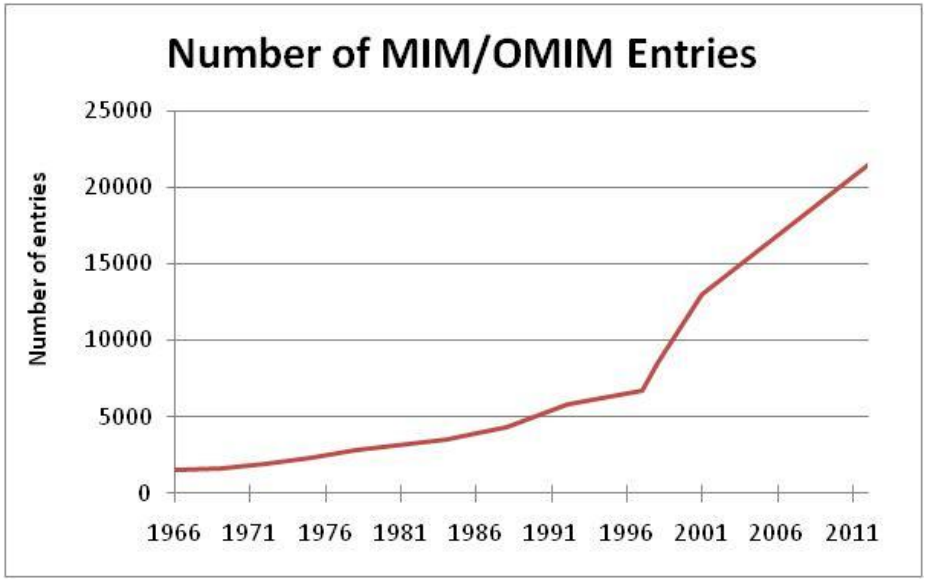
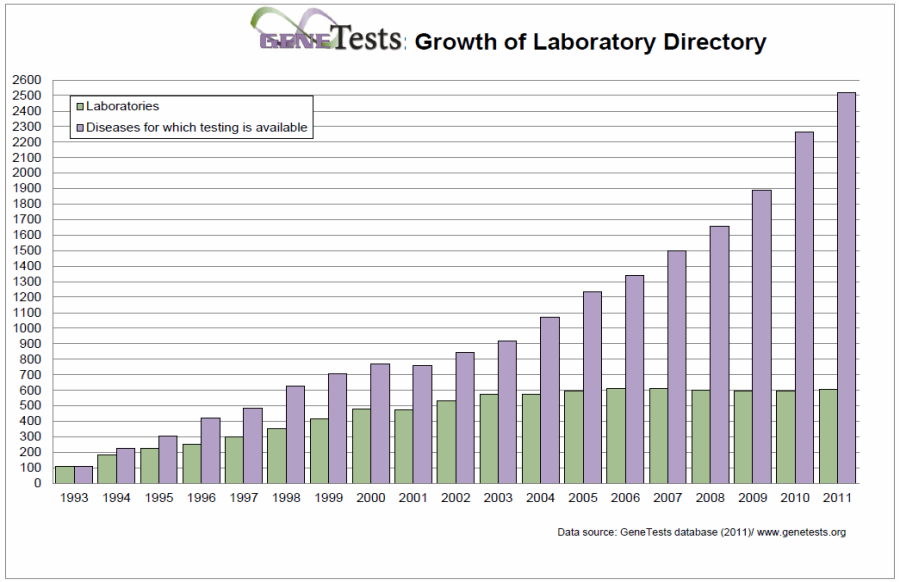
- Low predictive power
- Population variance
- Environment
- Complex cell and molecular biology

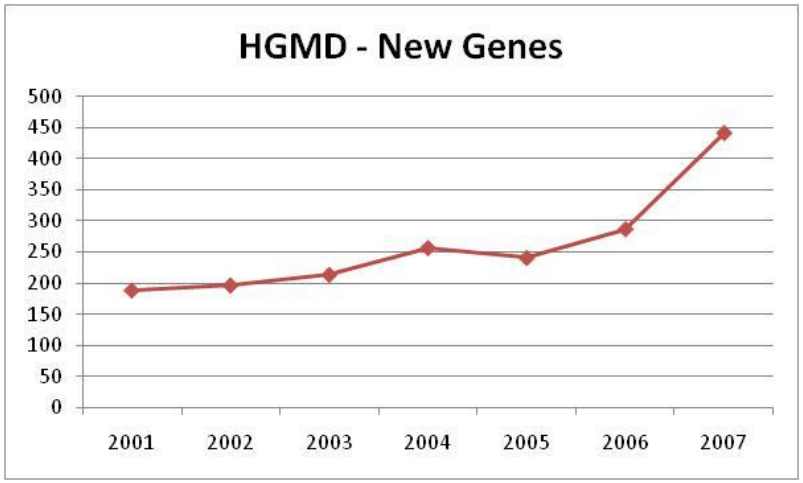


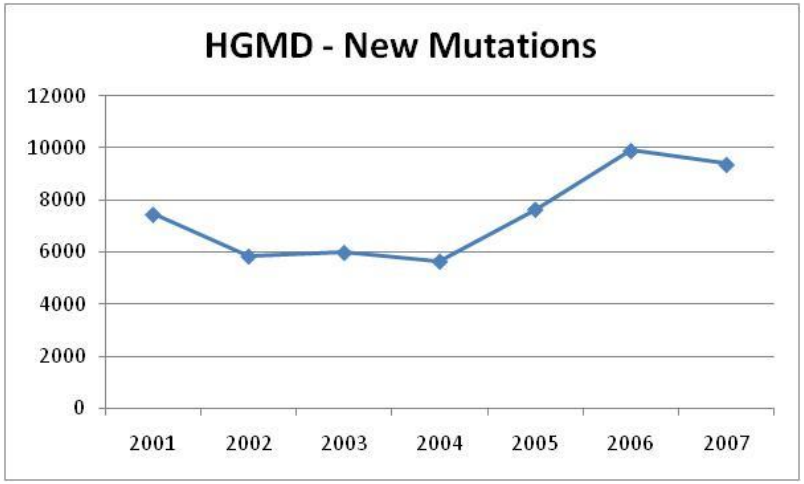
Solution:
High-throughput next generation sequencing

Clinical Translation









Pharmacogenomics

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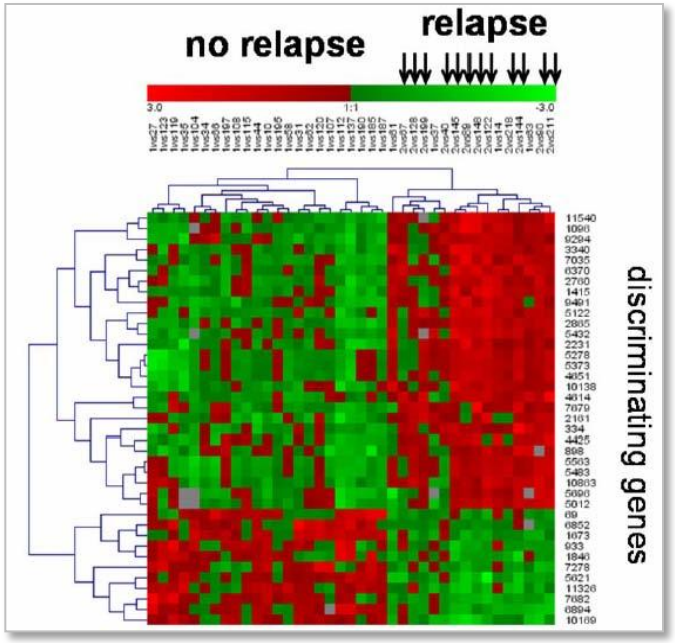
Effect of many genes on drug response and efficacy

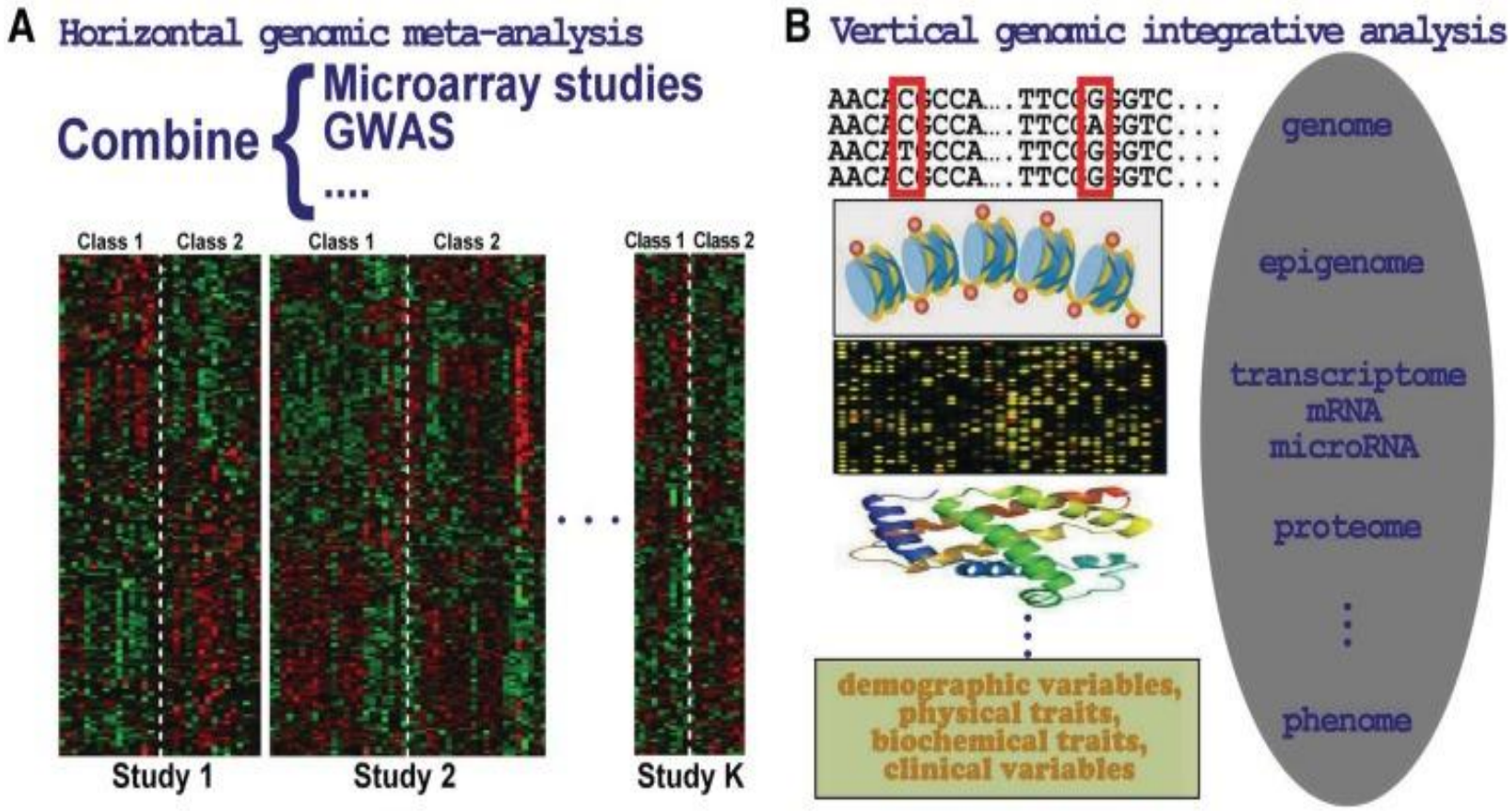
Drug	Adverse Reaction	Gene
Warfarin	Maintenance Dose	VKORC1, CYP2C9, CYP4F2, CYP2C18
Plavix®	Anti-platelet effect	CYP2C19
Methotrexate	Toxicity – childhood leukaemia	SLC1O1B1
Simvastatin	Induced myopathy	SLC1O1B1
Irinotecan	Increased toxicity	UGT1A1
Panitumumab; Cetuximab	Chemotherapy yielded ineffective	KRAS

Gene Expression Profiles

- Gene expression tumours
- Uses:
  - Pathological classification of tumour
  - Rate of recurrence (10 years)
  - Treatment protocols
- Intervention:
  - Chemotherapy or not
- Breast Cancer, Melanomas and Colon Cancer



Biology Systems



Whole Genomes for the Future

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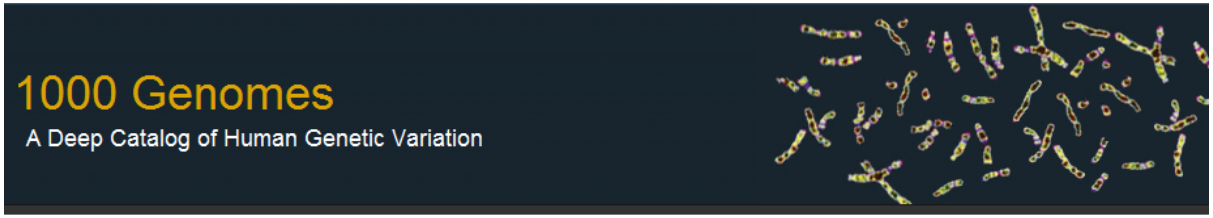
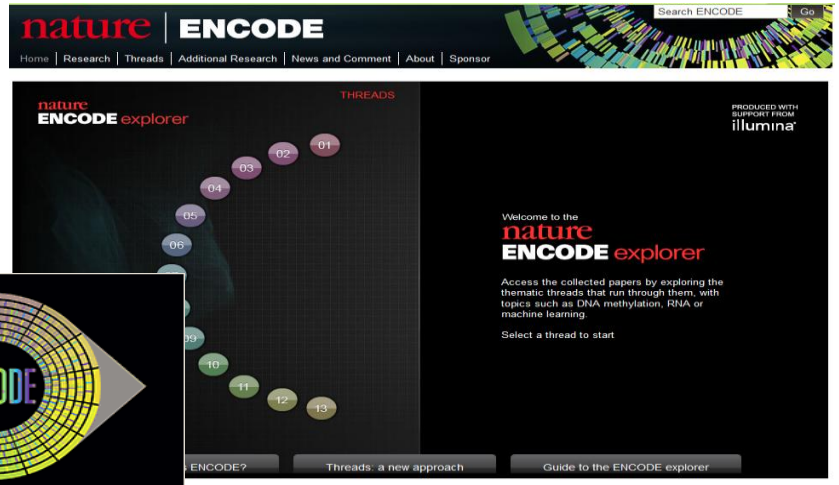


Personal Genome Project



ENCODE

HMP
NIH HUMAN MICROBIOME PROJECT

HEP
Human Epigenome Project

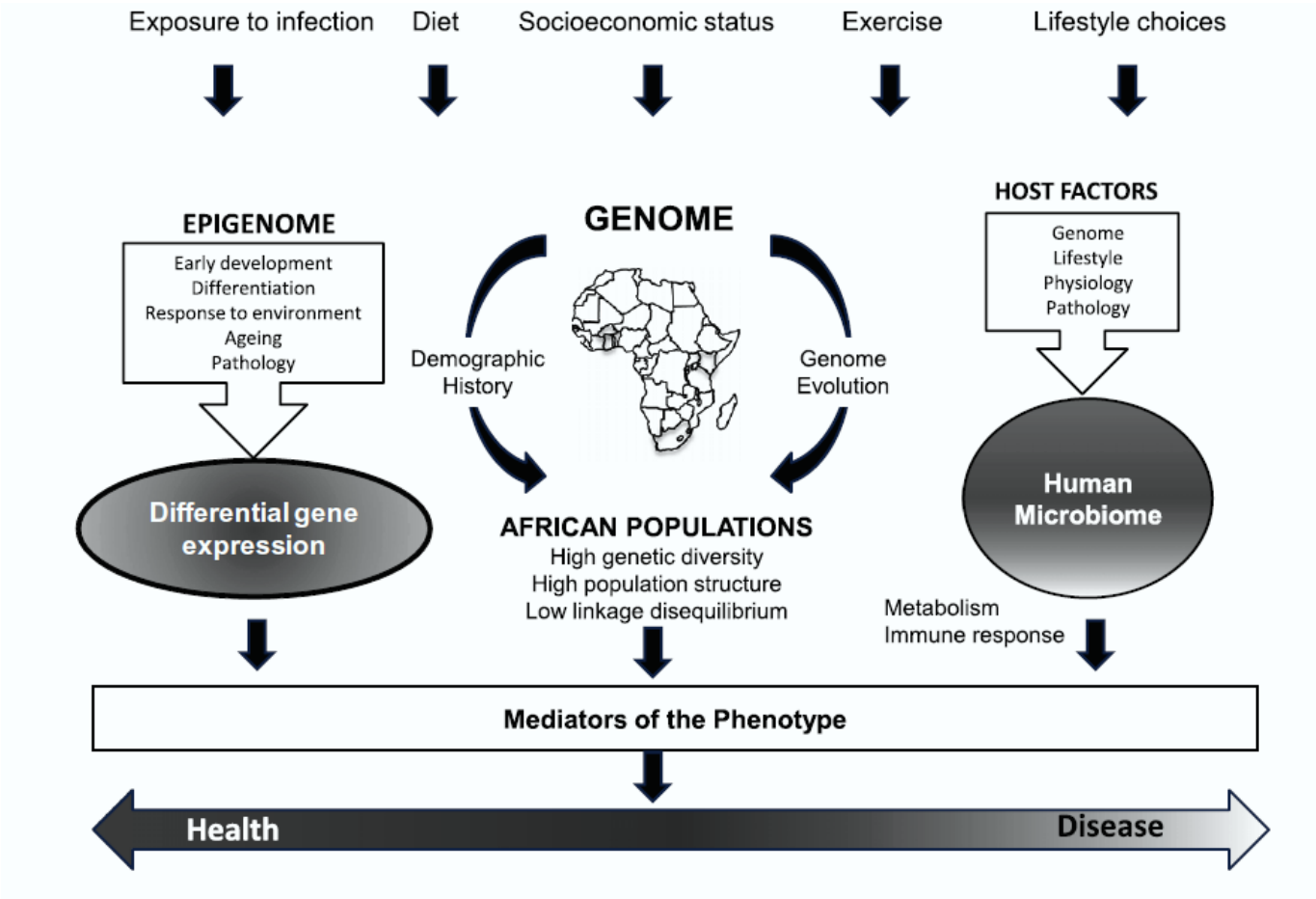
CGP

miRBase

NGS Exomes and Genomes

- Data acquisition
  - 3 million variants per run
- Computing power
  - Variant interpretation
- Clinical interpretations and translation
  - Improved prediction
  - Management and preventative options
  - Treatment

African Populations



"Genomic medicine premised on role of ancestral variants in disease processes" *Prof Michele Ramsay*

South African Genetic Services

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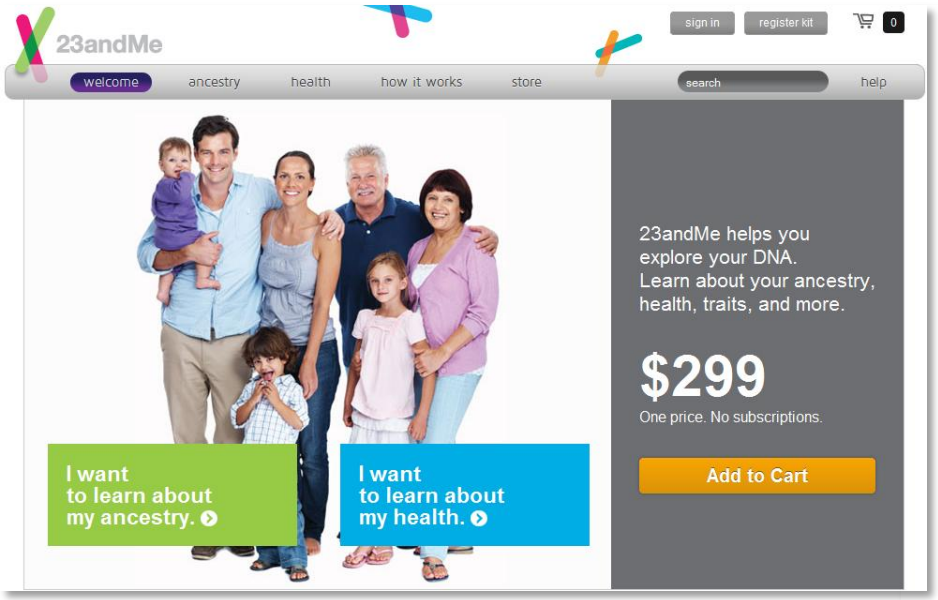
- To help people understand how genetics effects their lives and health
- Detect the genetic basis
- Predict risk of event
- Prevention and management

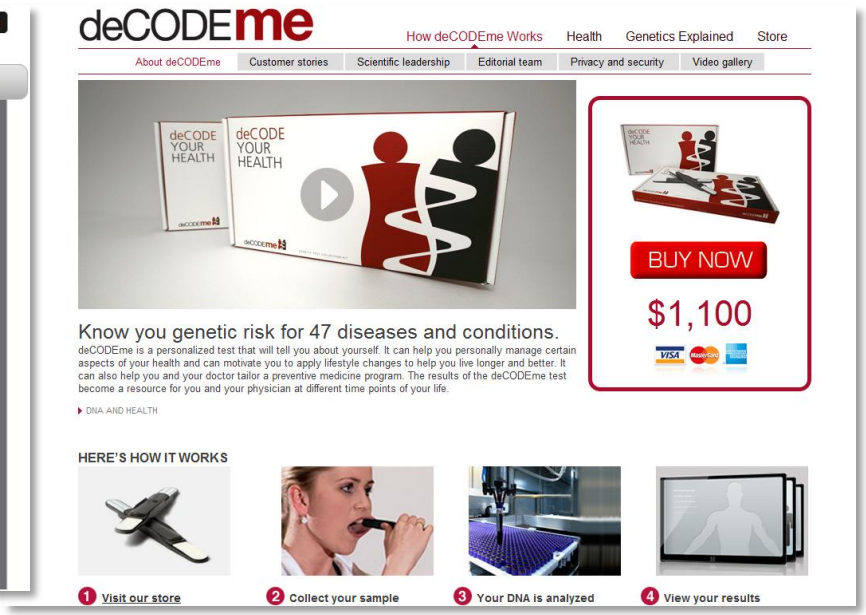
	1977	2008
Academic	2	6
Private	0	5
Types Genetic Test	Cytogenetics Biochemistry	Cytogenetics Serogenetics Molecular (including NGS)
Number of Test	?	200

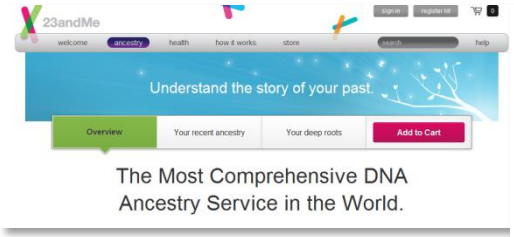
Diagnostic Genetic Test 2008

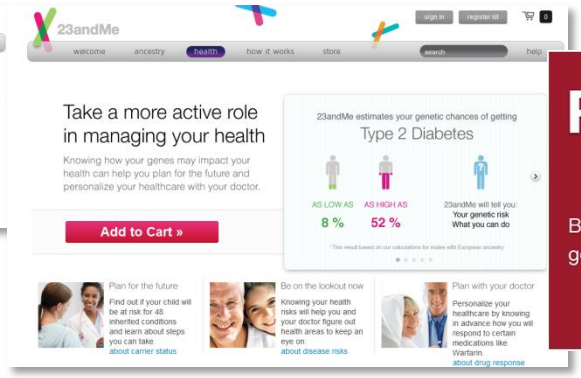
NHLS	16,073
Private	3,392

International Genomic Profiling









South African Genomic Profiling

gknowmix
genetic knowledge integration

GENEdiagnostics
POWER THROUGH KNOWLEDGE™

dna diet	dna health	dna diet
8 genes	20 genes	12 genes
R1,350	R2,700	R2,950

23andMe genetics just got personal.

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

welcome | ancestry | health | how it works | store

Personal Genome Service™

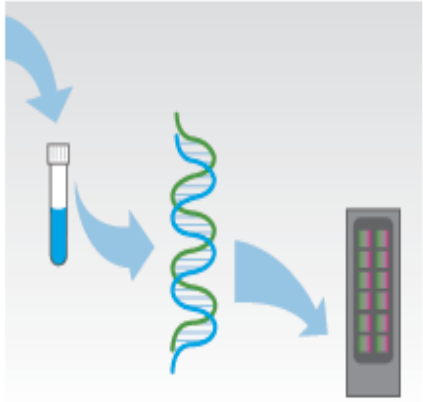
Get to know your DNA. All it takes is a little bit of spit.

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.

health overview

Print my health overview

Show results for Greg Mendel (Dad)

See new and recently updated reports »

23andWe 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

Medical Conclusions → Actuarial Questions

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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. Some overestimated the role of genetics – genetic determinism
4. Genetic testing is and will lead to improved medical diagnosis and treatment
5. This could reduce the cost and improve the effectiveness of healthcare - health providers may encourage it's use
6. Good for health and longevity
7. Life style improvements have already helped to increase life expectancy but newer preventive therapies will be developed
8. How much could this improve life expectancy in next 40 years?
9. Direct consumer testing by Google is a disruptor in innovation and users will increase exponentially outside any national control
10. 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?

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Science Non-Fiction: Genetics and Insurance

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

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- 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
  - Look what happened with the Gender Directive

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.

http://www.abi.org.uk/media/releases/2011/04/insurance_genetics_moratorium_extended_to_2017.aspx

South African Legislation and Guidelines

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Long-term Insurance Act

- Legal framework

Association for Savings and Investment South Africa (ASISA)

- Interests and concerns of life insurance industry and insured public
- LOA incorporated into the (ASISA), 2008.

- Long-term Insurance Ombudsman

ASISA Standard on Genetic Testing

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- Genetic test results (prior application) – underwritten risk information
- Genetic tests may not be requested
- Genetic test performed after policy commenced may not be requested
- No premiums lower than standard rates for negative genetic test
- Review policy terms based on predictive genetic test result
- Consider specialist screening, medical intervention and treatment

ASISA's view that in this area the insurance industry should follow rather than lead common medical practice and consumer attitudes

(ASISA, 2009)

Life Insurance

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- 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 (pa) in the US?

HTTP://WWW.CANCURE.ORG/MEDICAL_ERRORS.HTM

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 a 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!

Factors that can have a big effect

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

DATA FROM GAPMINDER, WITH THE ORIGINAL DATA BEING WHO/UNAIDS

Ethical questions

Closing comments

Outstanding questions

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

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- 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? (will that discourage or encourage testing? Is that a permissible side effect)
  - 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 be encouraged?
  - e.g. people presenting at ill-health annuity application or to show that they are healthier than their family history suggests?
  - is there a difference in mandatory or optional use?

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

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- 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 ...

Ending with a quiz
Raise your hand if you:

1. know what whole genome sequencing is?
2. know what a gene variant is?
3. have you heard of www.23andme.com?
4. think that we have all the answers relating to genetic testing?

Any questions or comments?

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