Genomic Medicine

An update on the current state of play within the UK

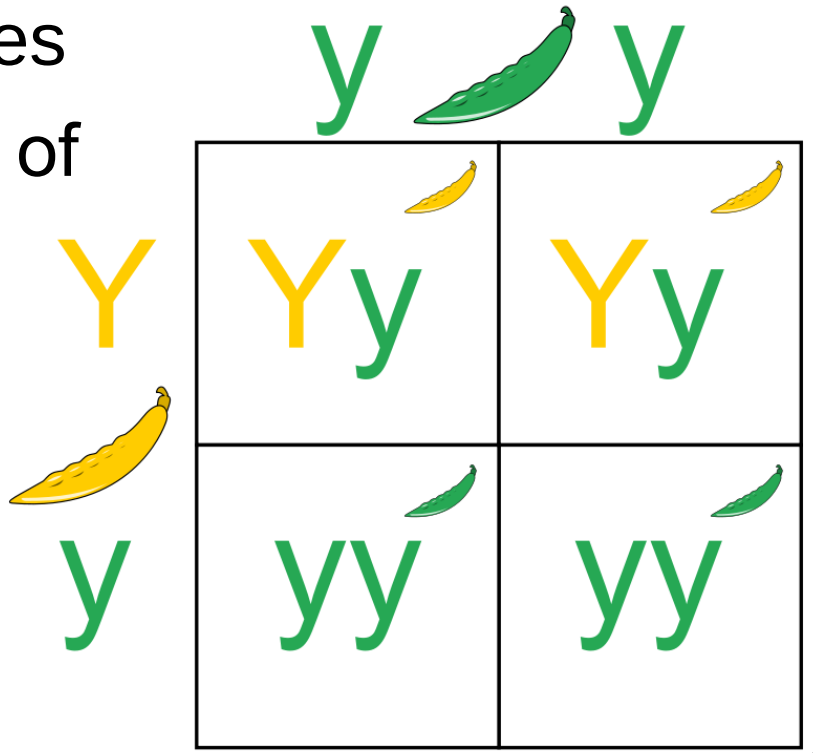
James Wingfield
Genomic and personalised medicine

Genetics Vs Genomics

Imperial College Healthcare NHS Trust

Genetics

- The study of heredity
- The study of the function and composition of single genes
- ‘Gene’: specific sequence of DNA that codes for a functional molecule



https://en.wikipedia.org/wiki/Punnett_square#/media/File:Punnett_Square.svg

Genetics Vs Genomics

Imperial College Healthcare NHS Trust

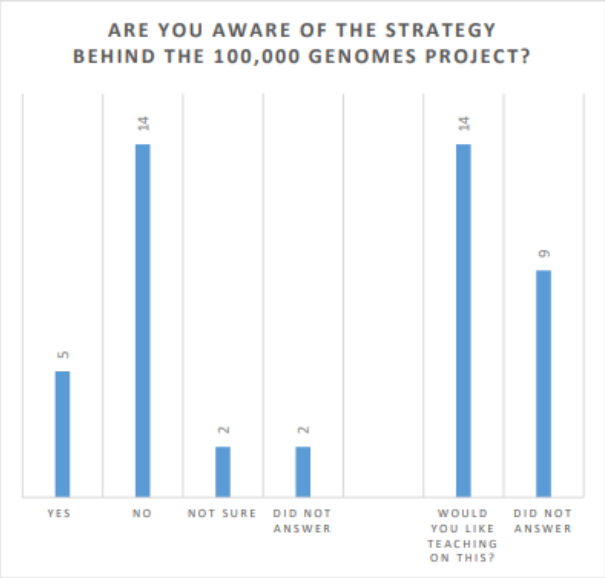
Genomics

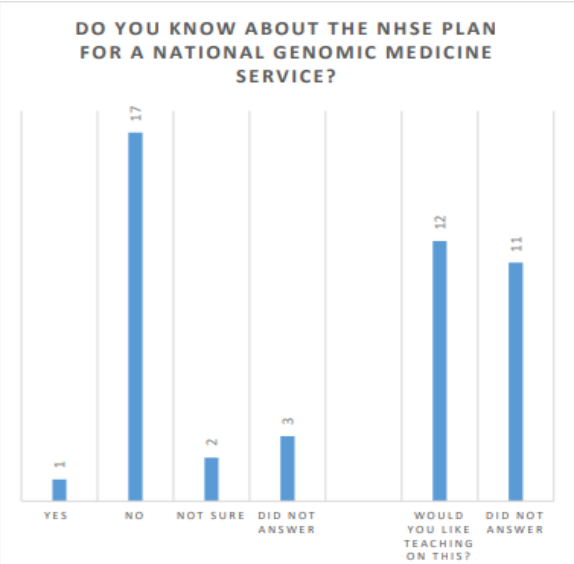
- The study of an organisms complete set of genetic information
- The genome includes both genes (coding) and non-coding DNA
- ‘Genome’: the complete genetic information of an organism

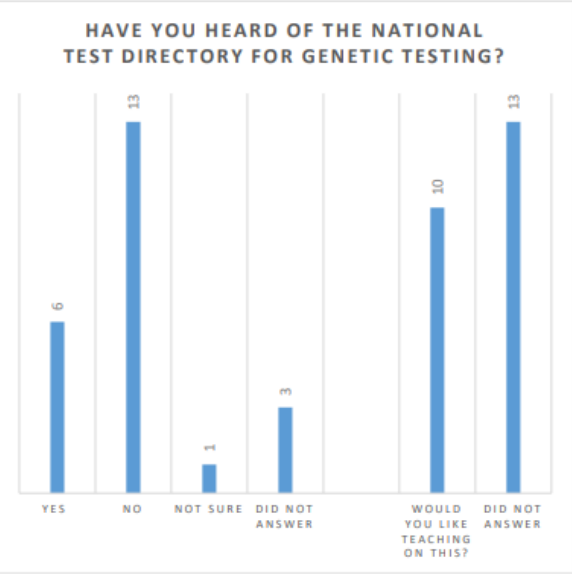
https://www.scripps.edu/science-and-medicine/translational-institute/translational-research/genomic-medicine/index.html

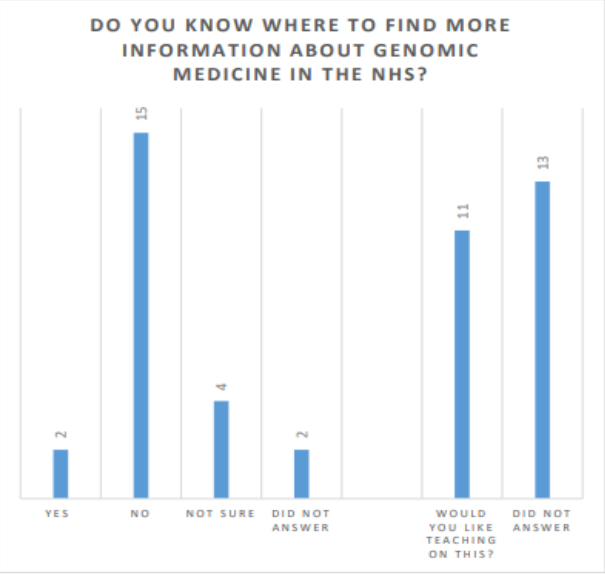
GP Genomics Survey

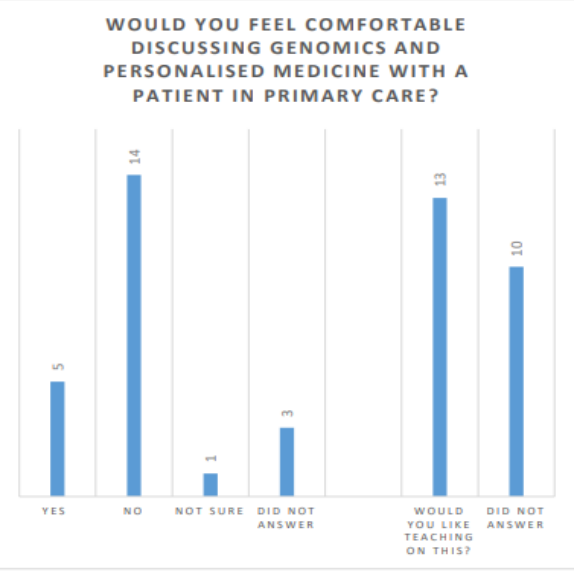
Imperial College Healthcare NHS Trust

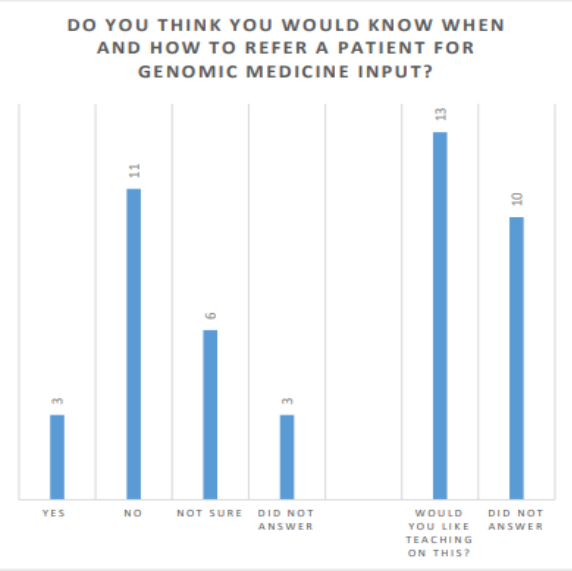






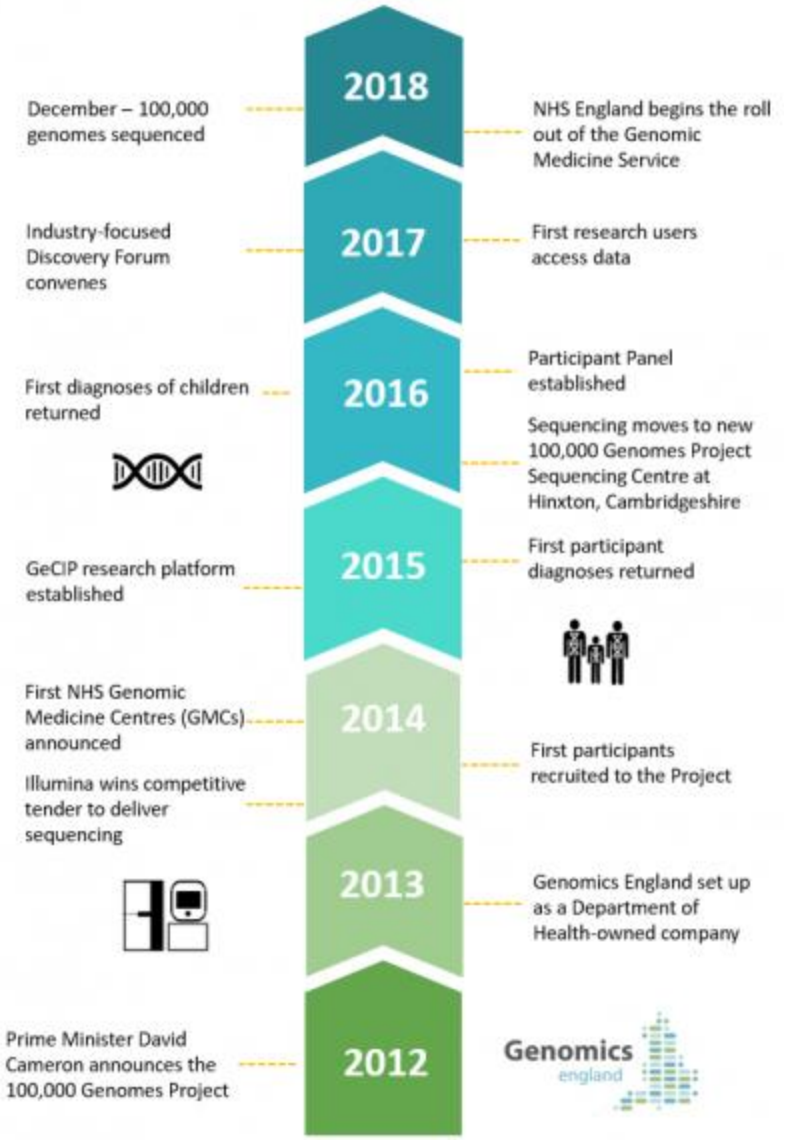


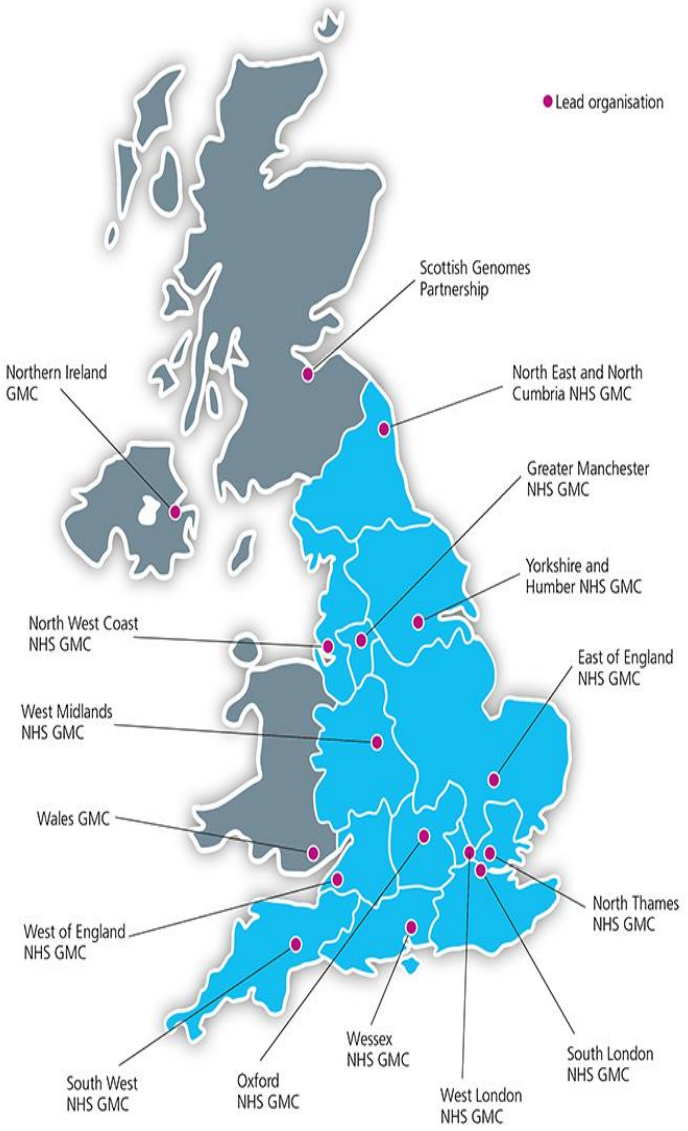




100,000 Genomes Project

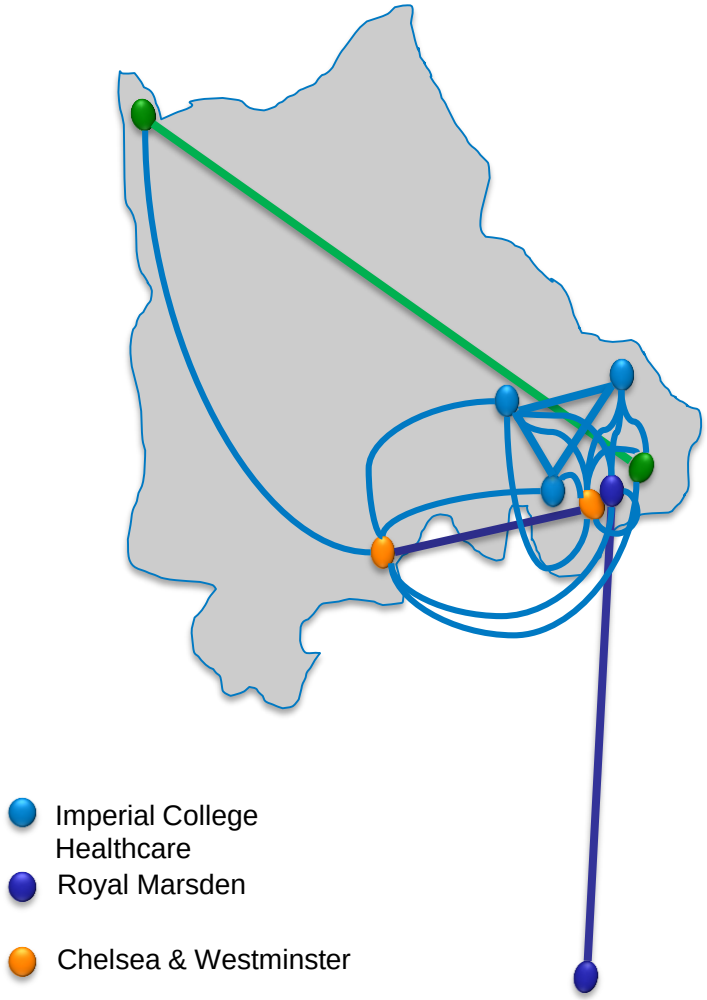
Imperial College Healthcare NHS Trust





West London Genomic Medicine Centre

Imperial College Healthcare NHS Trust



Serving a population of 2.5 million
Covering boroughs of:

- Kensington
- Chelsea
- Hammersmith & Fulham
- Sutton
- Hillingdon

NHS West London NHS Genomic Medicine Centre

100,000 Genomes Project

Imperial College Healthcare NHS Trust

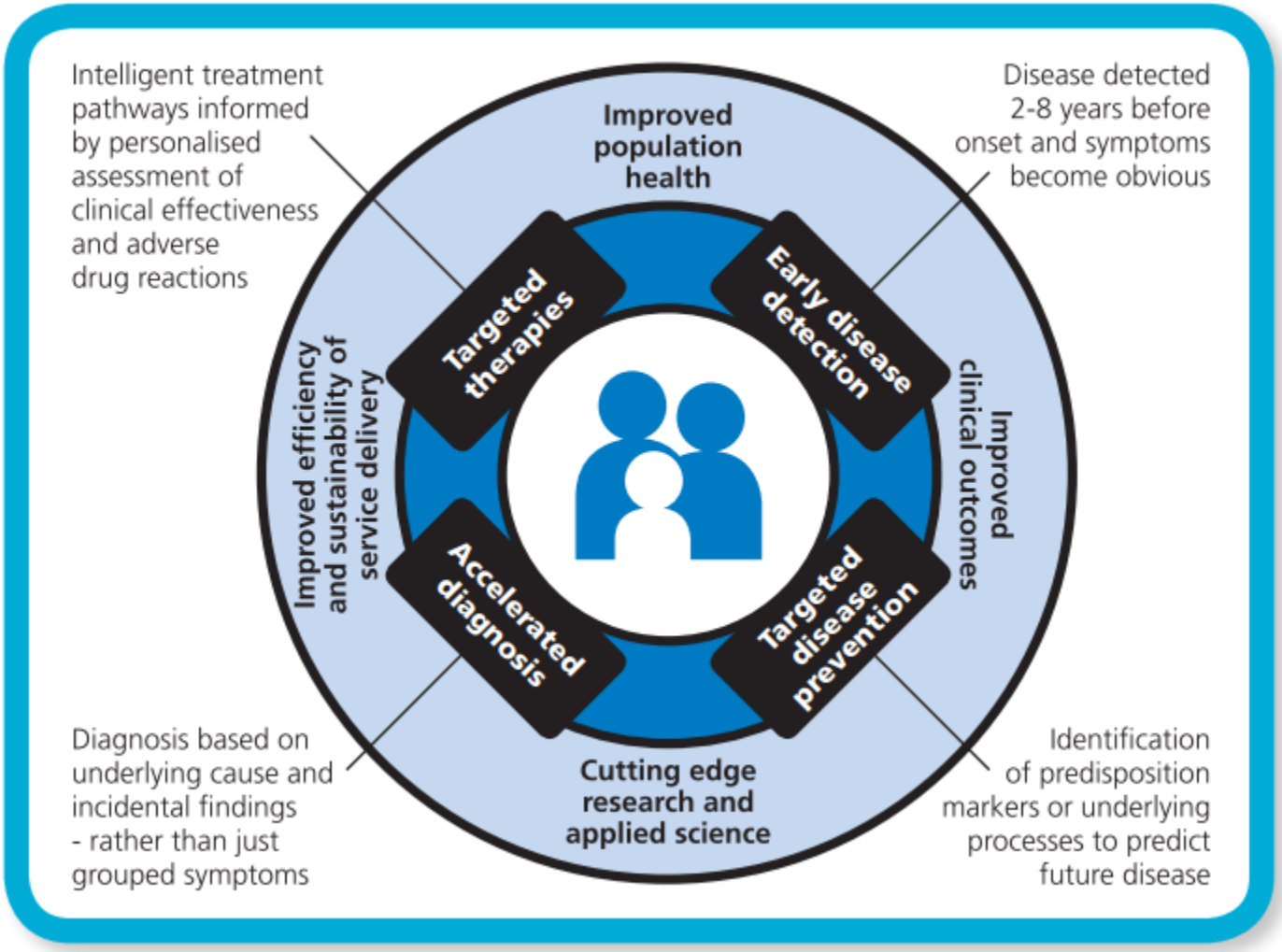
1. To bring benefit to NHS patients
2. To create an ethical and transparent programme based on consent
3. To enable new scientific discovery and medical insights
4. To kickstart the development of a UK genomics industry

Genomics england

Personalised medicine

Imperial College Healthcare NHS Trust

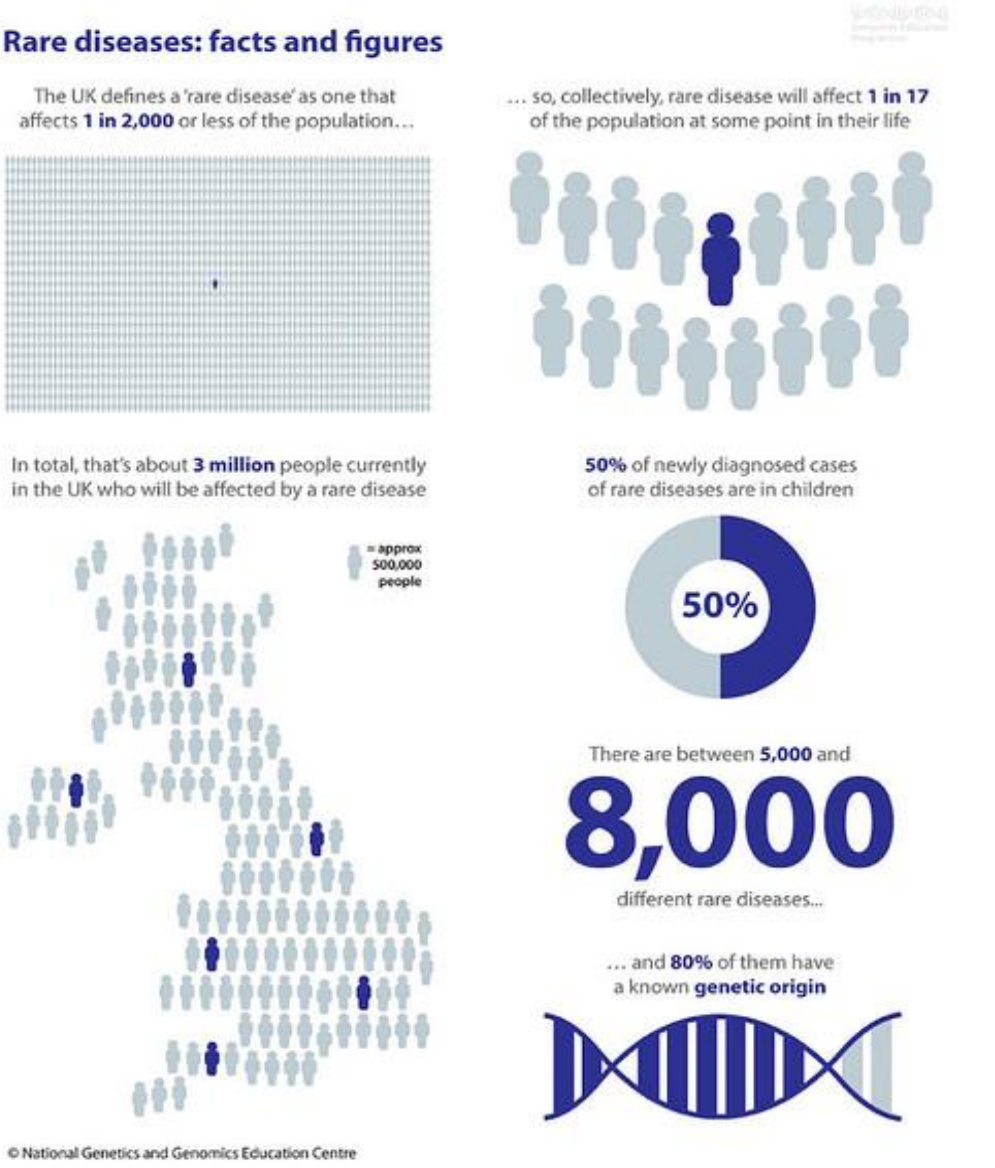
Figure 3



Improving outcomes through personalised medicine, NHS England 2016

Why rare disease?

Imperial College Healthcare NHS Trust



Why cancer?

Imperial College Healthcare NHS Trust

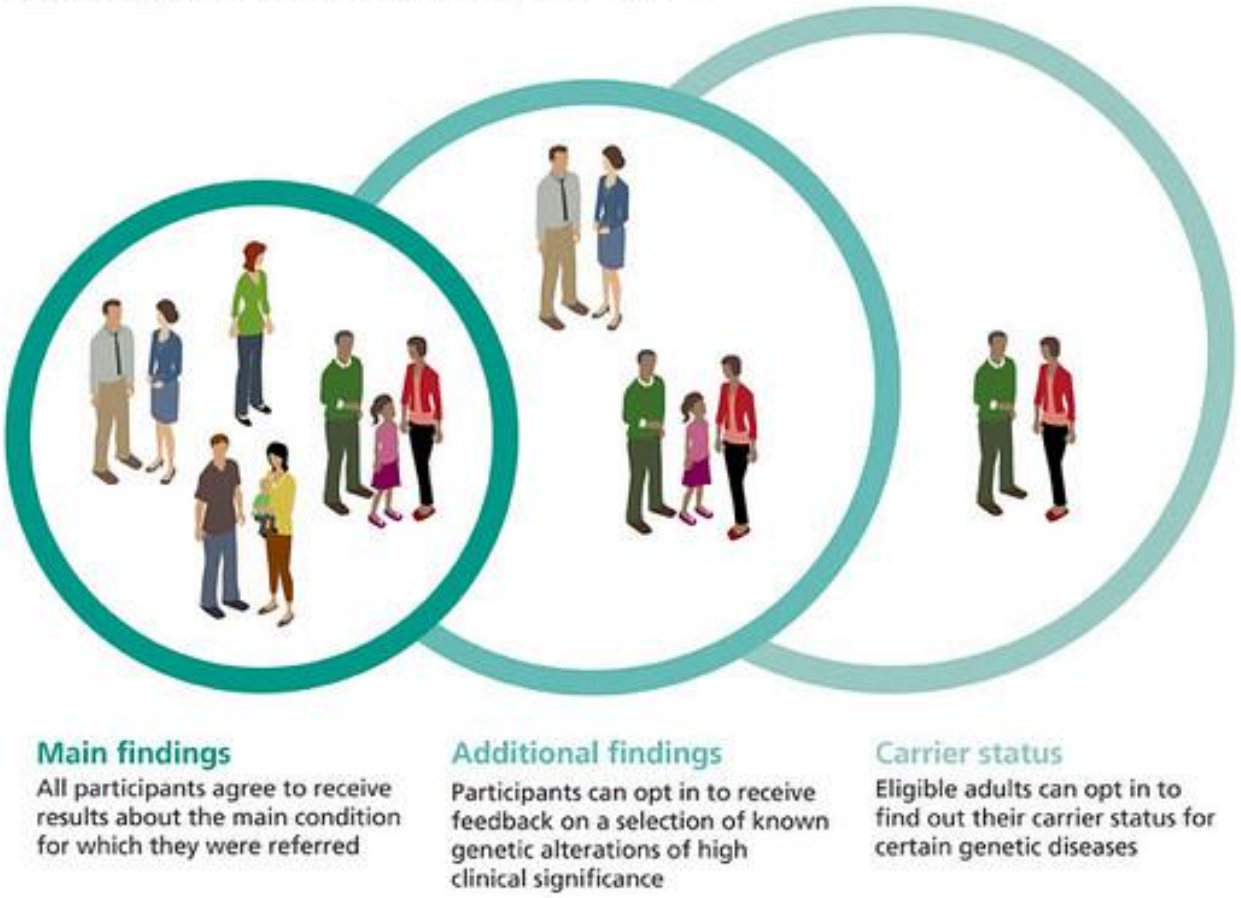
- Collectively the UK's largest killer
- 360,000 diagnoses every year
- 160,000 deaths
- Genomic disease

"Cancer is a disease of disordered genomes: acquisition of serial genomic mutations results in progressive escape from the mechanisms that regulate cell division, leading to tumourigenesis, invasiveness, and metastasis"

Garraway LA, Lander ES. *Lessons from the cancer genome. Cell2013;153:17-37*

Types of feedback

Imperial College Healthcare NHS Trust



Additional Findings (AFs)

Imperial College Healthcare NHS Trust

A carefully curated set of known pathogenic variants in selected genes:

1. Health-related AFs: genes which cause a disease which can be treated/screened for

2. Reproductive AFs: genes which cause severe disease in offspring

NB NOT incidental findings: these are defined as being anything which is neither ‘main’ nor ‘additional’, and won’t be reported, eg Variants of Unknown Significance (VUS), non-paternity (if not clinically relevant), health-related but non-actionable

Additional Findings (AFs)

Imperial College Healthcare NHS Trust

Bowel cancer predisposition:
MLH1 (adult only)
MSH2 (adult only)
MSH6 (adult only)
APC (adult and child)
MUTYH (adult only)

Breast and ovarian cancer predisposition:
BRCA1 (adult only)
BRCA2 (adult only)

Other cancer predisposition:
VHL (adult and child)
MEN1 (adult and child)
RET (adult and child)

Familial hypercholesterolaemia:
LDLR (adult and child)
APOB (adult and child)
PCSK9 (adult and child)

Autosomal recessive carrier status:
CFTR (Cystic fibrosis)

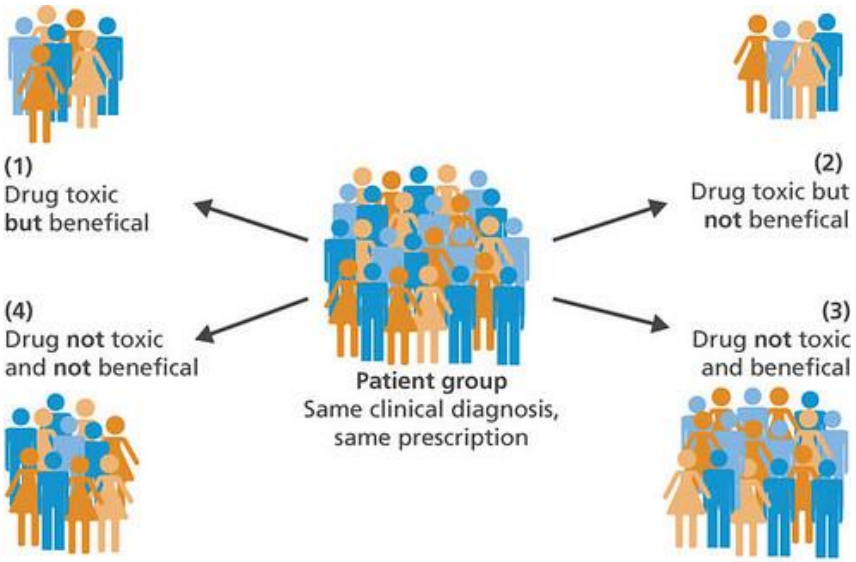
The list will change as new evidence and technical know-how are available

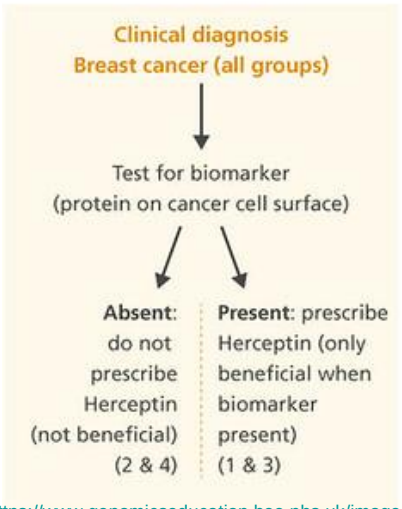
Results will be issued separately (later) than main findings

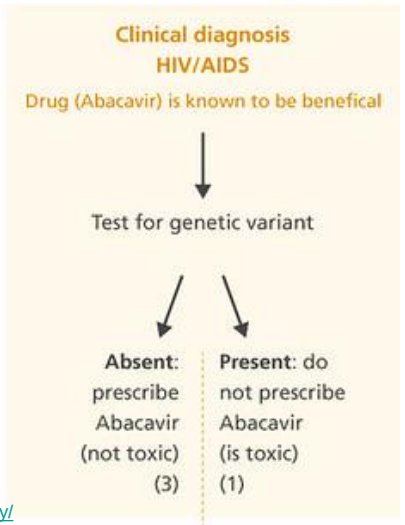
The chance of getting an AF is probably < 1 in 100

'Broad consent' aims to establish whether the participant wants this type of information or not; they can opt in or out of AFs at any time

Types of feedback - Pharmacogenomics







https://www.genomicseducation.hee.nhs.uk/image-library/

The use of genetic and genomic information to tailor pharmaceutical treatment to an individual

Imperial College Healthcare NHS Trust

Return of results

The West London Genomic Medicine Centre teams are currently working through the results from the 100,000 Genomes Project and expect to return results to consultants by the end of March 2020

Patient story

NHS
West London
NHS Genomic Medicine Centre

https://www.genomicsengland.co.uk/about-genomics-england/participant-stories/

Genomic Medicine Service

In response to the success of the 100,000 Genomes Project, the NHS has launched the the National Genomic Medicine Service in 2019. The aims of this service are to:

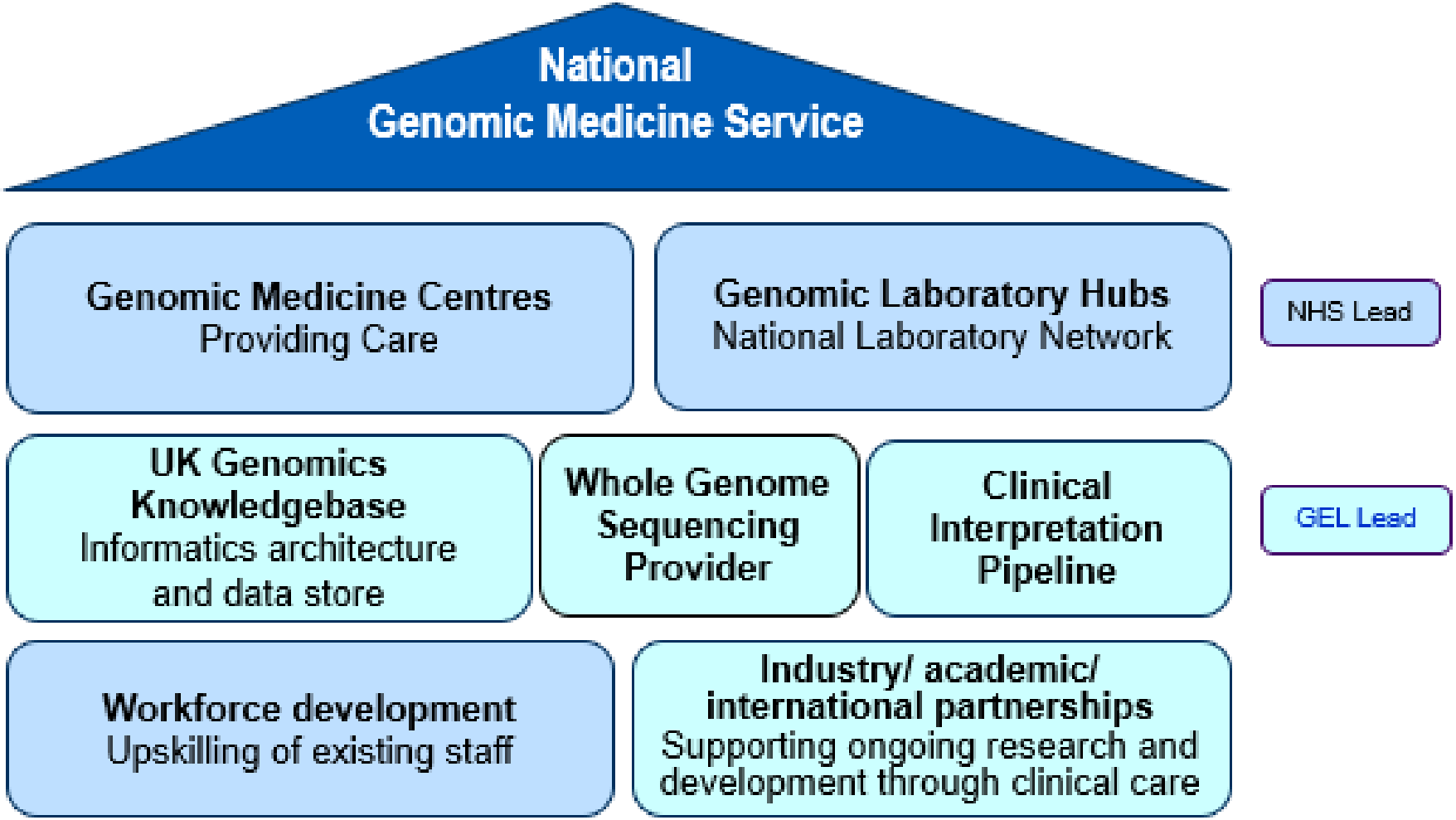
- Provide **equity of access** across England to the full range of clinically appropriate genomic & genetic tests
- **Standardise testing** for all patients
- **Keep the NHS up to date** with an annual review of available genetic and genomic tests, increasing the number of conditions eligible for Whole Genome Sequencing

Key elements

Imperial College Healthcare NHS Trust

1. A national genomic laboratory service through a network of **Genomic Laboratory Hubs**
2. A new **National Genomic Test Directory** to underpin the genomic laboratory network
3. A national **Whole Genomic Sequencing** provision and supporting informatics infrastructure developed in partnership with Genomics England
4. A clinical genomics medicine service and an evolved **Genomic Medicine Centre** service
5. A national co-ordinating and oversight function within **NHS England (Genomics Unit)**

Genomic Medicine Service



London North Genomic Laboratory Hub

What does this mean for patients?

Imperial College Healthcare NHS Trust

Whole genome sequencing has the potential to:

- Transform rare disease patients' lives through faster diagnosis, rather than years of uncertainty ('diagnostic odyssey')
- Matching people to the most effective medications and interventions, reducing the likelihood of adverse reactions
- Increase the number of people surviving cancer each year through more accurate diagnosis and more effective use of therapies

National genomic test directory

- The National Genomic Test Directory specifies which genomic and genetic tests are commissioned by the NHS, the technology by which they are available and patient eligibility
- There are 21 rare disease indications eligible for whole genome sequencings
- There are a small number of cancers eligible for whole genome sequencing. These include:
  - All paediatric tumours
  - Most sarcomas
  - Acute leukaemias

Available: https://www.england.nhs.uk/publication/national-genomic-test-directories/

Eligible rare disease indications

Clinical Indication
Ultra-rare and atypical monogenic disorders
Congenital malformation and dysmorphism syndromes - microarray and sequencing
Intellectual disability – microarray, fragile X and sequencing
Hypotonic infant with a likely central cause
Skeletal dysplasia
Rare syndromic craniosynostosis or isolated multisuture synostosis
Neonatal diabetes
Likely inborn error of metabolism - targeted testing not possible
Hereditary ataxia with onset in adulthood
Hereditary ataxia with onset in childhood
Early onset or syndromic epilepsy
Childhood onset hereditary spastic paraplegia
Arthrogryposis
Other rare neuromuscular disorders
Cerebellar anomalies
Holoprosencephaly - NOT chromosomal
Hydrocephalus
Cerebral malformation
Severe microcephaly
Childhood onset leukodystrophy
Cystic renal disease

Commissioning arrangements

- Most Rare and Inherited Disease genomic testing is funded directly by specialised commissioning
- Cancer genomic testing is funded from within tariff as part of the cost for diagnostic and imaging services
- WGS will be funded directly by NHS England
- Charging arrangements for tests associated with Highly Specialised Services should remain unchanged until 31st March 2020
- Funding for genomic testing is expected to be standardised from 1st April 2020

Educational resources

Imperial College Healthcare NHS Trust

Genomics Education Programme

Search (hit return for all results)

Health Education England

Home | Education | Genomics in Healthcare | Blog | News & Events | About us

HEE Genomics Education Programme

Delivering genomics education, training and experience for the healthcare workforce

Learn about the impact of genomics

Try our educational opportunities for health professionals. Get started below, or browse our full collection.

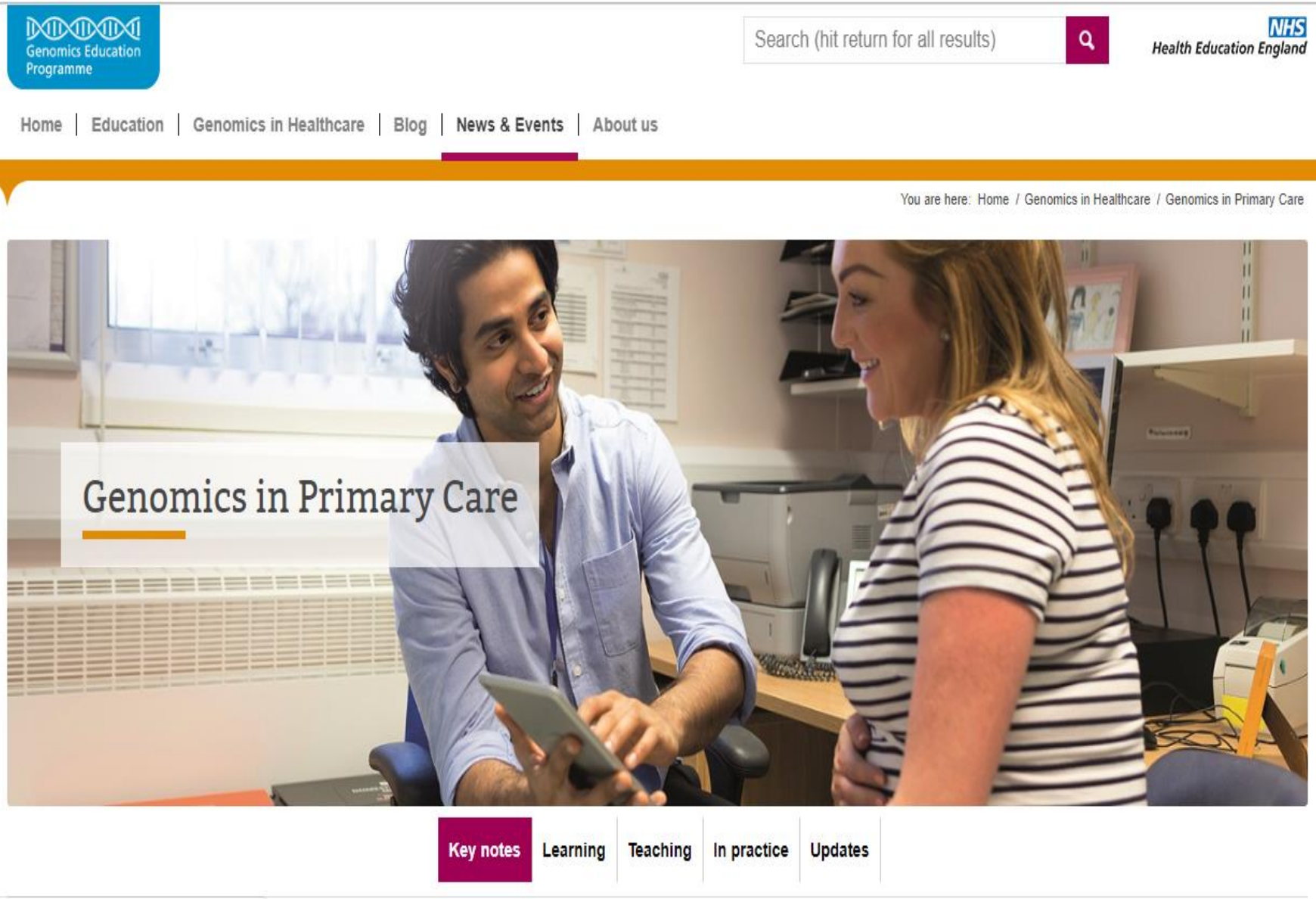
FEATURED PROFESSION

BITESIZE LEARNING

ENTRY-LEVEL COURSE

Educational resources

NHS
Imperial College Healthcare
NHS Trust



NHS long term plan

- Genomics has been identified as a priority in the NHS Long Term Plan and the NHS People Plan (2019) and the Topol Review (2019)
- Imperial College Healthcare NHS Trust is committed to working closely with our colleagues in Primary Care and Public Health

“Genomics will become integral to all medical specialties. While some aspects will remain with highly specialised professionals, many will become mainstream and embedded in routine healthcare delivery. The health workforce will play a key role in ensuring that genomic technologies are efficiently, appropriately and equitably deployed, so that individuals can understand how genetics can affect their health. ”

- Topol review

Thank you