Developing the NHS Genomic Medicine Service

Hilary Fanning on behalf of
Professor Sue Hill, Chief Scientific Officer and
The Genomics Unit, NHS England

May 2018
Why genomic medicine? Why now?

NHS Genetic Labs working since the 60s

Long term investment by Gov’t in genetic services & workforce

• Enabling a quicker diagnosis & ending the diagnostic odyssey
• Matching people to most effective medications & interventions
• Increasing people surviving cancer through accurate diagnosis & precision therapy

Major parliamentary reports setting out strategic direction

Cornerstone of Industrial Strategy to develop UK plc

>£600 million investment in 100,000 Genomes Project & NHS contribution

Building on our Inheritance – HGSG (2012)

Generation Genome - CMO (2017)
Alignment with key initiatives

**NHS England Five Year Forward View**

- NHS England’s Next Steps on the NHS Five Year Forward View signalled the intention to create a national Genomic Medicine Service

**Life Sciences Industrial Strategy**

- Potential to align with emerging developments in relation to AI and digital pathology
- The LSIS called for **continuation of sequencing of cohorts of cancer patients**. Initial proposal for £50m to support continued use of WGS for cancer

**CMO’s Generation Genome**

- The report set out how genomics can improve health and prevent ill-health.
- Recommendation for NHS England to **commission all genomics services nationally** to ensure a national network which enables equitable service provision across the country.

**Rare Disease Strategy**

- Support the delivery of England’s plan for rare disease

**International collaborations**

- The NHS will be the first healthcare system to introduce a comprehensive approach to genomic testing up to the level of whole genome sequencing and there are significant opportunities to work with other healthcare systems/governments on funded implementation aspects eg with US National Institutes of Health.
Establishing key principles for future care: The 100,000 Genomes Driver Project

<table>
<thead>
<tr>
<th>PRINCIPLES</th>
<th>INFRASTRUCTURE</th>
<th>LEGACY</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>100,000</strong> genomes from Rare Disease (families) &amp; Cancer (people &amp; tumours)</td>
<td><strong>13</strong> NHS Genomic Medicine Centres covering populations of <strong>3-7</strong> million</td>
<td><strong>4</strong> key legacies:</td>
</tr>
<tr>
<td><strong>4</strong> key principles:</td>
<td>Networked with <strong>90</strong> NHS hospital organisations (of circa 200) to ensure access – outreach clinics into other NHS orgs &amp; link to other UK countries</td>
<td>• Increased discovery of new pathogenic variants</td>
</tr>
<tr>
<td>• WGS extends current diagnostic scope</td>
<td>Contractual requirements include common protocols, data sharing, collation &amp; submission against agreed data standards &amp; sets</td>
<td>• Integrating advanced genomics into mainstream NHS</td>
</tr>
<tr>
<td>• Recruitment from routine care, treated through routine channels</td>
<td>National networking, groups &amp; events to drive standardisation, sharing of best practice &amp; to drive improvements</td>
<td>• Increasing public understanding &amp; support</td>
</tr>
<tr>
<td>• Participants consent to sharing of de-identified data for R&amp;D &amp; industry use &amp; for longitudinal access</td>
<td></td>
<td>• Stimulating and advancing UK life sciences industry</td>
</tr>
<tr>
<td>• Establishes model for transformational change</td>
<td></td>
<td>HEE Genomics Education Programme enhances system capacity across the NHS’s <strong>1.3</strong> million staff</td>
</tr>
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</table>

**GENOMIC MEDICINE - CORE PATHWAY**

- Identification of suitable patients from routine care
- Involvement of patients in ethics, data & consent issues
- Supply of high-quality processed samples
- Collection of linked phenotypic and clinical data
- Validation of WGS findings and feedback to patients
The proof of concept for a mainstream national genomic medicine service

Building from proven areas of clinical utility (rare disease & cancer)

Key principles for the NHS Genomic Medicine Service

• To ensure comprehensive and equitable access for the entire population (55 million)

• To improve the quality, value and sustainability of care by providing proampt diagnosis and personalised care

• To support learning, research & development through new collaborative partnerships between the NHS and with academia and UK life science sector and international collaborators/initiatives.

• To retain and build the political, ethical and moral trust of the UK in genomic medicine
NHS Genomic Medicine Service: Our aim

The NHS will have:

• A national Genomic Medicine Service providing consistent & equitable care for the country’s 55 million population

• Operating to common national standards, specifications & protocols

• Delivering to a single national testing directory – covering use of all technologies from single gene to whole genome sequencing

• Building a national database that will inform academic & industry research & discovery inc. clinical trials recruitment
The NHS Genomic Medicine Service: Assembling building blocks 18/19 to 20/21

NHS Genomic Medicine Service underpinning Personalised treatments and interventions

- **Genomic Medicine Centres & Genomic Clinical Services**
  - Integrated clinical genetics & providing population-based care

- **National Lab Network**
  - 7 ‘new’ Genomic Lab Hubs inclusive of cancer genomics

- **National Testing Strategy**
  - Inc annually refreshed testing directory (single gene – WGS)

- **Informatics architecture & data store**

- **Whole Genome Sequencing Provision – NHS requirement combined with others**

- **Clinical Interpretation Pipeline**

- **Workforce development**
  - Upskilling of existing staff & ongoing professional engagement in conjunction with Health Education England

- **Industry/academic/international partnerships**
  - Supporting ongoing research & development through clinical care

**Political oversight:**
Dept of Health & Ministerial Board

**Policy & strategy,** coordinating, contracting & evaluation function with a programme of care & fixed budget

**Overall service timetable:**
- **Procurement:** Currently live
- **Mobilisation:** Q1 18/19 – Q2 18/19
- **Operational:** Q3 ’18 onwards

**Advances in genomic & informatics technologies & other next generation diagnostics informing policy, strategy & regulation**
The National Genomic Test Directory – shaping routine care for the future

- From October 2018/19 the Test Directory will define all genetic and genomic tests available through the NHS in England – from single gene to WGS >300,000 tests/year
- Initially covering common cancers and rare and inherited diseases
- Sets out the What, Where, Why, When & How of each genetic test
- Structured by: Technology; Test name; Test scope; Targets/Genes; Clinical Indication
- Data and outcomes on testing will be collected, reviewed with other emerging evidence, with the directory updated annually
- Pharmacogenomic testing to be included as suitable evidence developed
- 25% of existing testing expected to be replaced by newer technologies, through the assessment of clinical utility, efficiency & effectiveness
Content of the Test Directory

- The Directory builds on the UKGTN directory and its development was supported by Genomics England and the Cancer and Rare Disease Transition Working Groups.

- Directory sets out specific test method(s) across 22 technology categories from single gene testing to Whole Genome Sequencing.

- The Directory covers:
  - 350 rare disease
    - WGS will initially be available for approximately 24 rare disease conditions
  - 196 cancer clinical indications
    - The majority of cancer testing is expected to be through large panel
    - WGS offered for paediatric cancers, sarcomas and relapsed ovarian cancer
    - Some karyotyping, FISH and targeted mutation testing will remain
    - Work aligns with NHS Improvement approach to transforming pathology services & improving cancer diagnostics

- The Directory will be updated annually and the process will be supported by a Scientific Committee.

- The Test Directory covers all genetic and genomic tests, and overtime we expect the testing repertoire to change as the evidence and new technologies develop.

<table>
<thead>
<tr>
<th>Technology types</th>
<th>Proportion of reports</th>
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</thead>
<tbody>
<tr>
<td>WGS</td>
<td>10-25%</td>
</tr>
<tr>
<td>WES or large panel</td>
<td>2-14%</td>
</tr>
<tr>
<td>Small panel</td>
<td>10-15%</td>
</tr>
<tr>
<td>Single gene sequencing</td>
<td>3-5%</td>
</tr>
<tr>
<td>Targeted mutation testing</td>
<td>20-25%</td>
</tr>
<tr>
<td>STR testing</td>
<td>10-15%</td>
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<tr>
<td>MLPA or equivalent</td>
<td>5-7%</td>
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<tr>
<td>Microarray</td>
<td>10-20%</td>
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<tr>
<td>Common aneuploidy testing</td>
<td>5-7%</td>
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<tr>
<td>Karyotype</td>
<td>3-5%</td>
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<tr>
<td>FISH</td>
<td>&lt;2%</td>
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<tr>
<td>DNA repair defect testing</td>
<td>&lt;2%</td>
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<tr>
<td>Methylation testing</td>
<td>&lt;2%</td>
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<tr>
<td>UPD testing</td>
<td>&lt;2%</td>
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<tr>
<td>X-inactivation testing</td>
<td>&lt;2%</td>
</tr>
<tr>
<td>Identity testing</td>
<td>&lt;2%</td>
</tr>
<tr>
<td>Microsatellite instability</td>
<td>tbc</td>
</tr>
<tr>
<td>NIPT</td>
<td>tbc</td>
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<tr>
<td>NIPD</td>
<td>&lt;2%</td>
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<tr>
<td>PGD</td>
<td>&lt;2%</td>
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<tr>
<td>Other</td>
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</table>
The personalisation journey

Technology, Innovation & Knowledge Base

DNA + omics

Genomic medicine in specific examples

2012

100,000 Genomes Project - use of WGS, panels & functional genomics for rare disease & cancer

2013-18

Policy, System & Regulatory Alignment

100,000 Genomes Project

Genomic medicine embedded within specific pathways

2018 - 2020

Clinical Change & Operating Model

Genomic medicine embedded as part of routine care – where appropriate

Clear role established for next-gen diagnostics

Infrastructure change - informatics & commissioning

Data analytics and bioinformatics

Other functional diagnostics

Phenotypic characterisation

Patient generated data & self-reporting

Technology, Innovation & Knowledge Base

\[\text{http://bit.ly/PMvision}\]

2018 - 2020

2020 and beyond

\[\begin{align*}
\text{Better prediction and prevention of disease} \\
\text{A more precise diagnosis} \\
\text{More targeted and personalised interventions} \\
\text{A more participatory role for patients}
\end{align*}\]
Aligning the routine NHS service to provide real world evidence

A much wider range of outcomes and research

Why do we need this product?

- Burden of disease (economic & humanistic)
- Patient journey and current treatment algorithms
- Patient subgroups and competition
- Unmet needs
- Patient outcomes
- Treatment costs & resource use
- Adherence
- Effectiveness/comparative effectiveness
- Safety/comparative safety

Why do we need this product?

- Product related research

Adaptive pathways

- post-launch
- pre-launch

Is this product value for money?
Personalisation providing significant advance in practice

**GENOMIC-LED PERSONALISATION**

- **Earlier Diagnosis**
  - Reduce ‘diagnostic odyssey’
  - More treatment possibilities with early stage disease

- **Greater diagnostic yield**
  - 60%+ actionable genes in cancer
  - 4-5x increase in rare disease

- **Prognostics/preventative approaches**
  - Providing clear identification of underlying cause of disease & segmentation of condition

- **Identifying predisposition markers**
  - By better characterisation of condition & driver targets

- **Eligibility for clinical trials**
  - Through identification of predisposition to side effects

- **Fewer adverse reactions**
  - Precise diagnosis allows better treatment selection & increased effectiveness

- **More effective treatments**
  - Earlier Diagnosis
  - Greater diagnostic yield
  - More precise diagnosis
  - More effective treatments
  - Fewer adverse reactions

- **Eligibility for clinical trials**
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The genomic medicine journey to 2025

Today:
• Variable patient access to cutting-edge genetic technologies
• Proof of concept project demonstrating benefits
• ‘One size fits all’ treatment based on symptoms
• Limited use of genomic markers
• Diagnostic & clinical data not linked

By 2020:
• National Genomic Medicine Service driving personalised treatments and interventions with consistent & equitable access across the country – underpinned by a National Genomic Test Directory
• Improved diagnosis of rare conditions and better understanding of cancer
• Integrated informatics platform to support comprehensive linking of genomic and clinical data to give a full picture to patients
• Routine care and treatment closely linked through to clinical research, academia and industry with many more patients eligible for clinical trials

By 2025:
• New taxonomy of medicine based on underlying case & personal response
• Integrated clinical services taking a ‘whole pathway’ approach
• Routine use of Whole Genome Sequencing and newer genomic technologies embedded across multiple clinical pathways
• Genomics included as a fundamental part of clinical training across all professions and levels
• Tailored, optimised & more effective therapies for better outcomes
WM Genomic Medicine Centre

A Regional Snapshot ..
Setting out on our Journey
Recruitment: Q1 2015/16 - Q2 2015/16

<table>
<thead>
<tr>
<th>Key</th>
<th>Local Delver Partner</th>
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<tbody>
<tr>
<td>1</td>
<td>University Hospitals Birmingham NHS Foundation Trust</td>
</tr>
<tr>
<td>2</td>
<td>Birmingham Women’s Hospital NHS Foundation Trust (BWH)</td>
</tr>
<tr>
<td>3</td>
<td>Birmingham Children’s Hospital NHS Foundation Trust</td>
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</tbody>
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Key:
- LDP: Local Delver Partner
- Rare Disease
- Cancer

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## Recruitment: Q1 2015/16 – Q4 2017/18

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<tr>
<td>4</td>
<td>Heart of England NHS Foundation Trust</td>
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<tr>
<td>5</td>
<td>The Royal Wolverhampton NHS Trust</td>
</tr>
<tr>
<td>6</td>
<td>University Hospitals Coventry and Warwickshire NHS Trust</td>
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<tr>
<td>7</td>
<td>The Royal Orthopaedic Hospital NHS Foundation Trust</td>
</tr>
<tr>
<td>8</td>
<td>Royal Stoke University Hospital</td>
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<tr>
<td>9</td>
<td>The Dudley Group NHS Foundation Trust</td>
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<tr>
<td>10</td>
<td>The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust</td>
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<tr>
<td>11</td>
<td>The Shrewsbury and Telford Hospital NHS Trust</td>
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<tr>
<td>12</td>
<td>Wye Valley NHS Trust</td>
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<tr>
<td>13</td>
<td>Sandwell and West Birmingham Hospitals NHS Trust</td>
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<td>14</td>
<td>Burton Hospitals NHS Foundation Trust</td>
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<td>15</td>
<td>George Eliot Hospital NHS Trust</td>
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<tr>
<td>16</td>
<td>South Warwickshire NHS Foundation Trust</td>
</tr>
<tr>
<td>17</td>
<td>Worcestershire Acute Hospitals NHS Trust</td>
</tr>
<tr>
<td>18</td>
<td>Walsall Healthcare Trust</td>
</tr>
</tbody>
</table>

### Key:
- **LDP**: Rare Disease
- **Cancer**

[Map of recruitment areas with key]

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Sarah, newly diagnosed with diabetes, also has early onset deafness.

Diagnostic testing:
Gene panel negative

Whole genome sequencing reveals variants in a new gene for diabetes

Diabetes team/GP order samples for genomic testing

Review back in clinic with genomics consultant/nurse counsellor – family testing

Sarah’s dad wants to know about treatment options.

Research group identify the underlying mechanism, common to other diseases

Electronic health data linkage shows outcomes of 25 other UK children with diabetes and deafness - some get kidney problems

Nephrology Review

2 drugs available: compare Sarah’s transcript signature profile to that of the drug that most closely reverses it

PERSONALISED Care is Routine
Thank You