The 100,000 Genomes Project

Henry Rogers – Recruitment team at SLaM
Rationale for the project

- The 100,000 Genomes Project is a government initiative set up by the Department of Health and NHS England to assess the feasibility of genomic medicine in the NHS.

- Cost of whole genome sequencing (WGS) has reduced to a reasonable amount ~£1,000.

- By developing the project pipeline to deliver WGS on such a large scale it should allow the transition to personalised medicine within the NHS.
Aims of the project

- It will help to build up a database of genetic information that can be used for research and can be fed back into the NHS to help improve clinical care.

- Precision medicine – by using WGS it may be possible to identify new targeted treatments and individually tailored treatment plans.
Put the NHS at the forefront of Genomic Medicine by investing in IT and technology.

Facilitate training for clinicians/academics in the interpretation and analysis of genetic data in the NHS.
The 100,000 Genomes Project in numbers

- **100,000 genomes**
- **70,000 patients and family members**
- **21 Petabytes of data.**
  - 1 Petabyte of music would take 2,000 years to play on an MP3 player.
- **13 Genomic Medicine Centres, and 85 NHS Trusts** within them are involved in recruiting participants.
- **1,500 NHS staff** (doctors, nurses, pathologists, laboratory staff, genetic counsellors)
- **2,500 researchers and trainees** from around the world

Rare Genetic Conditions

- The SLaM GMC is focussing on the following rare genetic conditions:
  - Kleine–Levin Syndrome.
  - Classical Tuberous Sclerosis.
  - Intellectual Disability.
  - Severe Familial Anorexia/Low–Weight.
  - Schizophrenia plus additional features (new condition recently added initially ~50 families to be recruited).
  - Severe early–onset/paediatric psychiatric disorders (TBC– has been proposed and is under review by Genomics England).
Intellectual Disability Criteria

**Inclusion criteria**

- Moderate to severe intellectual disability disproportionate to parental IQ
- Congenital onset
- Developmental delay
- Metabolic disorders have been excluded

**Exclusion criteria**

- Antenatal history suggestive of non-genetic cause
- Proven congenital or neonatal infection
- Known genetic cause already identified
The recruitment team works alongside clinicians to help identify eligible patients from caseloads.

Once eligible patients have been identified, they are contacted either by the clinician during routine clinical appointments or by the recruitment team on behalf of the clinician.

If the patient (and where possible family members) agree to take part in the project, then the recruitment team can arrange an appointment to consent them and take samples for sequencing.
Tool developed with funding from the 100,000 Genomes Project to help improve efficiency of identifying potentially eligible patients for recruitment.

Will allow clinicians/researchers to search electronic patient records more thoroughly using new data mining techniques.

It will be possible to search large numbers of records for key search terms in seconds freeing up clinician time.
Patient feedback – Main findings

These are related to the condition that the patient was recruited for. These results have the potential to provide patients with a diagnosis, a greater understanding of their condition or influence their clinical treatment.
Patient feedback – Additional findings

- This is an optional part of the project, allowing patients to decide whether they would like to know risk profiles of other known genetic conditions and cancers (not related to the condition they were recruited for).

- Examples of predispositions that can be explored:
  - Breast cancer (BRCA1, BRCA2)
  - Bowel cancer
  - Familial hypercholestrolaemia
While this project can have clinical implications, it is not currently designed to replace routine clinical testing.

If a genetic abnormality is suspected, genetic testing should be requested (in line with routine clinical care).

As results from this project can take between 12–18 months (sometimes longer), standard genetic tests can help to provide guidance for care in a much shorter time frame.
Research

- To get the most value out of the sequenced data, clinical academic groups have been formed. These groups have joined the Genomics England Clinical Interpretation Partnership (GeCIP).

- The aim of the GeCIP is to develop better understanding and interpretation of the sequenced data.

- There are currently 42 GeCIPs looking at various different domains across the project.

- Improving understanding and interpretation of the data can potentially lead to improvements in patient outcomes.
Patient experience – Jessica’s story

https://youtu.be/hxou7ayQSZQ?t=22s
Recruitment example – Southwark MHLD Team

**Stage 1**
- Eligible patient identified by clinician
- Project explained
- C4C conversation

**Stage 2**
- Micro-array requested
- Sample taken for both micro-array and 100K Project

**Stage 3**
- Patient is consented for the 100K Project
- Sample is sent for sequencing
- Phenotype data is collected to help the interpretation of the sequenced data.
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