The NHS Vision and Context: Genetic Laboratory reprocurement

Professor Sue Hill OBE @CSOsue
Chief Scientific Officer for England and SRO Genomics

November 2016 Market Engagement events
Drivers of change in healthcare

Demographics
Scientific Advance
Expectations
Social, political, economic, environmental
Service models
Carter efficiency review (2016)

Care & Quality Gap
Health & Wellbeing Gap
Finance & Efficiency Gap

Utilising technology & information
New models of Care
Improving integration
Multiprofessional working

NHS diagnostic spend >£10bn pa, drugs budget £15bn pa (but <50% meds effective)
System recognition of the potential of genetics & genomics

A proud heritage of UK genetic advance has triggered development of organisations and policy initiatives over the years - real appetite for 100,000 Genomes Project and its legacy in service
Genomics and Personalised medicine – backbone of the future NHS

The introduction of genomic medicine - particularly to inform the personalisation of treatment – is the most significant initiative to shape the future delivery of NHS care.

- **Dec 2012:** Government has commits to cementing the UK’s position as a world leader in this area through the £300 million launch of the 100,000 Genomes Project and establishment of Genomics England

- **Dec 2014:** First wave of NHS Genomic Medicine Centres established by NHS England

- **Sep 2015:** NHS England Board commits to the development of a Personalised Medicine Strategy for the NHS

- **Nov 2015:** Government commits a further £250 million to the 100,000 Genomes Project to ensure lasting legacy for the NHS *inc National Genomic Data Centre*
Genomic & computing advances have provided an exponential jump in diagnostic data.

Alongside WGS, information from the functional genomic pathway – the steps in translating the genetic code – provides a wealth of information and insight, with important implications for future testing.

**UKGTN:** since 2003
562 tests recommended, 95NGS with 231 sub-panels; 4800 genes can now be tested from clinical exome within NHS genetic laboratories - combined specialist and CCG funding.

**Molecular diagnostics** for cancer generally provided by pathology - mainly CCG funded.
...and a new depth of structural information

<table>
<thead>
<tr>
<th>Data Type</th>
<th>Targeted gene sequencing</th>
<th>SNP+ arrays</th>
<th>Array CGH*</th>
<th>Exome</th>
<th>Whole Genome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Large-scale Structural Changes</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Balanced Translocations</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Distant Consanguinity</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Uniparental Disomy</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Novel / Known Coding Variants</td>
<td>✗</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Novel / Known Non-coding Variants</td>
<td>✓</td>
<td>✗</td>
<td></td>
<td>✗</td>
<td></td>
</tr>
</tbody>
</table>

**Interpretation & analysis is a challenge**

Each genome contains:
- ~5-10 million variants
- ~3.5 million “known” SNPs
- ~0.5 million “novel” SNPs
- ~0.5 million small indels
- ~1000 large (>500bp) CNVs
- ~20,000-25,000 coding variants
- ~9,000-11,000 non-synonymous
  - 92 rare missense variants (MAF <0.1%)
  - 5 rare truncating variants (MAF <0.1%)
  - 0-2 de novo variants

+ Single Nucleotide Polymorphism
* Comparative Genomic Hybridisation
Aims & principles of the 100,000 Genomes Project

In 2012 PM David Cameron launches 100,000 Genomes Project made possible due to the decreasing cost of sequencing and developments in computational power and data analytics

“By unlocking the power of DNA data, the NHS will lead the global race for better tests, better drugs and above all better care.

Key Principles

1. A focus on rare inherited diseases (unmet clinical need) and common cancers
2. Patients to be drawn from routine care and treated through routine channels
3. All participants to provide a fully informed consent providing for a wide range of data and tissue capture and broad categories of use including research and industry
4. However neither data nor tissues to go outside NHS-controlled ‘safe havens’ and all users to be properly authorised and monitored
5. A separate (government owned) company – Genomics England – formed to coordinate the project under an independent board, providing a ‘start-up’ mentality and drive

Aligned with NHS strategies

Whole genome sequencing is providing a step change in the NHS diagnostic repertoire
NHS Genomics Medicines Centres

- Nationwide network of 13 NHS Genomic Medicine Centres (GMCs) for populations of ~3-5 million recruiting participants, providing DNA and other samples and data and undertaking validation and feedback against highly defined service specification
- Lead organisations working with additional local delivery partners (42 at present – will be 75 by March 2017)
- Clinical genetics, regional genetic laboratories and molecular pathology laboratories central to delivery
- Established operating models for the future driven by **focus on innovation** including:
  - Ethics, consent & patient participation
  - Standardisation and streamlined models of care
  - Data collation and handling, creation of 13 data hubs
  - Partnership and network working
  - Clinical Leadership for change
- Integrated with **workforce development** led by HEE Genomics Programme and underpinned by flexible HEI programme in Genomic Medicine
- Model now adopted across UK

NHS England provided £20 million in direct funding to GMCs and commissioned care pathways provides indirect funding
Rare disease – objectives & achievements

- 185 + **rare diseases** currently in scope with more being introduced with a clear process for assessing new conditions. Estimated 3 million affected by rare disease

- Aims of RD Programme include:
  - To inform the underlying cause of the disease through additional biological insights from WGS
  - To improve the current diagnostic return and enhance clinical interpretation of WGS.
  - To develop a programme of functional multiomics pathways & biomarkers
  - To create a unique dataset for rare diseases that may enable therapeutic innovation

*Data sets and use of HPO terms already providing a much richer way to describe and characterise disease*

*Enhanced diagnostic yield (approx 25-30 %) with some patients receiving diagnoses after many years of uncertainty and significant use of health care resources*

*Providing evidence for clinical use of WGS in context of current testing regime*
Cancer – objectives & achievements

• **13 common cancers** currently in main 100,000 Genomes project (inc Breast, Colorectal, Lung)

• Aligned with aspirations of Cancer Task Forcer recommendations

• Aims of Cancer Programme include
  • To identify novel driver mutations of common cancers and to understand its evolutionary genetic architecture
  • Identify value of WGS in predicting response to therapy and in new pathways for therapies
  • To use multiomic approaches to offer additional biological insights.

• New handling and fresh frozen processing pathway established providing significantly higher quality DNA including from diagnostic biopsies to facilitate the identification of previously unknown variants

• New approach to tumour genomic interpretation and reporting

• Novel findings from WGS enabling patients to enter other clinical trials

• Greater involvement of genetic laboratories and expertise including in DNA extraction

• Recognition that greater levels of genomic testing need to be performed - evidence emerging to support use of cancer gene panels or WGS and for more testing during clinical pathway
What laboratories have delivered

- **Established local sample collection, handling and processing networks** to agree working practices and standardisation inclusive of pathology in with new models of provision for routine histopathology emerging

- **Centralised and consolidated DNA extraction for blood and tumour and participated in new and innovative UK NEQAS schemes for DNA extraction** and open sharing of results including assessment of tumour cellularity (linked to approval and performance KPIs)

- **Coordinated and processed Multiomic samples** including cfDNA

- **Tracked samples across pathology and genetics** including developing custom software for sample management, for central sample collection and for reporting following validation

- Informatics developments to support sample metadata collation across geographies and submission

- **Working with Fresh Frozen tissue** rather than FFPE including world-leading protocols and processes for the identification, handling and processing to provide genomic blocks to maximise quality of extracted DNA

- **Establishing national approach to validation and to sharing of variant information** Involvement in new genomic MDTs
Where genomics is taking us

Tackling:
- Rare Diseases & Cancer
- Common Non-communicable disease (eg CVD, Diabetes)
- Other clinical priority areas (Mental Health, Dementia, LD)
- Infectious disease (inc AMR)
- Prevention & prognostics
- Pharmacogenetics
Building the NHS approach to personalised medicine

• The NHS England Vision for Personalised Medicine builds on:
  - knowledge & transformation of the 100,000 Genomes Project & the expectations for the future
  - Reprocurement of specialist laboratory infrastructure
  - other cutting-edge diagnostics available
  - wealth of patient and clinical data produced through the NHS’s unique integrated operation.
  - recognition of current spend on medicines and diagnostics

• The strategy defines personalised medicine as:

  *a move away from a ‘one size fits all’ approach to the treatment and care of patients with a particular condition, to one which uses emergent approaches in areas such as diagnostic tests, functional genomic technologies, molecular pathway, data analytics and real time monitoring of conditions to better manage patients’ health and to target therapies to achieve the best outcomes in the management of a patient’s disease or predisposition to disease.*
100,000 Genomes Project - use of WGS, panels & functional genomics for rare disease & cancer

Genomic medicine embedded within specific pathways

- Exemplar pathways and pilots
- Other diagnostics and screening
- Pharmacogenomics and profiling
- Phenotypic info over the life course

Genomic medicine embedded as part of routine care – where appropriate

- Better prediction and prevention of disease
- A more precise diagnosis
- More targeted and personalised interventions
- A more participatory role for patients

DNA + omics

Genomic medicine in specific examples

2012

Genomic medicine in specific examples

2012 - 2018

Genomic medicine in specific examples

2013-18

Genomic medicine in specific examples

2018 - 2020

Genomic medicine in specific examples

2020 and beyond

Integrating diagnostics for maximum impact

Determination of diagnostic approach will be shaped by:

- Diagnostic yield and impact on outcomes
- Turnaround times for clinical intervention
- Ability to intervene and to inform pharmacogenomics
- Impact on efficiency and value for money
- Collecting and sharing data and re-analysis
- Adoption of new technologies
- Distributed model of provision
- Flexibility in commissioning
- Overall coordination of provision and regular review of evidence

The use of WGS in the context of other testing is crucial, particularly in areas that capture information about multiomics and the functional genomic pathway.

Advances will be driven by technology and data inc: Circulating DNA; Micro RNA;
‘Next genomics’
the future rebalancing of testing

There will be a rebalancing of testing over coming years driven by, cost, improved efficiency and potential for enhanced outcomes including:

- WGS provision for defined Rare Disease applications by April 2018
- WGS/Gene panels for some cancers by April 2018 plus introduction of CtDNA
- Reduction in some of current tests undertaken (eg panels, arrays, single molecular markers)
- Specific genotype testing (POCT) for defined applications eg warfarin, FH
- Further genomic testing advances and multiomic analyses including in POCT opening up delivery options

NHS England has formed groups to look at WGS and the overall genomic testing strategy for rare disease and cancer
Informed by evidence including international
## Opportunities for a new model

<table>
<thead>
<tr>
<th>Current service issues</th>
<th>Opportunities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capacity and demand constraints</td>
<td>New models of care to tackle the quality &amp; equity gaps</td>
</tr>
<tr>
<td>Variability in Quality</td>
<td>Greater efficiency and use of high throughput robotic platforms</td>
</tr>
<tr>
<td>Variability in practice &amp; standardisation</td>
<td>Cost reduction and use of WGS + scale &amp; pace of change</td>
</tr>
<tr>
<td>Limited &amp; unstructured data collection &amp; sharing</td>
<td>Linkage to academic and other resources</td>
</tr>
<tr>
<td>Uptake of new technology</td>
<td>Sharing of data in agreed models &amp; dynamic &amp; enhanced interpretation</td>
</tr>
<tr>
<td>Facilitating future advance</td>
<td>Address issues from Cancer &amp; Rare Disease Strategies</td>
</tr>
</tbody>
</table>

*Maximising potential will require a flexible approach*
A framework for the future

- A network of high specification labs integrating Genetics and Genomics with broader Molecular Pathology (and over time working with NHS microbial genomic laboratories)
- Maximise utilisation of cutting edge technology, expertise in bioinformatics and clinical interpretation in routine clinical practice to establish strong links with research and industry and with training for wider workforce
- Shared service resource – local access and national UKGTN requirements and with other partners
- Optimise emerging genomic techniques such as whole genome sequencing and NGS in wider clinical context inclusive of cancer
- Enable and support introduction of new technologies at scale and pace to replace existing genetic technologies inclusive of POCT
- Standardise protocols, methods and sample pathways to improve quality, reduce variation and improve efficiency
- Structured data sets and formalised data sharing agreements
- Workforce with right skills and competences
- Key membership of genomic MDTs in rare disease, other conditions and cancer and in working with assigned NHS GMCs or successor arrangements
- Supporting pharmcogenomic profiling and establishment of personalised medicine
- Close working with clinical genetics services and supporting integration of genomic medicine into all clinical specialities
Overarching principles for national genomic laboratory service

- Local provision linked to local clinical needs
- Enhanced partnerships and explicit clinical/research role
- Genomic lab provision
- Data & Information Sharing
- Cost effective, efficient, flexible and responsive to change & adoption of new technology
- Standardisation and industrialisation of ‘wet laboratory’ functions
- Concentration of highly specialist expertise/knowledge for validation & interpretation

Inc near patient testing requirement and to support supply of tissues/materials and local referral and MDT decisions.
The new genomic laboratory infrastructure

- Whole genome sequencing provider
  - National Specialist Resource

  - ‘Regional’ Genomic Central Laboratory Hubs (GCLH)
    - Network of ‘regional’ centres providing routine diagnostic clinical sequencing and complex genome analysis - The core of the NHS Genomic Laboratory Service

  - ‘Local’ Genomic Local Laboratory Hubs (GLLH)
    - Providing rapid testing for clinical utility – will integrate pathology specialisms to provide broad diagnostic picture and provide the tissue handling for subsequent genomic analysis.

- Point of care ‘molecular’ testing
Key features: Genomic Central Laboratory Hubs (GCLHs)

- Configured around the concept of ‘diagnostic clinical sequencing’ and complex genome analysis supporting the full range of molecular and cytogenetic technologies (inc validation & interpretation of WGS)

- State of the art, high throughput laboratories operating across significant geographical population base, with explicit NHS regional partnerships in place and with procured WGS provider

- Responsive and evolving as evidence on the testing requirements for rare, inherited and acquired disease including cancer, emerges and changes in terms of best practice and greater efficiency.

- Credible scientific leadership to ensure maximum scientific and technological advance and competitiveness and robust operational management

- Integrated network of laboratories – not all labs will necessarily provide all tests, but will work together as a coherent national service.

- This strategic network will require significant informatics infrastructure with interoperability and data sharing at their core - providing benchmarking intelligence & expertise – via a National Coordinating Centre and collating and sharing data with the UK genomic knowledge centre

- Be able to demonstrate the translation of research into clinical practice. Will be aligned to established academic centres of excellence. (AHSN, BRU etc)

- Taking a lead role in teaching and training and embedding genomic medicine
Key features Genomic Local Laboratory Hubs

- Focussed around local planning and provision of clinical ‘genomic’ diagnostic testing and interpretation across a broad range of pathology specialities and preparation of material for Regional Hubs for a defined population (and in line with NHSI/Carter provider efficiency plans) – may incorporate a specialist/highly specialist genomic service

- Defined by the partnership arrangements with Regional Hubs and work closely with, and be supported by, the Regional Hubs as managed network sharing knowledge, expertise, technology and data

- Support local planning & provision of rapid testing for clinical utility including ‘genomic’ POCT for primary care and other distributed models of provision

- Support MDTs and local clinical teams in interpretation in conjunction where appropriate with Regional Hubs

- Will combine results of range of tests for integrated diagnostic reporting and have informatics capability and interoperability to share data across the local network, with the Regional Hub and with the UK Genomic Knowledge base

- Will network with other local hospitals/laboratories for sample handling and processing where appropriate

- Will also process genomic blocks from cancer patients and may be designated as a local DNA extraction service and will participate in the UK NEQAS QA schemes inclusive of cellularity assessment
Data paths across the service network
Networked and structured to deliver maximum benefit

To gain the full benefit from genomic testing, future provision should include information that is:

- **Collected** – gathered and retained in patient records. Test results should not be regarded as disposable.

- **Comparable** – collected using common protocols and standards for a given test – so results from one centre can be compared with another.

- **Consistent** – appropriate assurance and quality systems in place to ensure confidence and reliability in the results.

- **Connected** – available in a connected form so patients and clinical staff can access it wherever an individual presents.

- **Compiled** – assembled and analysed to paint a picture of an individual’s condition and population health. Informatics should be used to identify issues and support clinical decision systems.
Key elements of transformation

- Defining and ensuring quality - through data sharing and external QA

- Review and standardisation of repertoire of tests
  - Molecular / cytogenetics/molecular pathology
  - Stopping performing tests with low clinical utility
  - Ensuring most up to date methods are used

- Economies of Scale
  - Minimum no of tests / GenUs
  - Efficiencies in procurement eg consumables
  - Bioinformatics and interpretation

- Effective national networking of all services

- Professional engagement & joint working on variant classification

- Integral to future Genomic MDTs and engagement with wider groups of clinicians

- Review Technology platforms and plan for future advances
  - WGS, NGS – Arrays – Digital analysis - POCT
  - Maximum use of equipment with access by several departments

- Improved informatics and data infrastructure for interoperability and data sharing, populating data models and dynamic interpretation and reporting

- Workforce configuration & service integration
  - optimum and integrated workforce including new skills

Need to both: concentrate expertise where appropriate and localise to improve speed and access to testing services
The model for the future

- An **integrated Clinical, Laboratory and Academic** centre working with local genomic laboratories and the WGS provider partner
- Focus on rapid translation from **research to service**
- Serving a broad population base, with strong **regional partnerships and networks** to ensure patient access & knowledge flows into the UK genomic knowledge centre
- **Unified centralised laboratory** bringing together all genomic applications and overseeing local genomic laboratory provider network driving quality, efficiency, clinical utility and enhanced interpretation
Integration and collaboration is everything...

Partnerships – across services, specialisms, sectors and across the world – maximise the opportunities from discovery & innovation through the mainstreaming of genomic medicine.

Area of maximum advance
Patient, population & system benefits

- Intelligent treatment pathways informed by personalised assessment of clinical effectiveness and adverse drug reactions
- Improved efficiency and sustainability of service delivery
- Targeted therapies
- Accelerated diagnosis
- Early disease detection
- Targeted disease prevention
- Cutting edge research and applied science
- Improved population health
- Disease detected 2-8 years before onset and symptoms become obvious
- Diagnosis based on underlying cause and incidental findings - rather than just grouped symptoms
- Identification of predisposition markers or underlying processes to predict future disease
Hold & deliver the vision – the time has never been more right

The New Frontier is here whether we seek it or not. Beyond that frontier are uncharted areas of science and space… unsolved problems…. unanswered questions…

It would be easier to shrink from that new frontier, to look to the safe mediocrity of the past…

But I believe that the times require imagination and courage and perseverance

John F Kennedy, 1960
The re-procurement of Genomic Lab services

- Reconfigured service to create a world class resource in genomics and genetic technologies
- A new specification for NHS Genomic Lab Services was developed
- Consultation on the NHS Genomic Laboratory Services – service specification took place between January and April 2015.
- In addition, two provider information days were also held
- As a result of the consultation feedback, the core elements of the specification (e.g. intended service model) remained the same but the document was amended to better articulate the intentions behind the specification
- Service specification agreed by CPAG in September 2015
Service Model

- The service model will consist of Genomic Central Laboratory Hubs delivering core and national specialised testing services linked to Genomic Local Laboratory Hubs and the whole genomic sequencing provider.

- All Genomic Central Laboratory Hubs, will be a member of the National Co-ordinating Centre.

- The National Co-ordinating Centre will be established and accountable to NHS England within an agreed governance and operational framework that will oversee the test repertoire and support labs to work together.
Service Scope

• The procurement will include the provision of genomic testing for patients with, or at risk of, inherited disorders

• Sporadic genetic disorders,

• Stratified/personalised medicine

• The above is indicative and will evolve
Outcomes

• It is expected that there will be a measurable and defined impact on:

— Improved access to and reduction in the variations in genetic, genomic and molecular diagnostic testing.

— Improved quality through collation and sharing of data for participant benefit by standardisation of, and participation in, minimum agreed datasets and national audits, reporting, testing repertoires and methods and quality benchmarking.

— Earlier diagnosis, prediction and prevention of disease based on the complete functional genomic pathway from genomics (DNA) to transcriptomics and epigenetics, proteomics and metabolomics (products and biomarkers).

— Safe and effective targeted treatment
Outcomes continued

— Improved detection of genetic variants and structural changes across the genome, identification of variation that may encode diseases and may enable major new biological insights that will support new innovative diagnostics and therapies for patients.

— The development and delivery of point of care molecular diagnostics leading to improved diagnosis and management of long term conditions, for example the recurrence of diseases such as cancer.

— Enhanced working practice that is compatible with a seven (7) day working policy. This will optimise the utilisation and clinical effectiveness of the genomic technology platforms thereby delivering benefits to patients and the NHS.
The Procurement timeline

- November 2016  Market place events
- Spring 2017  Invitation to Tender
- Autumn 2017  Bidders advised of outcome
- Winter 2017  Contracts awarded
- Winter 2017 and Spring  Mobilisation
- 2018
- April 2018  Service commences
Geographical coverage

• To ensure complete geographical coverage, the procurement will be structured across 11 geographical lots

• This model is linked to the geographical boundaries of NHS England’s Specialised Regional Teams

• The lots will cover a population range of 3.1 – 6.9 m
The contract structure

• One GCLH to be selected for each of the geographical lots (a GCLH can be selected to cover more than one lot)

• Each GCLH to be responsible for the delivery for that geography of:
  
  — Core tests

  — Specialist tests (provided through (mandated) subcontractors

    ▪ There will be up to two testing services for category one sub specialist tests and up to four testing services for category two sub specialist testing services
Group work

• In your groups we want you to:

• Nominate a chair to enable a discussion about what we have said

• Record your comments

• Pick three top areas and feed them back to the larger group

• We did this on the 04 11 2016 and we work through all of the information received