Delivery of ethical and effective genomics health care

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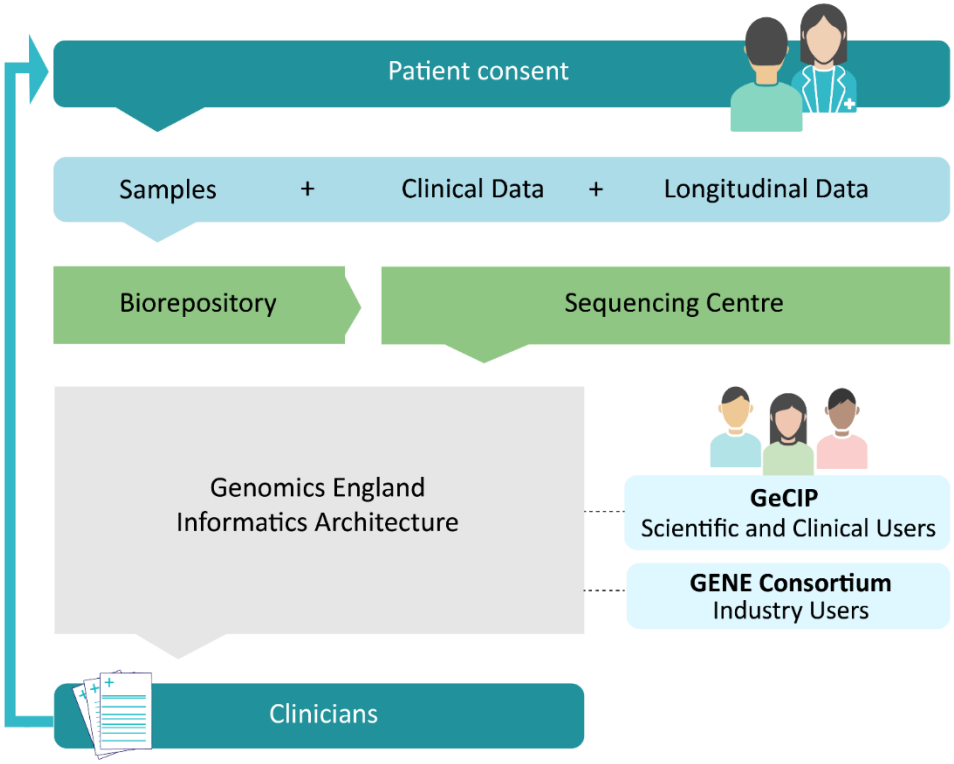
The 100,000 Genomes Project

- Launched by **UK Prime Minister,** led by Genomics England – Department of Health funded
- Whole genome sequencing NHS patients with **rare disease, cancer and infectious disease**
- Recruitment through **13 NHS Genomic Medicine Centres**
- Combining genome with longitudinal **health records** and **phenotypic** information
- Clinical **interpretation** through a semi-automated pipeline
- Clinically significant **results fed back** to NHS clinical teams for patients



Bring benefits to NHS patients

Enable new scientific discovery and medical insights

Ethical and transparent programme based on consent

Kick-start the development of a UK genomics industry

Progress to date

Figures as at 05/07/2019

Samples

122,751
Samples collected and received at the UK Biocentre

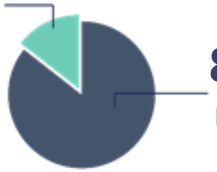
36,781 cancer

85,970
rare disease

Genomes

113,080
Genomes sequenced

29,822 cancer



83,258
rare disease

+882
genomes
since 1 June

Analysis and Results

Results for **93,276**
genomes sent to NHS GMCs

Equivalent to **25,070**
cancer genomes and
68,206 rare disease

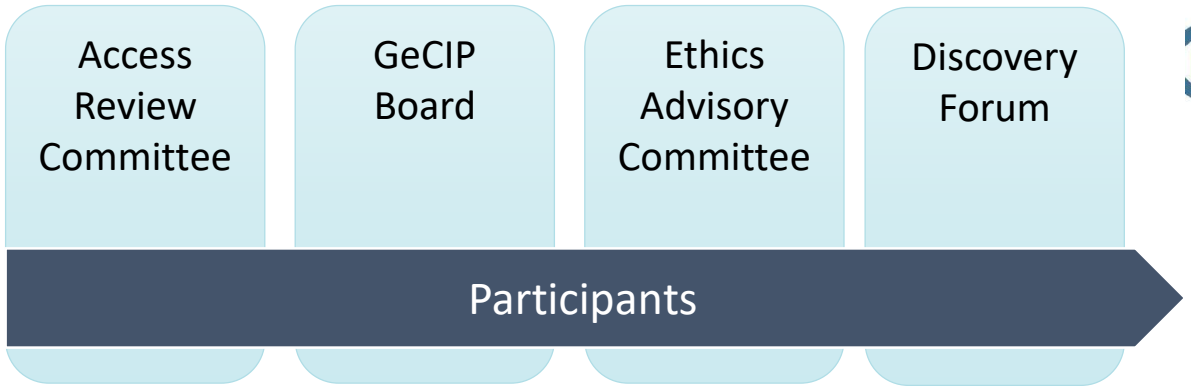
- 20-25% actionable findings for Rare Disease
- ~ 50% cancer cases contain potential for a therapy or a trial in our report

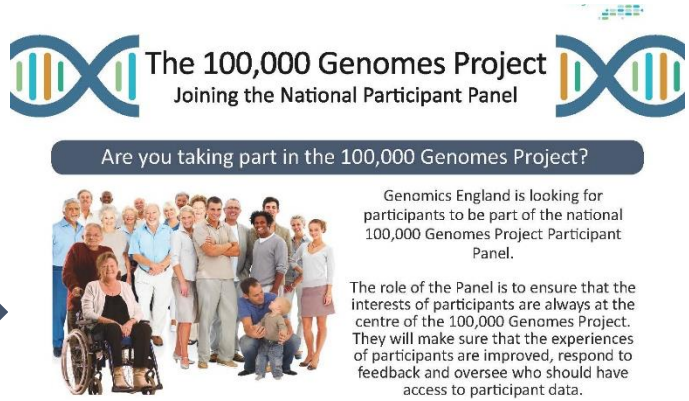
Patient involvement - the National Participant Panel

Role of the Panel is to ensure the interests of participants are always at the centre of the 100,000 Genomes Project.

They do this by:

- Making sure experiences of participants are at the heart of the project
- Responding to feedback
- Overseeing who should have access to participant data





Consent in the 100,000 Genomes Project

- Participants consented to
  - Whole Genome sequencing
  - Return of main findings
  - Option of return of limited list of secondary findings

- Revision of consent materials
  - Collaboration with participants
  - Recruiters
  - Independent ethics committee

National Genomic Medicine Service

National Test Directory

300,000 Tests reviewed
25% upgraded to new technologies

22 categories of rare disease

Cancer
4 cancers planned for WGS

Many more edge cases in cancer

Annual Test Directory Review

Pharmacogenetics

National
Genomic Medicine Service

Genomic Medicine Centres
providing care
(continue till 2021)

National Laboratory Network
Genomic Laboratory Hubs - 7 hubs doing single gene, panels, clinical exome

NHS Lead

UK Genomics Knowledgebase
Informatics architecture
& data store

Whole Genome Sequencing Provider

Clinical Interpretation Pipeline

Genomics England Lead

Workforce development
upskilling of existing staff

Industry/ academic/ international partnerships
supporting ongoing research & development through clinical care

500,000 whole genomes sequenced from the NHS in the next 5 years

- Offered consent for research
- Longitudinal Life Course
- Recall for research
- International researchers and industry

Learning from the 100,000 Genome Project

Health-care professionals need to be prepared to answer patients' questions about genetics to facilitate genome sequencing consent. Health-care professionals' education also needs to address how to effectively listen and elicit each patient's questions and views, and how to discuss uncertainty around the disease risks associated with secondary findings.

Opening the "black box" of informed consent appointments for genome sequencing: a multisite observational study.

Sanderson SC, et al Genet Med. 2018 Oct 1. doi: 10.1038/s41436-018-0310 [Epub ahead of print]

We found that interviewees' decisions to participate in 100 kG P were based on interpersonal and institutional trust in the NHS, and on an investment in improving care for the future. Interviewees relied upon receiving good ongoing NHS care for managing their own or their child's rare disease, but they worried about what their relationships with NHS healthcare professionals would be like in future. …….. To honour and foster participants' trust - which may easily be lost - and their clinical labour, we therefore recommend ongoing public engagement and consultation about how genomics is being integrated more widely across specialties (especially given current funding and staffing constraints in the NHS) within the newly formed NHS Genomic Medicine Service.

Fostering trust in healthcare: Participants' experiences, views, and concerns about the 100,000 genomes project.

Dheensa S et al Eur J Med Genet. 2018 Nov 29. pii: S1769-7212(18)30352-5. doi: 10.1016/j.ejmg.2018.11.024. [Epub ahead of print]

Vision of Patient choice

The patient choice framework will focus on two key aspects of choice – clinical care and research. The approach will see the two aspects presented as part of the clinical pathway.

- Aim to set **clear and informed choice** about use of NHS GMS and Genomic Tests to patients
- Choice **supported by plenty of information** to help patients understand the choice and consequences
- Will cover **both usual use of patient data** within healthcare services (e.g. clinical and administrative standards), as well **as innovative aspect of genomic care and data** use to support/develop service
- All patients to be given the **opportunity to participate in research**
    - **Access to deidentified data by researchers-for profit and not for profit**
    - **Recall for research**
    - **Lifelong collection of other routinely collected health data**
- **Clear and distinct choice to be part of research** programme (without impact on standard of clinical care of individual)
- Additional findings not being offered in first wave

To achieve this vision an iterative approach will need to be taken including to the record of discussion form and the education and training of clinicians to ensure uptake of the approachli

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Clinical Choice

All tests on offer as part of GMS are NHS-commissioned diagnostic tests for patients presenting with unexplained symptoms

The consent conversation with these patients is unchanged from current consent standards

With the exception of:

1. National storage of data
2. Discussions of pertinent germline results (for some cancers)

Research Choice

- The offer of research to all patients undergoing WGS for diagnostic purposes is designed to accelerate diagnosis, discovery, and development of new biomarkers, diagnostics and therapeutic agents
  - This offer is strongly supported by many patient groups
- Standards of informed consent apply under the usual procedure for research consent
  - for some rare conditions, the chance of getting a diagnosis may be higher for patients who do take up the research offer; larger numbers of experts will be working through their variant data and comparing it with others with similar conditions
- The research offer for WGS is considered part of the standard clinical pathway for patients - not a stand-alone project
  - This is in line with other developments embedding research in all aspects of NHS care and increases the potential for patient benefit

Patient first name:	
Patient last name:	
Date of birth:	
NHS number: (or Postcode, if not known)	

Record of discussion regarding genomic testing

Please note that all of the information presented in this form is relevant to you OR your child.

I have discussed genomic testing with my health professional and understand that:

Family and wider implications

1. The results of my test may have implications for me and members of my family. I understand that my results may also be used to help the healthcare of others nationally and internationally, through a process that will not personally identify me.

Uncertainty

2. The results of my test may have findings that are uncertain and not yet fully understood. To decide whether findings are significant for myself or others, my data may be compared to other patients' results across the country and internationally. I understand that this could change what my results mean for me and my treatment over time.

Unexpected information

3. The results of my test may also reveal unexpected results that are not related to why I am having this test. These may be found by chance and I may need further tests to understand their significance.

DNA storage

4. Normal NHS laboratory practice is to store the DNA extracted from my sample even after my current testing is complete. My DNA might be used for future analysis and/or to ensure that other testing, for example, that of my family members, is of high quality.

Data storage

5. The data from my genomic test will be securely stored so that it can be looked at again in the future if necessary.

Health records

6. Results from my genomic test and my test report will be part of my patient record, a copy of which is held in a national system only available to healthcare professionals.

Research

7. I understand that I have the opportunity to take part in research which may benefit myself or others, now or in the future. An offer to join a national research opportunity is available on the following page.

For any further questions, my healthcare professional can provide information. More information regarding genomic testing and how my data is protected can be found at www.nhs.uk.

Please circle your clinical choice:

A. I have had the opportunity to discuss information about genomic testing and agree to my sample being tested. **YES | NO**

Patient first name:	
Patient last name:	
Date of birth:	
NHS number: (or Postcode, if not known)	

The National Genomic Research Library

The NHS invites you to contribute to the National Genomic Research Library, managed by Genomics England.

Genomics England was set up in 2013 by the Department of Health and Social Care to work with the NHS to build a library of human genomes for researchers to study. Combining data from many different patients helps researchers to better understand disease and spot patterns in the data.

By agreeing to share your data you might get results which could lead to your own diagnosis, a new treatment, or offers to take part in clinical trials. Your taking part could enable diagnoses for people who don't have one.

Please read the following statements. Feel free to ask any questions before making a decision.

By saying 'yes' to research, I understand:

Security

1. Any samples and data stored by Genomics England and the NHS will always be stored securely. Genomics England will take all reasonable steps to ensure that I cannot be personally identified.

Re-contact

2. NHS staff, or Genomics England together with the NHS, can contact me if the data or samples reveals any clinical trials or other research that I might benefit from.
3. If something relevant to me or my family, there is a process by which this will be shared with my NHS clinical team.

Data and sample usage

4. Researchers may include national or international scientists, healthcare companies and NHS staff. To access the data, these researchers must all be approved by an independent committee of experts, including health professionals, clinical academics and patients. There will be no access to the data by personal insurers and marketing companies.

Data storage

5. Genomics England will collect different aspects of my health data from the NHS and other data from organisations listed at https://www.genomicsengland.co.uk/understanding-genomics/data. The collection and analysis of my health data for research will continue across my entire lifetime and beyond.

Withdrawal

6. I can change my mind about taking part at any time.

More information regarding research in the National Genomic Research Library can be found at: www.genomicsengland.co.uk. For any further questions, my healthcare professional can provide information.

Please circle your research choice:

B. I have discussed taking part in the National Genomic Research Library. **YES | NO**

If your answer is NO, please move directly to the next page to confirm your choice.
If your answer is YES, please circle your choice below:

C. I agree that my data and / or sample may contribute to the National Genomic Research Library. **YES | NO**

Considerations for implementation

100,000 genome project

- Complex project within the health care system
  - Regulated under Health Research Authority as a Tissue Bank

- Creation of New NHSE genomic medicine service
  - NHSE and Genomics England
  - System transformation
  - Workforce transformation
  - Clinical service and Research combined

- Ethical considerations are more than
  - Informed consent
  - Data access, use and sharing
  - Secondary/additional findings
  - Incidental findings
  - Familial information
  - Prenatal testing
  - Childhood testing
  - Etc etc

- Ethical considerations also emerge in ‘the doing’

Examples

- Consistent and accurate recording of patient choice
  - Including withdrawal from research
- How to manage changing capacity over time
  - Children attaining capacity
- Consistent accurate recording of changes in capacity
- Accurate records for recontact including recording deaths
- Governance structures

Choice for testing is just the beginning

In Reuben's case getting a diagnosis has made no difference at all because nothing is known about it as it's extremely rare. More research is needed so we have no idea what the future holds for him. We are still living with the unknown.

With Faith it made it easier as it gave answers to all her issues. Although it's rare there are a lot of other children with the same condition so we are able to speak with them. Also it meant that I got a diagnosis myself as I have the same condition as her and it's prepared us for future generations having the same condition.

Getting a diagnosis gave us closure. We knew that it was nothing I did during pregnancy or labour. Faith's diagnosis gave us a lot of answers and made us realise that several other family members have the same condition and we know that it will be passed down to future generations. With Reuben, his diagnosis reassured my older children that it wouldn't be passed down.

https://www.undiagnosed.org.uk/news-event/getting-a-diagnosis-reuben-and-faith/

https://www.geneticalliance.org.uk/news-event/participants-experiences-of-the-100000-genomes-project/

The Genomic Medicine Service promises a cutting edge approach to diagnosis, so it is appropriate to sound a note of caution about the post-diagnostic service available to patients, and its potential impact on patient satisfaction with health services.

The NHS is resource-constrained.

Results from WGS might not be clinically significant at the time they are reported back to patients, but could become actionable in the future

Research will be needed to deliver a meaningful finding.

There must be a clear message to patients and carers as to what to expect, and who has responsibility for renewing contact when appropriate.

It is clear that whether the Genomic Medicine Service ultimately delivers on its promise will depend on factors outside pure progressing genomic technology.