Developing a newborn genomes programme

Genomics England

RCPCH Webinar
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Genomics England newborns core team:

- Dr Richard Scott, Chief Medical Officer
- Alice Tuff-Lacey, Programme Lead
- Simon Wilde, Director of Engagement
- Amanda Pichini, Consultant Genetic Counsellor
- Dr David Bick, Consultant Clinical Geneticist & Clinical Advisor
- Arzoo Ahmed, Ethics Lead
- Mathilde Leblond, Human-Centred Design Researcher
- Sofia Garcia Noriega, Service Designer
- Christella Matoko, Delivery Coordinator
- Dasha Deen, Genome Data Scientist

The vision

- Exploring the benefits, challenges, and practicalities offering whole genome sequencing to all newborns
- Ethics-approved research pilot embedded into the NHS and including evaluation
- Co-production with stakeholders and the public
- Considering the impact on NHS clinical care and workforce
- Ensuring it is human-centred, ethical, and translatable into a clinical service

3 areas of exploration:

Early diagnosis and care for childhood-onset rare genetic conditions

Enabling research and new treatments for NHS patients

Exploring the potential of a lifetime genomic record

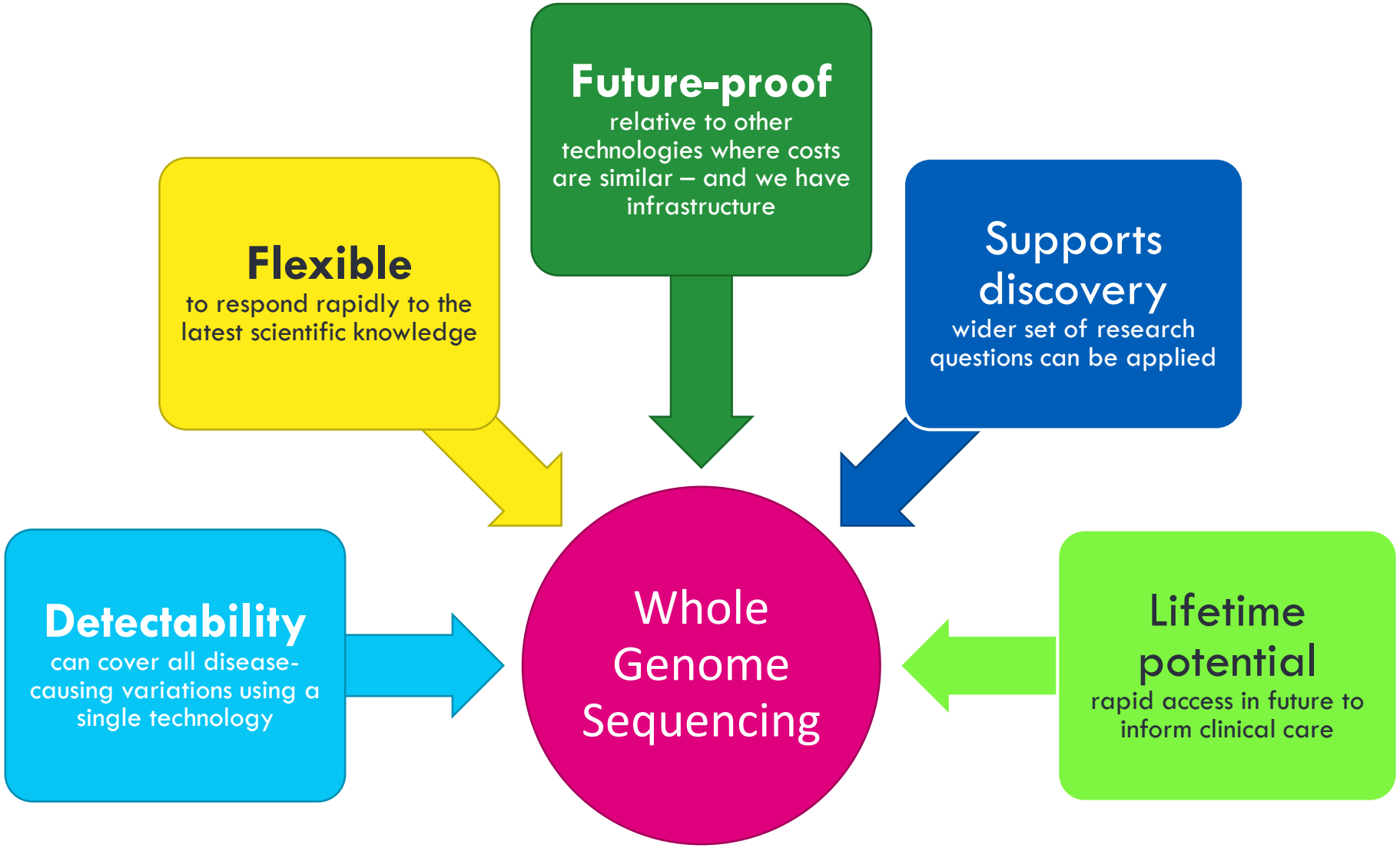
Newborn Genomes Programme: background

- Dame Sally Davies – 'Generation Genome' – 2018
- Genetic Alliance Patient Charter on Newborn Screening - 2018
- Genomics Analysis in Children task and finish group – 2019
- Genome UK: the future of healthcare - 2020

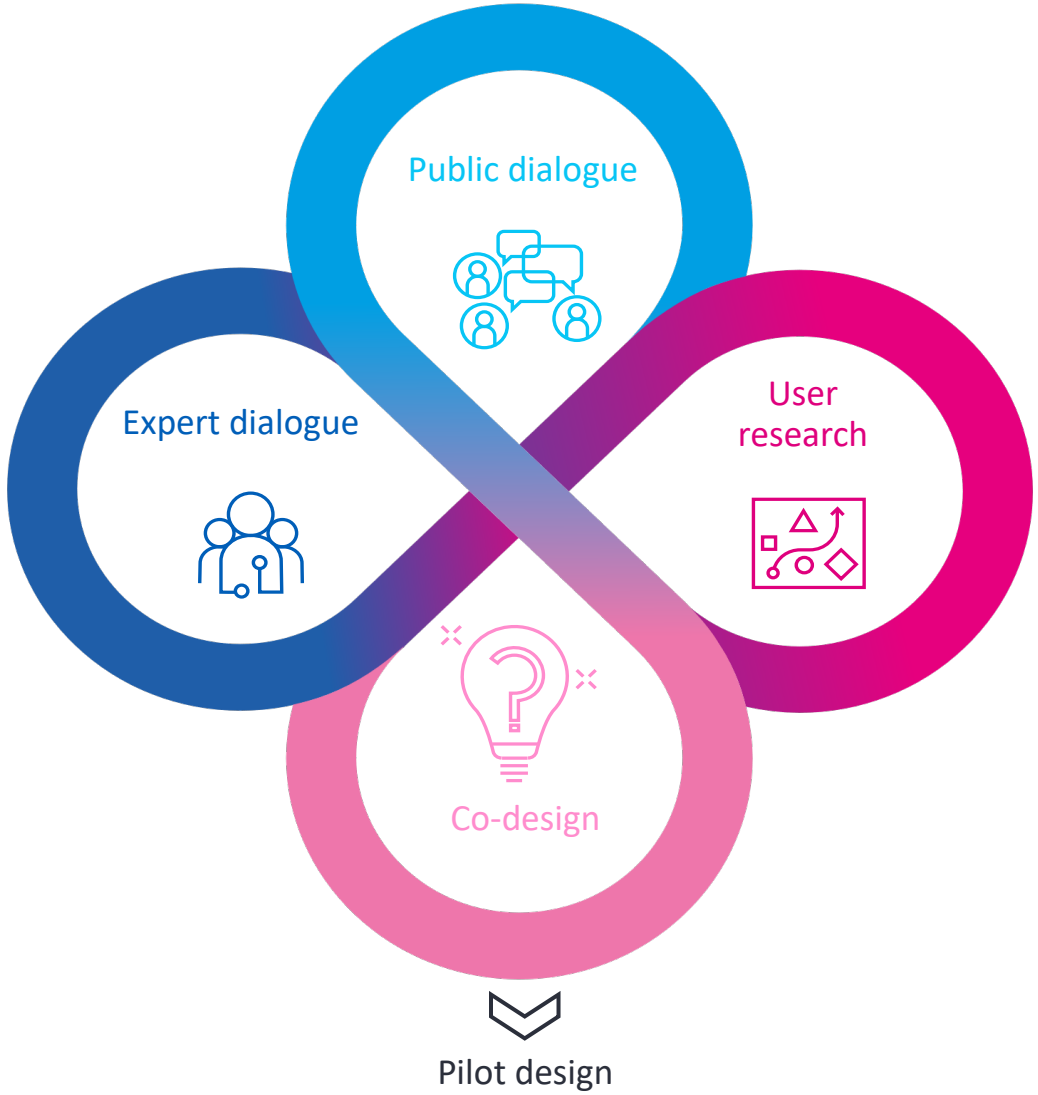
[we] support a high quality, large scale resourced research programme of whole genome sequencing for screening in healthy newborns. Now is the moment to investigate the value of this given the priority on genomics and prevention… The UK is uniquely placed to do this now with much of the infrastructure in place to develop a world leading programme to develop the evidence necessary to determine whether and how it should be introduced into clinical practice.

Genomic Analysis in Children Task and Finish Group

Why Whole Genome Sequencing?



A collaborative approach



- Public perspectives
- NHS Steering Group
- Specialist input
- Expert interviews

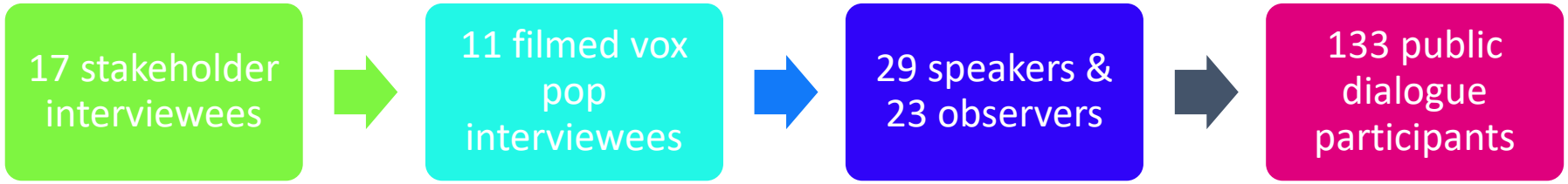
Genomics England / UK NSC Public Dialogue

What are the implications for the NHS and society of using whole genome sequencing (WGS) in newborn screening?

Explored in two contexts:

1. The potential use of WGS as a technology **in addition to or to replace** some parts of the current NHS newborn screening programme:
   - What might be the potential benefits and harms for the baby throughout their lifetime, for parents and the wider family, for others in society, and for the NHS?

2. The potential **novel or alternative** uses of WGS in newborns:
   - Exploring different purposes (e.g. lifetime monitoring, pharmacogenetics, family planning, research, information only), and the potential benefits and harms for the baby throughout their lifetime, for parents and the wider family, and for others in society, and for the NHS.



Genomics england

UK National Screening Committee

sciencewise

UK Research and Innovation

Creating Connections Hopkins Van Mil

Key findings

Participants are broadly supportive of the potential use of WGS for newborn screening, but they expect proper consideration of the design and planning of any future use of this technology.

1. WGS for newborn screening should identify a wider set of conditions than the current NHS newborn screening programme *if*:
   - they impact the infant in early childhood *and*
   - there are treatments and interventions to cure, prevent, or slow progression of the conditions.

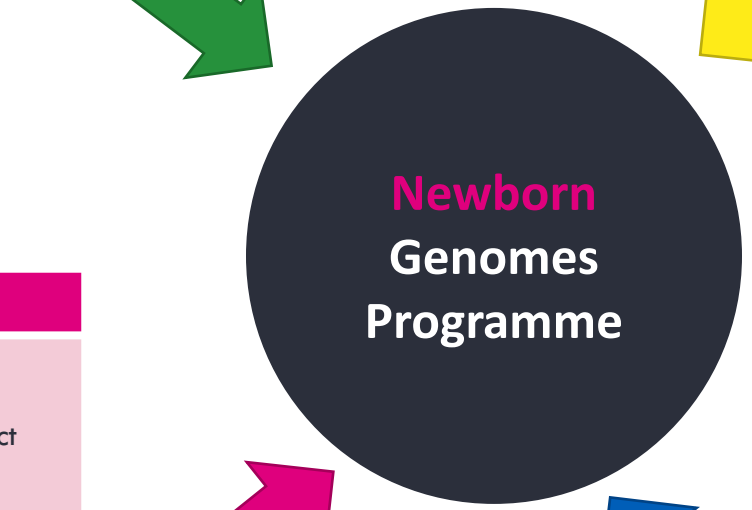
   There is also potential for WGS in newborn screening to bring health benefits to parents, siblings and the wider family.

2. Genetic counselling and mental health assistance must be available for those who receive a confirmed diagnosis to help them understand the health condition and to provide emotional and psychological support.

3. A comprehensive genetic database should be established so that people from ethnic minority backgrounds are not disadvantaged by receiving more uncertain, or less accurate, diagnoses than the rest of the population from newborn screening – and the accuracy of diagnosis for everyone is improved.

4. The full complexities must be recognised when designing consent processes. If consent is sought for WGS data to be used for research: the data must be anonymised and used to deliver improved diagnoses, treatment and care.

Public, participant and patient perspectives



Young People

Young person's panel

Genomics England

Participant Panel

Ethics Advisory Group

NHS Steering Group

Working Groups

Public dialogue

Newborns dialogue (2021):

Genomics and the social contract (2019):

Dialogue on consent issues: filling the gaps in our knowledge of public attitudes

Consultation

Public consultation on genes framework principles

Citizen's jury on research access to data

Pilot-site engagement and consultation including community groups

Standing ethics group to gather views / consult on ethical issues as they arise

Co-design

Parent ethnography

Recruitment working group

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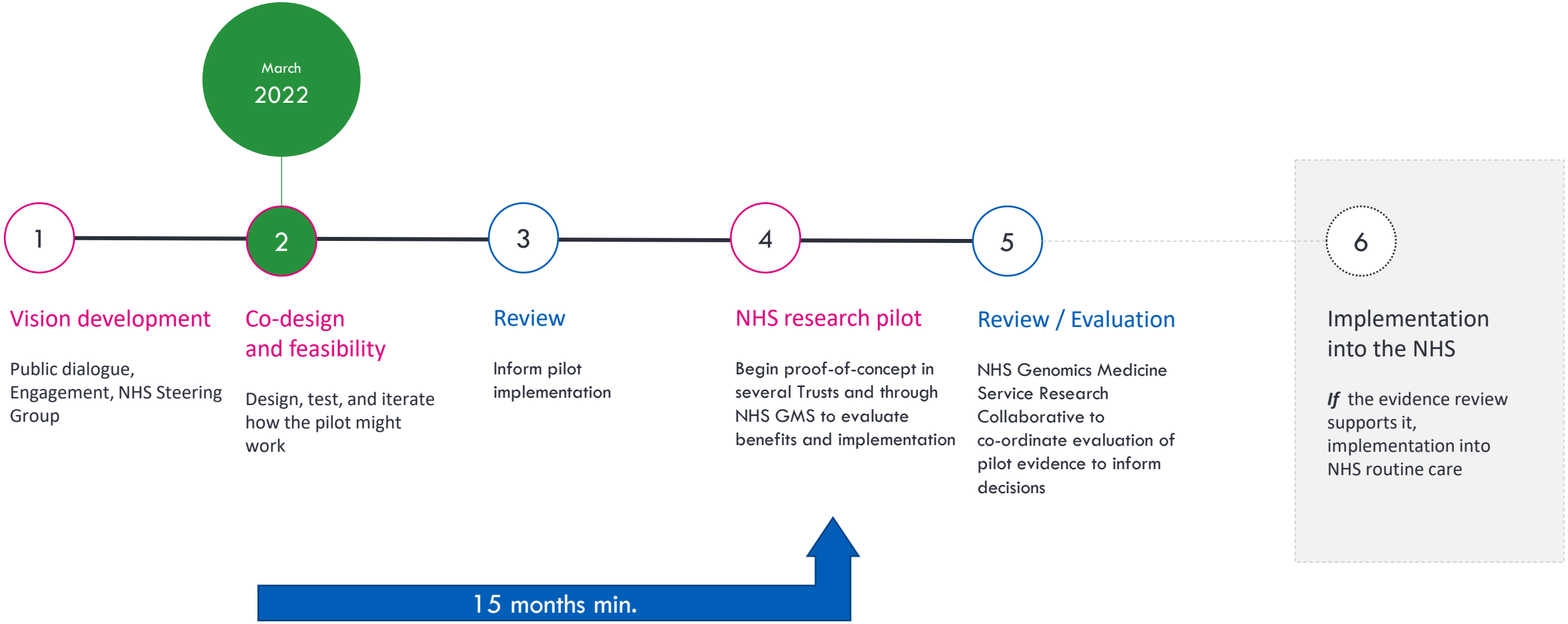
Where are we?


March
2022
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Vision development
Public dialogue, Engagement, NHS Steering Group
Co-design and feasibility
Design, test, and iterate how the pilot might work
Review
Inform pilot implementation
NHS research pilot
Begin proof-of-concept in several Trusts and through NHS GMS to evaluate benefits and implementation
Review / Evaluation
NHS Genomics Medicine Service Research Collaborative to co-ordinate evaluation of pilot evidence to inform decisions
Implementation into the NHS
If the evidence review supports it, implementation into NHS routine care
15 months min.

Emergent themes

- **The benefits, limitations and unknowns of WGS as a screening tool**
- **Co-developed principles for including conditions in the screening panel**
- **Person-centred consent across screening, research and reanalysis**
- **Supportive and inclusive experience for all families**
- **Trusted and future-proofed genomic data storage and usage**
- **A sustainable and scalable programme for the NHS**

"If we get it right, it will be fantastic and it's about doing it safely. Isn't it really so that actually families are really supported to understand their child better?"
Health Visitor

What we want is for every condition to be there or not there based on merit, and whether or not it is sensible to do so, with our own community's voice in there." Genetic Disease Charity representative

"I am a firm believer that emotional support is most effective from someone who has experienced the emotional turmoil that a patient's family is feeling. On completion of genetic counselling, ongoing support and follow-up could be carried out by that particular group (e.g. cystic fibrosis group)."
Public Dialogue Participant, Genetic Conditions Group

"Pregnant women already have a tsunami of information coming towards them. Genomics is difficult for many people to understand, it will need more than just giving them written information."
Obstetrician

Structure of workstreams in research and design phase

1. Ethics framework and protocol design

2. Design elements

Early Diagnosis and care for childhood onset rare conditions

Conditions framework → Recruitment → Consent → Sample and sequencing → Analysis and return result → Treatment pathways and support

3. Education and training

4. Workforce and pilot mobilisation

5. Evaluation framework

Enabling research and new treatments

Exploring potential of lifetime genome

Embedding ethics across the programme

- Dedicated Ethics Lead in core team
- Proactive work with Genomics England's Ethics Advisory Committee, internal ethics team and external stakeholders
- Developing a framework with key guiding ethical principles to consider in each 'workstream' of the programme
- Learning from and building on previous & parallel experiences (e.g. 100K, Genomic Medicine Service)

Balancing what we *should* do with what we *can* do

Developing a framework for including conditions, genes, variants…

What is the clinical **utility** for each condition or variant?

What is the clinical **validity** for each condition or variant?

- What is an acceptable level of confidence?
- What makes a condition 'actionable'?
- What is the max. age when treatment would need to start?
- Is treatment and/or support available in the UK?
- How much would the treatment cost?
- What is the prevalence of the condition?
- How variable are the clinical features & outcomes?
- What is the maximum age of onset of first symptoms?
- What is an appropriate level of evidence for treatment?

Care and Treatment Pathways

"Considering existing pressures in healthcare, the programme must understand the services and resources required to support children and families, and education and training needs for the workforce to provide high quality care."

Although the total number of test-positive babies in the lifetime of the pilot may be no more than 500, every one needs a structured care and treatment pathway in place before we begin.

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Questions

- To ensure the best outcomes for children, it is vital that we work with and learn from (long) established specialist teams and pathways

- How do we
    - ensure we are linking with the right teams?
    - best map the end-to-end clinical pathways?
    - ensure that children can access care and treatments rapidly?
    - model and prepare for impacts on capacity and workforce?

Newborn Sequencing NHS steering group

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Dr Ngozi Edi-Osagie Chair, Clinical Reference Group for Neonatal Critical Care, NHSE

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Dr Frances Elmslie Clinical Director, NHS South East Genomic Medicine Service Alliance

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Michelle Lyne Education Adviser, Royal College of Midwives

Prof Anne Mackie Director of Screening, PHE

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