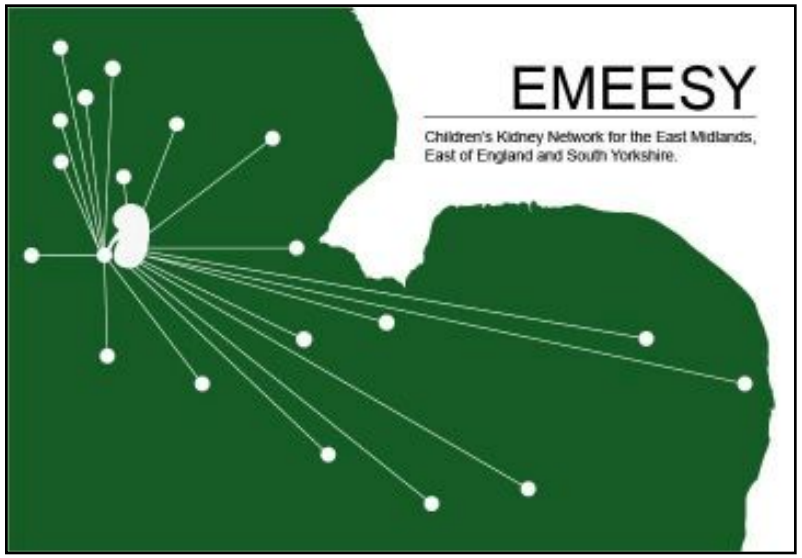
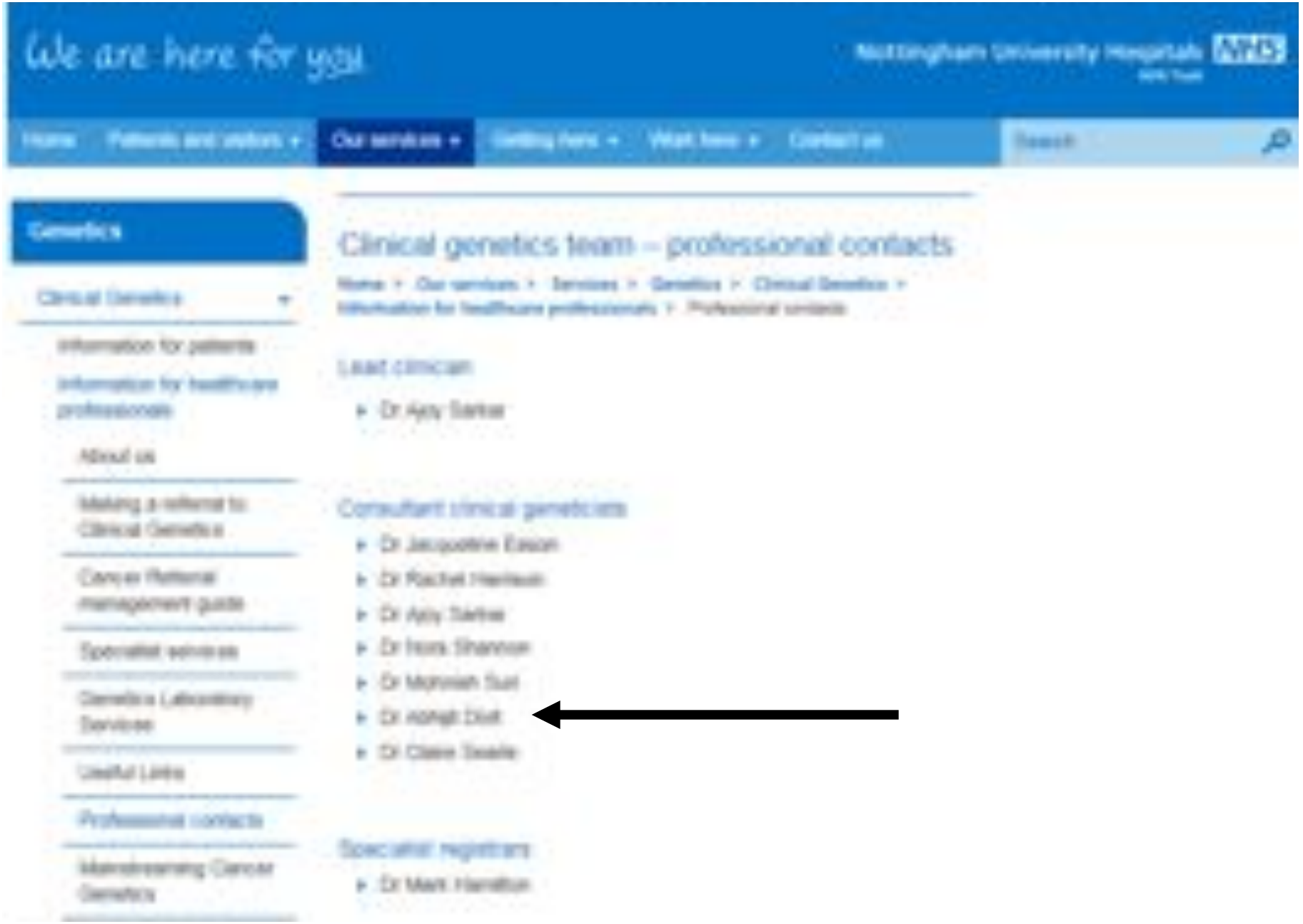


EMEESY Network Annual Education Day

Sedgebrook Hall
16th October 2015


We are here for you
Nottingham University Hospitals
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Our services
Genetics
Clinical Genetics
Information for patients
About us
Cancer Referral management guide
Useful Links
Professional contacts
Clinical genetics team – professional contacts
Lead clinician
Dr Ajay Sarkar
Consultant clinical geneticists
Dr Jacqueline Eason
Dr Rachel Hamlin
Dr Ajay Sarkar
Dr Moinish Suri
Dr Claire Searle
Specialist registrars
Dr Mark Hamilton

Ajoy → Dysmorphology, ethics

Jacq → Prenatal

Rachel → Cancer

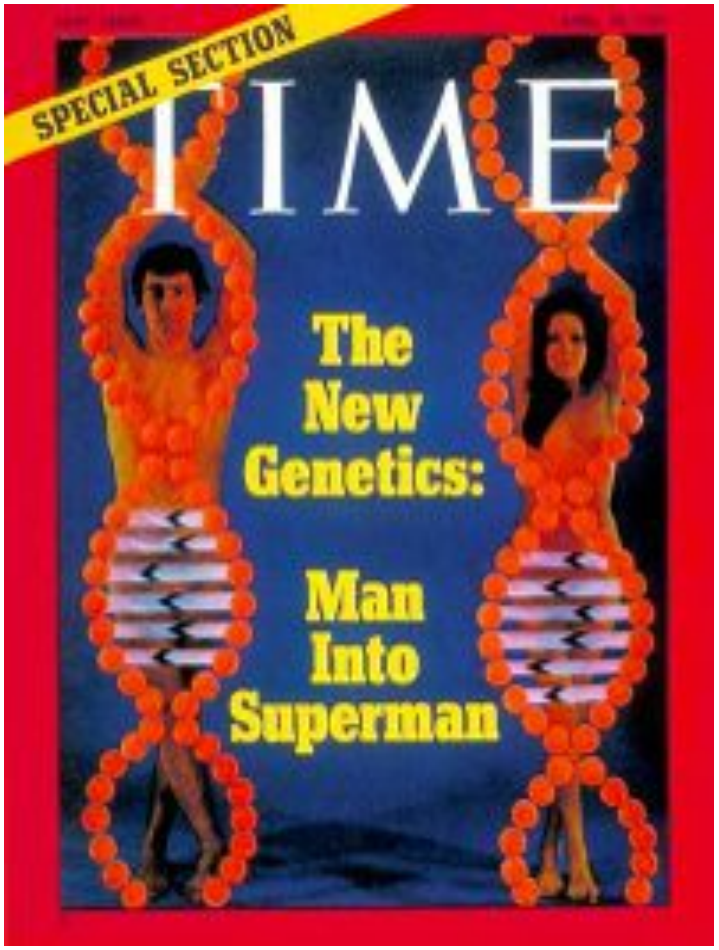
Nora → Cardiac

Mohnish → Dysmorphology, Skeletal, Neurology

Abhijit → Renal, Endocrine, Neurology

Claire → Ophthalmology, Cancer

Apr 1971

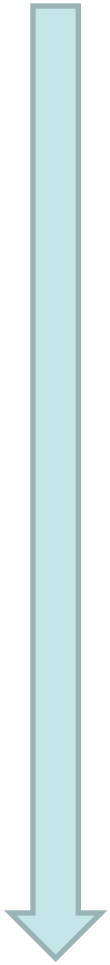


How will genetics influence medicine in the future?

Dec 2012

How will genetics influence medicine in the future?

The 5 year timeline



2010 **Next Generation Sequencing** technology established
ArrayCGH routine

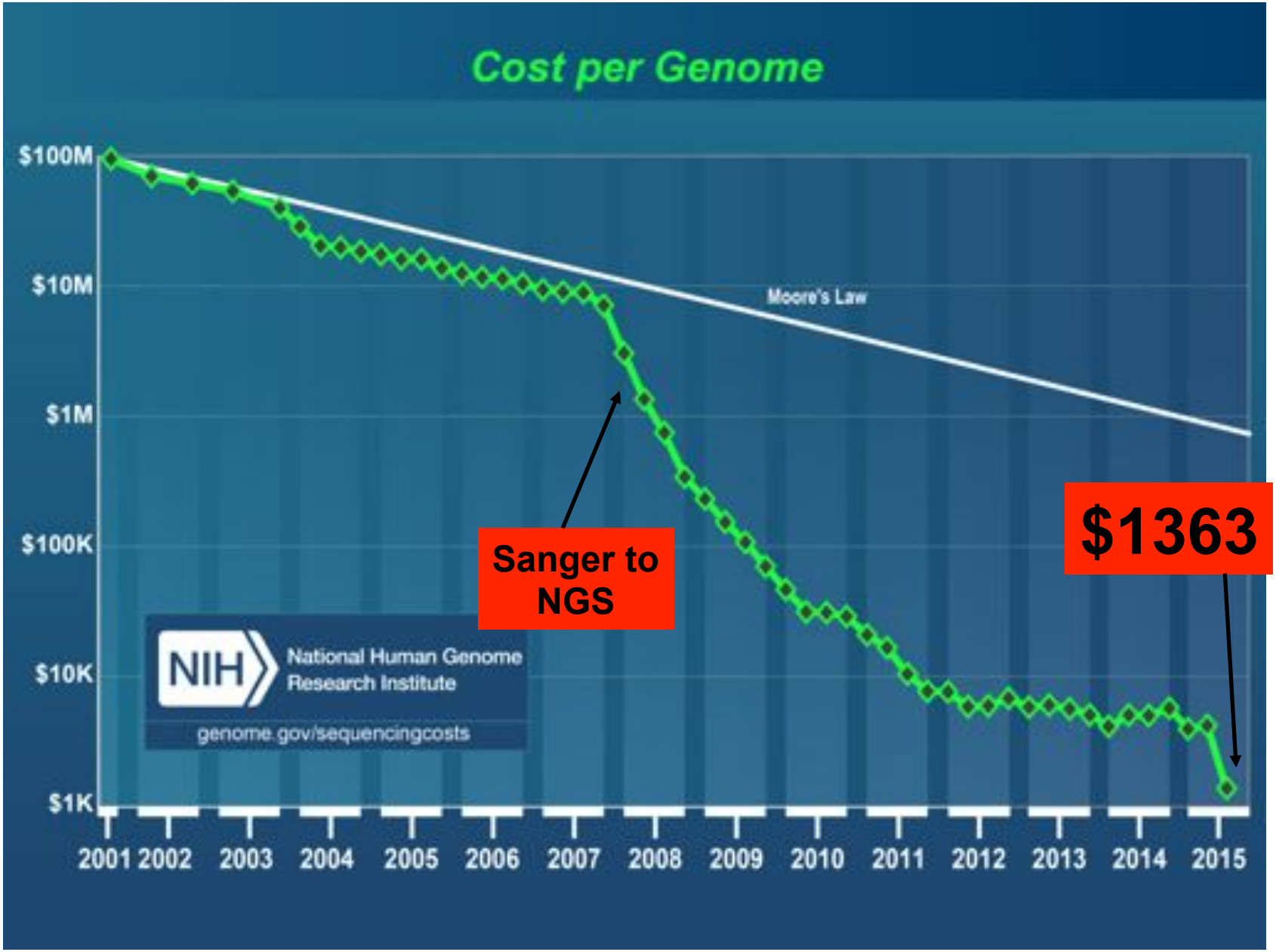
2011 'Small' gene **panels** (HCM 13 genes)

2012 'Larger' gene panels (Retinal Dystrophy 100+ genes)

2013 **Whole exome sequencing (WES)** technology established
Results from DDD Research Study

2014 Wide choice of panels
Talk of **'mainstreaming'** genetic testing

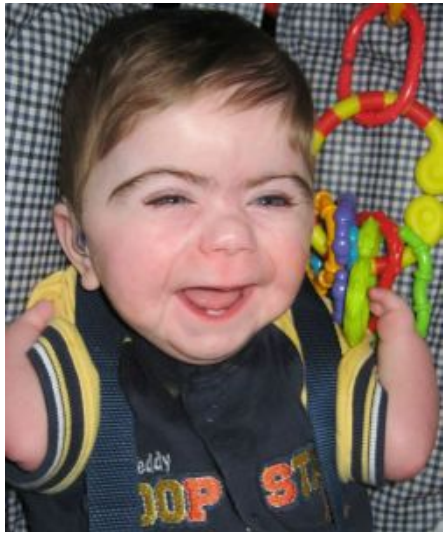
2015 WES available clinically
Whole Genome Sequencing via **100k Genomes Project**



Wetterstrand KA. DNA Sequencing Costs: Data from the NHGRI Genome Sequencing Program (GSP)
Available at: www.genome.gov/sequencingcosts. Accessed [12 Oct 2015].

Next-gen sequencing

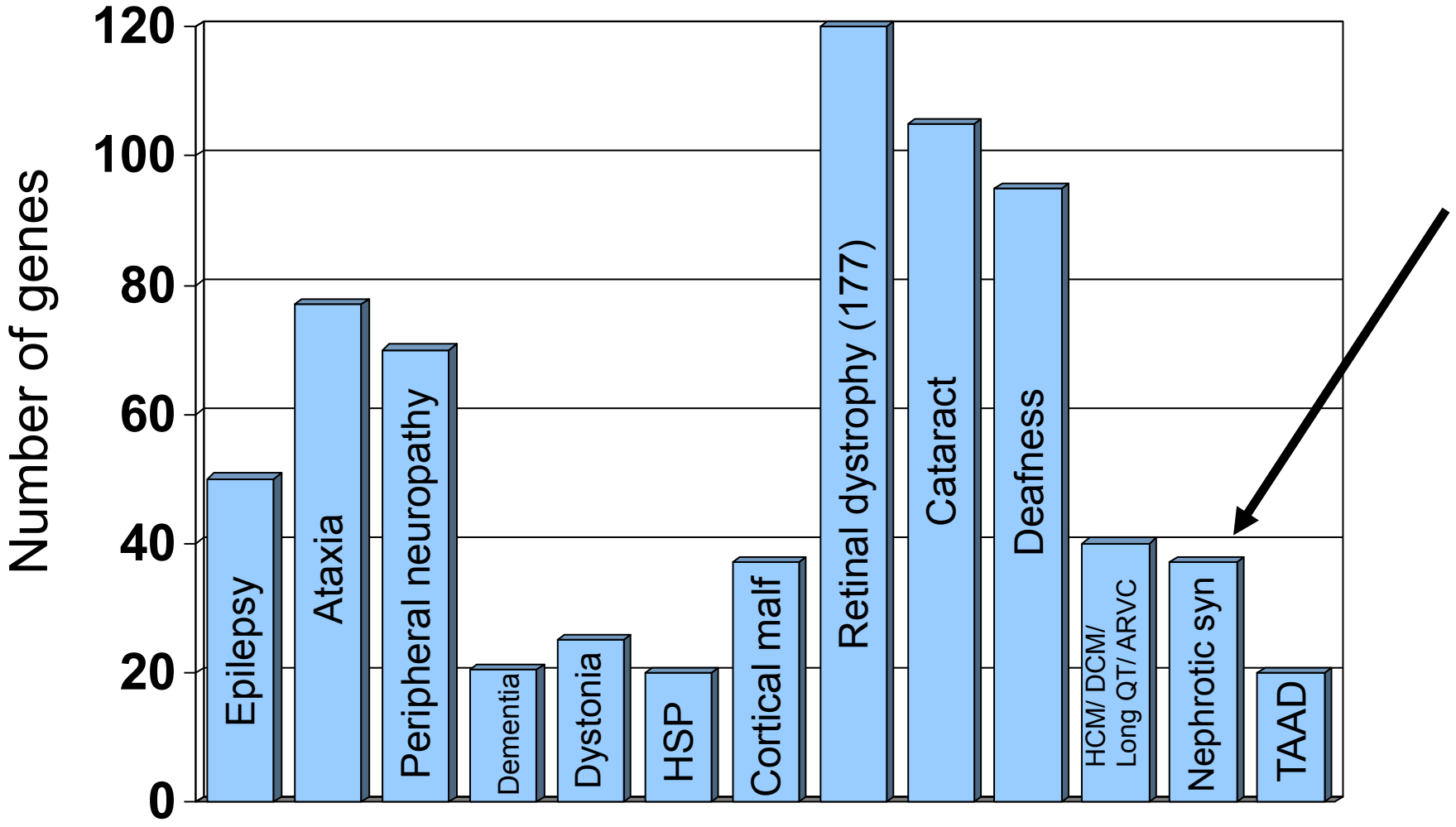
- Simultaneous analysis of multiple genes
- Fraction of cost vs Sanger sequencing
- 8-16 week turnaround



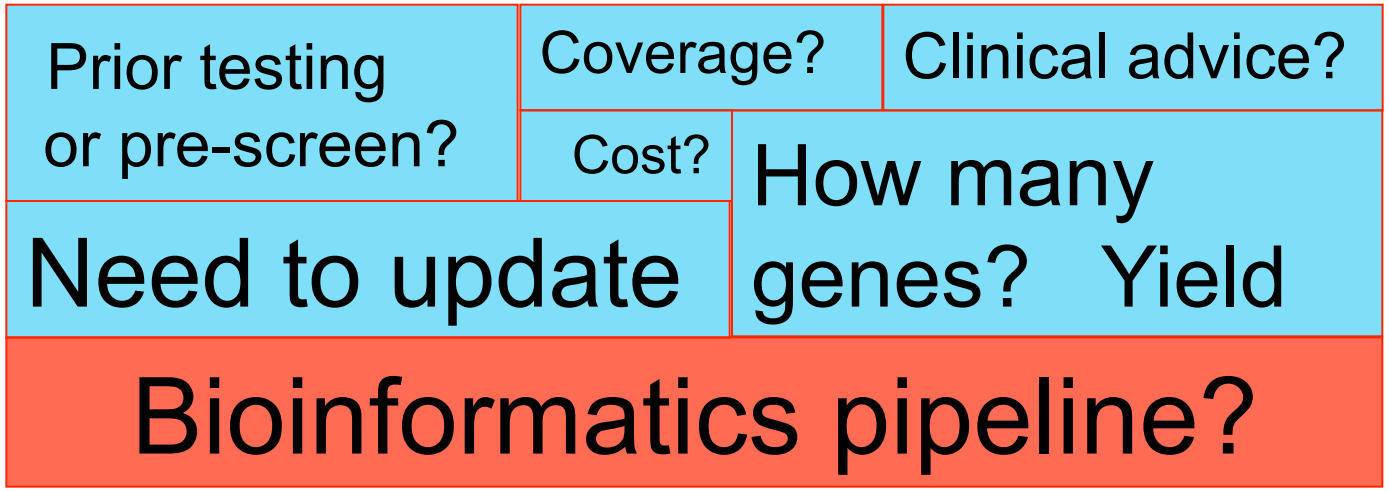
‘Syndrome’
Cornelia de Lange

Not syndrome
Eg, renal failure

Panels


Number of genes
120
100
80
60
40
20
0
Epilepsy
Ataxia
Peripheral neuropathy
Dementia
Dystonia
HSP
Cortical malf
Retinal dystrophy (177)
Cataract
Deafness
HCM/ DCM/
Long QT/ ARVC
Nephrotic syn
TAAD

How to build a panel?



Exome

- All **ex**ons in the gen**ome**
- ~180,000 exons in 20,000 genes
- 1-2% of whole genome

Deciphering Developmental Disorders

Whole exome sequencing
Parents-child trio

RECRUITMENT CLOSED in April 2015

- **Total ~14000 patients**
  - 538 Nottingham (~4%)
  - 35 results so far
  - Finish analysis by Oct 2016
- **Renal phenotypes**
  - 67 renal agenesis
  - 24 renal insuff or ESRD
  - 14 nephrotic syndrome

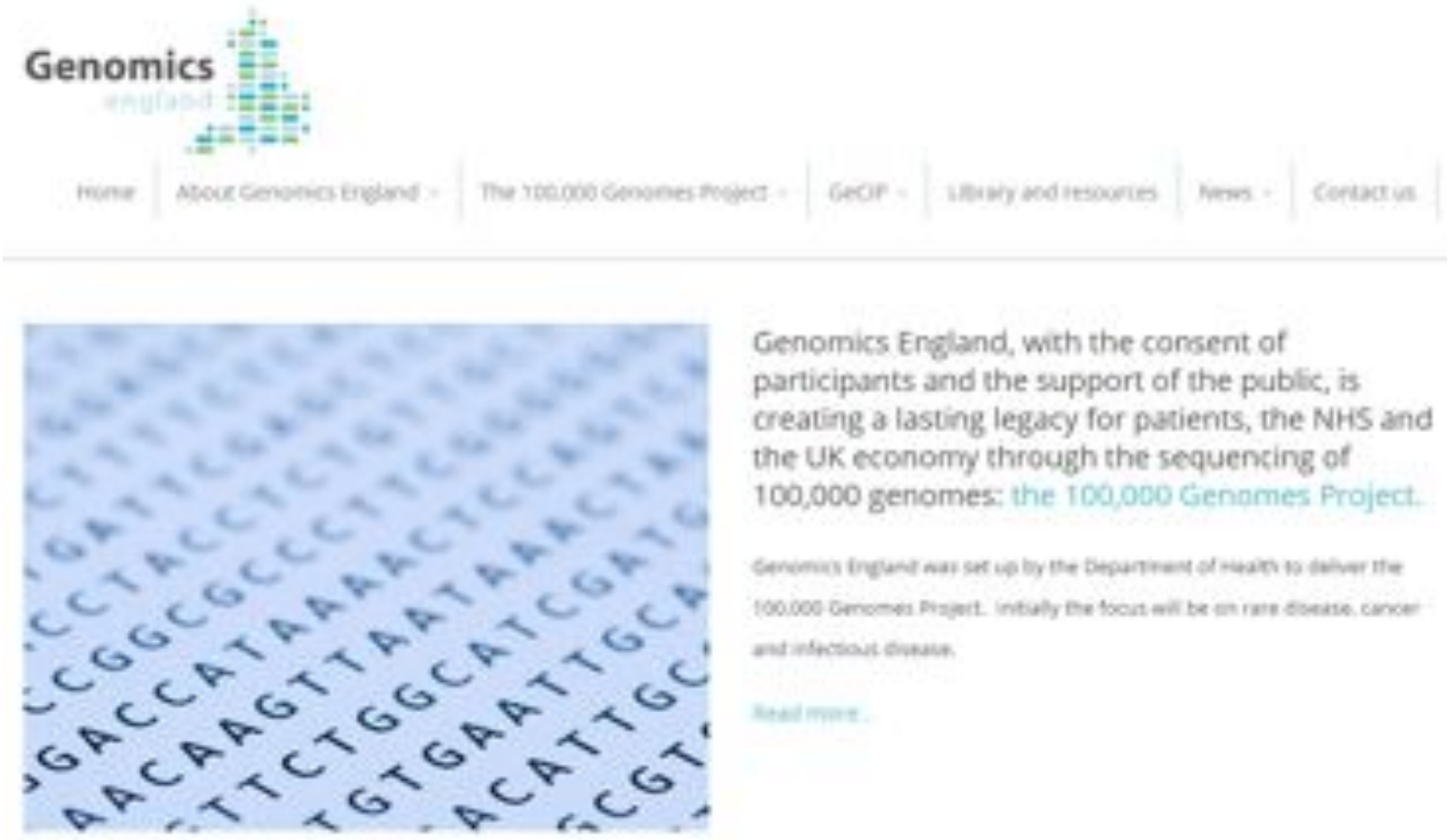
Clinical exome

- Presently offered via Cambridge Genetics Lab
- ~4800 genes known to be associated with genetic disorders
  - Off the shelf or customised panels
  - Sequencing of all genes possible in patients with very complex multisystem phenotypes
- £650
- Report in 6 months

Genome

- Everything!
- Exons and introns (genes) AND intergenic DNA
- 3.3 billion base pairs

100,000 Genomes Project



Who can have their genome sequenced?

Rare disease

~17000 probands

Broad categories

'Eligibility' criteria

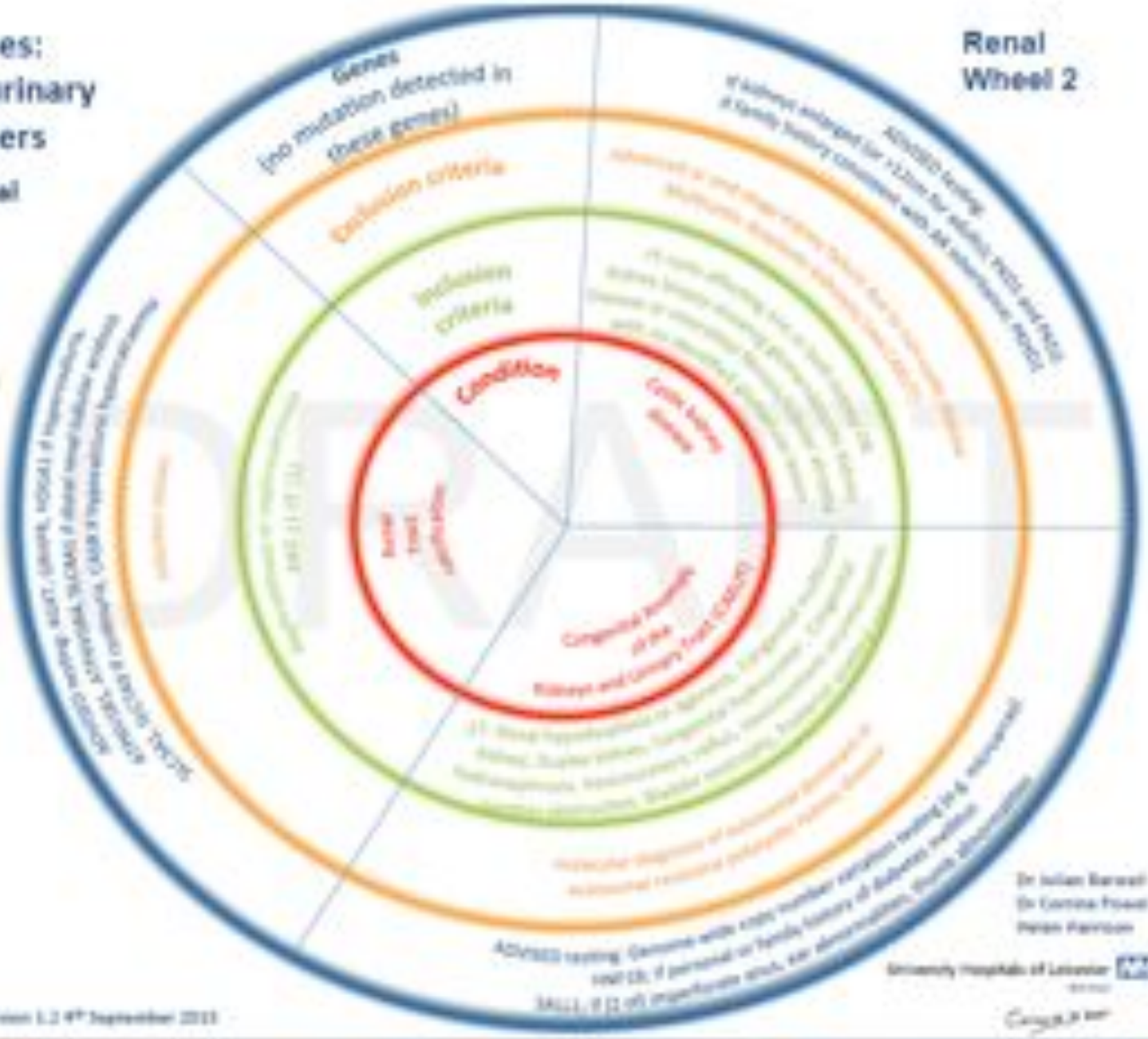
146 page pdf

Cancers
(blood and tumour)

~25,000 patients

Rare Diseases: Renal and urinary tract disorders

Renal Structural and Tubular Dysfunction



Dr Julian Barwell
Dr Corinna Proud
Helen Harrison
University Hospitals of Leicester NHS

2nd October 2015
Eligibility Statement version 1.2 4th September 2015

Nottingham, Leicester and Cambridge are the East of England GMC

Consent and recruitment of patients by Specialist Nurse(s)

First 2 Nottingham families recruited in Sept 2015

http://www.genomicsengland.co.uk/

http://www.genomicseducation.hee.nhs.uk/genomicsmsc/

The White House
Office of the Press Secretary

For Immediate Release

January 30, 2015

SHARE THIS:

FACT SHEET: President Obama's Precision Medicine Initiative

Building on President Obama's announcement in his State of the Union Address, today the Administration is unveiling details about the

Personalised Medicine

The 100,000 Genomes Project

The project will sequence 100,000 genomes from around 70,000 people. Participants are NHS patients with a rare disease, plus their families, and patients with cancer.

The aim is to create a new genomic medicine service for the NHS – transforming the way people are cared for. Patients may be offered a diagnosis where there wasn't one before. In time, there is the potential of new and more effective treatments.

The project will also enable new medical research. Combining genomic sequence data with medical records is a ground-breaking resource. Researchers will study how best to use genomics in healthcare and how best to interpret the data to help patients. The causes, diagnosis and treatment of disease will also be investigated. We also aim to kick-start a UK genomics industry. This is currently the largest national sequencing project of its kind in the world.

Challenges and pitfalls

Sanger sequencing

NGS, WES and WGS……

Bycatch

Variants of uncertain significance, variants in more than one gene and incidental but very significant changes in other (eg cancer) genes

The analytical bottleneck

- Exome
  - 12000 variants
- Genome
  - 5000000 variants

The key to interpreting the significance of genetic difference(s) noted in an individual is to distinguish

- **Benign natural variation**

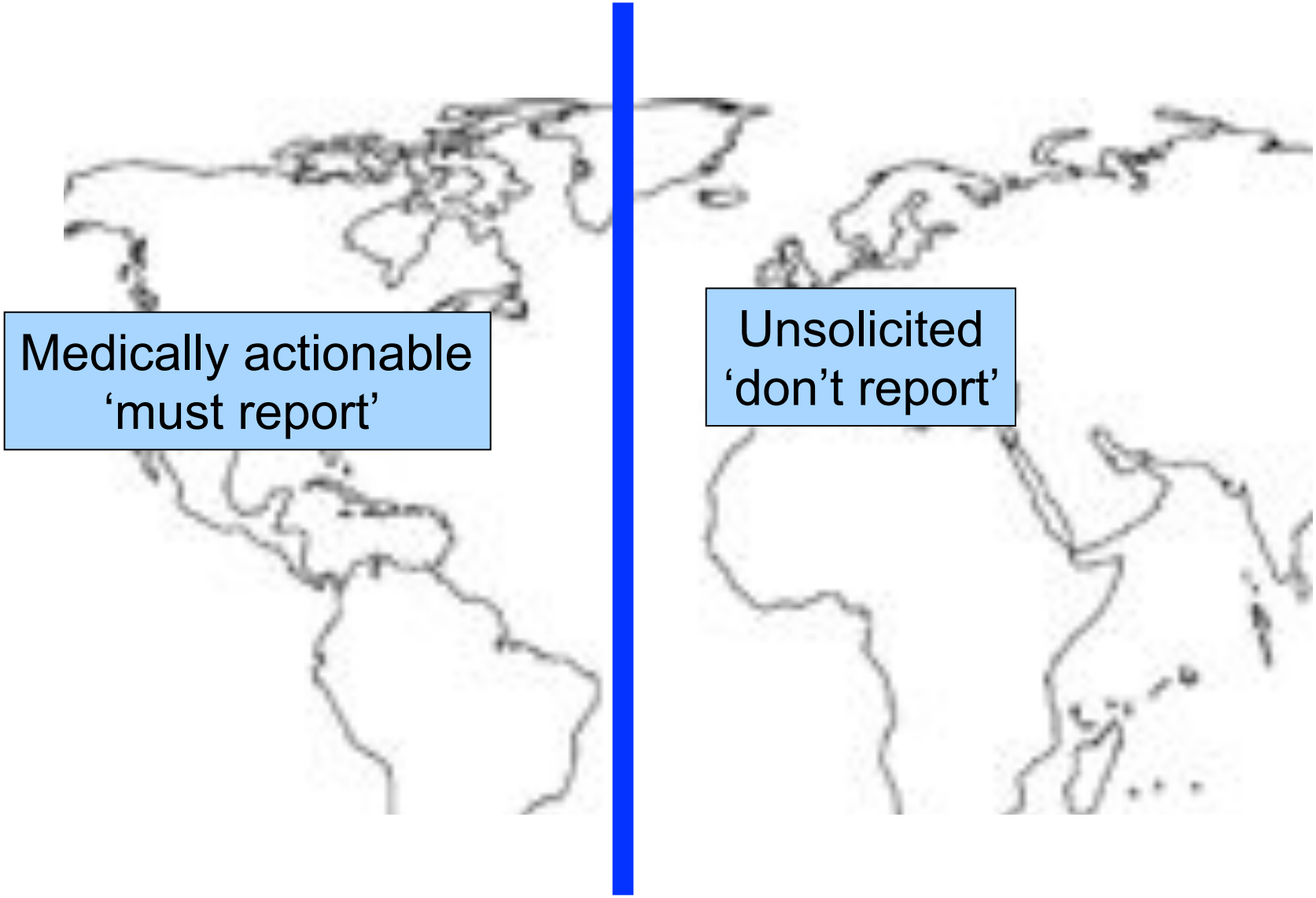
vs

- **Pathogenic mutation**

and minimise (hopefully)

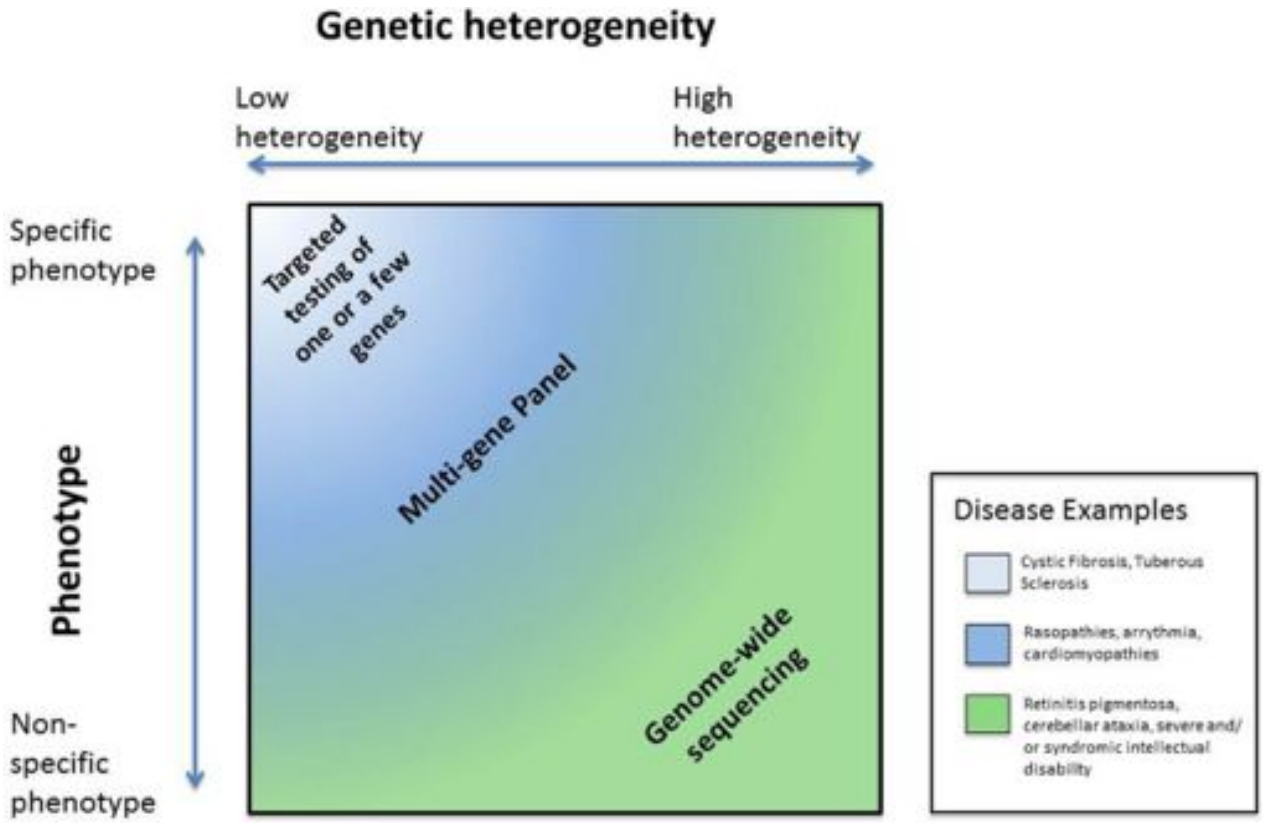
- Variants of unknown significance

Incidental findings



POSITION STATEMENT

The clinical application of genome-wide sequencing for monogenic diseases in Canada: Position Statement of the Canadian College of Medical Geneticists



J Med Genet 2015;52:431–437

Genomics for ALL

Delivery of genetic testing by geneticists is unsustainable and unnecessary

- Education
  - Genetics ⟺ Nephrology
- MDTs and joint clinics

http://www.genomicseducation.hee.nhs.uk/genomicsmsc/

Where are we now?