

# Personalised Medicine; made for you

**Martin Elliott**

37th Gresham Professor of Physic

RX 4407687-1333

JOHN SMITH  
ONE CAPSULE  
BEFORE BEDTIME

10 MG TABLETS  
REFILLS: 0  
QTY: 30

# TAKE IT PERSONALLY



Parkinson's



Melanoma



Dementia



Diabetes

Rh Arthritis



Emphysema



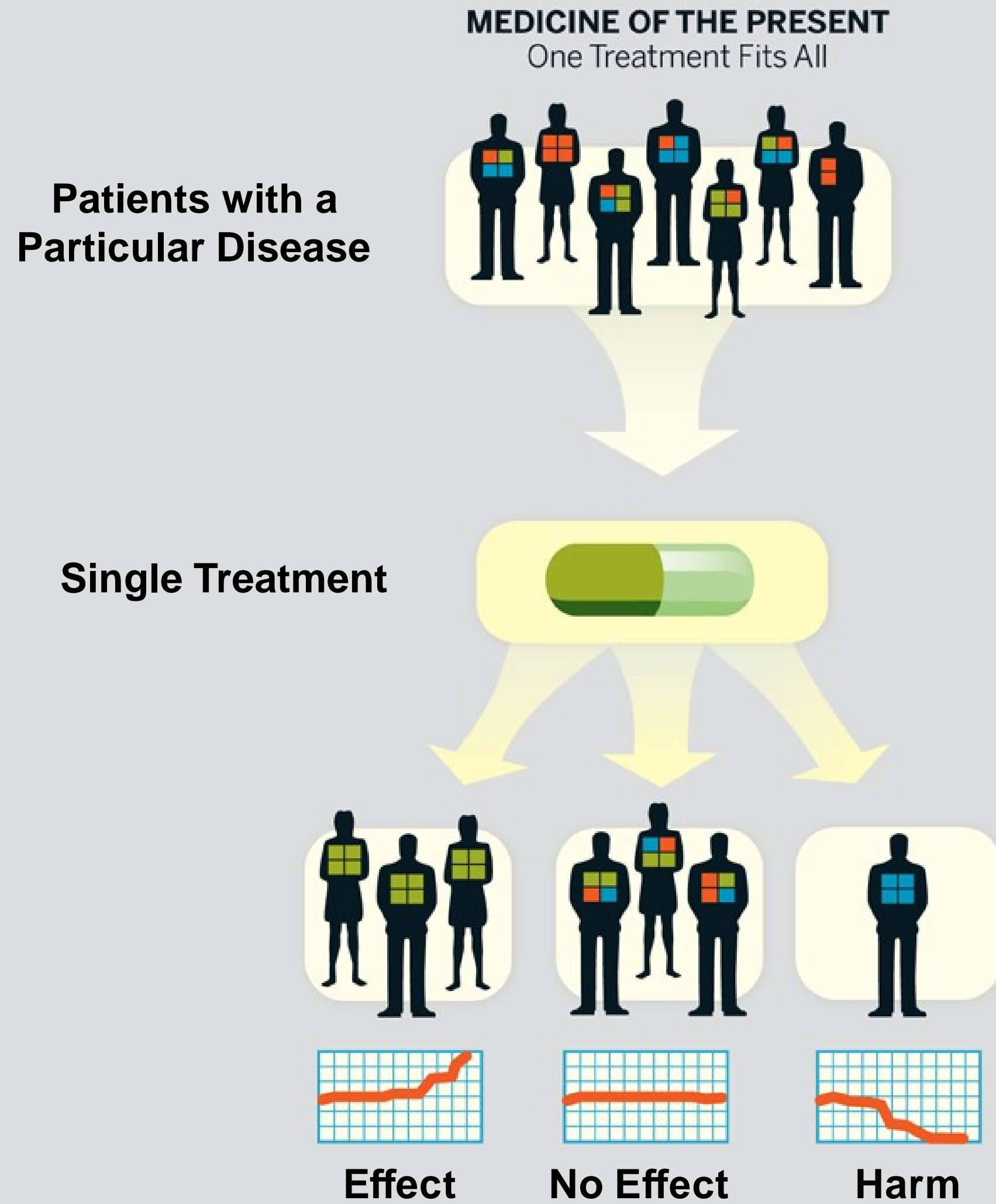
Breast Cancer



Depression



# PERSONALIZED MEDICINE: Tailored Treatments

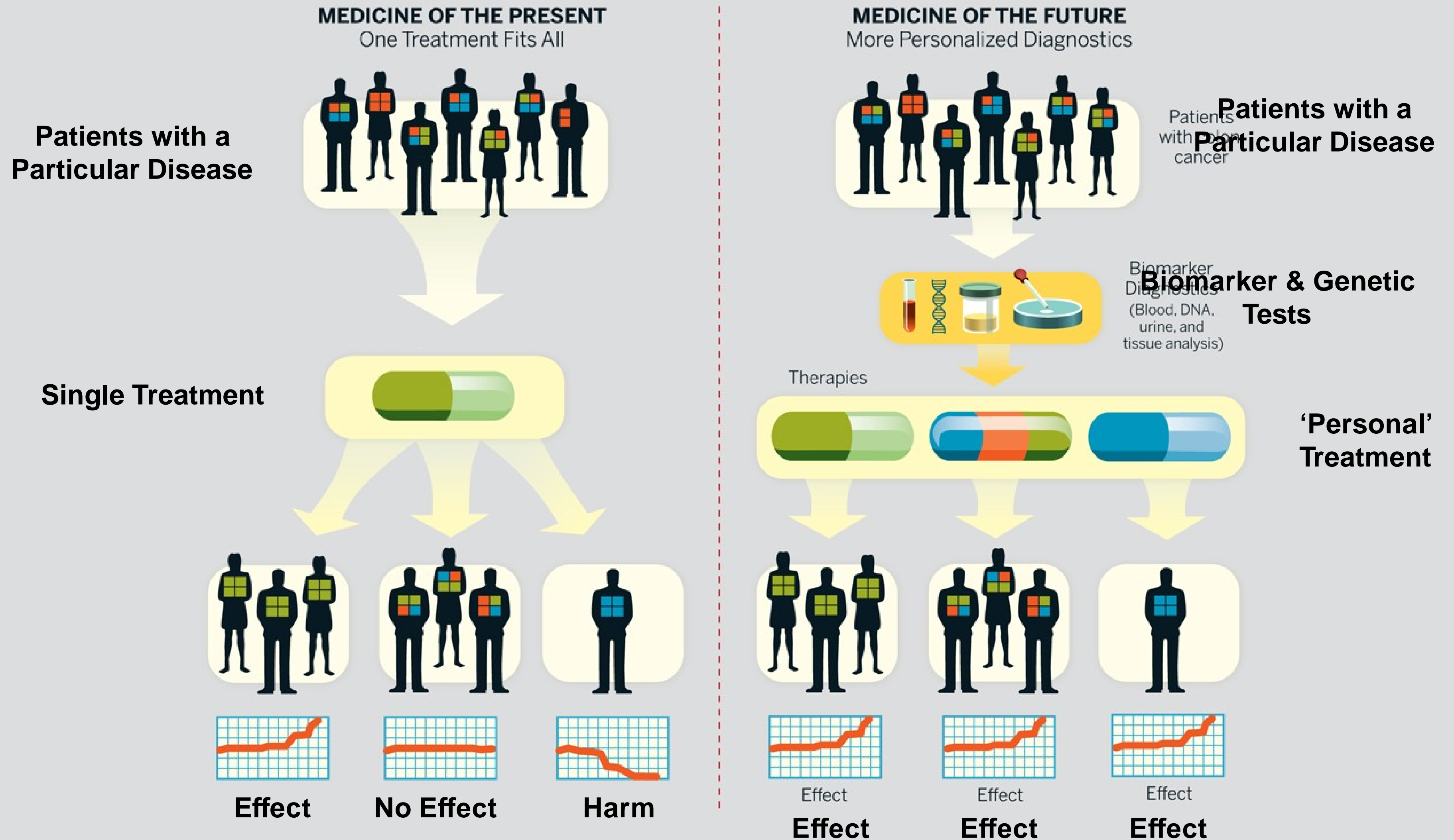


**Effect**

**Effect**

**Effect**

# PERSONALIZED MEDICINE: Tailored Treatments



**“the tailoring of medical treatment to the specific characteristics of each patient.**

**.....it involves the ability to classify individuals into subpopulations that are uniquely or disproportionately susceptible to a particular disease or responsive to a specific treatment”**

# GENES

## IMPORTANT POINTS ALONG THE WAY



**1911**

Researcher Alfred Sturtevant discovers how to map the locations of fruit fly genes, creating the first gene map

**1953**

James Watson and Francis Crick describe the now-familiar double helix structure of DNA, the compound that contains the genetic instructions for building, running and maintaining living organisms

**1977**

Walter Gilbert and Fredrick Sanger devise techniques for sequencing DNA

**1990**

The Human Genome Project (HGP) begins as the National Institutes of Health (NIH), the Department of Energy and international partners come together to sequence all three billion letters in the complete set of DNA in human beings

**2003**

Researchers publish the full report of HGP results, ahead of schedule

# DNA

## IMPORTANT POINTS ALONG THE WAY



**1911**

Researcher Alfred Sturtevant discovers how to map the locations of fruit fly genes, creating the first gene map

**1953**

James Watson and Francis Crick describe the now-familiar double helix structure of DNA, the compound that contains the genetic instructions for building, running and maintaining living organisms

**1977**

Walter Gilbert and Fredrick Sanger devise techniques for sequencing DNA

**1990**

The Human Genome Project (HGP) begins as the National Institutes of Health (NIH), the Department of Energy and international partners come together to sequence all three billion letters in the complete set of DNA in human beings

**2003**

Researchers publish the full report of HGP results, ahead of schedule

# GENES

# DNA

## IMPORTANT POINTS ALONG THE WAY



**1911**

Researcher Alfred Sturtevant discovers how to map the locations of fruit fly genes, creating the first gene map

**1953**

James Watson and Francis Crick describe the now-familiar double helix structure of DNA, the compound that contains the genetic instructions for building, running and maintaining living organisms

**1977**

Walter Gilbert and Fredrick Sanger devise techniques for sequencing DNA

**1990**

The Human Genome Project (HGP) begins as the National Institutes of Health (NIH), the Department of Energy and international partners come together to sequence all three billion letters in the complete set of DNA in human beings

**2003**

Researchers publish the full report of HGP results, ahead of schedule

# GENES

# Sequencing



# DNA

# HGP Starts

## IMPORTANT POINTS ALONG THE WAY



**1911**

Researcher Alfred Sturtevant discovers how to map the locations of fruit fly genes, creating the first gene map

**1953**

James Watson and Francis Crick describe the now-familiar double helix structure of DNA, the compound that contains the genetic instructions for building, running and maintaining living organisms

**1977**

Walter Gilbert and Fredrick Sanger devise techniques for sequencing DNA

**1990**

The Human Genome Project (HGP) begins as the National Institutes of Health (NIH), the Department of Energy and international partners come together to sequence all three billion letters in the complete set of DNA in human beings

**2003**

Researchers publish the full report of HGP results, ahead of schedule

# GENES

# Sequencing

# DNA

# HGP Starts

## IMPORTANT POINTS ALONG THE WAY



**1911**

Researcher Alfred Sturtevant discovers how to map the locations of fruit fly genes, creating the first gene map

**1953**

James Watson and Francis Crick describe the now-familiar double helix structure of DNA, the compound that contains the genetic instructions for building, running and maintaining living organisms

**1977**

Walter Gilbert and Fredrick Sanger devise techniques for sequencing DNA

**1990**

The Human Genome Project (HGP) begins as the National Institutes of Health (NIH), the Department of Energy and international partners come together to sequence all three billion letters in the complete set of DNA in human beings

**2003**

Researchers publish the full report of HGP results, ahead of schedule

# GENES

# Sequencing

# HGP Published



Genotype

**codes for**

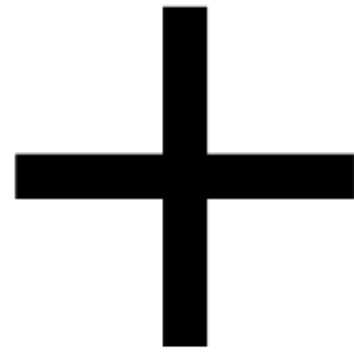


Phenotype

**“the collection of noticeable properties of an organism, representing its physiology, biochemistry, morphology at different levels (including cellular) and behaviour”**



Genotype

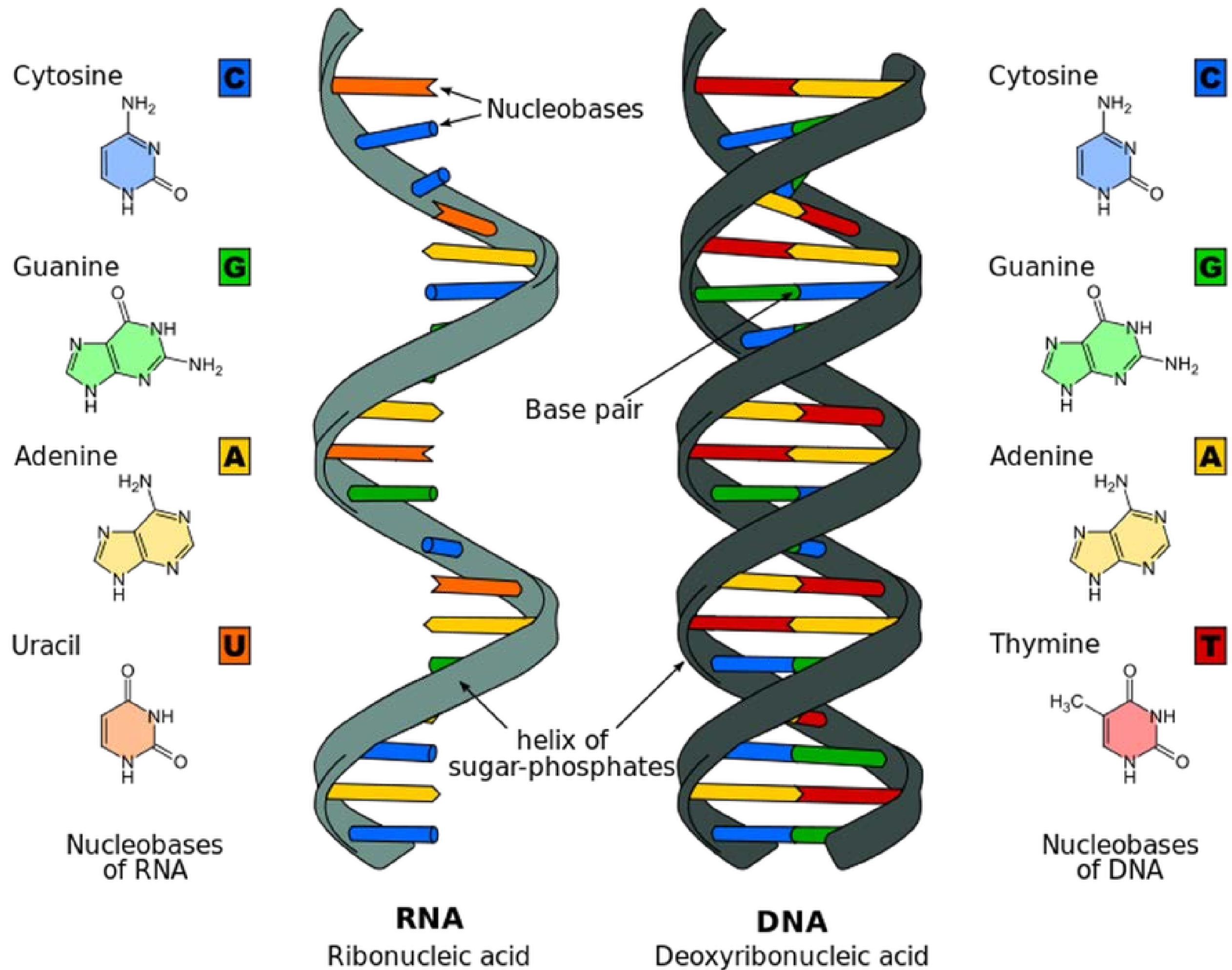


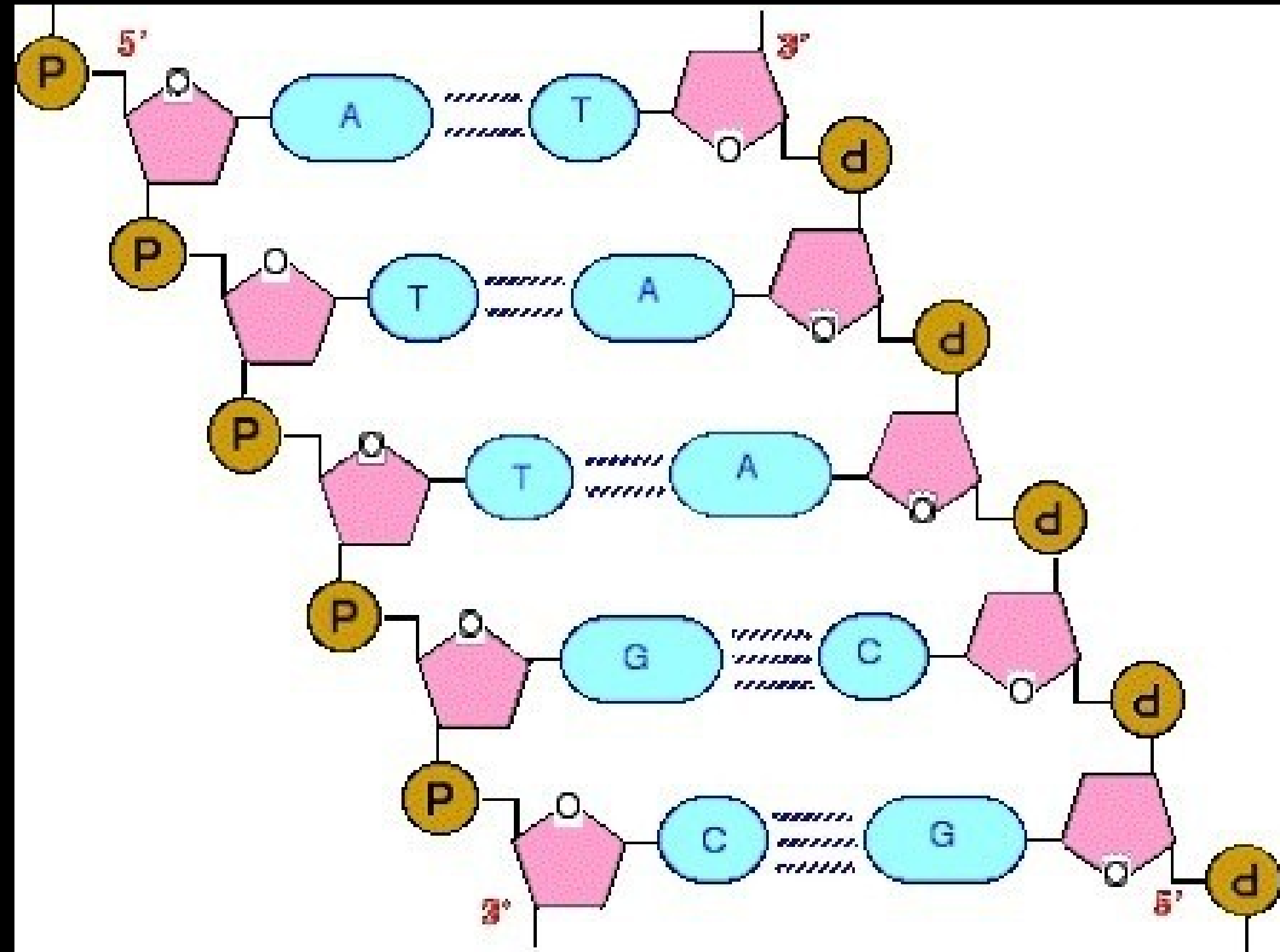
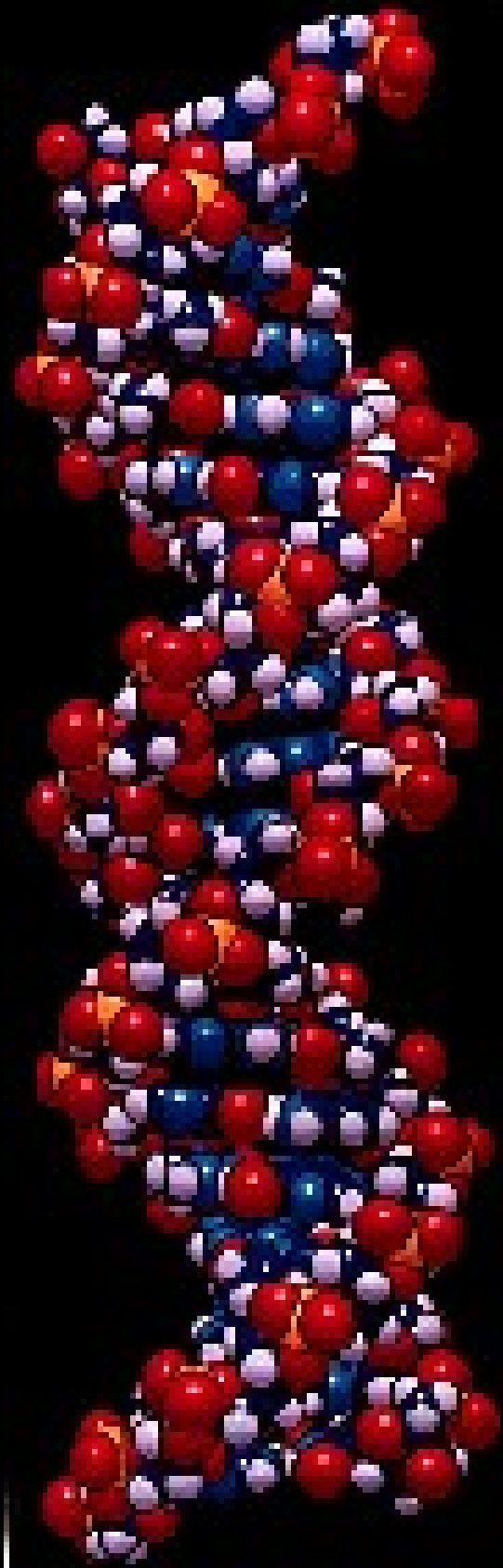
Environment



Phenotype

# The Genome





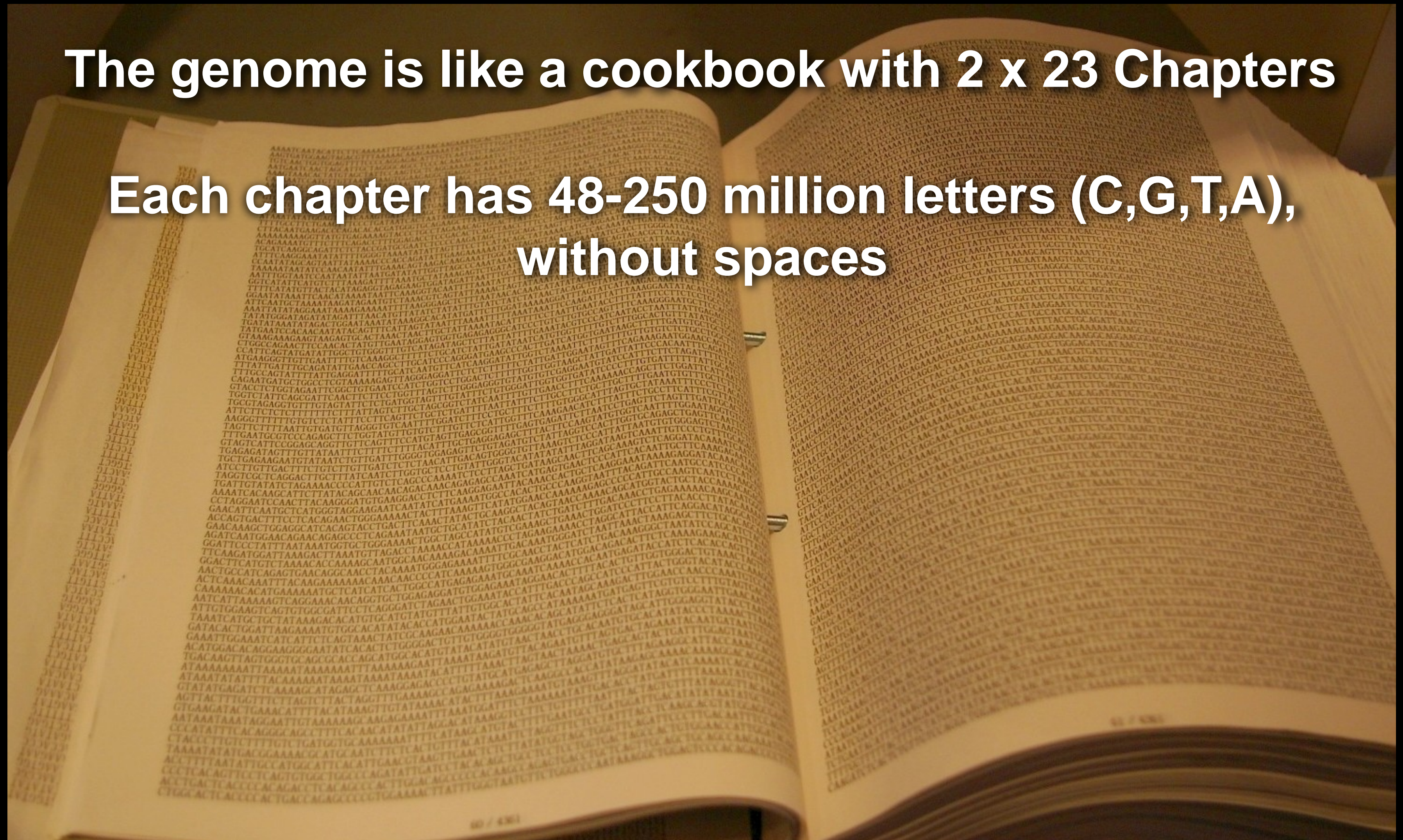
**1 human gene is roughly 27,000 base pairs long**  
**around 20,000 protein-coding genes**  
**The Human genome has 3 billion base pairs**





The genome is like a cookbook with 2 x 23 Chapters

Each chapter has 48-250 million letters (C,G,T,A),  
without spaces



**The genome is like a cookbook with 2 x 23 Chapters**

**Each chapter has 48-250 million letters (C,G,T,A),  
without spaces**

**The book has >3.2 billion letters**

**The genome is like a cookbook with 2 x 23 Chapters**

**Each chapter has 48-250 million letters (C,G,T,A),  
without spaces**

**The book has >3.2 billion letters**

**There are > 20,000 different recipes (genes),  
but these make up < 2% of the letters**

**The genome is like a cookbook with 2 x 23 Chapters**

**Each chapter has 48-250 million letters (C,G,T,A),  
without spaces**

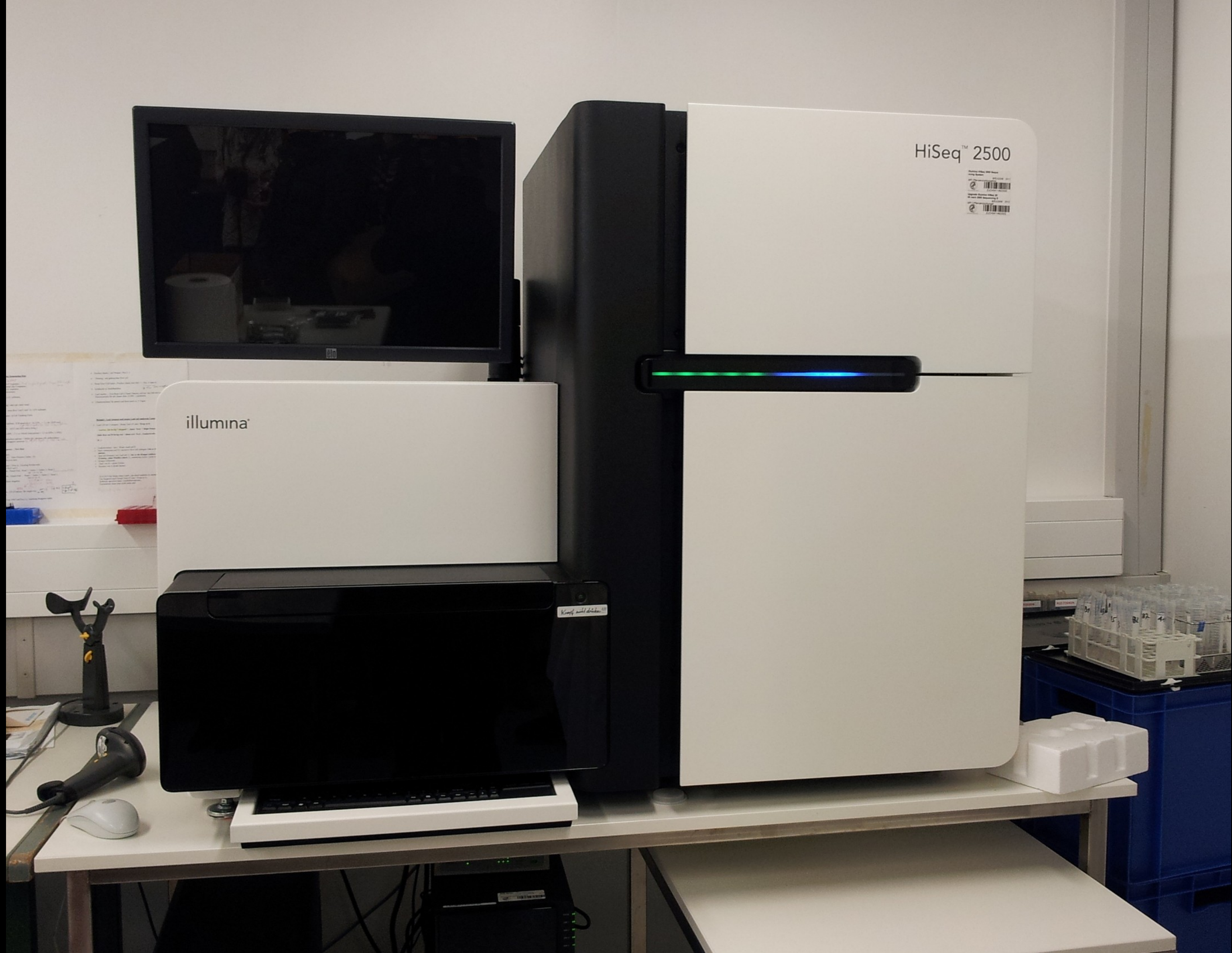
**The book has >3.2 billion letters**

**There are > 20,000 different recipes (genes),  
but these make up < 2% of the letters**

**The whole book fits into a cell nucleus,  
< the size of a pinpoint**



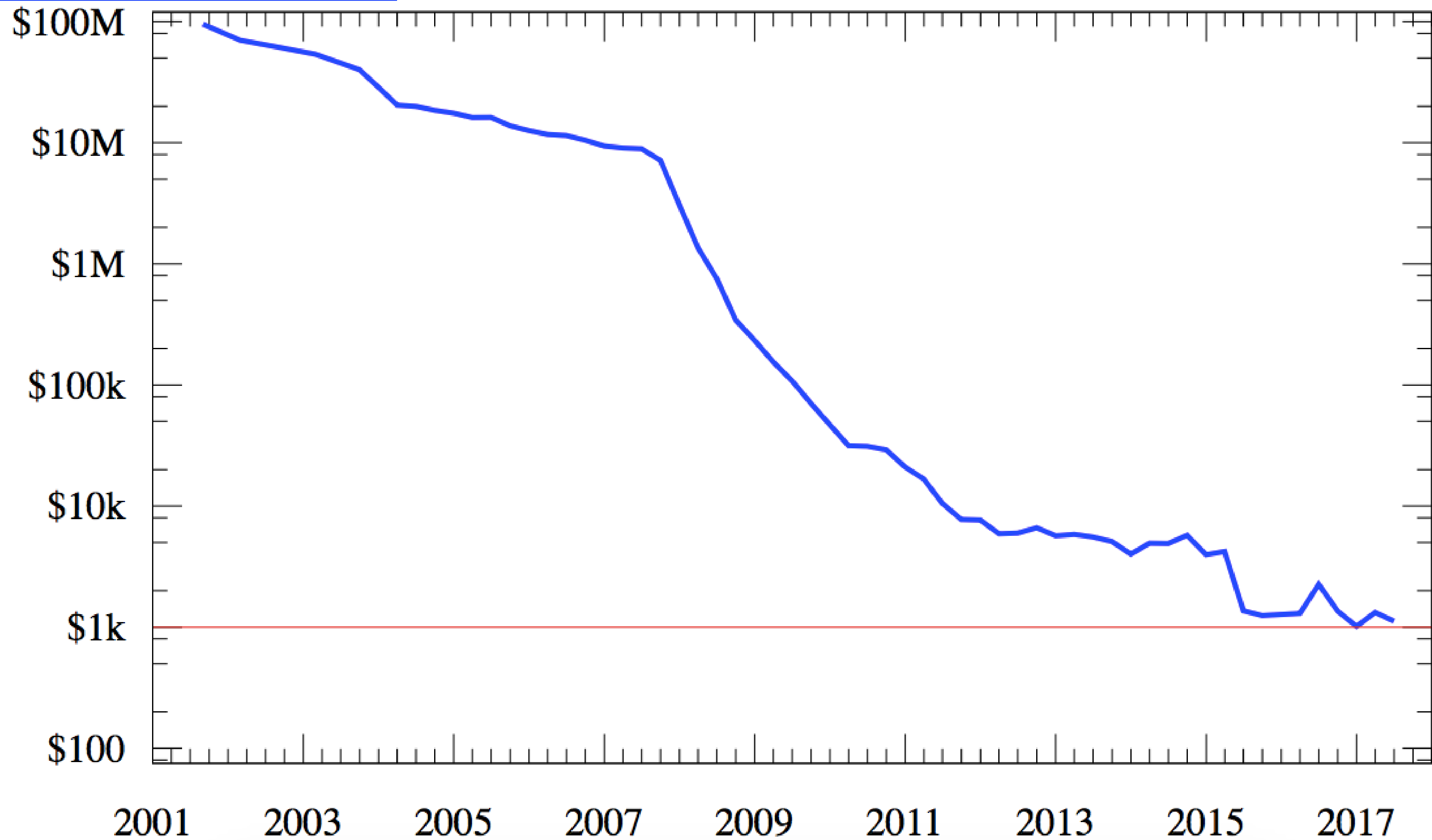
# DNA Sequencing



HiSeq™ 2500

illumina

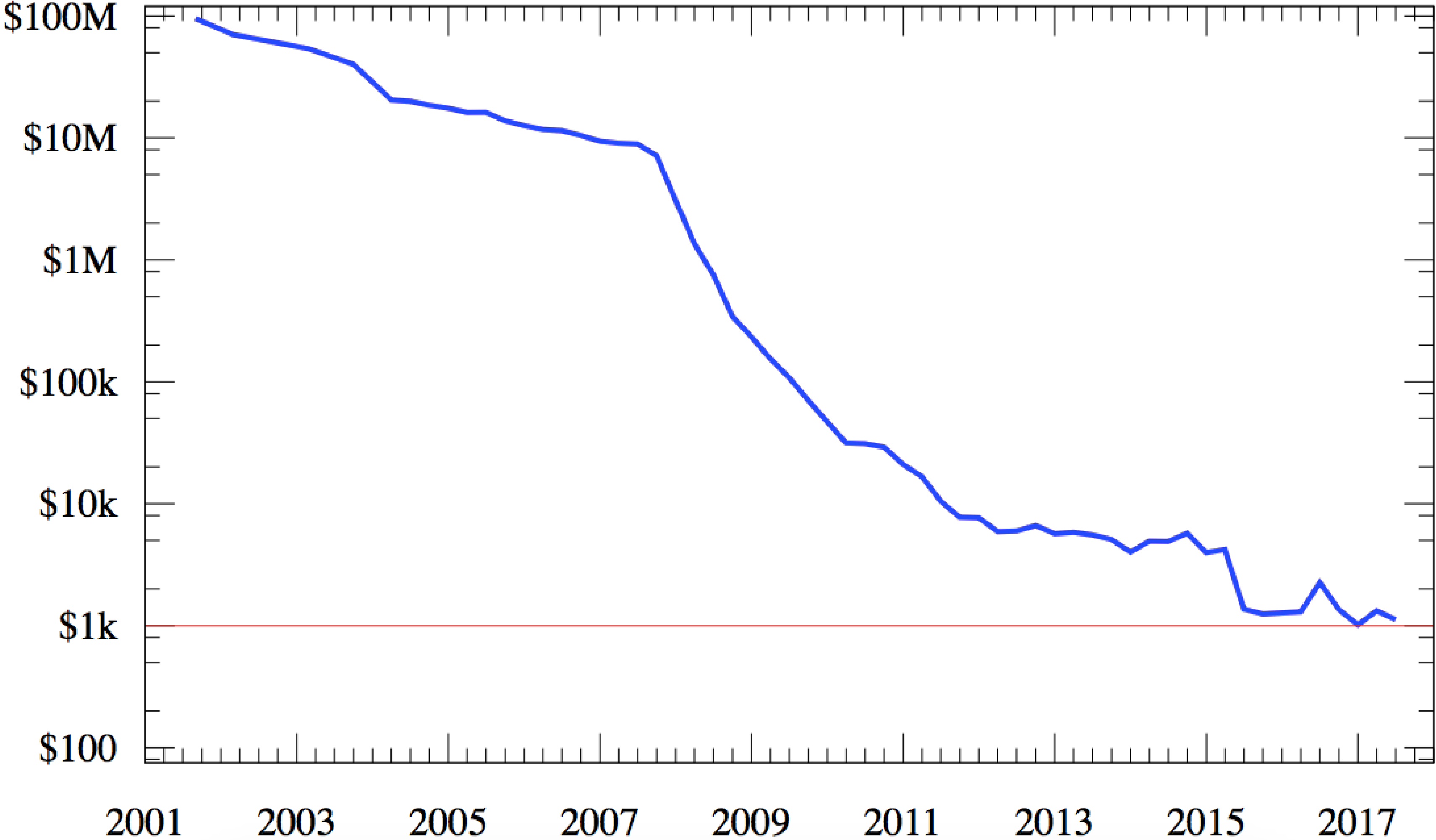
Cost to sequence a human genome (USD)





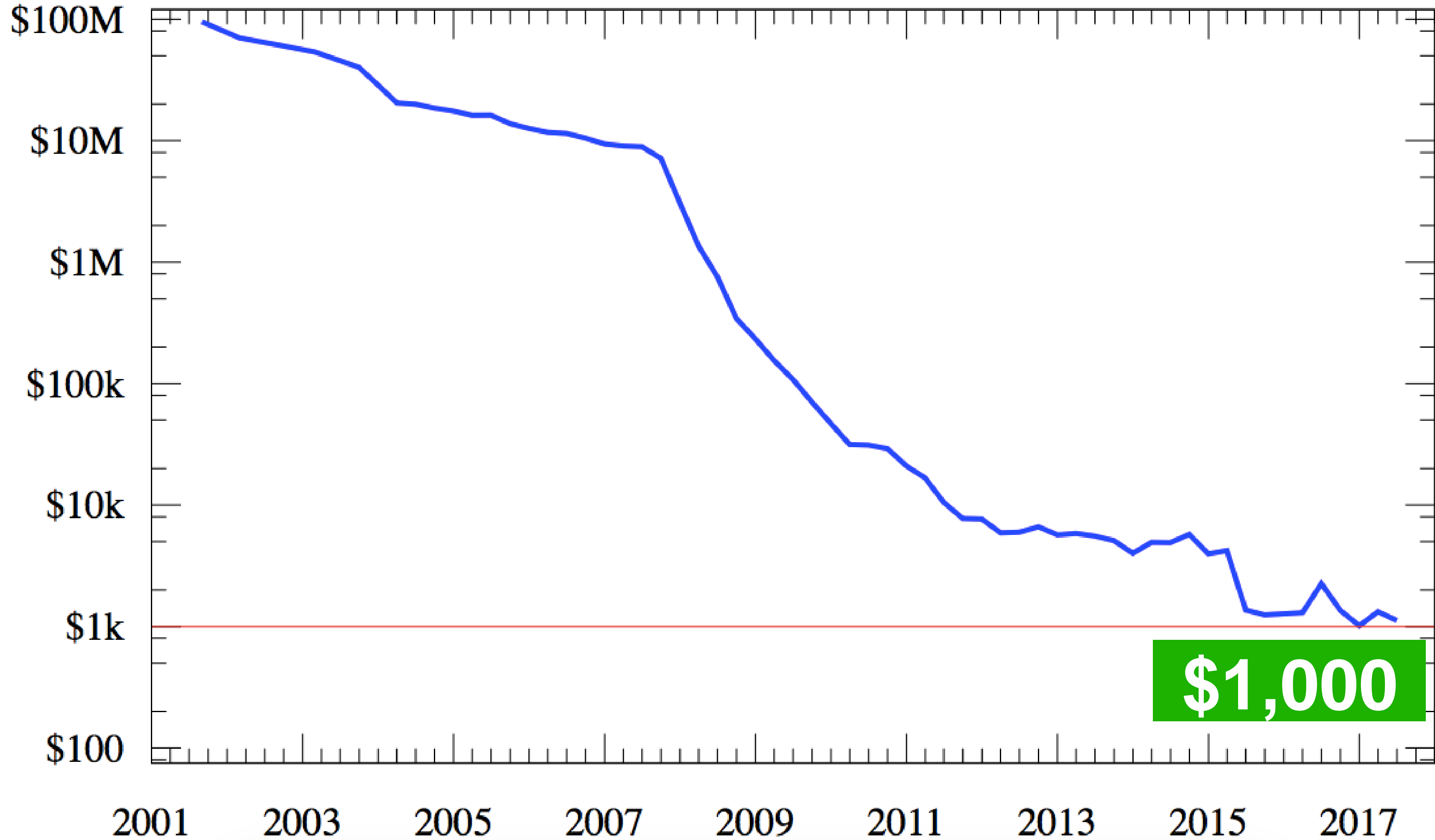
Cost to sequence a human genome (USD)

**\$100,000,000**



Cost to sequence a human genome (USD)

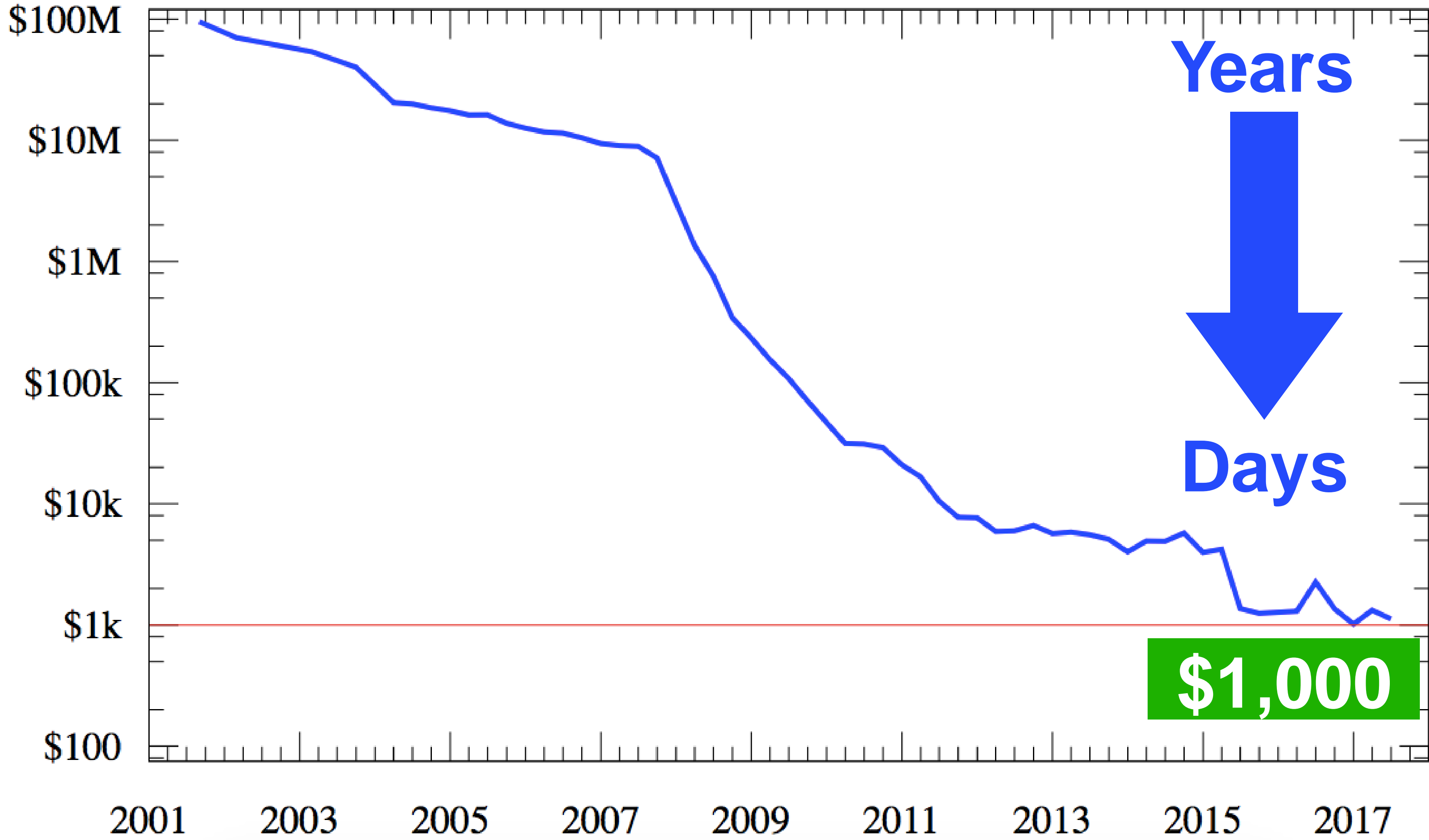
**\$100,000,000**



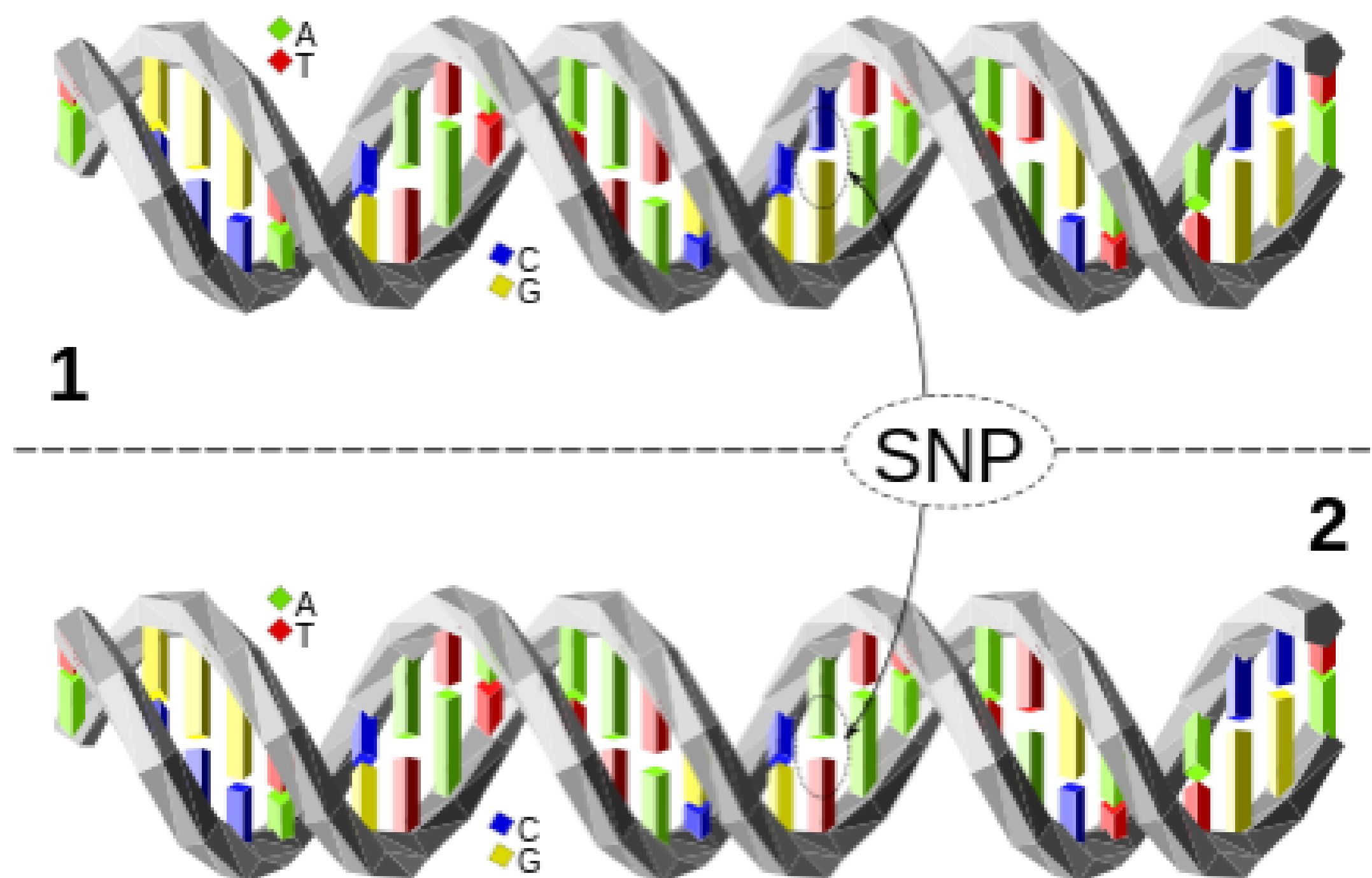
**\$1,000**

Cost to sequence a human genome (USD)

**\$100,000,000**



**\$1,000**

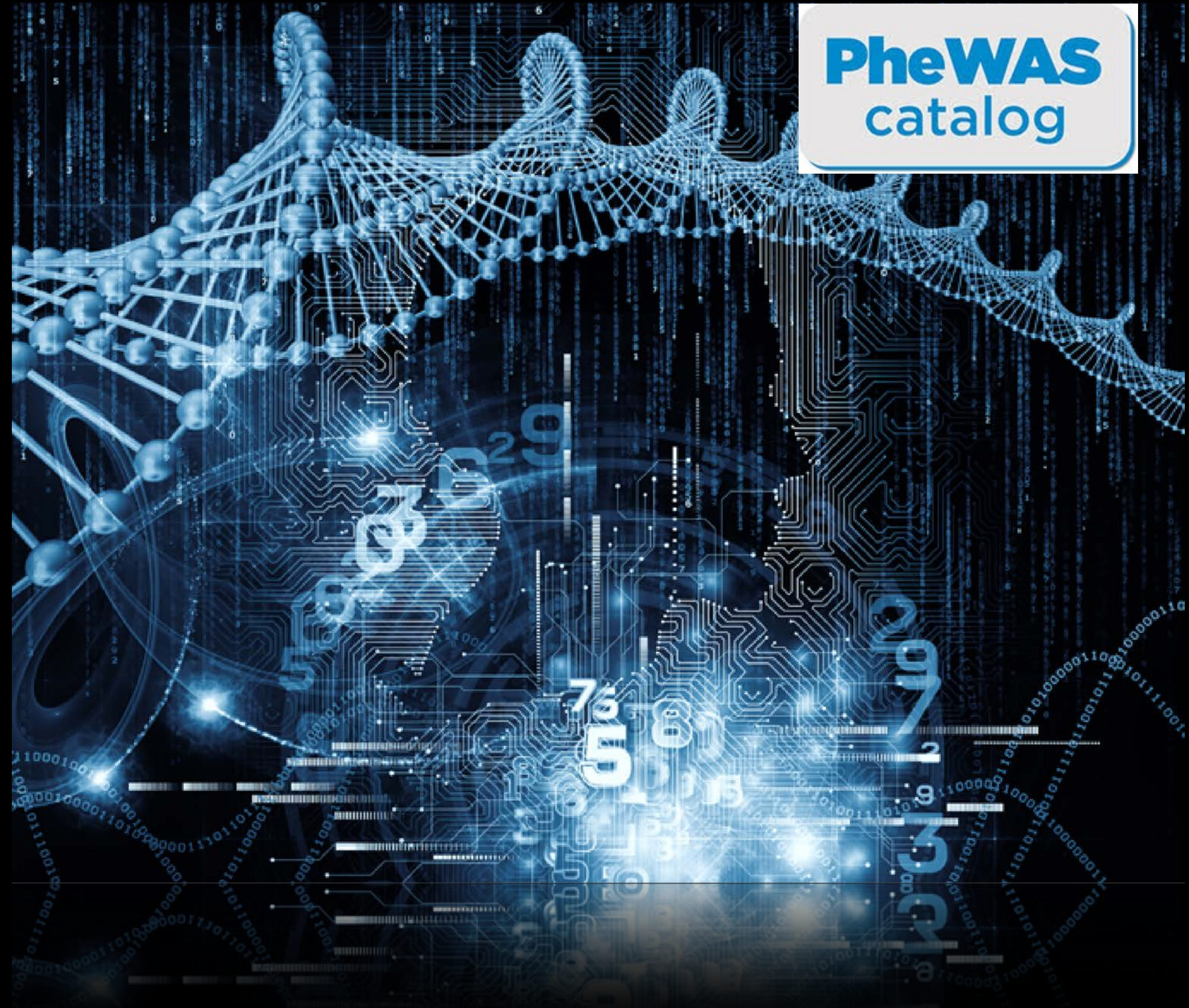


**SNPs; Single Nucleotide Polymorphisms**

# International HapMap Project



**PheWAS**  
catalog



**GWAS; Genome-Wide Association Studies**

**Trial  
and  
Error?**

for every person they help,



the 10 highest-grossing drugs in the USA fail to improve the conditions of

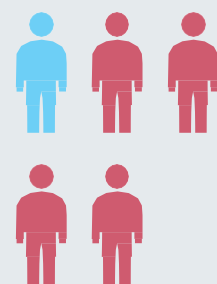
between 3 and 24 people



## IMPRECISION MEDICINE

For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

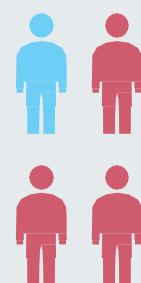
1. **ABLIFY** (aripiprazole)  
Schizophrenia



2. **NEXUM** (esomeprazole)  
Heartburn



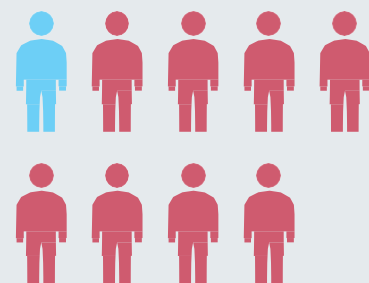
3. **HUMRA** (adalimumab)  
Arthritis



4. **CRESTOR** (rosuvastatin)  
High cholesterol



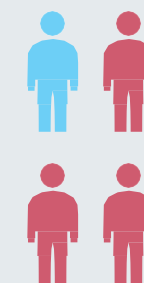
5. **CYMBALTA** (duloxetine)  
Depression



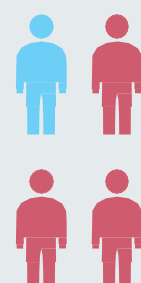
6. **ADVARDISKUS** (fluticasone propionate)  
Asthma



7. **ENBREL** (etanercept)  
Psoriasis



8. **REMICADE** (infliximab)  
Crohn's disease



9. **COPAXONE** (glatiramer acetate)  
Multiple sclerosis



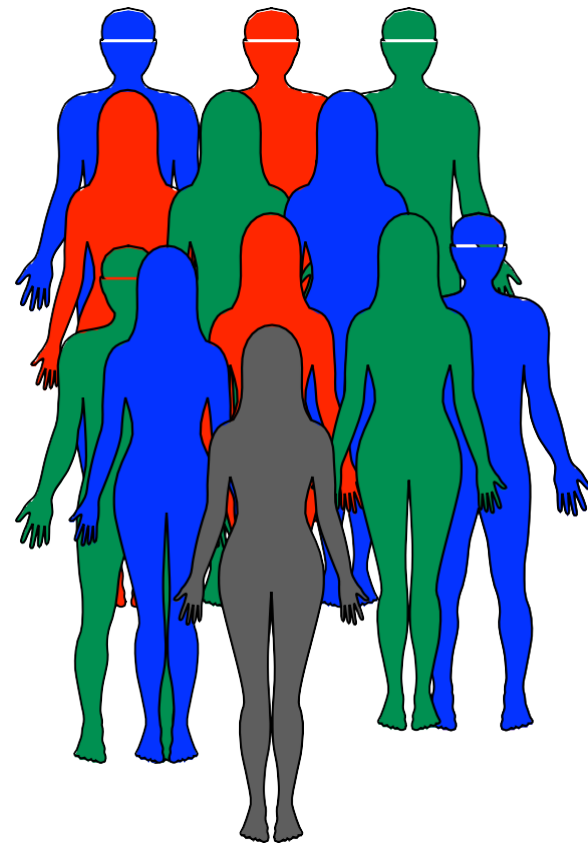
10. **NEULASTA** (pegfilgrastim)  
Neutropenia



Based on published number needed to treat (NNT) figures. For a full list of references, see Supplementary Information at [go.nature.com/4dr78f](http://go.nature.com/4dr78f).

from Schork, N  
Nature, 2015

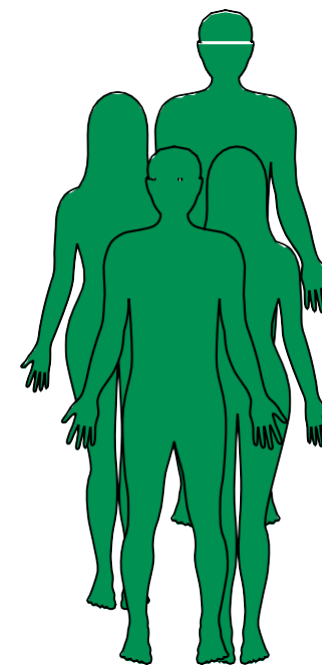
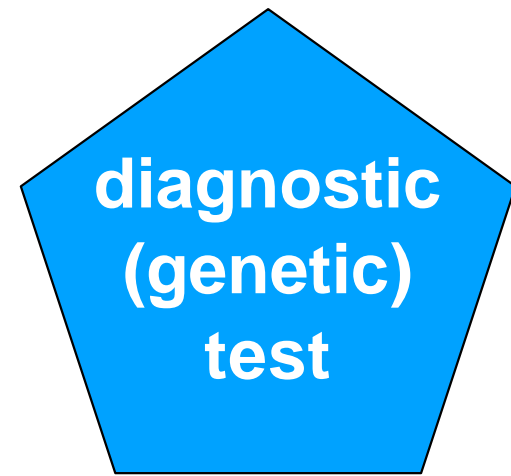
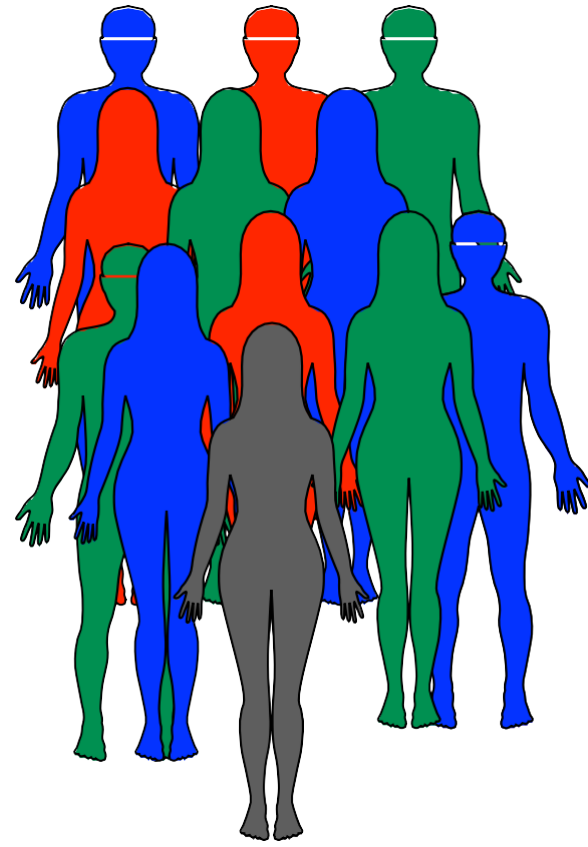
# Pharmacogenomics



diagnostic  
(genetic)  
test

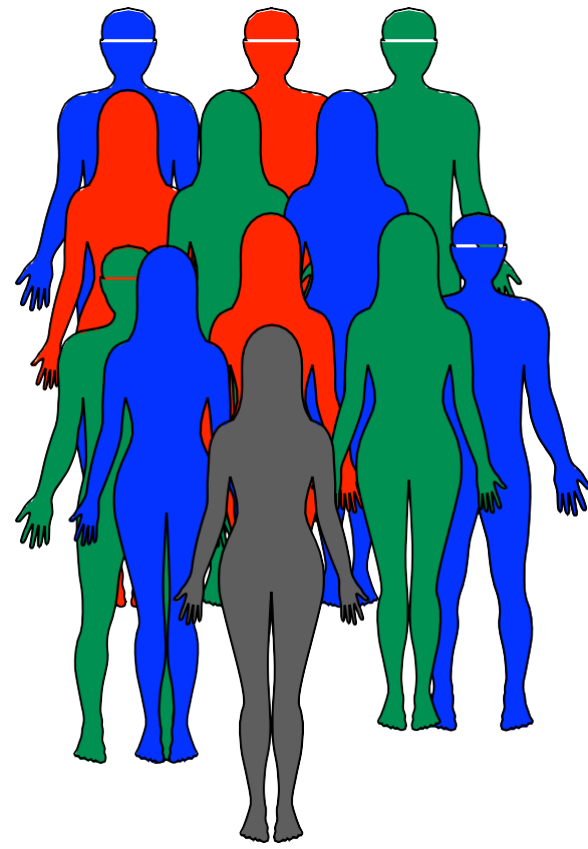


# Pharmacogenomics

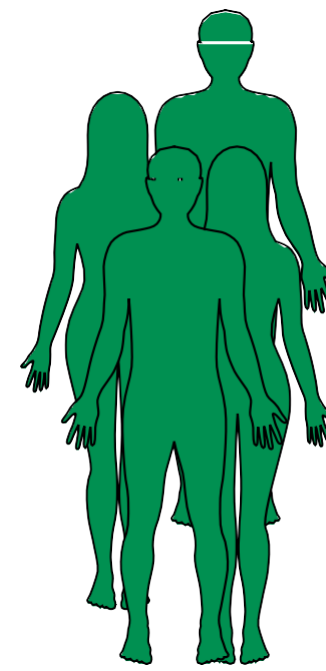


responders for Drug A

# Pharmacogenomics



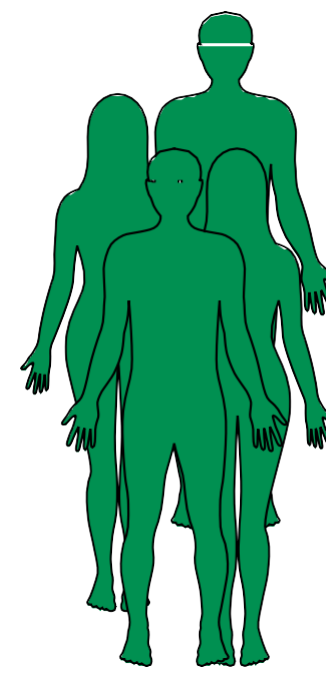
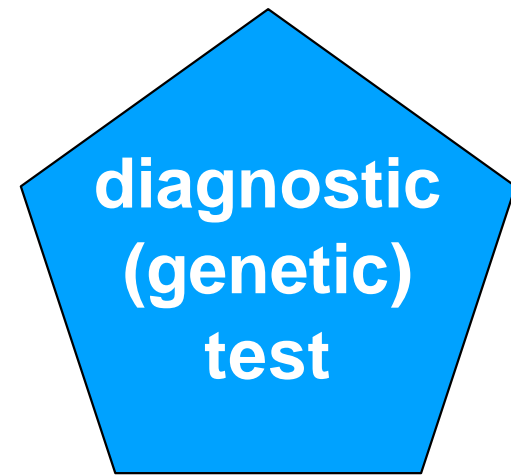
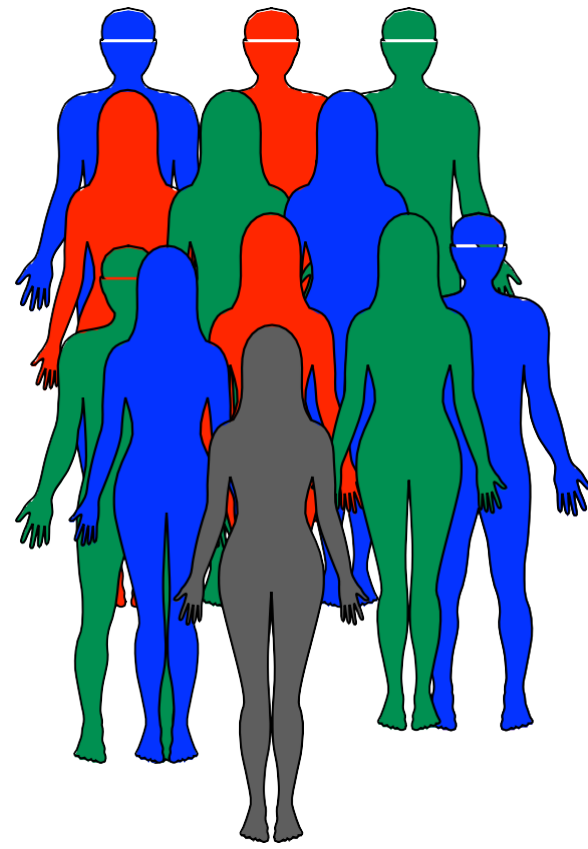
diagnostic  
(genetic)  
test



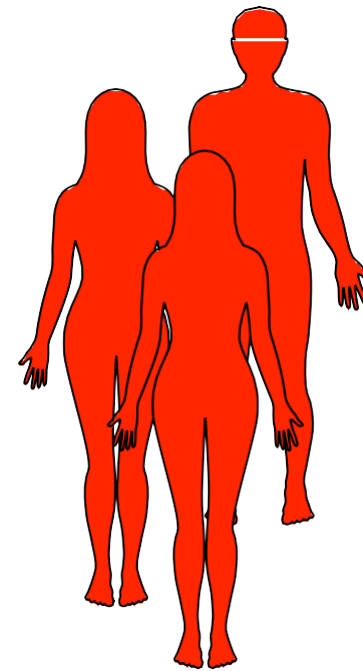
responders for Drug A



# Pharmacogenomics



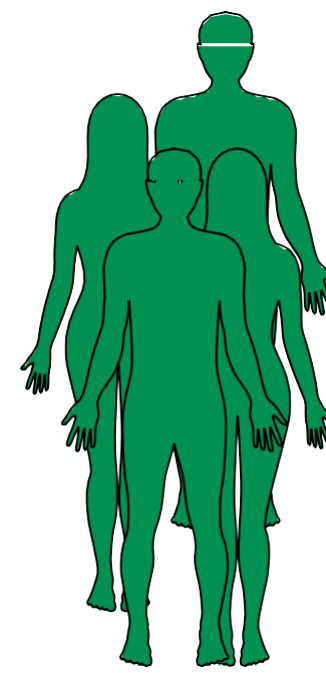
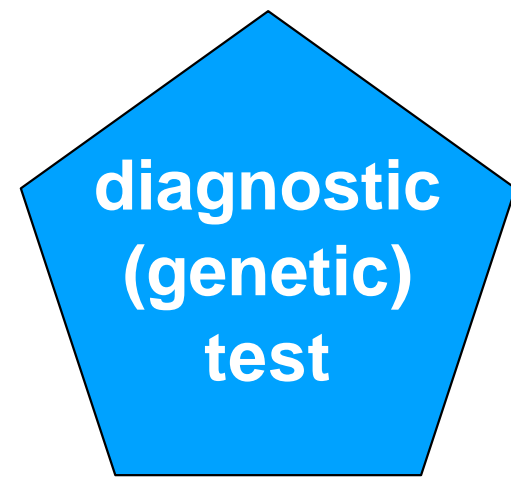
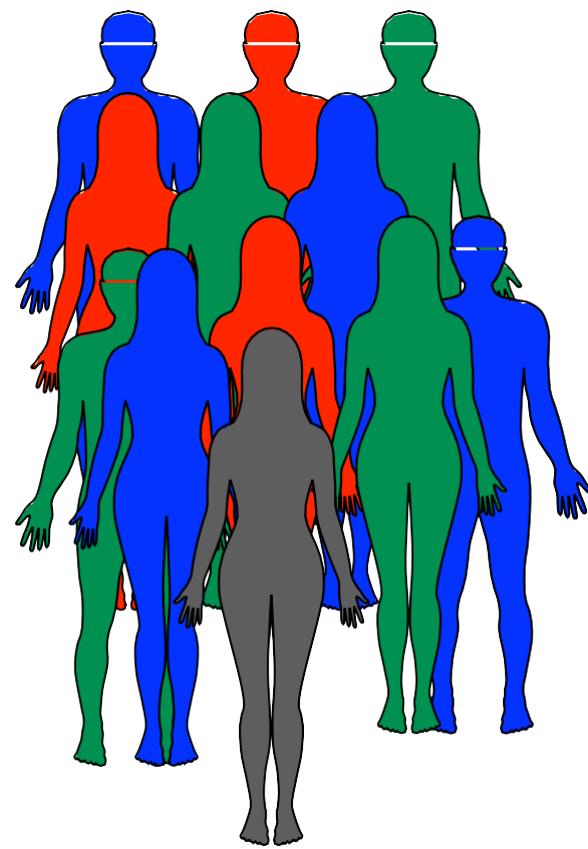
responders for Drug A



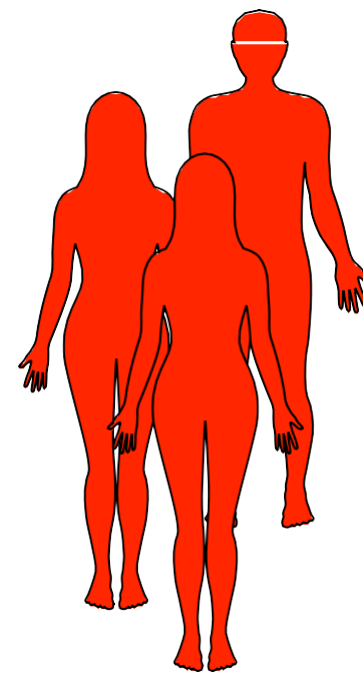
non-responders for Drug A



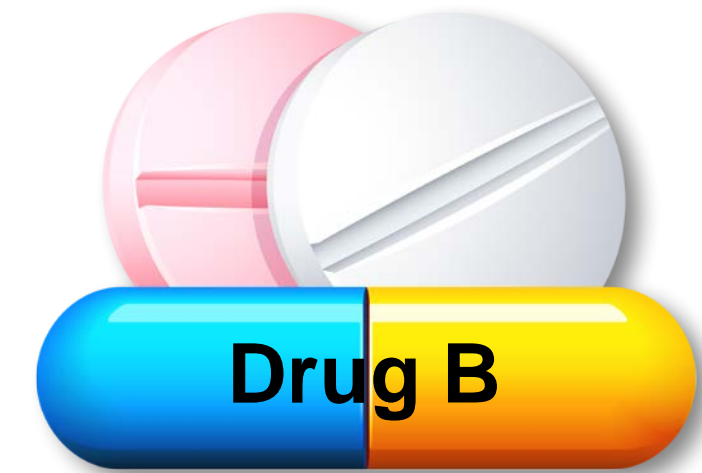
# Pharmacogenomics



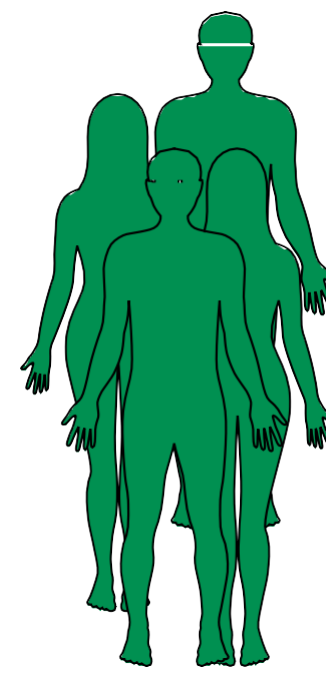
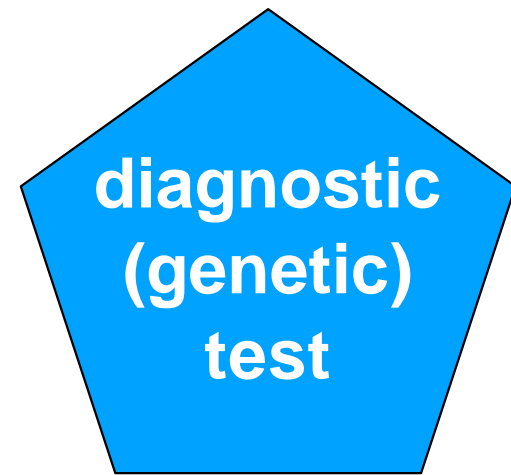
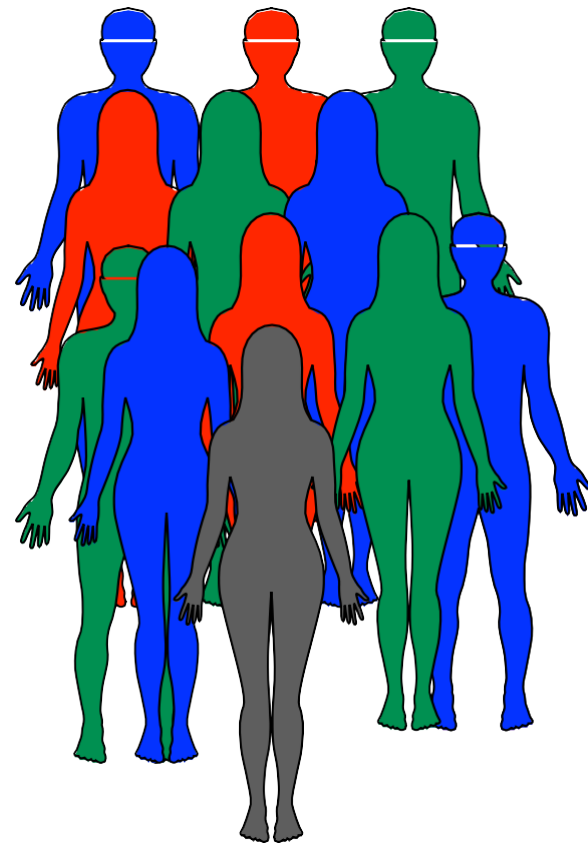
responders for Drug A



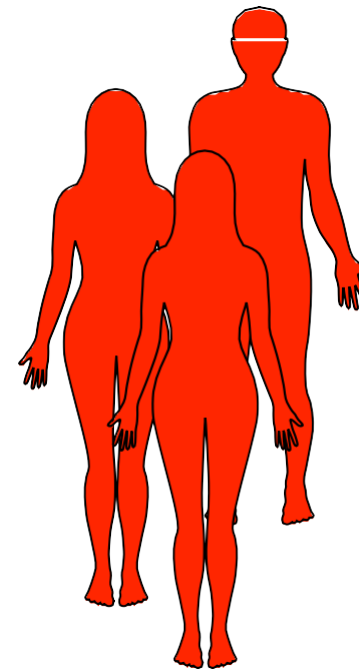
non-responders for Drug A



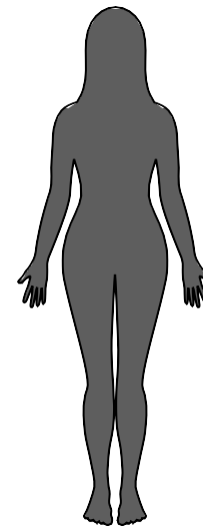
# Pharmacogenomics



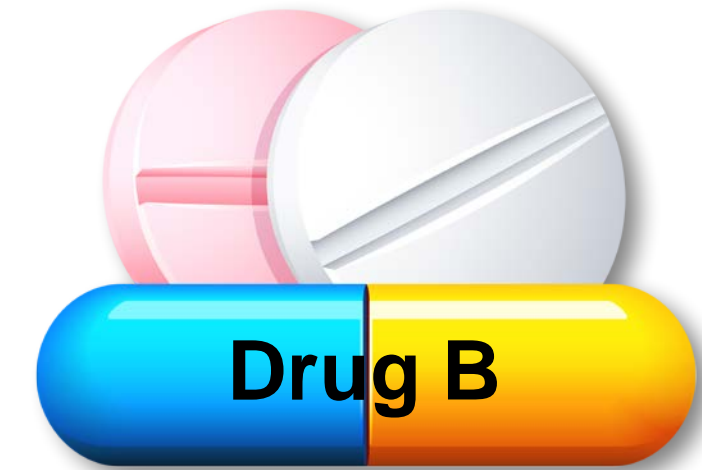
responders for Drug A



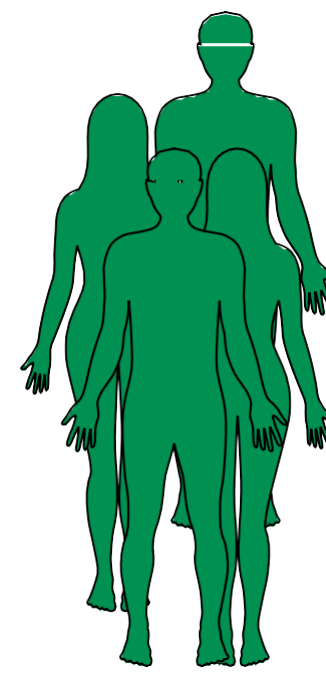
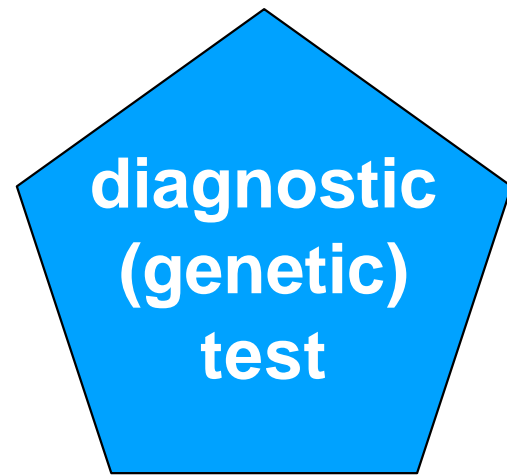
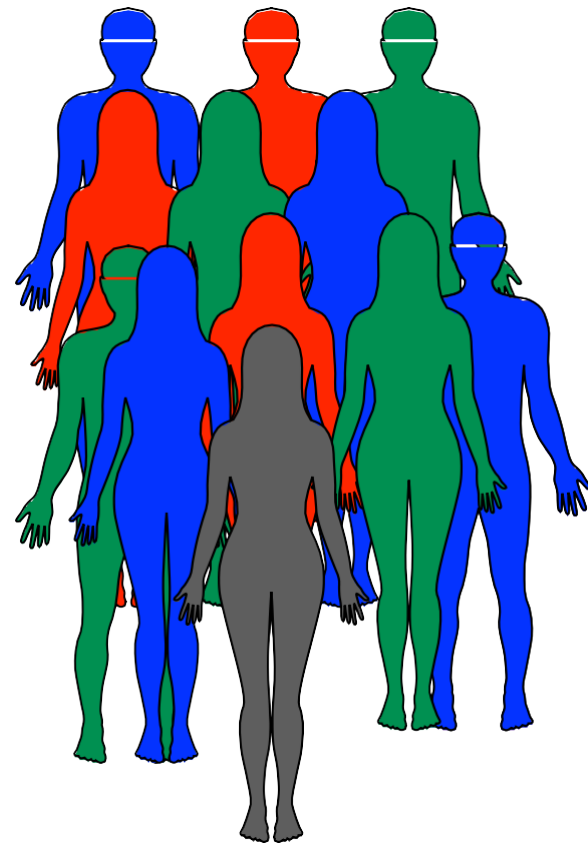
non-responders for Drug A



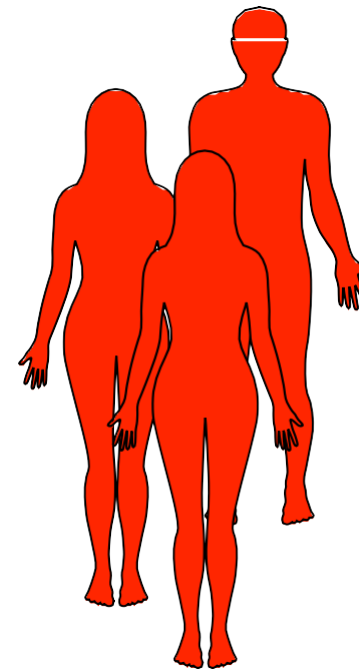
severe side effects predicted



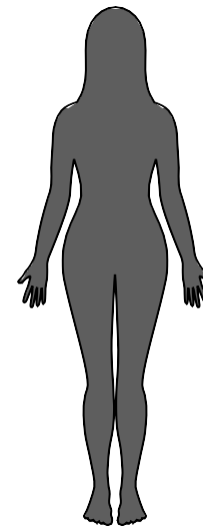
# Pharmacogenomics



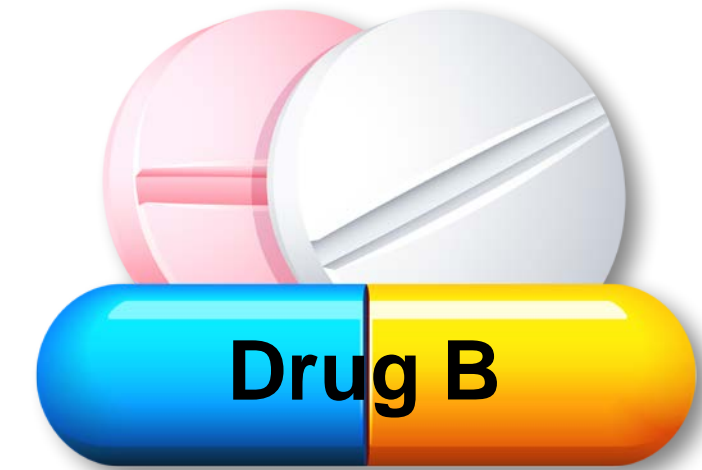
responders for Drug A



non-responders for Drug A



severe side effects predicted



**Personalised?**

**Personalised?**

**Precision?**



**Personalised?**

**Precision?**

**Stratified?**

# Precision Medicine

# Precision Medicine

- a **precise diagnosis**
- the **right drug**
- at the **right dosage**
- at the **right time**
- for the **right patient**
- at the **right price**

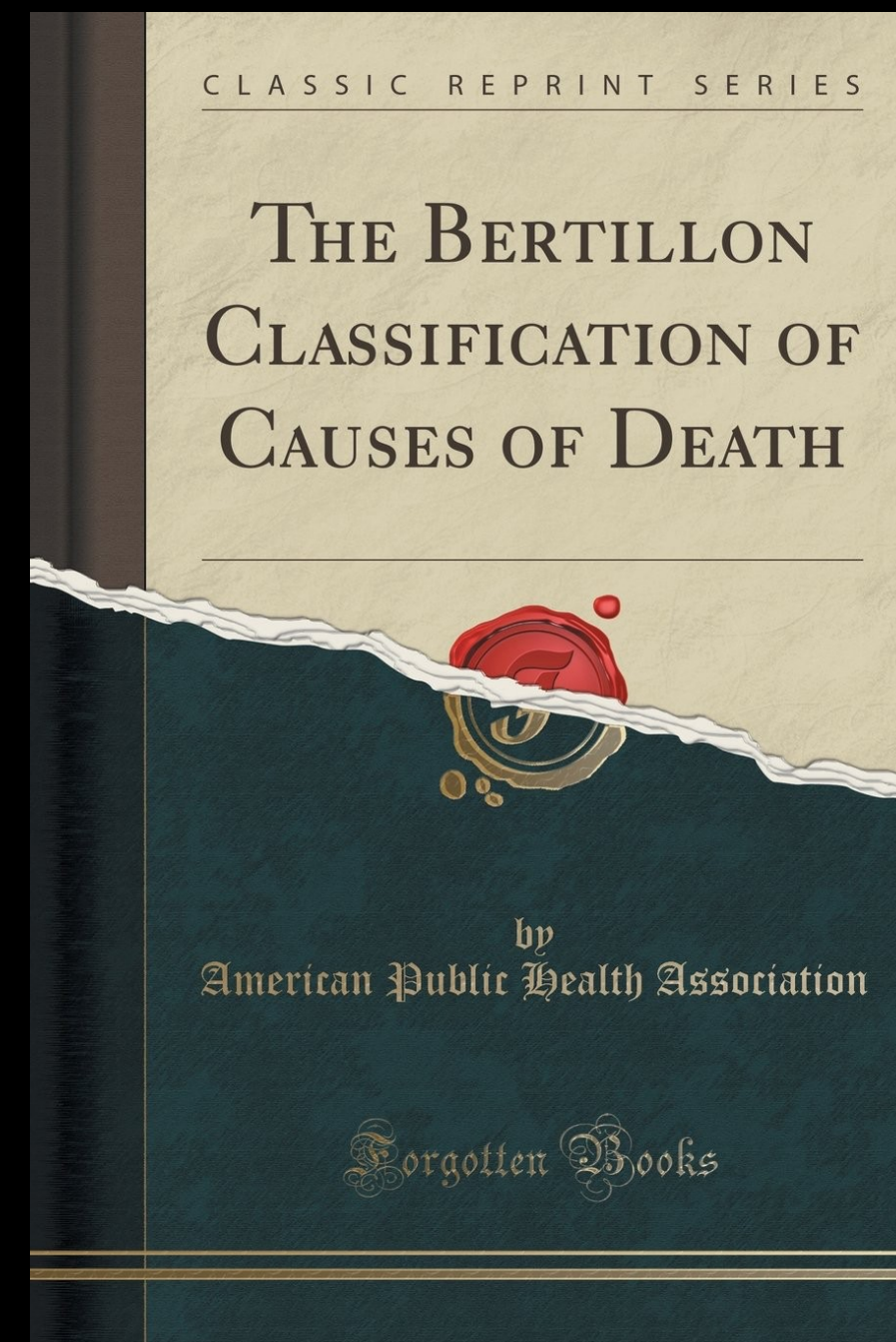
**With  
more detailed  
diagnosis  
comes the need for  
a new **taxonomy****



**Jacques Bertillon (1851-1922)**

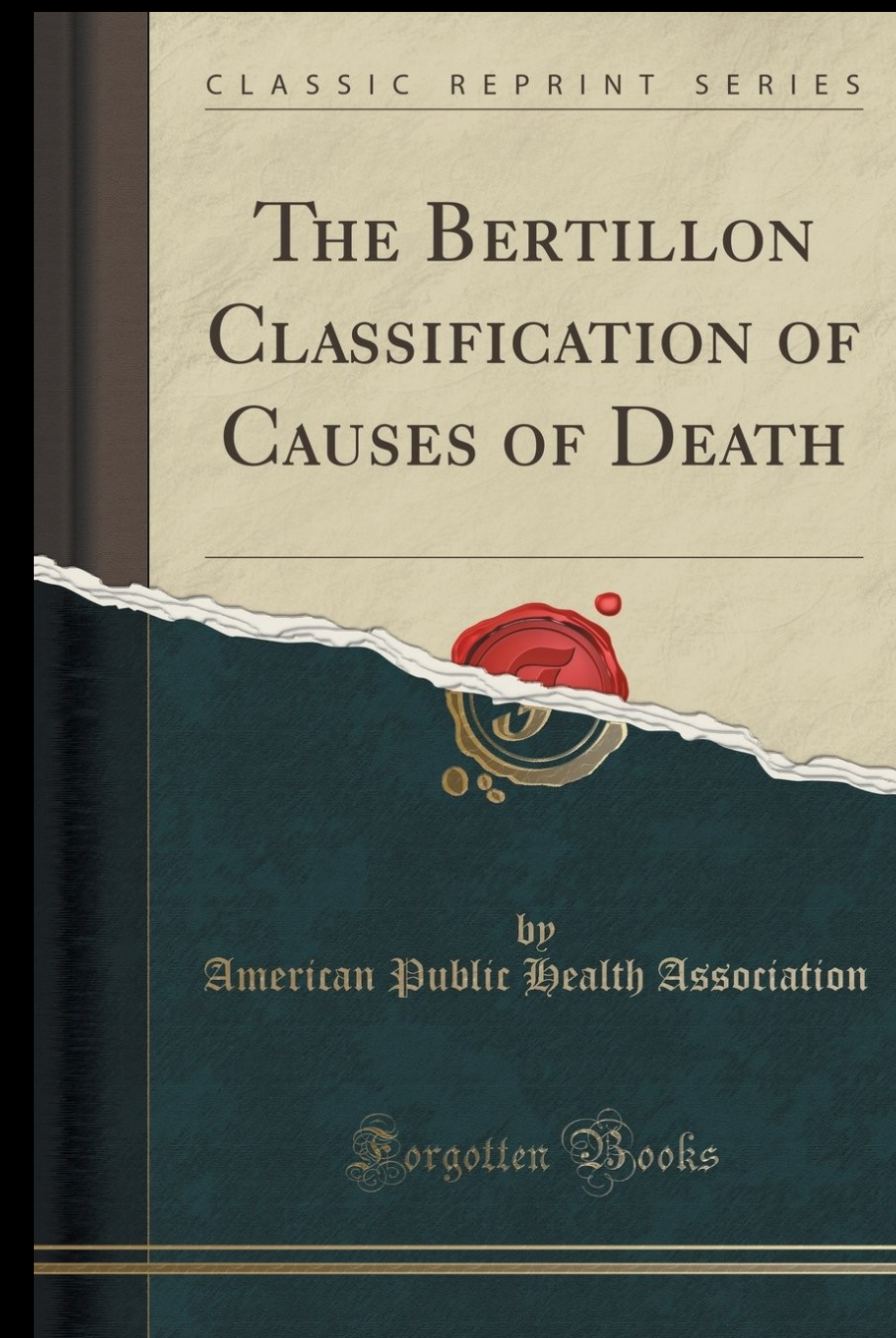


**Jacques Bertillon (1851-1922)**





**Jacques Bertillon (1851-1922)**



TENTH REVISION

# ICD-10

INTERNATIONAL CLASSIFICATION OF DISEASES

---

ICD-10 is a new code set for reporting medical diagnoses & inpatient procedures.

## CODING DIABETES MELLITUS

# Structural difference

## in ICD-10-CM versus ICD-9-CM

ICD-9-CM

1979-98

ICD-10-CM

1999-now

**249** Secondary diabetes mellitus

**E08** Diabetes mellitus due to underlying condition  
**E09** Drug or chemical induced diabetes mellitus  
**E13** Other specified diabetes mellitus

**250** Diabetes mellitus

**E10** Type 1 diabetes mellitus  
**E11** Type 2 diabetes mellitus

**648.0** Diabetes mellitus complicating pregnancy, childbirth, and the puerperium

**O24** Diabetes mellitus in pregnancy, childbirth, and the puerperium

**775.1** Neonatal diabetes mellitus

**P70.2** Neonatal diabetes mellitus



# CODING DIABETES MELLITUS

## Structural difference

### in ICD-10-CM versus ICD-9-CM

ICD-9-CM

1979-98

ICD-10-CM

1999-now

**249** Secondary diabetes mellitus

**E08** Diabetes mellitus due to underlying condition  
**E09** Drug or chemical induced diabetes mellitus  
**E13** Other specified diabetes mellitus

**250** Diabetes mellitus

**E10** Type 1 diabetes mellitus  
**E11** Type 2 diabetes mellitus

**648.0** Diabetes mellitus complicating pregnancy, childbirth, and the puerperium

**O24** Diabetes mellitus in pregnancy, childbirth, and the puerperium

**775.1** Neonatal diabetes mellitus

**P70.2** Neonatal diabetes mellitus

Source: Contexo Media

| Type                  | OMIM                  | Gene/protein                         |
|-----------------------|-----------------------|--------------------------------------|
| MODY 1                | 125850                | hepatocyte nuclear factor 4 $\alpha$ |
| MODY 2                | 125851                | glucokinase                          |
| MODY3                 | 600496                | hepatocyte nuclear factor 1 $\alpha$ |
| MODY 4                | 606392                | inulin promoter factor-1             |
| MODY 5                | 137920                | hepatic nuclear factor 1 $\beta$     |
| MODY 6                | 606394                | neurogenic differential 1            |
| MODY 7                | 610508                | Kruppel-like factor 11               |
| MODY 8                | 609812                | Bile salt dependent lipase           |
| MODY 9                | 612225                | PAX4                                 |
| MODY 10               | 613370                | INS                                  |
| MODY 11               | 613370                | BLK                                  |
| Permanent neonatal DM | 606176                | KCNJ11 and ABCC8                     |
| Transient neonatal DM | 601410,610374, 610582 | ABCC8                                |

**OMIM<sup>®</sup>**

**Online Mendelian Inheritance in Man<sup>®</sup>**

**An Online Catalog of Human Genes and Genetic Disorders**

Updated February 28, 2018

All Content

Search

[Advanced Search](#)

[< Previous Article](#)

Online First

[Next Article >](#)

Articles

## Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables

Emma Ahlqvist, PhD, [Petter Storm](#), PhD, [Annemari Käräjämäki](#), MD<sup>†</sup>, [Mats Martinell](#), MD<sup>†</sup>, [Mozhgan Dorkhan](#), PhD, [Annelie Carlsson](#), PhD, [Petter Vikman](#), PhD, [Rashmi B Prasad](#), PhD, [Dina Mansour Aly](#), MSc, [Peter Almgren](#), MSc, [Ylva Wessman](#), MSc, [Nael Shaat](#), PhD, [Peter Spégel](#), PhD, Prof [Hindrik Mulder](#), PhD, [Eero Lindholm](#), PhD, Prof [Olle Melander](#), PhD, [Ola Hansson](#), PhD, [Ulf Malmqvist](#), PhD, Prof [Åke Lernmark](#), PhD, [Kaj Lahti](#), MD, [Tom Forsén](#), PhD, [Tiinamaija Tuomi](#), PhD, [Anders H Rosengren](#), PhD, Prof [Leif Groop](#), PhD  

**Additional phenotypic sub-divisions**

## Novel subgroups of adult-onset diabetes and their association with outcomes: a data-driven cluster analysis of six variables

Emma Ahlqvist, PhD, Petter Storm, PhD, Annemari Käräjämäki, MD<sup>†</sup>, Mats Martinell, MD<sup>†</sup>, Mozhgan Dorkhan, PhD, Annelie Carlsson, PhD, Petter Vikman, PhD, Rashmi B Prasad, PhD, Dina Mansour Aly, MSc, Peter Almgren, MSc, Ylva Wessman, MSc, Nael Shaat, PhD, Peter Spégel, PhD, Prof Hindrik Mulder, PhD, Eero Lindholm, PhD, Prof Olle Melander, PhD, Ola Hansson, PhD, Ulf Malmqvist, PhD, Prof Åke Lernmark, PhD, Kaj Lahti, MD, Tom Forsén, PhD, Tiinamaija Tuomi, PhD, Anders H Rosengren, PhD, Prof Leif Groop, PhD

## Additional phenotypic sub-divisions

### Summary

#### Background

Diabetes is presently classified into two main forms, type 1 and type 2 diabetes, but type 2 diabetes in particular is highly heterogeneous. A refined classification could provide a powerful tool to individualise treatment regimens and identify individuals with increased risk of complications at diagnosis.

#### Methods

We did data-driven cluster analysis (k-means and hierarchical clustering) in patients with newly diagnosed diabetes (n=8980) from the Swedish All New Diabetics in Scania cohort. Clusters were based on six variables (glutamate decarboxylase antibodies, age at diagnosis, BMI, HbA<sub>1c</sub>, and homoeostatic model assessment 2 estimates of  $\beta$ -cell function and insulin resistance), and were related to prospective data from patient records on development of complications and prescription of medication. Replication was done in three independent cohorts: the Scania Diabetes Registry (n=1466), All New Diabetics in Uppsala (n=844), and Diabetes Registry Vaasa (n=3485). Cox regression and logistic regression were used to compare time to medication, time to reaching the treatment goal, and risk of diabetic complications and genetic associations.

#### Findings

We identified five replicable clusters of patients with diabetes, which had significantly different patient characteristics and risk of diabetic complications. In particular, individuals in cluster 3 (most resistant to insulin) had significantly higher risk of diabetic kidney disease than individuals in clusters 4 and 5, but had been prescribed similar diabetes treatment. Cluster 2 (insulin deficient) had the highest risk of retinopathy. In support of the clustering, genetic associations in the clusters differed from those seen in traditional type 2 diabetes.

#### Interpretation

We stratified patients into five subgroups with differing disease progression and risk of diabetic complications. This new substratification might eventually help to tailor and target early treatment to patients who would benefit most, thereby representing a first step towards precision medicine in diabetes.

## Findings

We identified five replicable clusters of patients with diabetes, which had significantly different patient characteristics and risk of diabetic complications. In particular, individuals in cluster 3 (most resistant to insulin) had significantly higher risk of diabetic kidney disease than individuals in clusters 4 and 5, but had been prescribed similar diabetes treatment. Cluster 2 (insulin deficient) had the highest risk of retinopathy. In support of the clustering, genetic associations in the clusters differed from those seen in traditional type 2 diabetes.

## Additional phenotypic sub-divisions

### Summary

#### Background

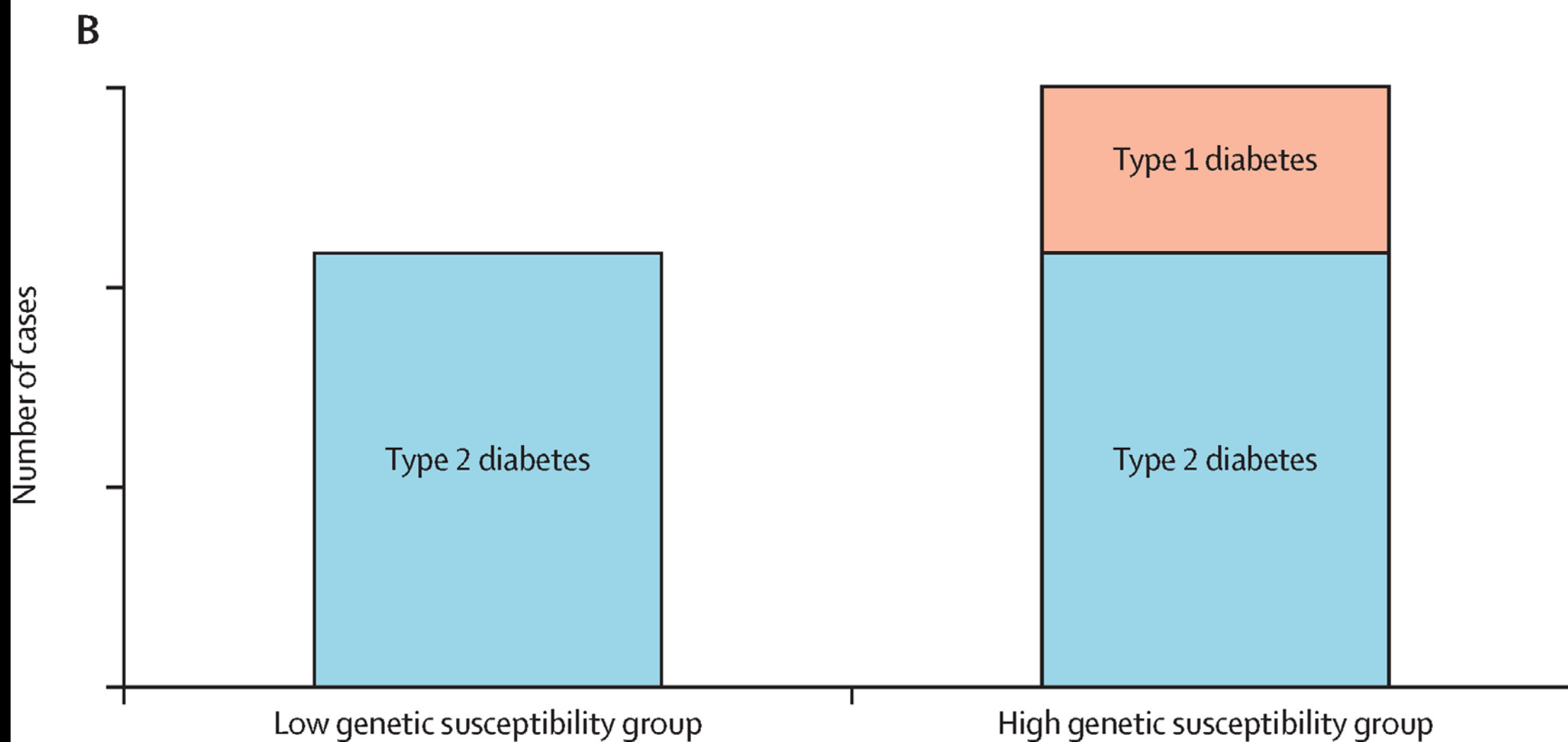
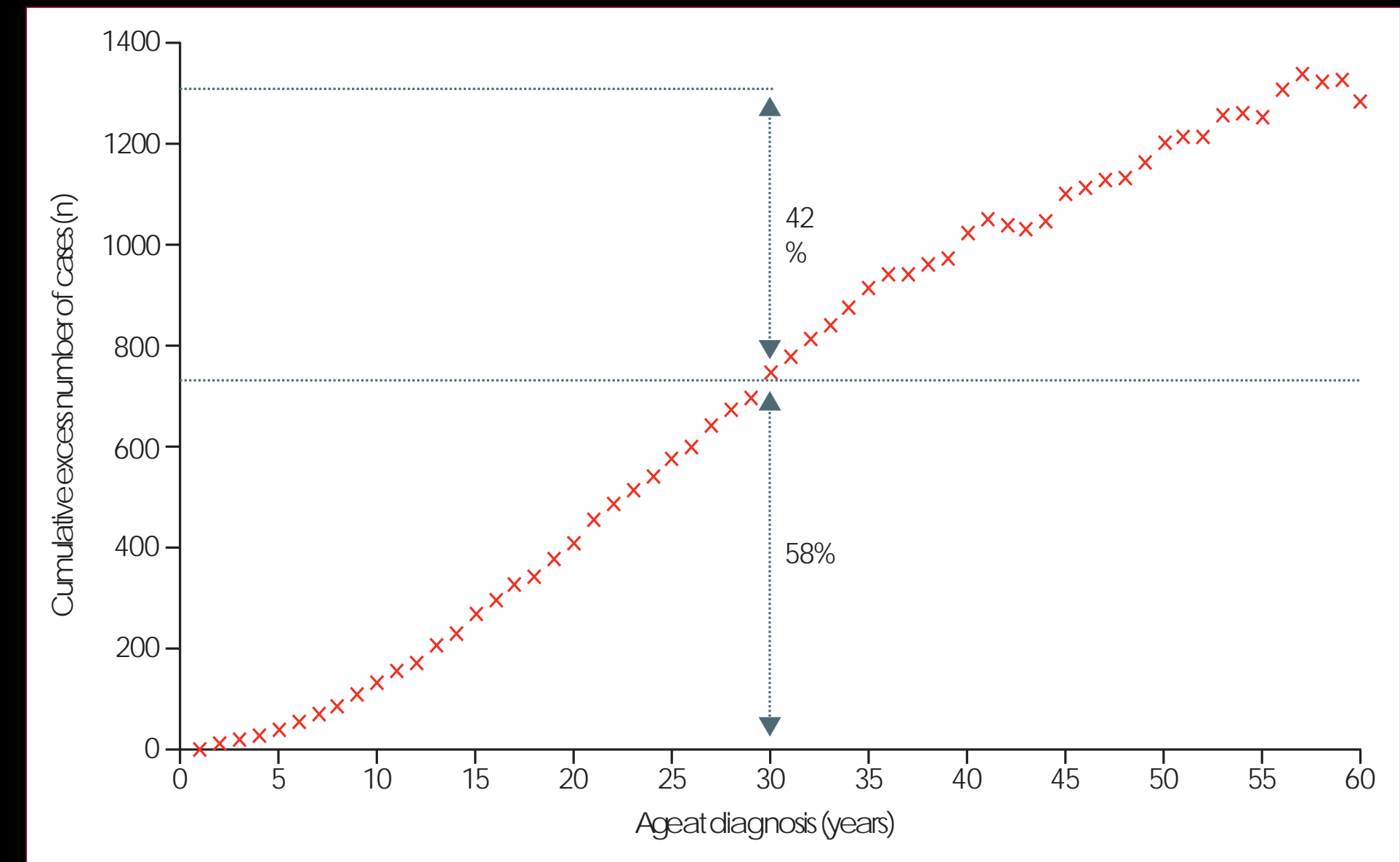
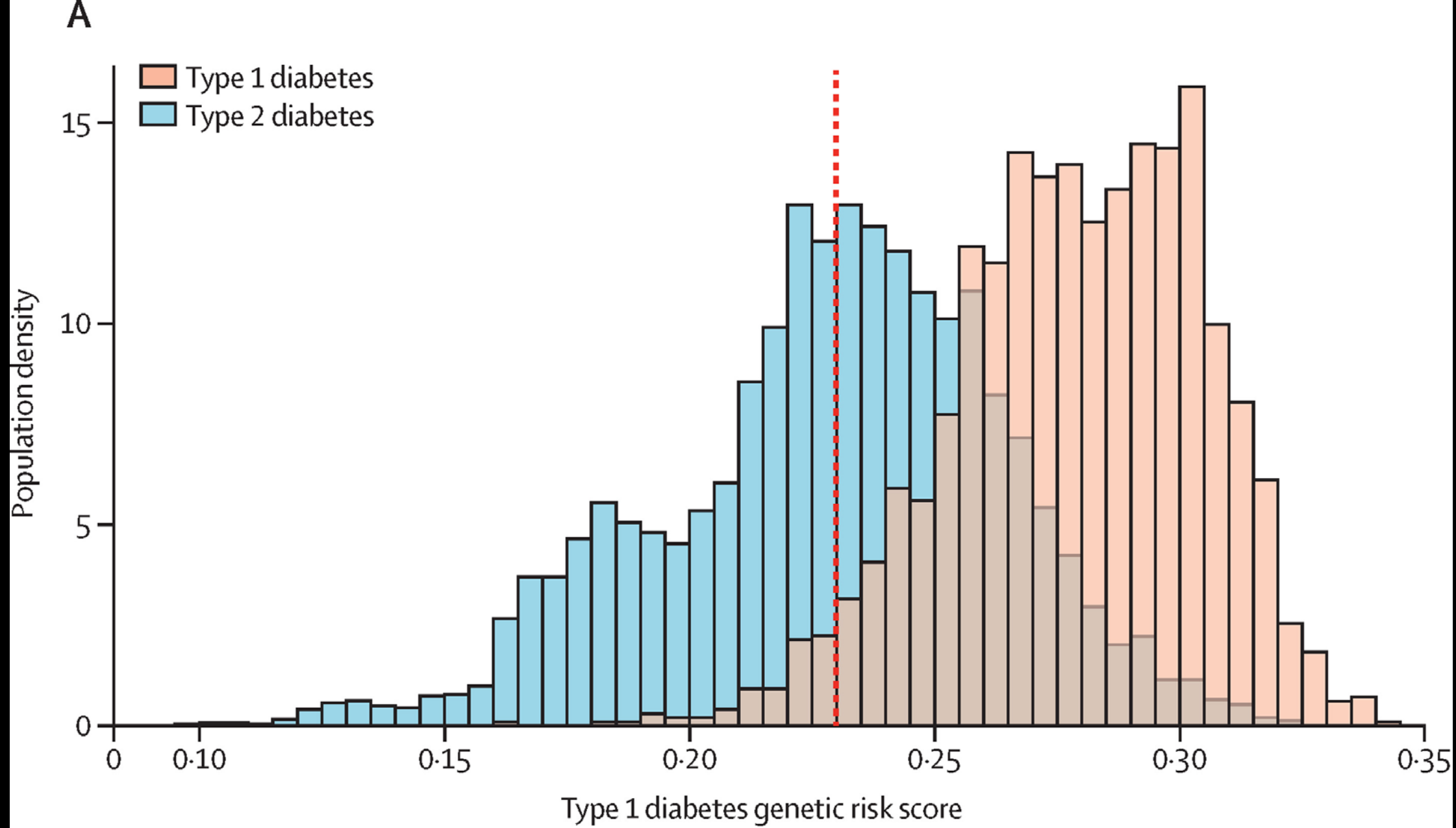
Diabetes is presently classified into two main forms, type 1 and type 2 diabetes, but type 2 diabetes in particular is highly heterogeneous. A refined classification could provide a powerful tool to individualise treatment regimens and identify individuals with increased risk of complications at diagnosis.

#### Methods

We did data-driven cluster analysis (k-means and hierarchical clustering) in patients with newly

#### Interpretation

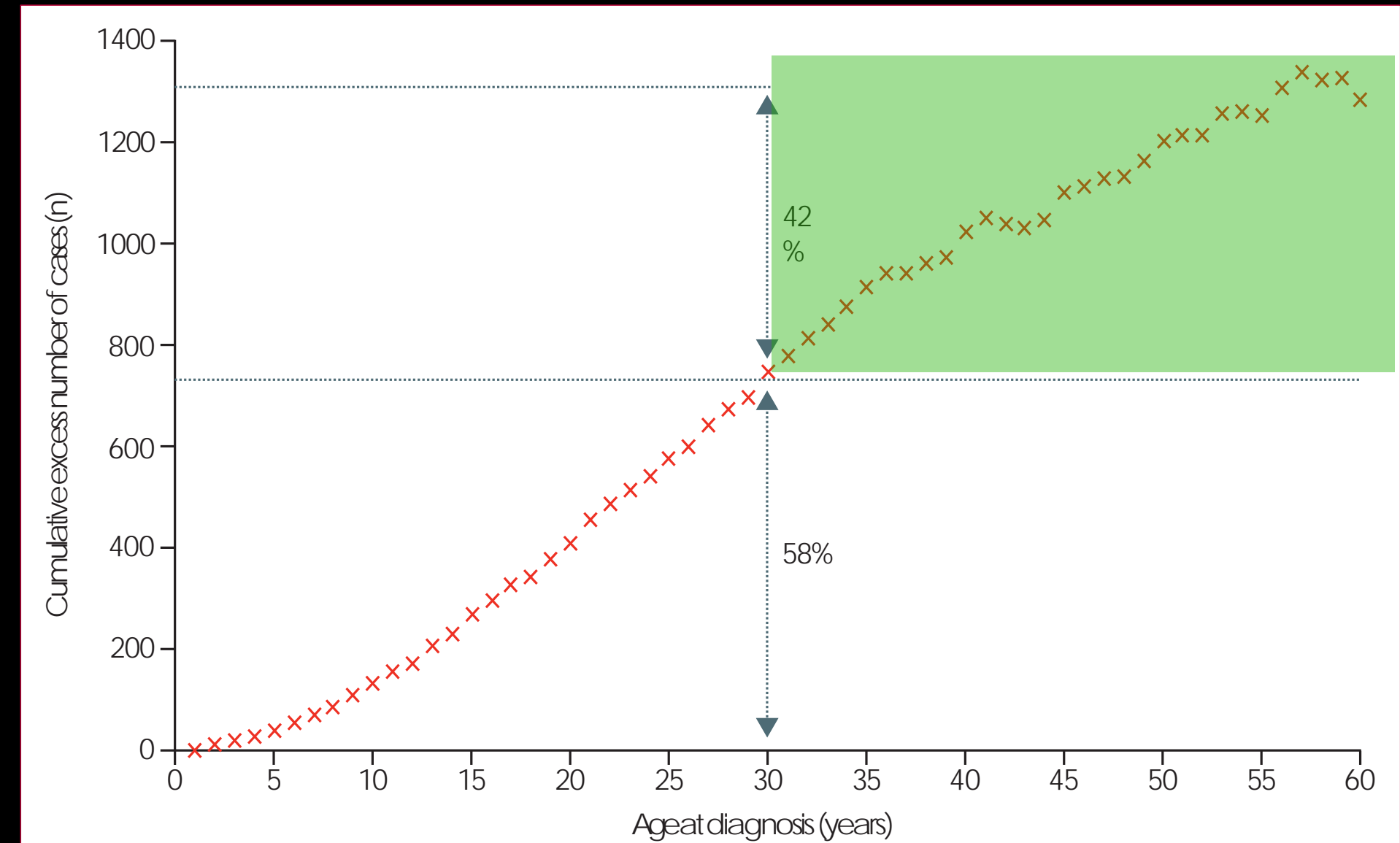
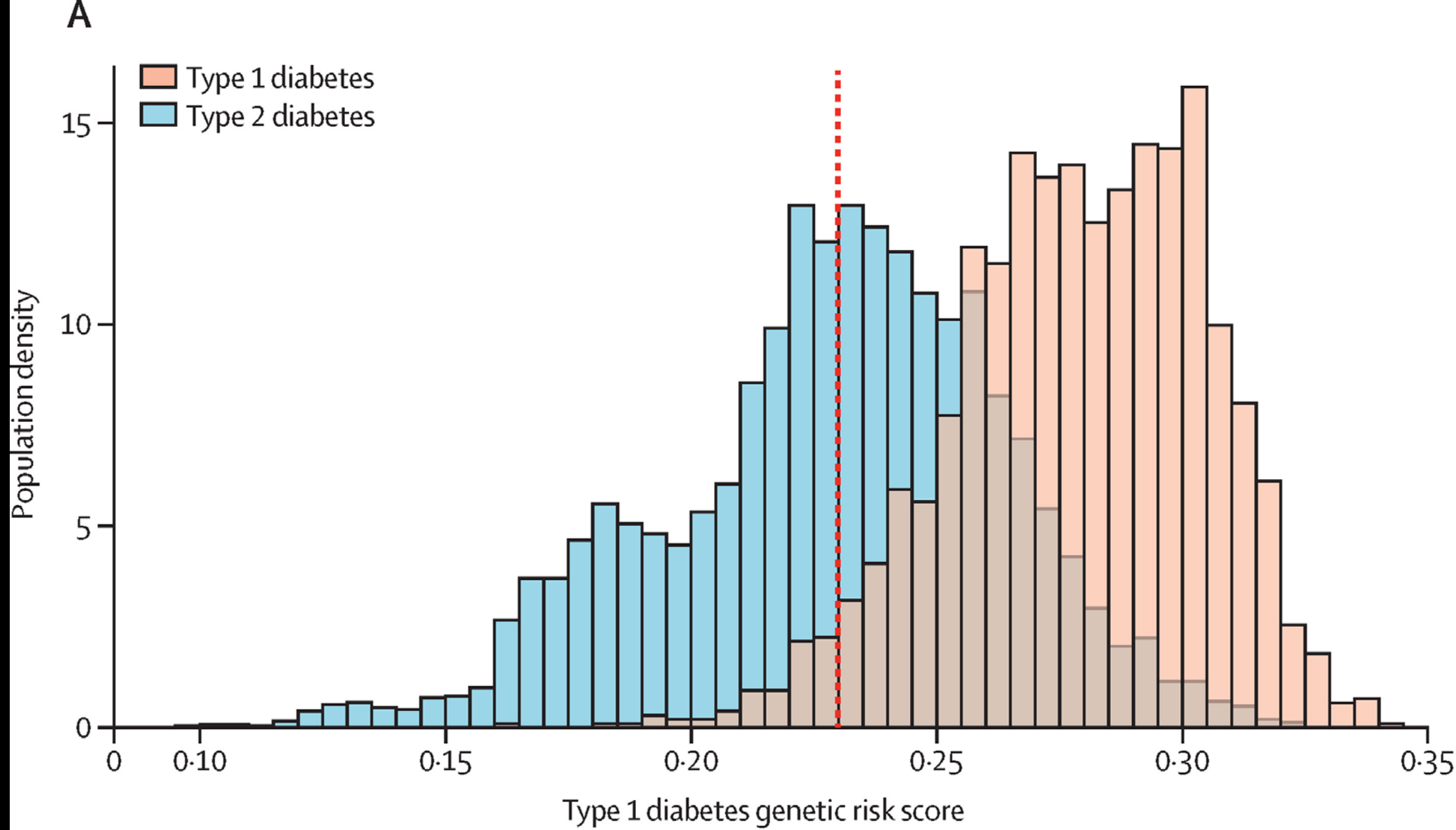
We stratified patients into five subgroups with differing disease progression and risk of diabetic complications. This new substratification might eventually help to tailor and target early treatment to patients who would benefit most, thereby representing a first step towards precision medicine in diabetes.



*Figure 3: Cumulative excess of genetically defined cases of type 1 diabetes occurring throughout the first six decades of life*

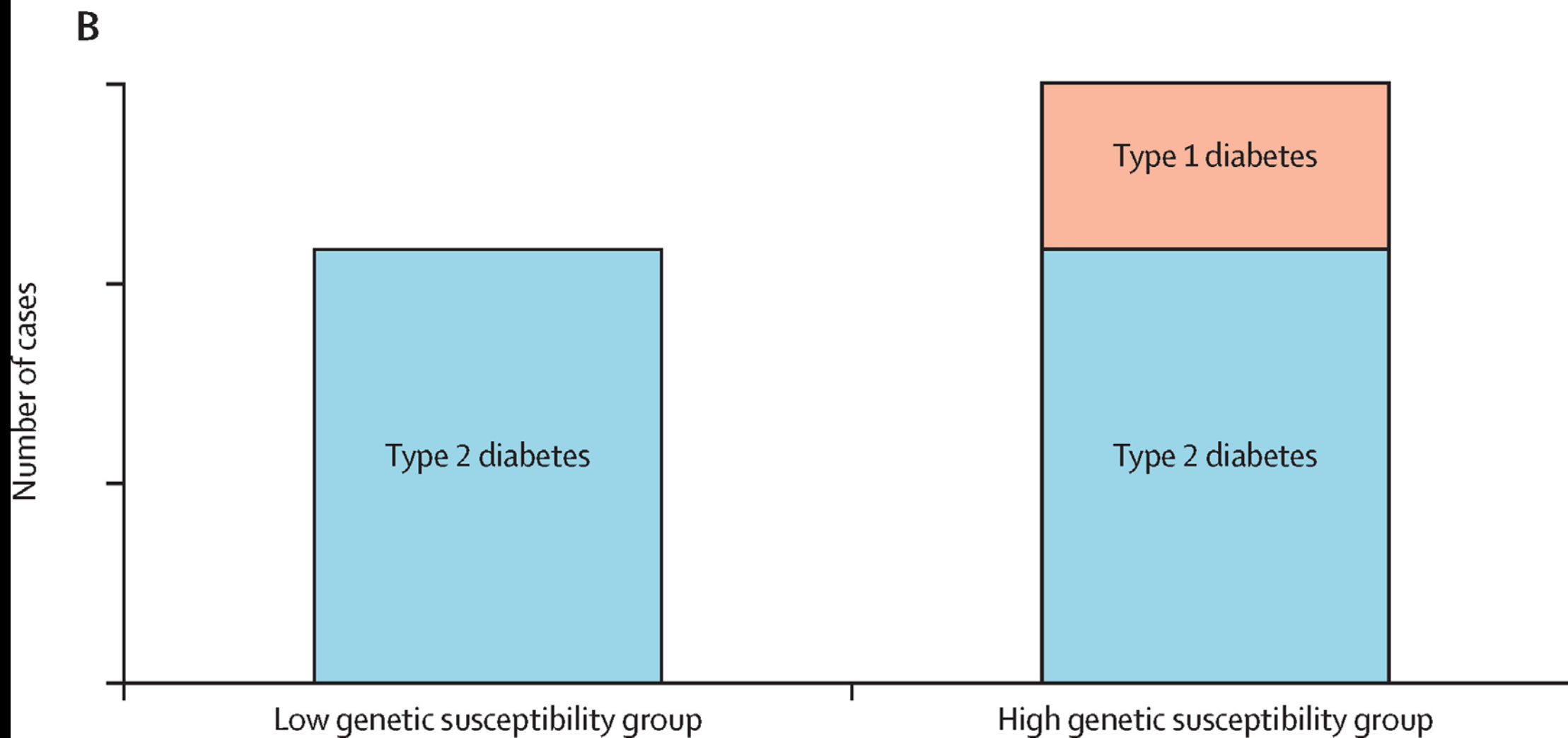
58% (749/1286) of type 1 diabetes cases were diagnosed when individuals were aged 30 years or younger; 42% (537/1286) were diagnosed when individuals were aged 31–60 years.

**Thomas, NJ et al**  
**Lancet Diabetes Endocrinol 2018; 6: 122–29**

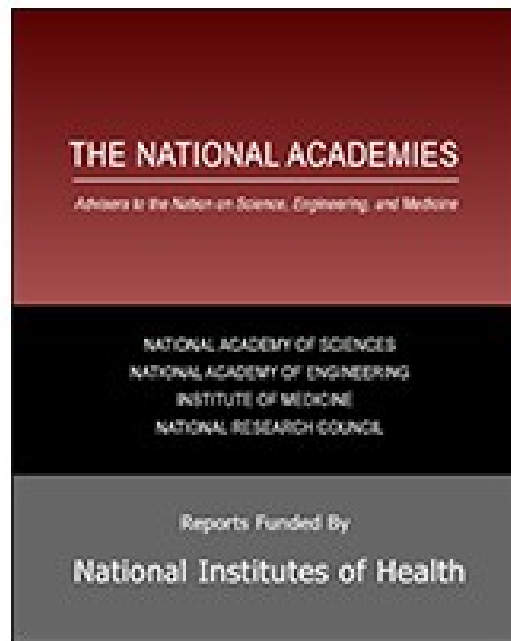


*Figure 3: Cumulative excess of genetically defined cases of type 1 diabetes occurring throughout the first six decades of life*

58% (749/1286) of type 1 diabetes cases were diagnosed when individuals were aged 30 years or younger; 42% (537/1286) were diagnosed when individuals were aged 31–60 years.



**Thomas, NJ et al**  
**Lancet Diabetes Endocrinol 2018; 6: 122–29**



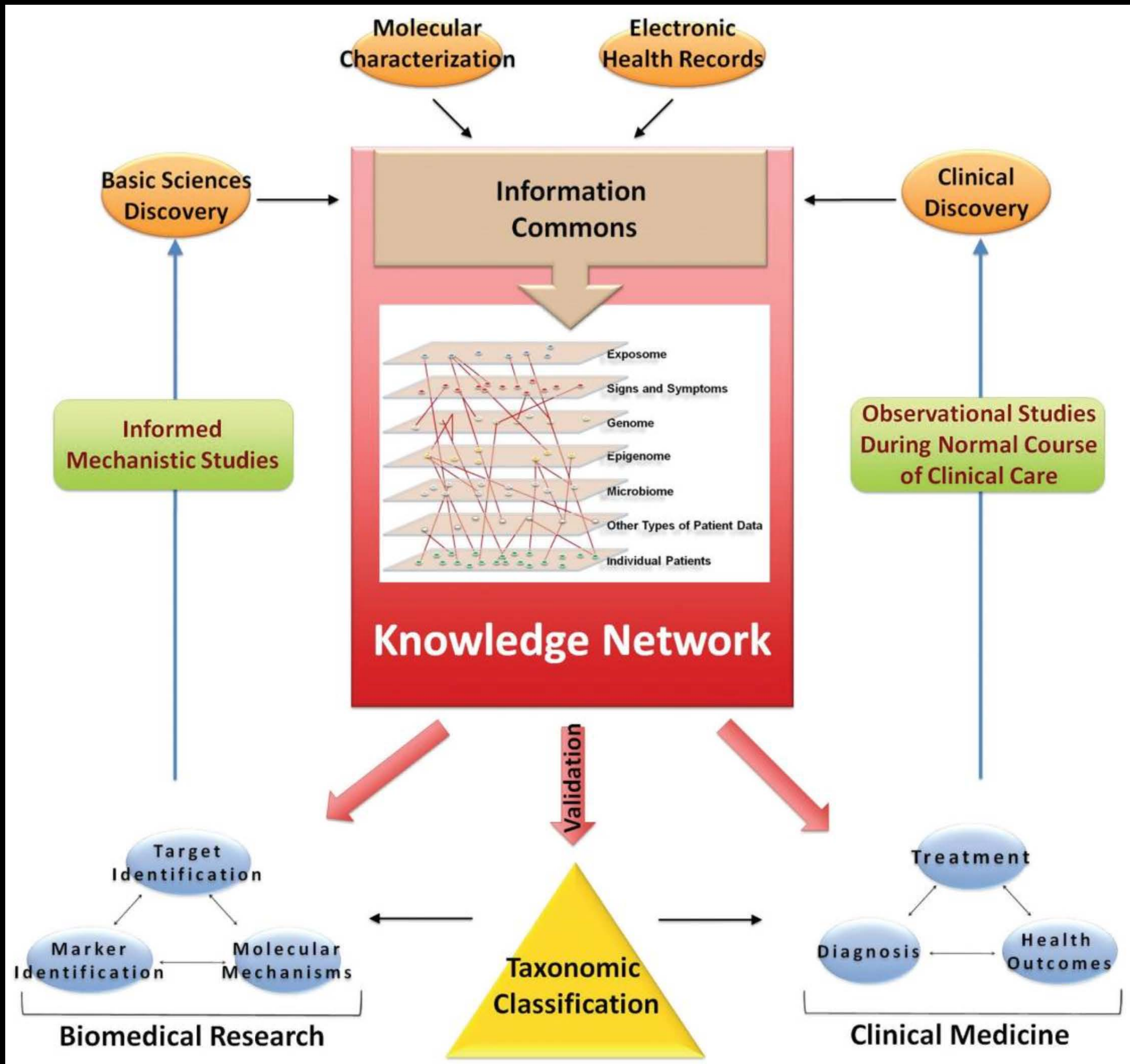
# Toward Precision Medicine: Building a Knowledge Network for Biomedical Research and a New Taxonomy of Disease.

## ▼ [Show details](#)

National Research Council (US) Committee on A Framework for Developing a New Taxonomy of Disease.

Washington (DC): [National Academies Press \(US\)](#); 2011.





# Genetic Testing to Guide Treatment in Cancer

- **Philadelphia Translocation in Chronic Myeloid Leukaemia**
  - **treatment with imatinib doubled survival rates**
- **Tumour cells carrying mutated EGFR gene (and not a mutated KRAS gene) in colon cancer**
  - **improved survival with cetuximab**



BRCA Gene 1

**Chromosome 17**



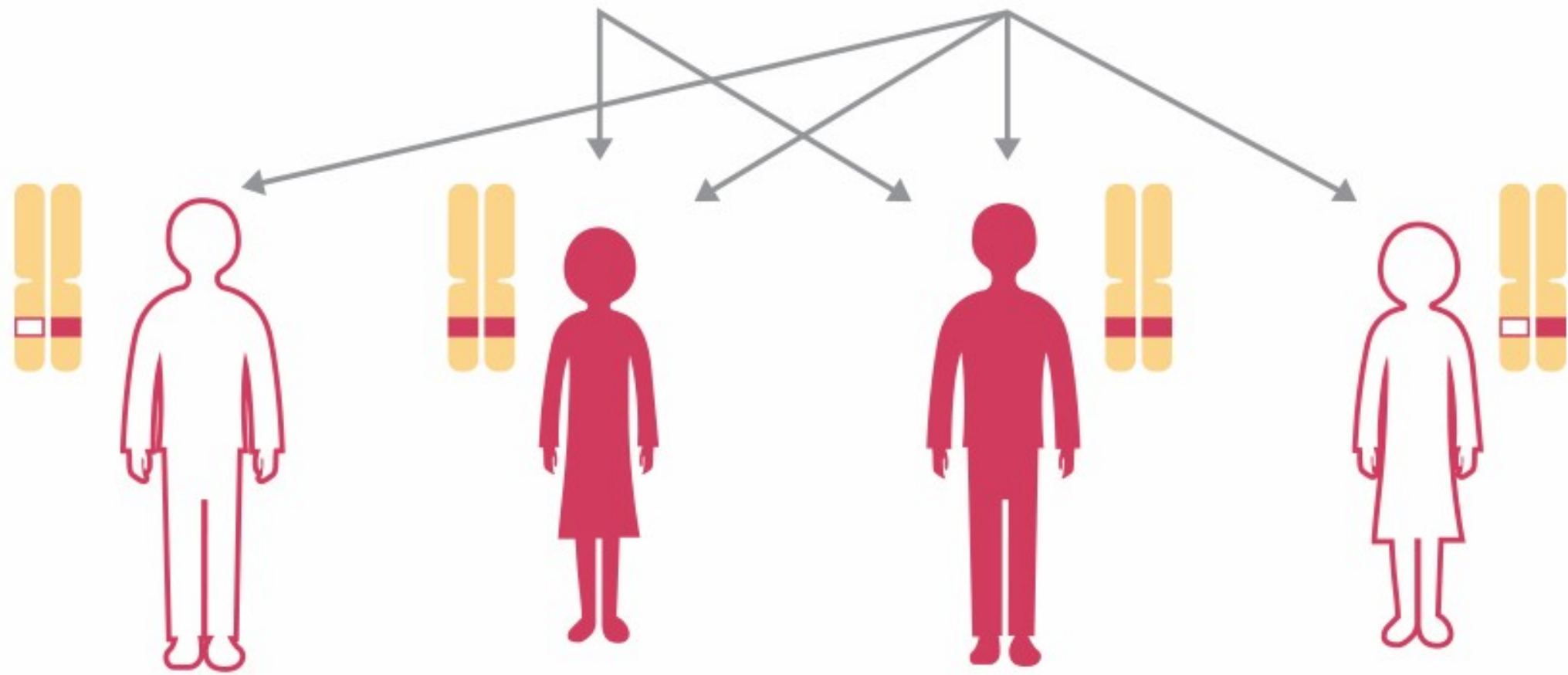
BRCA Gene 2

**Chromosome 13**

Affected  
Father



Unaffected  
Mother

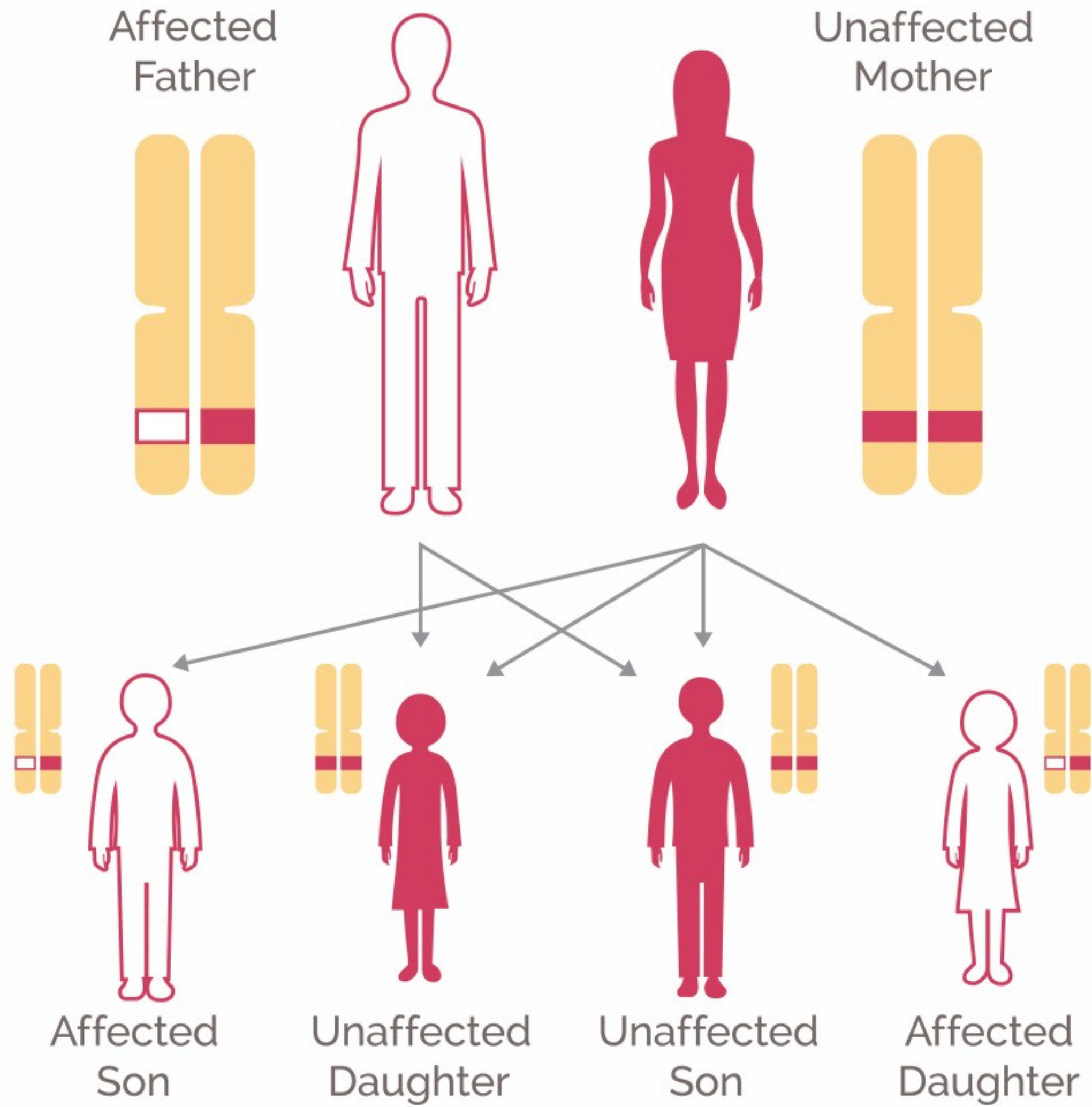


Affected  
Son

Unaffected  
Daughter

Unaffected  
Son

Affected  
Daughter



# PCSK-9\* and hypercholesterolaemia

a few patients were identified with very low blood LDL cholesterol levels, without having changed their lifestyle

\* Proprotein Convertase Subtilisin Kexin 9

# **PCSK-9\* and hypercholesterolaemia**

**a few patients were identified with very low blood LDL cholesterol levels, without having changed their lifestyle**

**these individuals had a 'loss of function' mutation in the gene PCSK9**

**\* Proprotein Convertase Subtilisin Kexin 9**

# **PCSK-9\* and hypercholesterolaemia**

**a few patients were identified with very low blood LDL cholesterol levels, without having changed their lifestyle**

**these individuals had a 'loss of function' mutation in the gene PCSK9**

**monoclonal antibodies developed to inactivate PCSK9 in the liver.**

**\* Proprotein Convertase Subtilisin Kexin 9**



# **PCSK-9\* and hypercholesterolaemia**

**a few patients were identified with very low blood LDL cholesterol levels, without having changed their lifestyle**

**these individuals had a 'loss of function' mutation in the gene PCSK9**

**monoclonal antibodies developed to inactivate PCSK9 in the liver.**

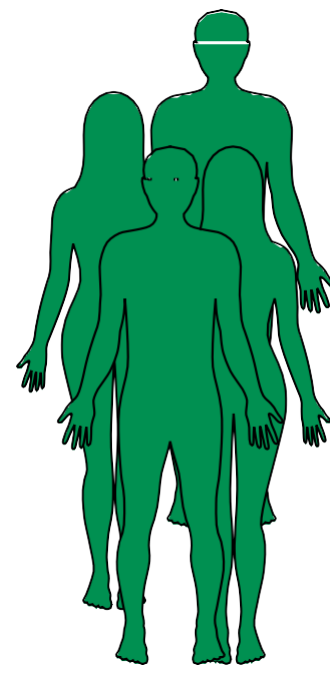
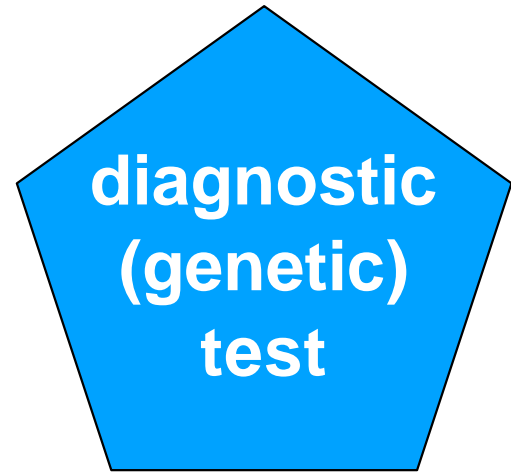
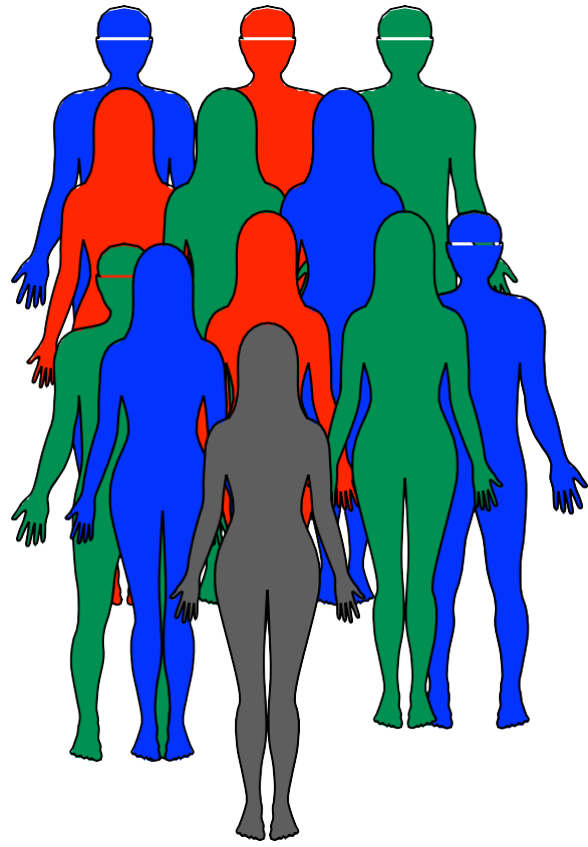
**treat patients with statin-resistant hypercholesterolaemia**

**\* Proprotein Convertase Subtilisin Kexin 9**

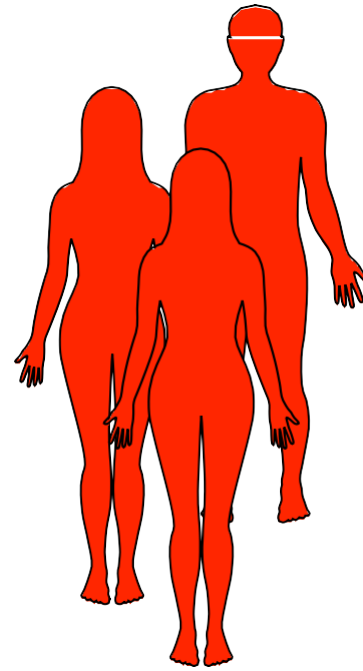


# Biomarkers

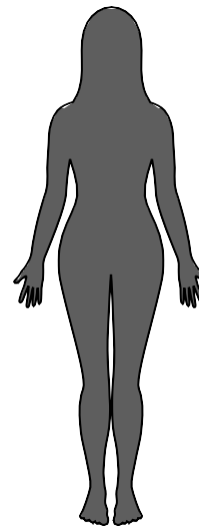
**“any substance, structure or process that can be measured in the body or its products and influence or predict the incidence or outcome of disease”**



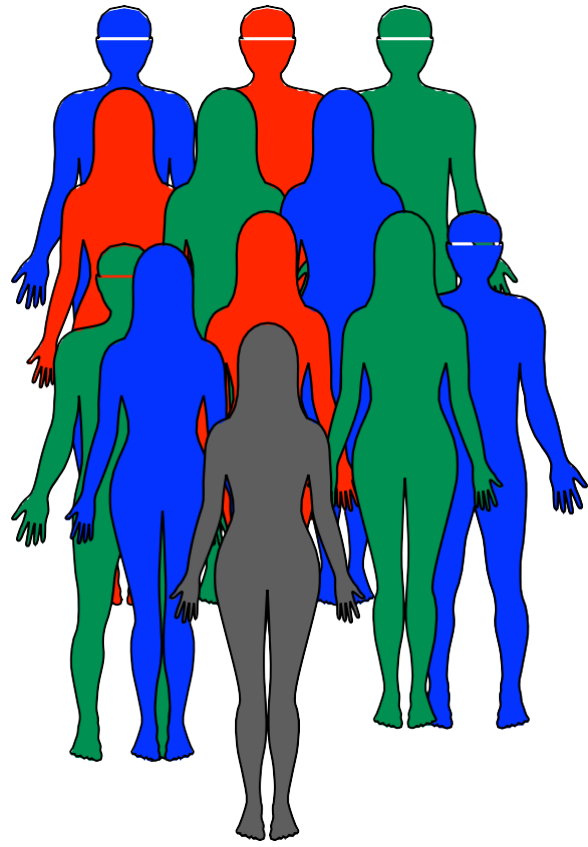
**responders for Drug A**



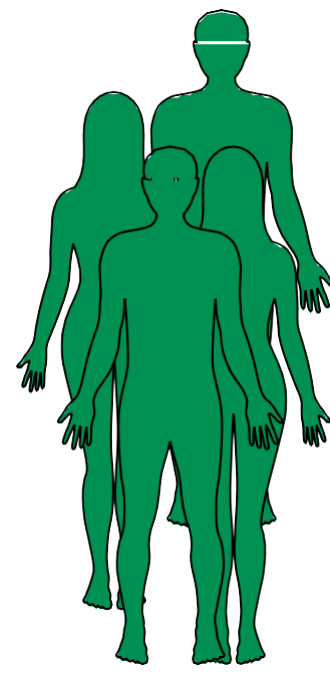
**non-responders for Drug A**



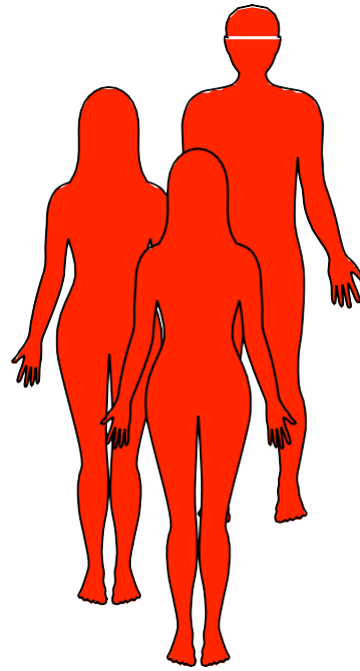
**severe side effects predicted**



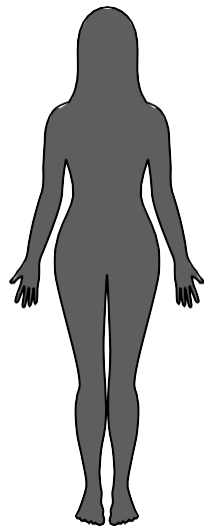
diagnostic  
(genetic)  
test



responders for Drug A

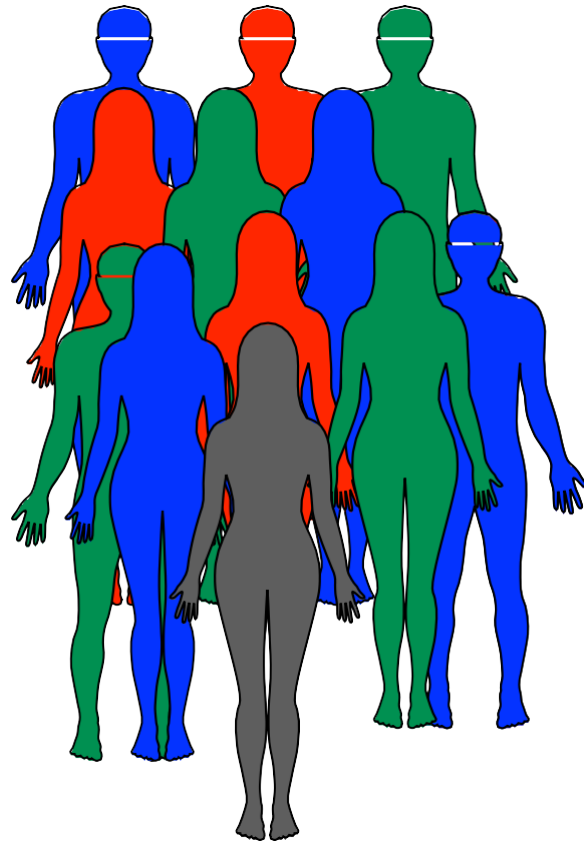


non-responders for Drug A

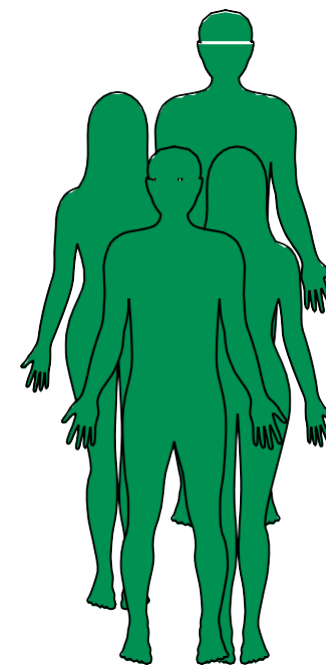


severe side effects predicted

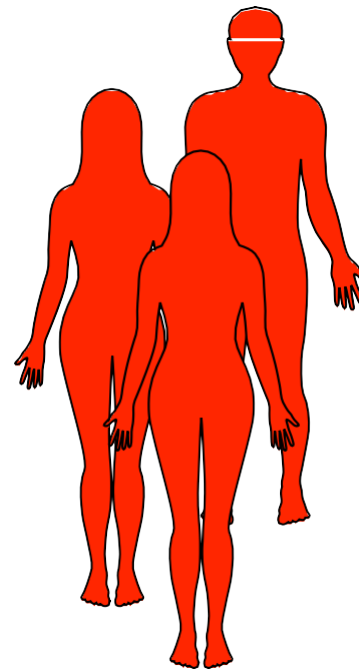
monitoring  
biomarker



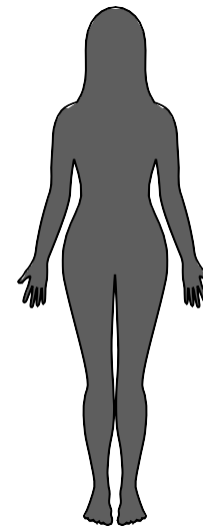
diagnostic  
(genetic)  
test



responders for Drug A



non-responders for Drug A



severe side effects predicted

monitoring  
biomarker

- blood sugar
- HbA1
- creatinine
- cholesterol
- troponin
- specific antibodies
- circulating tumour DNA
- etc.

# Bioinformatics







**Technology**

**Interoperability**



**Security**

**Trust**

# NEWS

Home

UK

World

Business

Politics

Tech

Science

Health

Family & Education

## Technology

# NHS trust fined for 56 Dean Street HIV status leak

By Chris Foxx  
Technology reporter

9th May 2016



Share



**An NHS trust has been fined £180,000 after a sexual health centre leaked the details of almost 800 patients who had attended HIV clinics.**

Malware

# WannaCry, Petya, NotPetya: how ransomware hit the big time in 2017

Most first encountered ransomware after an outbreak shut down hospital computers and diverted ambulances this year. Is it here to stay?



▲ Marcus Hutchins, who stopped the WannaCry ransomware attack from spreading. Photograph: Frank Augstein/AP

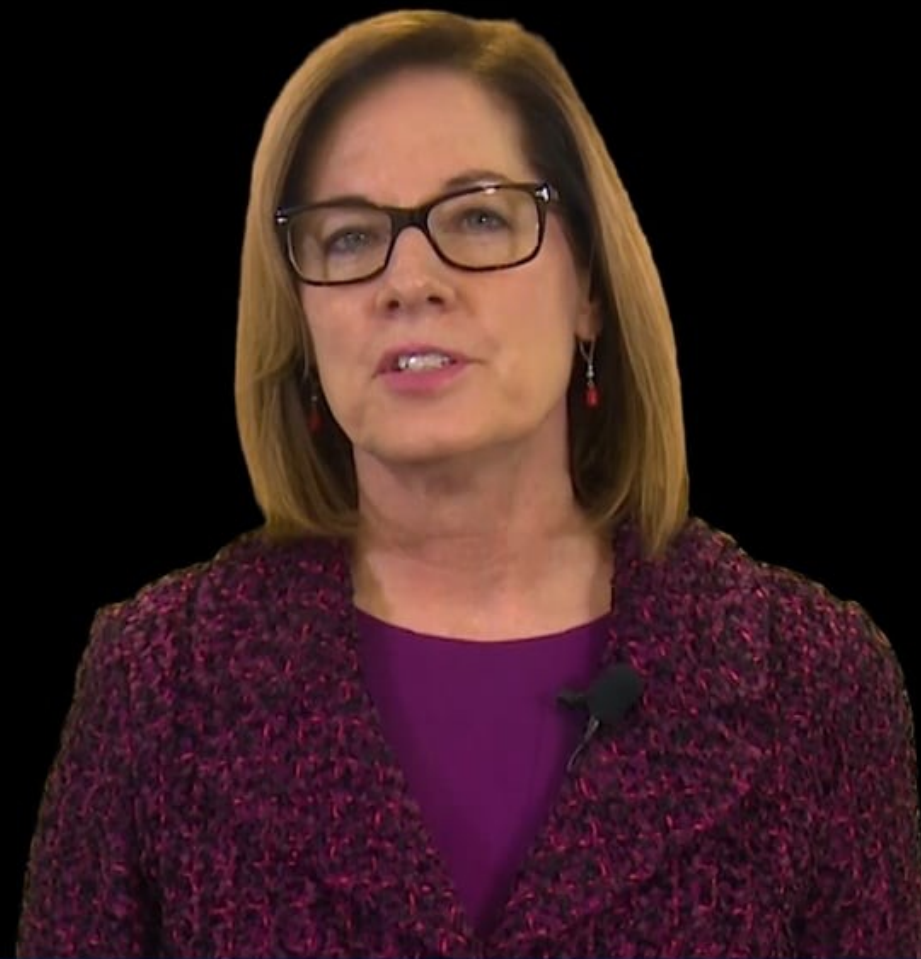
# Royal Free breached UK data law in 1.6m patient deal with Google's DeepMind

**Information Commissioner's Office rules record transfer from London hospital to AI company failed to comply with Data Protection Act**



▲ 'We underestimated the complexity of the NHS and of the rules around patient data' - DeepMind. Photograph: Alamy Stock Photo

**“the price of innovation didn’t need to be the erosion of legally ensured fundamental privacy rights”**



**ico.**  
Information Commissioner's Office

Elizabeth Denham, Information Commissioner

# Biobanks

## Genetics

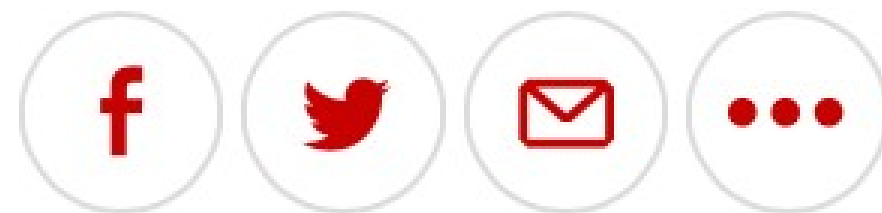
# Icelandic DNA project hit by privacy storm

---

---

**Robin McKie**, *science editor*

Sun 16 May 2004 10.22 BST



  
18

---

It was meant to give Iceland a global lead in medical research and create one of the world's most powerful drug companies. But the launch of DeCode [Genetics](#) is threatening to become a national embarrassment.



**Genetics**

# Icelandic DNA project hit by privacy storm

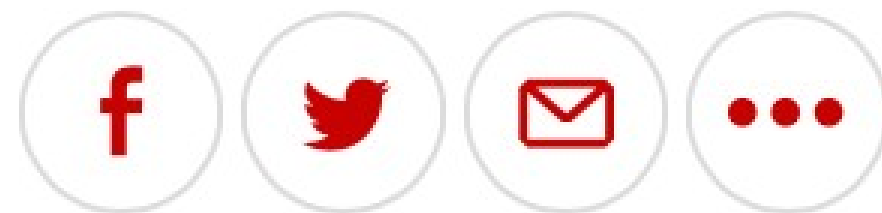
# AMGEN

---

---

**Robin McKie**, *science editor*

Sun 16 May 2004 10.22 BST

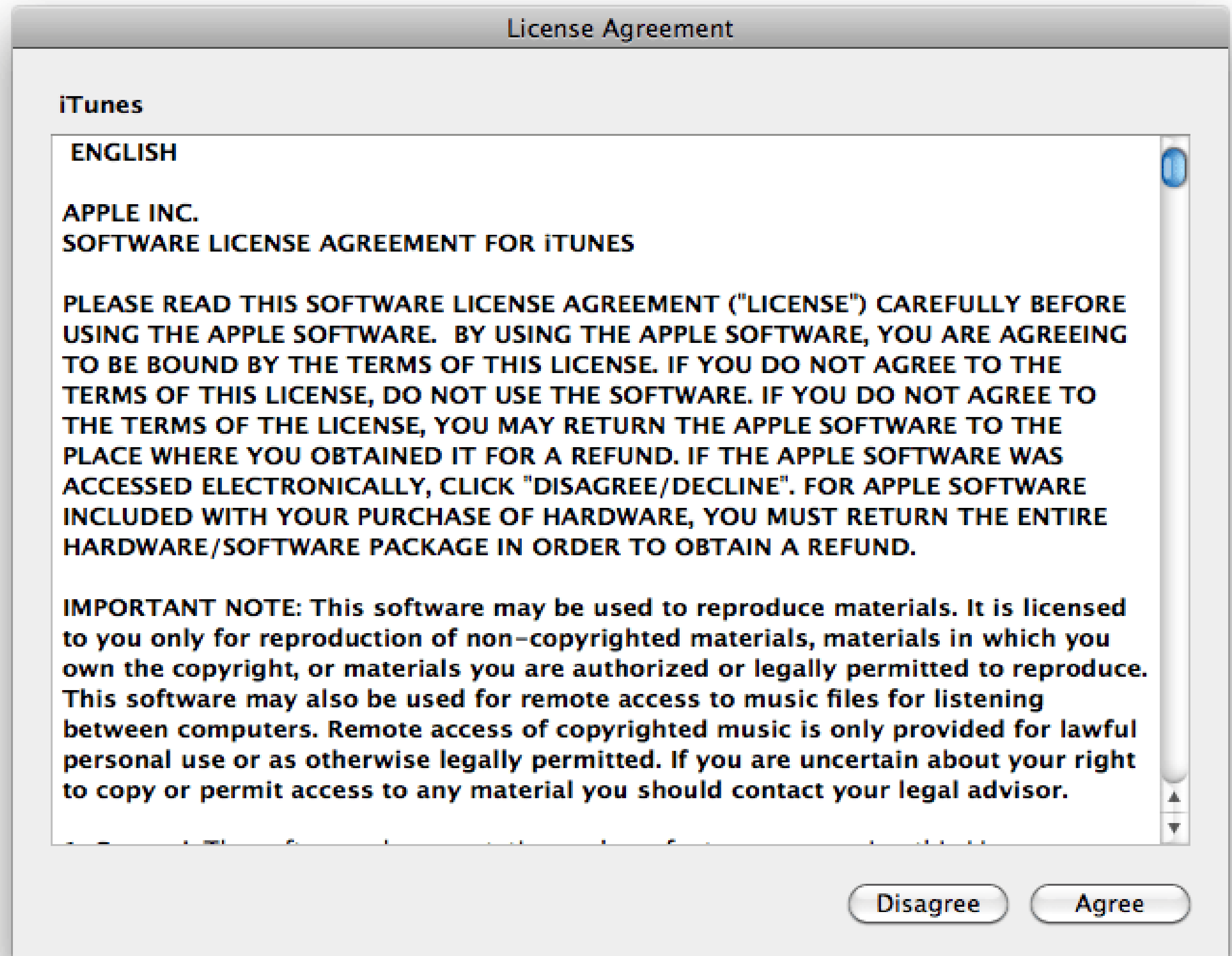


  
18

---

It was meant to give Iceland a global lead in medical research and create one of the world's most powerful drug companies. But the launch of DeCode [Genetics](#) is threatening to become a national embarrassment.

# terms & conditions





# **100,000 Genome Project**

**to create an ethical and transparent programme based on consent;  
to bring benefit to patients and set up a genomic medicine service for the NHS;  
to enable new scientific discovery and medical insights;  
and to kick start the development of a UK genomics industry.**

**rare diseases and cancer**







credit

information

steals

years

purpose

someone

theft

become

ashamed

feel

shock

reason

often

learn

found

Finding fraudulent

known

might

takes

turn

True

actual

charges

past-due

quickly

immigrants

making

happening

years

example

thought

years

years

years

years

years

years

years

years

years

years

years

years

years

years

days

established

like

without

right

starts

account

take

idea

personal

creating

deleted

downright

man

never

mus

evidence

doesn't

way

apply

may

name

complete

false

show

illegal

graduates

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

wages

Number

notice

dollars

think

first

Everyone

Imagine

even

experience

knowledge

changed

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

problem

fell

thousands

times

find

man

decade

emotion

learned

people

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

days

established

like

without

right

starts

account

take

idea

personal

creating

deleted

downright

man

never

mus

evidence

doesn't

way

apply

may

name

complete

false

show

illegal

graduates

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

wages

Number

notice

dollars

think

first

Everyone

Imagine

even

experience

knowledge

changed

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

days

established

like

without

right

starts

account

take

idea

personal

creating

deleted

downright

man

never

mus

evidence

doesn't

way

apply

may

name

complete

false

show

illegal

graduates

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

wages

Number

notice

dollars

think

first

Everyone

Imagine

even

experience

knowledge

changed

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

years

days

established

**the data are valuable to us all**

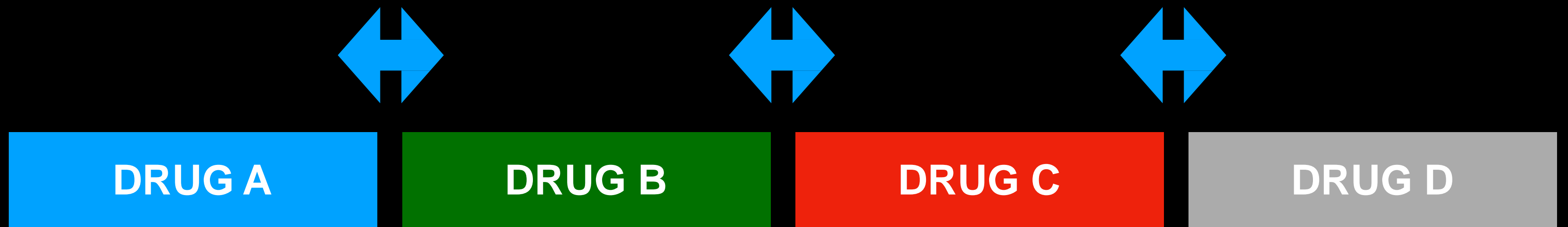
**the data are valuable to us all**

**that value must not be lost  
because of breaches of trust**



**How can we study therapies aimed at small populations?**

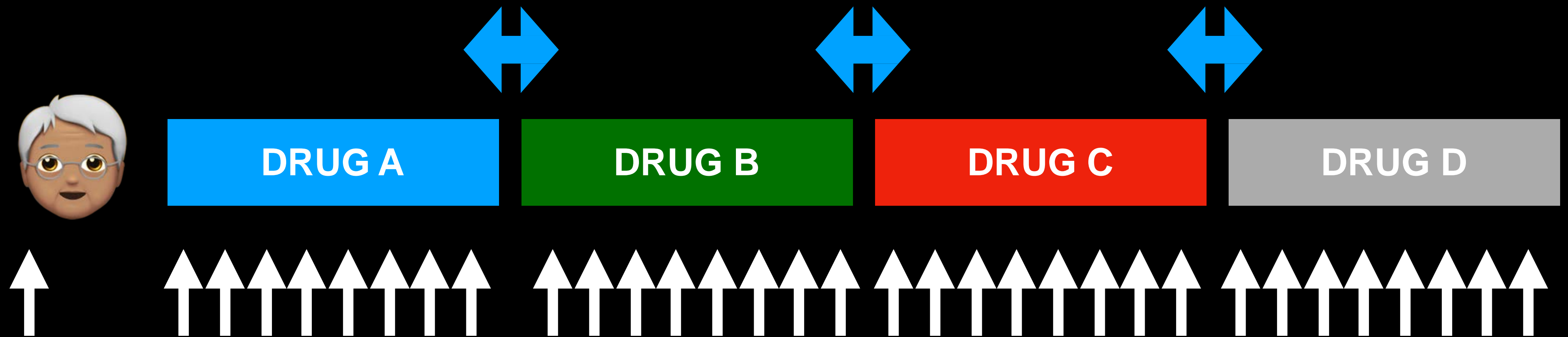
# How can we study therapies aimed at small populations?



# How can we study therapies aimed at small populations?



# How can we study therapies aimed at small populations?



**“the genomic information allows the population to be divided into groups with different **probabilities** of responding to particular types of medication or developing an adverse reaction—one group has a high probability, another a lower probability, but **for neither group is there certainty**”**

**Nikolas Rose 2010**

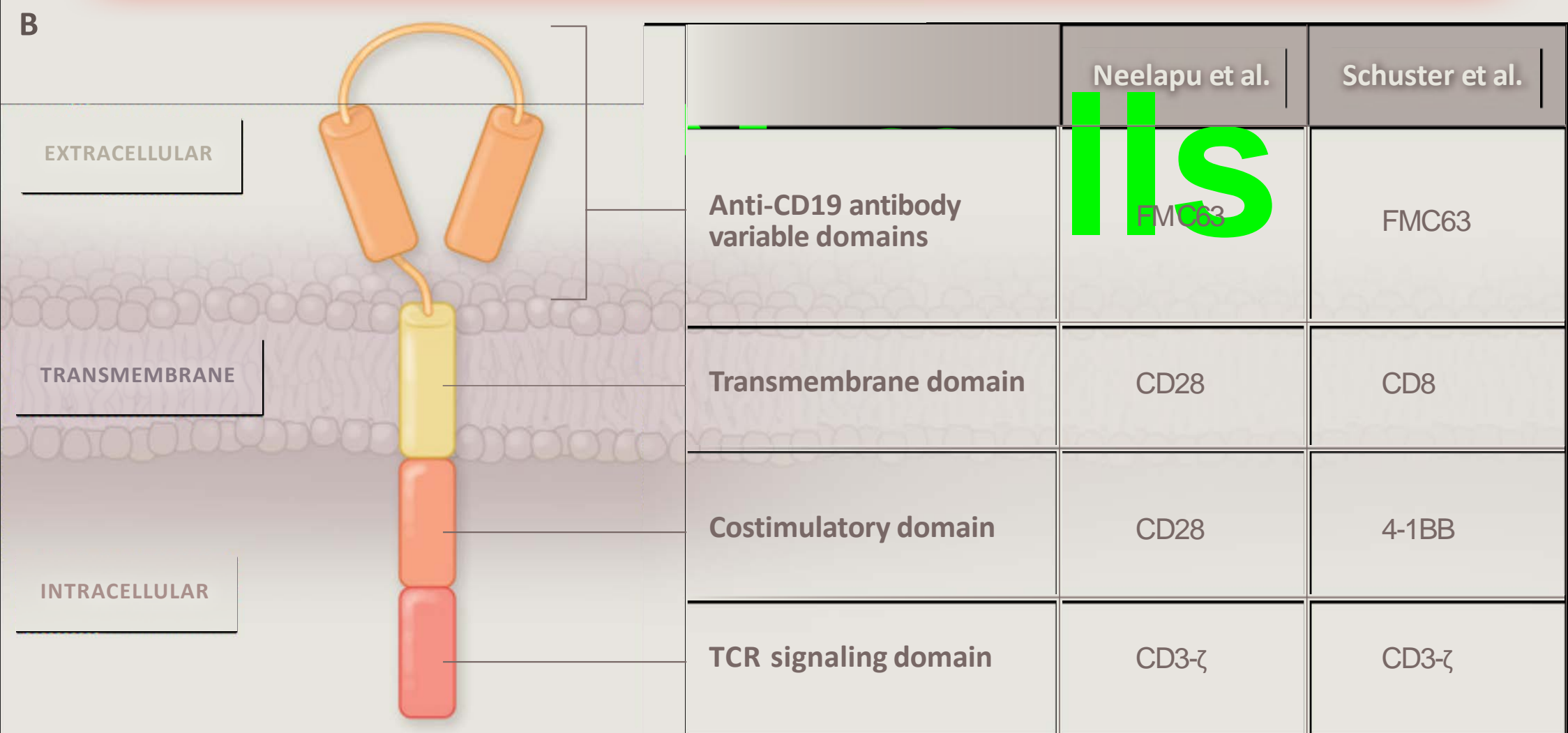
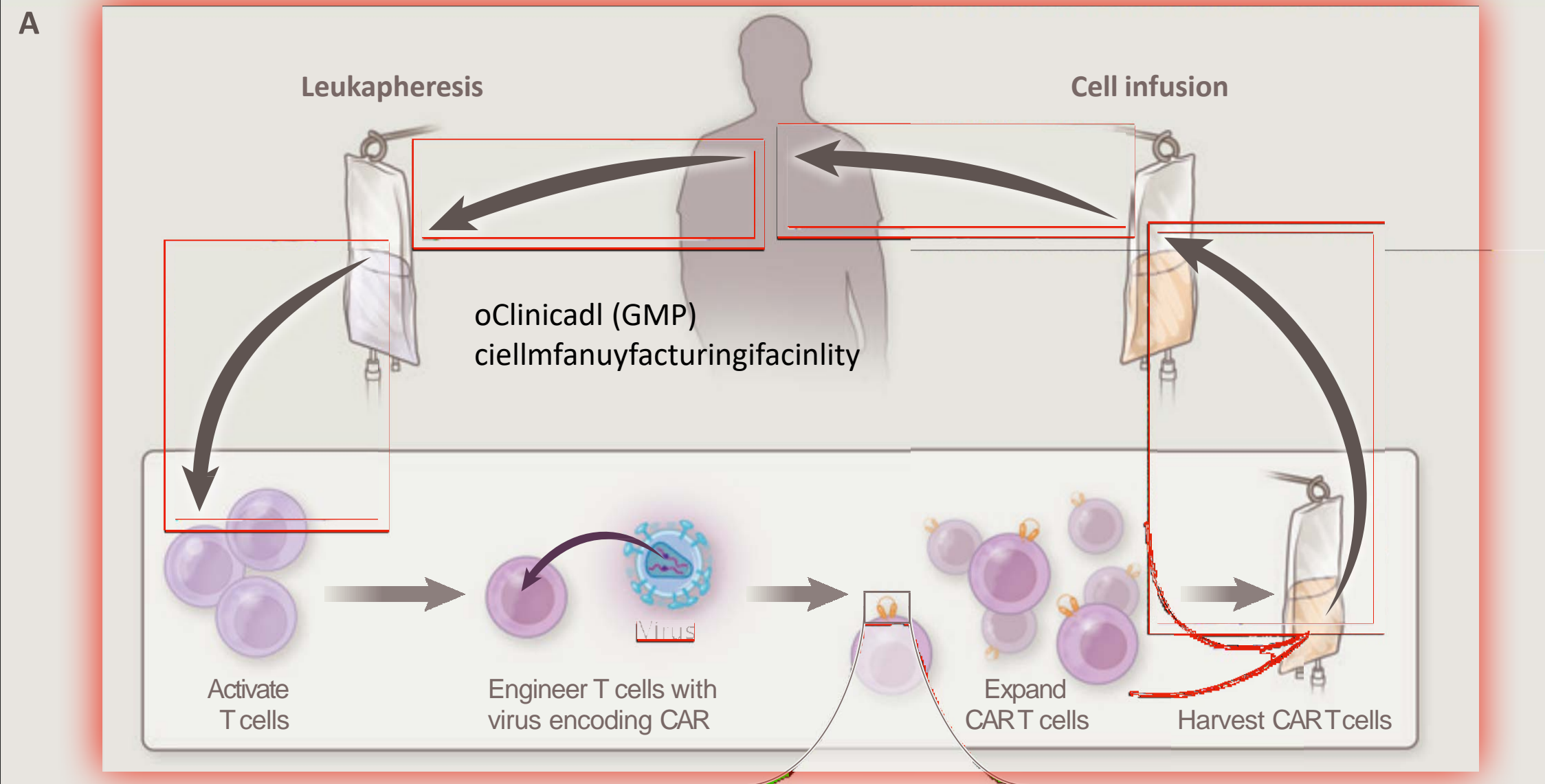
**treatment specific to an  
individual**

# CAR-T

**Modifying  
the patient's  
OWN cells**

# chimeric antigen receptor T-cell therapy

# CAR-T





chimeric antigen receptor T-cell therapy

**CAR-T**

**ICU**

**Side effects**

**Cost**

# CAR-T

ICU

Side effects

Cost

£288 - 360,000

per administration

**Can we afford  
precision medicine?**

# Potential Savings

# Potential Savings

- **more accurate diagnosis (fewer patients per treatment)**

# Potential Savings

- **more accurate diagnosis (fewer patients per treatment)**
- **no drugs for non-responders**

# Potential Savings

- **more accurate diagnosis (fewer patients per treatment)**
- **no drugs for non-responders**
- **avoidance of predictable side-effects**

# Potential Savings

- **more accurate diagnosis (fewer patients per treatment)**
- **no drugs for non-responders**
- **avoidance of predictable side-effects**
- **improved outcome (less burden of disease)**



# Potential Additional Costs

# Potential Additional Costs

- costs of diagnostics/biomarkers

# Potential Additional Costs

- **costs of diagnostics/biomarkers**
- **population screening**

# Potential Additional Costs

- **costs of diagnostics/biomarkers**
- **population screening**
- **complex IT**

# Potential Additional Costs

- **costs of diagnostics/biomarkers**
- **population screening**
- **complex IT**
- **data security/confidentiality**

# Potential Additional Costs

- **costs of diagnostics/biomarkers**
- **population screening**
- **complex IT**
- **data security/confidentiality**
- **drug development and pricing**

# Diagnostics is not a Money-Spinner

diagnostic  
(genetic)  
test



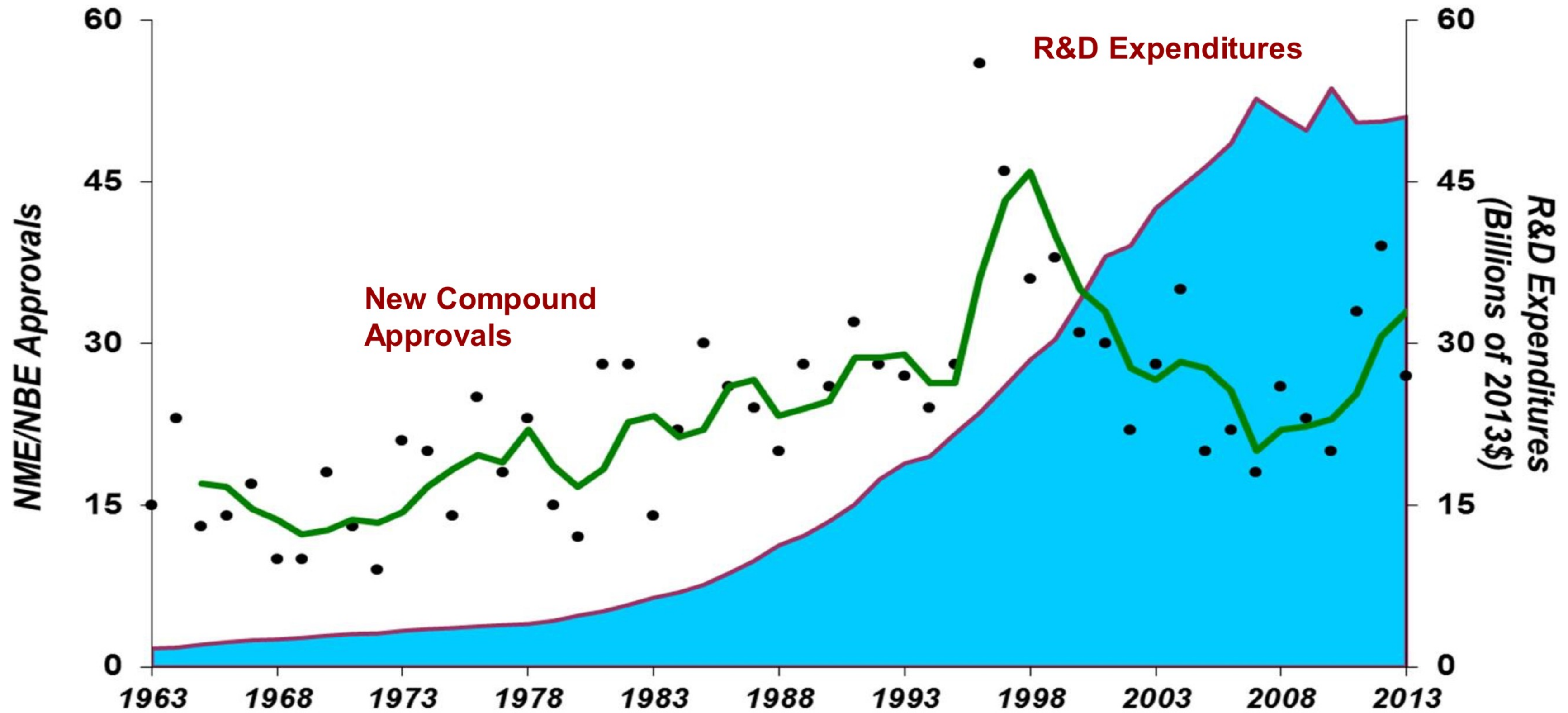
**Cheap Diagnostics and Expensive Drug**

# £1.87 billion

**the average pre-tax industry cost per new prescription drug approval  
(inclusive of failure and capital costs)**

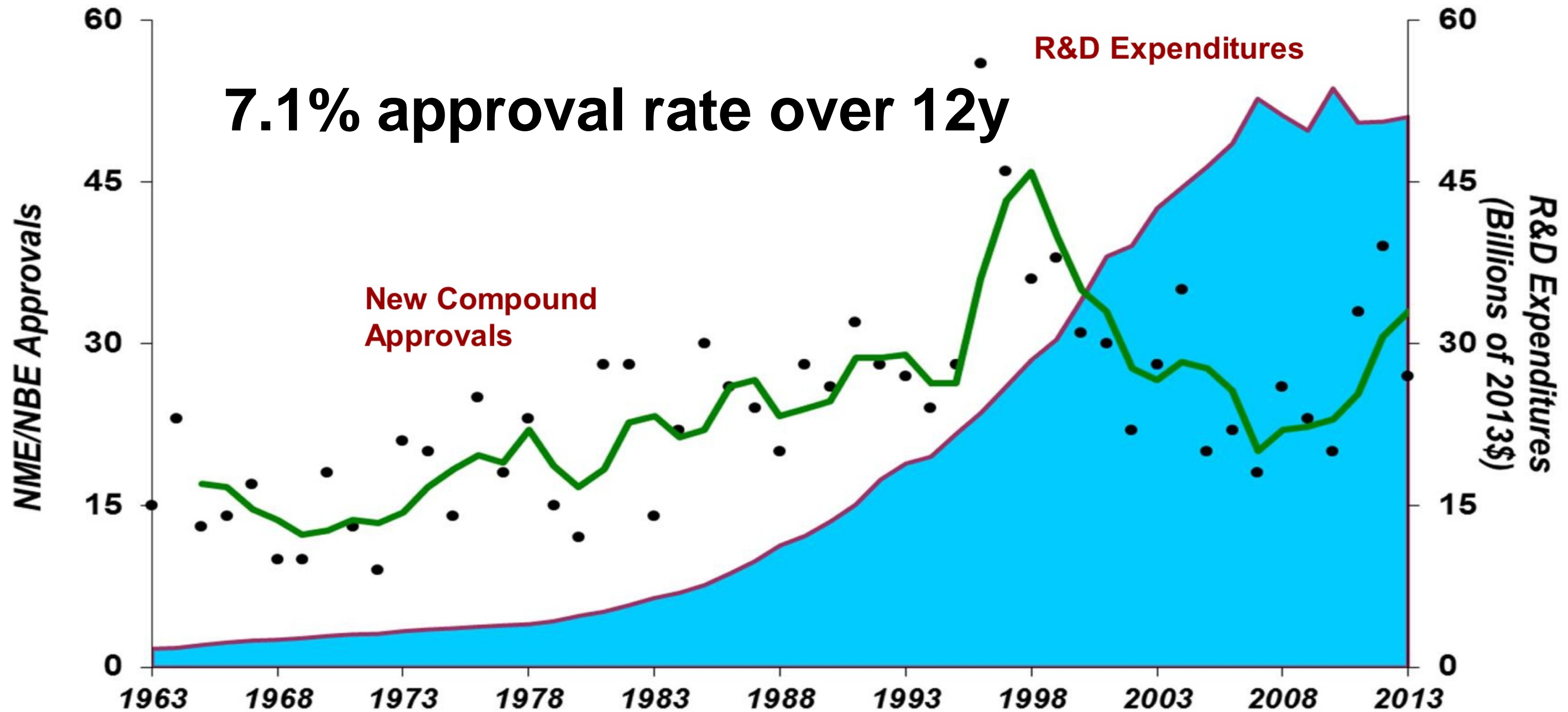


# New Drug and Biologics Approvals and R&D Spending



R&D expenditures are adjusted for inflation; curve is a 3-year moving average for NME/NBEs  
Sources: Tufts CSDD; PhRMA, 2014 Industry Profile

# New Drug and Biologics Approvals and R&D Spending



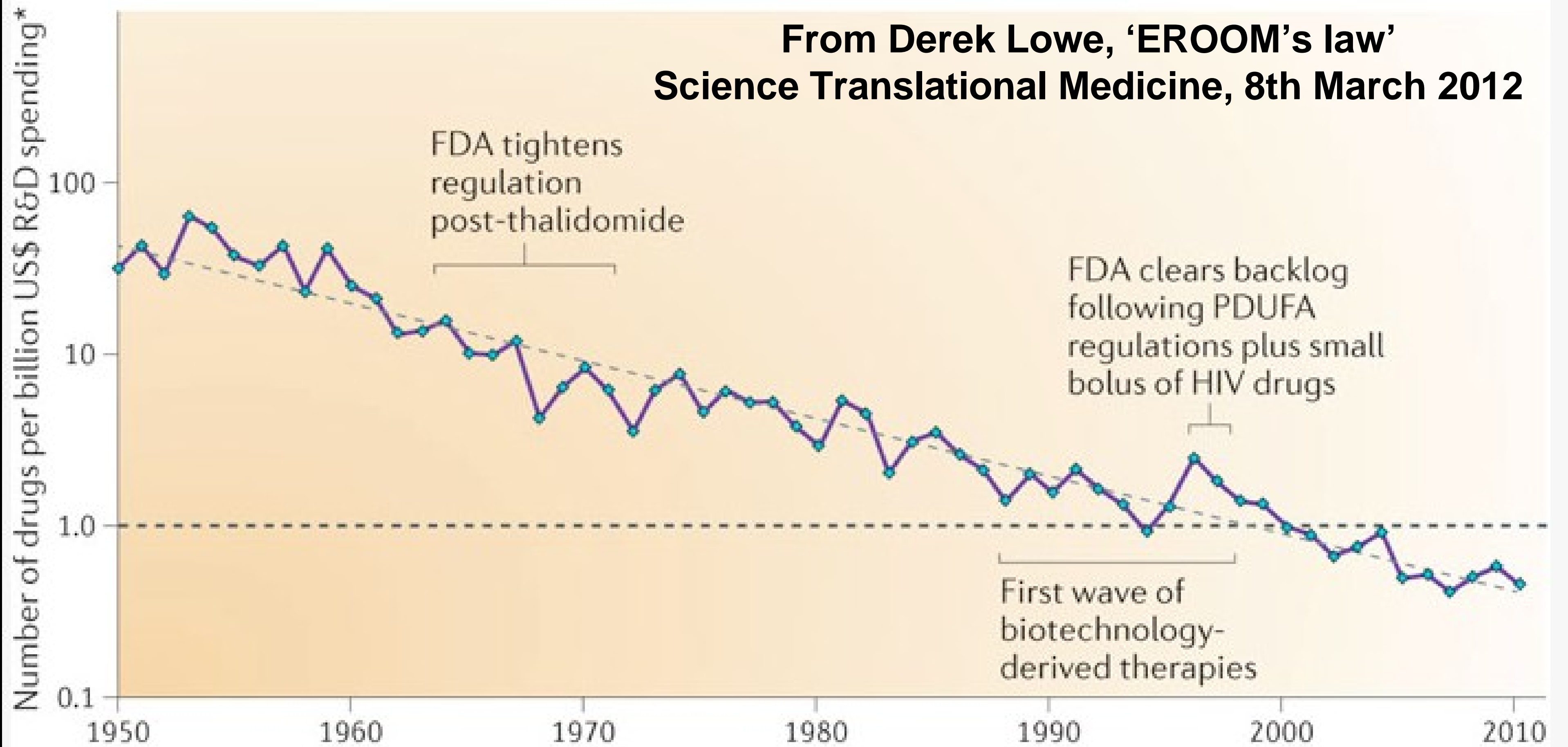
R&D expenditures are adjusted for inflation; curve is a 3-year moving average for NME/NBEs  
Sources: Tufts CSDD; PhRMA, 2014 Industry Profile

# Orphan Drugs

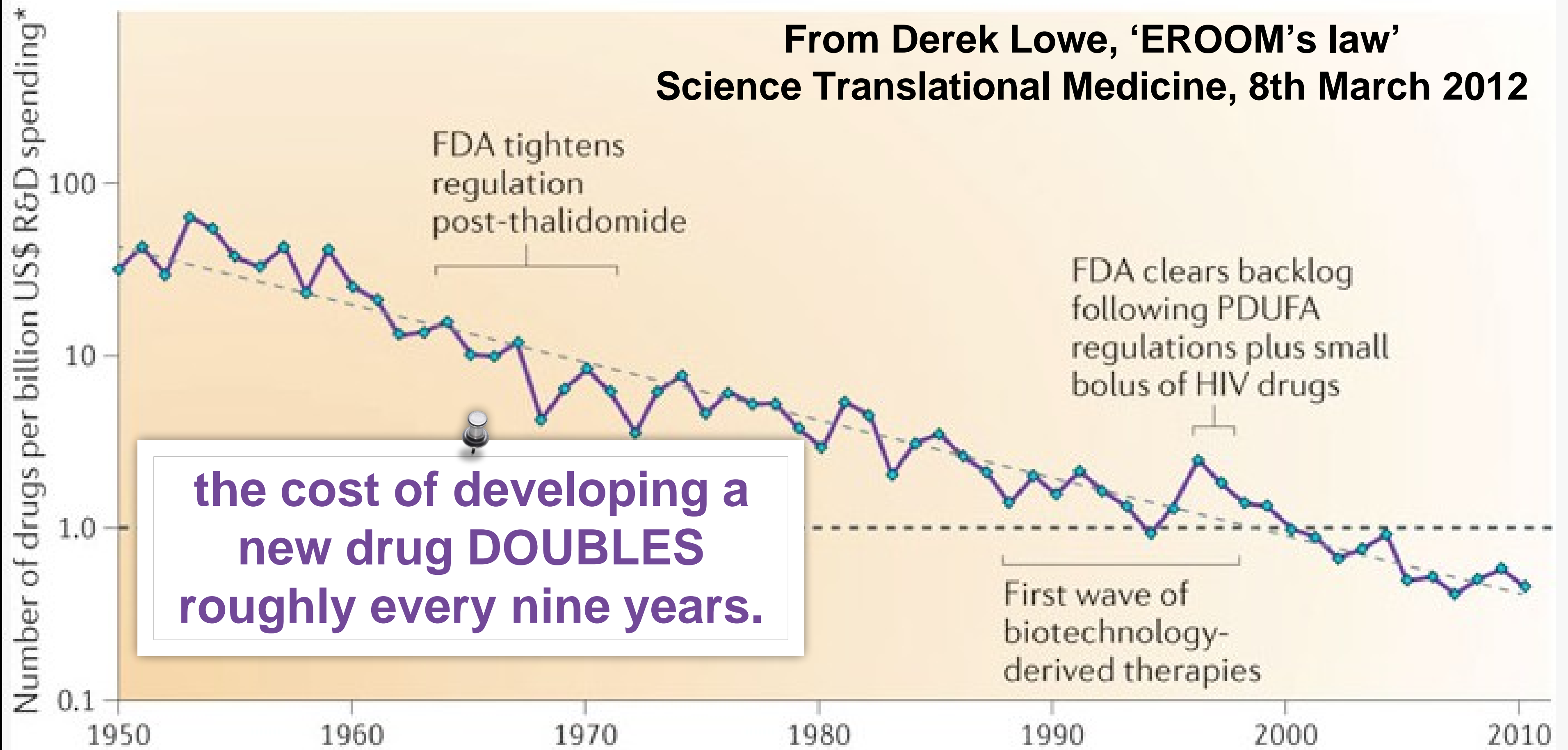
Agents that are **not developed by the pharmaceutical industry for economic reasons**, but which respond to a public health need.

The indications for such a drug may also be considered as 'orphan' since a substance may be used in the treatment of a frequent disease but may not, previously, have been developed for another, rarer, indication

**From Derek Lowe, 'EROOM's law'**  
**Science Translational Medicine, 8th March 2012**



From Derek Lowe, 'EROOM's law'  
Science Translational Medicine, 8th March 2012



# A Market Problem

# A Market Problem

high  
development  
costs

# A Market Problem

**high  
development  
costs**

**expensive  
diagnostics/  
biomarkers**



# A Market Problem

**high  
development  
costs**

**expensive  
diagnostics/  
biomarkers**

**high IT and  
regulation  
costs**

# A Market Problem

high  
development  
costs

expensive  
diagnostics/  
biomarkers

high IT and  
regulation  
costs

small market

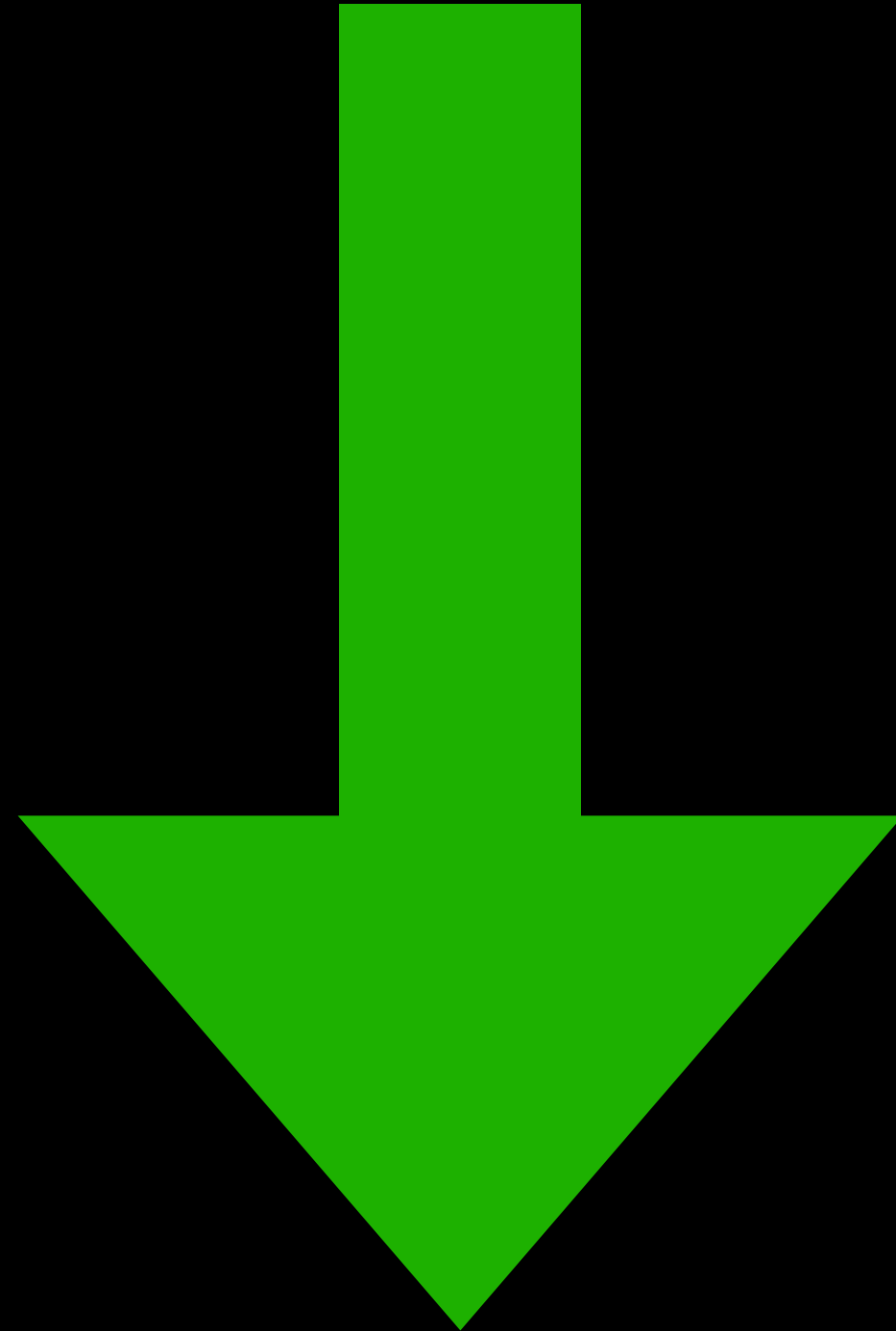
# A Market Problem

high  
development  
costs

# A Market Problem



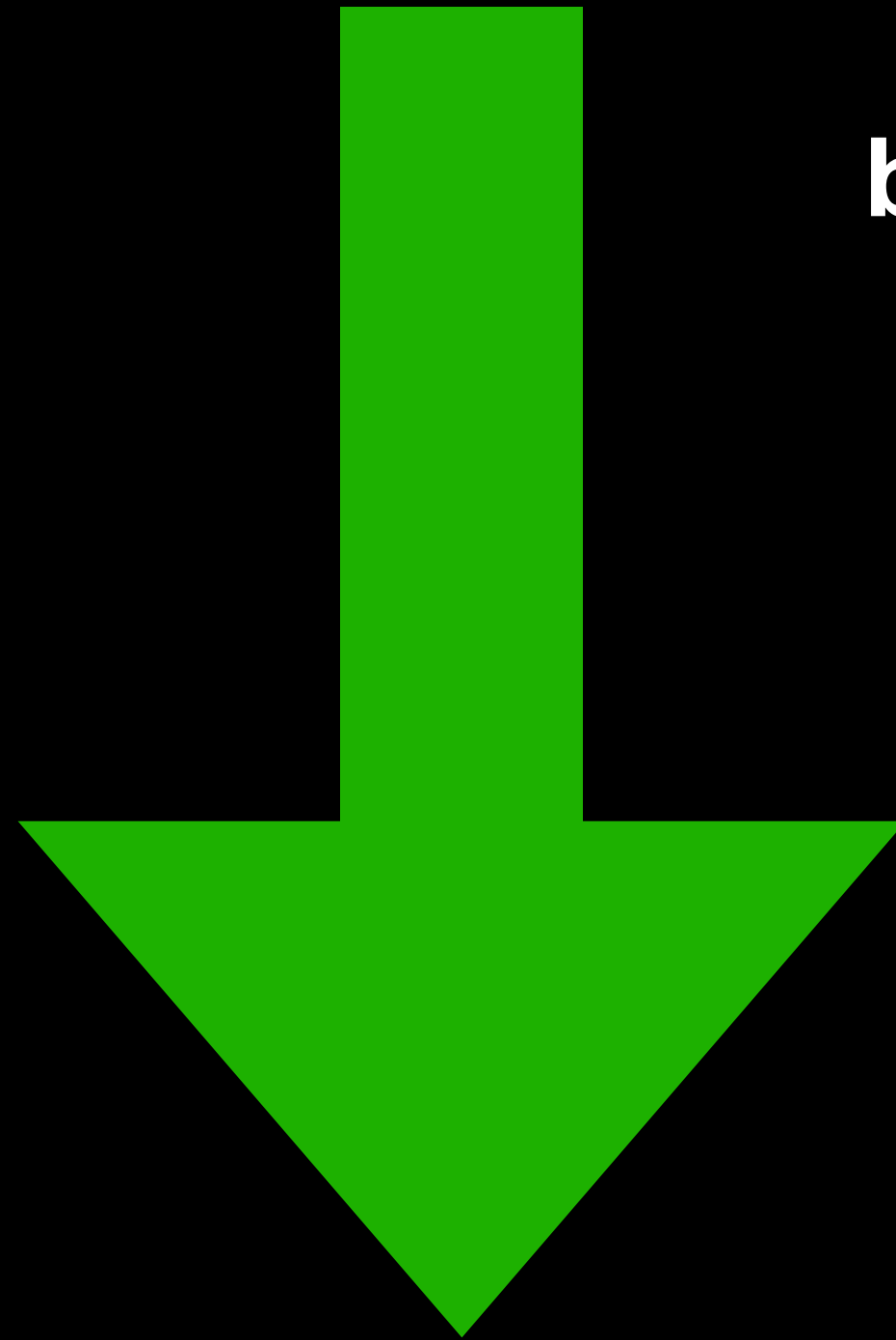
high  
development  
costs



# A Market Problem

high  
development  
costs

better biometric testing to reduce  
the size of trial populations



# A Market Problem

high  
development  
costs

better biometric testing to reduce  
the size of trial populations

different trial designs

# A Market Problem

**high  
development  
costs**

**better biometric testing to reduce  
the size of trial populations**

**different trial designs**

**modified regulation?**

# A Market Problem

high  
development  
costs

market  
test and drug  
together

expensive  
diagnostics/  
biomarkers



# A Market Problem

high  
development  
costs

market  
test and drug  
together  
re-market  
old drugs with  
new test

expensive  
diagnostics/  
biomarkers

# A Market Problem

high IT and  
regulation  
costs

small market

# A Market Problem

**simplify regulation**

**high IT and  
regulation  
costs**

**small market**

**Ethics**

# Ethical Issues and Biobanks

# Ethical Issues and Biobanks

- **What use is the sample going to be put to? Was the donor asked?**

# Ethical Issues and Biobanks

- **What use is the sample going to be put to? Was the donor asked?**
- **Will there be secondary uses of the samples, and can they be sold on? What should be the contract Ts & Cs?**

# Ethical Issues and Biobanks

- **What use is the sample going to be put to? Was the donor asked?**
- **Will there be secondary uses of the samples, and can they be sold on? What should be the contract Ts & Cs?**
- **Do you need to re-consent for secondary use or sale and if so how do you find the donor?**



# **Ethical Issues and Biobanks**

- **What use is the sample going to be put to? Was the donor asked?**
- **Will there be secondary uses of the samples, and can they be sold on? What should be the contract Ts & Cs?**
- **Do you need to re-consent for secondary use or sale and if so how do you find the donor?**
- **Can the donor change their mind and, if so, should their samples be destroyed? Who can authorise destruction?**

# Ethical Issues and Biobanks

- **What use is the sample going to be put to? Was the donor asked?**
- **Will there be secondary uses of the samples, and can they be sold on? What should be the contract Ts & Cs?**
- **Do you need to re-consent for secondary use or sale and if so how do you find the donor?**
- **Can the donor change their mind and, if so, should their samples be destroyed? Who can authorise destruction?**
- **What information (how much and how often) should be fed back to the donor?**

# Ethical Issues and Biobanks

# Ethical Issues and Biobanks

- **What if secondary testing turns up something important re risk or disease? Is there a duty of candour?**

# Ethical Issues and Biobanks

- **What if secondary testing turns up something important re risk or disease? Is there a duty of candour?**
- **If a family trait is identified, should the family be told? What should be the contract Ts & Cs?**

# Ethical Issues and Biobanks

- **What if secondary testing turns up something important re risk or disease? Is there a duty of candour?**
- **If a family trait is identified, should the family be told? What should be the contract Ts & Cs?**
- **What if data are lost, stolen, hacked or exploited? What rights should the donor have?**

# Ethical Issues and Biobanks

- **What if secondary testing turns up something important re risk or disease? Is there a duty of candour?**
- **If a family trait is identified, should the family be told? What should be the contract Ts & Cs?**
- **What if data are lost, stolen, hacked or exploited? What rights should the donor have?**
- **What if the bank crosses international boundaries? Whose regulatory authority trumps the others?**

**Who OWNS the data?**



You can own your pants .... but

we own your genes

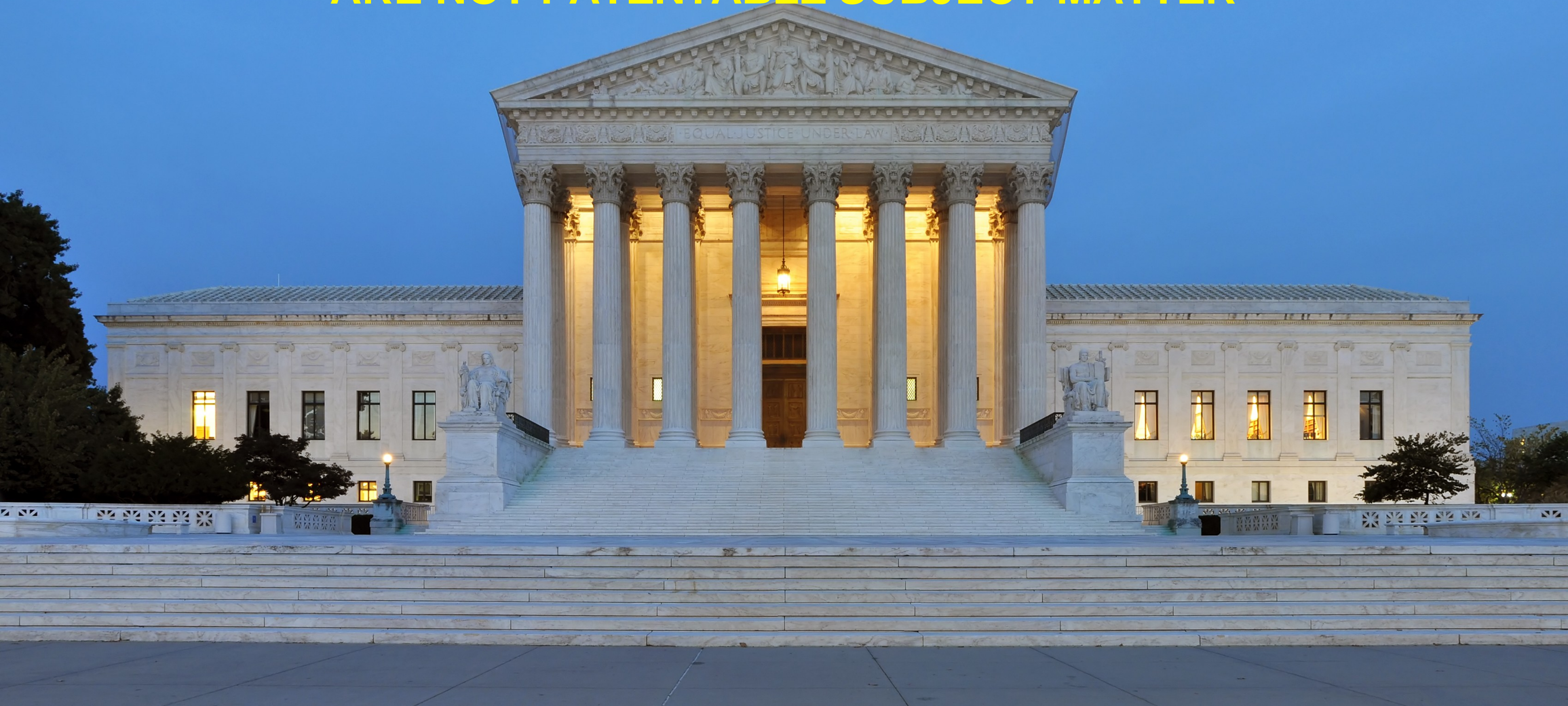
We are ruthless and treat your  
myriad genes as our private property

MYRIAD<sup>®</sup>

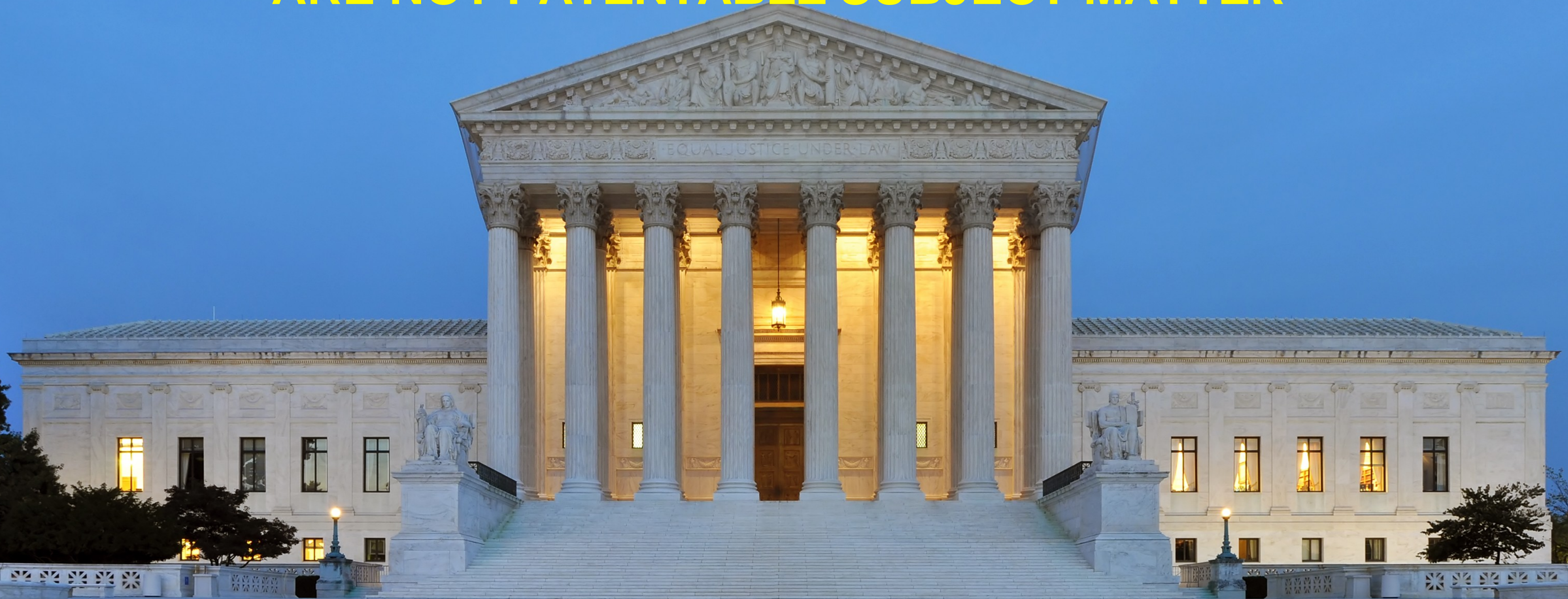


Myriad Genetics, Inc.  
San Diego, CA

All nine Justices on the Supreme Court agreed that  
**THE SEGMENTS OF DNA THAT MAKE UP HUMAN GENES  
ARE NOT PATENTABLE SUBJECT MATTER**



All nine Justices on the Supreme Court agreed that  
**THE SEGMENTS OF DNA THAT MAKE UP HUMAN GENES  
ARE NOT PATENTABLE SUBJECT MATTER**



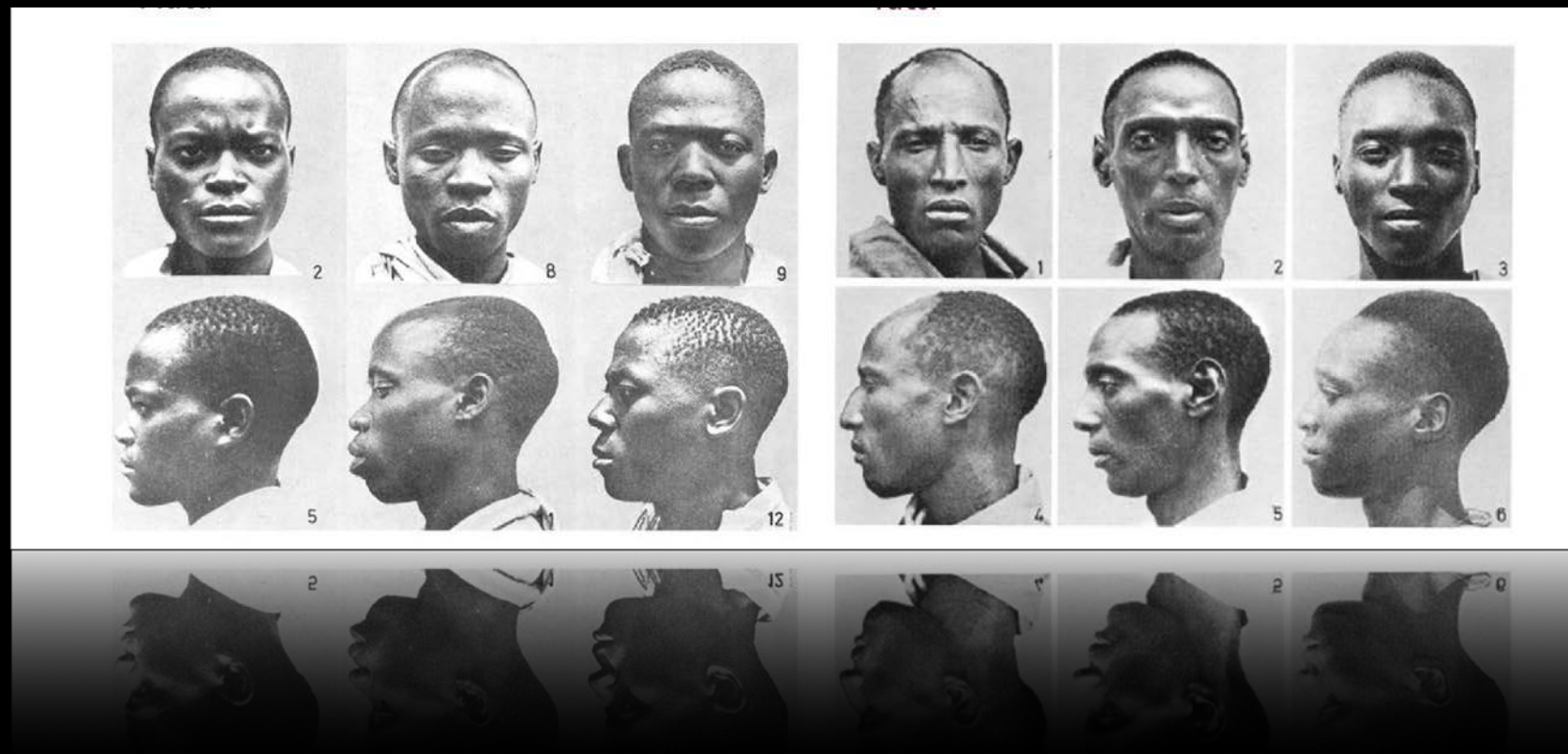
**Universal Declaration on the  
Human Genome and Human Rights**

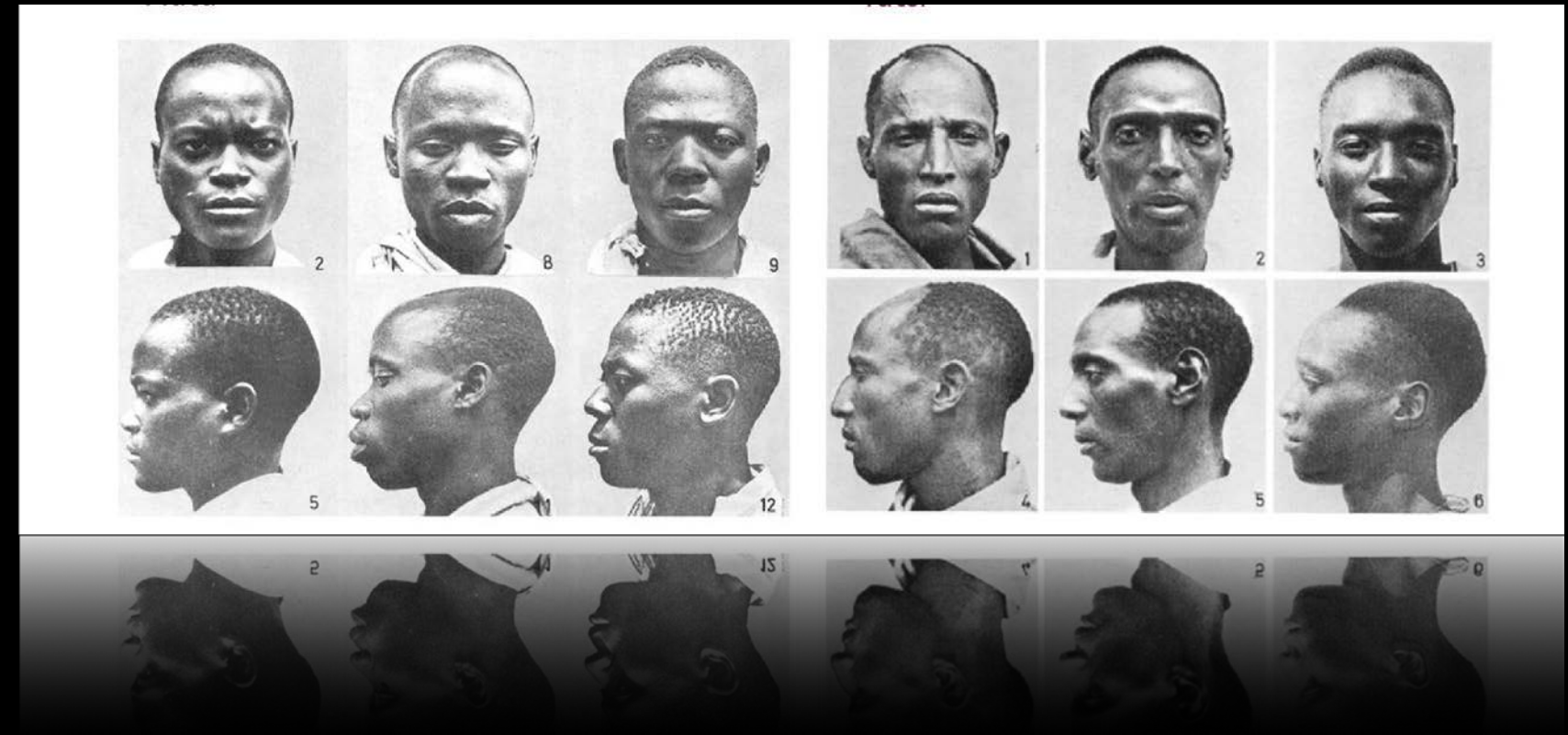




**“My dream is that by including all peoples in understanding and reading the genetic code we will realise that all of us belong in one big global family – that we are all brothers and sister. Wow!”**











**“Find me all the people  
with....”**

Voices

# *Erdogan has released the genealogy of thousands of Turks – but what is his motive?*

In 2003, the Armenian newspaper Agos, whose editor Hrant Dink was assassinated outside his office in 2007, reported that the Turkish government was secretly coding minorities in registers

Robert Fisk | @indyvoices | Thursday 1 March 2018 11:00 GMT



6K  
shares

Like

Click to follow  
Independent Voices



Erdogan has made Turkey's population registers public AP

# Access to Treatment

**“The focus of all this activity is on the  
diseases of affluence  
and not on the conditions that ail most people  
on our planet, curtailing their life expectancy  
and bringing them to an early death”**

*Nikolas Rose, London School of Economics, 2013*



commentaries

# Lack of Access to Targeted Cancer Treatment Modalities in the Developing World in the Era of Precision Medicine: Real-Life Lessons From Bosnia

**Amina Kurtovic-Kozaric, Semir Vranic, Sabira Kurtovic, Mirza Kozaric, Nermir Granov, and Timur Ceric**, Clinical Center of the University of Sarajevo; **Amina Kurtovic-Kozaric, Semir Vranic, Nermir Granov, Timur Ceric and Azra Hasic**, University of Sarajevo, Sarajevo, Bosnia and Herzegovina.

Downloaded from [ascopubs.org](http://ascopubs.org) by 82.27.14.52 on March 12, 2018 from 082.027.014.052  
Copyright © 2018 American Society of Clinical Oncology. All rights reserved.

**BIG PHARMA**



**EVERYONE**

**BIG PHARMA**

**TRUST**

**EVERYONE**




ARTICLE

DOI: 10.1038/s41467-018-03202-2

OPEN

# Gene-by-environment interactions in urban populations modulate risk phenotypes


Marie-Julie Favé<sup>1,2</sup>, Fabien C. Lamaze<sup>1</sup>, David Soave<sup>1</sup>, Alan Hodgkinson<sup>2,3</sup>, Héloïse Gauvin<sup>2,4</sup>, Vanessa Bruat<sup>1,2</sup>, Jean-Christophe Grenier <sup>1,2</sup>, Elias Gbeha<sup>1</sup>, Kimberly Skead<sup>1</sup>, Audrey Smargiassi<sup>5</sup>, Markey Johnson<sup>6</sup>, Youssef Idaghdour<sup>7</sup> & Philip Awadalla<sup>1,2,8,9</sup>

ARTICLE

DOI: 10.1038/s41467-018-03202-2

OPEN

# Gene-by-environment interactions in urban populations modulate risk phenotypes

Marie-Julie Favé<sup>1,2</sup>, Fabien C. Lamaze<sup>1</sup>, David Soave<sup>1</sup>, Alan Hodgkinson<sup>2,3</sup>, Héloïse Gauvin<sup>2,4</sup>, Vanessa Bruat<sup>1,2</sup>, Jean-Christophe Grenier <sup>1,2</sup>, Elias Gbeha<sup>1</sup>, Kimberly Skead<sup>1</sup>, Audrey Smargiassi<sup>5</sup>, Markey Johnson<sup>6</sup>, Youssef Idaghdour<sup>7</sup> & Philip Awadalla<sup>1,2,8,9</sup>

**Our findings demonstrate how the local environment directly affects disease risk phenotypes and that genetic variation, including less common variants, can modulate individual's response to environmental challenges.**

# Exciting Innovations

**Exciting Innovations**

**Access and Equity**

**Exciting Innovations**

**Access and Equity**

**Privacy and Security**

**Exciting Innovations**

**Access and Equity**

**Privacy and Security**

**Economic Issues**

**Exciting Innovations**

**Access and Equity**

**Privacy and Security**

**Economic Issues**

**Profit, Subsidy, Sharing**

**Exciting Innovations**

**Access and Equity**

**Privacy and Security**

**Economic Issues**

**Profit, Subsidy, Sharing**

**Ethical and Regulatory Control**





**Exciting Innovations**

**Access and Equity**

**Privacy and Security**

**Economic Issues**

**Profit, Subsidy, Sharing**

**Ethical and Regulatory Control**

1066

AND ALL THAT

A Memorable History of  
ENGLAND

comprising all the parts you can  
remember, including

103 GOOD THINGS,  
5 BAD-KINGS

and

2 GENUINE DATES

By

WALTER CARRUTHERS SELLAR

Aegrot.: Oxon.

AND

ROBERT JULIAN YEATMAN

Failed M.A., etc. - Oxon.

ILLUSTRATED BY

JOHN REYNOLDS,

Gent.

# Personalised/Precision Medicine

**Good Thing > Bad Actors**

## WITH SPECIAL THANKS

This was a tough topic for a surgeon.

It didn't exist when I graduated, and much of the basic science now taught at medical school passed me by.

I could not have written this without the help of these great colleagues and advisors;

# Thank You

[@profmjelliott](#)