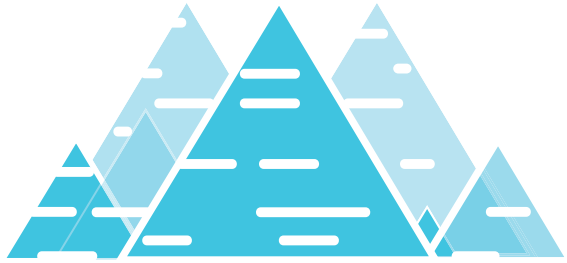


PERSONALIZED MEDICINE

SUMMIT

TRANSFORMING THE PRACTICE OF MEDICINE

June 7-9th 2015, UBC, Vancouver, BC

Be part of the Personalized Medicine Revolution

personalizedmedsummit.com

#PMSummit2015

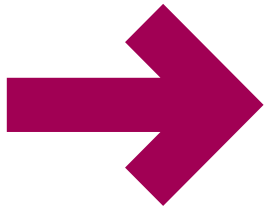
Developing personalised medicine in the NHS: the 100,000 Genomes Project

Personalised Medicine Summit
Vancouver, 9 June 2015

Professor Sir Malcolm Grant
Chairman NHS England

Drivers for success

- NHS as single payer/provider; 55m registered patients



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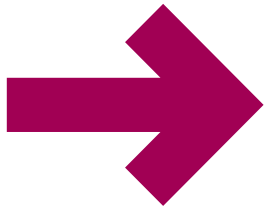

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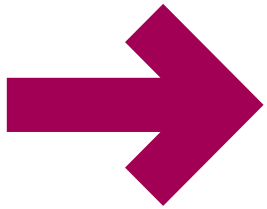

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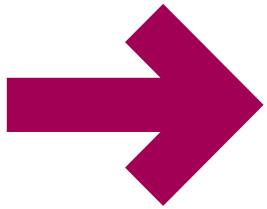

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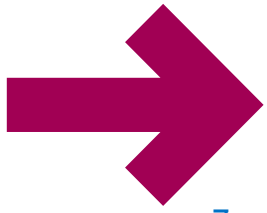

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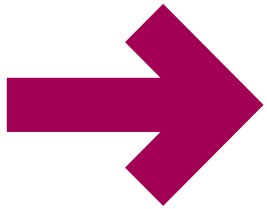

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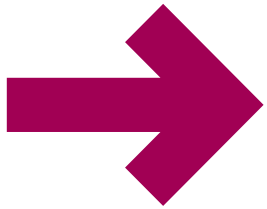

The first steps

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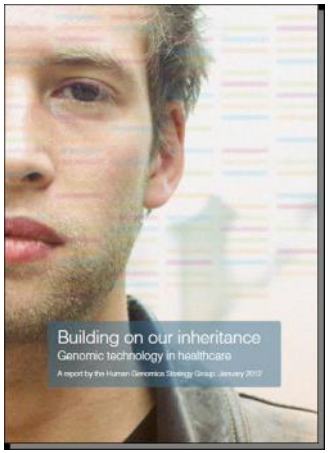

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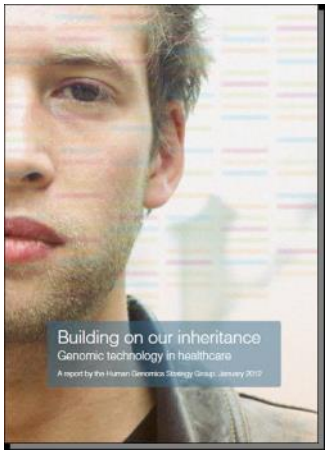

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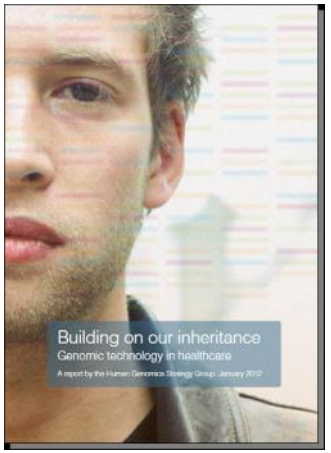

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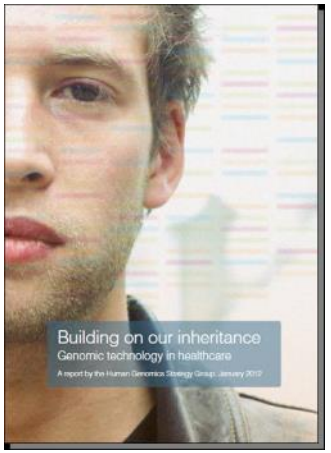

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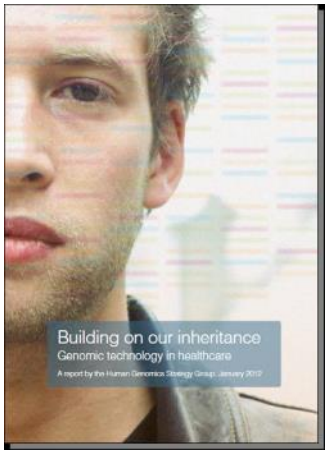
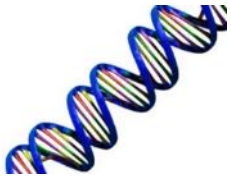
- Establishment of Genomics England Ltd
  - Ownership
  - Board



21st Century: Transforming medicine through functional genomics

- *Functional genomics*: a structured analysis of the relationship between ***genotype*** and ***phenotype***, typically using high throughput methods to look at the various steps of the transcription process
- Allows more accurate diagnosis of disease and targeted treatment



DNA

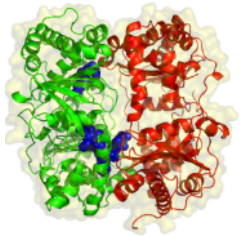
Genomics

>30k genes. Sets out '*potential*'

RNA

Transcriptomics

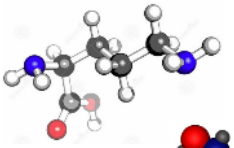
>30k Sets out the '*implementation strategy*'



Proteins

Proteomics

>100k products Shows '*the process happening*'



Metabolites

Metabolomics

>6500 metabolites - the '*final outcome as products*'

Desired benefits of the 100,000 Genomes Project

Not a research project: need to spearhead NHS transformation

Desired benefits of the 100,000 Genomes Project

Major legacies for patients, the NHS and the UK economy by 2017

Enhanced discovery of pathogenic variants leading to **new treatments, devices and diagnostics**

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Accelerate uptake with advanced genomic medicine practice **integrated into the NHS**

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Increased discovery of pathogenic variants leading to **new treatments, devices and diagnostics**

Accelerate uptake with advanced genomic medicine practice **integrated into the NHS**

Increase public understanding and support for genomic medicine

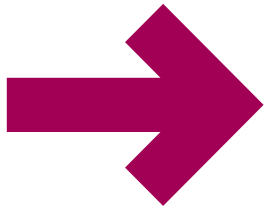
Stimulate and advance UK life sciences industry and commercial activity in genomics

Design features for the 100,000 Genomes Project

- Structurally integrated with **National Health Service**
- Selected **patient cohort**
- Patients give informed **consent**
- Sequencing undertaken in new **state-of-the-art sequencing** centre
- Data held in a **secure and monitored environment** with strictly regulated access to ensure public confidence
- Engagement of large number of scientists and clinicians in interpretation
- **Commercial companies** to have defined routes to access
- Common pool of **Intellectual Property** available for licence
- Genomic medicine **education programme**

Making it happen: the early stages

- Identification of medical conditions for priority for sequencing



Disease selection: cancers, rare and infectious diseases

- Cancers: breast, bowel, lung, ovarian, prostate and chronic lymphocytic leukaemia (CLL)
- Rare diseases: As a group, rare diseases affect 6% of the population, and >85% are caused by a single gene defect. Many are chronic, and associated with substantial morbidity and premature mortality. Early diagnosis enables accurate genetic counseling and prevention, and may lead to new treatments based on genetic stratification. Inherited cancer and immunodeficiencies fall within this group
- Infectious diseases: HIV, Hepatitis C and TB

Making it happen: early stages

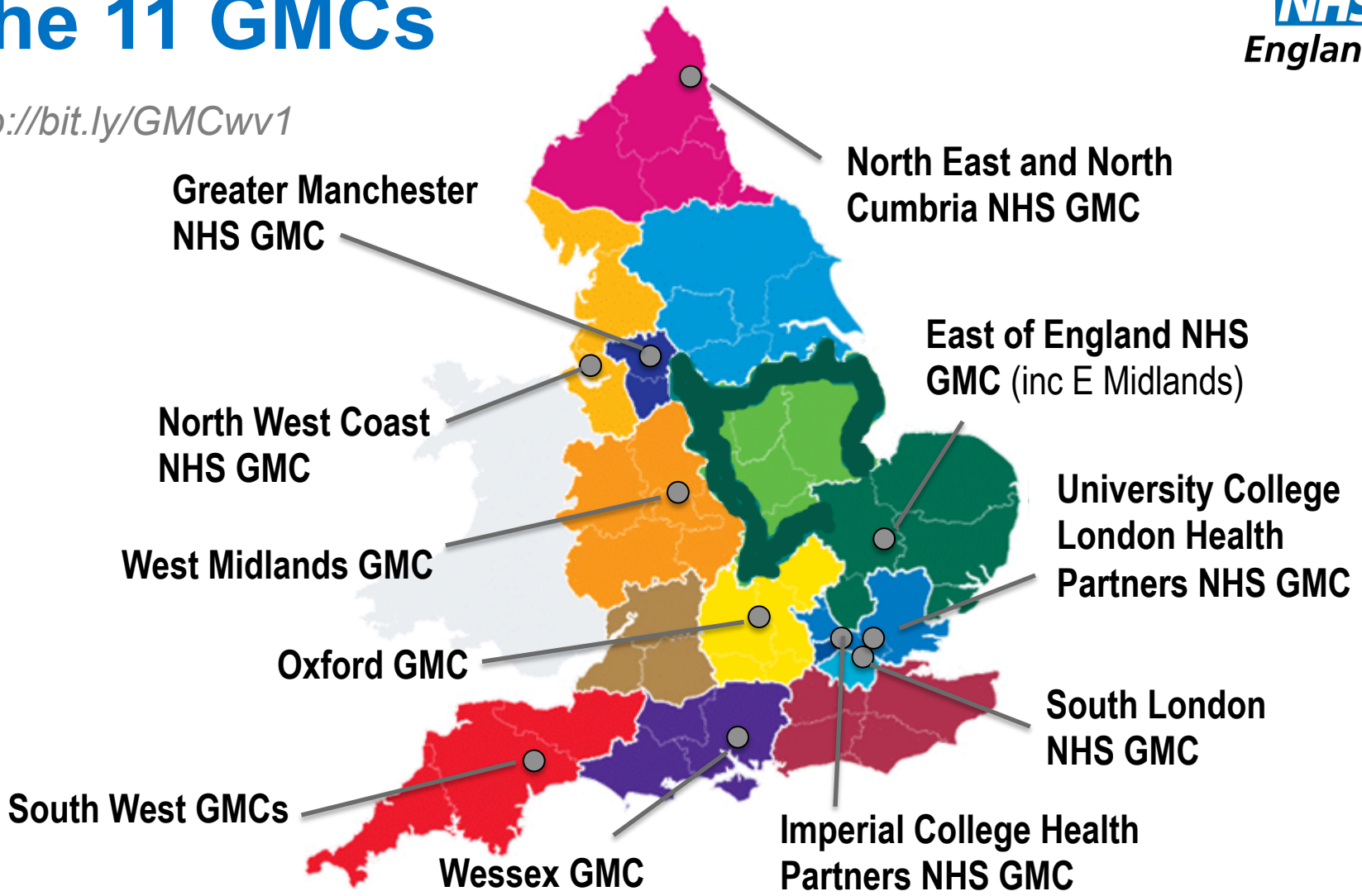
- Identification of medical conditions for priority sequencing
- Learning through Oxford pilot study
- Engaging NHS clinicians and institutions in the project

Setting up the NHS Genomic Medicine Centres

- Selection through 2 step competitive process
- Leading to designation of 11 NHS Genomic Medicine Centres (geographically dispersed and with multiple local delivery partners)
- 'Go Live' from March 2015 (rare diseases), May 2015 (cancer)
- Duties of the Centres:
  - acquire and process 90,000 samples from participants with rare disease (and their family members) and with cancer
  - capture clinical phenotypic information
  - validate the findings from whole genome sequencing and provide feedback to participants and clinical teams
  - measure and monitor impact

The 11 GMCs

http://bit.ly/GMCwv1

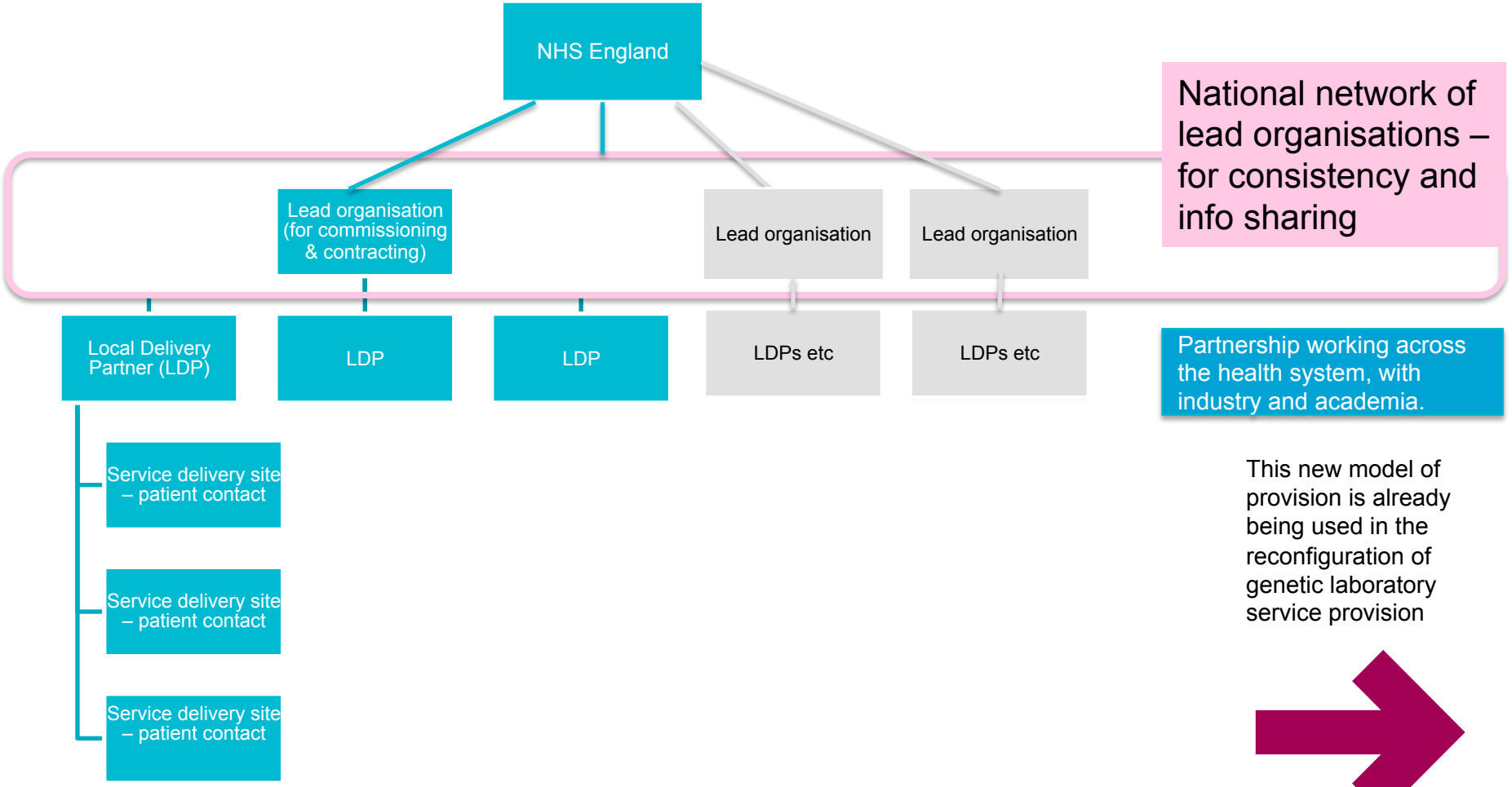


NHS GMCs working in partnership with academia, patients and industry through the Academic Health Science Networks across the geographical footprint

The operating model

- NHS England is the prime contractor and funder (internal budget of £20 million over 3 years)
- Designated NHS Genomic Medicine Centres operate over a significant geographical area with partnership agreements with NHS Local Delivery Partners for some or all of the services to be delivered
- NHS GMCs as Lead Organisations appoint specific leads eg informatics, rare diseases to have oversight across the geography
- NHS GMCs work together in a network to share good practice
- Supported by NHS England's Implementation Unit, overseeing contracting arrangements and providing improvement support

GMCs – coordinating a network of delivery organisations



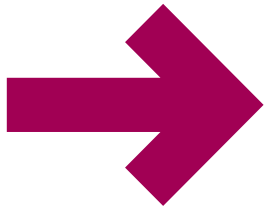
National network of lead organisations – for consistency and info sharing

Partnership working across the health system, with industry and academia.

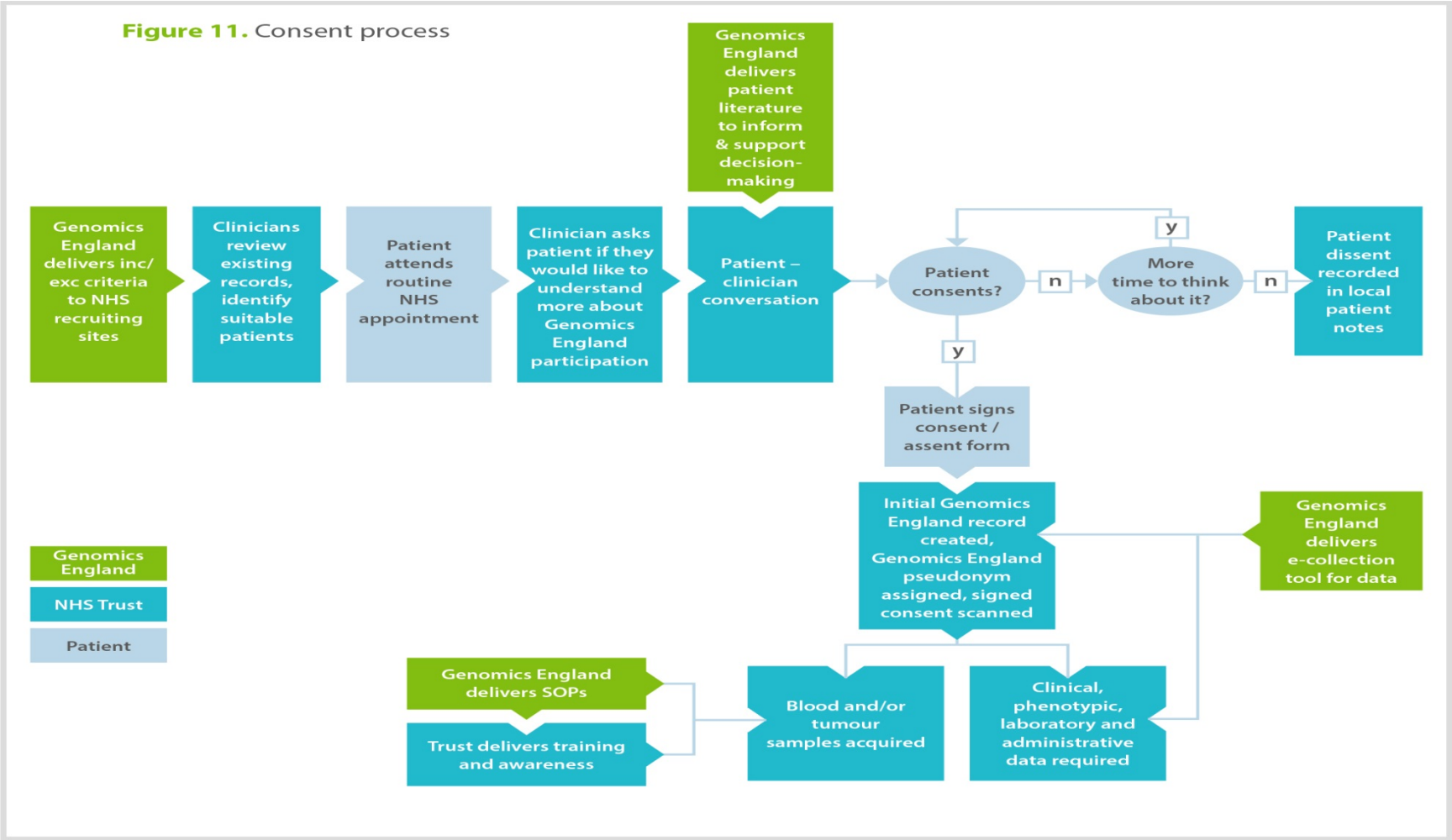
This new model of provision is already being used in the reconfiguration of genetic laboratory service provision

Contractual arrangements

- Contract with robust KPIs, reporting metrics and financial schedule based on full payment for successful samples assessed following sequencing
- Approval to extract DNA locally based on successful participation in a newly established and NHS England sponsored UK NEQAS scheme
- Detailed service specification covering all aspects of the delivery pipeline from consent through to clinical feedback and service transformation
- Detailed outcome specifications for certain functions eg sample processing and DNA extraction

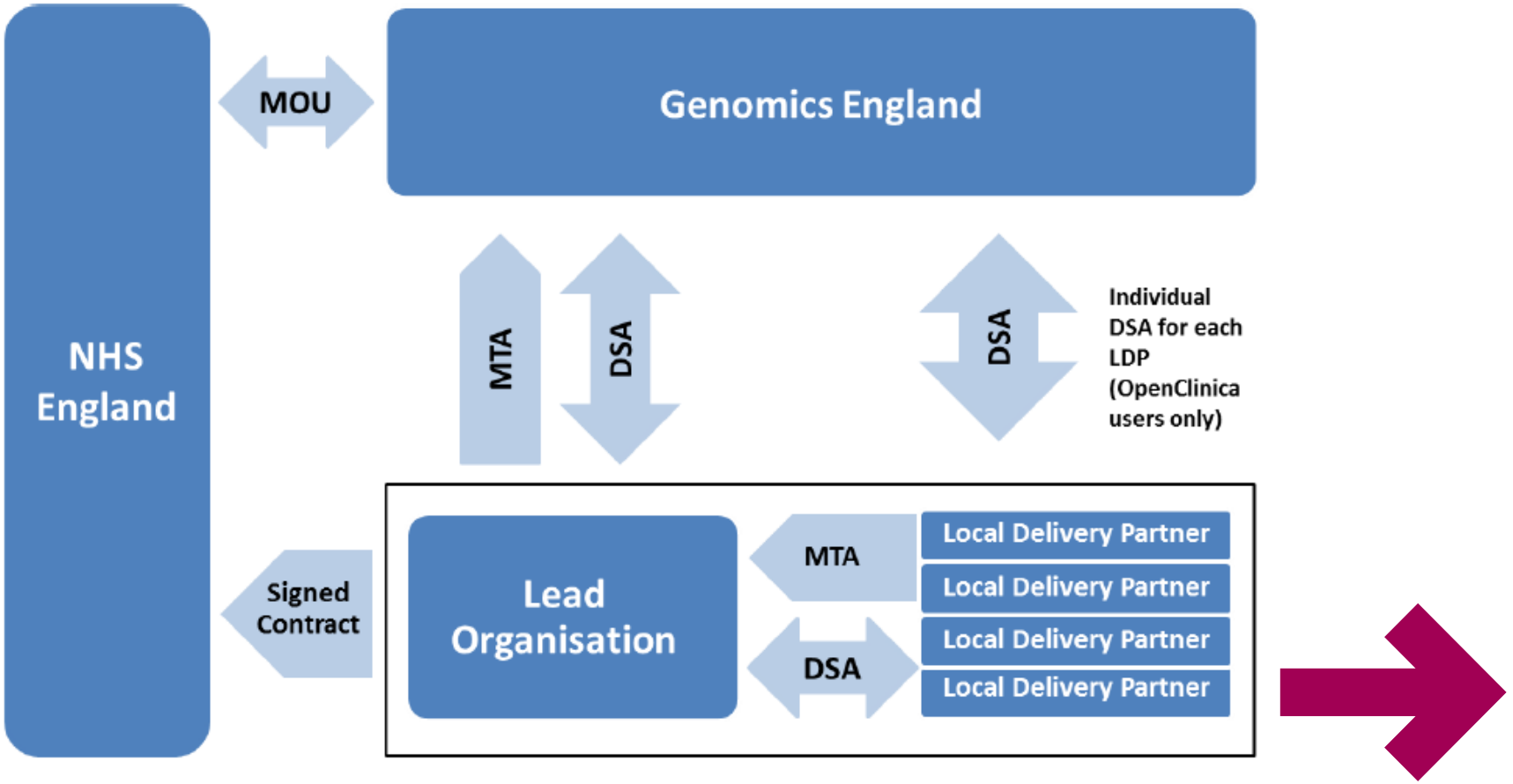


Informed consent



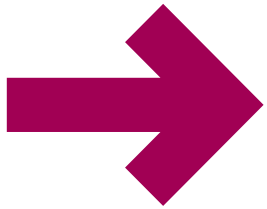
Assuring material and information

Material transfer & data sharing agreements govern the flows between the various NHS partners and Genomics England

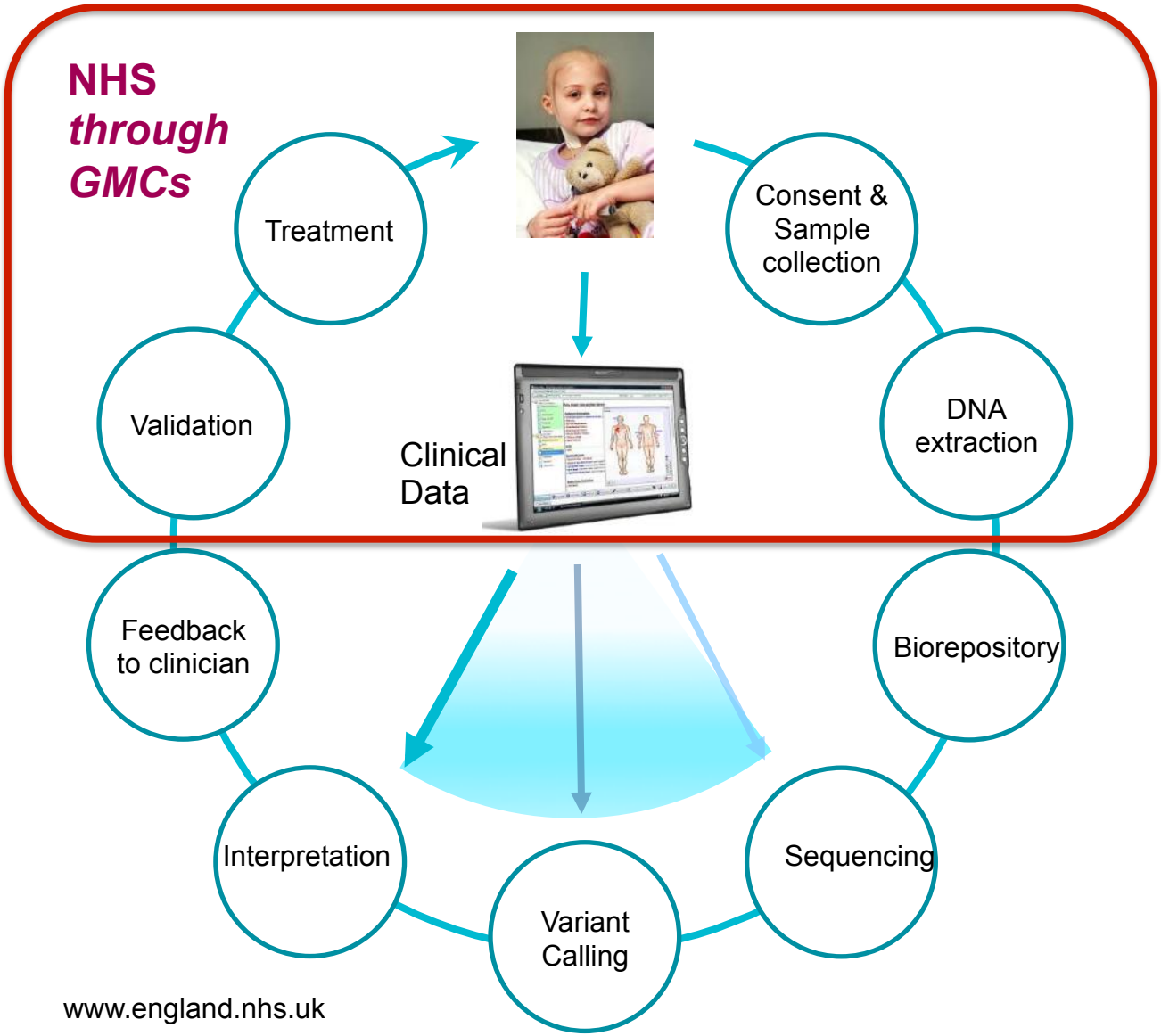


Making it happen: early stages

- Procurement of sequencing technology through commercial partnership with illumina; Silexa
- Developing approaches to securing viable tumour samples – study currently underway of how quality of extracted DNA has been affected by different preparations
- Trios of germline, tumour (Formaldehyde Fixed-Paraffin Embedded – FFPe) and tumour fresh/frozen
- Banking samples for future proteomic, metabolomic etc analysis – towards comprehensive molecular-level information



The Genomic Medicine Cycle – The role of the NHS through GMCs

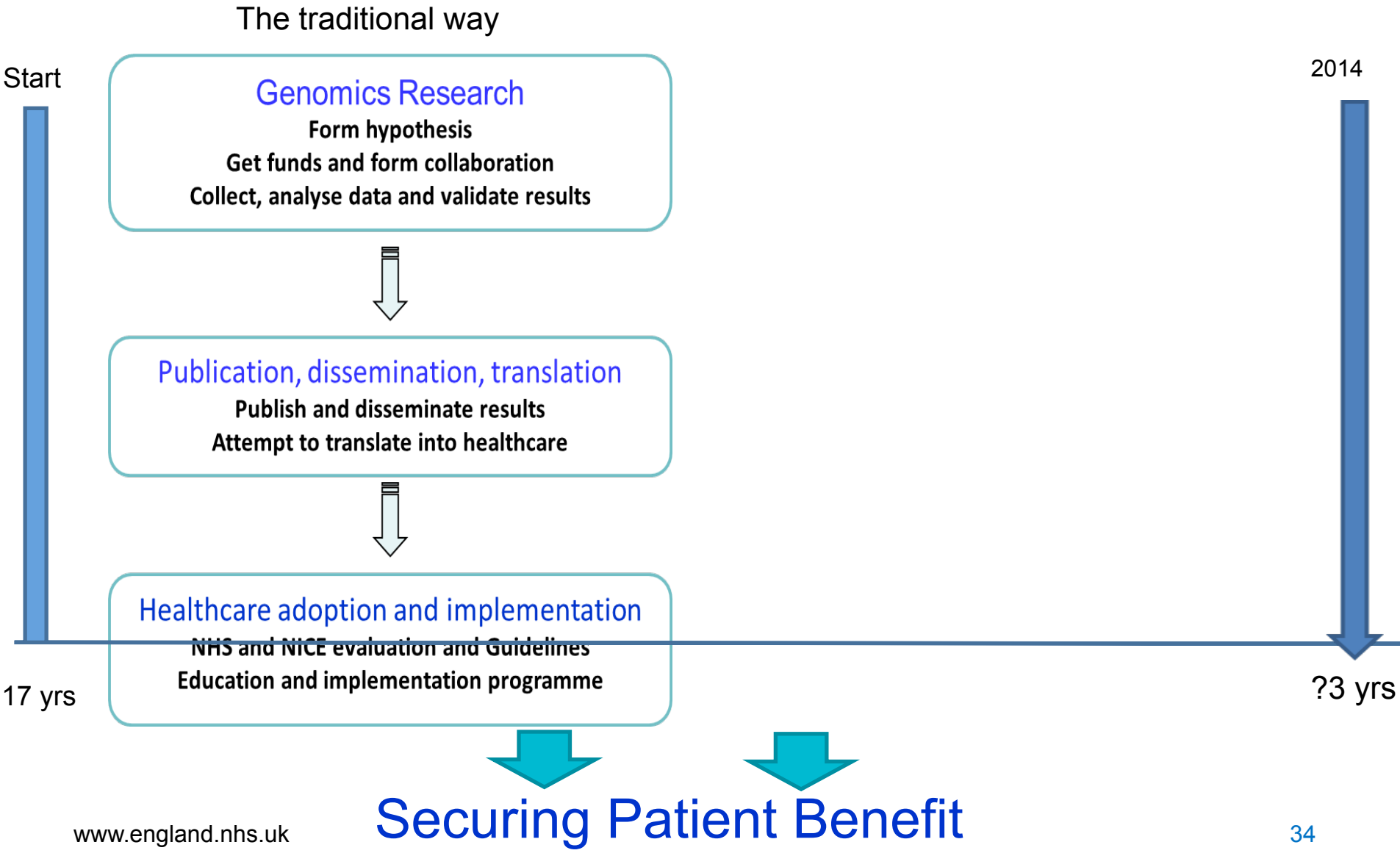


The treatment cycle for the 100,000 Genomes project combines the patient-facing work of the NHS - through Genomic Medicine Centres - with a number of highly-specialised processes

Current processes are not optimised for genomic medicine so the task is truly one of initiating a transformation in medical practice across the workforce, particularly relating to routine use of coordinated data.

Interpretation partnerships to speed up delivery of new interventions

NHS England



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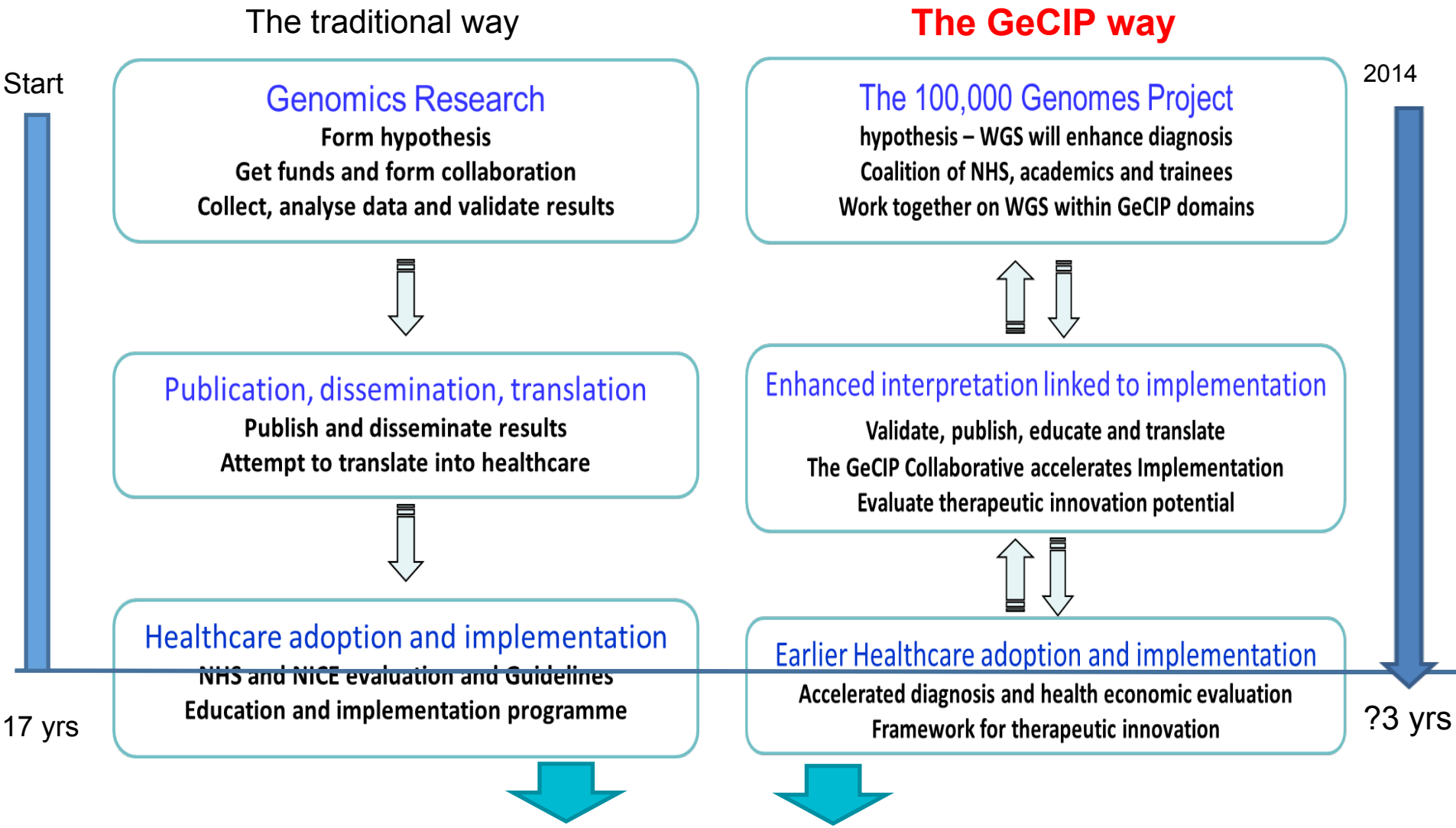


Securing Patient Benefit

The idea of GeCIPs

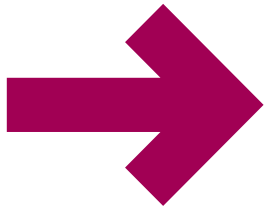
- Improve fidelity of clinical interpretation of WGS
- Accelerate academic/industry partnership and development of diagnostics and therapies.
- Partnership with researchers, the NHS and equip trainees with skills
- Portal for international collaborators
- All data generated contribute to the Genomics England Dataset and are available to all.
- Getting to a therapy will require significant additional R&D which will be deliberately stimulated in the UK.

Key GeCIP domains

- Rare diseases: (15), eg cardiovascular, endocrine and metabolism, neurological, renal, respiratory, schizophrenia
- Cancer (8): breast, colorectal, lung, ovarian, prostate, childhood solid cancers, haematological malignancy, pancreatic
- Functional (8): EMR, validation and feedback, ethics and social science, functional effects, health economics, machine learning, population genomics, translational research, functional cross cutting

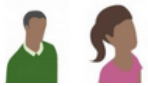
IPR agreements

- GEL owns the samples and the data relating to them supplied by the GMCs
- GMCs continue to own clinical data relating to their patient but grant GEL a wide licence
- Likewise IPR developed in preparation of samples
- GEL owns sequence data, analysis, GMC results and Reports; grants licence to GMC to use for clinical purposes; no research rights
- GEL owns GeCIP outputs and IPR
- GeCIP members need to disclose/get consent to dealings
- GENE Consortium: large and small companies
- Patent strategy



The big picture

NHS England



Patients & Families

NHS Genomic Medicine Centres
Rare diseases, cancers and pathogens
Broad consent, characteristics, molecular pathology and samples

Local Delivery Partners

DNA & multi-omics
Repository

Sequencing Centre
Wellcome Trust

Refreshable identifiable
Clinical Data
Life-course regi

Linked to anonymised
Whole Genome Sequence

Farr
Oxford Big Data

Primary Care
Hospital episodes
Cancer Registries
Rare Disease Registries
Infectious Disease
Mortality data
Patient entry

MRC Research Data Infrastructure (GeCIP)
Sequential builds of pseudonymised data and WGS
Safe haven- users work within

Annotation & QC
Scientists & SMEs
Product comparison

Fire wall
Patient data stays in safe haven

Only processed results pass outside

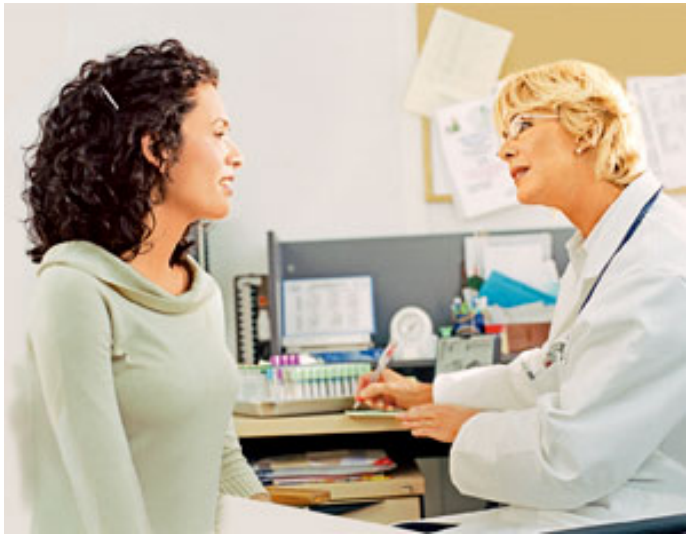
Clinicians & Academics

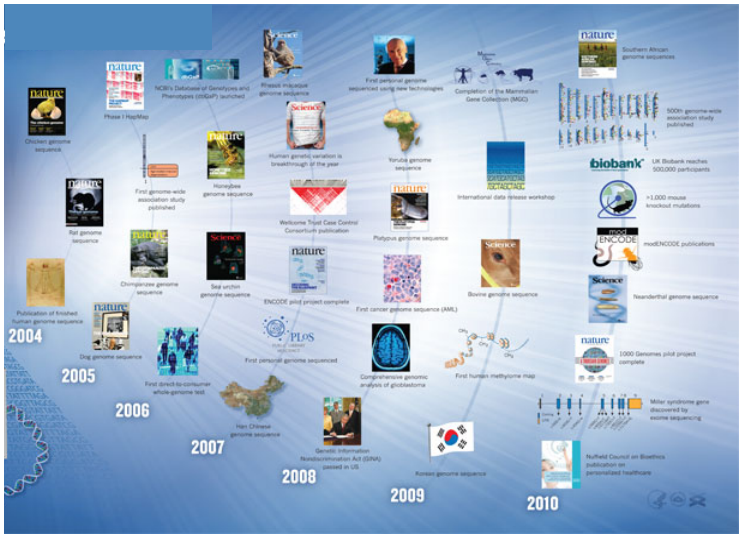
Training & capacity

Industry

Formalising clinical data collection has wider benefits

Capturing, analysing and sharing phenotypic information is hard





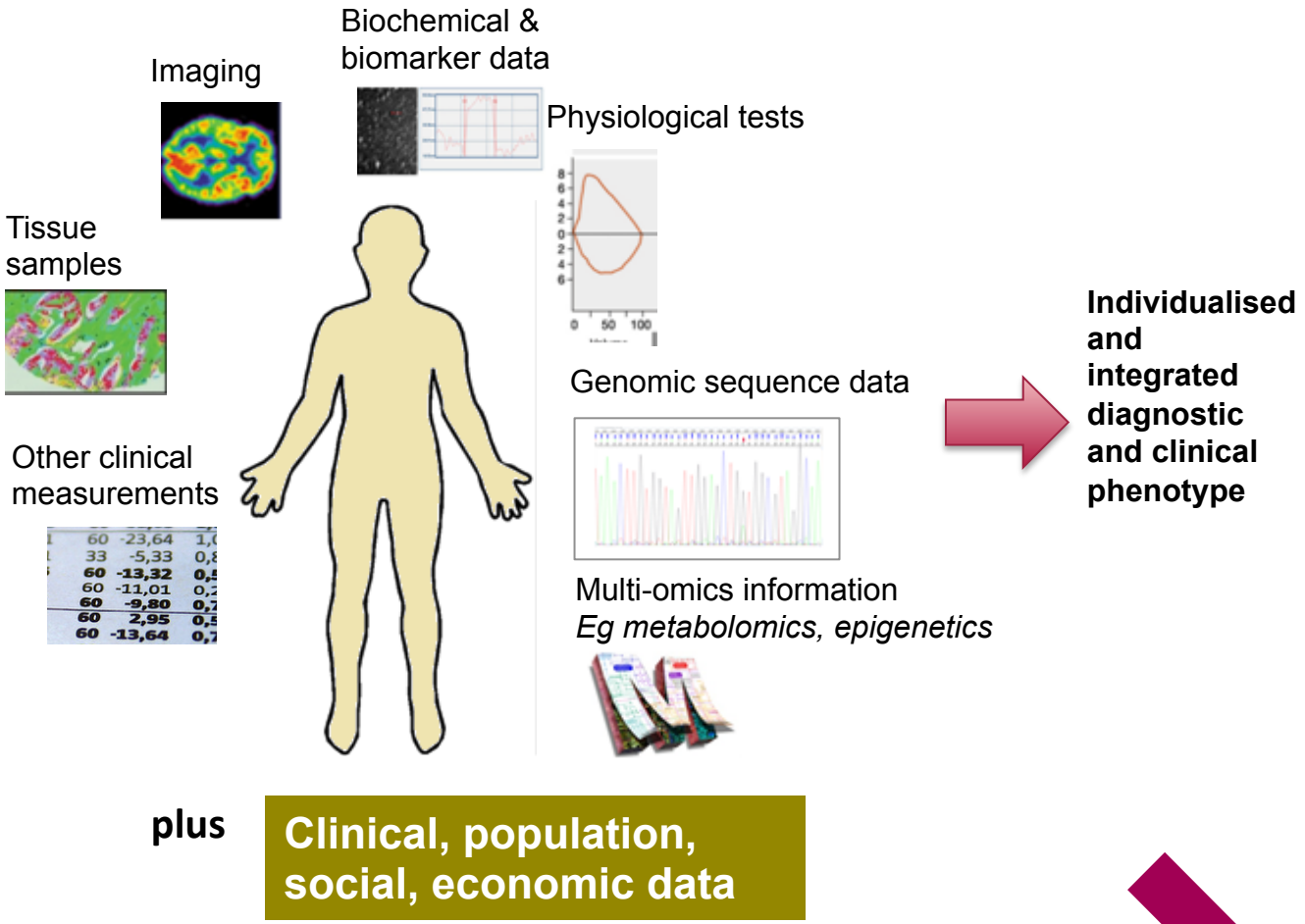
ED Green *et al. Nature* **470**, 204-213 (2011) doi: 10.1038/nature09764

Much harder to capture, analyse and share phenotypic as compared to genomic data: need to rethink the phenotype from the genotype; incorporate the things that patients and their families experience; wearable technologies

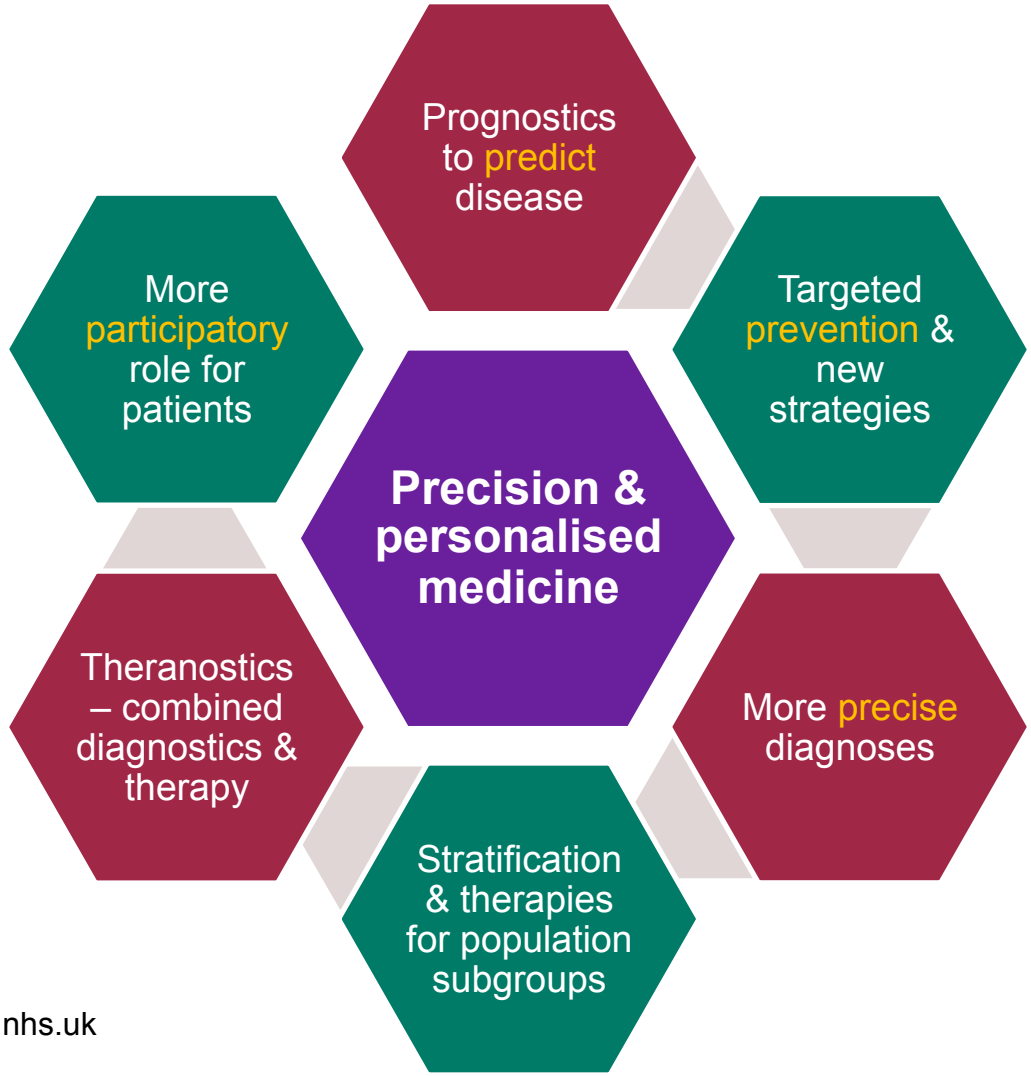
Data collection, combination and analysis

Data needs to be combined, analysed and correlated to enable decisions about precision targeting to be made

Opportunities for insight through machine learning, data mining and population-level analysis

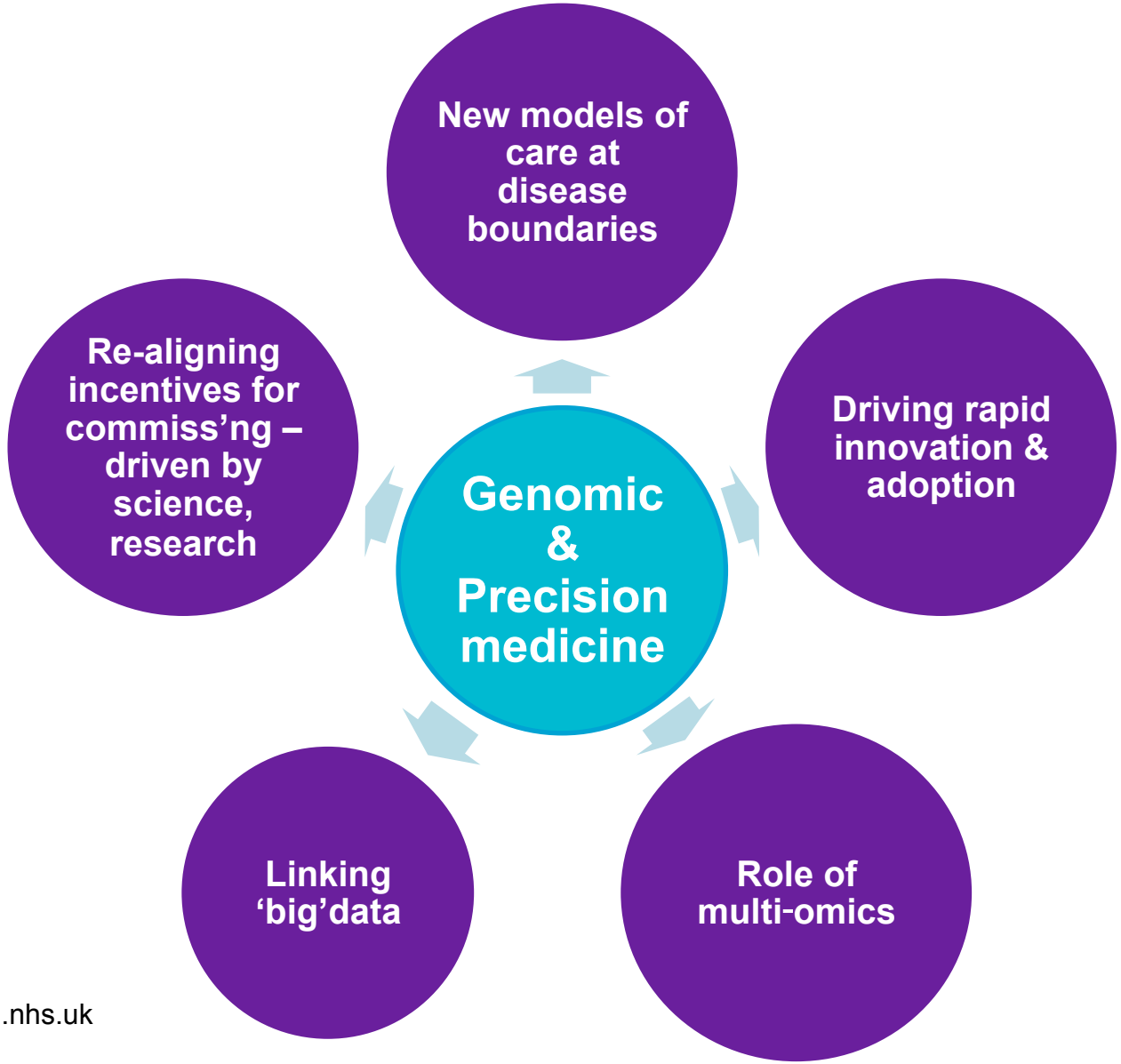


The future – personalised medicine

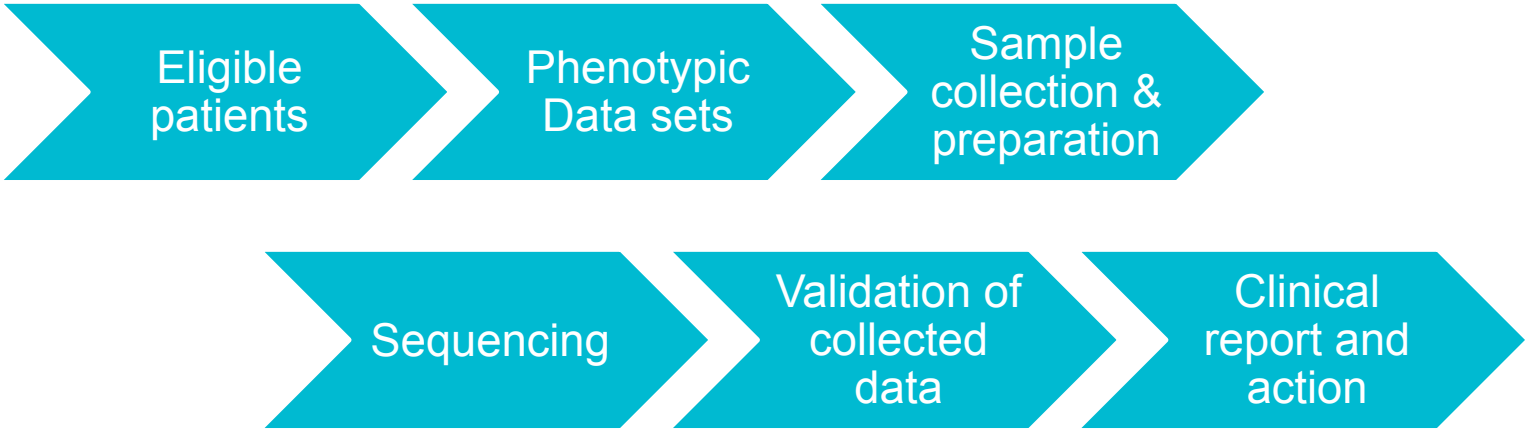


Highlighting the 4 P's of precision medicine

Genomic & Precision medicine – transforming clinical practice



The vision: what could it mean for the NHS?



Legacy requirements include

- High quality sample preparation and use of high throughput and novel genomic technologies
- Increased Bioinformatics capability
- Molecular Pathology capacity
- Richer phenotypic data linked to genetic abnormalities and markers
- Stronger link between clinical practice and applied genomics
- Standardisation of data and clinical practice

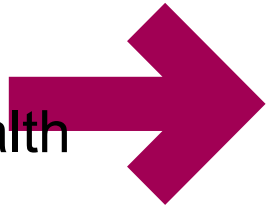
More than just technology – the role of medical & system leaders

Integrating medical technologies across the NHS:

- Building an understanding of the new taxonomy of disease coming from genomic understanding and its consequences for future healthcare
- Data context; development of better algorithms for variant calling; robust, scaleble, implementable
- Ensuring clinical leaders engage with and support the work of NHS GMCs
- Leading the development of new models of care in services and commissioning processes to integrate genomic & other precision medicine technologies (*eg molecular pathology*)
- Driving the development of knowledge, skills and experience across the service through engaging with the HEE Genomics Education Programme

After 2017?

- Entire population as the research cohort
- Rapid move through diagnosis to therapy – ICU
- Routine component of healthcare; everyone sequenced as norm; ADRs;
- From fixed genomics to temporal multi-omics
- International consortia of knowledge
- Researcher-clinician-patient-partnership in which knowledge goes into the knowledge base as well to diagnosis/treatment of individual patient
- Proof of costs/savings for healthcare systems
- From cottage industry to efficiency, safety at scale
- From crisis management to management of good health



Developing personalised medicine in the NHS: the 100,000 Genomes Project

Personalised Medicine Summit
Vancouver, 9 June 2015

Professor Sir Malcolm Grant
Chairman NHS England