

NHS ENGLAND – BOARD PAPER

Title:

Creating a genomic medicine service to lay the foundations to deliver personalised interventions and treatments

Lead Director:

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Purpose of Paper:

This paper sets out NHS England's strategic approach for building a genomic medicine service, building on the legacy of the 100,000 Genomes Project. Further planning to develop detailed implementation plans is now required, the immediate next steps of which include formalising the partnership approach with Genomics England, and launching the procurement process for the genetic laboratories by the end of Quarter 1 of 2017/18.

To help inform and shape the detailed implementation plans, NHS England's Board is asked to approve the high-level approach set out within this paper.

The Board invited to:

- Note the progress of the delivery of the 100,000 Genomes Project; and
- Approve NHS England's strategic approach to create a genomic medicine service to deliver personalised treatments and interventions.

Creating a Genomic Medicine service to lay the foundations to deliver personalised interventions and treatments

Introduction

1. The NHS has a long tradition of undertaking genetic testing in patients with rare and inherited disease and more recently in the molecular testing of cancer tissue. Since the early 2000s there has been significant government investment in genetic laboratory and clinical services and more recently by NHS England as part of its commissioning responsibilities.
2. The 100,000 Genomes Project (the project) commenced in 2012 to harness advances in whole genome sequencing (sequencing all 3.3 billion letters of an individual's genetic code) computing power and data analytics to improve diagnoses and deliver more informed care as well as to enable the development of better tests and better drugs.
3. The project is being delivered in partnership with Genomics England, underpinned by the NHS commitment to deliver 90,000 DNA samples and associated clinical data from participants with rare disease (and their family members) and cancer, is due to complete in 2018.
4. Since its inception the expectation has been that by the end of the project NHS England, working in partnership with Genomics England, will commission whole genome sequencing and embed genomic medicine into routine care pathways where it is clinically and cost effective to do so, in line with NHS constitution for to continue to operate at the limit of science.
5. To help inform and shape the detailed implementation plans, NHS England's Board is asked to approve the high-level approach set out within this paper.

Potential benefits of Genomic technologies

6. Across the world, scientific discoveries and technological advances in genomics, informatics, analytics and bio nanotechnology, are transforming our ability to more precisely diagnose illness and target treatment of disease.
7. The concept of tailoring interventions to individuals is not new, but never before has it been possible to identify the underlying cause of disease, predict how each of our bodies will respond to specific interventions, or determine which of us is at risk of developing an illness.
8. The systematic application of genomic technologies (up to the level of a whole genome sequence) has the potential to transform patient's lives by:
 - enabling a quicker diagnosis for patients with a rare disease, rather than years of uncertainty, often referred to in rare disease as the 'diagnostic odyssey';

- matching people to the most effective medications and interventions, reducing the likelihood of an adverse drug reaction; and
 - increasing the number of people surviving cancer each year because of more accurate and early diagnosis and more effective use of therapies.
9. There are also significant benefits for research and development that can be leveraged on behalf of the NHS, taxpayers and the wider economy. The NHS as the single biggest integrated healthcare system in the world is in a unique position to harness the potential of whole genome sequencing to benefit NHS patients but also, through the forthcoming life sciences industrial strategy, demonstrate the nation's competitive advantage in enhancing understanding of diseases, and developing products for earlier detection and treatment.

Delivering the 100,000 Genomes project

10. Through the project, NHS England has established 13 NHS Genomic Medicine Centres (GMCs) working across geographical areas of approximately 3 to 5 million people and involving over 85 hospital trusts. The GMCs have been working closely with Genomics England, the government owned company overseeing the project. Genomics England have established elements of the national infrastructure including procuring the whole genome sequencing provider and creating a national genomic knowledge database.
11. The GMCs have enabled patients, clinical laboratory and informatics teams to participate within the project. They are responsible for: recruiting and consenting patients; providing DNA samples from both blood and cancer tissue and clinical information for analysis; establishing mechanisms for validating results; and working with clinical staff to broaden the use of genomics across clinical specialities.
12. As of March 2017, the 13 NHS GMCs have consented participants and processed a total of 28,205 DNA samples:
- **Rare Diseases** - 24,268 samples from patients and family members across over 180 different rare diseases. The NHS is currently recruiting over 2,000 patients and family members per month from routine clinical care.
 - **Cancer** - 3,937 samples (tumour and a matching blood sample) from 15 different cancer types representing around 1,900 patients given that in some patients, more than one sample was collected. To date the majority of samples have been collected in breast cancer, colorectal cancer and renal cancer. Across all of the GMCs and participating Trusts there are over 80 different cancer pathways live and actively seeking patients for enrolment.
13. Delivery of the rare disease element of the project is delivering to plan, with the original commitment to provide 45,000 samples expected to be delivered by December 2017 and 60,000 by the end of the Project. Delivery of the cancer programme has been more challenging and complex. One of the biggest challenges has been to ensure high quality samples for sequencing, requiring the

NHS to embed a new process for obtaining tissue samples (fresh-frozen), which has necessitated a significant reengineering of the diagnostic cancer pathway. A review of the NHS approach to cancer tissue handling and DNA extraction processes is underway, including work to assess the feasibility of using biopsy tissue samples to simplify this pathway for the future.

14. All 13 NHS GMCs have established patient and public engagement groups working with charities and other third sector partner organisations. These patient and public networks have been critical in:

- raising awareness and understanding of genomics;
- informing the development of information on consenting materials;
- identifying barriers within the consenting process;
- informing the design of the cancer patient pathways;
- supporting patients and their families to prepare for the receipt of results and explaining where to find further information.

Early findings from the project

15. Ten of the NHS GMCs have now received a number of results for rare disease (1532 rare disease results from the pilot and main programmes) and three NHS GMCs have received a small number of cancer results. Examples of the impact of the results for individual patients are included in Annex A. It is expected that the rate of results being returned, for both cancer and rare disease, will accelerate significantly, with additional results expected to be returned in April 2017.

16. In rare disease, the results returned so far indicate there is an increased diagnostic yield of at least 20-25%, signifying new diagnostic findings and information about the underlying cause for a person's disease where existing tests have failed. Furthermore, the results are demonstrating the importance of collecting detailed medical information regarding patients to help better understand the findings that are being obtained from a WGS.

17. In cancer, although only a small number of results have been returned, analyses of the tumour tissue are revealing new genomic information such as signatures (distinctive 'scars' of mutation across the genome), which are directing patients towards clinical trials for which they previously would not have been eligible. We are also identifying new genomic mutations in the blood of a subset of these cancer patients, which provide information about that patient's high risk of additional cancers and what needs to be tested in relatives to enable provision of enhanced screening and preventative health measures in the family members who carry the mutation.

International approaches

18. Within the UK the 100,000 Genomes Project is: mainstreaming the use of whole genome sequencing within a healthcare system with the consent of participants to enable ongoing scientific discovery; developing informatics, data and analytical

platforms capable of storing, linking and interrogating genomic, clinical and longitudinal information; and introducing a new way of working with academia and industry. The approach taken within the UK has involved the NHS from the outset, recruited participants from routine care pathways, and involved routine laboratory and clinical care services.

19. There is global recognition of the potential benefits of genomics to underpin personalised medicine (also known as precision or stratified medicine). Health systems including the United States of America, Germany, France, Canada, Australia, China and India are formulating policy and research programmes in the application of genomic technologies to support the adoption of more personalised treatments and interventions.
20. In France, the 'French Genome 2025 Project' is pursuing a vision to establish a network of up to twelve sequencing centres for rapid, high-throughput genome sequencing and two national centres for storage and for expert analysis that will be able to deliver whole genome sequences for 20,000 rare disease and 50,000 cancer patients annually by 2020 (equivalent to 235,000 whole genomes per year). The French Government is providing EUR 630 million from healthcare funding, accompanied by commercial contributions of EUR 230 million.

Establishing a Genomic Medicine Service

21. The project is demonstrating that significant transformational change is required across the NHS to embed genomic medicine into routine care. From the way consent is taken, processes for collecting and handling samples, the role of clinical genetics within clinical specialities, to the informatics infrastructure enabling data to be brought together, shared and analysed. These transformations are beginning through the project and considerable investment has already been made to transform the infrastructure.
22. Despite the successes there is still more to be done to fully establish the application of genomic technologies (not just whole genome sequencing) across the whole of the NHS and ensure equitable access. This is particularly in primary care where new molecular point of care testing devices could provide real time data to guide more appropriate prescribing in a number of areas. As genomic analysis is becoming routine in infectious disease diagnosis, and other molecular analyses and biomarkers are incorporated into routine diagnostic practice and patient risk assessment, genomics is set to become inextricably linked to all branches of clinical practice.
23. To create the future infrastructure to deliver a genomic medicine service, NHS England will need to continue to work in partnership with Genomics England. The partnership will need to create the following elements until at least 2020/21:
 - **Whole Genome Sequencing Provision** – provision of expertise to sequence blood and cancer tissue samples supplied by the NHS as part of a routine diagnostic pathway. It will require delivery at the appropriate scale, quality and price point.

- **Clinical Interpretation Pipeline** – continued development and leadership by Genomics England, of the unique bioinformatic and interpretation analytical platform to assist the NHS in the timely interpretation of the WGS, informing clinical decision making in relation to genomic diagnoses and subsequent interventions based on pharmacogenomic profiling.
- **Data and informatics environment** – an integrated platform to support data sharing within the NHS for patient and commissioners that interfaces with the WGS provider, enables interpretation of the whole genome sequence and supports the UK genomics endeavour through the further evolution of the UK Genomic knowledge base. This will be established by Genomics England in partnership with NHS Digital and NHS England.
- **Horizon scanning and evidence building** - ongoing expertise to ensure the NHS's strategic approach is focused on adoption of the most effective and relevant technologies, whilst remaining competitively priced.

24. Successful implementation will require the NHS to establish the following underpinning elements:

- **A new networked genetic laboratory and genomic medicine service infrastructure** – consolidated genomic laboratory infrastructure for rare, and inherited diseases and cancer operating to a defined service model, and a transitional role for the existing Genomic Medicine Centres to establish comprehensive coverage and access to genomic medicine across the NHS.
- **A comprehensive genomic testing strategy for the NHS** - initially for rare, and inherited disease and cancer, that encompasses the entire testing repertoire from whole genome sequencing to tests for single genes, molecular markers and other functional genomic tests that are important to fully determine the patients predicted response to treatment. The NHS will require a single directory of tests, informed by evidence and based on the latest technological advances, to ensure that the tests that are no longer clinically or cost effective are decommissioned or replaced.
- **A joint-commissioning model with CCGs** to achieve standardisation, equity of access, economies of scale and the high quality required for the future. For example panel tests for cancer and WGS will need to be delivered at a centralised and aggregated level, which will not be possible without a joined-up approach to commissioning.
- **Further evolution of the NHS informatics environment** through continued HMT capital investment to ensure that the interoperability and data sharing across the NHS is fully functional and can interface effectively with the Genomics England platforms.

Conclusion

25. This paper has set out NHS England's strategic approach for building a genomic medicine service, building on the legacy of the 100,000 Genomes Project. Further planning to develop detailed implementation plans will now begin. The immediate next steps include formalising the partnership approach with

Genomics England, and launching the procurement process for the genetic laboratories by the end of Quarter 1 of 2017/18.

Recommendations

26. The Board is asked to:

- Note the progress of the delivery of the 100,000 Genomes Project; and
- Approve NHS England's strategic approach to create a genomic medicine service to deliver personalised treatments and interventions.

Annex A

Patient benefit examples

Jessica, a 4 year old who was being treated at Great Ormond St Hospital, received a diagnosis of her rare condition after being recruited to the 100,000 Genomes Project. Her diagnosis means a treatment could be recommended too. It was found that she had a genetic mutation known as the Glut1 deficiency syndrome. Research has shown that in some patients who have Glut1 deficiency syndrome, a special low-carbohydrate diet can help reduce the number of seizures they experience. This treatment was applied to Jessica's and her symptoms improved dramatically.

Three sisters, Mary, Sandra and Kerry Lloyd all developed breast cancer within 15 months of each other. They joined the 100,000 Genomes Project at Leicester's Hospitals. They had already undergone genetic testing for changes in the BRCA1 and BRCA2 genes – which can be a cause of breast cancer. But these tests didn't find anything. The sisters donated a small amount of blood and had their genomes sequenced. We are still trying to find out the causes for their cancers. But by taking part in the 100,000 Genomes Project, the Lloyd sisters are contributing to research. Their de-identified data, together with data from other participants, is available to researchers through our secure database.

A 10 year old girl who was admitted to the intensive care unit at the Royal Manchester Children's Hospital with life threatening chicken pox infection received a diagnosis of her rare condition through the 100,000 Genomes Project. She was found to have mutations in a gene called *CTSP1*, which leaves her prone to infections. This has changed the way she is looked after and she is now being considered for a bone marrow transplant, which would cure her. This finding has also raised awareness of her condition, which is now considered in other children who have had life threatening chicken pox.

A 29 year old man with severe learning disability under the care of the Manchester Genetics Service was recruited to the 100,000 Genomes Project. His sister was planning to start a family and concerned about the risk of a child being born with similar problems. Through the project, he was found to have a very rare and recently recognised condition caused by a mutation in a gene called *ZSWIM6*. This brought to an end a wait of many years of search for a diagnosis. The condition had started for the first time in the family in him as a result of a new mutation, meaning that his sister can be reassured that the risk of her having a child with similar problems is very low.