100,000 Genomes & Genomics England

Tim Hubbard
Genomics England
King's College London, King's Health Partners
Wellcome Trust Sanger Institute

Global Leaders in Genomic Medicine
Washington 8-9th January 2014

UK Health System 101

- Four separate health services
  - NHS England
  - NHS Wales
  - NHS Scotland
  - Health & Social Care in Northern Ireland (HSC)
- NHS (England)
  - ~1.4 million employees
  - ~£110 billion annual budget
- Structure in England changed 1st April 2013

https://www.gov.uk/government/organisations/department-of-health

GOV.UK

Search

Inside Government

How government works | Get involved | Departments | Worldwide | Topics
Announcements | Consultations | Policies | Publications | Statistics

Department of Health

- Dementia challenge
- A paperless NHS
- Compassionate care
- Reducing avoidable deaths

15 May 2013 — News story

Report marks progress in first year of Dementia Challenge

The Dementia Challenge champion groups have produced a report on their progress since the challenge was launched in March 2012.

26 March 2013 — Guidance

The Health and Care System Explained

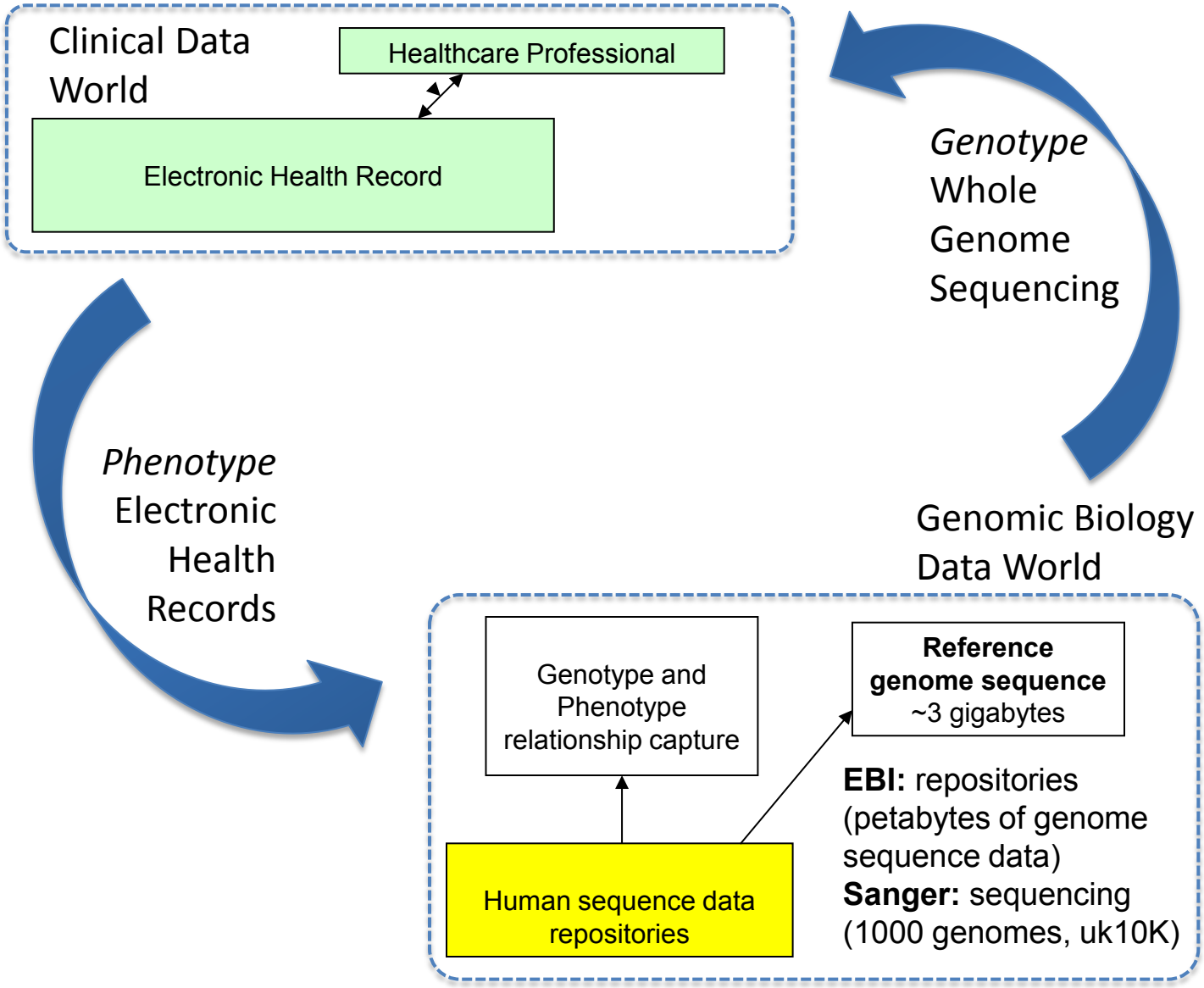
The health and care system helps people lead healthier lives, recover well from illness and live better for longer.

14 May 2013 — News story

National partners make commitment to join up health and social care

Care and Support Minister Norman Lamb has launched plans to join up health and social care.

Linking Health data to Research



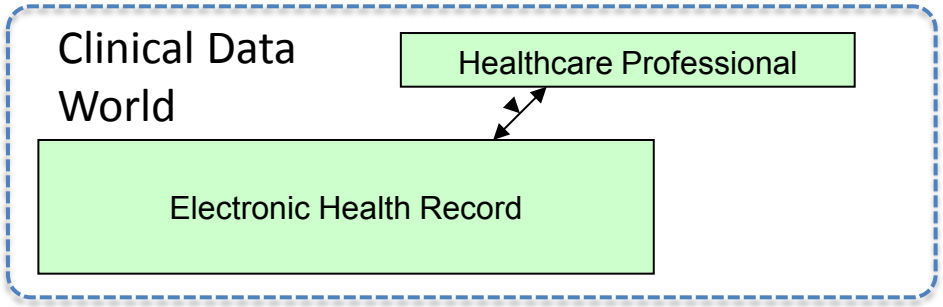
Steps in UK towards E-Health Research, Genomic Medicine

- Health data to Research
  - 2006 Creation of OSCHR
    - Increase coordination between funders: MRC and NIHR
  - 2007 OSCHR E-health board
    - Enable research access to UK EHR data
    - Build capacity for research on EHR data
- Genomics to Health
  - 2009 House of Lords report on Genomic Medicine
  - 2010 Creation of Human Genomic Strategy Group (HGSG)

2011: UK Life Sciences Strategy

No10: http://www.number10.gov.uk/news/uk-life-sciences-get-government-cash-boost/
BIS/DH: http://www.dh.gov.uk/health/2011/12/nhs-adopting-innovation/

Linking Health data to Research

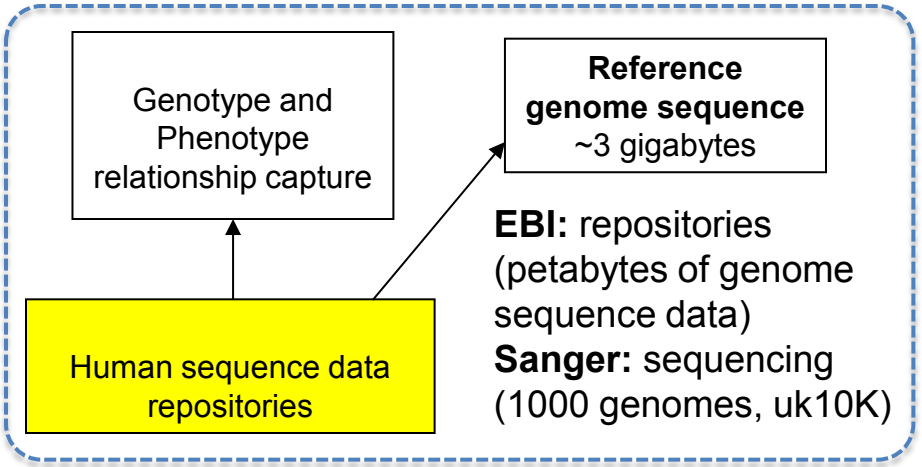


Clinical Practice Research Datalink (CRPD)

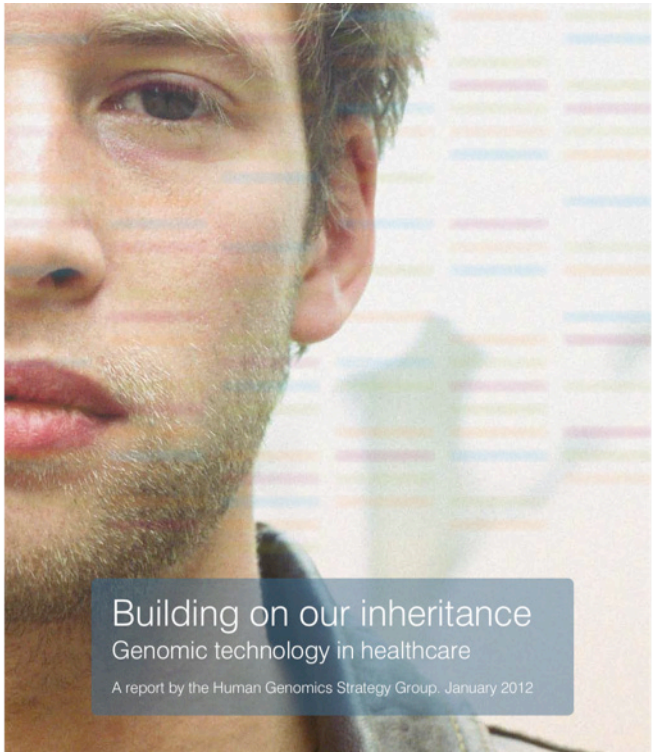
Phenotype Electronic Health Records

Farr Institute

Genomic Biology Data World



2012: Human Genome Strategy Group report
UK Life Science Strategy Update; 100K Genomes



DH: http://www.dh.gov.uk/health/2012/01/genomics/
BIS: http://www.gov.uk/office-for-life-sciences/

Genomics England

Genomics england

Home | About the 100K Genome Project | About us | How we work | News | Contact us

Home > Archive by Category "News"

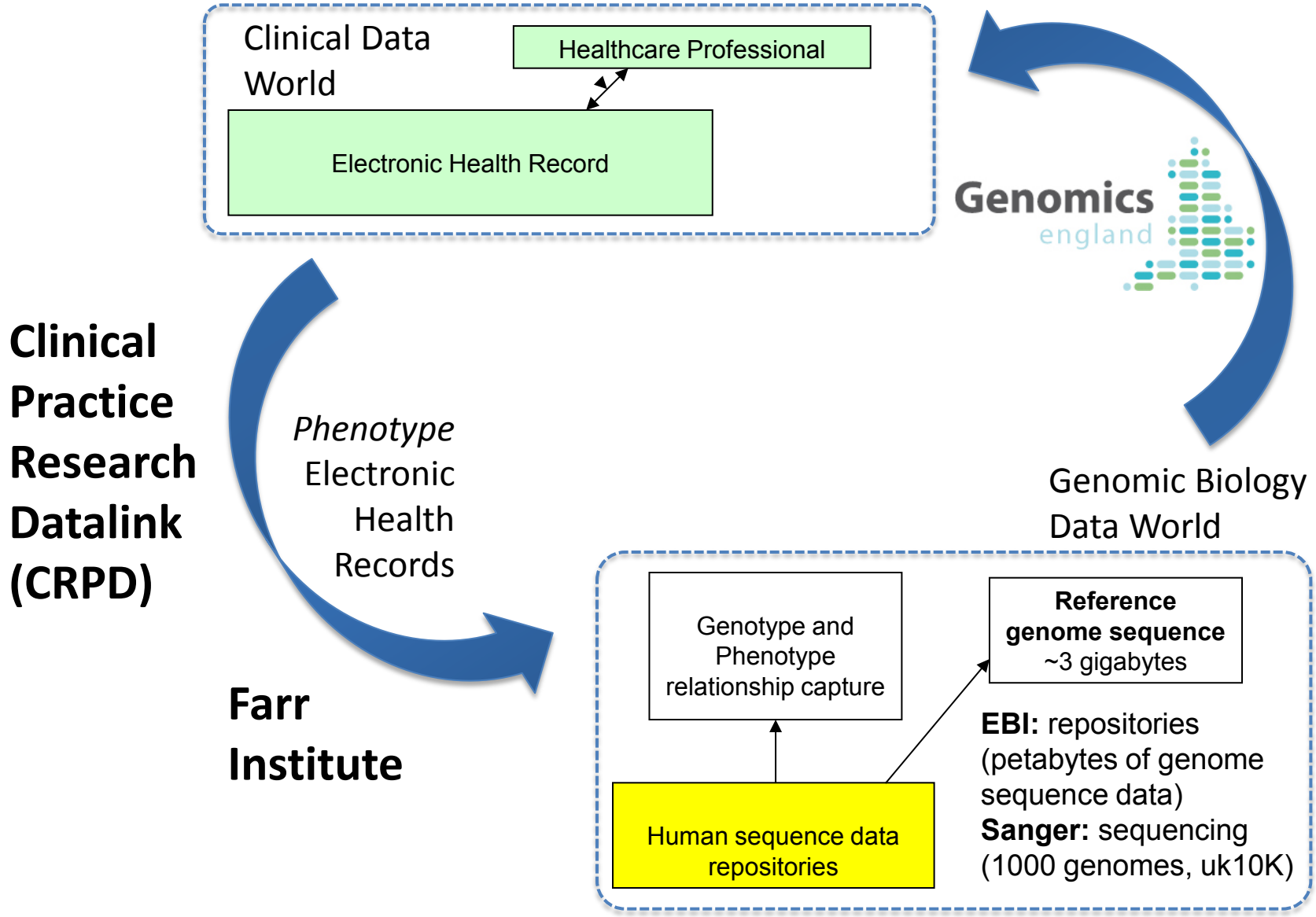
JUL
5

Genomics England launched, mapping DNA to better understand cancer, rare and infectious diseases

http://www.genomicsengland.co.uk/

@genomicsengland

Linking Health data to Research



Genomics England- mission

- 100,000 patients with rare inherited disease, common cancers and pathogens from the NHS in England
- Whole Genome Sequencing
- Generate improved health and wealth for UK
- Legacy of infrastructure, human capacity and capability
- Become World-leader in Healthcare application of Genomic Medicine
- £100m funding over the next 5 years

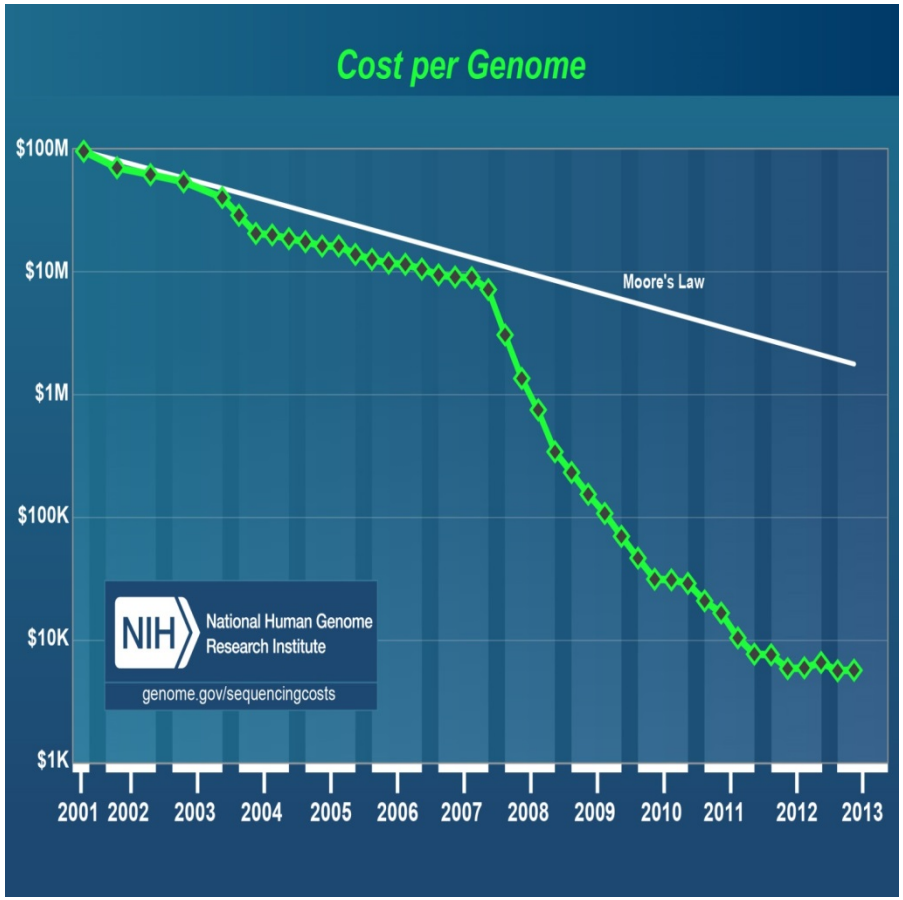
Genomics england

Scale compared to existing WGS

- 1000 genomes and UK10K
  - low coverage genomes (~4x illumina)
- Limited number of ‘clinical grade’ WGS
  - TCGA: ~700
  - ICGC: ~700
  - WGS 500: 500

Genomics england

Is now the moment to commit to WGS



Data Type	Large-scale structural changes	Balanced translocations	Distant consanguinity	Uniparental disomy	Novel/known coding variants	Novel/known non-coding variants
Targeted gene sequencing	⊗	⊗	⊗	⊗	☑	⊗
SNP arraya	☑	⊗	⊗	☑	☑	⊗
Array CGH	☑	⊗	⊗	⊗	⊗	⊗
Exome	☑	⊗	⊗☑	⊗☑	☑	⊗
Whole Genome	☑	☑	☑	☑	☑	☑

Genomics england

Rare inherited diseases

- 7% of the population or about 5/10,000 people
- 7000 rare disorders- disabling, shorten life, costly
- Circa 85% have a single gene defect
- Early knowledge may avoid disability
- Testing for >700 disorders extant within the NHS diagnostic laboratory network (UKGTN)
- Represents <1/4 of known disease genes.
- Whole Genome Sequencing 25-50% increase in discovery

Genomics england

Genomics England
Will look for mutual wins

- NIHR Translational Research Collaborative
- NHS Clinical Genetics Service & Organ Based Specialists
- WGS500 - Oxford
- International Rare Diseases Consortium
  - Aiming for 200 new treatments
- Deciphering Developmental Disorders (Exome)

- Link to trial opportunities for new therapies
- Increased recognition from industry of the value of niche markets

Genomics england

Cancer

- Lung Cancer -40 000 cases/year in the UK, (35K die/year)
- Largest cause of cancer death, therapies modestly effective only applicable to 10-15% of patients
- CRUK Stratified Medicine's initiative

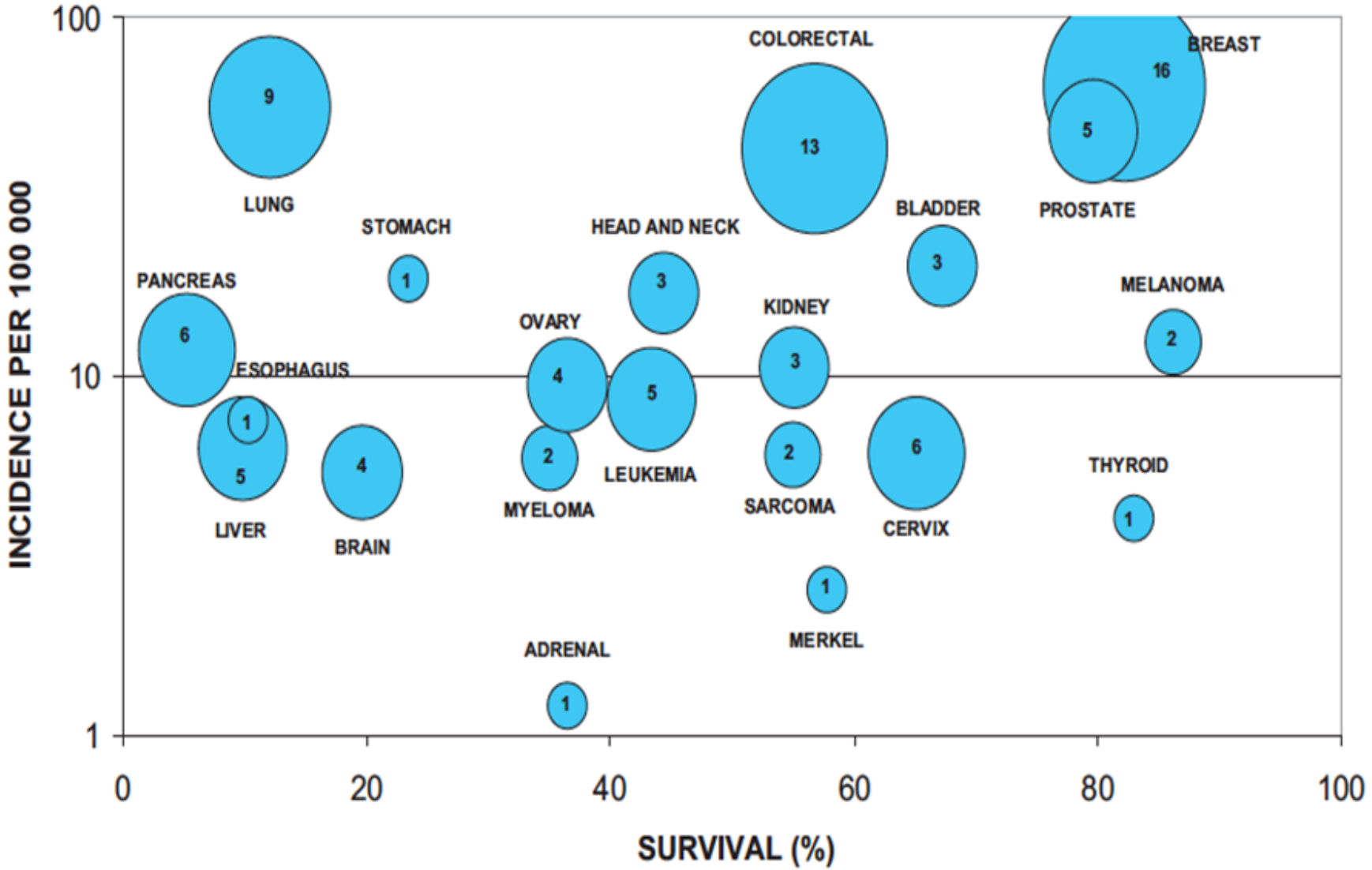
- Other Cancers - Breast, colon, prostate and unknown primary

- Rare and Childhood Cancers

- Drugs target mutations
- Tumour heterogeneity

Genomics england

Incidence v survival at 5 years

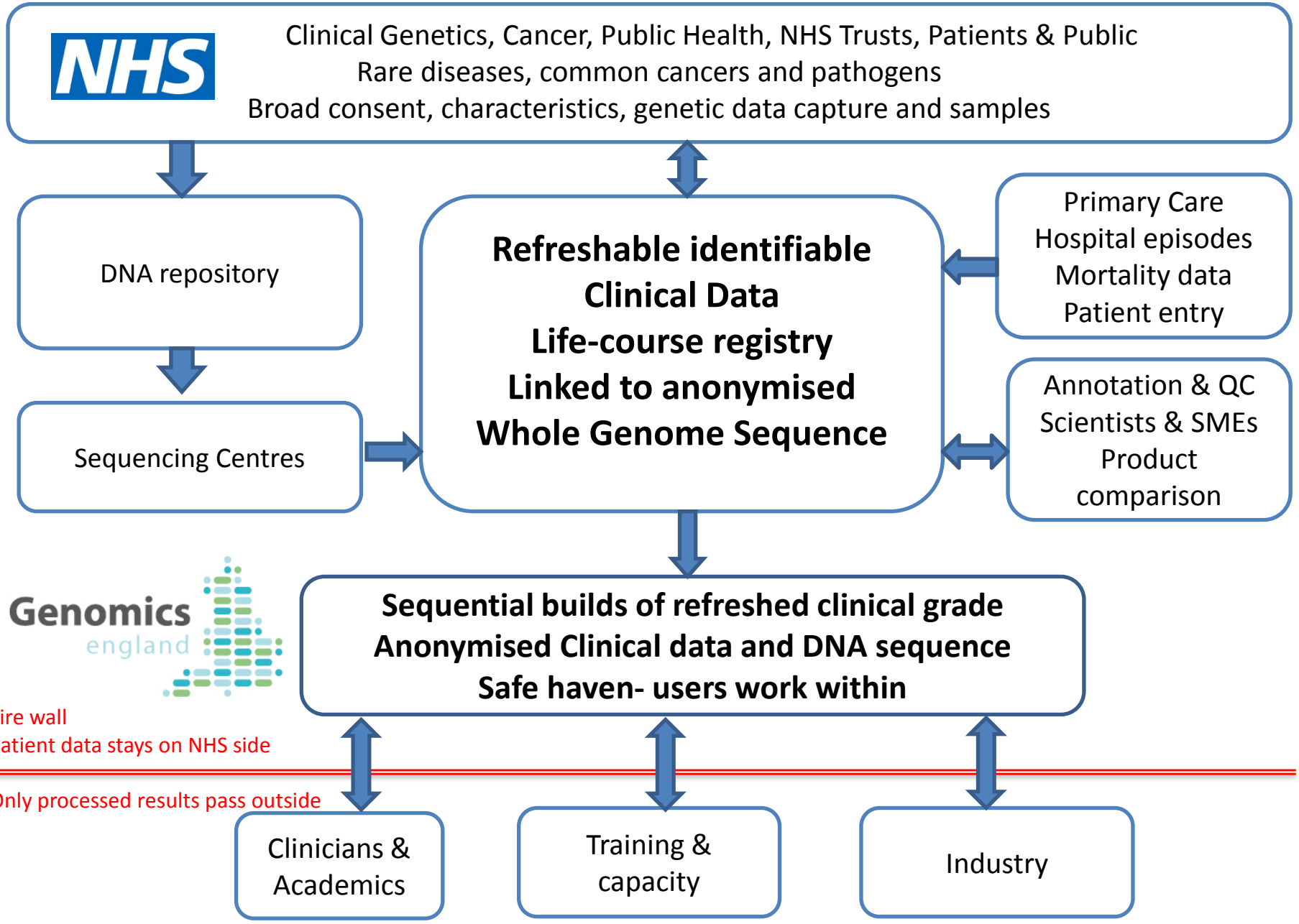


Pathogens

- Stratifying response, minimising adverse events and tracking outbreaks
- HIV –Treatment for life and resistance testing is in the care pathway.
- Hepatitis C genotype selects therapy
- M. Tuberculosis resistance and epidemiology

Genomics england

Genomics England – Operational Plan

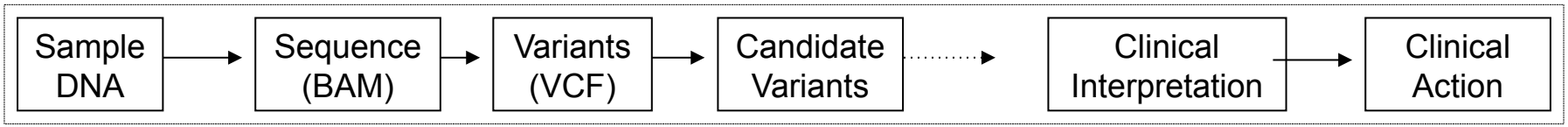


Genomics England – Implementation Plan

- Phase 1: bake-offs
  - Sequencing comparison underway
  - Annotation comparison to follow
- Phase 2: Pilots
  - 2000 Rare Inherited Disease WGS- 30x depth –January 2014
  - 3000 Cancer Patients (Lung, Breast & Colon)
  - Each 1000 somatic (50x) and 1000 germline (30x) – tender imminent
  - Pathogens pilot will be planned with Public Health England
- Phase 3: Main study
  - 30,000 WGS per year
- Education
  - Developing a National Programme to transform capacity and capability
  - UK Universities and Medical Schools

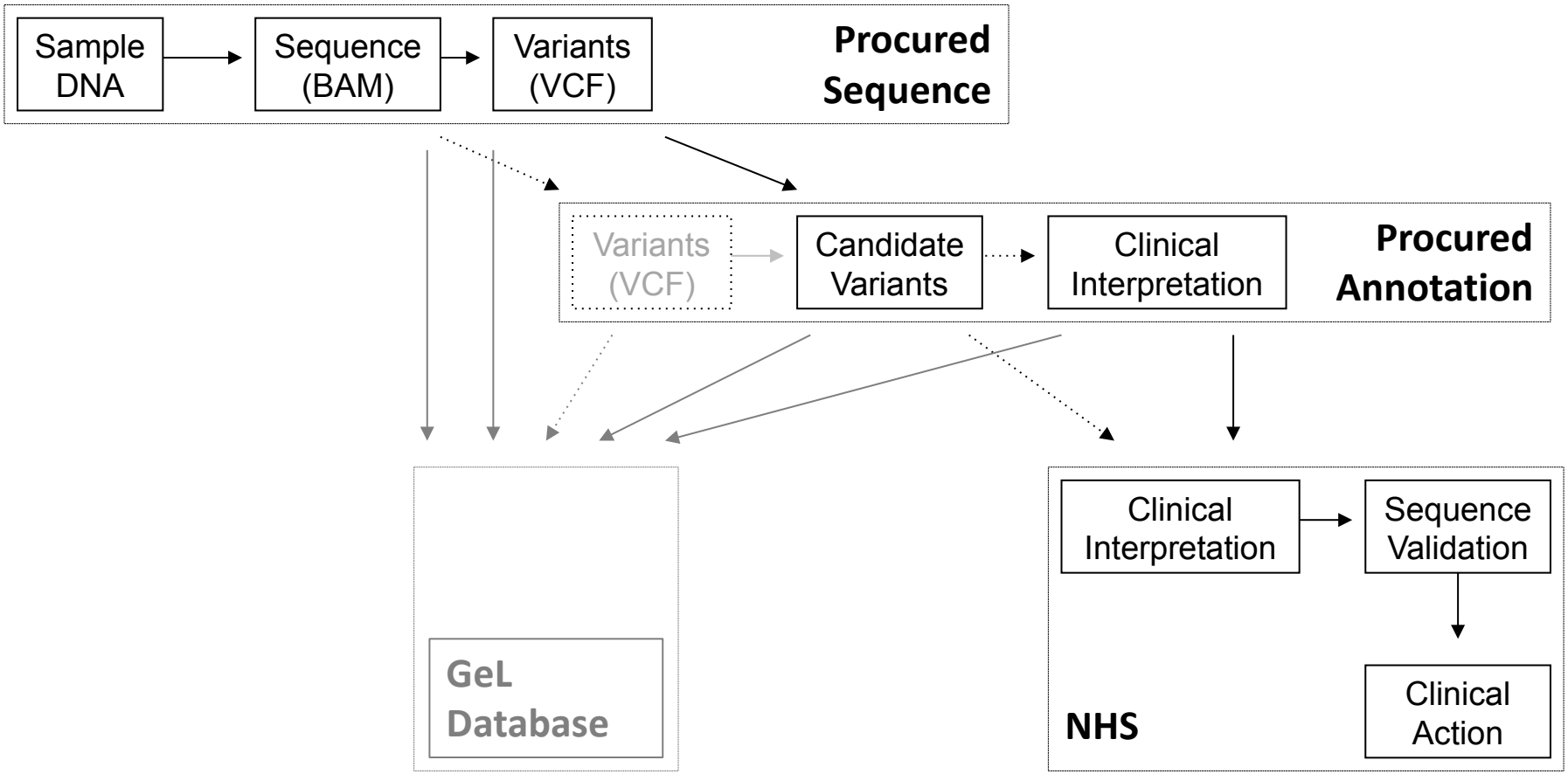
Genomics england

Process Overview

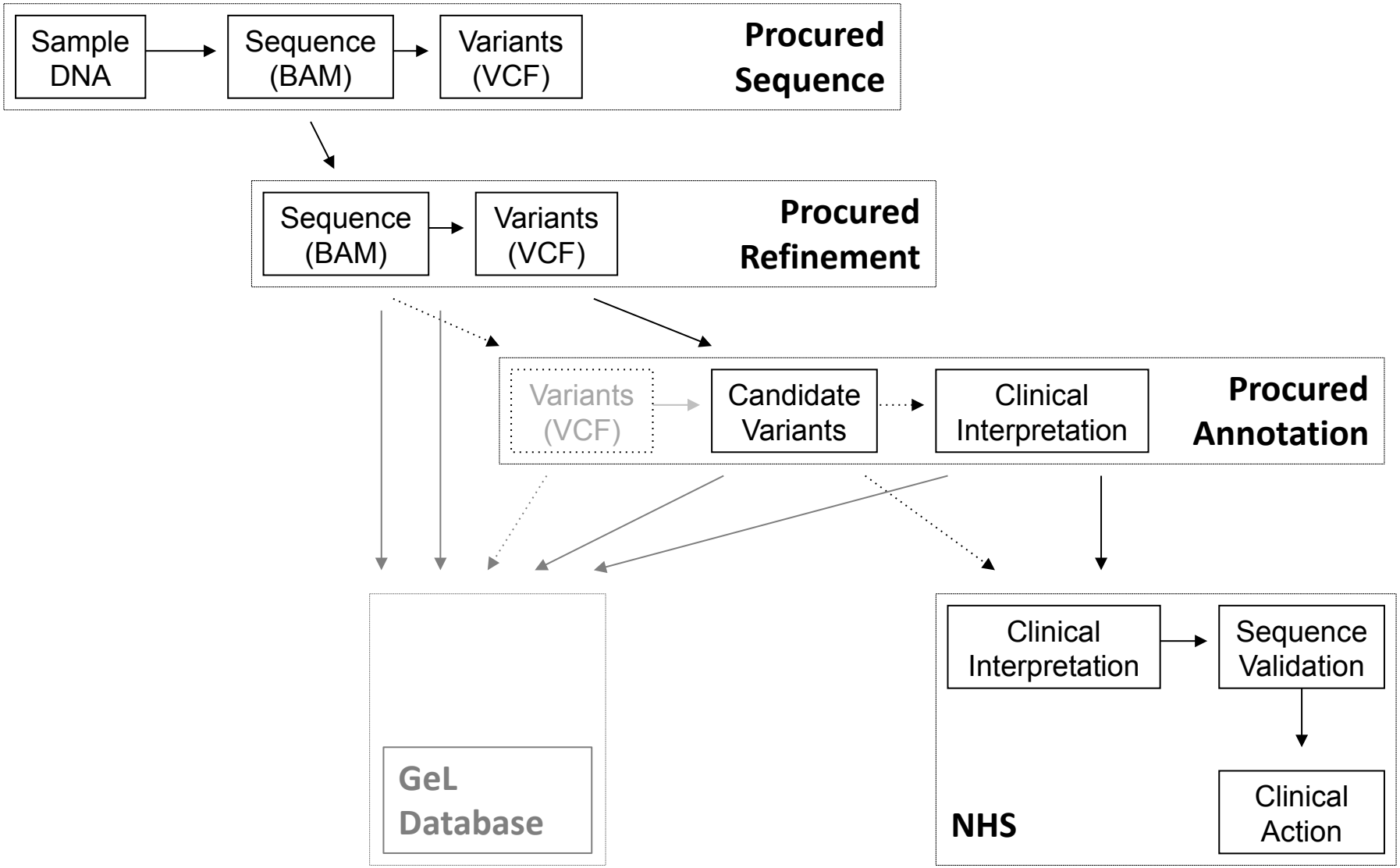


Genomics england

Process Overview



Genomics england



Genomics england

Sequencing assessment

- Bake off in progress – samples with suppliers
- Evaluation will be on quality and coverage

Genomics england

Annotation assessment

- Harder than assessing sequencing
- Gold standard less well defined
- Lack of established data standards

Genomics england

Past assessment exercises

- CASP – Critical Assessment of Structure Prediction (since 1994, CASP11 in 2014)
- GASP, RGASP – Gene prediction and RNAseq assessments

- CLARITY Challenge – 2012
  - http://genes.childrenshospital.org/
- CAGI – 2010, 2011, 2013
  - https://genomeinterpretation.org/

Genomics england

Data provided by GeL

- Sequence from providers (BAM+VCF)
  - Rare diseases: trio
  - Cancer: germline + tumour
- Phenotype data available to clinicians

Genomics england

Types of annotation anticipated

- Filtered, ranked lists of variants with estimates of pathogenicity and confidence
- Expected impact at level of genes, pathway
- Tools organising literature around affected genes, pathways
- Clear, simple clinical reports
- Suggested clinical interventions

Genomics england

Assessment criteria

- Accuracy
- Clinically informative
- Rapid turnaround
- Understandable output
- Standardised output data formats
- Ability to operate at scale
  - 2014: ~25 samples/day (pilot)
  - 2015: ~50 samples/day
  - 2017: ~100 samples/day

Genomics england

Initial annotation assessment

- Information collection exercise on 15 samples
  - Investigate levels of annotation available
- Minimal file format requirements
  - Will inform future specifications for file formats

- Will select multiple suppliers for pilot
  - Ability to deliver timely, consistent data, etc.

Genomics england

Ongoing assessment during Phase 2

- Precise file format requirements, with optional sections

- Best suppliers will be invited to tender to provide annotation for main programme (2015-2017)

Genomics england

Annotation expectations for Phase 3

- Software will run as Virtual Machines within GeL datacentre, c.f. Apps
- Software will be subject to evolving compliance requirements, c.f. CLIA dry lab

- No need for 'Apps' to be comprehensive: potential for specialist software, e.g. specific diseases, pharmacogenomics etc.

Genomics england

Genomics England

- 100,000 WGS on NHS patients and pathogens
- Aware of the challenges
- Working with NHS, academics and industry to drive Genomic Medicine into the NHS
- Support that with education
- Leave a legacy of NGS Centres, sample pipeline and biorepository, large-scale data store that makes this usable by the NHS
- New diagnostics and therapies and opportunities for patients
- By end of 2017

NHS England

Public Health England

Acknowledgements

Genomics England
NHS England Genome Strategy Board
Department of Health Human Genome Strategy Group

Wellcome Trust Sanger Institute
Discussions with many at Wellcome Trust, OSCHR, NIH, ENCODE