The 100,000 Genomes Project: Transforming healthcare through genomic medicine

“This project represents a great opportunity to translate our world class genomic science into world leadership in genomic medicine.”

Sir John Chisholm, former chair of the Medical Research Council.
Aims today

• Provide an overview of the project and its aims
• Explore the future of ‘consenting for genomic tests’
• Consider the implications around ‘testing in families’
• Examine the issues around ‘my data/your data’
100,000 Genomes Project: The vision

1. Sequence 100,000 Genomes…
2. To bring benefit to patients
3. To create an ethical and transparent programme based on consent
4. To enable new scientific discovery and medical insights
5. To kick-start the development of a UK genomics industry

Sue Hill OBE Chief Scientific Officer for England
What is a genome?

- A genome is an organism’s complete set of DNA, including all of its genes.

- In humans, a copy of the entire genome—more than 3 billion DNA base pairs—is contained in all cells that have a nucleus.

- Each genome contains the information needed to grow, maintain and repair that organism.

- There are 3.2 billion letters in a genome—enough to fill a stack of paperback books 61 m high.
What is the 100,000 Genomes Project?

- NHS healthcare transformation programme to improve diagnosis and treatment
- Currently available for patients with certain types of cancer and rare diseases
- Based on patient consent – opt-in
- Blood, tissue or saliva samples collected
- In addition, results can be used for research to provide greater understanding of disease
How does it work?

- Patients and sometimes their families are referred by their clinician.
- Participants read a Patient Information Sheet before being able to give consent.
- Blood or saliva samples are collected for patients and their families (Rare Disease).
- Blood and tissue or saliva samples are donated by patients (cancer/suspected cancer).
- Participants can choose to ask for ‘looked for’ findings.
- Results can be used for research to provide greater understanding of disease.
- A diagnosis may be identified to help treatment.
Why is this important?

- 5000-8000 rare diseases affecting around 3 million people in the UK
- 80% have a genetic cause
- 50% of new cases are in children

- Over 350,000 people are diagnosed with cancer every year
- Over 160,000 people die from cancer every year
- Cancer can be described as a genomic disease
What does it mean for participants?

- Provide a **diagnostic test** for a known condition
- Provide samples for testing for **additional findings**
- **Support research** in the future

‘Big Data’
What does it mean for NHS?

- **Targeted disease prevention**
  Identification of predisposition markers or underlying processes can predict future disease

- **Early disease detection**
  2-8 yrs before onset & symptoms become obvious with low cost stratification

- **Accelerated diagnosis**
  Based on underlying cause

- **Targeted therapy**
  Identification of effective personalised treatments

- **Improves outcomes**
  - Greater efficiency from streamlined care pathways
  - Earlier and more precise diagnosis and treatment
  - Fewer and less complicated surgical interventions
  - Fewer patients getting cancer and other diseases
Providing a better diagnosis

Sophie
Diagnosed with type 1 diabetes at 3 months
4 insulin injections a day
major problems with low
and high glucose

Genetic testing
Mutation in
KCNJ11 gene
Diagnosis
not type 1 diabetes
but neonatal diabetes

Can replace insulin
injections with
glibenclamide tablets

Glucose much lower and
more stable
No problem with hypos
Genomics and cancer therapy

Mrs K, 62 year old keen golfer, rapid deterioration, metastatic lung cancer

2\textsuperscript{nd} opinion as “Unfit for chemotherapy”, almost bed bound

Test tumour for EGFR mutations in genetics lab

EGFR Mutation detected

EGFR mutation predicts response to gefitinib

Dramatic response
Cooked/entertained Xmas dinner for 10!
Better prevention - BRCA1 mutation

- Lifetime risk of breast cancer: 80%
- 2-3% pa 30y onwards
- Lifetime risk of ovarian cancer: 20-60%
- Most over 50y

- Early breast surveillance - mammography and MRI
- Chemoprevention
- Risk-reducing surgery
- No proven surveillance for ovarian cancer
- Risk-reducing salpingo-oophorectomy

Autosomal dominant inheritance
1 in 2 offspring will have mutation
The 100,000 Genomes Project
South West Genomic Medicine Centre
(SWGMC)

1587 people already taken part
Working in partnership:

- 592 families with rare disease
- 273 cancer participants
Current rare disease eligible categories:

- Intellectual Disability
- Multiple Epiphyseal Dysplasia
- Charcot-Marie-Tooth disease
- Ketotic hypoglycaemia
- Silver Russell syndrome
- Congenital Hearing Impairment
- Syndromic Congenital Heart Disease
- IUGR and IGF abnormalities
- Familial Focal Epilepsies
- Congenital Anomaly of the Kidneys and Urinary Tract
- Non-CF bronchiectasis
- Silver Russell syndrome
15 eligible cancer types

- Adult Brain Tumours
- Bladder
- Breast
- Childhood Solid Tumours
- Colorectal
- Endometrial
- Haemtaological Malignancies (AML, CLL, myeloma)
- Lung
- Melanoma
- Ovarian
- Prostate
- Renal
- Sarcoma
- Testicular
- Upper GI

- All invasive malignancies are eligible for submission to the cancer programme
- Patient can be newly diagnosed, have received neoadjuvant treatment, chemotherapy, radiotherapy or be ‘recurrent’
- Resection most common route of specimen capture - biopsy pathway may be a possibility in the future
Access for patients with rare disease

Index cases referred by Trust and Speciality (n=727)

Patients referred by each Trust Q2 2017-2018 n= 57

Participants seen at each Trust Q2 2017-2018 n= 186
Access for patients with cancer
Number of cancer samples donated @30/09/2017  n= 216
What happens next?

“This technology has the potential to change medicine for ever but we need all NHS staff, patients and the public to recognise and embrace it’s huge potential”.

Dame Sally Davies (Chief Medical Officer for England)
The 100,000 Genomes Pathway

- **Patient Information Sheet** provided
- **Consent form** completed
- Provide a sample for examination to provide a *genetic diagnosis*
- Agree to share your data for that examination and to be used for research both now and later
- Results returned
The Genomes Pathway

- Whole Genome Sequencing as a test outside of clinical genetics
- The test should be requested and provided as part of normal clinical pathways
- Patients should still have the benefit of additional screening
- The valuable information resulting from testing can be used by researchers to further diagnosis and treatments and the health sciences
What should consent look like when genetic tests become part of routine care?

Working Group overview

- NHSE Consent Transition Working Group formed May 2017
- Membership includes:
  - NHSE – implementation unit, information governance and legal teams
  - Genomics England
  - NHS GMC representatives
  - BSGM/Royal Colleges consent and confidentiality working group representatives
  - Patient representation including charity representatives and 100,000 Genomes Project participant

- Objective: to develop a national consent model to cover all genetic and genomic testing
Different types of consent

**Consent in clinical practice and research has a different emphasis**

**Clinical consent**
Clinical treatment or intervention deemed necessary for health. Need to know risk/benefit balance. Consent often just one part of clinical relationship involving trust.

**Research consent**
Consent to take part in research for future health benefit. Focus on altruism, information, minimising risks, Helsinki principles. More contractual ‘free standing’ Obligatory consent forms.
Valid consent

1. Voluntary (free from coercion)

2. Informed “full” information risks and benefits of proposed treatment/intervention [“Healthcare professionals should not withhold information”]

3. Capacity Person must have capacity to decide and be able to “use the information to make an informed decision”
Consenting for genomic tests Questions:

Think about how consent looks now and how it might look in the future.

• What are the benefits of going through a consent process for a genetic test?

• How does this compare with your experience of agreeing to a hospital test?

• Can you think of a similar test or procedure and how did you give your consent?

• If the results are also used for research- is that valid consent? Does it matter?
But what about the family?
Case 1

Incidental findings
Case 1

• The microarray result identifies:
  – 17p12 deletion associated with hereditary neuropathy and pressure palsy
  – Xp21.1 deletion associated with X-linked muscular dystrophy
Case 1

• Neither of these findings are associated with Rehan’s learning difficulties or short stature

• Should the paediatrician reveal these findings?
Case 1

• The paediatrician informs the parents of the findings
• They are also referred to clinical genetics at this stage
• However the parents are really upset as they did not feel that there was a chance the test could reveal such unexpected information
• They are now very concerned about Rehan and the rest of the family
Case 4

Unexpected information
Case 4

- 11 month old Evie is investigated due to delayed motor milestones and hypotonia

- She is diagnosed with Spinal Muscular Atrophy (SMA)
Case 4

- Parents, Gail and Chris, are expected to be carriers
- Testing is offered to Gail and Chris to confirm this
- Gail is initially reluctant but eventually agrees to testing
Case 4

• Following the appointment Gail contacts the genetic counsellor and asks for the test results for both of them to be given to Gail.

• On discussion the genetic counsellor explains that the results will be given individually to both of them as it was his information.

• On discussion, Gail admits that she had an affair before Evie was born.
Testing in Families Questions:

Think about how our responsibility in health care changes when we start to diagnose and treat the whole family.

- Can we safeguard family members from unwanted information?
- Think about your family, would everyone agree and should they?
- What other issues can you see might arise from a genetic test as routine?
A 10 year-old girl with life threatening chicken pox

- Ten year old girl admitted to intensive care in Manchester because of life threatening chicken pox
- She had previously had other unusual infections. Detailed immune testing had not determined why.
- Mutations in CTSP1 gene found via 100KGP
- Likely benefits of diagnosis
  - A (curative) bone marrow transplant is now planned for the girl
  - Her siblings have been tested and shown not to be at risk of these infections
  - The gene wasn’t recognised by immunologists as a cause of bad chicken pox. A change in practice is now planned to test many more children for changes in this gene to identify others with the condition
29 year-old man with severe learning difficulties and epilepsy

- Known to Manchester Genetics Dept for over 2 decades
- Many genetic tests done, all negative
- Sister pregnant and concerned about recurrence risk
- Truncating mutation identified in a new gene by 100KGP
- Mutation not present in either parent
- Likely benefits of diagnosis
  - Sister had a baby at Christmas, and the result was available in time for her to be reassured that her baby would not have the same condition as her brother
  - This is a newly recognised disease gene. It’s recognition will help diagnose other families. The case is being written up as academic paper to improve its recognition and knowledge of the condition
Data

I agree that the Project can access and collect electronic copies of my past and future health records.

- This includes personal information from all of my records from the NHS, my GP, and other organisations, including information about any illnesses or stays in hospital – even ones that appear unrelated to the rare condition in my family.

- The data is from different sets of records, including hospital or clinic records, medical notes, social care and local or national disease registries. It includes images from my NHS records, such as MRI scans, X-rays or photographs.

- To get this data, the project will need to send some details about me (for example, my NHS number and date of birth) to the organisations holding this information. This will allow them to find the health data they hold about me.

- The data may be used to study many different medical conditions, not just ones that affect me.

- It can be collected at any point in my life and will continue after my death, unless I have withdrawn from the project.

- Approved individuals from Genomics England, the NHS and other study monitors can look at this information at any time.
I understand the following.

- all information about me held by the project will be treated as confidential;
- my data, and information from my samples, will only be used by researchers in a form that protects my identity;
- research organisations who are accessing my data and samples may include commercial (for-profit) companies;
- researchers won’t be allowed to copy or remove any of my information; and
- I will not benefit financially if research data from the project (which includes my data), leads to new treatments or medical tests.

Initial here to show you agree.
‘My data – your data’ questions:

Collecting and understanding data is an important part of innovation and development. Consider the impact of collecting data on this scale

- What could be the problems around a WGS data bank?
- What issues can you see in asking to collect this data?
- Should data from WGS be automatically available to the research community
Imagine could only tell man if you had his written consent.

What if he’d given consent to lots of information but not about drowning dog?

should i tell him?
Resources

www.genomicsengland.co.uk/
www.swgmc.org
www.genomicseducation.hee.nhs.uk/

Further study
• Online modules
• PGC, diploma, MSc
For more information

Genomic Nurse Champions

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