

2018 Bio Future Forum

The 100,000 Genomes Project – realising the potential of population data

November 2018

Sir John Chisholm, Chair, Genomics England

UK Commitment to Genomics is long and deep



Francis Crick and James Watson first discover the double helix structure of DNA in 1953.

First draft of the human genome announced by President Clinton and PM Blair in 2000. The Sanger Centre in the UK was alone responsible for 30% of that draft.



In 2006 the MRC and the Wellcome Trust announced the creation of a cohort of 500,000 well people aged between 45 and 60 years, called UK Biobank. Deep data has been collected including medical incidents, primary records, images, and genotypes.

In 2017 it was announced that these would be extended to whole genomes.

In 2012 PM Cameron announced that the UK would be the first country to use routine health records to link with 100,000 whole genomes.

A company, Genomics England, was created to manage the 100,000 Genomes Project.



Genomics England's Mission

I was tasked by the Prime Minister to:



1. Create the infrastructure to introduce genomic medicine to the NHS

2. Build a genomic/clinical dataset capable of enabling important health discoveries

3. Accelerate commercial investment in the genomics industry in the UK

4. Carry public support

Genomics England's Mission



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1. Carry Public Support

Put patients at the centre

This is all about patients and participants having the confidence to knowingly and willingly offer their data



1. **Consent** must be obtained after explaining in straight forward terms and must be honest, thorough, efficient, and positive.



2. **Processes** must be courteous and respectful and deal with the difficulties such as samples or relatives as smoothly as possible.

3. Worries such as **data security**, data sharing, and feedback issues must be acknowledged and faced openly.

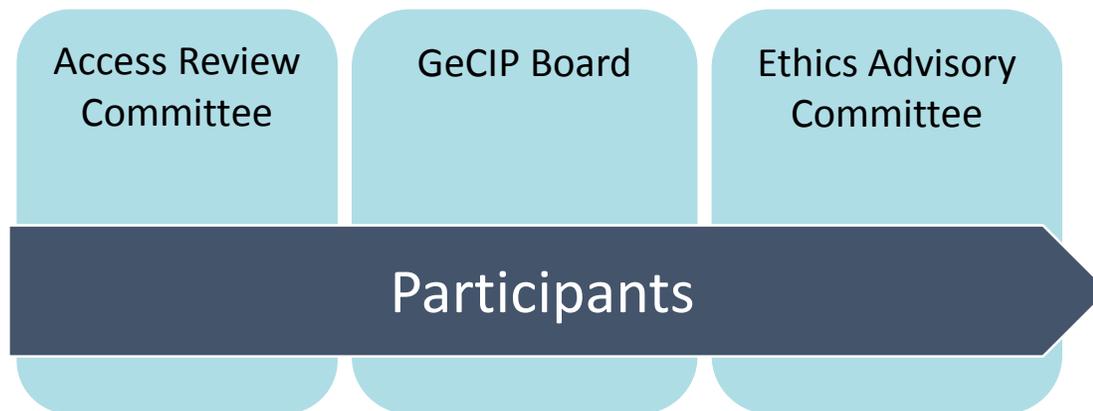


4. Participants must be kept in touch and **informed of progress**.

5. And we have learned that the only way to win support in the face of hard issues is to **listen** to participant concerns, design process to deal with them, and stick to them no matter what difficulties that gives you.

Participant Panel

- Role of the Panel is to ensure the interests of participants are always at the centre of the 100,000 Genomes Project.
- They do this by:
 - Making sure experiences of participants are at the heart of the project.
 - Responding to feedback.
 - Overseeing who should have access to participant data.
 - Representing the views of participants to the Board, the executives, and the public.



Are you taking part in the 100,000 Genomes Project?



Genomics England is looking for participants to be part of the national 100,000 Genomes Project Participant Panel.

The role of the Panel is to ensure that the interests of participants are always at the centre of the 100,000 Genomes Project. They will make sure that the experiences of participants are improved, respond to feedback and oversee who should have access to participant data.

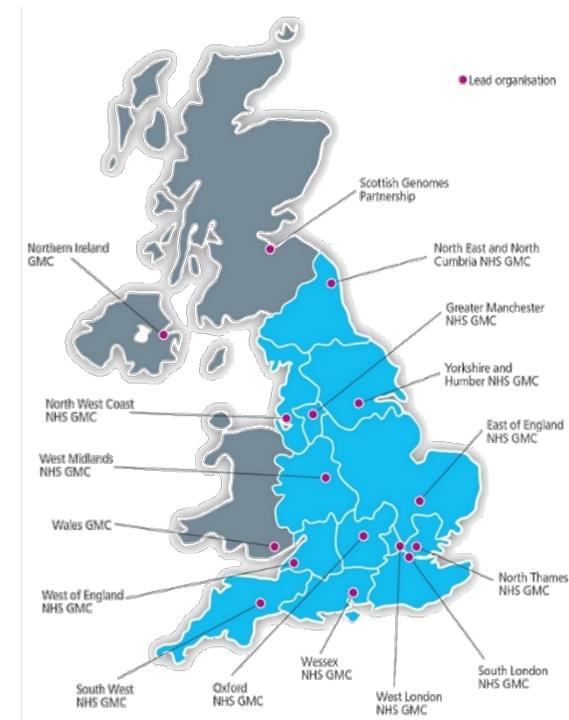
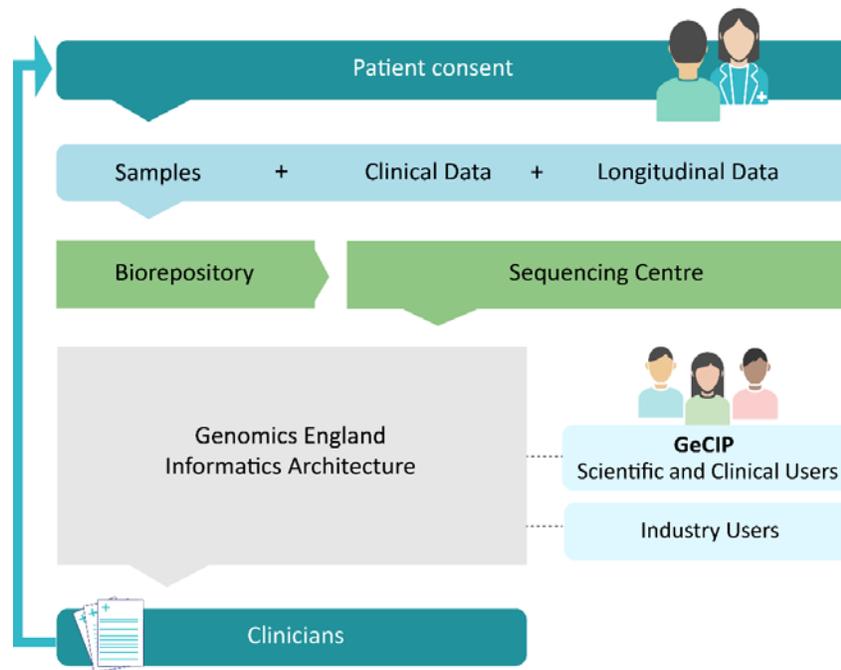
Public commitments

- Your data will **never leave the NHS**.
- Your data will only be used in identifiable form in relation to your direct care. **For all research purposes it will be used in de-identified form.**
- While it is impossible to provide an absolute guarantee, your data will be **guarded with the utmost diligence** and we will always inform you if there has been any event that could be of possible concern to you.
- Your data will only be accessed **according to the consent you have given us**.
- **Anyone who accesses your data will have been through a scrutiny process** examining the person, their organisation, and the task they want your data for.
- If you ask for it we will be able to provide **a list of those who have accessed** your data.
- **You may withdraw your consent at any time.** In that case your data will no longer be available in the research environment, but those analyses that have already used your data can continue to use their processed results.
- **If you require it we will give you a copy of your data for you to use for your own purposes.**

2. Create and prove the infrastructure to systematise Genomic Medicine in the NHS

How the 100,000 Genome Project Worked

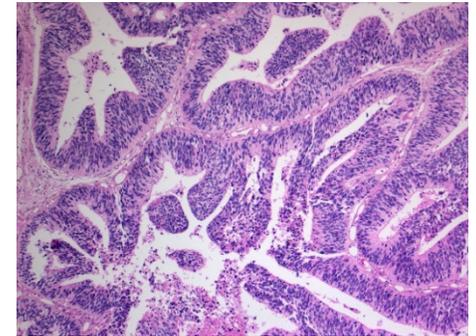
- Private company, 100% owned by the Department of Health, under **Independent Board**
- Close **Partnership** with NHS who commissioned recruitment and feedback via NHS Genomic Medicine Centres covering over 85 hospitals and 50 million people
- Built single **Centralised** platform for informatics, sample storage and whole genome sequencing
- Industry and academic research collaboration in a **Single, Safe** environment
- Evidence based process to establish consistent **Standards and Protocols**



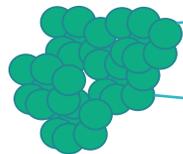
Whole genome diagnoses requires new Standards and Protocols, e.g. Pathology

This requires a transformation of routine health practice, which is now underway

- Tumour samples are traditionally preserved in formalin then fixed in paraffin (FFPE) to preserve cellular architecture for diagnosis under the microscope
- DNA extracted from samples treated like this is damaged and broken



The new
protocol



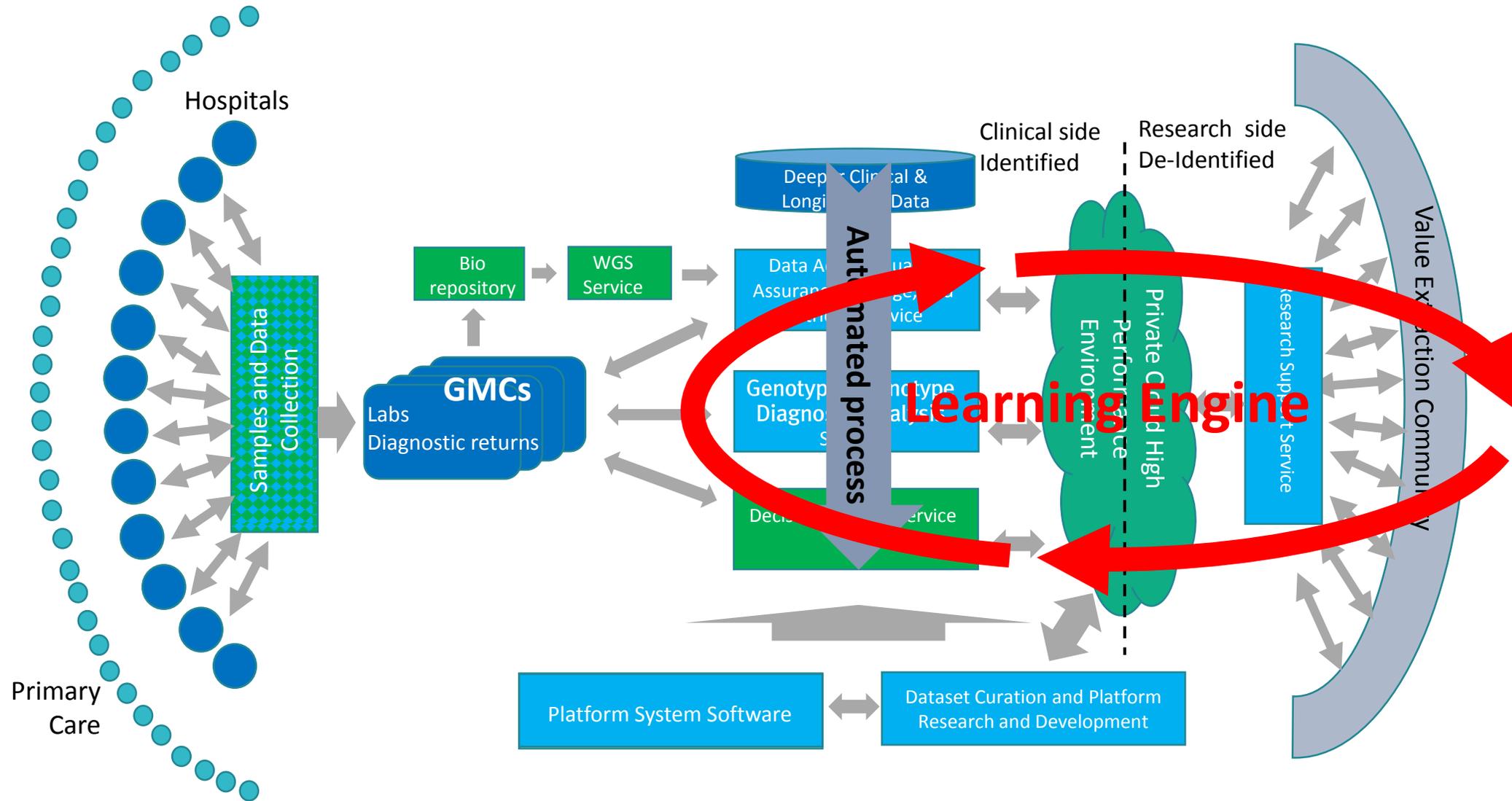
Use part of the sample for FFPE and histology

Freeze part of the sample for genetic tests

- Need to make sure the sample contains mainly tumour cells

- This new pathway requires very significant changes in sample handling, affecting nurses, surgeons, interventional radiologists, pathologists and oncologists

100,000 Genomes Project platform



What are participants expecting?

- Information about a patient's main condition
- Information about additional 'serious and actionable' conditions (optional)
- Carrier status for non affected parents of children with rare disease (optional)

Types of potential feedback to participants



Main findings

All participants agree to receive results about the main condition for which they were referred

Additional findings

Participants can opt in to receive feedback on a selection of known genetic alterations of high clinical significance

Carrier status

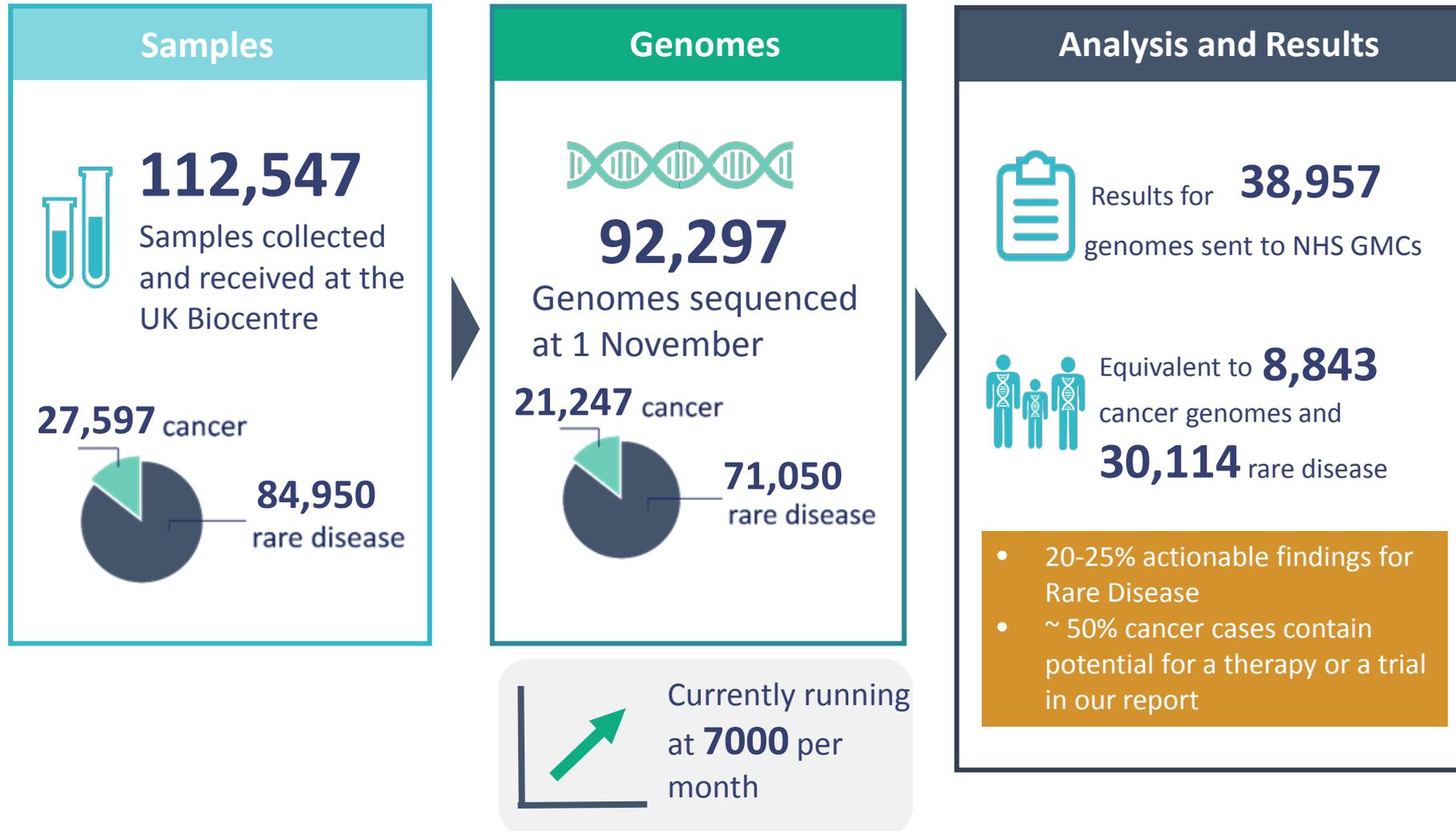
Eligible adults can opt in to find out their carrier status for certain genetic diseases

Image courtesy of Health Education England

3. Build a genomic/clinical dataset capable of enabling important health discoveries

Progress to date

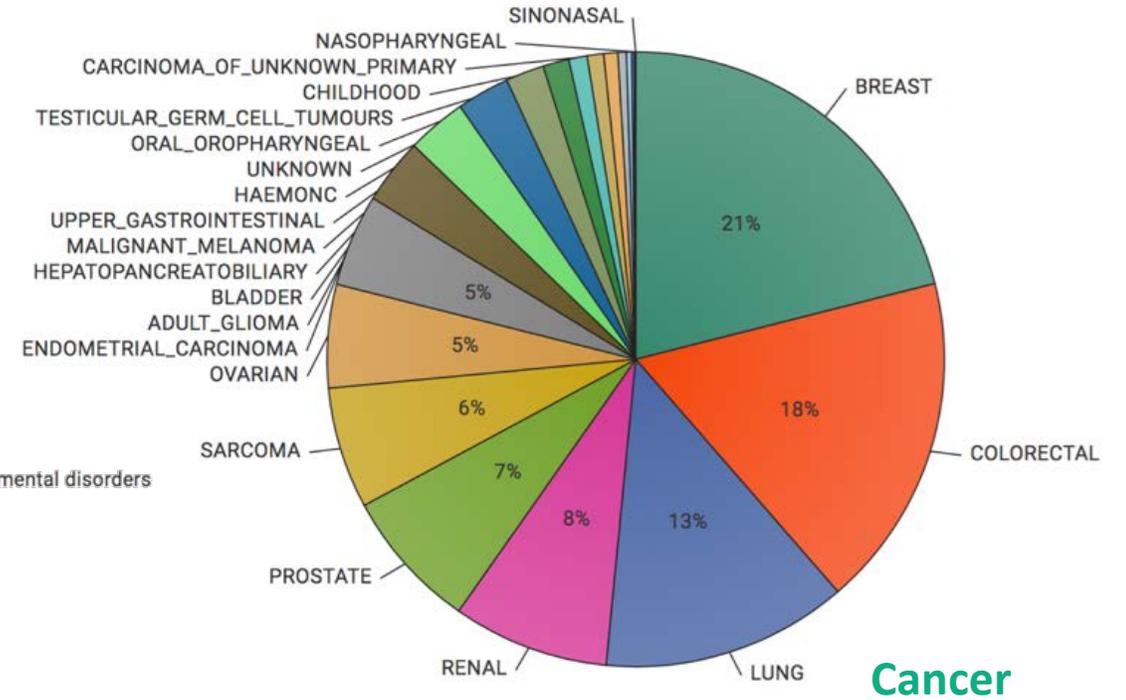
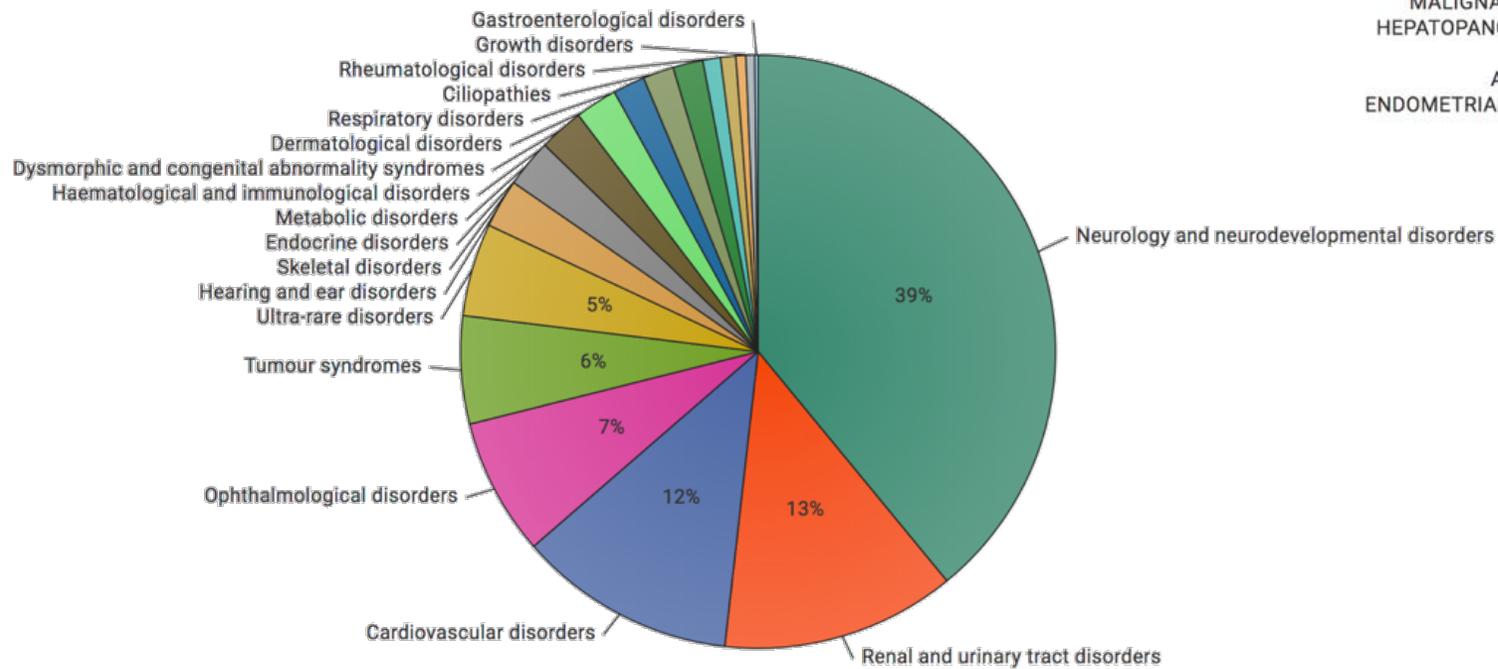
Figures as at 05/11/2018



Disease cohorts

Consented for longitudinal follow up, re-contact and additional samples

Rare disease



Cancer

Researchers across the world are getting access to the data: Genomics England Clinical Interpretation Partnership (GeCIP)



GeCIP launched in **June 2014**



3032 researchers world-wide



387 academic institutions

108 signed Participation Agreement

1821 researchers with access to data



33/42 Approved domains

4. Accelerate commercial investment in the genomics industry in the UK

Discovery Forum – more than 90 members



R&D companies [48]

Biopharmaceuticals [28]

Molecular diagnostics [20]

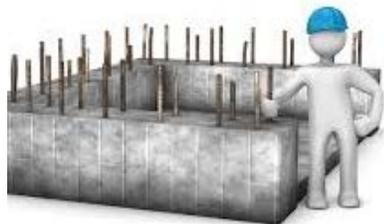


Platform partners [20]

Sequencing & Bioassay
[5]

Informatics &
Databases [15]

Contract research [1]



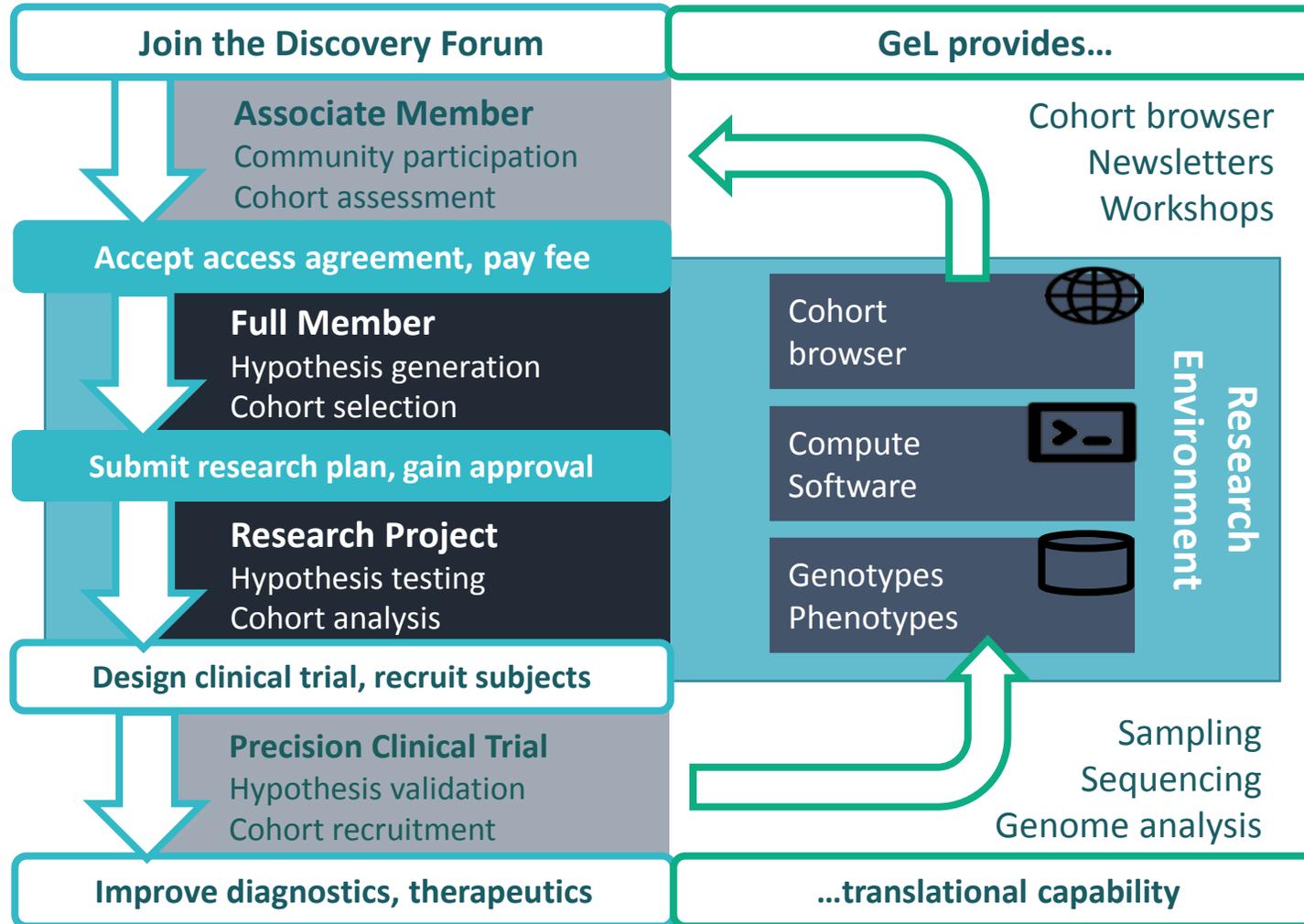
Finance, support and regulation [15]

Finance & Investment
[7]

Regulatory & Trade
bodies [2]

Charities [6]

The Discovery Forum process



So where next?

Future: Building the future NHS Genomic Medicine Service

By January 2019 the National Health Service in England will:

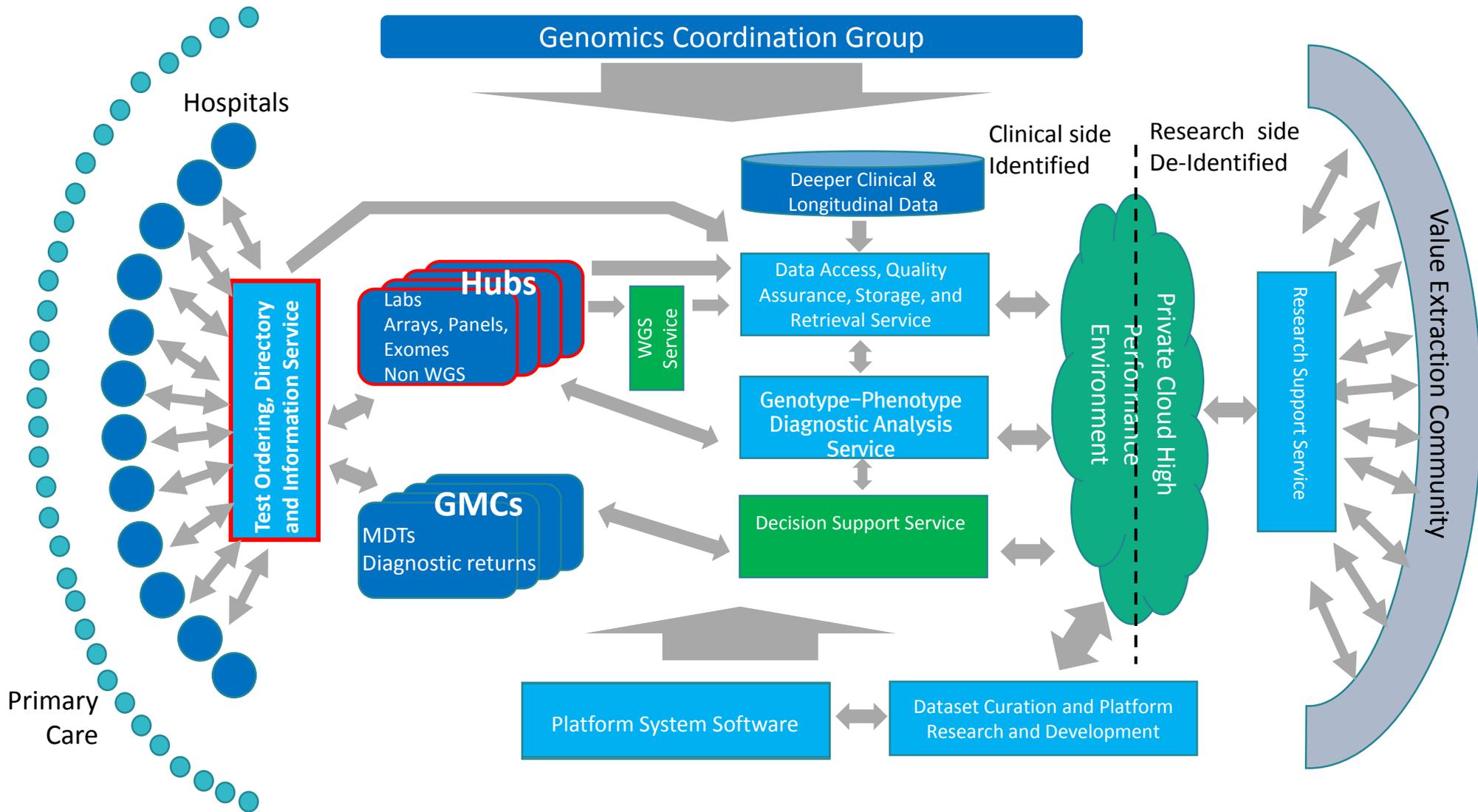
- Have a national **Genomic Medicine Service**
- Be operating to **common national** standards, specifications & protocols
- Have standardised **Genomic Consent** for NHS care and Research
- Be delivering an approved **National Testing Directory**
- Have **7 Genomic Laboratory Hubs**

Plus

- A single **UK Genomic Knowledgebase** with de-identified data for academic & industry research

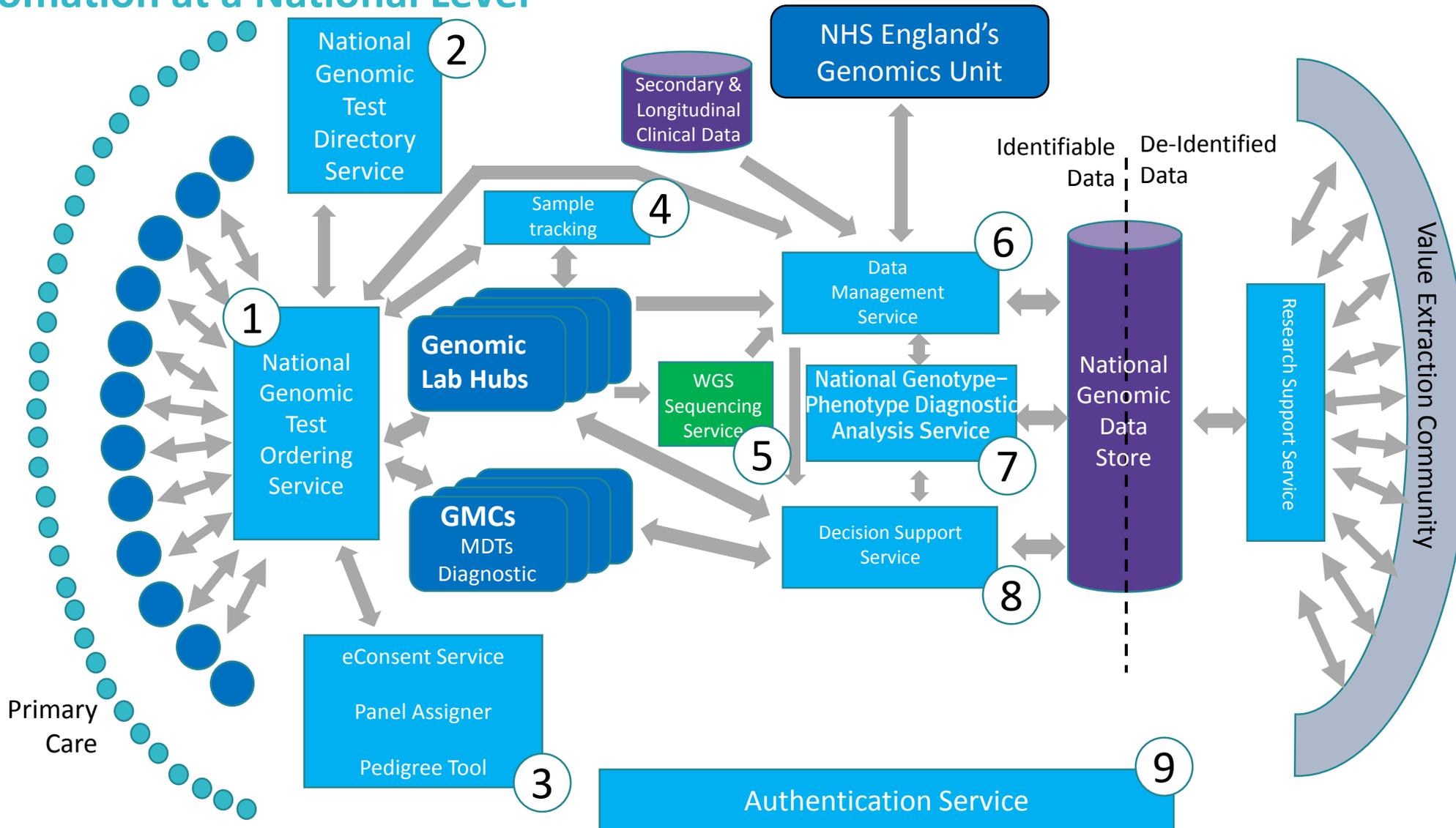


Genomic Medicine Service schema



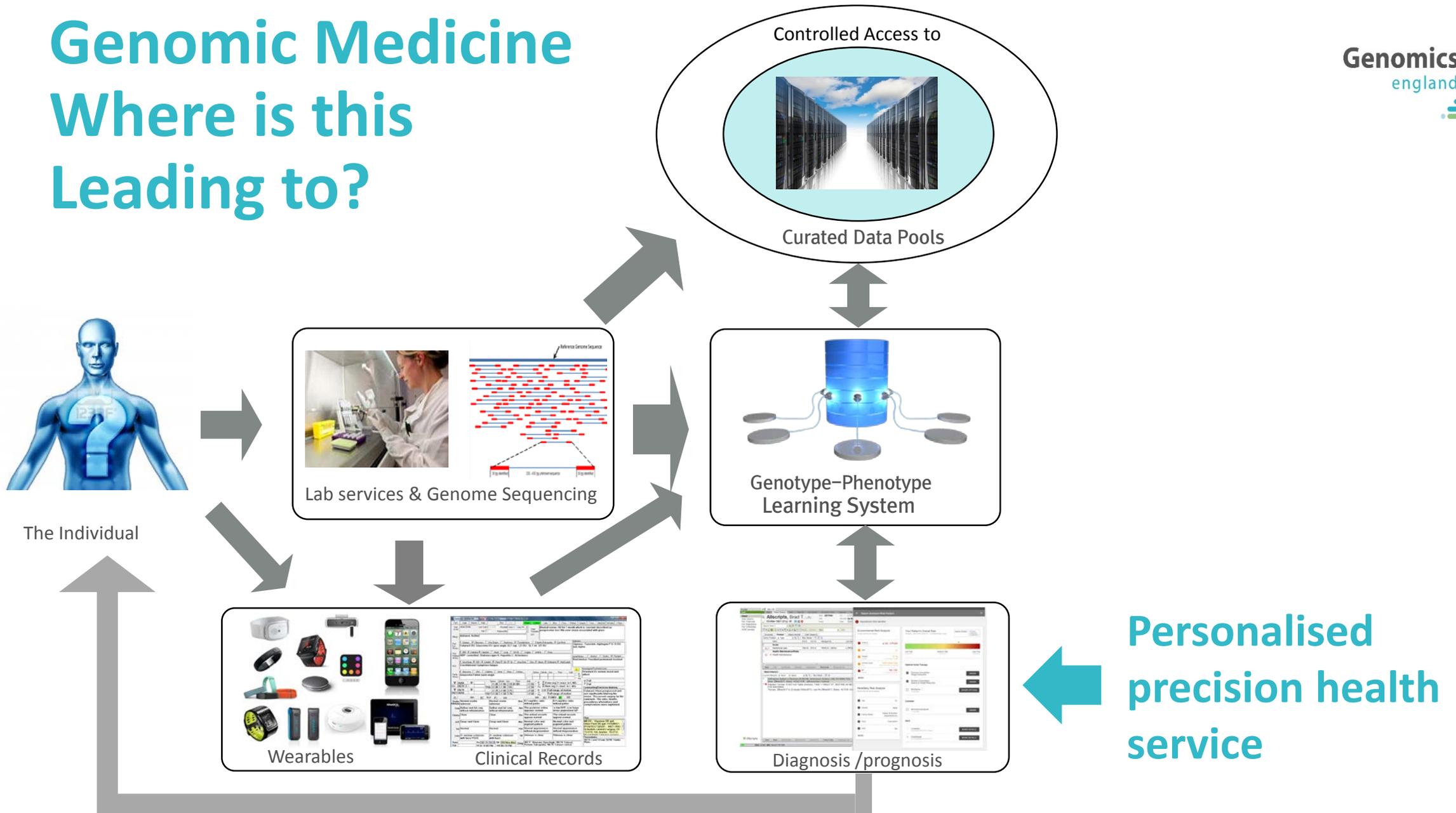
National Genomic Informatics Service

A modular integrated system designed to provide Genomic Medicine automation at a National Level



Genomic Medicine

Where is this Leading to?



Clinical Record + Wearable Data + Genomic Analytics



Provider: Hide VTB

Chart: Allscripts, Brad T. (JR) MRN: ZZZTW04 FYI: No Re

03-Mar-1967 (51y) M

Optum View 2

| Encounter | Problem | Patient Worklist | Chart Viewer(2) |
|---------------------------------|---------|------------------|-------------------|
| Active Problem | Type | Rec: Never | |
| Name | ICD-9 | ICD-10 | Managed By |
| Acute | | | |
| Abdominal pain | 789.00 | R10.9 | Medicin, James... |
| Health Maintenance/Risks | | | |
| Health Maintenance | | | |

Meds/Orders(3)

Current Meds/O: None Alpha Rec: Never

- Ceftriaxone Sodium in Dextrose 20 MG/ML Intravenous Solution; USE AS DIRECTED; T Done: 29Mar2017; Status: HOLD FOR - Administration Ordered
- Zolpidem Tartrate 10 MG Oral Tablet (Ambien); TAKE 1 TABLET AT BEDTIME AS NEEDED FOR INSOMNIA; Therapy: 29Mar2017 to (Evaluate:31Mar2017); Last Rx:29Mar2017; Status: ACTIVE Ord

View New Verify/Add Record D/C Order D/C Temp Defer Complete On

User: imedici Site: Second TW Clinic

Optum Assistant Risk Factors

Hypertension Risk Identified

Environmental Risk Analysis

Factors that can't be changed

- Sodium Lab Results **▲ 145 CYP3A5**
- BMI **27**
- Weight Withings **91 kg** 11.10.2018 @ 10:15 AM
- Activity Level Filbit **4000 Steps Daily** 2800 // 23.10.2018 @ 11:40 AM
- BP Withings **150 / 102** 11.10.2018 @ 10:15 AM

MORE

Hereditary Risk Analysis

Factors that cannot be changed

- Age 51
- Gender Male
- Family History Father & Brother (Hypertension)
- Race Caucasian
- CKD No

MORE

Your Patient's Overall Risk

Sources — 80,076,043 UK & US - 17 Similar Profiles Found

Genetic Variants • CYP3A5 • CYP2C9*3 • CYP2C19*17

Low Risk Hypertension Medium Risk Hypertension High Risk Hypertension

Optimal Initial Therapy

- Exercise Consultation Weight Reduction **ORDER**
- Nutrition Consultation Sodium & Weight Reduction **ORDER**
- Nifedipine **ORDER OPTIONS** 90 mg Daily

Consider

- Bendroflumethiazide **ORDER** 2.5 mg daily

Alert

- !** Losartan Low Dose (CYP2C9*3) <50mg **MORE DETAILS**
- ×** Clopidogrel Contraindicated (CYP2C19*17) **MORE DETAILS**

And what will a Personalised Precision Health Service Enable?



The Individual

Lab services & Genome Sequencing

Wearables Clinical Records

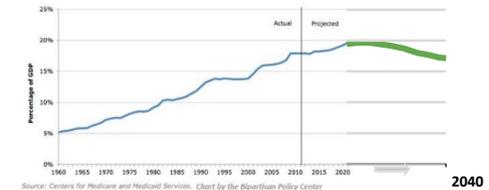
Controlled Access to
Curated Data Pools

Genotype-Phenotype Learning System

Diagnosis /prognosis



Figure 2: U.S. National Health Expenditures as a Share of GDP, 1960-2021



Source: Centers for Medicare and Medicaid Services. Chart by the Bipartisan Policy Center

Affordable Population Health Care

Everyone who has engaged in this project deserves thanks and congratulations, but the real heroes are our participants



Stay in touch



@genomicsengland

#genomes100k



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