The NHS approach to personalised medicine in respiratory disease

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“Genomics is probably the biggest breakthrough in the last 50 years.

“For many years, it’s been talked about that medicine is going to be personalized. We’re finally starting to get there.”

Dr Eric Topol
Leading researcher in US Precision Medicine Institute
Into the next generation – science moving beyond genomics alone

Profound scientific & technological innovation influencing NHS transformation and effectiveness; as outlined in 5 Year Forward View and the next steps in implementation
Harnessing genomics for a significant advance in diagnostic yield & reach

Building on history and tradition of genetic advance and genetics in NHS

Exponential growth in information – much more that is actionable today and currently available in NHS

Informatics: Combining information to objectively define disease phenotypes

Opportunities to further increase diagnostic yield, coupling with functional genomics

POCT developments providing real-time clinical opportunity

Patient Push  GENOMICS  Science Pull
NHS Genomic Medicine Centres: delivering the genomic future

- Established to provide NHS contribution to 100,000 Genomes Project - patients from routine care, treated through routine channels
- Coordinating care for populations of ~3-7 million, responsible for pathways & services across their geography.
- Lead organisation builds networks with other trusts as Local Delivery Partners (over 90 Trusts will be involved at completion of Project)
- Provide transformative leadership to the system including as Clinical Programme Leads
- Capture improvements in clinical outcomes and drive change in clinical utility (4-5x increase in RD diagnosis and greater actionability in cancer)
- Underpinned by HEE Genomics Education Programme and investment in genetic scientists and bioinformatics
Project has created a World-Leading Infrastructure for genomic medicine

National elements

- National Biorepository
- Whole Genome Sequencing Provider
- National Genomic integrated Database
- National Genomic Interpretation Pipeline
- National Knowledge Base

Network of 13 NHS Genomic Medicine Centres
- serving ~3-5m population, inc data hubs
- 13 Lead organisations & 75 local NHS trust delivery partners
- Multiple hospital sites and outreach locations

NHS molecular diagnostic and genomic laboratories

Access through a range of specialties & services

Pharma, Biotech and Diagnostic Companies investing in the UK

2500 Researchers providing Insights and Discoveries
Birth of the NHS Genomic Medicine Service

Mar 2017: NHS England Board agrees strategic approach for building a genomic medicine service from 2018/19, delivering personalisation of treatment and intervention building on the legacy of the 100,000 Genomes Project.

The key principles for the NHS genomic medicine service are:

- To ensure **comprehensive and equitable access** for the entire population
- To improve the **quality, value and sustainability** of care by providing prompt 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.
- To **retain and build the political, ethical and moral trust** of the UK in genomic medicine
Assembling all the building blocks

NHS Genomic Medicine Service underpinning Personalised treatments and interventions

Genomic Medicine Services providing population-based care
National Lab Network inc Genomic Laboratory Hubs
National Testing Strategy from single gene - WGS
Informatics architecture & data store
Whole Genome Sequencing Provider
Clinical Interpretation Pipeline
Workforce development inc upskilling of existing staff
Industry/academic/international partnerships supporting ongoing research & development through clinical care

Advances in genomic and informatics technologies and in other next generation diagnostics
Delivering genomic-based personalisation for patient benefit & service sustainability

- Technology available and affordable
- Patients/Public ready for change
- Clinical Leadership & workforce upskilling
- Proof of concept for routine care established
- New service networks and patient pathways set up
- Health economics established
- System planning & commissioning aligned

GENOMIC MEDICINE FOR PERSONALISATION

Transformed pathways of care based on careful characterisation of patients facilitating tailored interventions

Spectrum of delivery
At home
Specialist Care
Moving forward – activity to deliver personalisation

Improving Outcomes through Personalised Medicine (Sep 2016) sets out a 10-year framework for the delivery of personalised medicine across the NHS, including:

- improved **prediction & prevention** based on underlying predisposition
- more **precise** (and prompt) diagnosis based on cause
- targeted interventions through the use of companion diagnostics to identify & **personalise** effective treatments
- better use of **diagnostic spend** to provide objectivity to **medicines use**

Key activity from national partners:

- **Build the commissioning, data & informatics infrastructure**
- Roll out personalised medicine approach in a **number of clinical areas**, linked to NHS England’s priorities & informed by AMS exemplar pathways
- **Engage & involve** the public, patients & patient groups, clinicians, academics, industry & others to inform and shape the approach
- **Develop the enabling framework** to ensure that personalised medicine approaches are proactively adopted based on strong evidence, value & ethics

[Improving Outcomes through Personalised Medicine](http://bit.ly/PMvision)
Transforming the patient pathway

Patient presents → Next-gen diagnostic → Clinical Decision → Intervention decision → Outcome

- Precise diagnosis – precise treatment selection - Fewer non-responders/ADRs
- Greater multi-professional involvement in MDT
- Role for community-based diagnostics/screening
- Working across the care continuum, moving burden of disease from late stage care to early identification & diagnosis
Personalised Medicine in practice - tailoring treatment & management to a patient’s individual makeup

Increasingly precision interventions based upon carefully identified subgroups within the broader population

‘One size fits all’ treatments & intervention

Individually-tailored approach

Diagnostics (inc WGS)

Data and analytics

Medicines & other interventions
- Existing and repurposed drugs
- Targeted medicines
- Non-pharma
- New discoveries

Providing effective coupling of diagnosis and treatment
Genomics and Medicines optimisation

Precise diagnosis leads to precise treatment selection and fewer non-responders

Patient response to a particular pharmaceutical can be predicted by genomic & phenotypic characterisation

£1bn pa spend on respiratory inhalers in primary care alone

NHS England working on plans for mainstreaming genomic testing & pharmaco genomic profiling linked to sharing of patient record

Genomic screening can identify potential adverse drug reactions

Principle 1: Aim to understand the patient’s experience
Principle 2: Evidence based choice of medicines
Principle 3: Ensure medicines use is as safe as possible
Principle 4: Make medicines optimisation part of routine practice

Improved patient outcomes

Patient-centred approach

Aligned measurement & monitoring of medicines optimisation
A whole pathway approach to developing personalisation across care continuum

<table>
<thead>
<tr>
<th>NHS Clinical priorities</th>
<th>Opportunities for population health approaches</th>
<th>Medicines optimisation &amp; reduction of ADR</th>
<th>Where significant utility from next-gen diagnostic approaches</th>
<th>Where significant variation in access</th>
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<tbody>
<tr>
<td>• Diabetes</td>
<td>• Familial Hypercholesteremia</td>
<td>• Warfarin</td>
<td>• Rare Diseases, • Cancer</td>
<td>• Renal • Cardiovascular</td>
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<td>• Mental health</td>
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<td>• Respiratory</td>
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Evaluation of candidate conditions assesses:

- Potential for **high impact of next-generation diagnostics** including functional genomics and for **medicines optimisation**
- Evidence base for utility/cost effectiveness and health economics
- Responsiveness & turnaround time for results
- Evolution of **Informatics and analytical platforms including decision support**
- Whole pathway approach
- Adoption of new technologies

The asthma challenge

- > 4 million people are prescribed asthma therapies in the UK
- > 500 deaths per year. Asthma exacerbations lead to
- > 65,000 hospital admissions from exacerbations
- > £900m pa on pharmaceutical costs alone.
- A direct cost to the NHS of £1 billion and an indirect cost to society, (time off work and loss of productivity etc) of £1.2 billion
- Vast majority of patients have potential to be well controlled with existing therapies - A small proportion (<5%) have severe asthma.
Rethinking respiratory conditions and diagnosis – segmenting disease

Cluster analysis of asthma phenotypes shows the heterogeneity of the condition – with the clusters changing depending on the selection of markers.

Genomic and functional genomic data has the potential to give an extra dimension to this analysis.
Multilevel approach to personalisation in respiratory conditions

- The multi-faceted nature of respiratory conditions are increasingly making them ideal candidates for a personalised approach at many levels,
- Rather than assign broad diagnostic labels (‘asthma’, ‘COPD’) across the continuum of patient presentation, precise diagnosis will allow the identification of specific ‘treatable traits’ (pulmonary, extrapulmonary & behaviour/lifestyle) allowing more personalised care & better outcomes.

Network model of condition drivers

Personalised approach to airway disease

Adult with symptoms, signs or events suggestive of airway disease

History, clinical examination and risk factors
- Spirometry/Foxa/blood eosinophils

Strong history and/or risk factors present and/or abnormal test results

Atypical history, no risk factors and normal test results

High probability of airway disease

Low probability of airway disease

Assess and manage treatable traits (Tables 1-3)

Assess and manage non-airway treatable traits (Tables 2 and 3), consider alternative diagnosis and follow-up
A (near) future personalisation pathway–improving cardiovascular care

Blood analysed (WGS) to determine if patient at risk of CVD events

Biomarker and remote telemonitoring determines when to intervene (reducing hospital readmission)

Genomic and biomarker data used to select most effective medication

Drug platform enables designer drugs for personalised treatment

Urine/Biomarker monitoring is used to check treatment efficacy, modifying as required

Improves patient outcomes & experience, while reducing pressure on acute services

Approach developed by Cardiovascular Precision Medicine Initiative – a multi-partner US project

Aim: emphasize predictive analytic methodology to provide quality care, reduce cost and provide cutting edge cardiovascular technology to community of 3 million
Alignment & partnership driving research advance, future care & innovation

Future plans structured to actively engage & support research endeavours by clinicians, academia & the life science industry for patient benefit

This includes:
- Providing an evidence base to inform identification of new treatment targets & approaches
- Analysis of evidence base to improve understanding of conditions & their heterogeneity
- Supporting trial design & patient selection
- Repurposing of existing drugs & treatment
- Better tests for clinicians to check patients for suitability; Patients more confident in fit of medicine - benefits for adherence, support & monitoring
- Mining data for findings that boost understanding of real world response
The personalisation journey over the next decade

**Today:**
- ‘One-size-fits-all’ treatment based on symptoms
- Services and professions organised according to organ/speciality
- Limited use of genomic and molecular markers
- Diagnostic and clinical data not linked

**By 2020:**
- Whole genome sequencing for specific conditions
- Improved diagnosis of rare conditions and better understanding of cancer
- Comprehensive, linked diagnostic data coupled with effective informatics analysis to give a full picture of patients

**By 2025:**
- New taxonomy of medicine based on underlying cause and personal response
- Integrated clinical services taking a ‘whole body’ approach
- Tailored, optimised and more effective therapies for better outcomes
- New NHS relationships with academia, industry, patients & patient groups