The 100,000 Genomes Project

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North East & North Cumbria Cancer Alliance Launch Event
30th March 2017
The first human genome sequence

- 26th June 2000 - Cost $3.2 billion
- 100,000 Genomes at Millennium Prices - Cost $320 trillion
Genomic Medicine - time for translation

• 3.3 billion letters
• Variation every 300 letters
  • Single letter changes
  • Insertions and deletions
  • Bits copied or repeated
• Human Genome Mapping Project

• Next Generation Sequencing
• Whole genomes
The 100,000 Genomes Project

Origins

Announced by the Prime Minister in December 2012

An Olympic Legacy

Genomics England announced by Secretary of State for Health in speech during NHS 65th Anniversary Celebrations, July 2013
Mission

• 100,000 whole genome sequences in NHS patients with rare inherited disease, cancers and pathogens from the NHS
• Returning new diagnoses to the NHS now
• Legacy of infrastructure, human capacity and capability
• Generating inward investment
• World-leaders in the application of Genomic Medicine for healthcare
The 100,000 Genomes Project

.........in a nutshell

• **June 2000**: World’s 1\textsuperscript{st} sequence cost $3.2 billion (1$ per 3.3 billion letters) and **12-years later**, PM’s announces 100,000!

• **Genomics England** (owned by SoS) established to deliver biorepository + sequencing + annotation + research interface.

• **NHS transformation**: 90,000 whole genomes from NHS patients (from routine care) and their families with rare disease or cancer, completion by December 2018

• **Consent**: Understanding of genomics + additional findings + sharing with research + longitudinal record

• **Clinical Data**: Linked with sequence data and lifelong medical record data to create dataset available for research including access by drug companies

• **Genomic Friendly Samples**: NHS Formalin cancer sample processing is not adequate.
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
How it works

Patient consent

Samples + Clinical Data + Longitudinal Data

Biorepository

Sequencing Centre

Genomics England Informatics Architecture

Clinicians

GeCIP
Scientific and Clinical Users

GENE Consortium
Industry Users
The role of NHS England

• NHS England has committed to delivering 90,000 genomes from 70,000 NHS patients (and their families) with rare disease and cancer by September 2018 with corresponding phenotypic data.

• There is circa £20 million to support the delivery of this (£200 per sample plus £20m of IT capital funding in 2015/2016 and 2016/17).

• NHS England’s Implementation Unit manages the interface with NHS Genomic Medicine Centres (NHS GMCs).

• Our role is to prepare the NHS to harness the power of genomic technology and science to improve the health of our population. The NHS will be the world-leading healthcare system in its use of cutting edge genomic technologies to predict and diagnose inherited and acquired disease, and to personalise treatments and interventions.

• The NHS will be able to support a greater understanding of disease and its evolution, building new strategic partnerships with Research and Development and Industry for the benefit of patients and the public in this country and beyond.
The infrastructure for delivery

• Nationwide network of **13 NHS Genomic Medicine Centres** – each serving ~3-5 million population

• Each NHS GMC lead ‘contractual’ organisation works with local hospitals as delivery partners (over 70 further hospitals across England)

• Integrated with existing regional genetic laboratories and clinical genetic services and local pathology laboratories

• Mapped to Academic Health Science Networks (AHSNs)

• National network of 10 universities providing upskilling of workforce through HEE Genomics Education Programme – with E&T leads within each NHS GMC
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The collection of rare disease samples continues to be hard work but good progress has been made; momentum is building and risks are manageable.

- **41%** of the target sample have now been recruited (24.8k of 60k)
- Weekly recruitment now averaging **c500** (compared to target of 400).
- **134** results were returned by the end of October with 25% diagnostic yield.
- **53** Local Delivery Partners now ‘live’
- Excellent family structures for optimised diagnostic yield (only 16% singletons)
- Sample quality remains exceptional
- Good spread of recruitment across **164** of 193 approved RDs
- **Current focus** = Collection of linked clinical data
The recruitment of cancer DNA samples is very challenging

- **13%** of the target sample have now been recruited (3.9k of 30k)
- Current weekly recruitment is averaging >100 (vs target of 250).
- **34** Local Delivery Partners now ‘live’
- **69** cancer pathways are now ‘open’ (# of tumour types across GMCs)
- **Twelve** (12) reports returned to 3 sites this month (just starting)
- Expecting 97% FF samples to QC/sequence (vs c 70% FFPE)
- Biopsy collection just starting
- Mobilisation of FF takes time - c200+ pw from April 17?
- **Current focus** = improve cancer recruitment rates
# Operational Progress (as at 17th March 2017)

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<th>NHS GMC</th>
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<th>Total no. of LDPs Gone-Live</th>
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<th>Still to go live for cancer</th>
<th>Live for RD</th>
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Structures for quality improvement

- UKNEQAS DNA EQA scheme including cellularity assessment
- Biorepository QA assessment
- Standardised protocols informed by evolving experimental pathway evidence
- Contract incentives and KPIs
Patient and public involvement (PPI)

- PPI groups contribute to the project within each GMC
- National Participant Panel - members will sit on committees including the Data Access Review Committee
Genomics England Clinical Interpretation Partnership (GeCIP)
Working with the research community

- Launched at the Wellcome Trust in June 2014
- Partnership between over 2,000 researchers from academia and the NHS, trainees, plus international collaborators.
- Designed to accelerate academic/industry partnership and development of diagnostics and therapies
- Over 35 topics (domains) of research and most domains cover a single disease or group of diseases and some are wider e.g. epigenomics, health economics and technology.
- All data generated contributes to the Genomics England Dataset
Health Education England
Genomics Education Programme

• 10 University providers of MSc in Genomic Medicine
  • Aimed at NHS healthcare professionals working in England
  • Full/part time study
  • Fully funded places available through HEE
  • Individual (CPPD) modules available for range of professional backgrounds and groups (e.g. medicine, nursing, healthcare scientists and technologists).

• Online training courses and resources
  • The fundamentals of genomics
  • Sample handling and DNA extraction
  • Bioinformatics
  • How to support patients through the consent process
GENE Consortium
Working with industry

• 13 companies = the Genomics Expert Network for Enterprises (GENE) Consortium to oversee a year-long Industry Trial

• Aims to identify most effective and secure way to accelerate development of new diagnostics and treatments for patients

• Range from big pharma to small biotech

• Working in a pre-competitive environment

• AbbVie, Alexion, AstraZeneca, Berg, Biogen, Dimension Therapeutics, GSK, Helomics, Roche, Takeda, NGM Biopharmaceuticals, UCB, Intellia Therapeutics
What are we telling participants?

- Information about a patient’s main condition
- Information about additional ‘serious and actionable’ conditions (optional)
- Carrier status for non affected parents of children with rare disease (optional)
Consent materials

Information sheets and consent forms – REC Approved

• Available to download on our site: bit.ly/participant-info

• General leaflets:
  • *Introduction to the 100,000 Genomes Project* leaflet – what is involved, results and feedback, data access and privacy and insurance.

• Cancer and RD information sheets and consent forms, withdrawal forms, opt-in/opt-out of additional findings

• Large print Word versions available for all materials.

13 April 2017
Updated Materials

- Outcome of the National Service Evaluation of the Consent Materials and Process, led by North West Coast NHS GMC
- All have a crystal mark from the Plain English Campaign
- Received approval from REC in March 2017
- New materials now available to download from Genomics England website
- Both new and old consent materials can currently be used. This transition period will end on 30th April 2017 and after that point only the new versions will be accepted.
“Our goal is personalised treatment and care for everyone diagnosed with cancer. Targeting treatments and providing individualised care depends on the best technology, equipment, expertise, and innovations being available throughout the patient pathway.”

Cancer Main Programme

- The Cancer Main Programme started with seven common cancers ‘Live’ in the 100,000 Genomes Project. They were: Breast, Colorectal, Lung, Ovarian, Prostate, Sarcoma and Renal
- A further six were added in May 2016: Adult Brain Tumour, Bladder, Endometrial, Melanoma, Testicular and Upper GI
- Two more were added in December 2016: Childhood Solid Cancers and haematological malignancies
- Head and neck cancers (excluding endocrine), and cancer of unknown primary were added earlier this year
Cancer

• **Genomic technologies** are accelerating our understanding of cancer by providing more granular analysis of tumour cells and their mutations, leading to more personalised cancer treatment.

• NHS England has established **13 NHS Genomic Medicine Centres** to deliver DNA samples and clinical and diagnostic data for the 100,000 Genomes Project. This nascent infrastructure plus advances in informatics technology and analytics are introducing whole genome sequencing into the NHS mainstream.

• NHS Genomic Centres, Genomics England and industry partners are developing a standardised high quality national approach to **validation and feedback of whole genome sequencing results**. This ground-breaking work will lead to a new genomic results ‘pipeline’: harnessing the power of data to deliver more precise, personalised diagnostics for patients.

• We envisage that in the future the majority of cancer patients will have access to genetic testing (or ‘molecular diagnostics’), that will enable more personalised and tailored cancer treatments.

• **Molecular diagnostics** through whole genome sequencing will help us meet our goal to deliver personalised treatment and care for everyone diagnosed with cancer.
Molecular pathology

Complex NHS transformation underway

Tumour samples are traditionally preserved in formalin then fixed in paraffin (FFPE) to preserve cellular architecture for diagnosis under the microscope.

DNA extracted from samples treated like this is damaged and broken.

- Use part of the sample for FFPE and histology
- Freeze part of the sample for genetic tests
  - Need to make sure the sample contains mainly tumour cells

This new pathway requires very significant changes in sample handling, affecting surgeons, interventional radiologists, pathologists and oncologists.
The drive for quality

- Quality of genomic sequence data reliant on quality of DNA and quality of the identification of the tumour
- Early findings showed that sequences from tumours processes through the established FFPE methodology were ‘noisy’ and variable
- Cancer experimental phase set up to examine every step of the tumour identification, processing and DNA extraction process to see how this could be refined and optimised
- Recognition that protocol had to be effective in all environments – LDP centres as well as NHS GMC Lead Organisations
Cancer results

A small number of clinically actionable driver mutations with treatments known to work/not work
[may already have been tested for in the clinical context]

Germline results which affect cancer development
eg a BRCA1 mutation in a patient with breast cancer but without a strong enough family history to be tested for BRCA1 in the genetics clinic

Remainder of results are mostly of research interest for now, but in future may assist:
• Drug development
• Targeted treatment selection
• Prediction of prognosis
• Monitoring of disease progression
Cancer whole genome analysis report

Preliminary analysis report:
• Domain 1 variants - directly relevant to cancer treatment
• Domain 2 variants – other cancer related genes

New cancer programme webpages include resources around reports: www.genomicsengland.co.uk/information-for-gmc-staff
Human Tissue Authority consensus statement

- Draft consensus statement that **tumour samples are diagnostic**
- With support from: HTA, HRA NHS England, RCPath, 12 GMCs

**Impact**: simplify; help recruit LDPs; introduce biopsy pathways

**Potential changes to cancer eligibility**

- Open up to all invasive malignancies -benefits:
  - Increase recruitment
  - Simplify eligibility
    - much easier message for those at front line
    - no checking complex eligibility
    - No patients becoming ineligible because of rare diagnosis
  - Start building up cohort of rare conditions
“We always overestimate the change that will occur in the next two years and underestimate the change that will occur in the next ten”

Bill Gates
with the first version of Microsoft Windows
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