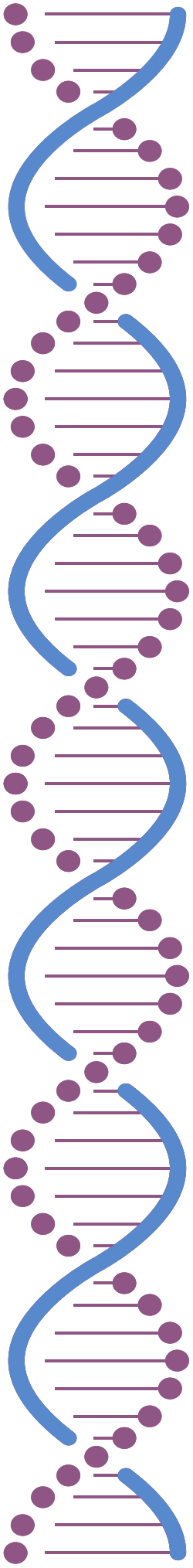
HM Government

GENOME UK

The future of healthcare



Contents

Ministerial Foreword

The UK is a global leader in genetics and genomics. From seminal discoveries in fundamental science through to translation into clinical practice and improved patient outcomes, the UK has made a vast contribution to this rapidly evolving and exciting field. In this strategy we set out our plan to maintain and extend our leadership position: to deliver the future of healthcare; enabling the provision of world-leading genomic healthcare to patients in the UK and across the world.

We are committed to a future where genomics greatly improves the mental and physical wellbeing of the UK population and millions more worldwide. This will mean developing a better understanding of the genetic causes of disease, along with provision of tailored therapies so that patients get the treatments and advice that work for them. Predictive interventions – addressing diseases before they appear – are also starting to deliver on the promise of preventative medicine at scale.

We now find ourselves at a tipping point. The cost of sequencing is falling, and it is now quick and efficient enough to inform clinical and even critical care. We are building a holistic ecosystem in which genomics research is no longer the preserve of the laboratory scientist. The biggest gains are being made through collaborations across a range of expertise from clinicians, engineers, social scientists, mathematicians, and data scientists. Combined with world leading research projects to better understand COVID-19 and a nascent, exciting genomics industry, the UK can and must ensure we maintain our leadership role in the genomics revolution.

The societal cost of healthcare is rising as people live longer and the prevalence of long-term, complex diseases increases. We must take advantage of the developments in genomics to increase prevention and early diagnosis of disease. Clinical, scientific and industry innovations, scaled through trusted technologies and delivered through the NHS must continue to ensure that the UK healthcare system delivers the best possible care to all patients. This will require both bold steps and careful consideration. We will need the right partnerships with patients, the public and the clinical community, so we will engage with these communities to build trust and understand and address concerns. We will ensure that our approaches are anchored on equity of access, data security and privacy, and we will always be responsible and transparent where patient data are used to advance scientific understanding and direct care.

This strategy sets out an ambitious and compelling vision for how we will create the most advanced genomic healthcare ecosystem in the world, underpinned by the latest scientific advances and public support to deliver better health outcomes for our population.

Lord Bethell of Romford,
Parliamentary Under Secretary of State (Minister for Innovation)

Executive Summary

Over the next ten years our ambition is to **create the most advanced genomic healthcare system in the world, underpinned by the latest scientific advances, to deliver better health outcomes at lower cost.** We will do this by working together across our four nations and reducing boundaries between clinical care and research. We will support earlier detection and faster diagnoses, use genomics to target interventions to specific groups of patients, support patients in understanding what genomics means for their health, and bring the full might of our capabilities in this field to bear against new global pandemics and threats to public health. This will support the commitments, set out in the 2019 Conservative manifesto[1], to invest in world class computing and health data systems that can aid research and make the UK the leading global hub for life sciences.

In this strategy we set out an exciting and compelling vision for the future which is focused on three key areas:

1. **Diagnosis and personalised medicine: we will incorporate the latest genomics advances into routine healthcare to improve the diagnosis, stratification and treatment of illness.** We will focus on:

    - **The NHS England Genomics Medicine Service:** We will be the first national healthcare system in the world to offer whole genome sequencing (WGS) as part of routine care, delivering on our promise to sequence 500,000 whole genomes.

    - **Pharmacogenomics:** We will enable the most effective provision of effective therapies so that patients get the treatments and advice that work for them, including tailoring drug treatments.

    - **Cancer:** We will introduce a new operating model for cancer, ensuring multi-disciplinary teams can draw on a range of genomic, imaging and longitudinal health and care data to improve patient outcomes.

2. **Prevention: Enabling predictive and preventative care to improve public health and wellness.** We will focus on the role genomics can play in:

    - **Expanding screening in early life:** The UK is uniquely positioned to conduct a high quality, large-scale research programme to determine whether and how sequencing should implemented for screening in newborns. We will study the opportunities, risks, ethical issues, and regulatory implications of such a programme, ensuring that we progress a public conversation to generate better understanding of patient and public attitudes.

    - **Targeted screening:** We aim to better use genomics to improve population health through improved disease prevention including better screening. This includes the use of personalised and risk stratified screening and testing of the family members of cancer patients to identify where they are at increased risk of cancer. We also expect to see development of Non-Invasive Prenatal Testing using sequencing to identify diseases.

1 Get Brexit Done, Unleash Britain's Potential (The Conservative and Unionist Party Manifesto 2019): https://www.conservatives.com/our-plan

3. **Research: Supporting fundamental and translational research and ensuring a seamless interface between research and healthcare delivery.** We will focus on:

    - **Data to support innovation:** We will make the UK the best place in the world to access genomic data for research. We will also get the underpinning infrastructure and standards right, and coordinate the development and adoption of standardised data access processes, tools and conventions for the major health data controllers.

    - **Responsible use of data:** We want genomics to be an exemplar for the responsible use of health data for patient benefit and will make this a core tenet of our approach.

    - **Ensuring diversity and equity of access:** We will develop robust systems of outreach and communication to diversify our genomic datasets. This will address the ethnic bias historically seen in most large genetic datasets and help ensure equity of access to genomic healthcare.

Alongside these three pillars, we will focus on five cross-cutting themes:

A. **Engagement and dialogue with the public,** patients and our healthcare workforce, placing the patient and the diverse UK population at the heart of this journey.

B. **Workforce development** and engagement with genomics through training, education and new standards of care.

C. **Supporting industrial growth in the UK,** facilitating entrepreneurship and innovation for projects and companies of all sizes, through common standards, funding, procurement, and R&D structures.

D. **Maintaining trust** through strong ethical frameworks, data security, robust technical infrastructure and appropriate regulation.

E. **Delivering nationally coordinated approaches to data and analytics.** This will enable healthcare professionals and approved researchers to easily access and interpret our world-leading genomic datasets.

At the end of each section we set out measures of success; a mixture of specific targets, and long-term ambitions to monitor progress in delivering on this vision which, combined, will deliver on the Government's overall commitment to reach five million genomic tests and analyses.

The UK has prioritised clinical impact, research, and innovation in genomics for decades. Our continued funding for and focus on the power of genomics has resulted in a diverse and complementary ecosystem of projects and programmes which draw together our key strengths in science, research and technology. We believe we can achieve the aims of this strategy because we have all of the ingredients to succeed: the commitment at Budget 2020 to increase public spending on R&D by £22 billion by 2025, putting the UK on track for 2.4% of GDP being spent on R&D by 2027, a world leading academic and science base with access to skilled people, and technology and financial expertise to collaborate and deliver maximum impact for patients.

The strategy is UK-wide, but it is important to note the differences in the evolution and development of genomics in healthcare across the four nations. Since health is devolved, decisions about whether and how to implement specific elements of this strategy will necessarily be made separately by the four administrations. These decisions will differ to accommodate the different needs of the populations in the four nations and the structures and systems of the NHS in each administration. This brings great opportunities for sharing of expertise and best practice, but also some challenges, in particular around data sharing and equity of access. Through working together we can help realise the potential for genomics to improve healthcare across the UK and globally.

Strategy structure

Diagnosis and personalised medicine

Incorporating the latest genomic advances into routine healthcare to improve the diagnosis, stratification and treatment of illness

Prevention

Enabling predictive and preventative care to improve public health and wellness

Research

Supporting fundamental and translational research and ensuring a seamless interface between research and healthcare delivery

Engagement and dialogue with the public, patients and our healthcare workforce, placing the patient and the diverse UK population at the heart of this journey.

Workforce development and engagement with genomics through training, education and new standards of care.

Supporting industrial growth in the UK, facilitating entrepreneurship and innovation for projects and companies of all sizes, through common standards, funding, procurement, and R&D structures.

Maintaining trust through strong ethical frameworks, data security, robust technical infrastructure and appropriate regulation.

Delivering nationally coordinated approaches to data and analytics. This will enable healthcare professionals and approved researchers to easily access and interpret our world-leading genomic datasets.

Chapter 1: Introduction

We have a long and proud history of advancing genomic medicine to benefit patients. From the discovery of the structure of DNA almost 70 years ago, through our vital contribution to the Human Genome Project at the turn of the century, to the delivery of the 100,000 Genomes Project less than two years ago, the UK remains at the vanguard of pioneering science and healthcare.

Genomics is revolutionising the way we think about healthcare. It is providing us with a far more detailed understanding of what causes illness and infectious disease and is underpinning the development of new interventions that would have been unthinkable even a decade ago.

We are at an important juncture in the history of genomic healthcare. Rapidly decreasing sequencing costs combined with increased computing power mean we are able to understand the human genetic code like never before. We are well-placed to harness advances in our understanding of genomics to respond quickly to evolving threats, including COVID-19.

We are clear that all of our work in this area must be done in a way that addresses historic imbalances and inequity of access, and it is therefore fundamental to our vision that diversity in genomic datasets is improved.

We must re-focus the healthcare system more towards prevention, earlier detection of disease, and promotion of wellbeing, rather than simply the diagnosis and treatment of illness. Genomics will be an integral and crucial aspect of the future of the NHS, and our vision is for genomics to be used widely in mainstream healthcare, having established our leadership in the science over recent years. As the UK recovers from the COVID-19 pandemic it makes it all the more important that the NHS moves effectively from a treatment to a prevention organisation.

A thriving genomics industry composed of companies of all sizes will be key to achieving our ambitions. We will create high quality jobs and generate inward investment through our ground-breaking research: developing products, services, and intellectual property in the UK, which can be exported to the rest of the world. Alongside traditional life sciences companies, smaller genomics companies are being created across the UK and are part of a growing £1.9bn economic contribution in 2018/19. Industry participation is vital to achieving our goals, and we will ensure that the UK is open for business and remains the go-to destination for genomics companies.

To achieve this, it is essential that we – government, patients, the public, healthcare professionals, researchers, charities, and anyone working in this area – work together and develop our understanding, so that we are all informed, educated and able to communicate about genomics and health effectively.

There is a huge breadth of world leading genomic activity in the UK, and we have set out some of the key population-level projects across the genomics space below. But beyond this, major cohorts, small scale studies and a multitude of programmes are underway to understand and enhance the role of genomics in healthcare, from small academic research groups to multi-million pound research programmes. These initiatives all have different focuses and approaches, but what unites them is the commitment to delivering tangible benefits for patients through genomics, both now and in the future, and the opportunity to bring data together for patient benefit.

There are of course a huge number of factors that affect our physical and mental health and wellbeing. This strategy focuses on genomics in healthcare, but the determinants of health are enormously influenced by environment and lifestyle, often entirely independently of our genome. Any future healthcare approach must combine and incorporate these various factors. It is implicit throughout this document, but should be explicitly stated here, that the decision to implement new genomic technologies must be based on the latest, robust evidence. We will consider a broad range of evidence and advice including across medical and social sciences, ethics, and economics.

In order to make the whole greater than the sum of the parts, we are calling for the adoption of a shared set of principles that the genomics community can unite behind. We worked with a wide range of stakeholders and experts from across the UK to identify the principles which the community believes underpin the work they do and the decisions they take. We have done so under the leadership of the National Genomics Board, which advises on the development and implementation of genomics policy in the UK. We hope that by setting out these principles here we can provide a framework and reference point for decision makers to carry out their work, whether that be clinical care or research.

Working together on genomics: Our shared principles

1. Patients and the public will be at the heart of everything we do. We will work to reduce health inequalities, ensuring evidence-based genomics-driven healthcare is valuable and accessible to all.

2. Health care systems and research programmes will work in partnership for patient benefit. This will include the public, third and private sectors. We will encourage the availability and appropriate use of data for research and innovation that serves the public interest, while promoting the protection of privacy and data security.

3. Patients and the public should be enabled to have access to their own genomic and health information and have an appropriate voice in the use of their data for research.

4. We will prioritise workforce training and development to keep pace with our ambitions.

5. All genomics healthcare and research programmes will incorporate robust ethical frameworks to maintain best practice, transparency, and trust.

6. We will be open to working internationally to advance our shared understanding of genomics, including in infectious disease response.

7. We will adhere to a common set of protocols and standards to ensure data, information, and samples can be widely accessed and re-used for research and health benefits.

8. The four nations of the UK will work together to realise the potential of genomics for the benefit of patients and ensure that the genomics services thrive in each nation. We will engage in open dialogue and collaboration, recognising that health is devolved and there are differences in NHS structure and systems.

Improved Patient Outcomes

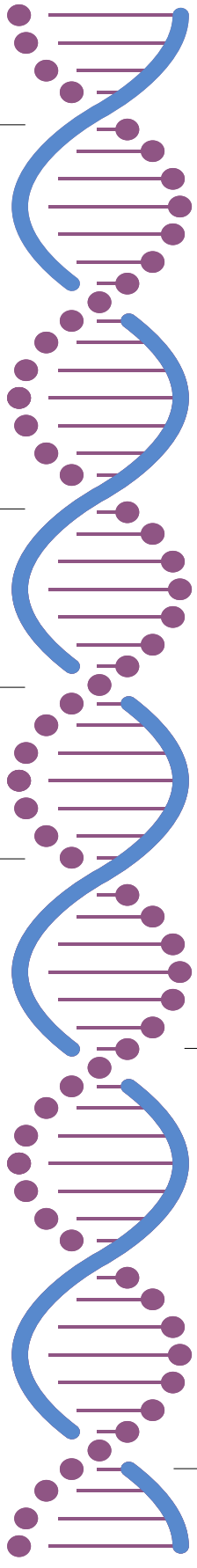
Diagnosis and personalised medicine

Prevention

Research

Key UK infrastructure	Genomics England and genomic testing in the NHS		ADD challenge	UK Biobank	NIHR BioResource
Unique capability	Delivering cutting-edge genomics services to the NHS A pioneering research library powering academic and industry research	Clinical diagnostic testing for NHS patients embedding WGS into routine care for the first time	Long-term prospective cohort for early detection research at an unprecedented scale	World leading long-term prospective cohort research	Vast recruitment platform to support early translational research
Population	**100,000** participants with rare diseases and cancer	Provision of genomic testing across the UK, including at least **500,000** whole genomes in England by 2024	**5 million** participants	**500,000** participants healthy at the time of recruitment	**200,000-400,000** participants with rare or common diseases or healthy at the time of recruitment
Genomic data	Whole genome sequencing	Whole genome sequencing and non-whole genome sequencing	Genotyping – PRS	Whole exome sequencing and whole genome sequencing	Whole genome sequencing or genotyping
Complementary data	Phenotypic and long-term clinical data collection	Phenotypic and long-term clinical data collection	Health-related data	Deep phenotyping and health-related data	Deep phenotyping, metabolomics, health-related data, medical records
Bio-sampling	✓	✓	✓	✓	✓
Clinical feedback	✓	✓	✓	×	✓
Recontact	✓	✓	✓	✓	✓
UK-wide	✓	✓	✓	✓	✓

Milestones in genomics



1953
The DNA double helix structure is identified

1961
Genetic code deciphered

1977
Sanger sequencing is developed

1983
Polymerase chain reaction (PCR) is developed

1985
First NHS funded DNA diagnostic service is launched

1990
Human Genome Project begins

1997
DNA sequencing used within NHS diagnostic services

1999
First human chromosome (22) is sequenced

2001
Molecular testing for BRCA1 and BRCA2 mutations in high-risk families

2003
Human Genome Project is completed

2007
Landmark Wellcome Trust Case Control Consortium genome wide association study of seven common diseases

2012
UK government announces 100,000 Genomes Project

2013
First multi-gene sequencing diagnostic test for tumour profiling in the NHS

2015
First patients enrolled in 100,000 Genomes Project receive diagnoses

2017
Release of genome-wide genotype data on all 500,000 UK Biobank participants

2018
100,000 Genomes Project reaches its target of 100,000 whole genomes sequenced

2020
Routine use of whole genome sequencing in the NHS

2020
First 50,000 UK Biobank participants receive a whole genome sequence

Page intentionally blank

Chapter 2: Three pillars

Pillar 1: Diagnosis and personalised medicine – incorporating the latest genomics advances into routine healthcare to improve the diagnosis, stratification and treatment of illness

Vision: We will help people live longer, healthier lives by using new genomic technologies to routinely identify the genetic determinants of rare diseases, infectious diseases and cancer. We will detect cancers earlier, and we will provide personalised treatments to illness.

Over the next ten years we will continually evaluate genomics technologies and their applications to bring the greatest benefit to UK patients, ensuring they are implemented into our healthcare system at the earliest opportunity.

As we learn more about the role and function of the genome in disease, the implementation of genomic technologies in routine healthcare becomes ever more impactful. Most patients with genetically mediated disease will not be aware that the genes responsible may not yet have been identified and that it is only through detailed further analysis of their genomes that the cause of their disease can be uncovered. Concerted efforts will need to be made to facilitate this process for the benefit of patients whose diseases are not yet fully understood.

As part of NHS England and NHS Improvement's contribution to the UK Government's broader aims to reach five million genomic tests and analyses, NHS Genomic Medicine Service (GMS) will sequence 500,000 whole genomes by 2023/24. This builds on the legacy of the ground-breaking 100,000 Genomes Project, which was made possible because of the unique partnership between Genomics England and the NHS. Under the GMS seriously ill children who are likely to have a rare genetic condition, children with cancer, and adults suffering from certain rare conditions or specific cancers, will be offered WGS.

And, as we introduce WGS into mainstream care, we must also integrate new ways of working to interpret rare variants: bringing clinicians and approved disease-expert researchers together to solve individual patient cases. This means creating a new learning healthcare environment where clinicians and researchers can work together effectively to maximise learning from genomic data and implement that learning into healthcare.

Using genomics to diagnose and stratify both inherited and acquired disease is already becoming a reality together with targeting treatments to known genomic variants. Pharmacogenomics will enable the most effective provision of tailored therapies so that patients get the treatments and advice that work for them. This not only leads to improved outcomes for the patient but reduces negative outcomes such as adverse drug reactions, which have a considerable impact on the NHS. This will increase as the evidence base grows, enabling the expansion of personalised treatments.

This makes it all the more essential that we are able to translate these advances through to rapid development, assessment, and access to innovative new medicines for patients. Tackling the complex barriers faced when bringing new medicines into the NHS will require strong joined up pathways across the health system, exploring new commercial flexibilities, better use of real world data and updated assessment methodologies.

Headline Initiative – Genomics England, the 100,000 Genomes Project and the NHS Genomic Medicine Service

Genomics England and the NHS delivered the 100,000 Genomes Project, proving the value of WGS for rare disease and cancer in routine care. This legacy is being built upon by the NHS Genomic Medicine Service (GMS) in England, which will provide WGS as part of routine care.

The new NHS GMS will be supported by an informatics platform – the National Genomic Informatics Service (NGIS) – and a network of National Genomic Laboratory Hubs (GLHs) that will deliver an integrated system for genomic testing. NHS England and NHS Improvement, in collaboration with Genomics England, will work to further transform pathways of care and create the multi-disciplinary teams and cross-professional infrastructure that will be critical for the future.

The NHS GMS is supported by a comprehensive National Genomic Test Directory of genomic tests for specified cancers and rare diseases that encompasses the entire testing repertoire from WGS to single gene tests. This will be updated on an annual basis, ensuring that everyone has equitable access to high quality genetic testing, where the evidence shows it could improve their care.

A new NHS Genomic Medicine Service Research Collaborative led by NHS England and NHS Improvement, the NIHR, and Genomics England will establish a coordinated approach to embedding research and discovery to advance clinical care ensuring patients gain maximum benefit from research and innovation, with breakthroughs enabling prevention of ill-health, earlier diagnosis, more effective treatments, better outcomes and faster recovery.

The Genomics England research library will continue to be populated through these initiatives ensuring that genomics is at the centre of transformation of healthcare in the UK by providing researchers with access to high quality data and informatics. This research is fundamental to improving diagnoses, treatments and care for patients across the world.

The Scottish Genome Partnership

The Scottish Government, with co-funding from the Medical Research Council, has invested in the Scottish Genomes Partnership (SGP) – a collaboration of Scottish Universities and NHS building on WGS capabilities at the Universities of Edinburgh and Glasgow. SGP is piloting genomic testing of patients in Scotland with rare genetic diseases in collaboration with Genomics England and the 100,000 Genomes Project and has been supporting genomic research on a range of cancers, rare genetic diseases, and also an established Scottish population cohort. This has provided a platform to enable academics, NHS Scotland as well as industry to engage in genomics research, development, and implementation. The research has found new genes and genomic structural information which can lead to new diagnoses and strategies for managing disease. The investment in infrastructure, skills and joint working practices is expected to have long term impact. As well as new genomic analysis pipelines and datasets, SGP has enabled training of new clinical scientists, genetic counsellors and bioinformaticians in addition to growing the skills, knowledge and understanding of those already working in the field.

1: Cancer

Cancer is primarily an acquired disease of the genome. Genetic variations and rearrangements all contribute to the make-up of the disease, meaning genomics-led diagnosis is critical to understanding cancer better.

Half of all people born in the UK will be diagnosed with cancer in their lifetime[2]. For many of these, early diagnosis means better prospects for treatment and longer survival. To take one example, when bowel cancer is diagnosed at the earliest stage, more than 9 out of 10 people survive at least ten years. However, if diagnosed at late stage survival falls to below 1 in 20.[3]

Similarly, delayed treatment can lead to a lower likelihood of survival, greater treatment morbidity, and higher costs of care. The current waiting time target is no more than one month between the date a hospital receives an urgent referral for suspected cancer and the start of first treatment. Fast turnaround times for molecular diagnostics are therefore a vital aspect of informing treatment decisions and reducing treatment delays.

Our aims are to:

(1) prevent and identify cancer earlier by harnessing emerging genomics technologies including long-read sequencing, circulating tumour DNA, and RNA sequencing.

---

2 Smittenaar CR, Petersen KA, Stewart K, Moitt N. Cancer incidence and mortality projections in the UK until 2035. *Br J Cancer*. 2016;115(9):1147-1155. doi:10.1038/bjc.2016.304

3 Achieving World-Class Cancer Outcomes: A Strategy for England 2015-2020 Report. https://www.england.nhs.uk/publication/achieving-world-class-cancer-outcomes-a-strategy-for-england-2015-2020/

(2) design, pilot and iterate a new operating model for cancer involving multiple genomic testing approaches and ensuring multi-disciplinary teams can draw on multimodal data across imaging, genomics and longitudinal health and care data.

(3) develop the next generation of technology-enabled infrastructure to support cancer clinical teams in maximising the impact of the new operating model.

(4) delivering on the promise of genomic-enabled clinical trials, with more cancer patients than ever participating.

We will continue to extend the use of molecular diagnostics and, over the next ten years, the NHS will routinely offer genomic testing to all people with cancer for whom it would be of clinical benefit. Our ambition for the future system is that genomic tests will be linked with medical records and other data such as digital pathology information, to identify the optimal treatments for cancer. We expect that most future cancer therapies will be targeted to tumours based on specific genomic and other biomarkers. Panel testing is widespread in the diagnosis of cancer but in the next few years, as the cost of sequencing falls below these tests and where turnaround times meet clinical needs, where appropriate WGS will be used to further stratify cancers to inform intervention and treatment options.

We also expect to start to see long-read sequencing technology increasingly deployed for cancer patients. Initially, short reads may be combined with longer reads since the two methodologies have differing, but complementary strengths in detecting different categories of DNA mutations, rearrangements, and methylation patterns. The validation provided by comparing the two outputs may lead to a reduction in the total number of reads required, thus reducing overall cost. In addition, other components of the functional genomics pathway, such as RNA based sequencing, will be employed in the diagnosis of cancer.

We anticipate the increasing implementation of new tests to detect cancer relapse earlier and more effectively. Using certain types of tumour DNA, relapsing cancer could be detectable as much as 200 days before relapsed disease appears on a CT scan, enabling any recurrence to be swiftly identified. This could allow more regular testing for early detection, facilitate rapid development and deployment of targeted immunotherapies, and better more targeted monitoring relieving the burden on high-demand NHS services.

In Wales and Scotland circulating tumour DNA (ctDNA) technologies have led to the early implementation of clinical services for cancer patients. Since 2017, Wales has offered a ctDNA service for Non-Small Cell Lung Cancer (NSCLC) patients and metastatic colorectal cancer. This technology has presented an opportunity for improved stratification of these cancer patients for treatment.

Genomics in practice: Comprehensive, precise molecular diagnosis of Chronic Lymphocytic Leukaemia (CLL)

Chronic Lymphocytic Leukaemia has a number of well recognised subtypes, defined by differences in the underlying genomic changes, each of which has a different prognosis and response to treatment. Comprehensive genomic analysis is therefore an essential part of the diagnostic process for CLL, enabling patients to benefit from a personalised approach to the management of their disease.

Researchers based at the University of Oxford Department of Oncology have pioneered the development of a long-read nanopore sequencing based assay that delivers the complete molecular analysis of CLL in a single test, by combining long read WGS with targeted deep sequencing of specific genes that are implicated in the disease to deliver highly accurate results. Taking advantage of the real time nature of nanopore sequencing this group has developed a fast, accurate, affordable test to improve the delivery of precision medicine for CLL[4].

2: Rare and Inherited Diseases

Although rare diseases are individually uncommon there are more than 6,000 of such conditions meaning that 1 in 17 people, or 6% of the population, will be affected by a rare disease at some point in their lives. This equates to approximately 3 million people in the UK, and a single rare disease may affect up to 30,000 people.

80% of rare diseases have a strong genetic component. Some conditions are discoverable by relatively simple genomic assays but whole genome and exome sequencing for rare diseases provides several important benefits. Diagnosis not only provides an often long sought-after answer to what is causing a condition but can also inform treatment decisions for the patient, as well as providing insight to parents into the potential risk of future children being similarly affected.

The NHS in England will be the first national healthcare system to offer WGS as part of routine care via the NHS Genomic Medicine Service. Currently, most of the genetic testing performed within the NHS does not extend to WGS, but this will become increasingly possible as approaches to genetic testing in rare diseases are standardised and the use of WGS is extended to all rare disease patients without a genetic diagnosis. However, most of the genetic testing performed within the NHS is currently non-WGS.

Our aims are to:

(1) continue to increase the diagnostics rate from genomic testing and explore opportunities for re-analysis of genomic databases where we have increased our understanding over time.

(2) continue to reduce the time people wait for a rare disease diagnosis.

---

4 Burns, Adam et al. “The diagnostic chronic lymphocytic leukaemia genome by nanopore sequencing.” Biorxiv (2019). https://www.biorxiv.org/content/early/2019/08/28/750059.full.pdf

(3) make it easier for researchers to feedback findings that are relevant to a patient's care, in a way which protects privacy and maintains trust.

(4) make it easier for patients with rare diseases to be enrolled in specialist clinical trials working in their disease area.

In the short to medium term, the current centralised provision of short-read sequencing will continue to be the model for sequencing of rare diseases. We will look to extend the use of advanced diagnostics such as WGS to all rare disease patients and we will continually evaluate genomics technologies and their applications to make sure we give the right test to the right patient at the right time. Genomics England has built, together with clinicians in the NHS and involving patients from across the UK, the largest single dataset of rare genetic variants, their associated clinical phenotypes, and healthcare data anywhere in the world. We expect to see increasingly productive collaborations between clinicians and researchers to decipher rare variants that are currently of unknown clinical significance. Furthermore, understanding the functional genomics of rare variants can provide crucial clues to potential therapies for more common diseases.

As the Genomics England dataset continues to be analysed and these collaborations develop, research will feed into clinical practice so that more patients will receive a diagnosis, more families will be able to make informed decisions about having children, and more new treatments will be developed to offer hope to those with currently untreatable conditions. It is vital that we can translate this through to rapid assessment, and access to innovative new medicines for rare disease patients.

Genomics in practice: Genomic testing to fast track diagnosis for critically ill babies and children

Genomic testing is being introduced into routine care for patients in neonatal or paediatric intensive care units who have serious health problems with a likely genetic cause. The use of sequencing not only increases the chance of a diagnosis but can reveal the underlying genetic cause of a condition within a matter of days. The NHS in England has implemented Whole Exome Sequencing whilst NHS Wales has already developed a limited rapid WGS service.

3. Pharmacogenomics

Genetic variants in an individual can be used to predict the likelihood that a particular drug will (a) be effective and (b) cause unintended harm through an adverse reaction.

Adverse reactions to medications account for 6.5% of UK hospital admissions and result in a median hospital stay of eight days. Admissions related to Adverse Drug Reactions (ADRs) cost the NHS an estimated £466m annually.[5]

Increasing routine genomic testing in the NHS particularly in England includes relevant targets to guide treatment or eligibility for clinical trials particularly in cancer. This ambition was set out in NHS England's 'Improving outcomes through Personalised Medicine'[6] vision published in 2016.

To further understand the opportunity to introduce pharmacogenomic panels for gene drug pairs for more common medicines, NHS England and NHS Improvement and Genomics England have established a pharmacogenomics working group, composed of experts from across the UK. This group has been reviewing the evidence to understand the implication of implementing targeted pharmacogenomic testing in the NHS and the approach to implementation including data and messaging requirements.

The Welsh Government's Genomics for Precision Medicine Strategy[7] notes the anticipated increase in the clinical utility and requirement for pharmacogenetic testing in the near future and advises that services will be prioritised based on clinical need and Welsh expertise. A commitment is made to release funding for genomic investigations through the substitution of more costly investigations, or the cost-avoidance of treatments where these will be ineffective or harmful. The Medicines Strategy for Wales[8] commits to reducing the burden of adverse drug reactions. A pilot study is underway to address and inform the challenges of implementing a national pharmacogenetics service in Wales. The outcomes of the pilot study will be to direct future testing strategy for patient benefit and identify further funding opportunities.

---

5 Pirmohamed, Munir et al. "Adverse drug reactions as cause of admission to hospital: prospective analysis of 18,820 patients." BMJ (*Clinical research ed.*) vol. 329,7456 (2004).

6 Improving Outcomes Through Personalised Medicine (NHS England, September 2016): https://www.england.nhs.uk/publication/improving-outcomes-through-personalised-medicine

7 Genomics for Precision Medicine Strategy (Welsh Government, July 2017): https://genomicspartnership.wales/genomics-precision-medicine-strategy/

8 All Wales Medicines Strategy Group (AWMSG) Five-year Strategy 2018–2023: https://awmsg.nhs.wales/about-us1/our-strategy-and-annual-reports/awmsg-5-year-strategy-2018-2023/

The Welsh Government's Genomics for Precision Medicine Strategy

The Welsh Government's Genomics for Precision Medicine Strategy, published in July 2017, sets out an ambitious plan 'to create a sustainable, internationally-competitive environment for genetics and genomics to improve health and healthcare provision for the people of Wales'.

'Partneriaeth Genomeg Cymru – Genomics Partnership Wales (GPW)' was established in 2018 to support a collaborative approach to genomics in Wales. It represents several disciplines coming together to deliver a transformational programme of work that will realise the benefits from collaborative action. Partners include: patients and the public, NHS Wales' All Wales Medical Genomics Service, Public Health Wales' Pathogen Genomics Unit, Wales Gene Park, Higher Education Institutions in Wales, Welsh Health Specialised Services, NHS Wales Informatics Service, Health Education Improvement Wales, NHS Wales and Welsh Government.

The national programme follows the Prudent Healthcare philosophy and represents our approach to ensure that genomics for precision medicine becomes mainstreamed across health and care in Wales through its five core themes; co-production, clinical and laboratory services, research and innovation, workforce, and strategic partnerships. The programme is in line with 'A Healthier Wales'[9] - our long term plan for Health and Social Care, as well as the UK Life Sciences Strategy[10], in recognising the importance of earlier and more personalised diagnostics to prevent illness, intervene appropriately and prolong independent living. Our genomics strategy also aligns with the principles of the Quadruple Aim; 1) Improved population health and wellbeing, 2) Better quality and more accessible health and social care services, 3) Higher value health and social care and 4) A motivated and sustainable health and social care workforce.

9 A Healthier Wales: Our Long Term Plan for Health and Social Care (Welsh Government, June 2018): https://gov.wales/healthier-wales-long-term-plan-health-and-social-care

10 Life Sciences Industrial Strategy – A report to the government from the life sciences sector (August 2017): https://www.gov.uk/government/publications/life-sciences-industrial-strategy

Within the next ten years, if supported by the evidence, it is the ambition of this strategy that we adopt a pre-emptive approach whereby patients have a pharmacogenomic profile attached to their medical records. This will support clinicians in all cadres in making therapeutic decisions for the benefit of patients. We also expect to see a combination of simple gene-drug pairing analysis and generation of pharmacogenomic profiles based on common variant analysis. Successful implementation in England will necessitate coordinated working across a wide range of stakeholders including the NHS, Genomics England, MHRA, and NICE.

This will benefit patients by increasing the efficacy of their treatment and reducing the incidence and severity of adverse drug reactions; and contribute to the fight against anti-microbial resistance through overall efficiency of drug prescription.

Genomics in practice: DPYD gene testing

Fluoropyrimidines (5-fluorouracil, capecitabine and tegafur) are drugs used in colorectal cancer chemotherapy, and are also commonly used in other cancers (including oesophago-gastric, breast, head, and neck cancer). Treatment with fluoropyrimidines is generally well tolerated. However, 3-6% of patients suffer serious adverse drug reactions as a result of genetic mutations in their DPYD gene which mean they are unable to properly metabolise and breakdown these drugs. This can result in prolonged hospitalisation in intensive care and, in some cases, can be fatal.

All four nations of the UK are introducing genetic testing for the common DPYD mutations in cancer patients. Although the test does not remove all treatment risk, it does reduce the incidence of toxicity which can save lives. Furthermore, the test will continue to be improved as more becomes known about the mutations that alter the metabolism of this class of cancer drugs.

4: Infectious Disease

Genomics has already transformed the way disorders caused by pathogens are diagnosed, studied, and treated. The UK was among the first in the world to use pathogen WGS for public health management of communicable disease. WGS is recognised as a transformative technology in understanding transmission of disease in populations, and in identifying and managing outbreaks. It can also be used to predict antimicrobial resistance and describe how pathogens evolve.

In England, our National Infection Service (NIS) laboratories have sequenced almost 200,000 microbial genomes, including for serious and highly infectious diseases such as TB, influenza and Hepatitis C, and pathogens associated with foodborne outbreaks. As part of the Welsh Government Genomics for Precision Medicine Strategy, the Pathogen Genomics Unit was launched within Public Health Wales in 2018, and now provides accredited diagnostic and surveillance services for a range of pathogens including HIV, TB, C. difficile and Influenza. The pre-existing capacities within England and PHW have formed an important part of the COVID-19 Genomics UK Consortium (COG-UK), which

represents a truly national collaboration covering the NHS, all four UK Public Health Agencies and research institutes from across the UK. COG-UK has sequenced more than 50,000 SARS-CoV-2 genome sequences, data that is being used in real time as part of the pandemic response across the UK at every level – from local outbreaks up to the provision of advice to SAGE.

These data enable researchers to assess the emergence of resistant mutations arising from health interventions and treatments, identify genetic markers associated with clinical severity and, when combined with human genomic data, can assess multifactorial disease risk determinants and their correlation with clinical severity. Viral sequencing for SARS-CoV-2 is being used increasingly across the UK to support the understanding of transmission and outbreaks and will be considered as part of our future testing response.

Our aims are to:

(1) use genomics to deepen our understanding of how and why different people's immune systems respond in different ways to pathogens e.g. COVID-19.

(2) explore the potential to develop genetic tests for individual risk stratification for a given infectious disease.

(3) use genomics to support, where appropriate, the development of vaccines and therapeutics to respond to infectious disease.

To underpin and further expand WGS services it is vital to maintain and develop the right data analytics systems to process, analyse and interpret genomic data, and it is critical that results produced are comparable between laboratories. The public health agencies are working with world leading UK research expertise to collaboratively design and implement improvements to their genomic data systems, using best coding practices and cloud-based technologies. These platforms will help to ensure that results are generated consistently across the UK, will ensure that every patient in the UK is able to benefit from the application of genomics to fight infectious disease and will collectively keep the UK at the forefront of clinical pathogen genomics.

Technological advances mean that sequencing is being increasingly performed locally to provide rapid turnaround time data. Miniaturised sequencing technology is increasingly being deployed near to the patient, giving real-time sequence data to inform clinical decision-making. This is only set to increase and improve as new sequencers become more readily available and clinically useful, allowing close to real time genomic analysis of disease.

Genomics in practice: GenOMICC COVID-19 Human Whole Genome Sequencing Programme

Susceptibility to COVID-19 is almost certainly, in part, genetic. The Genetics of Mortality in Critical Care (GenOMICC) consortium is a severe infection network of over 160 Intensive Care Units (ICUs) across the UK, to deliver WGS of up to 20,000 people who required intensive care due to COVID-19, and up to 15,000 people who had mild symptoms of COVID-19.

Led by Edinburgh University, the consortium will read the data from the entire genomes of participants and compare the genomes of the two cohorts, along with clinical characteristics, with the aim of finding out whether genetic factors influence the severity of response to COVID-19.

The GenOMICC study[11] complements the UK COVID-19 Viral Sequencing Programme (COG-UK) which is sequencing the genomes of viruses isolated from COVID-19 patients.

To achieve, maintain and measure success over the next ten years we will:

- Ensure the NHS is ready to evaluate and implement all clinically-relevant, genomic technologies and novel genomic healthcare applications based on the latest, robust evidence from experts at the forefront of their fields across the UK and globally.
- Support the join up of the NHS and research community with scalable and secure informatics systems, both for clinical decision support and large-scale data processing and analytics.
- Secure the best value per clinical whole genome sequence anywhere in the world, and help ensure that new clinically-relevant technologies become more widely available at a competitive price.
- Offer genomic testing to all people with cancer for whom it would be of clinical benefit.
- Create a healthcare environment where clinicians and researchers can work together effectively for the benefit of individual patients; breaking down the current cultural and structural barriers that prevent this model from being standard of care for all.
- Offer all patients with a rare genetic disorder a definitive molecular diagnosis using tests that will support research into their condition wherever possible.
- Have a clear evidence-based position on whether and how pharmacogenomics should be implemented in the health service at scale.
- Sequence pathogens quickly and easily using point of care sequencing technology,

11 https://genomicc.org/

helping us control outbreaks and fight antimicrobial resistance.

- Understand the role of the genome in differing patient outcomes from infectious disease.

- Rapidly utilise advances in sequencing technology to develop and deploy new diagnostics and support better, more integrated, surveillance of infectious diseases.

- Provide international leadership in supporting the development of best practice in infectious disease genomics and public health, through international projects such as the Global Alliance for Genomic Health, the Public Health Alliance for Genomic Epidemiology.

Pillar 2: Prevention – Enabling predictive and preventative care to improve public health and wellness.

Vision: We will use genomics to accurately predict the risk of chronic diseases and our national screening programmes will use genomics to identify at-risk populations.

Preventing disease before it begins is key to our future healthcare system and requires the right technology, large diverse datasets, and validated analytical tools to predict the risk of disease. Effective disease prevention benefits not just the individual but the healthcare system as a whole. We know that waiting until a patient presents to hospital with a condition leads to worse health outcomes and increased care costs.

As healthcare costs continue to rise, investing in genomics-based screening – with the enduring principles we apply to all screening programmes – can help to mitigate disease through effective early intervention. We will shift away from a health and care system focused on diagnosing and treating illness and towards one that is based on preventing ill health and promoting wellbeing.

1: Expanding screening in early life

The newborn blood spot test currently tests for nine rare but serious conditions to diagnose conditions for which interventions are available before symptoms appear. We know there are other similar, rare but treatable, genetic conditions that cannot be detected using this approach.

Recent improvements in genomic sequencing offer the chance to rethink our approach. The UK National Screening Committee recently reported that there is clear potential for genomics in the testing for many of the conditions currently included in the blood spot test.[12] WGS could significantly increase the diagnoses of other genetic conditions, which is particularly valuable if early detection reduces or avoids harm in early life or improves long term outcomes from the condition. Initial investigations indicate that this has the potential to enable a major NHS transformation, delivering benefit to thousands of children who

12 Generation genome and the opportunities for screening programmes (Public Health England, 2019) https://www.gov.uk/government/publications/generation-genome-and-the-opportunities-for-screening-programmes

would benefit from early intervention to reduce or avoid harm in early life.

The UK has in the region of 97% uptake of newborn screening and strong public engagement in genomic medicine. Together with our world-leading genomic infrastructure embedded in the NHS, this makes the UK uniquely placed to conduct a high quality, large-scale research programme to determine whether and how sequencing should be implemented for screening in newborns.

Such research would need to include a study of opportunities, risks and the ethical and regulatory issues involved. Following a recommendation from the previous Chief Medical Offer (CMO), Professor Dame Sally Davies, there is in progress a public conversation to generate better understanding of patient and public attitudes. Thinking about a genome sequence as a resource to be accessed at particular times in life (rather than disclosed all at once), may be a helpful starting point for the ethical discussions that need to accompany a large-scale research programme.

2: Reproductive genomic screening

The recognition that fetal DNA circulates in maternal blood led to Non-Invasive Prenatal Testing (NIPT) based on sampling maternal blood to detect aneuploidies such as those associated with Down's Syndrome, reducing the need for invasive tests which are associated with an elevated risk of miscarriage.

We expect to see development of NIPT using sequencing to be able to identify conditions such as sickle cell disease in the near future, and it is foreseeable that WGS could detect inherited variants as well as de novo mutations causing severe paediatric conditions. The observations that led to this technology were made in the UK and we see it as our responsibility to fully explore the ethical issues presented by future testing strategies alongside the developing science.

Pre-implantation genetic diagnosis (PGD) is a type of embryo testing that can be used by people who have a serious inherited disease in their family to avoid passing it onto their children. Only embryos that have been tested and found to be free of the condition are transferred into the woman's womb. Nearly 600 conditions have been approved for testing in the UK by the Human Fertilisation and Embryology Authority.

Genomics in practice: Non-invasive Prenatal Testing – first for Wales

Wales was the first UK nation to introduce Non-Invasive Prenatal Testing (NIPT). The test substantially reduces the number of pregnant women being offered invasive prenatal tests which come with an associated risk of miscarriage. The introduction of NIPT for fetal aneuploidies (Down syndrome, Edwards syndrome, Patau syndrome) has changed the field of prenatal screening in Wales and demonstrated significant cost efficiencies.

3. Adult screening

Analyses of UK Biobank have established proof of concept for the use of genetic information to substantially improve risk prediction for all the common diseases and cancers. These approaches, which combine information from large numbers (often millions) of common genetic variants across the genome into "polygenic risk scores" (PRS) offer a step change, through a new generation of robust risk prediction tools. The UK has played a central role in the scientific research underpinning these approaches and is well placed to lead the world into the new era of "genomic prevention": a prevention-first approach to healthcare built on targeting appropriate interventions and screening to high-risk individuals and subpopulations. Increasingly sophisticated risk-prediction tools will combine the genetic drivers of risk with non-genetic risk factors, including biomarkers and environmental and social factors.

Professor Sir Mike Richards' October 2019 Independent Review of Adult Screening Programmes in England highlighted the potential that genomic techniques, including PRS, could have in targeted screening. It is clear that the screening programmes of the future will need to be more targeted, NHS England's Long Term Plan and the Government's Advancing our health: prevention in the 2020's green paper published in July 2019 sets out our ambition to embed genomics into routine healthcare, to improve population health through disease prevention enabled by better screening. This includes the use of personalised and risk stratified screening and testing of the family members of cancer patients to identify where they are at increased risk of cancer.

One major advantage in applying genomic tools to define risk of common diseases is that it could allow prevention strategies to start early, for example initiating cardiovascular protection strategies in individuals in their 40s rather than waiting until other risk factors become evident in later life. Having established the potential, the next step is for implementation studies to learn how and where improved risk prediction can be used, disease by disease, in clinical pathways and in screening programmes, and how to do so in a way which reduces rather than increases the burdens on healthcare professionals. Parallel studies should assess the use of these approaches in population health management.

Of course, there are many societal, ethical, and logistical factors to consider, not least that benefit must outweigh harm. We do not take these lightly, and the UK advisory bodies will continue to assess them. But if we can identify people at higher risk of developing a condition, then the direction of travel must be towards more genomically-targeted screening and interventions. The intention is to take advantage of this to deliver a more efficient and effective screening service to patients.

Headline Initiative: Accelerating Detection of Disease Challenge

Built on the principles and lessons from the successful UK Biobank programme, the Accelerating Detection of Disease (ADD) challenge will recruit up to 5 million diverse participants to provide an unprecedented research resource which will empower the next generation of diagnostics, clinical tools, drug development, and smart clinical trials.

Polygenic risk scores will be calculated for at least three million of these participants. The scores will be made available alongside other data to researchers, while participants will be given the option of receiving personalised risk assessments incorporating their polygenic risk score results. The project will generate evidence that will help us understand the impact of giving people personalised health and risk information. This will contribute to decisions on whether and how polygenic risk scores should be implemented at scale in the health service and provide us with a basis for future screening decisions.

We know that polygenic risk scores have the potential to identify people with greater risk of diseases, who might then benefit from smarter, more targeted interventions and prevention approaches. By building the evidence now, we will maximise the likelihood that this rapidly developing area of science will translate into actionable benefits for patients in the future.

Analysis of the ADD data will yield powerful new insights. The ability to embed smart prospective medical studies within the ADD, with appropriate individual consent, will be transformational.

To achieve, maintain and measure success over the next ten years we will:

- Enable the NHS to move from a system that primarily detects and treats illnesses to one that utilises genomics to predict and prevent ill health.
- Continue to develop a public health and screening system that uses genomics to intensify screening and interventions in those at high risk.
- Establish a clear, evidence-based position on whether and how genomic sequencing should be implemented for newborns, and how that genomic data could inform their care later in life.
- Formulate a clear evidence-based position on whether and how PRS can be best utilised at scale in the health service.
- Explore how genomic testing can continue to be best used in reproductive medicine to support parents to make informed choices.

Pillar 3: Research – Supporting fundamental and translational research and ensuring a seamless interface between research and healthcare delivery.

Vision: We will extend the UK's world-leading position at the forefront of discovery-led and translational genomics research, continually expanding our collective genomics knowledge base. We will develop an ecosystem of world-leading secure genomics datasets, powering international research and supporting a seamless transition of impactful research findings into the healthcare setting backed up by robust implementation research programmes.

The UK leads the way in genomic research, and we will support a virtuous circle of health and genomic data feeding and accelerating research, which then provides new insights that are integrated into healthcare systems at pace. Datasets of significant depth and breadth, readily accessible and well curated, are necessary to maximise the benefits of research. This means integrating vast amounts of genomic data with rich phenotypic data – including routine clinical and genomic data – and biosamples at scale, for which the UK has unique capabilities.

Our existing large-scale initiatives including but not limited to, Genomics England, the NIHR Bioresource, UK Biobank, and ADD are necessary, but not sufficient for the UK to maintain our global leadership. It is of paramount importance that we maximise, through functional analysis, the early returns from these data resources in terms of valuable new products and services capable of delivering transformational patient benefit. The development of new phenotyping technologies in addition to sequencing and the linking of consented genomic data and other health data will be essential features of this ecosystem. We will draw together the nation's capabilities across the academic, clinical, charitable, and industrial sectors and create an integrated discovery ecosystem that will be the envy of the world.

Finally, we must ensure that our datasets reflect the diversity of the UK population to ensure that research can power equitable benefit from focused healthcare.

1: Data-driven innovation and meeting patients' expectations about data use

The mainstreaming of emerging fields such as genomics and artificial intelligence (AI) will change the face of medicine. Advancements must be introduced in a way that involves and engages patients and the public in shaping implementation, is transparent about how data is used, and meets all legal and regulatory requirements.

Providers who are introducing new, data-driven technologies have called for clearer guidance about respecting the legal framework for data protection and confidentiality. The National Data Guardian intends to work with the Information Commissioner and others to improve the advice available so that innovation can be undertaken safely. And at the same time the Health Research Authority is clarifying and updating guidance on the lawful use of patient data in the development of healthcare technologies.

We want genomics to be an exemplar for the responsible use of health data for patient benefit. We do not take the trust that patients and the public put in us lightly. We will make

responsible patient data use the core tenet of our approach to genomics.

Coordination across the system is vital to achieving these objectives and an important first step has been the establishment of the Health Data Research Alliance which aims to coordinate the development and adoption of standardised data access processes, tools and conventions for the major health data controllers, to drive greater use of healthcare data for research and innovation.

All organisations working with Health Data Research UK (HDR UK) sign up to their 'Principles for Participation' to guide working practices and draw on national and international best practice frameworks. These include the 'five safes' – safe people; safe projects; safe settings; safe outputs and safe data – which provide multiple safeguards for ensuring the security and privacy of patient health data. This will ensure privacy and the ability to audit how data are being used.

HDR UK is developing guidance that will recommend that research on health data is undertaken in what's known as a Trusted Research Environment or Safe Haven rather than having data travel from the data controller to the data user. This approach was pioneered for genomic data by the Genomics England research library.

Health Data Research UK

Health Data Research UK (HDR UK) was established to enable the safe and responsible use of health-related data at scale. Working in partnership with patients, NHS, academia and industry across the UK, HDR UK has established the inter-related national capabilities necessary for a robust and scalable UK health data research infrastructure.

The UK Health Data Research Alliance is a partnership between the NHS and HDR UK. The purpose of the Alliance is to work in partnership to unite the UK's health data to enable discoveries that improve people's lives through the development and adoption of agreed standardised data access, processes, tools and conventions.

The UK Health Data Research Innovations Gateway is a common portal and a set of open software tools that will provide discovery, accessibility, security and interoperability to find data, support linkage, and enable health data science to take place in a safe and efficient manner.

2: Harmonising consent frameworks to maximise participation in research

Standardisation in consent processes increases consistency and familiarity for clinicians and patients, and facilitates greater interoperability between datasets.

A new consent model, termed 'hybrid patient choice', will support patients to make an informed decision about both whether they have a genomic test, coupled with discovery-led analysis into new variants discovered by sequencing, and whether they want to participate in research. Furthermore it is the Government's intention that a framework that builds on that being put in place for WGS will be extended to all types of genetic testing.

The differences in NHS structures and systems across the four nations will mean that each nation will need to develop its own hybrid patient choice model to be fit for purpose in their own context, however we are committed to working together to ensure that our consent frameworks are developed using a shared set of principles.

Obtaining specific consent for follow-up contact is crucial to realising the wider benefits of genomics. Re-contact enables patients to participate in follow-on research studies or clinical trials, as well as providing additional findings of clinical utility from re-interpretation of their genome.

Secondary, or additional, findings are genomic test results that provide information about changes within a person's DNA that are unrelated to the primary purpose for the testing. This might include an increased disposition to certain types of cancer. The information provided by secondary findings can be important because they could help prevent a disease from occurring or influence how a patient's care is managed. It is our ambition that the opportunity for patients to receive secondary findings will become a key principle of standardised consent processes. The NHS will use the evidence from the 100,000 Genomes Project to evaluate the ethical and resource implications of returning additional findings as part of the NHS Genomic Medicine Service.

Genomics in practice: Patient choice and consent

NHS England and NHS Improvement has worked with Genomics England to develop a hybrid patient choice model for patients in England undergoing clinical WGS to make a choice about whether they have a WGS and whether they want to participate in research. A version of this model will be adapted to apply across all clinical genomic testing offered by NHS England and NHS Improvement. Digitisation of consent will be a key feature of the National Genomics Informatics System (NGIS) which is being developed by Genomics England on behalf of the NHS and will provide a modern, digital service for collecting consent. This will result support uptake of research and benefit potential research participants through a quicker and easier to understand consent system.

The model for consent to genomics research in Wales is being developed by a group with expertise in ethics, legal frameworks, biobanking and information governance, as well as representatives from clinical and laboratory teams. The proposals for how patient consent for research should be managed will take into account existing ethical and legal principles, Welsh Government policy, and the consent approach implemented by other UK nations. The importance of research to patient benefit is central to discussions, and the group are working with the Genomics Partnership Wales (GPW) Patient & Public Sounding Board to ensure true co-production is taking place.

3: Functional analysis of genomic variation

Functional genomics is the study of how genes and other regions of the genome contribute to biological processes. Genome-wide functional analyses focus on the dynamic expression and interaction of gene products in specific contexts, for example in a diseased organ or tissue. The aim is to gain a better understanding of the functional impact of variants and thereby facilitate better understanding and diagnosis of disease and support more targeted drug discovery. In order to conduct tissue-specific analysis, it is important to have access to high-quality samples. We will explore how existing bio-sampling capabilities could be used to complement ongoing longitudinal research. The ability to prospectively collect bio-samples for research, within a clinical setting, will be an important part of the UK's functional genomics offer.

Functional genomic assays already have direct clinical relevance in the NHS, for example, RNA sequencing has started to be used more routinely in cancer diagnostics to increase diagnosis rates. As we move forward, we expect to see multiple assays across the functional analysis pathway offered to individual patients within the health service. The NHS National Genomic Test Directory, which mandates the tests available through the NHS in England, will be updated annually and it is anticipated that over time all evidence based use of components of the whole functional analysis pathway will be included.

Genomics in practice: Understanding the role of epigenetics in Inflammatory Bowel Disease

Inflammatory bowel diseases (IBDs) are chronic inflammatory disorders affecting the gastrointestinal tract. The genetics of IBD are complex, and genome-wide association studies (GWAS) have identified more than 200 genetic regions thought to increase IBD susceptibility. However, many of these polymorphisms are found in noncoding regions of the genome and are thought to contain transcriptional regulatory elements. The activity of these regulatory elements and the genes whose expression they control are influenced by epigenetic modifications.

Linking specific epigenetic modifications with disease phenotype is challenging, and large scale, high-throughput studies will be necessary to assess the penetrance of epigenetic modifications in IBD with confidence. Assays such as ATAC-seq and Capture-C are set to be powerful techniques for identifying genome-wide changes to chromatin accessibility in patient samples

Headline Initiative: UK Biobank

UK Biobank is a national and international resource for health research providing unparalleled opportunities for understanding the determinants of disease. The resource offers non-preferential access to researchers undertaking health-related research that is for the public good. UK Biobank aims to improve the prevention, diagnosis and treatment of a wide range of serious and life-threatening illnesses.

Following the health and well-being of its 500,000 volunteer participants, UK Biobank provides detailed health information, in a manner which does not identify them, to approved researchers in the UK and overseas, from academia and industry. The resource is increasingly detailed and is already the most genetically characterised medical research resource in the world.

Funded primarily by the MRC and the Wellcome Trust, UK Biobank recruited people aged between 40-69 years in 2006-2010 from across the country to take part in the project. They have undergone measures, provided blood, urine and saliva samples for future analysis, given detailed information about themselves and agreed to have their health followed. More recently, UK Biobank has embarked on a project to Magnetic Resonance Image (MRI) key organs of 100,000 participants and has previously undertaken biochemistry and genetic analysis of samples.

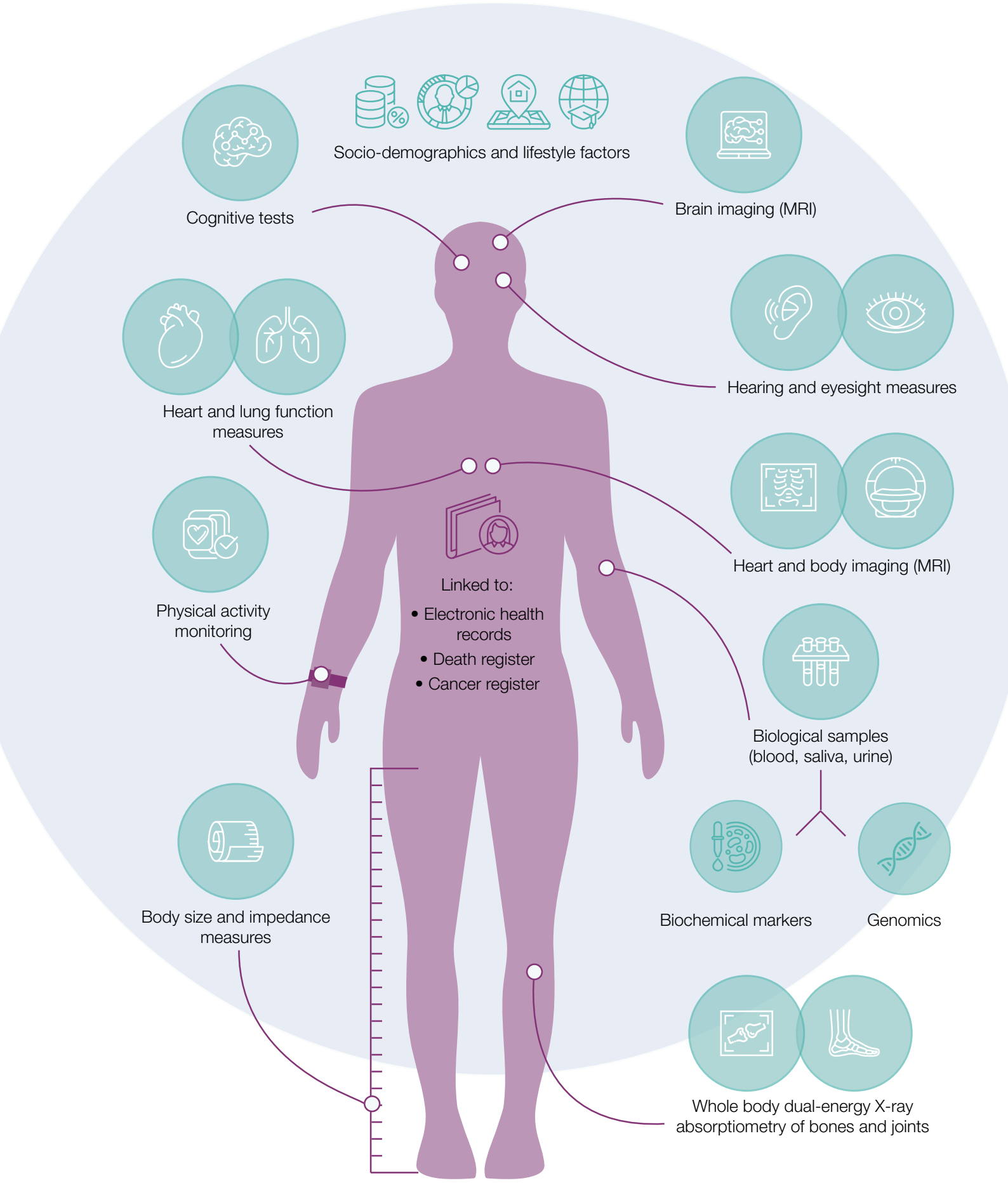
In September 2019, a £200 million investment from government, industry and charity was announced to further cement UK Biobank's reputation as a world-leading health resource. The investment secures the WGS of all UK Biobank participants.

The addition of the whole genome sequence data from all 500,000 participants will dramatically enhance the ability of the resource to support innovative and imaginative research. It will enhance the ability of scientists to understand how genetics combine with lifestyle and the environment in which we live to cause disease.

At the time of publication, UK Biobank has approved over 12,000 registrations from researchers working in over 1,500 institutes in 68 countries, and has approved over 1,500 applications to enable these researchers to access this valuable resource. To date, more than 900 journal articles using UK Biobank data have been published.

All bona fide researchers from the UK and overseas and from academia, government, charity and commercial companies can apply to use the resource by following UK Biobank's access procedures found at: http://www.ukbiobank.ac.uk.

UK Biobank Measurements



4: Informatics

Implementation of a unified informatics strategy will be the defining step in alignment of the UK's genomics ecosystem. The genomics community will work together to maximise the impact clinicians and researchers can have through the use of genomic and other health data. We will use common standards and ensure systems are interoperable, so that researchers and clinicians can work together on improving outcomes for patients. Patients and the public must be confident that their data are safe and that being used appropriately and responsibly. We will involve and engage patients and the public in our projects, and privacy and security will be critical to our shared success.

The MRC Cloud Infrastructure for Microbial Bioinformatics (CLIMB) provides a national capability to support microbial genomics, and has supported over 1,000 researchers examining a diverse range of questions – from mining bacterial genomes for new antibiotics through to examining the spread of Ebola in real time. As part of the COVID-19 pandemic CLIMB has provided the core platform for the analysis and sharing of viral sequence data and patient metadata across the UK. The recent pandemic work has seen close working between CLIMB and HDR-UK, and this provides a platform for the development of better integration of pathogen genomic data with other patient metadata.

Access to the UK Biobank, NHS and Genomics England datasets will be improved through a federated, standards-led informatics infrastructure for UK genomics, spanning research and healthcare domains. This informatics infrastructure will enable integration of genomics from the academic research domain to secondary use of healthcare data for research. At its core will be a coordinated network of interoperable standards, wherever possible aligned with global standards.

European Bioinformatics Institute

In 1992, the European Molecular Biology Laboratory (EMBL) voted to establish the EMBL-European Bioinformatics Institute (EMBL-EBI) and locate it on the Wellcome Genome Campus in Hinxton, UK, where it would be in close proximity to the major sequencing efforts at the Wellcome Sanger Institute. The EMBL is an international governmental organisation, of which the UK is a member.

EMBL-EBI develops databases, tools and software that make it possible to align, verify and visualise the diverse data produced in publicly-funded research, and make that information freely available to all. They collaborate with scientists and engineers all over the world, and provide the infrastructure needed to share data openly in the life sciences.

Genomics in practice: Rare Diseases Sprint Exemplar Innovation Project

The NIHR Bioresource Rare Diseases Sprint Exemplar Innovation Project aims to develop a secure cloud research platform with the potential to transform the understanding of rare genetic disorders, drive improvements in diagnosis, and provide proof of principle for use in other diseases.

The collaboration will build on the advances that clinical imaging, pathology, and genomic technologies have made in understanding rare diseases by creating a secure, anonymised platform to draw together and integrate data from the NHS with research data. The project team worked with patients from three rare disease cohorts enrolled in the NIHR BioResource, enabling de-identified phenotype and genotype data to be integrated and made available for approved research studies.

This model is now being developed and scaled in other disease areas. The long-term goal is to use this model to provide a world-class, multi-dimensional integrated data resource for research and innovation that is based on open data standards, protects the privacy of participants, and can be readily scaled and replicated for other disease areas.

5: Equity and genetic diversity

There is currently an ethnic bias in most large genetic datasets and the bioinformatics tools used in healthcare. The main global genome databases are predominantly from European ancestries, although there are now significant efforts to improve the global coverage. The 100,000 Genomes Project has involved a diverse range of patients with rare disease and cancer, through the recruitment from patients attending NHS services. Although there was under-representation in cancer it still provides researchers with one of the largest human genetic variation resources ever collected. However, we recognise that there is a continuing need to address any barriers to inclusion in genomic medicine services and research. Indeed, to fully understand genetic diversity, simply being representative of our population will not be sufficient. We will need to include a much larger number of people from ethnic minority groups than their overall population size might otherwise suggest: a process known as ‘over-sampling’.

In 2017, Genomics England commissioned a qualitative review of people from black African and black Carribean backgrounds’ views on participation in the 100,000 Genome Project. It identified some suspicion and distrust within many of these communities and also highlighted that some healthcare professionals may assume refusal from ethnic minorities and are less active in recruiting from these populations. We will not shy away from the results of this study, because it is absolutely vital that our datasets are reflective of the ethnic diversity in the UK:

- If people from ethnic minority groups are not appropriately represented in datasets, their information will be compared with people of a different genetic background to them, and the information they receive might not be as personalised. For example, PRS are calculated by looking at patterns within large

population datasets. For the PRS to have predictive utility for an individual it is vital that their ethnic group is adequately represented within that underlying population data.

- Use of pharmacogenomics in medicines development: companies and regulators need to understand whether new products will work and the adverse drug reaction profile in the population that will use them. Knowing this information requires a diverse underlying dataset and is vital to successfully treating the disease in those patients, supporting global health.

Improving diversity and equity of access will be fundamental to successfully achieving the vision of this strategy. We will develop robust systems of outreach and communication to diversify our datasets and ensure that we increase equity of access as much as possible, as well as identifying opportunities for international collaboration to increase our understanding of ethnic diversity and genomics.

The Wellcome Sanger Institute

The Wellcome Sanger Institute is one of the premier centres of genomic discovery and understanding in the world. It leads ambitious collaborations across the globe to provide the foundations for further research and transformative healthcare innovations. The Sanger Institute was established in 1993 and sequenced one third of the first human genome in the global Human Genome Project, the single largest contributor and over the last 25 years has pioneered multiple large-scale global projects. It is located at the Wellcome Genome Campus, Cambridge, UK and its success is founded on the expertise and knowledge of its people. The Institute seeks to share openly its discoveries and techniques with the next generation of genomics scientists and researchers worldwide.

The Institute has pioneered responsible clinical genomic data sharing initiatives, such as DECIPHER, which are used daily in clinical genomic testing around the world. The Institute has also catalysed genomic medicine through landmark translational research projects such as the DDD[13] and PAGE[14] studies, which were co-funded by the Department of Health and Social Care and laid the foundations for the 100,000 genomes project.

13 https://www.ddduk.org/intro.html

14 https://www.sanger.ac.uk/collaboration/prenatal-assessment-genomes-and-exomes-page/

6: Opportunities to participate in clinical research

It is vital that patients are offered opportunities to participate in disease-focused research and clinical trials whenever these are available. Linking and correlating genomics, other healthcare data and data from patients provides routes to new treatments, diagnostic patterns and information to help patients make informed decisions about their lifestyle and care.

We will ensure that there are streamlined pathways for contacting patients who want to participate in research, delivered through exemplars such the NIHR Bioresource, Be Part of Research, and the NIHR Clinical Research Networks and their counterparts in the devolved nations. We will work at a UK-level to ensure there is equitable access to opportunities to participate in clinical trials.

A new NHS Genomic Medicine Service Research Collaborative led by NHS England and NHS Improvement, the NIHR, and Genomics England will establish a coordinated approach to embedding research and discovery to advance clinical care with the aims of ensuring maximum gain for patients, and prioritising areas of unmet need in the NHS. This research will support breakthroughs enabling prevention of ill-health, earlier diagnosis, more effective treatments, better outcomes and faster recovery.

This will provide a forum to agree strategic needs for genomic research in the NHS and to identify knowledge gaps, areas of unmet need and research priorities.

The NIHR BioResource

The NIHR BioResource for Translational Research in Common and Rare Diseases (NIHR BioResource) is a national resource of around 100,000 volunteers who have consented to be recalled for research based on their genotype and/or phenotype. This includes around 70,000 participants from the general population, almost 20,000 participants with rare diseases, and more than 28,000 patients with inflammatory bowel disease.

The NIHR BioResource provides researchers from academia and industry with unprecedented access to highly characterised patients with common and rare diseases and volunteers from the general population diseases who are interested in participating in early translational research. The Bioresource is a unique resource that is recognised as a rapid and highly efficient mechanism for recruitment to clinical trials and studies by:

- Enabling the identification of highly characterised individuals and cohorts of patients who have volunteered to be recalled for research;
- Facilitating seamless, one-stage central identification and recall of volunteers who meet precise entry criteria for clinical research studies; and
- Supporting recruitment to clinical trials that could not be delivered without access to stratified national patient cohorts.

The BioResource has supported over 200 studies involving recall of participants to research studies.

7: Translation

Wherever you are in the world, the translation of basic science discoveries into clinical practice is not straightforward. But it is a vital part of unlocking improved health outcomes for patients, as well as realising economic benefits from advances in fundamental research.

The Life Sciences Strategy highlighted the progress the UK has made so far in delivering large-scale clinical trials with industry over the last ten years. However, it also noted that there are opportunities to further improve translational science and attract more clinical trials from industry, a significant source of inward investment in the life sciences sector. It set a strategic goal to support a 50% increase in the number of clinical trials over the next five years, and to grow the proportion of 'change of practice' trials and trials with novel methodology over the next five years. Additionally, NHS England's Long Term Plan has committed to significantly increase the number of NICE evaluations for medical technologies, giving greater scope for assessment of digital products in particular.

The NIHR, funded through the Department of Health and Social Care, provides the support, expertise, and facilities the NHS's need to undertake world-leading research. It funds a range of infrastructure facilities including: Biomedical Research Centres (BRCs), Clinical Research Facilities (CRFs), MedTech and In Vitro Diagnostics Cooperatives and the Experimental Cancer Medicine Centre (ECMC) network jointly with Cancer Research UK. The NIHR Clinical Research Network (CRN) also supports the set-up and timely delivery of studies and trials in the NHS in England. In 2019/20 the NIHR CRN supported 438 rare disease studies to recruit 19,000 participants in England.

NIHR Biomedical Research Centres

The NIHR funds 20 Biomedical Research Centres (BRCs) created to support the transfer of new scientific discoveries into early translational and clinical research. The BRCs are partnerships between English NHS organisations and universities, bringing together academics and clinicians to translate discoveries from basic science through into potential new treatments, diagnostics and medical technologies.

BRC funding supports researchers of the highest calibre to develop innovative research ideas that can attract investment from other funders, furthering the nation's economic growth.

The BRCs provide a focus for experimental medicine and undertake research on a wide range of disease and therapeutic areas and more than half of the BRCs have research themes which include genetics and genomics research. The BRCs also work together as part of the NIHR BioResource for Translational Research in Common and Rare Diseases.

To achieve, maintain and measure success over the next ten years we will:

- Coordinate the UK's existing and future genomics ecosystem, enabling ground-breaking-research at scale for the benefit of patients.
- Incentivise the genomics research community to prioritise areas of high NHS unmet need.
- Ensure that clinical genomic testing and genomics research contribute to powerful national data resources and maximising impact.
- Support hypothesis-driven identification, recruitment, phenotyping, and biosampling of uniquely informative cohorts of patients.
- Enable and empower genomics research, providing capabilities at a unique scale.
- Develop consent and data standards that support innovation for the benefit of patients and the NHS, whilst maintaining trust in the safe, appropriate, and responsible use of data.
- Achieve greater diversity within our reference genomes, and future Genome Wide Association Studies (GWAS) will reflect the UK's diverse populations.
- Work at a UK level to ensure there is equitable access to opportunities to participate in clinical trials informed by genomic data.

Chapter 3: Cross-cutting themes

The three pillars will be supported by work in five thematic areas – these enablers cut across our three pillars and are individually, and collectively vital to successfully delivering our strategic ambition.

A. Engagement and dialogue with the public, patients, and our healthcare workforce, placing the patient and the UK population at the heart of this journey.

Vision: We will build and maintain trust in genomic healthcare with patients, the public and NHS workforce, ensuring that they are involved and engaged in how we design and implement genomic healthcare, including the use of data and ethical considerations.

Genomics in healthcare can only be successful with the trust, consent and support of patients, the public and the NHS workforce. Patients and the public must be confident that their data is safe and also that it is being used in order to deliver the best possible care, to them and other patients. Genomics England's public dialogue on genomic medicine found that the public are enthusiastic and optimistic about the potential for genomic medicine but have clear red lines on use of data and want assurances that there is a robust governance framework and consent process in place that makes it clear what the intended use of their data is.

We recognise these points and are committed to open, collaborative engagement. We will commit to communicating openly with patients and the public and make increasing understanding of genomics and health literacy central to our communications and outreach approach over the next ten years. We will safeguard opportunities for patients and the public to tell us what matters to them, as users of the genomic healthcare system. It is not enough to have an advanced genomic healthcare service; we must also have a public who believe in its potential and are empowered to help shape its delivery.

We must also continue to work with the NHS workforce, both clinical staff and senior leaders, to understand what the embedding of genomics in healthcare means for them. It is vital, as discussed in the next section, that staff are confident in communicating genomic results and analyses and that they have the tools they need to do their jobs effectively.

Genomics in practice: Genomics Cafes initiative across Wales

Organised by Wales Gene Park on behalf of Genomics Partnership Wales, Genomics Cafes are free events for people affected by a rare or genetic condition and are held in various locations across Wales. Genomics Cafes are a relaxed and informal opportunity for individuals to meet others and find out more about new advances in genomic medicine in Wales. These events provide a chance for people to come together and tell Genomics Partnership Wales how this group of people can be better supported. Genomics Cafes are a networking opportunity, and also guest speakers are present to highlight new initiatives and give attendees the chance to shape activities in genomics.

The first Genomics Cafes were held in June 2019 with events in Cardiff and Carmarthen, and further events have taken place across Wales. These cafés continued to take place virtually during the period of COVID-19 pandemic restrictions with great success.

To achieve, maintain and measure success over the next ten years we will:

- Ensure that patients, the public and the NHS workforce have an increased awareness and understanding of the potential benefits of genomic healthcare by increasing its visibility and committing to open, honest engagement about what is involved.
- Set out clearly how patient data can be used to advance research and inform the public about research that has successfully used their data to improve diagnosis, understanding or treatment of patients in the UK.
- Ensure that appropriate measures are in place to protect patient privacy and confidentiality, so that patient data are used in ways that are acceptable to the public.

Genomics in practice: Genomics England public engagement

Patient and public involvement is central to making the most of our world leading genomics ecosystem. Patients and the public need to continue to trust that healthcare data will be used in ways they expect, by approved parties, for their mutual benefit, in order to continue to be willing to share it.

Patient trust is engendered by inspiring confidence that healthcare data is being used wisely and overseen by people who have their best interests at heart. From the outset of the 100,000 Genomes Project, Genomics England have involved patients and their families in decisions about how their data is used, and by whom. By inviting a Participant Panel of users with direct lived experience to contribute to these decisions, Genomics England are ensuring that they retain the trust of the people whose data they hold – as well as keeping senior leaders informed about how genomic healthcare is being delivered in practice.

Public trust is engendered by exploring ethical and practical aspects of genomics with the public and understanding what they consider to be the limits of acceptable use. To this end, in 2019, Genomics England engaged in a public dialogue[15] to explore aspirations, concerns, and expectations about the development of genomic medicine in the UK. This is an important foundation for this strategy and will continue to inform policy making here and around the world in the future.

15 https://www.genomicsengland.co.uk/public-dialogue-report-published/

B. Workforce development and engagement with genomics through training, education and new standards of care.

Vision: We will support the NHS workforce, academia and industry workforce to develop and acquire the necessary scientific and clinical skill sets and understanding of genomics, including bioinformatics. We will support the workforce across all sectors to communicate about genomics in an accessible way. We will prioritise workforce and training in spending and policy considerations. We will implement a framework of skills across the sectors, identifying the major skills shortages in each and propose new ways of training to keep up with demand. We will develop clinical pathways and standards of care that fully incorporate the latest genomic testing and results.

Delivery of the full benefits of genomics within healthcare is dependent upon having staff who are confident in understanding, interpreting and communicatinge genomic results and analyses, and with the appropriate knowledge and skills. We cannot realise a genomic healthcare system without giving those who care for patients the skills and tools to do their jobs effectively.

Workforce planning in the face of such rapid development will be challenging. There will be an ongoing requirement for genomics education to be built into the academic and training pathways of the whole healthcare workforce. However, given the rapidly expanding knowledge base, the approaches for upskilling the existing workforce and developing the prospective workforce will need to be responsive and flexible. There is an opportunity to look at introducing more collaborative training models bringing together the NHS, academia and industry partners. This will need to be coupled with clinical academic training, and joint academic appointments, with the NHS and other bodies.

At the same time, adoption and integration of new technology will be about much more than just the clinical workforce. Senior leaders in a range of organisations from data to service delivery will need to understand more about genomics, what it means for them, and how they can work together to deliver the ambitions of this strategy.

1: Workforce training and development

In 2014, Health Education England (HEE) launched a four-year £20 million Genomics Education Programme (GEP) to ensure that the NHS workforce has the knowledge, skills and experience to keep the UK at the heart of the genomics revolution in healthcare. The programme is now established within HEE and continues to deliver its innovative programme of work to support the NHS Genomic Medicine Service in England and the aspirations for genomics as set out in the NHS Long Term plan, as well as having accessible products for use across the UK health systems. This includes the highly successful Genomic Medicine Master's framework delivered by 7 leading HEI's plus a range of short and bitesize formal and informal courses to support both the novice and specialist practitioner. The GEP is active in working directly with each professional group, for example primary care, nursing and midwifery, pharmacy and with the Academy of Medical Royal Colleges across a number of areas including development of genomics competency frameworks, the incorporation of genomics into the pre- and postgraduate curricula and the development of educators toolkits.

The Department for Health and Social Care has instructed HEE to undertake detailed workforce planning and modelling and work to embed

genomics into relevant curricula and revalidation requirements, with the goal of embedding genomics education at all levels of the current and future workforce.

Genomics in practice: Genomics Roadshows

In Wales, genomics clinicians are visiting a wide range of clinical disciplines in all hospitals to highlight genomics and how it can be used to improve patient care. These Genomics 'Roadshows' are tailored to the clinical audience and regular updates are communicated to participants. Alongside this engagement work, a nursing and midwifery survey is in progress to understand the level of genomics knowledge within this group as well as their preferred methods for participating in training and education.

As the gateway to the NHS, primary care practitioners are vital to the early identification of genomics issues and to ensuring appropriate management and quality of care – often throughout a person's lifetime. In particular the implementation of PRS in the NHS at scale will necessitate an ability to communicate the information learned from the genome and how to interpret risk.

The Royal College of General Practitioners have developed a genomics toolkit[16] in partnership with the GEP, designed to be used by the entire clinical primary care team. It aims to explain how genomic medicine impacts primary care, and how to manage issues relevant to primary care. It is intended that the toolkit can be used as a quick reference resource or as a package for continuing professional development, to deliver awareness-raising and educational events, and in supporting trainees preparing for Membership of the Royal College of General Practitioners (MRCGP) entrance exams.

As we look across the different employment sectors requiring genomics knowledge and skills it is evident that there is a shortage of genomic healthcare scientists, particularly bioinformaticians and genomic data scientists.

In 2013, HEE's National School of Healthcare Science added Bioinformatics to its range of Scientist Training Programmes. This can take individuals from masters level (STP) through to doctoral level. Individuals who qualify for higher speciality training can apply for medical consultant level equivalent roles. Health Data Research UK is also funding masters programmes in health data science at six universities helping to boost data science skills in the UK. Health and Care Professions Council (HCPC) registered bioinformaticians emerging from the NHS scientists training programmes are highly sought after across all sectors. Given the need for this specialist workforce across different employment sectors the opportunity to establish a framework for skills and knowledge exchange and development must be actively pursued.

We recognise much work will be required: to support the development of the highly specialised scientific and medical workforce; to meet the needs for the pathology workforce to support cancer genomics; and increase the numbers entering training. This needs to be

16 https://www.rcgp.org.uk/clinical-and-research/resources/toolkits/genomics-toolkit.aspx

a priority for HEE working with government and other stakeholders. Furthermore, we must work with academia and industry to explore new ways of engaging them to support training and education.

Apprenticeships combining practical on the job training with study offer another route to training in skills shortage fields. Apprenticeships are available in a number of in-demand occupations of relevance to genomics including AI, bioinformatics, and data science. We will assess and promote the relevant apprenticeship frameworks and standards to ensure that they are fit for purpose and that there is sufficient uptake within the community. Having a pipeline of trainable, motivated staff is vital for the success of genomics in the UK, and we will keep this pipeline under review across the duration of the strategy.

The NHS People Plan interim report committed to ongoing roll-out of education and training interventions and multi-professional workforce development programmes to support the NHS Genomic Medicine Service. This needs to be fully supported by HEE, NHE England and NHS Improvement and other partners within the context of the plan.

2: Clinical Pathways

Adoption of genomics into routine care needs a clinical workforce with understanding of how and where genomic testing fits into current clinical pathways and how to use it. The NHS publishes the National Genomic Test Directory, which specifies which genomic tests are commissioned by the NHS in England, the technology by which they are available and the patients who will be eligible to access tests. To ensure that models of care support the mainstreaming of genomics will require broader development of the managerial and commissioner workforce.

Clinicians must be empowered and supported to identify which patients require genomic testing, to identify the appropriate genomic test to offer their patient and to capture the phenotypic information required for an effective referral. Clinicians must also know how to seek expert advice, which services to refer the patient to, and how to handle findings that are based on genomic analyses.

Genomics in practice: Genomic Champions

NHS England, working in partnership with the Academy of Medical Royal Colleges, has sponsored and established a UK-wide network of Genomic Clinical Champions. The network is made up of clinical representatives from across all the Royal Colleges in the UK to lead the embedding of clinical genomic medicine into the NHS across clinical specialities.

The network meets on a quarterly basis and aims to:

- Align and coordinate genomics activity across the clinical community to ensure information is shared, efforts are not duplicated and there is clarity about the future direction and approach
- Discuss key issues, such as establishing multidisciplinary teams and referral pathways, shared decision making with patients, research and collaboration and training and education
- Establish cross-cutting programmes of work on clinical pathways and education and training

As well as participating in the UK-wide network, GPW have also launched their own Genomics Champions initiative to lead integration of genomics as part of mainstream patient care across many health disciplines. The initiative involves a diverse group of healthcare professionals across all disciplines, health boards and trusts in Wales, who have a passion to be part of the genomics revolution. Similarly within the NHS in England key leadership positions in genomics have been funded within Genomic Laboratory Hubs and linked to the proposed Genomic Medicine Service Alliances is planned multiprofessional clinical leads and champions

3: Technological solutions

Innovative informatics approaches to training, analytics and decision support will be a key part of readying the health service for the genomics revolution. We anticipate a vibrant economy of startups working in partnership with NHS staff to develop tools that will support them to implement genomics into their daily practice. This will include training tools and analytical and decision support, which is vital for GPs in particular.

Genomics in practice: Innovative online Genomics training portal

Guy's and St Thomas' NHS Foundation Trust (GSTT) is working with an innovative technology company to solve the problems in training a global clinical community in the complexities of this emerging scientific field.

By working in partnership with Medics.Academy, GSTT Clinical Cancer Genetics team have been able to combine their clinical expertise with innovative interactive technological solutions, to create an easily accessible education and training platform. This partnership has resulted in a co-developed best in practice education and training offer to staff.

The GSTT and Medics.Academy online training portal and dashboard will be able to quickly adapt and send relevant clinicians updates in a timely fashion, responding to and supporting the dynamic nature of information and genomic practice in the future.

To achieve, maintain and measure success over the next ten years we will:

- Ensure that all new graduating doctors, nurses, midwives, pharmacists, allied health professionals, dental and relevant non-clinical staff have a level of awareness and knowledge of genomics that is relevant to their role.
- Ensure that the healthcare science workforce continues to have advanced genomic training and education within their programmes.
- Put in place continuing professional development programmes to ensure all relevant staff maintain an up-to-date and role-appropriate understanding of genomics.
- Utilise workforce modelling data to inform investment decisions for training numbers across all professions and support workforce growth to meet the needs of the genomic medicine service particularly in specialist scientific and medical workforce areas.
- Establish and invest in training pipelines for in-demand occupations such as bioinformatics to build capacity within the health service and the wider sector.
- Redevelop clinical pathways and standards of care to that fully incorporate the latest genomic testing and results.
- Support the NHS workforce by providing simple, practical, informatics solutions for training, genomic analysis and decision-support.

C. Delivering nationally coordinated approaches to data and analytics, enabling healthcare professionals and approved researchers to easily access and interpret our world-leading genomic datasets.

Vision: We will standardise the way we record and store genomic, phenotypic and healthcare data to support the use of advanced analytics in both care and research and to ensure that a patient's genomic data can repeatedly inform their care throughout their life.

The true healthcare benefits of genomics can only be realised when genome sequences are analysed alongside health data at population level scales, and there is significant opportunity for AI and machine learning tools to be applied to analyse these large datasets. As the volume of genomic, multi-omic, clinical, and other healthcare data continues to expand rapidly, these tools will become ever more important. We have the opportunity to transform the application of genomic medicine in healthcare across the world and support the development of life science and healthcare-focused AI expertise within the UK which will drive the emergence of a new breed of companies with new-found expertise at their foundation.

We need to establish shared standards for the storage and structure of, and access to genomic data across the entire UK genomics research ecosystem and the NHS. A single data repository for all genomic tests performed within the NHS in England will provide a national genomic record for all patients that can be recalled and reanalysed throughout their life to provide additional insights and patient benefits. With appropriate consent and governance, this single repository could be federated with research datasets (such as UK Biobank) and lead to new national and international research collaborations.

Patients and the public must be confident that their data are safe and that being used appropriately and responsibly. We will ensure that our approach to the use of data aims to simplify and clarify processes, embedding privacy and security and that we are transparent about how data are used, so that patients and the public are involved and engaged in shaping this approach.

1: The Global Alliance for Genomics and Health

Data standards enable the effective, responsible, and secure sharing of genomic and health-related data and play a vital role in strengthening national and international collaboration.

The Global Alliance for Genomics and Health (GA4GH) is a coalition of over 500 organisations worldwide working together to establish frameworks and standards for responsible, voluntary and secure sharing of international genomic and health-related data. The ultimate goal is to advance healthcare and enable benefits to biomedical research through facilitation and implementation of agreed international standards. The consortium advocates for responsible data sharing and produces the necessary practical standards.

The GA4GH has been working on a number of specifications related to genomic data that can contribute to these capabilities across its various work streams steered by the relevant Driver Projects. GA4GH Driver Projects are real-world genomic data initiatives that help guide the development efforts and pilot the tools designed for and by the Driver Projects.

2: Machine Learning and Artificial Intelligence

Machine learning is already being used within Genomics England to automate genome quality control. Using machine learning it has been possible to identify genomes that are outliers, based on their sequencing or sample characteristics. Machine learning has improved the ability to process genomes rapidly and to high standards and soon will help improve genome interpretation.

The research community has also started using various types of AI based methods to derive insights from the UK Biobank data and within the Genomics England research environment. For example, researchers are using such methods for identifying genetic mutation signatures associated with certain cancers, helping to identify and classify sub-types of the disease and find targets for new treatments. This has the potential to improve cancer diagnosis by making more accurate predictions of disease progression, and to better stratify patients for more effective and efficient treatment. Similar work is ongoing with rare disease, to identify driver mutations of particular conditions. These and other AI models will be able to better predict the severity of outcomes based on genomic and clinical data.

The genomic revolution can only be realised with a smart, modern approach to data and informatics. We want the UK to be the home of genomic-enabled research, and simple, secure access to high quality data is a critical component. We want the UK to be the home of genomic-enabled research, and simple, secure access to high quality data is a critical component.

At the same time, there is a unique data sharing challenge within the four nations, and it is currently difficult to compare and share data across borders. This benefits no-one, and we commit to working in partnership across the administrations to realise effective data sharing.

To achieve, maintain and measure success over the next ten years we will:

- Through the use of machine learning and AI, understand how genomically informed healthcare and prevention could be improved and how these could be implemented in the NHS, embedding potentially lifesaving technologies quickly and efficiently in the NHS.
- Establish a clear set of standards for genomic and health data.
- Develop systems to enable federated access to data for research use to enable comparisons across multiple datasets.
- Track the usage of our datasets and maintain an upward trajectory of both numbers and user experience.
- Learn from the growing number of AI based businesses in the UK on how to turn these applications into healthcare interventions.

D. Supporting industrial growth in the UK, facilitating entrepreneurship and innovation for projects and companies of all sizes, through common standards, funding, procurement, and R&D structures.

Vision: We will make the UK the best location globally to start and scale new genomics healthcare companies and innovations, attracting direct investment in genomics by the global life sciences industry and increasing our share of clinical trials in the UK.

Innovation by industry of all sizes is vital to the delivery of the UK genomics healthcare ambition. Maintaining and extending the UK's leadership position in genomics and delivering world-leading, genomics-driven healthcare to patients cannot be driven by the NHS or government investments alone.

Genomics England Discovery Forum

Genomics England's Discovery Forum provides a platform for collaboration and engagement between Genomics England, industry partners, academia, the NHS and the wider UK genomics landscape. Companies have come together within the Discovery Forum to work in a pre-competitive environment with access to a selection of whole genome sequences.

The Forum promotes collaboration in – and access to – the UK genomics environment, utilising industry expertise to maximise patient benefit through the 100,000 Genomes Project. Ultimately, the Discovery Forum will help the 100,000 Genomes Project and its partners to turn research findings into treatments, diagnostics and benefits for patients as soon as possible.

1: A vibrant start-up economy

It is the Government's job to create and nurture an environment that enables start-ups to thrive, growing and scaling their business here in the UK. Over the next ten years we expect to see a surge in new start-ups in areas we couldn't have predicted before the UK assumed its world leading position in genomics: bringing together genomic data, AI, new technologies and novel business models. The dynamics of building and growing life sciences startups differ from other areas of technology, requiring access to specialist equipment, facilities and funding. Accelerators, incubators, support for entrepreneurial academics and other startup support programmes, alongside proportionate costs for access to data and biosamples, will be key pillars of a thriving startup ecosystem in the UK.

Genomics in Practice: Illumina Accelerator

Illumina recently announced the expansion of its Accelerator to Cambridge. Founded in the San Francisco Bay Area in 2014, the Illumina Accelerator focuses on partnering with entrepreneurs to build breakthrough genomics start-ups. During each six-month funding cycle, the Illumina Accelerator will provide selected start-ups with access to seed investment, access to Illumina sequencing systems and reagents, as well as business guidance, genomics expertise, and fully operational lab space adjacent to Illumina's campus in Cambridge. Since launching in 2014, Illumina Accelerator has invested in 33 genomics start-ups from across the globe, which have collectively raised over $300 million in venture capital funding.

2: Industry, charities, and government working in partnership

Industry has also come together to fund vital genomics initiatives, recognising the role they have to play in nurturing the development of genomic healthcare. The WGS of UK Biobank is funded by a combination of UK Government, The Wellcome Trust and industry partners, with Johnson and Johnson, Amgen, GSK and AstraZeneca providing a combined £100m to the project. The Accelerating Detection of Disease programme will leverage large amounts of industry and charity funding, with around £100m already committed.

Genomics in practice: Working in partnership with industry to provide patients with a diagnosis

Global biopharmaceutical company Alexion, a member of Genomics England's Discovery Forum, have identified 14 previously undiagnosed 100,000 Genomes Project participants with a life-threatening kidney disease

Nephronophthisis (NPHP) is a childhood genetic disorder primarily affecting the kidneys. It is rare (around 1 in 60,000 births) and usually results in kidney failure by the age of 15. It is responsible for 15% of cases of childhood end-stage renal failure – with no preventative treatments currently available.

Using Genomics England's dataset, Alexion identified 14 undiagnosed participants, recruited as part of the 100,000 Genomes Project's rare disease programme, who carry the gene deletion causing the disease. These findings were shared with Genomics England and fed back to the participants' NHS clinical teams.

The Government recognises and celebrates the vital role that industry plays in providing the funding, expertise and scalability for many of the most exciting new discoveries. We will continue to actively engage with industry, look for new opportunities to collaborate and provide the right environment and incentive structure to start, locate and grow a genomics business in the UK and, ultimately, produce new genomics-based treatments to be sold globally from a UK base.

The UK has not always been able to realise the benefits of its outstanding science linked to its single payer health system, but we now have a promising platform which will play a big role in the burgeoning genomics industry. Two significant problems in the past have been absence of capital at scale and slow take up by the NHS of innovation. To solve both issues requires symbiotic relationships to be fostered between the NHS, capital investors, companies and the public. As part of the Government's efforts to address the shortage of available capital, we have committed to invest £200m into a dedicated Life Sciences Investment Programme. This programme will be delivered through the British Business Bank and will leverage approximately £400m of private sector investment to increase the supply of venture growth finance available to the most exciting life sciences companies. In addition, the emerging trend for Environmental, Social and Governance (ESG) funds and Impact funds provide additional capital sources likely to be respected by the health community. The pandemic has given the NHS real life experience of sourcing innovation at speed. The opportunity is there to foster a virtuous circle whereby the close relationship between UK scientists and clinicians stimulates potentially compelling health products in cooperation with NHS partners, which provides the package for ESG or Impact funds to offer capital against clear health and financial goals, which in conjunction with informed and responsive regulatory authorities clears the way for uptake, and thus feeds the whole virtuous ecosystem into greater effort. We will keep looking at our incentive structures and identify opportunities to make it easier and more efficient for businesses to grow and thrive in the UK.

How we will achieve, maintain and measure success. Over the next ten years, we will:

- Develop integrated data resources, biosampling capabilities, and collaborative academic and clinical expertise that will make the UK the most attractive location globally for genomic healthcare start-ups.

- Help to increase life science industry research and development spend in the UK by identifying new opportunities for innovative and cutting-edge industry partnerships.

- Work to improve the availability of capital, including through the Life Sciences Investment Programme, which will deliver around £600m of investment – both public and private – to be deployed with a significant focus on UK Life Sciences companies over the next 10-15 years.

E. Maintaining trust through strong ethical frameworks, data security, robust technical infrastructure and appropriate regulation.

Vision: All our genomic data systems will continue to apply consistent high standards around data security and the UK model will be recognised as being the gold standard for how to apply strong and consistent ethical and regulatory standards that support rapid healthcare innovation, adhere to legal frameworks, and maintain public and professional trust.

As well as focussing on patients, trust must also be built through robust policies, processes, systems, regulations and clear adherence to the legal framework for data-sharing. A strong ethical framework must be established around the use of and access to genomic data, and furthermore our data storage and access systems must be robust and have sufficient controls in place.

We understand public views around the use of their data. We commit to open conversation and engagement on ethical and regulation standards. We will not be complacent about our regime and we will ensure that we keep it continually updated and fit for purpose. Genomic progress depends on the public participating with their data. It is essential that their trust is maintained. Breach of this trust must be vigorously pursued, if necessary with additional legal sanctions.

Regulations around genomics must be regularly reviewed to ensure that they remain relevant as the science and technology evolves and we will continue to work with MHRA to help them develop a clear direction on the development and regulation of medicines and diagnostics related to genomic technologies.

How we will achieve, maintain and measure success. Over the next ten years, we will:

- Keep an open dialogue and will continue to openly engage with relevant patient and participant groups, continuing to involve the public, building on the engagement through the 100,000 Genomes Project.

- Establish a gold standard UK model for how to apply strong and consistent ethical and regulatory standards. We will share these standards and expertise globally and help partners across the world develop and implement their own frameworks.

- Ensure that our regulatory and ethical frameworks support rapid healthcare innovation, whilst reflecting legal frameworks and retaining public and professional trust. We will keep under review the balance between regulation and innovation.

Chapter 4: Conclusion

Delivering this strategy will take commitment to achieving mainstream genomic healthcare, and collaboration between the constituent parts of the genomics community to make the whole greater than the sum of its parts, delivering the future of healthcare for UK patients.

We are committed to a future where genomics greatly improves the mental and physical wellbeing of the UK population and millions more worldwide, and global pandemics like COVID-19 can be rapidly brought under control. This will mean a better understanding of the genetic causes of diseases, how to predict and prevent them, and how to tailor therapies so that patients get the right medications at the right time.

But we are not coming from a standing start. The UK has built and nurtured a culture of collaboration and partnership between government, industry and medical research charities. The Government has shown commitment to growing the UK life science and genomics industries through the Industrial Strategy Challenge Fund and two Life Sciences Sector Deals[17]. The next generation of innovators in the field of genomics and data sciences will be trained using assets such as UK Biobank and the ADD, and the Genomics England dataset, strengthening our science base even further. We will become a leading global hub for life sciences, which will be at the very core of our economic recovery after COVID-19. We are in an excellent position to take the next step and lead the world in genomic healthcare.

This will not be easy. There are significant challenges to overcome not least of which being that other nations are making their own gains, and there will inevitably be areas of divergence in how we do things and where we focus our efforts. To unite these efforts and ensure we are pulling in the same direction, we will adhere to the set of principles developed by the community and ensure that we are getting the maximum value from our inputs.

The Government has set out a strategy that is ambitious in scope, whilst being grounded in what is deliverable over the next ten years. The challenge for us all now is to turn this vision into a reality. It is not enough to set out our ambitions and hope they will be achieved, so we will monitor the implementation of our commitments, holding ourselves and our stakeholders to account to ensure we are making progress. We will publish progress updates on a regular basis to show the steps we are taking and where we need to do more. The future of healthcare - a genomic healthcare system - is within our grasp and we owe it to our and future generations to deliver it.

17 Life Sciences Sector Deal 1, 2017; and Life Sciences Sector Deal 2, 2018: https://www.gov.uk/government/publications/life-sciences-sector-deal

Page intentionally blank

Glossary

Data federation: A mechanism for virtually combining datasets whilst the data itself remains in its primary source location. Authority for data access approval remains with the original data sources individually.

De novo mutations: genetic alterations that are present for the first time in one family member

Epigenetics: DNA modifications that do not change the DNA sequence can affect gene activity. Chemical compounds that are added to single genes can regulate their activity; these modifications are known as epigenetic changes. Epigenetic changes can help determine whether genes are turned on or off and can influence the production of proteins in certain cells, ensuring that only necessary proteins are produced. These effects account for how every cell can have the same DNA blueprint but can be very diverse from each other due to differential gene activation.

Functional genomics: is the study of how genes and other regions of the genome contribute to biological processes. Genome-wide functional analyses focus on the dynamic expression and interaction of gene products in specific contexts, for example in a diseased organ or tissue.

Genome Wide Association Study (GWAS): the study of a genome-wide set of genetic variants in different individuals to see if any variant is associated with a phenotype. Comparisons to the reference genome are in important part of these studies, so it is vital that the reference genome is an accurate representation of the species.

Polygenic risk scores (PRS): a way of assessing risks of developing certain diseases by observing a combination of variants spread across the genome. These variants are often changes to single letters of the DNA code and individually confer a very small increased risk of disease, but cumulatively increase an individual's probability of developing a disease. A polygenic risk score can be calculated using Whole Genome Sequencing, or more commonly using a SNP array that scores 100s of thousands of variants in a single inexpensive test.

Reference genome: a digital DNA sequence database that aims to act as the 'master copy' of a species' genome. An individual's genome can be compared to the reference and any differences identified.

Stratification: the process of identifying subgroups of patients with distinct mechanisms of disease, or responses to treatments. It allows us to identify and develop treatments that are effective for particular groups of patients.

Whole genome sequencing (WGS): the process of determining the complete DNA sequence of an organism's genome at a single time. **Short read sequencing** works by breaking down DNA into short fragments (typically 100 – 500 base pairs long) that are amplified and then sequenced. Bioinformatic techniques are then used to piece together the short sequences into a continuous genomic sequence. **Long read sequencing** involves reading sequences much longer strands of DNA (typically 10,000 – 100,000 base pairs long) in one go without the need to cut up and amplify DNA samples.