The 100,000 Genomes Project

Cancer of Unknown Primary

Prof Mark Caulfield FMedSci

Chief Scientist

William Harvey Research Institute
Queen Mary University of London

Genomics England

- 100,000 whole genome sequences in NHS patients with rare inherited disease, cancers and pathogens from the NHS in England
- Whole Genome Sequencing
- Generate health and wealth
- Legacy of infrastructure, human capacity and capability

Cancer

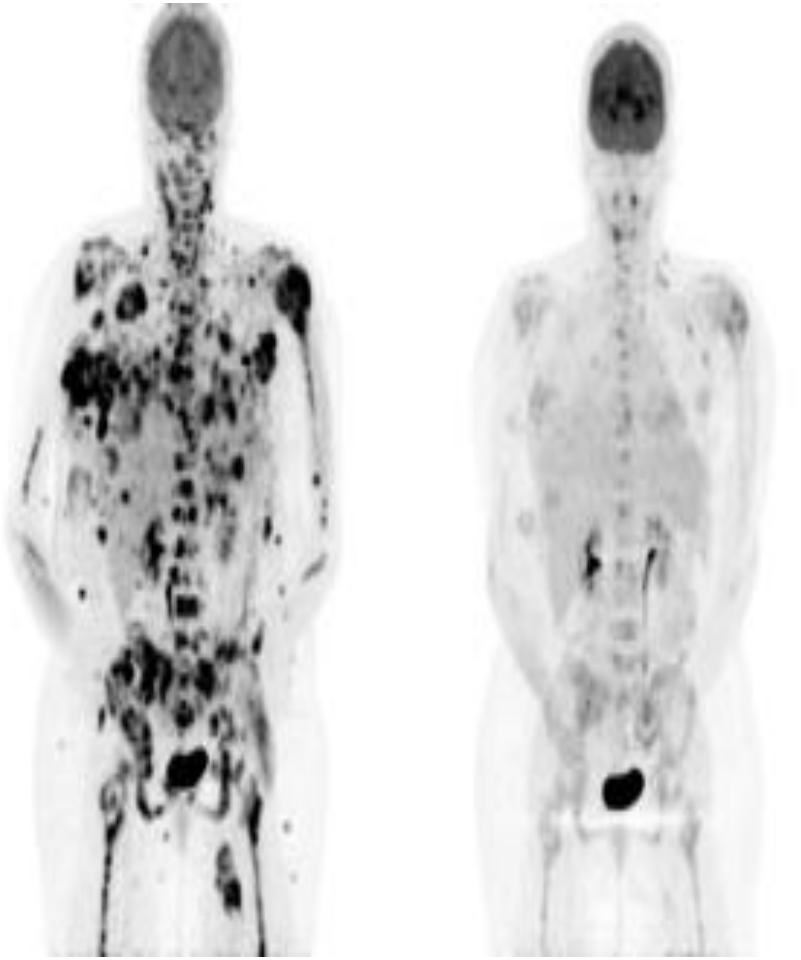
- Disease of disordered genomes – over 200 drivers known
- Drugs targets, Tumour heterogeneity, evolution of cancer, Stratified medicine

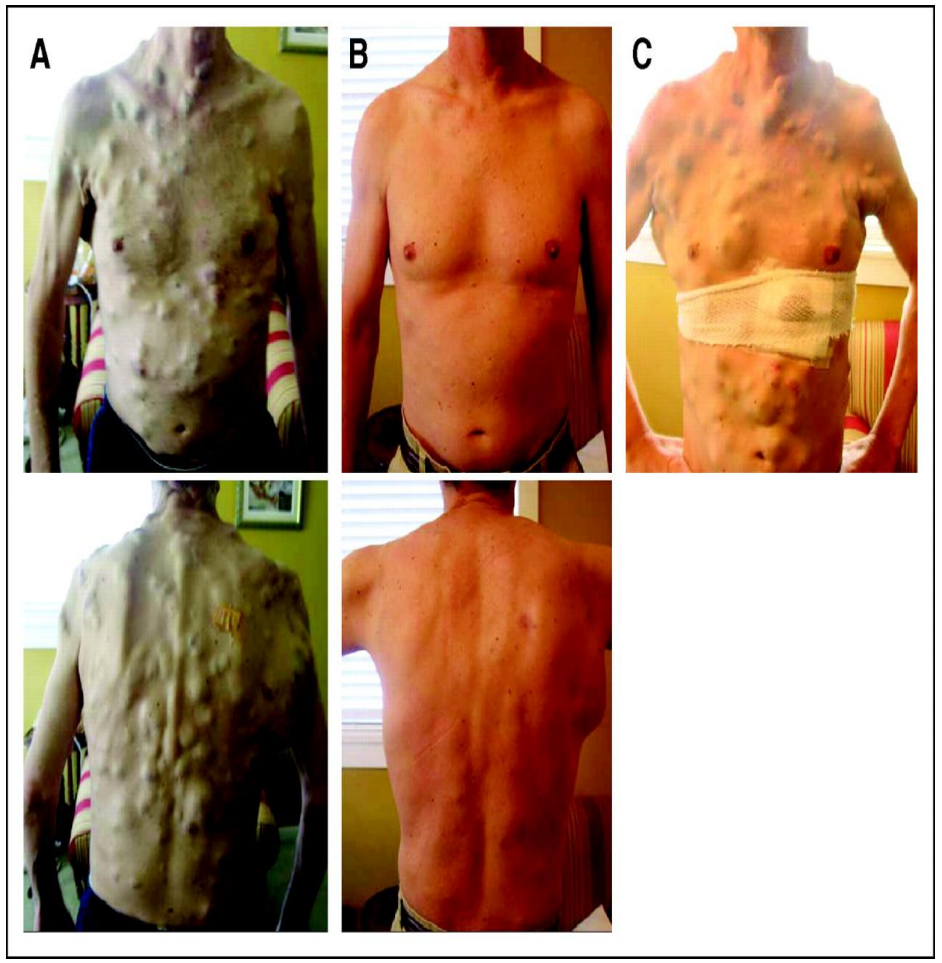
- Lung, breast, colon, prostate, ovary and, Leukaemia and
- Sarcoma and Renal
- Rare and Childhood Cancers, unknown primary

- Sequential biopsy of recurrent cancer
- Stratified medicine- Focus 4
- Optimise Molecular Pathology
- WGS at 75x somatic and 30x germline

- International Cancer Genomes Consortium- the Cancer Genome Atlas

BRAF inhibitors for Melanoma





Cancer – current plans

Tumour type	Allocation
Breast Cancer	2,000
Colorectal Cancer	2,000
Ovarian cancer	2,000
Lung Cancer	2,000
Prostate Cancer	2,000
Childhood solid	500
Renal	750
Sarcoma	500
Unknown Primary	250
Reserve	**10,500**

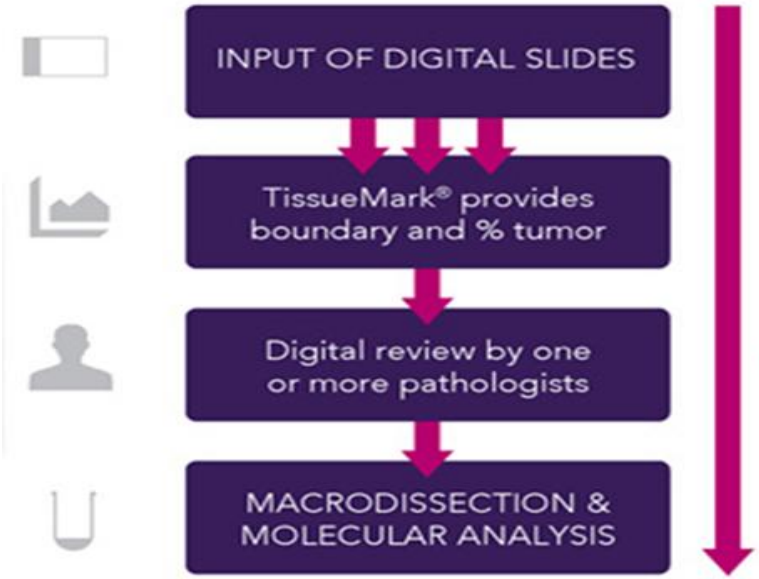
100,000 Genomes current thinking

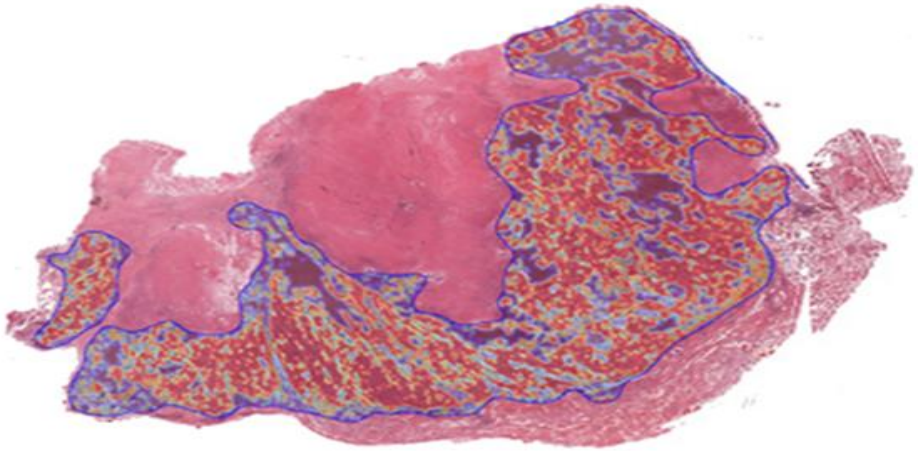
- 50,000 genomes on cancer
- 25,000 Tumour- Normal Pairs

Clinical Interpretation Partnership roles

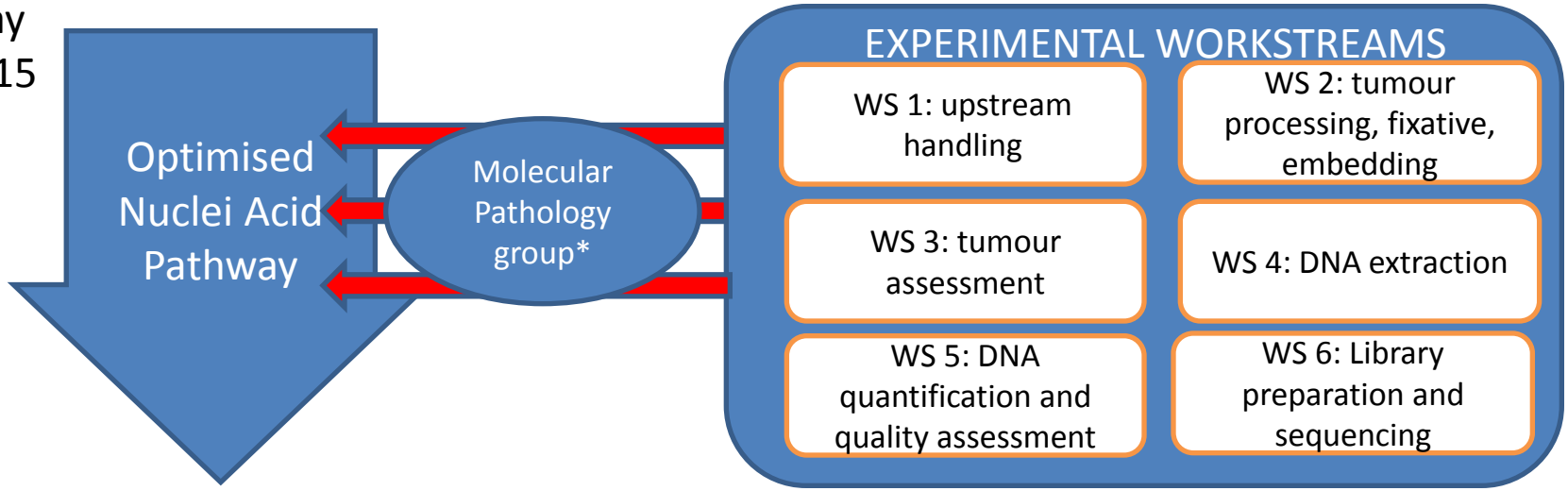
- Help set scientific priorities
- Focus on global-leading cancer programme
- Get additional WGS
- Stratified healthcare/ CFCT DNA
- Sequential and multiple biopsy
- Stimulate and support GMCs to enrol
- Organise yourselves to do research to drive up clinical interpretation

Cancer Programme- piloting molecular pathology





May 2015



September 2015

)Molecular pathology leads: Schuh, Verrill, Henderson, Flanagan, Gonzalez del Castro, Thomas

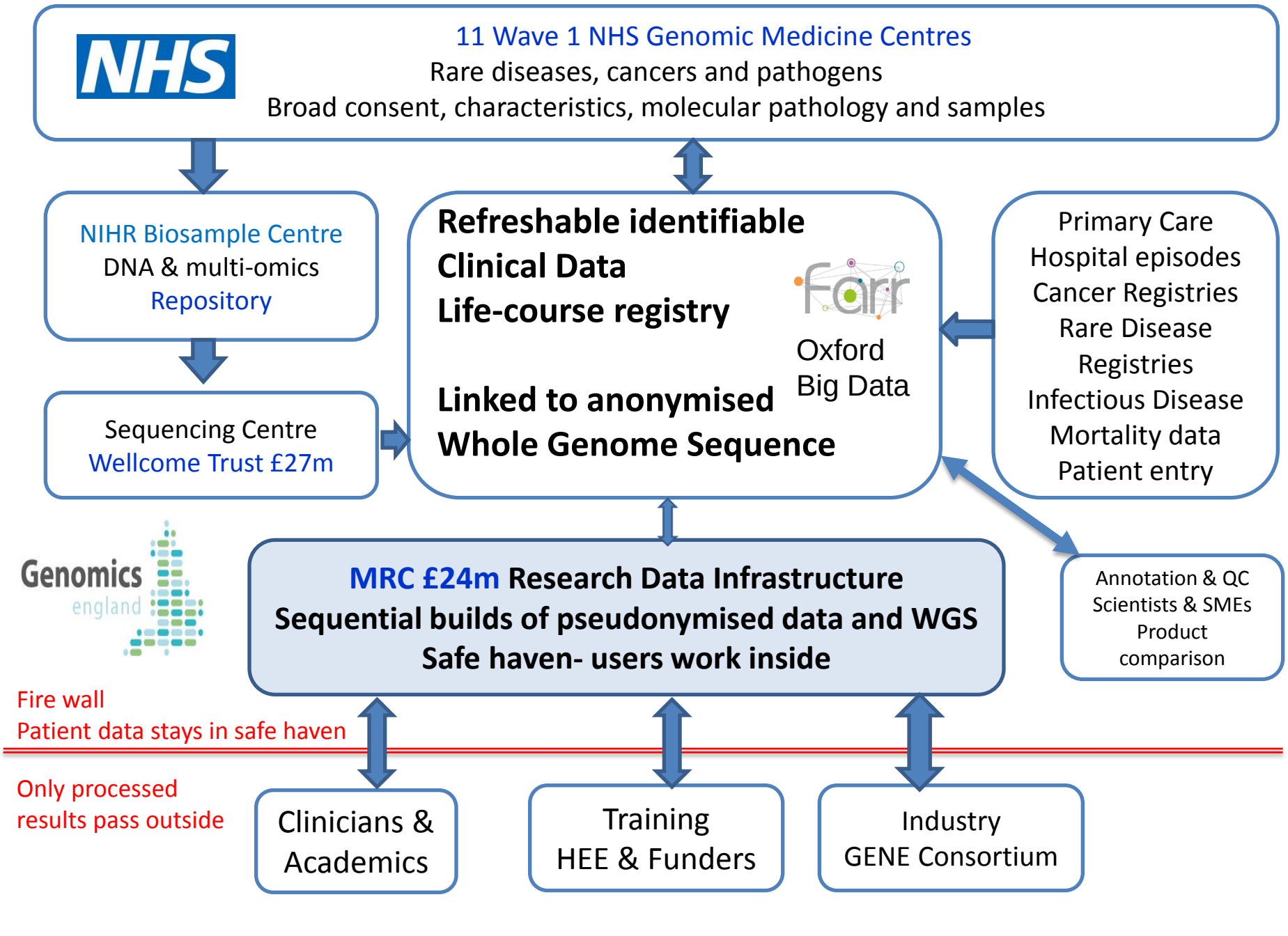
Implementing the programme

Ethics

- Ethics Advisory Group- Mike Parker
- Working toward an NHS Genomic Medicine Consent

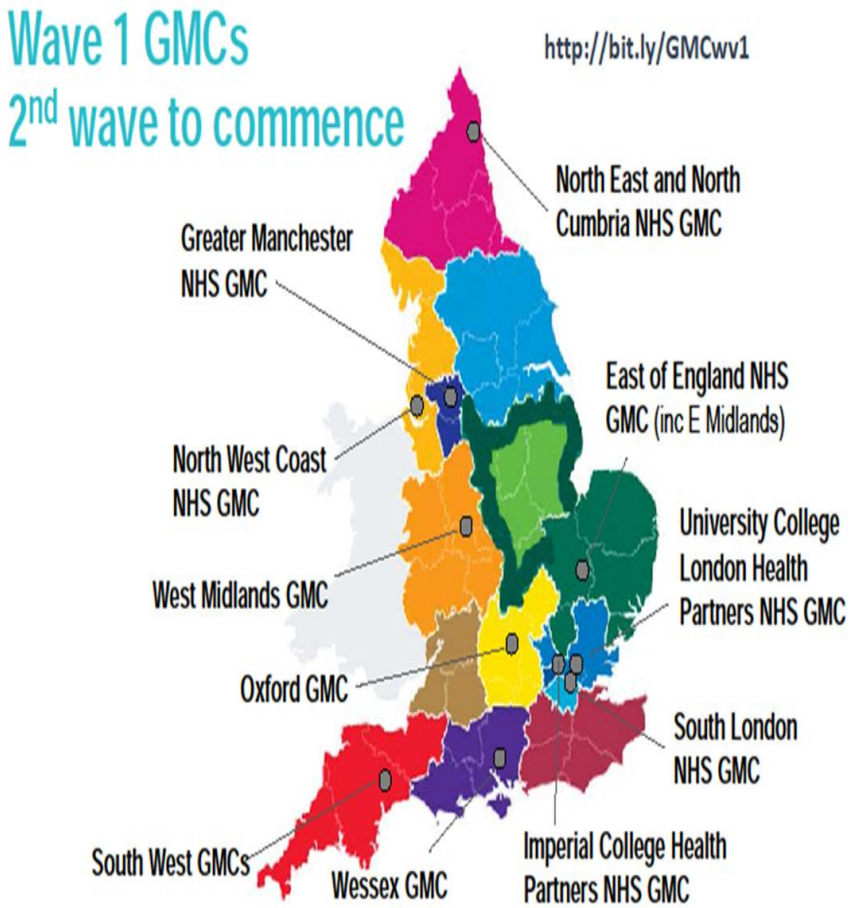
- Genomics England
- Life Course Refreshable Dataset
- Return of findings
- Release of data to third parties – academics, clinicians and industry
- Recall for research

Genomics England – The main programme



NHS England

11 NHS Genomic Medicine Centre
Awarded 20th December 2014

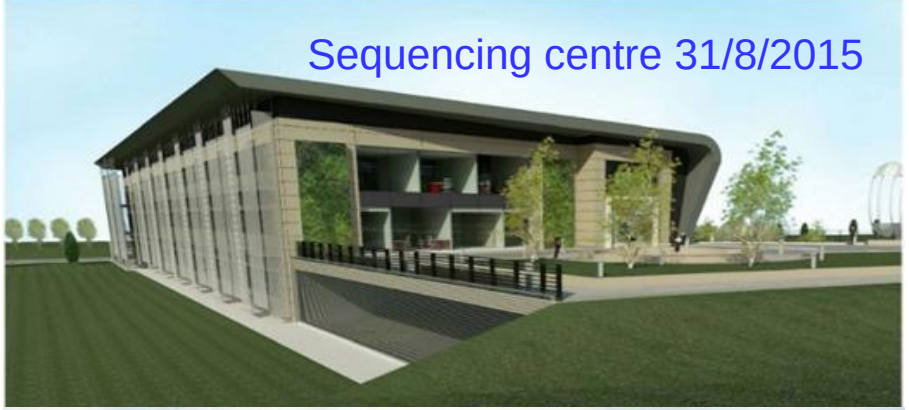


NHS GMCs working in partnership with academia, patients and industry through the AHSNs. Regional Genetics Labs and Clinical Genetics Services central to all GMCs

Contracted NHS GMC Lead Organisation working with Local Delivery Partners across the geographical footprint

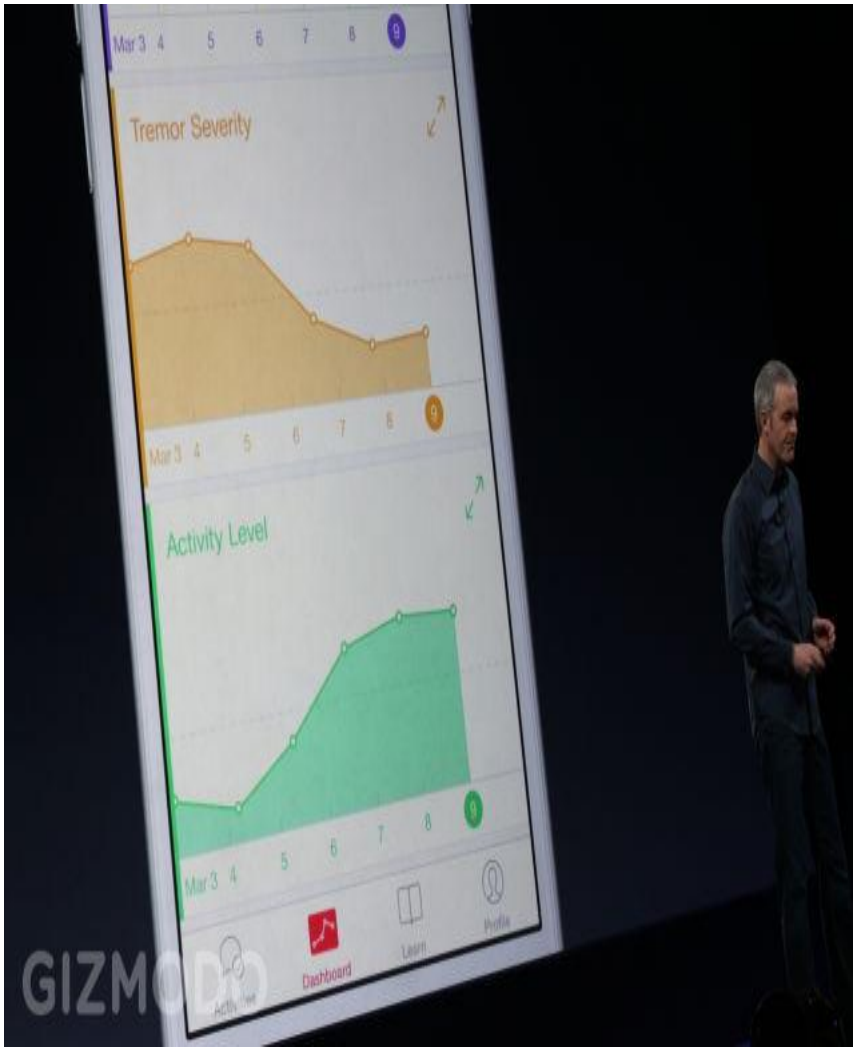
Biosample centre March 2015

Sequencing centre 31/8/2015



MRC funded Data Centre November 2014

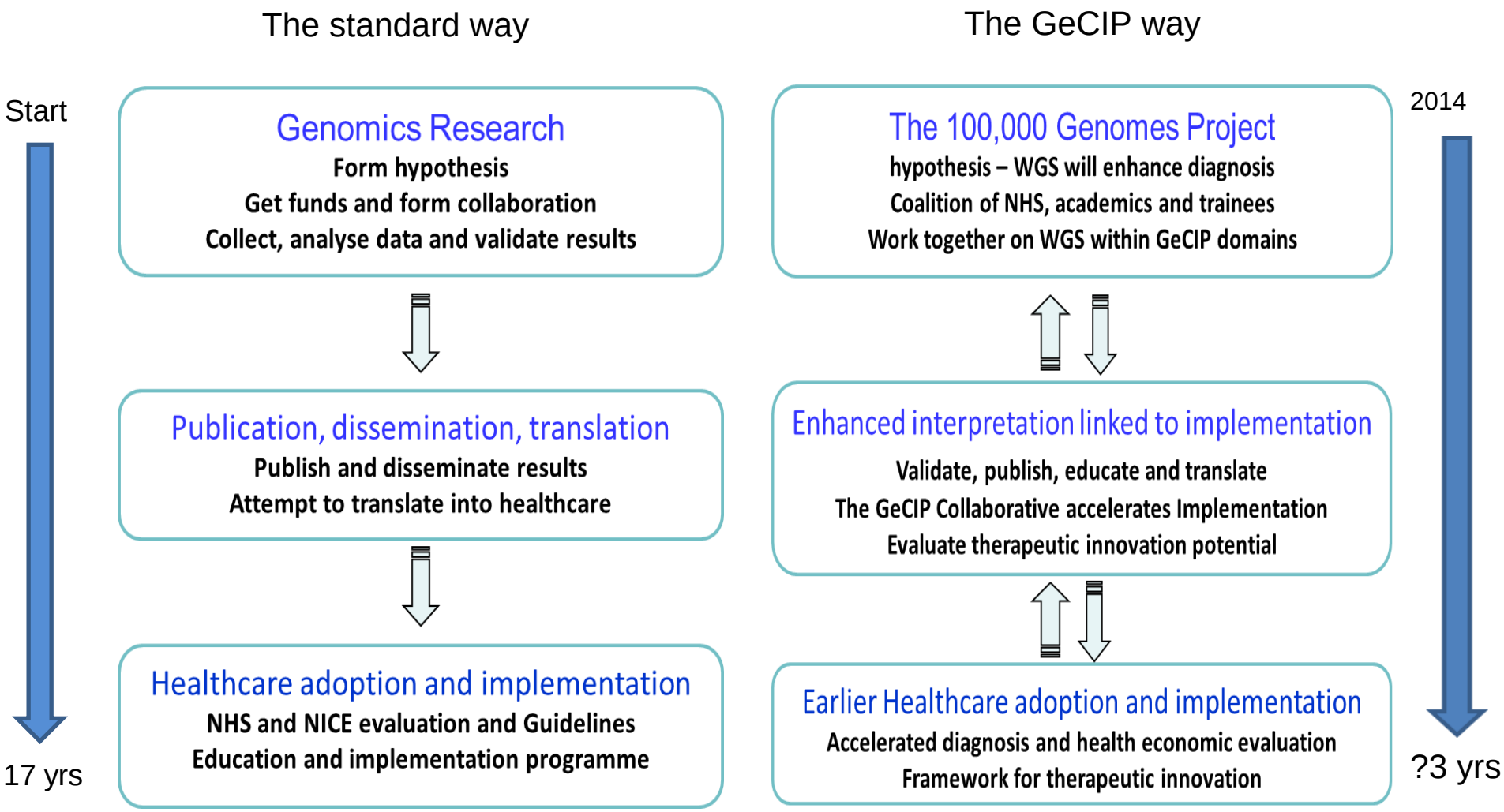
Apple ResearchKit



Opportunity for clinical trials inside the 100,000 Genomes Project

- Novel drug targets
- Combine sequence and Clinical Trials
- Test novel molecules for rare disease and Cancer
- Stratified Healthcare
- Enhanced patient enrolment
- Identify the right genotype and predictive biomarkers
- Identify important genetic predictors of adverse effects
- Adaptive designs

Why do we need a Clinical Interpretation Partnership?



Securing Patient Benefit

Genomics england

Final list of GeCIP restructured Domains		
Rare Disease	Cancer	Functional
Cardiovascular	Breast	Electronic Records
Endocrine and Metabolism	Colorectal	Validation and Feedback
Gastroenterology and Hepatology	Lung	Ethics and Social Science
Hearing and Sight	Ovarian	Functional Effects
Immunology and Haematology	Prostate	Health Economics
Inherited Cancer Predisposition	Childhood Solid Cancers	Machine Learning, Quantitative Methods and Functional Genomics
Musculoskeletal	Haematological Malignancy	Population Genomics
Neurological	Pan Cancer	Translational Research
Paediatric Sepsis		Functional Cross Cutting
Paediatrics	Renal	
Renal	Sarcoma	Stratified healthcare
Respiratory		
skin		

GENE Consortium

- 12 pharma/diagnostics/SMEs
- Precompetitive consortia
- Work together on 5000 WGS
- To shape data centre

- Larger consortia
- Individual company interactions

- AbbVie
- Alexion Pharmaceuticals
- AstraZeneca
- Biogen
- Dimension Therapeutics
- GSK
- Helomics
- Roche
- Takeda
- UCB*
- Berg
- Boehringer Ingelheim

Genomics england

International Partnership

- Global Alliance for Genomic Health
- Veterans Administration
  - Large cohort (1M), contract let for 5000 WGS
- US Integrated Healthcare Systems
  - Scripps – Wellderly Study sequenced 2000 volunteers to study lifestyle
  - Inova Health – aims to provide worlds largest WGS database, 1500 completed thus far
- Clinical Research programmes
  - Oxford 500 WGS, DDD (Sanger) up to 12,000 children (mainly exomes)
  - International Cancer Genome Consortium
  - Seattle – 100K WGS –Lee Hood
  - Garvan Institute
  - Genome Canada/British Columbia
  - UPenn - Prenatal
  - St Jude and the Moffit Cancer Centres
  - Middle Eastern programmes in Saudi, Abu Dhabi and Quatar
  - Chan Shoon-Shiong Foundation
  - Personal Genome Project – aims for 100k, all open data

Genomics england

Genomics England- the future

- 100,000 WGS on NHS patients and pathogens
- WGS deployed routinely- also in other diseases
- Harnessing electronic health records
- Patient reported outcomes and more remote monitoring
- New diagnostics and therapies and opportunities for patients
- By end of 2017

NHS England

Public Health England

NHS National Institute for Health Research

CANCER RESEARCH UK

Genomics England – who are we?

- **Officers:** Sir John Chisholm (Executive Chair)
- Mark Caulfield (Chief Scientist), Nick Maltby (Company Secretary), Jim Davies (Informatics), Viv Parry (Outreach), Graham Colbert (COO)
- **Board:** Prof Dame Sally Davies (CMO), Kevin Dean (Cisco), Prof Sir John Bell, Jon Symonds (Audit), Prof Sir Malcom Grant (NHSE)
- **Advisory Committees:**
- Science: Sir John Bell, IT: Kevin Dean and Ethics: Mike Parker

Team members

- **Science-** Tom Fowler, Jeanna Mahon-Pearson, Laura Riley, Nora Wong, Andrew Devereaux, Suzanne Wood, Ellen Thomas, Mina Ryten, Clare Turnbull.

- **Informatics -** Jim Davies, Tim Hubbard, Augusto Rendon, Matthew Parker, Katherine Smith, Ellie McDonagh, David Brown

NHS National Institute for Health Research

MRC Medical Research Council

wellcome trust

CANCER RESEARCH UK

Thanks

Cambridge, UCLH, GOSH, Moorfields, Newcastle, Manchester, Guys and St Thomas's, Oxford, Liverpool, Sheffield, Leeds, Birmingham, Royal Marsden, Southampton, UK CLL Consortium, CRUK, RCPath, NHSE, DoH, Biobank UK, Sanger, EBI, KCL, UCL and QMUL