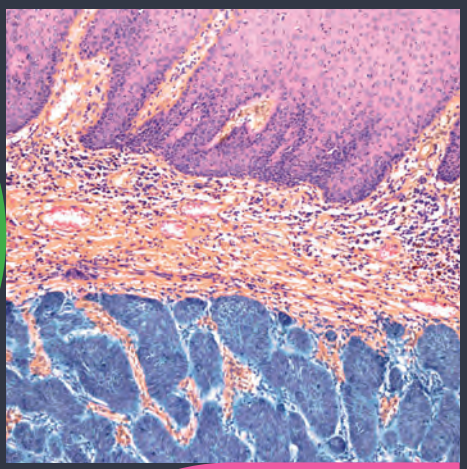
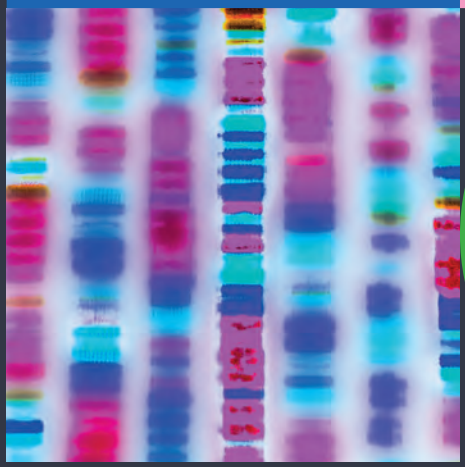
Genomics England

Annual report 2022





Transforming science into healthcare, together.

Contents

About Genomics England

UK leads the world in genomic healthcare and research

The UK has a long and illustrious history of making scientific discoveries and translating them into clinical practice for patient benefit.

It is home to:

Some of the richest genomic datasets in the world

The world's first national healthcare system to offer whole genome sequencing (WGS) in routine care, introduced by the NHS

A thriving genomics sector, with over £1.9 billion of venture investment and an estimated market cap of over £3.5 billion based on deals since 2017[1]

Years of significant and ongoing government investment in world-leading healthcare and research initiatives have positioned the UK as a genomic healthcare superpower. This position is driven forward by the NHS infrastructure, including the NHS Genomic Medicine Service (GMS) – a national service that provides access to genomic testing for patients with specific conditions – and its unique partnership with Genomics England.

Almost a decade since our mission began

The 100,000 Genomes Project launched in 2013. This was the world's largest national sequencing programme, and Genomics England was formed to guide it in partnership with the NHS.

Our focus is to integrate genomic information into clinical practice to improve diagnosis, treatment and care.

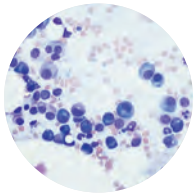
Nearly a decade on, we continue this mission at the forefront of the UK's genomics ecosystem. We've built on the incredible foundations laid by the 100,000 Genomes Project, enabling others to deliver advances in genomic healthcare both nationally and internationally.

Benefits to participants and patients

We help the NHS GMS to deliver WGS.

We provide approved researchers with secure access to genomic data and their work can lead to scientific discoveries in rare conditions and cancer. In turn, those insights can enable, more precise diagnoses and personalised interventions for NHS patients.

Analysis continues on the original data from the 100,000 Genomes Project. In addition, we launched 3 initiatives in 2022.



Cancer 2.0

- Uses new technology to enable faster and more accurate diagnoses
- Combines imaging, genomic and clinical data to build the world's largest multimodal cancer research platform

Diverse Data

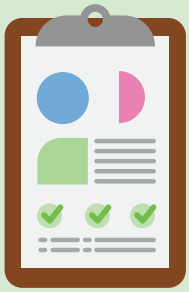
- Conducts research and communicates with minoritised communities to ensure that genomic healthcare can benefit everyone, regardless of their geographic or ancestral background
- Plans to sequence the genomes of 15,000 participants from minoritised communities

Newborn Genomes Programme

- Explores the benefits, challenges and practicalities of sequencing and analysing the genomes of newborns
- Is an NHS-embedded research study – the world's first publicly funded newborn genome programme at a national scale

"With the pace of change of knowledge and the emergence of new technologies, it is crucial that we continue to learn."

Dr Richard Scott,
Chief Medical Officer, Deputy CEO,
Genomics England



In December 2022, the government announced a UK-wide funding boost of over £175 million for cutting-edge genomics research in a 3-year plan, bolstering the above initiatives.[2]

A new era of personalised medicine

Genomics is continuously evolving. Working with the NHS, we aim to remain at the forefront of technology and scientific breakthroughs to revolutionise healthcare and improve millions of lives.

Our history

July 2013

Launch of the 100,000 Genomes Project

March 2015

First patients diagnosed as a result of the 100,000 Genomes Project

April 2016

Participant Panel established

July 2017

England's Chief Medical Officer Dame Sally Davies launches Generation Genome, to explore how genomics can improve health and prevent ill health; and the Life Sciences report – the government's plan to create a thriving life science sector – was published

December 2018

The 100,000th genome is sequenced

January 2019

NHS Long Term Plan outlines integration of genomics into healthcare as a priority

January 2020

GenOMICC COVID-19 study established to identify the genetic factors involved in why some people are more severely affected than others

September 2020

Launch of the Genome UK strategy

November 2020

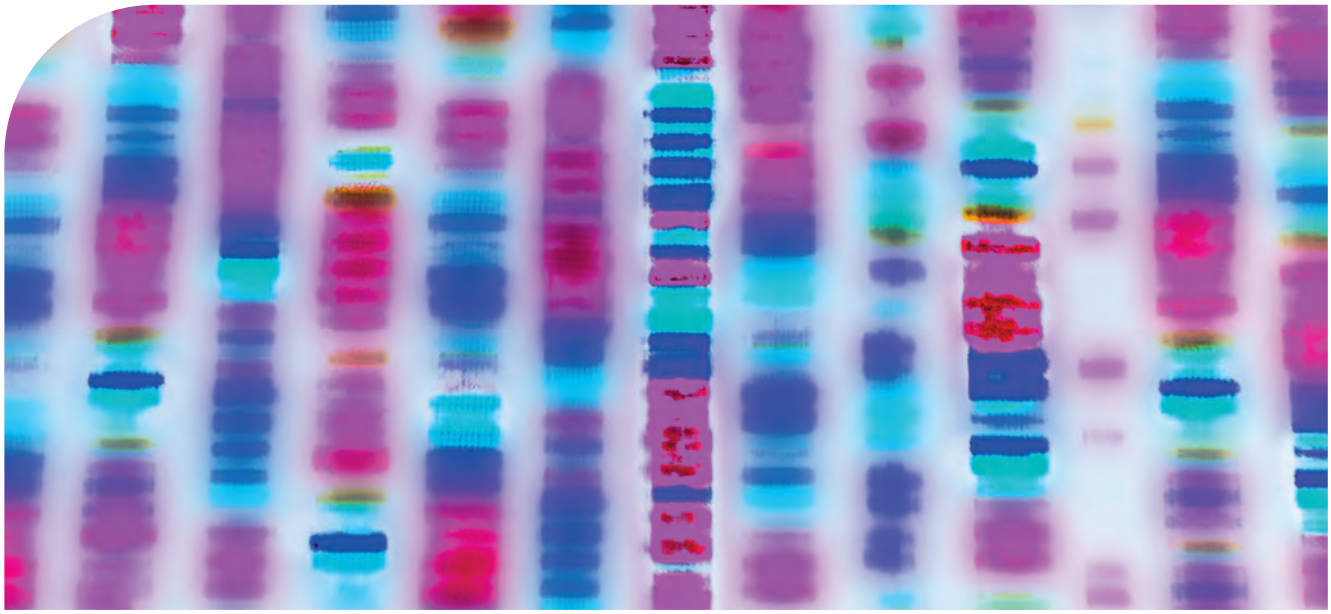
First whole genome sequenced in the NHS Genomic Medicine Service

October 2021

Newborn sequencing pilot and Diverse Data programme announced

December 2022

The government publishes the Genome UK: 2022 to 2025 implementation plan for England, highlighting our Cancer 2.0 and Diverse Data initiatives and Newborn Genomes Programme



100,000 Genomes Project: building foundations for the future

In 2013, Genomics England was set up to deliver the 100,000 Genomes Project. This moonshot project had the goal of harnessing WGS technology to uncover new diagnoses and improve treatments for patients with rare inherited conditions and cancer.

Just 5 years later, the project reached its target: the 100,000th genome was sequenced.

The impact continues

Many patients and their families consented to add their genomic and health data to a secure library, where approved researchers could analyse it. This analysis continues to contribute to the development of new diagnostic tests, treatments and therapies for a range of conditions.

A foundation of clinical care

The 100,000 Genomes Project laid the foundations for the NHS GMS – the first healthcare system in the world to offer WGS as part of routine clinical care.

Through the 100,000 Genomes Project:

6,625

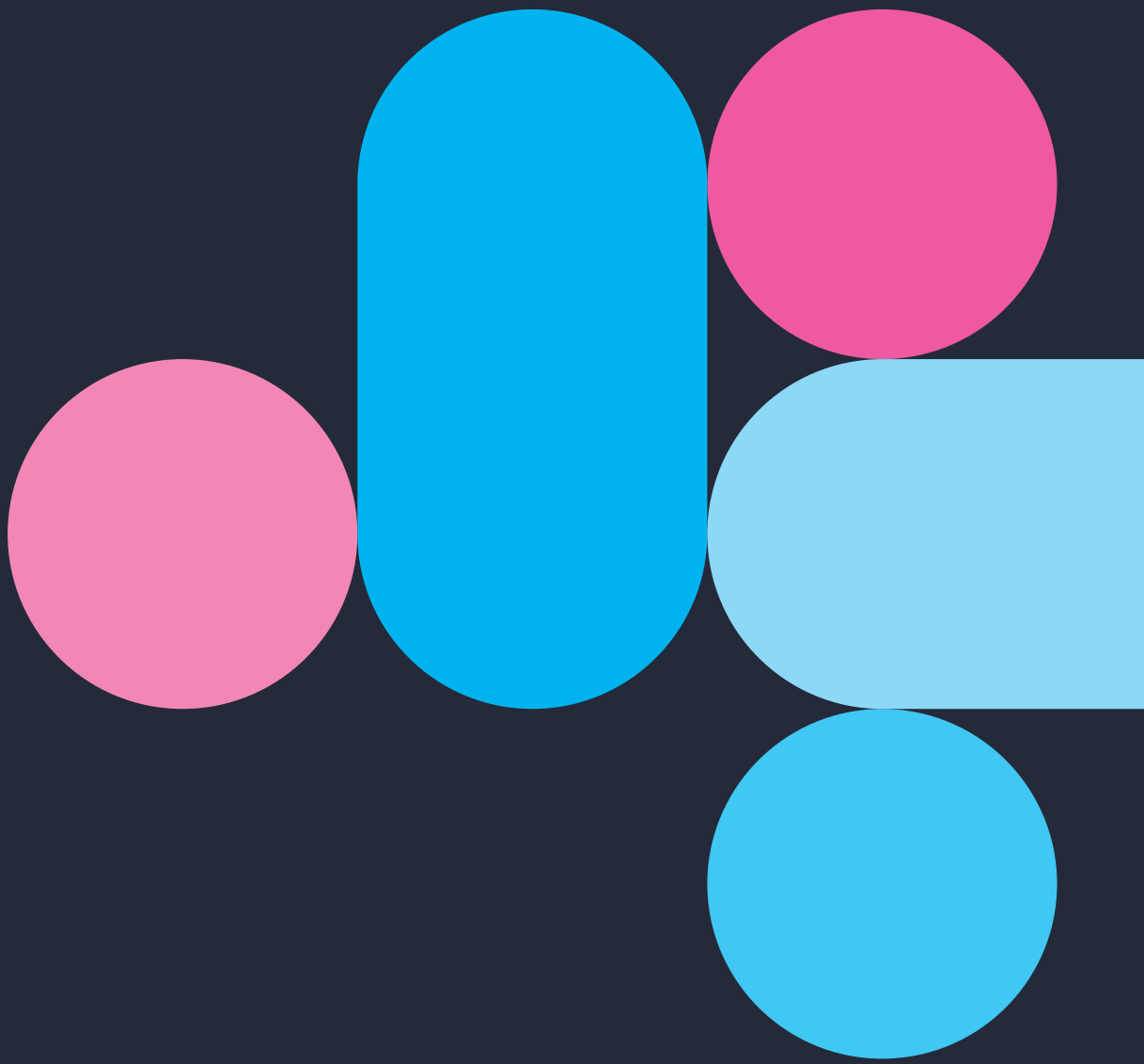
participants with rare conditions received a diagnosis that had not been possible through routine care

50%

of participants with cancer received diagnostic results or changed treatment course

See page 77 for details of references

Reviews



Ministerial review

Steve Barclay
Secretary of State

£175m
boost in genomic funding

10-year plan
to create the most advanced genomic healthcare and research system in the world

> “Our success in years to come will be underpinned by our bold and exciting Genome UK strategy: our 10-year plan to create the most advanced genomic healthcare and research system in the world.”

As the NHS turns 75 later this year, most people cannot remember a world before our national health service. Over the next 75 years, there will be more and more people who cannot remember a world before the transformative power of genomics.

One of them is a boy called Oliver, who was born last year. Whole genome sequencing (WGS), available on the NHS, spared him from unnecessary chemotherapy and surgery to treat a tumour on his leg (page 22). Our mission now is to make the most of such advances in genomic testing technology, so they are available to many more people in the NHS.

We could not ask for a better partner in this mission than Genomics England – a genuine world leader in the field. As this report highlights, Genomic England’s work continues to go from strength to strength.

Our success in the years to come will be underpinned by our bold and exciting Genome UK strategy – our 10-year plan to create the most advanced genomic healthcare and research system in the world.

As part of this, I was especially proud to announce a £175 million boost in genomics funding, including £150 million for Genomics England to progress Cancer 2.0, Diverse Data and the Newborn Genomes Programme. All these initiatives are truly groundbreaking and will help us generate the evidence we need to extend the benefits of genomics further in the NHS.

Genomics has the potential to transform the NHS in more ways than one. Genomics can – and must – play a central role in preventive healthcare. For example, the Newborn Genomes Programme will study the effectiveness of using WGS to speed up the diagnosis and treatment of rare genetic conditions in newborns, potentially leading to life-saving interventions for thousands of babies.

This year, we have a lot to celebrate – but much more still to do. The mission ahead for us is to ensure that everyone, including children like Oliver, have access to the most advanced genomic healthcare system in the world to ensure we can all live long, healthy and productive lives – and help make the next 75 years of the NHS a success.

Chair review

It is a great privilege to chair the board of Genomics England. Our role is to provide oversight of all activities the company undertakes, ensuring that we deliver on our mission, with good value for money and without compromising safety or ethics in any way.

From our origins as a vehicle to deliver the 100,000 Genomes Project, commissioned by then Prime Minister David Cameron, we could not have predicted the company it has become – an organisation of more than 500 talented and dedicated people, overseeing five major programmes in both research and clinical settings.

Together with our colleagues at GenOMICC, we contributed to the identification of several new genetic markers associated with critical illness in COVID-19, and offered supportive evidence for the potential relevance of baricitinib for patients hospitalised with severe COVID-19. The ability to adapt and react in the face of new challenges is fundamental to our success and I am very proud of our role as a driver of innovation in the life sciences sector.

Participants and patients are at the heart of all we do, and I am determined they will remain central to our guiding principle of best practice. It is important to recognise that, alongside cutting-edge scientific innovation, we are world leading in the human aspect of our work, including consent management. The key to this is consultation with participants throughout the process and the Participant Panel provides a vital resource for this. I would like to extend my personal gratitude to Jillian Hastings Ward, Rebecca Middleton and all the Panel members who work so diligently to play a vital role in all that we accomplish.

This year has seen continued progress by the genomics industry, particularly in the UK. We are seeing a strong drive towards mRNA vaccines, and we play a vital role in this through the Cancer Vaccine Launch Pad in partnership with NHS England. All of our programmes push the envelope of genomic medicine and its applications in line with NHS England's strategy – Accelerating Genomic Medicine in the NHS.

These include diversifying the ancestry of genomes available for research, validating new sequencing technologies and sequencing newborn babies with a view to determining whether this could and should be part of routine maternity care. We continue to play a vital role for the NHS Genomic Medicine Service (GMS), helping genomic tests to become the go-to choice for clinicians where they are appropriate. This is an important step in reducing the diagnostic odyssey – the time taken to receive a rare disease diagnosis – that still causes so much harm to patients with such conditions.

Our world-leading research, using genomic data to drive discovery such as the identification of multiple new cancer mutational profiles, enables a new approach to personalised cancer medicine. Our work with the NHS Genomic Laboratory Hubs delivers significant outcomes for NHS patients, like baby Oliver who captured the hearts of the nation when he made headlines last September. Thanks to WGS, Oliver's NHS clinicians were able to discover in time that his tumour was not cancer, sparing him chemotherapy and surgery.

From the discovery of the double-helix structure of DNA, to the desire to first sequence the human genome, the UK has long been at the forefront of genomic science. This remains true at Genomics England. Our unique structure allows us to integrate effectively into the NHS, supported by our academic and industry partners, and work in lockstep with our partners across the genomics and international life sciences ecosystem. This means we can continue to push the boundaries of genomic medicine – always in the service of our mission, which is bringing the benefits of genomic healthcare to all.

Baroness Nicola Blackwood

Chair

Nicola became Chair of Genomics England in May 2020. She is also Chair of Oxford University Innovation, a Trustee of the Alan Turing Institute, a member of the Royal Society Science Policy Expert Advisory Committee and a member of the House of Lords. She served as the Minister for Innovation in the Department for Health and Social Care under two prime ministers.

She chaired the Human Tissue Authority before becoming Baroness Blackwood of North Oxford in 2019.

> "Participants and patients are at the heart of all we do, and I am determined they will remain central to our guiding principle of best practice."

Chair of the Participant Panel review

Jillian Hastings Ward
Chair of the Participant Panel

Jillian is the Chair of the Participant Panel, which represents the interests of participants. Her family joined the 100,000 Genomes Project in 2015, in search of answers for her young son who is severely disabled. She brings professional analytical, strategic and communication skills from a career in consultancy and the Civil Service. She also brings her years of lived experience with a child who has complex needs.

The Participant Panel celebrated its sixth birthday this year and continues to go from strength to strength.

We were pleased to help shape the return of 'additional findings' results this year. Many participants requested these at the outset of the 100,000 Genomes Project as they wanted to find out whether they had a predisposition to certain forms of cancer or familial hypercholesterolaemia. Around 75% of participants had requested this information, and almost all these results have now been provided to them via the NHS. Participants with a positive finding have been offered treatment.

We appreciate the hard work of everyone across the genomics ecosystem who made this possible, especially the service desk staff at Genomics England who fielded thousands of queries from participants over a very short period, and the 7 NHS GMS Alliances who were responsible for returning the verified results to each participant.

Several Participant Panel members were on stage at the Genomics England Research Summit in May, setting out what patients and their families want from genomics in the foreseeable future, based on our lived experience as cancer patients and people affected by rare conditions. This type of collaboration brings genomics alive for a broad audience and shows researchers and members of the public alike how relevant this discipline is for all of us. Great stuff!

At the Genomics England Research Summit, we also launched our Guide to Language and Terminology[3] – a document that is already proving useful to professionals across the genomics world who have been wondering how best to describe the reasons why people like us need help from people like them. I was delighted to hear from Dr Francesca Faravelli, Clinical Director at North Thames GMS Alliance, that after 20 years as a clinical geneticist, she has adjusted the way she speaks to her patients after reading it. This type of impact will never be quantified but, if we have made even one conversation less difficult for patients and their families, we are making a positive difference.

We continue to meet regularly with the senior leaders across Genomics England and our members continue their work on the Access Review Committee, Ethics Advisory Committee and Genomics England Clinical Interpretation Partnership Board, recently helping to appoint new chairs to several of these bodies. Our Vice Chair, Rebecca Middleton, sits on the steering group for the Newborn Genomes Programme and several other Panel members are on working groups focusing on elements of this research.

On 4 October 2022, the Panel published an article in the European Journal of Human Genetics about their work: Research Participants: Critical Friends, Agents for Change.[4] This article sets out the Panel's perspective on their contributions to Genomics England over the years and offers advice to other organisations seeking to embed patient and participant voices in their work too.

> "If we have made even one conversation less difficult for patients and their families, we are making a positive difference."

We live with daily reminders about the importance of genomics in healthcare. We and our loved ones are still looking to Genomics England and its partners to find more diagnoses and treatments for people like us and the communities we are here to represent. We look forward to continuing to support Genomics England in doing the right things for its participant population in the year ahead.

Observer of the Genomics England Board review

Professor Dame Sue Hill
Chief Scientific Officer and Senior Responsible Office for Genomics in the NHS

We are now offering WGS routinely alongside other tests for more than

3,200

rare conditions

As this annual report clearly demonstrates, genomics can transform care for patients in the NHS by enabling them to receive more accurate diagnoses and more targeted treatments. It's a field that has a strong history in the NHS, with genetics playing a role since its inception nearly 75 years ago.

Since then, we have gone from strength to strength, initially through a collaborative partnership between NHS England and Genomics England to deliver what remains of the world-leading 100,000 Genomes Project, which laid the foundations of the NHS GMS. Through this service, we are now offering WGS routinely alongside other tests for more than 3,200 rare conditions and over 200 cancers.

This is underpinned by our new strategy – Accelerating Genomic Medicine in the NHS[5] - which sets out the vision for embedding genomics in the NHS over the next 5 years and where we will work with Genomics England on innovation in further areas to bring benefits to patients and their families.

Collaborations are essential in ensuring patients continue to benefit from genomics, and we in the NHS can rapidly capture and embed cutting-edge scientific and technological advances. We're delighted to be working closely with Genomics England on important research projects such as Cancer 2.0, Diverse Data and the Newborn Genomes Programme. These initiatives have the potential to allow the NHS GMS to accelerate the discovery of new diagnostic tests and new genomic targets for treatments, as well as the analysis and understanding of genomic variants. This work will also ensure we understand how genomic variants are reflected within our diverse communities and population and the significance of this.

We are going one step further with the NHS GMS Research Collaborative. This brings together the expertise of the NHS GMS, Genomics England and the National Institute for Health and Care Research to facilitate genomics research and innovation using the GMS infrastructure and continue to enhance Genomics England's National Genomics Research Library.

It's a truly exciting time to be involved in genomics. Genomics is the future of healthcare and the NHS and Genomics England are at the forefront of this revolution.

> "Collaborations are essential in ensuring patients continue to benefit from genomics, and we in the NHS can rapidly capture and embed cutting-edge science and technological advances."

CEO statement

This has been quite a year to remember. Our people – the patients and participants we serve – continue to demonstrate their agility and resilience in the face of instability.

I am especially pleased in that context to reflect on several highlights as Genomics England has continued to grow and develop its impact in support of our mission.

Perhaps the most obvious of these changes is the recent move to our new Canary Wharf office, along with opening a presence in Leeds and expanding our footprint in Hinxton at the Wellcome Sanger Institute. After a couple of years of mostly remote working, you can feel the buzz from our people being back together again as you walk the floor, with training sessions, workshops, team socials – it's great!

> "In 2022, we welcomed more than 100 new joiners, representing a diverse range of talent from 37 nationalities."

On that note, it has been inspiring to welcome some extraordinary new colleagues as we have grown our team to reflect our expanded scope and mission (for instance, the launch of our Newborn Genomes Programme). I am constantly impressed by the talent we continue to attract from around the world in a competitive industry. In 2022, we welcomed more than 100 new joiners, representing a diverse range of talent from 37 nationalities.

Chris Wigley

CEO

Chris was previously COO at QuantumBlack, a bespoke machine learning and AI technology company, and a Partner at McKinsey, working on technology strategy topics. He is a Trustee of the New Entrepreneurs Foundation, and on the advisory board of deep-tech VC Entrepreneur First. He previously worked for the UK Foreign Office, establishing and leading analytical work at the Counter Terrorism Policy Department to counter chemical, biological and nuclear terror threats. During the COVID-19 crisis, Chris was seconded as Senior Responsible Officer for Data to NHSX. He lives in London with his wife Tara and their three children.

We have sharpened our focus on delivery of our 5 key commitments:

We reached the milestone of having helped over 20,000 individuals and families with genomic insights and diagnoses in partnership with the NHS GMS – this is the world's first service of this kind at a national scale

Our cancer research has identified multiple new mutational profiles, enabling an advanced approach to cancer aetiologies and personalised cancer medicine

The Newborn Genomes Programme was launched to a very positive reception and has begun testing the feasibility of collecting different types of samples through the Babies and Mums Sample Study

In line with our goal of accelerating genomic research, we are now powering discoveries with a wider range of data than ever before including multi-omics, imaging and the data from the NHS GMS collaboration, which is held safely and securely in our Research Environment after appropriate consent

The Diverse Data team initiated sequencing partnerships in sickle cell, launched link23 – an open-source initiative for tools for genomic equity and kick-started a national priority-setting exercise with patients to understand the opportunities for genomics in sickle cell

We exist as part of a world-leading genomics ecosystem. The government's Genome UK strategy paper sets out a vision for this ecosystem that will drive the future of healthcare. We share an appetite for innovation with our partners that allows new technologies to come to the fore, and new ways of working that embed these into routine care.

Collaboration with the NHS is a driver in our ability to provide positive outcomes for patients. We are proud to support the NHS GMS and to continue working with the NHS on both the clinical and research sides of the infinity loop (page 35). This year we developed a variant-based approach to increase the number of potential new diagnoses identified through research. Using this approach alongside our existing work through the Clinical Research Interface, we were able to return over 1,500 potential diagnoses back to the NHS. Our Newborn Genomes Programme, an NHS-embedded research study, will also continue to demonstrate the positive impacts of this foundational partnership.

Our wider partnerships are also essential to our delivery capabilities. Our relationship with Illumina, our sequencing partner for the NHS GMS and much of our research work, continues to go from strength to strength as we rapidly increase our caseloads. The work of Oxford Nanopore Technologies is central to our cancer long-read sequencing programme. Incidentally, I was honoured to speak at its Population Scale Genomics Summit in Singapore this year and was pleased to learn more about work that is already under way in the Asia-Pacific region. We also place immense value on our industry and academic partners who access our Research Environment to conduct research. This is essential for delivering the research side of the infinity loop.

Nothing we do at Genomics England has value without our participants. They are our North Star, guiding all we do. We are very fortunate to have the Participant Panel, who are as driven by our mission as we are and support us by providing oversight and offering crucial perspectives. Their voices continue to play an integral role, in particular when we're working through new challenges such as research consent for the Newborn Genomes Programme. We are excited to be expanding the Panel soon to ensure it reflects the diversity of the communities we serve.

Times of reflection such as these inevitably provide opportunities to look to the future. Our ongoing focus is the delivery of our core commitments. We will be conducting a strategy review to plot our course over the next 3, 5 and 10 years – which will align with the next spending review period.

> "An appetite for innovation that we share with our partners allows new technologies to come to the fore."

I am more optimistic than ever before that we, as a country, will sustain our leadership in the genomics space. We will continue to partner in support of the NHS's genomic healthcare offer and work to develop it to provide more proactive and personalised medicine. We will facilitate groundbreaking research through our Research Environment to allow the development of new drugs and therapies. We will do it all for the patients and participants we serve.

See page 77 for details of references

We partner with the NHS to provide whole genome sequencing diagnostics.

Genomics England

We also equip researchers to find the causes of disease and develop new treatments – with patients and participants at the heart of it all.

Vision

Paving the way for personalised medicine

The genome and beyond

Our focus has always been on whole genome sequencing (WGS) and how to best use it to help people living with rare diseases, cancer and other conditions.

WGS allows us to look at millions of fragments of DNA at once. Clinicians can therefore use one test to screen each patient for many genetic conditions.

Our original goals were shaped by the technological capabilities of the time. Technology has since advanced, and we've adapted to these changes to ensure that new developments in research are delivered into the clinic to directly impact patients. We are already supporting the NHS with short-read WGS in routine care. Now, we are piloting long-read sequencing and looking to combine genomic data with broader health information, which is known as multiomics.

Building a better picture of health

As technology advances, genomics has the potential to revolutionise the field of predictive medicine by providing more personalised and effective strategies for disease prevention and treatment.

We're working towards a world where multiomic, clinical and real-world health data are becoming increasingly linked. It is where machine learning and expert teams can deliver deep insights, at scale, and where researchers can access a world-leading genomic data library to make scientific discoveries.

Our partnership with the NHS will continue to help us create a world where genomics enables personalised medicine and can be accessed by everyone.

Multiomics
Linking genomics to information about proteins (proteomics), metabolism (metabolomics) etc

Whole genome (long-read)
Sequence complex regions of the entire genome

Whole genome (short-read)
Sequence the entire genome, introns and exons

Whole exome sequencing
Sequence coding regions of all 22,000 genes

Disease focused panels
Test multiple genes associated with specific condition

Single gene test
Search for changes in individual gene associated with specific condition

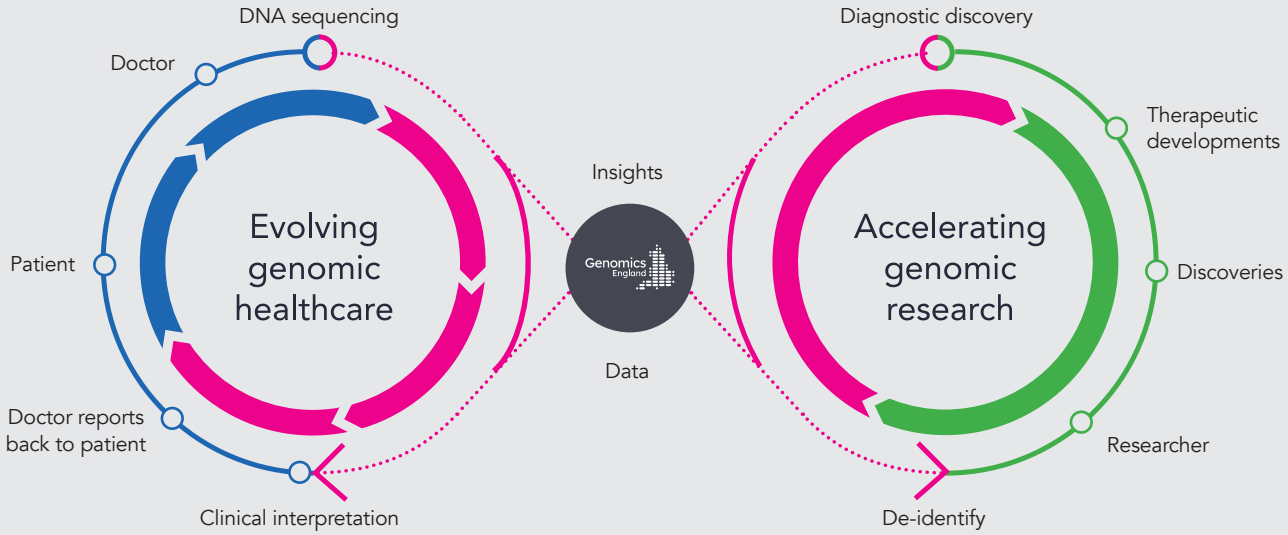
Genetic parental test
Count individual chromosomes

Our strategy

The infinity loop: connecting healthcare and research in genomics

Evolving genomic healthcare
We support the NHS to offer whole genome sequencing to patients who might have genetic conditions and help to interpret results before they go back to a patient's clinician.

Accelerating genomic research
Many patients and their families opt to share their genomic and health data for research. We securely hold their data and facilitate secure access to it for approved researchers. They use the data to unlock scientific breakthroughs in rare conditions and cancer.



Healthcare data feeds into research, and research generates new insights that might improve diagnoses and treatments for NHS patients

Fostering collaboration between research and clinical communities

The Clinical Research Interface (CRI) provides a safe and effective pathway for insights and data to be exchanged between researchers and NHS clinical teams to bring research findings into clinical care and benefit research.

This helps to:

- provide research-identified diagnoses to participants through their healthcare professionals
- facilitate collaboration to enable fundamental and translational research in diagnostics and therapeutics

How the CRI pathway works:

1. A researcher may identify a potential new diagnosis for a participant with a rare disease – known as diagnostic discovery. Alternatively, they may make a scientific discovery and wish to collaborate with a clinician for further information.
2. The researcher contacts the CRI team by submitting a request from the Research Environment.
3. The CRI team review the request for scientific and clinical validity and confirms participant consent.
4. Potential new diagnoses that meet criteria (agreed between Genomics England, NHS England and Genomic Laboratory Hub (GLH) representatives) are returned to NHS laboratories for formal evaluation and reporting.
5. To initiate collaboration between researchers and clinicians, the CRI team contact clinicians to invite them to get in touch with the appropriate researcher.
6. The CRI team continue to facilitate collaboration between NHS laboratories, clinicians and researchers to ensure the CRI pathway operates effectively.

This process enables all participants to benefit from new knowledge and analytical methods discovered by researchers. Findings can inform future developments in the NHS Genomic Medicine Service (GMS).

Noah's story

Ten years on from its launch, the 100,000 Genomes Project continues to deliver benefits and clarity for participants such as Noah and their families.

Diagnosis supported by continued research

Noah was diagnosed before the age of 3 with autism and a learning disability, but his parents always wondered if something else was going on. They noted that he looked different from his 4 siblings, 2 of whom also had autism diagnoses but didn't have the same learning difficulties.

In 2015, the family's geneticist invited them to take part in the 100,000 Genomes Project. While the first round of genomic results found nothing of significance, the family were told additional testing would continue to be done over time.

Rare variant found

Seven years on from their initial involvement in the 100,000 Genomes Project, Noah's parents Carys and Andy received a phone call asking them to make an appointment with the genetic team in Exeter. When they met with their geneticist, the family were told that the team believed a genetic 'spelling mistake' in a recently discovered gene known as FOXP4 was the cause of Noah's condition.

They were told the variant found was incredibly rare – only 10 children worldwide have the same diagnosis. As it is a de novo variant, neither parent has it and it is highly unlikely that their other children have it, too.

While scientists are still learning about FOXP4, it's thought that conditions caused by variants in the gene include neurodevelopmental conditions, delays in speech and language and some conditions present from birth.

An opportunity to learn more

While the diagnosis doesn't change things in a practical sense for the family or in terms of different treatments for Noah, it does provide them with an explanation and gives them the opportunity to learn more about Noah's condition. Both parents were relieved and grateful to find the cause and took comfort in knowing the diagnosis came without any additional health implications for Noah.

Noah's dad, Andy, says: "It was so good to find out there was no reduced life expectancy or any other health risks associated with the diagnosis."

> "While the diagnosis doesn't change things in a practical sense for the family or in terms of different treatments for Noah, it does provide them with an explanation and gives them the opportunity to learn more about Noah's condition."

Noah

Rachel's story

How we work in practice

At the age of 15, Rachel Gilbert was diagnosed with gastrointestinal stromal tumour (GIST), an incurable and incredibly rare type of sarcoma that occurs in the gastrointestinal tract. WGS via the 100,000 Genomes Project enabled Rachel to find out more about her cancer and allowed her doctor to identify the most suitable treatments for her.

Rachel initially saw her GP in 2001 after feeling increasingly dizzy, tired and experiencing stomach pain. After receiving treatment for low iron, her haemoglobin continued to fall to dangerously low levels and, following an endoscopy, she was diagnosed with GIST. GIST tumours form in the gastrointestinal tract, which includes the stomach and intestines. Doctors discovered she had been bleeding internally from the tumours for up to 5 years and she had developed secondary cancer on her liver.

15

people are diagnosed with sarcoma every day, which is about 5,300 people a year

Getting a diagnosis

Genetic factors can increase the risk of having GIST and, in 2017, Rachel's doctor suggested genomic sequencing to help her find out more about her cancer. The results showed that Rachel had wild-type GIST, a rare sub-type, caused by a glitch in her genes. The results helped identify the most suitable treatments for her, along with those she would not be able to tolerate. The process also indicated that Rachel's type of sarcoma could be hereditary, so her family were offered screening. It additionally highlighted that she was at a higher risk of developing other rare cancers, which she is now screened for annually.

"Genomic testing has been really helpful to myself and my family," she said. "It's reassuring to be regularly screened for other cancers and to know that my doctors are using the best information available to them to treat me as, sometimes in the past, treatment would make me really sick. It may also be useful for my family to be screened to see if they are more at risk of developing cancer."

Hope for the future

Now 35 years old, Rachel has undergone 3 different types of chemotherapy and has had 16 stomach tumours removed, along with 90% of her stomach. Today, Rachel devotes her time to raising awareness about cancer on social media. By sharing her experience, she hopes to help others in similar situations to seek medical help earlier, where there is a better chance of treatment success. She will be taking part in a new clinical trial at Addenbrookes Hospital in Cambridge, which she hopes will pave the way for more effective, personalised treatment options for those with her condition.

Rachel said: "I feel excited about the possibilities of the trial and more positive than I have in a long time. I am hoping it will be the resulting treatment that cures my cancer and that I will finally get better. I'm hopeful, too, that agreeing to donate my sample to the National Genomic Research Library will help researchers to find a cure for all sarcoma cancers one day."

> "I feel excited about the possibilities of the trial and more positive than I have in a long time. I am hoping it will be the resulting treatment that cures my cancer and that I will finally get better."
>
> Rachel Gilbert

Rachel

Oliver's story

WGS via the NHS GMS

When baby Oliver was born with a large tumour on his leg, his parents feared the worst. But, thanks to WGS via the NHS GMS, the lump was revealed to be harmless, and Oliver was spared chemotherapy and surgery.

Just a few days before Oliver's birth, his parents received concerning news when an ultrasound scan showed a large tumour on his right leg. Doctors initially thought Oliver's tumour looked like a type of sarcoma called infantile fibrosarcoma.

The family were referred to the paediatric oncology team at Cambridge University Hospitals NHS Foundation Trust, where Oliver underwent a series of blood tests. However, the standard molecular tests failed to confirm the diagnosis.

Uncovering a different diagnosis

To help solve the mystery of Oliver's diagnosis, consultant paediatric oncologist Dr Sam Behjati suggested WGS, a test offered routinely for children with cancer, via the NHS East GLH.

By sequencing the whole genome of Oliver's tumour and comparing this to the sequenced DNA in his blood cells, WGS revealed a subtle and unusual error in the lump's genetic code, which changed the diagnosis from cancer to myofibroma, a benign type of tumour.

Speaking about the life-changing diagnosis, Oliver's mother Sarah said: "For the first 8 weeks of Oliver being born, we lived with the prospect of cancer dominating all our lives and chemotherapy being the next step. Two weeks after his whole genome test, everything changed. We couldn't be more relieved."

A new approach to treatment

The initial diagnosis of infantile fibrosarcoma would have meant that

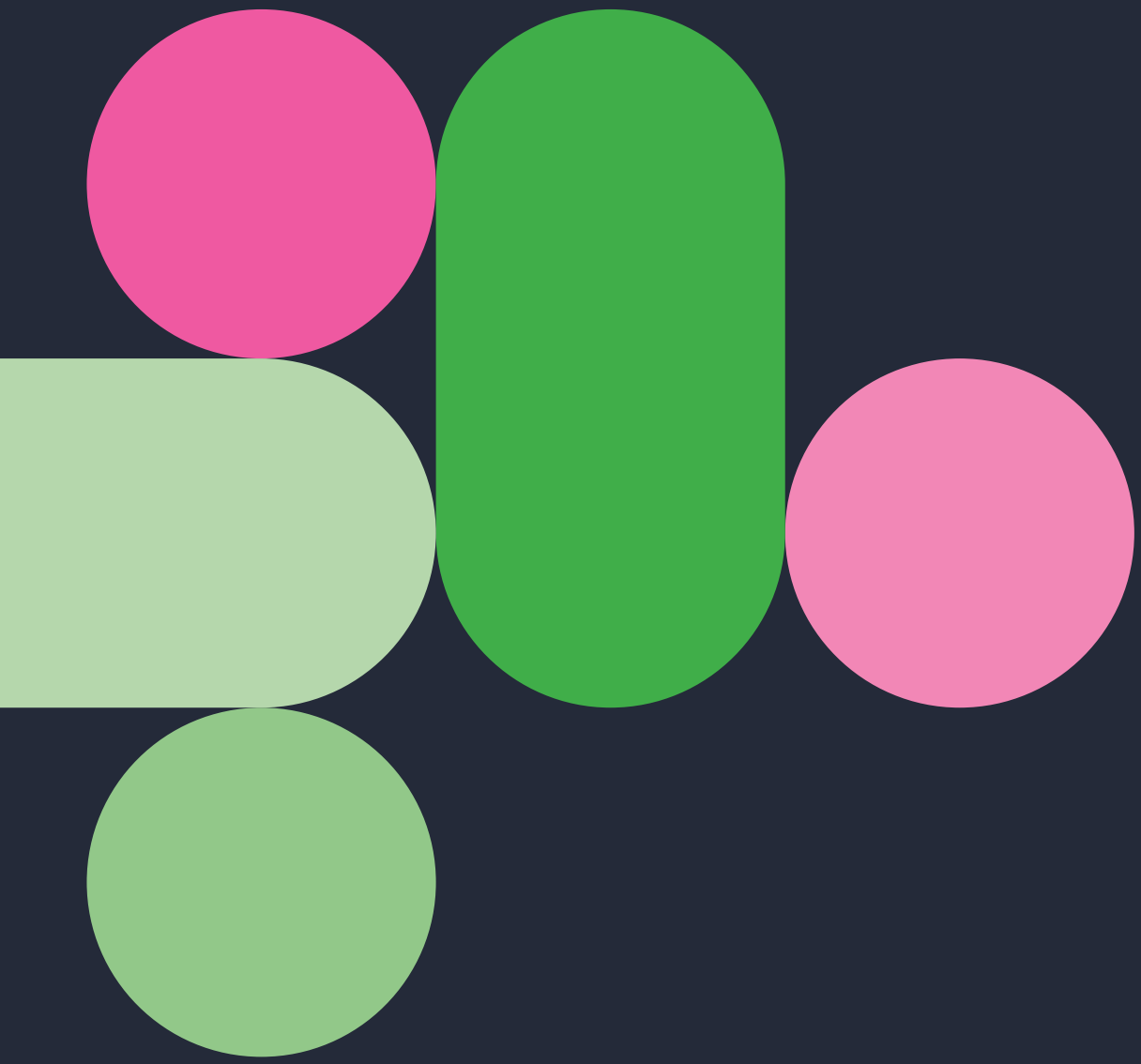
Oliver needed surgery, chemotherapy or other drugs to treat the cancer. Instead, with the revised diagnosis, Oliver's doctors were able to change their treatment plan, opting to observe the tumour first instead. They found that the lump started to shrink without any treatment, sparing Oliver from unnecessary surgery and chemotherapy.

Oliver's father Michael added: "Our lives were turned upside down when we thought Oliver would need surgery and chemotherapy. Receiving such clarity on the type of tumour we were dealing with was so important. It was like a miracle – a miracle test that told us he didn't have cancer and we could go back to our normal lives."

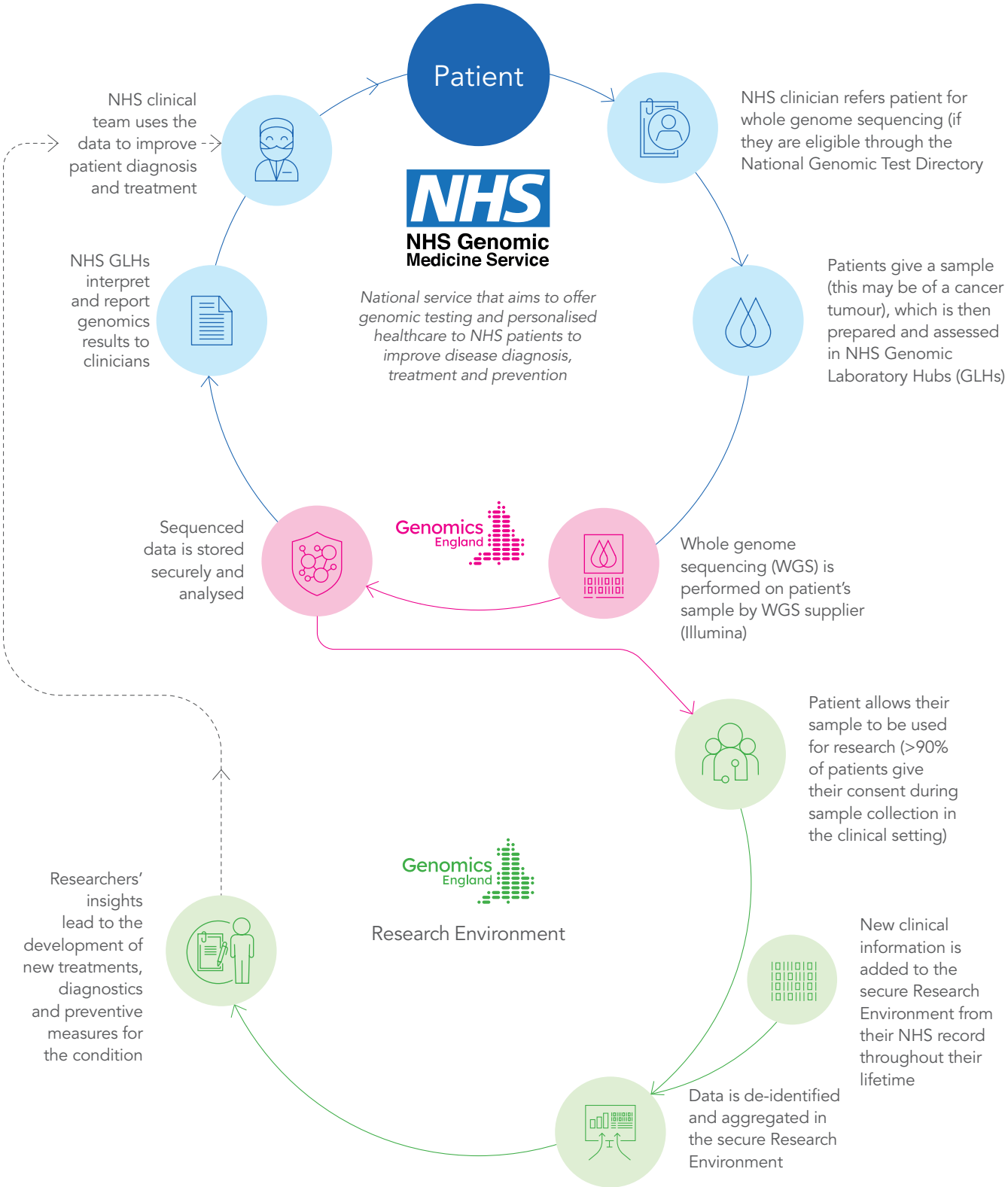
> "Our lives were turned upside down when we thought Oliver would need surgery and chemotherapy."
>
> Oliver's father

Oliver

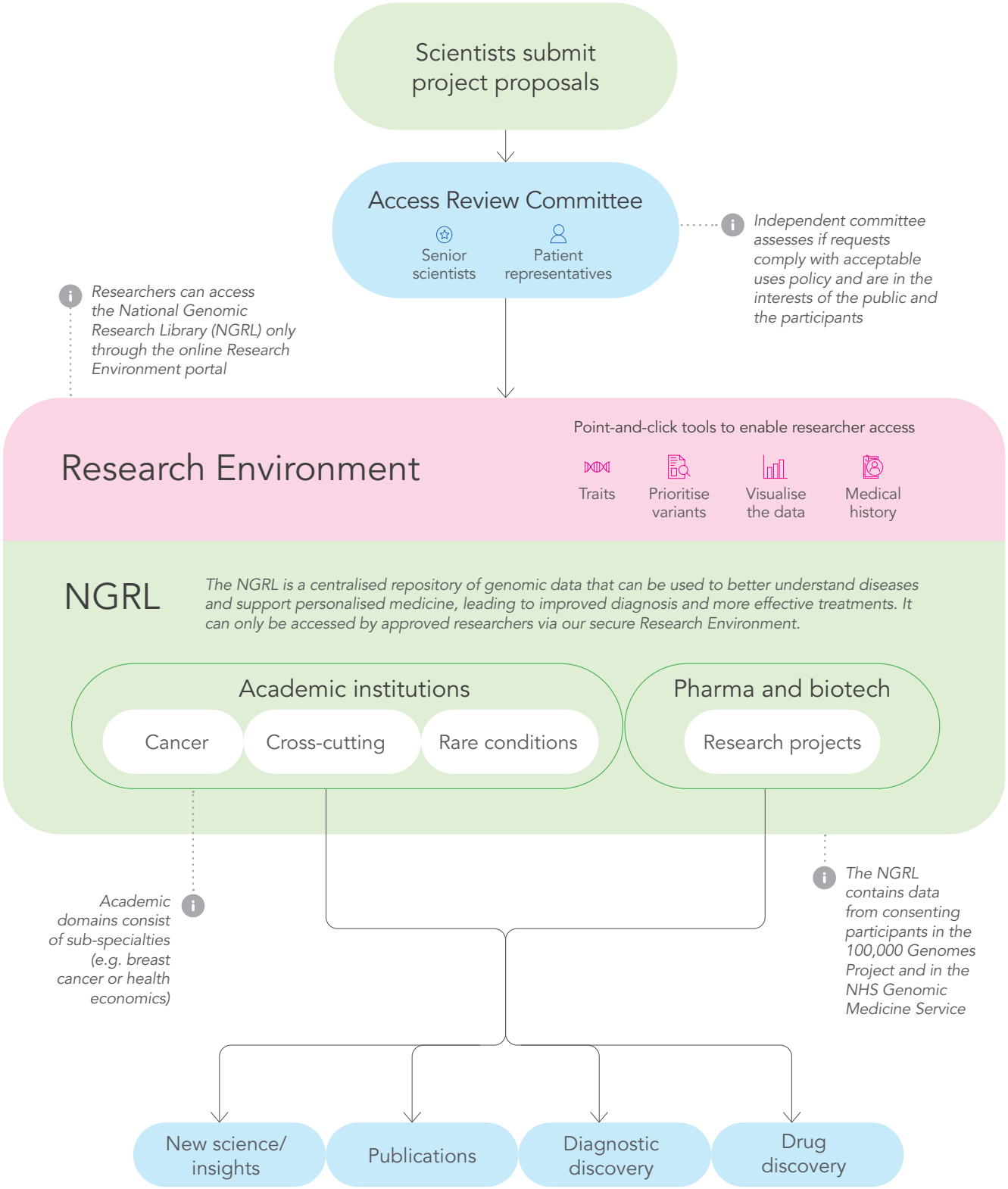
At a glance

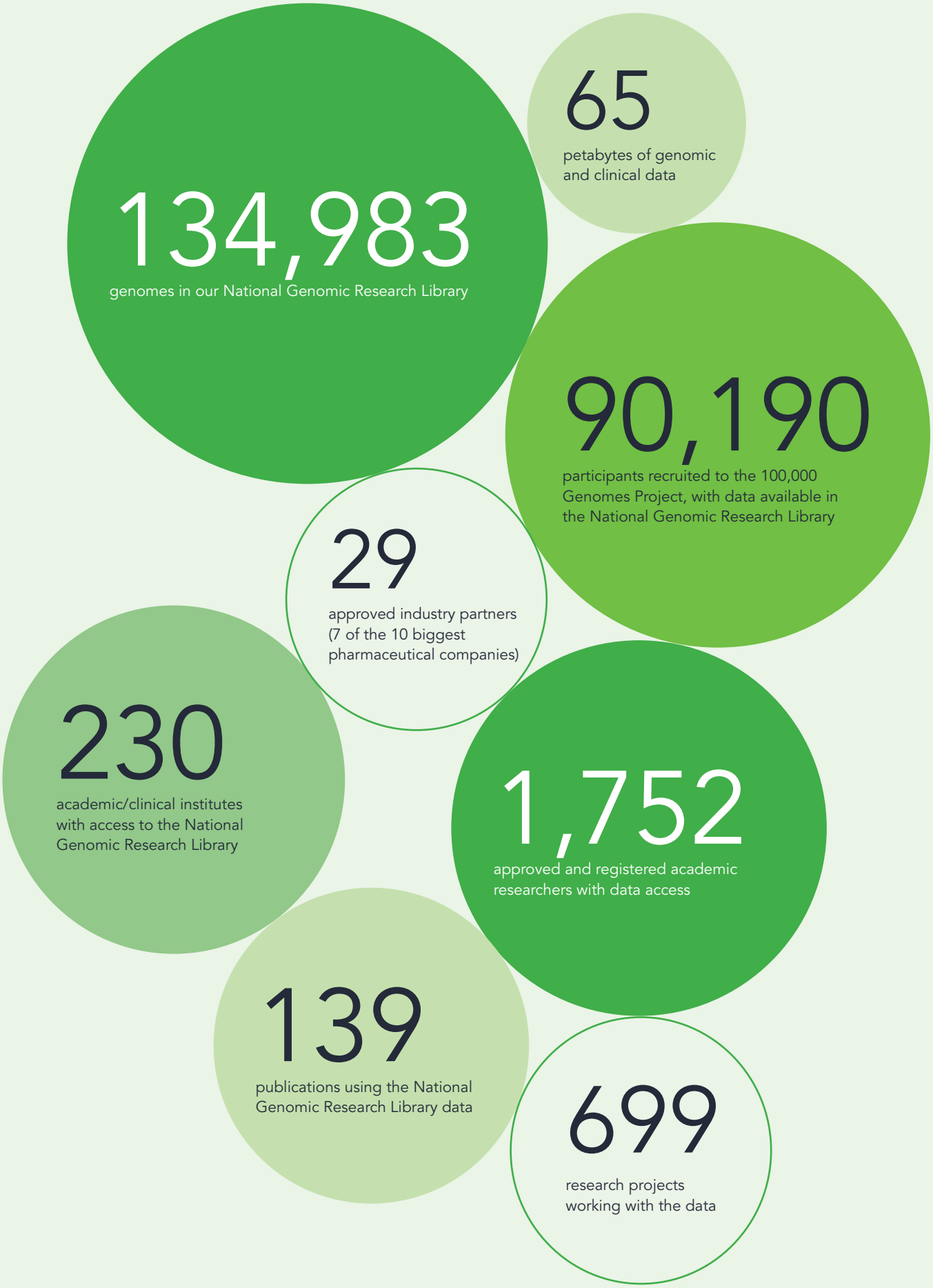


Whole genome sequencing, the patient journey and the NHS Genomic Medicine Service



The National Genomic Research Library and how to access it




134,983
genomes in our National Genomic Research Library
65
petabytes of genomic and clinical data
90,190
participants recruited to the 100,000 Genomes Project, with data available in the National Genomic Research Library
29
approved industry partners (7 of the 10 biggest pharmaceutical companies)
230
academic/clinical institutes with access to the National Genomic Research Library
1,752
approved and registered academic researchers with data access
139
publications using the National Genomic Research Library data
699
research projects working with the data

Our virtues

"There's an interesting debate whether **speed** is the enemy of quality. We see genomics medicine as part of the future and, if we want to be a future-maker, then we simply have to move faster than at present... there are patients at the other end of this who today are often on clinical pathways that are 15 years long and that's such a deeply frustrating thing for a patient, and they deserve better."

Parker Moss
Chief Ecosystems and Partnership Officer
Genomics England

"**Empathy** is the ability to share and understand the feelings of others. It's completely central to what we do. If you think about our most important users, it's the patients, the participants – understanding their illnesses, their challenges and what's important to them is completely at the heart of it."

Dr Richard Scott
Chief Medical Officer, Deputy CEO
Genomics England

"Much of what we're doing is amazing science and amazing tech and this is why **curiosity** is important. We've got huge amounts of data – it's all fascinating stuff. But we also need to understand what impact that has on people at the other end of the line; it's what keeps us going day to day."

Professor Matt Brown
Chief Scientific Officer
Genomics England

"Once you start thinking as a collective, everyone is coordinated. There needs to be some coherence of communication because everyone needs to know where they're going. Ultimately, **focus** is the way we channel all that energy... and deliver it in a way that will cause impact."

Nick Maltby
General Counsel, Company Secretary and Data Protection Officer
Genomics England

"**Connection** is about making time and engaging fully with other people so we can challenge, discuss, learn from each other, innovate and empathise. We need to help break down silos, understand people's needs and desires and help bring those components and parties together so that we are thoughtful about how the ecosystem can be built and also how it can run and be effective."

Rakhi Rajani
Chief Digital and Strategy Officer
Genomics England

"**Integrity** is all about how we engage with each other in an honest way... we come from a set of worlds where integrity is paramount. This is especially against a government background; integrity is an absolutely core part of the Civil Service and that concept of speaking truth to power."

Catherine Byers
Chief Financial and Performance Officer
Genomics England

"**Impact** is about making a significant and long-lasting difference and leaving a mark on people's lives. It's about measuring the outcomes that we've achieved. We are measuring as we go to make sure we're actually doing the thing we wanted to achieve."

Pete Sinden
Chief Information Officer
Genomics England

The ecosystem

An overview of the genomics ecosystem

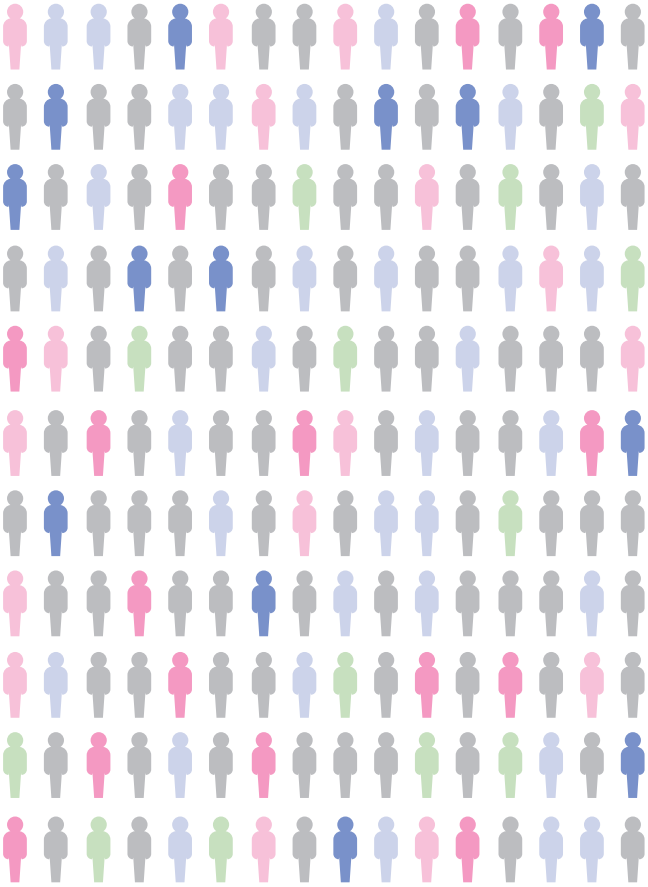
The wider UK genomics sector has approximately

121 companies

A market capitalisation of over

£3.5bn

based on deals since 2017, according to the Genomics Nation 2022 report[6]



Over 3,500 employees

Genomics England is one part of a wider UK ecosystem that has been built through years of consistent investment. We work with our partners and funders to deliver genomic healthcare for patients and have played an important role in accelerating genomic research.

Our work is overseen by the government, with responsibilities shared between the Department of Health and Social Care (DHSC) and the Office for Life Sciences (OLS). OLS – a joint unit of the DHSC and the Department for Science, Innovation and Technology – champions research, innovation and the use of technology to transform healthcare.

Our biggest partner is NHS England, which we help to deliver the NHS Genomic Medicine Service (GMS).[7] We collaborate with a range of life science and tech organisations, including small and medium-sized enterprises (SMEs) and start-ups. On the next page, we highlight some of the new partnerships and collaborations developed over 2022.

Working with industry

Genomics England has a mandate from our participants, expressed clearly by the Participant Panel and the Access Review Committee, to allow the biopharmaceutical industry to use the National Genomic Research Library (NGRL) for a fair economic return.

We charge an access fee for our commercial partners; 7 of the biggest 10 pharmaceutical companies in the world pay to access the data. We also recognise the huge contribution to research and development made by the SME industry, including start-up companies. For this reason, SMEs are charged a reduced access rate. Funding received is reinvested to improve the experience for all our users.

We've also partnered with 3 accelerators, which help us find some of the best early-stage start-ups with a specific genomics focus in cancer and rare disease. We're proud to support start-ups to build companies based on the data, and to focus on improving the lives of participants who we represent.

Public sector

NHS England

Office for Life Sciences

Department of Health & Social Care

Department for Science, Innovation & Technology

Major tech

aws

Provides a secure, cloud-based way for researchers to access the data stored in the NGRL

illumina

Provides whole genome sequencing for NHS GMS and supported the 100,000 Genomes Project

Oxford NANOPORE Technologies

Developed a new generation of sequencing technology based on nanopore sequencing, which allows for the direct, real-time sequencing of DNA molecules

Innovators

Congenica
Enabling genomic medicine

Hosts a decision support platform, used by the NHS GMS, which allows the rapid analysis and interpretation of genomic data in patients with rare conditions

lifebit

Provides a cloud-based platform to support the secure and efficient processing, storage and analysis of previously inaccessible genomics data

insitro

Uses machine learning and AI to accelerate the discovery and development of drugs and therapies

Nostos Genomics

An AI-driven start-up looking to use sequencing data to reduce rare condition diagnosis time by 99%

See page 77 for details of references

Research

Impact of genomic research

We support a thriving research community of academic, clinical and industry partners from around the globe.

Research community

Academic, clinical and industry researchers work together on the data in the National Genomic Research Library (NGRL) to address unsolved diagnoses for patients and make breakthroughs in genomic science that could lead to therapeutic discoveries and opportunities for clinical trials. We enable researchers to report these findings directly back into the NHS.

Below, we highlight the wide range of research done from that published in scientific papers (the standard measure of academic impact) to ongoing research projects, which promise even more impactful discoveries on the horizon.

Research projects

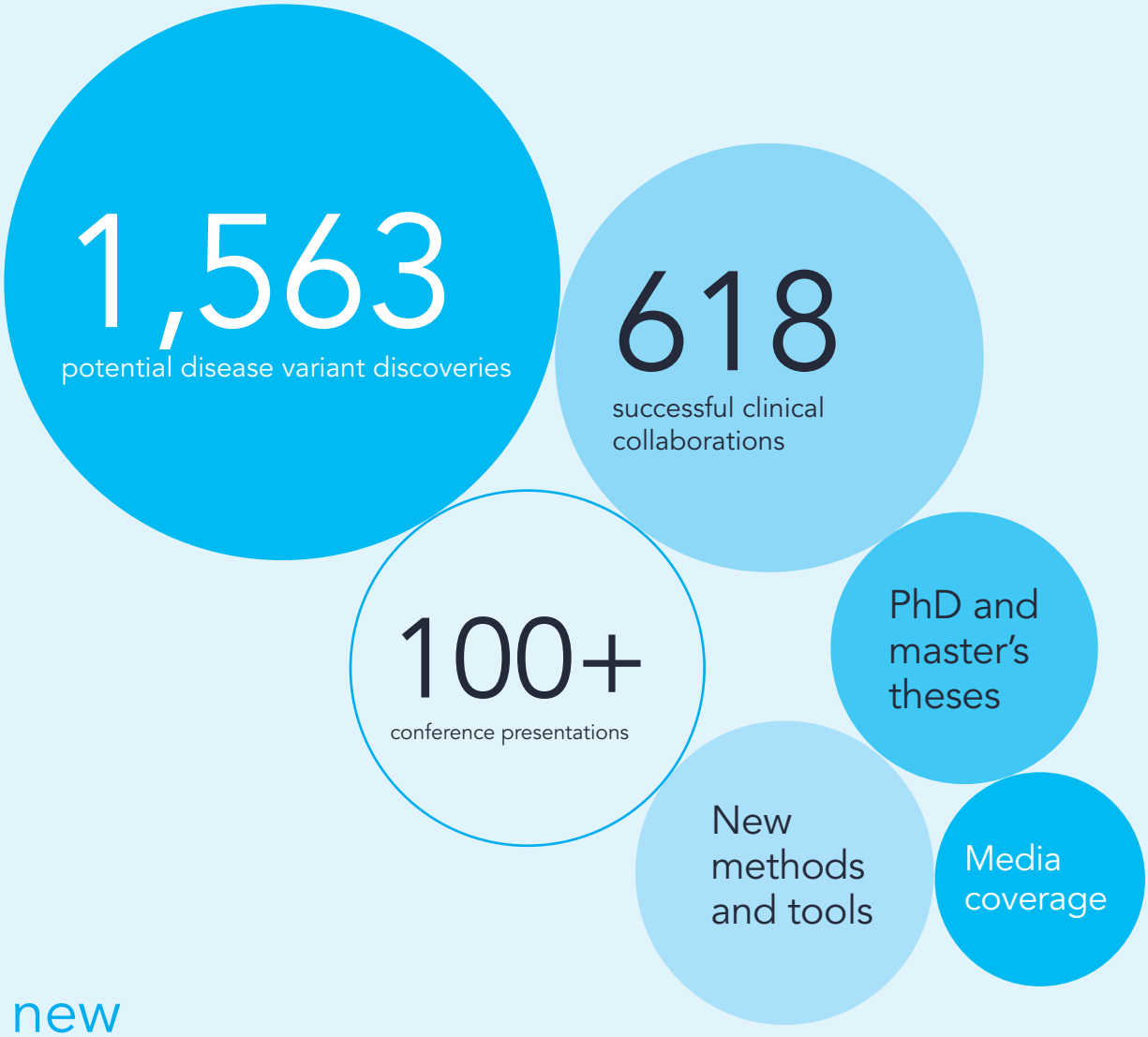
Groundbreaking research under way

- Exploring how genetic changes in blood cells can be used to better understand and diagnose diseases
- Using genomics to understand how ancestry influences cancer
- Understanding how rare structural genetic variants cause deafness in babies
- Investigating the genetic causes of motor neurone disease to drive therapeutic discovery

632
projects in progress

67
projects completed

Numerous research outputs…



A new research strategy

When Genomics England was first established 9 years ago, our goals were shaped by the technological capabilities of the time. We focused on how to best use whole genome sequencing (WGS) for rare conditions and cancer, including research into diagnostic and therapeutic approaches.

Since then, technology has advanced, and genomics has rapidly evolved. Now, we can conduct large-scale laboratory investigations, take AI-led analytical approaches and develop extensive publicly available bioinformatic resources.

Our new research strategy will focus on unlocking the power of one of these advances: multiomics.

That means we are adapting beyond WGS to focus on a more holistic personalised medicine approach.

Through multiomics, novel insights can be uncovered. Cell processes are interconnected, and multiomics allows a multi-layered, deeper analysis and gives the biological context of disease-causing genetic variants.

Our research strategy will also expand our focus in ethics, functional genomics and sequencing methodology.

Research impact

How can we help achieve research goals?

- Generate unique datasets using a multiomic approach to support new discoveries in rare conditions and cancer
- Ensure that our Research Environment is easy for researchers to access and use
- Lead strategic research projects to integrate innovative technologies such as long-read sequencing
- Ensure the data and services reflect and benefit our communities in their full ancestral diversity
- Continually expand the NGRL by adding WGS data through programmes and services such as the NHS Genomic Medicine Service
- Enable the use of AI to study the increasing complexity of genomics
- Collaborate with leading research institutes and the global academic community to increase our number and diversity of partnerships

Our vision is to provide outstanding data and researcher experience on a global scale. By enabling the collection of genomic and health data across the UK to be used globally, we can inform fundamental science, new diagnostics, therapies, technologies and clinical pathways.

"The rapid advances of genetic research capabilities create so many exciting opportunities to improve healthcare, from rare diseases to cancer. It's a great time to work with Genomics England in research across the spectrum of genomics to improve human health."

Professor Matt Brown
Chief Scientific Officer, **Genomics England**

Research events

Genomics England Research Summit

4 May 2022

At the first big in-person UK genomics event since the pandemic, we and our partners shared our latest research and technology innovations. It highlighted our ability to bring the extraordinary ecosystem together and emphasised the UK's world-leading role in genomics – in both research and how research is integrated into healthcare for the benefit of patients.

"I was blown away by looking at the agenda in terms of the types of science that this resource enables on both the oncology and rare disease side."

Daphne Koller
CEO and Co-founder, **insitro**

Research events

Discovery Forum 8

22 November 2022

A showcase of our strategy and initiatives, with a mix of talks from a range of genomics experts, including our research partners AstraZeneca and Boehringer Ingelheim. Roundtable discussions encouraged expert conversations in biomarker discovery, clinical trial design, newborn sequencing, multimodal data and diversity in research and development.

> "It was an amazing day, meeting key stakeholders in the transformation of medicine with genomics."

Manolis Kellis
Professor of Computational Biology and Computer Science,
MIT and Broad Institute

Research seminars

last Tuesday of every month

This series provides an opportunity to share the most exciting and interesting research being performed on the data within the genomic research and participant community.

Research and development

Our researchers at the Wellcome Sanger Institute in Cambridge are developing new tools to help improve genomic healthcare.

We are focused on 3 key areas:
long-read sequencing, transcriptomics and proteomics.

Long-reads

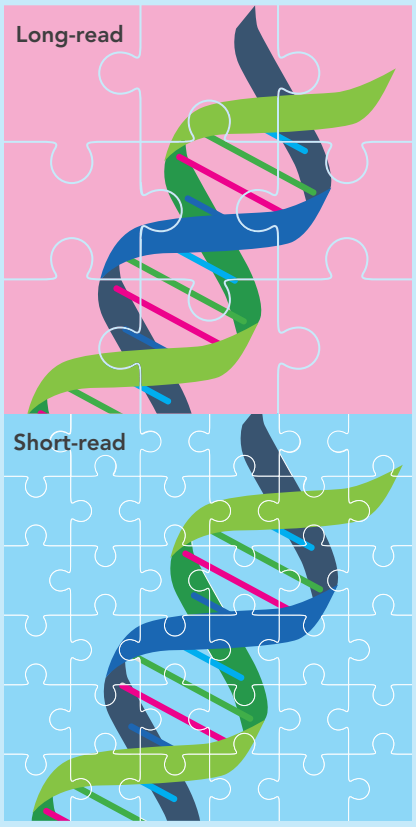
Long-read sequencing can read longer strands of DNA (up to 100,000 base pairs and beyond) than the existing short-read sequencing technology (300 base pairs) used at Genomics England.

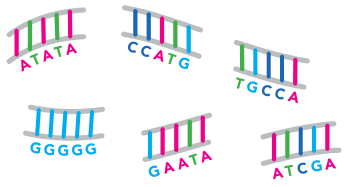
This allows for:

- faster sequencing
- deciphering of additional sequence features, such as methylation
- easier assembly of the genome
- better reading of certain sections of the genome

Ultimately, this could reduce turnaround times for test results and improve treatment options for patients We are exploring the different available long-read technologies (Oxford Nanopore Technologies and PacBio) to see which work best for our cancer and rare disease pipelines.

If sequencing a genome were like solving a jigsaw puzzle, long-read sequencing would make it easier by making all the pieces larger.





In short-read sequencing, DNA must first be broken into short pieces (<500 base pairs) to be sequenced.

Gaps in reconstruction

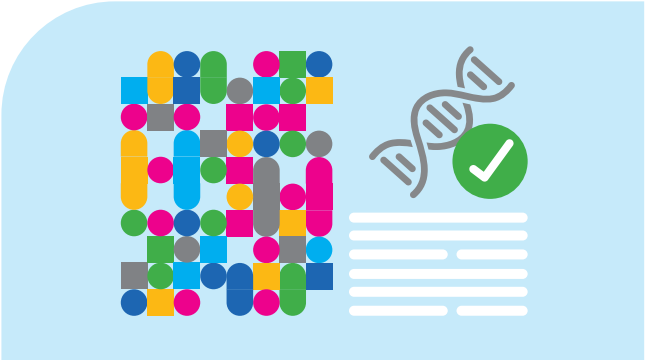
The whole sequence is then reconstructed digitally by computer algorithms.

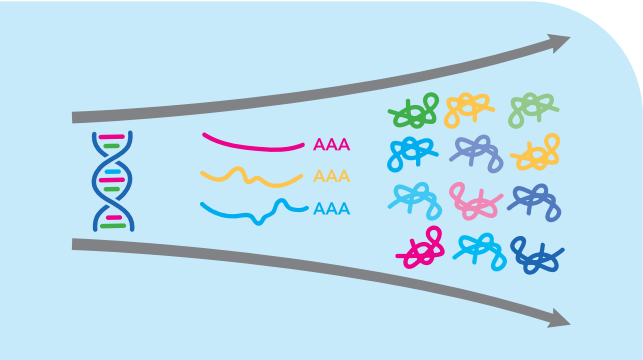
Long-read sequencing does not require this initial fragmentation.

Therefore, sequences can be reconstructed from larger building blocks.

"The scientific research and development team at Genomics England provide an essential bridge between emerging cutting-edge research technologies and clinical implementation. We are very excited about the potential of long-read sequencing and complementary 'omics' approaches using RNA and protein analyses."

Greg Elgar
Director of sequencing, **Genomics England**





Transcriptomics

Transcriptomics analyses RNA produced by cells in the body. RNA is the first molecule produced upon reading a cell's DNA and is responsible for directing the production of proteins.

We are working with UK Biocentre and Illumina, as well as researchers at the University of Southampton and the Wellcome Sanger Institute, to analyse the transcriptome of around 6,200 undiagnosed participants (the first to present with a disease in their family) from the 100,000 Genomes Project.

This work allows us to:

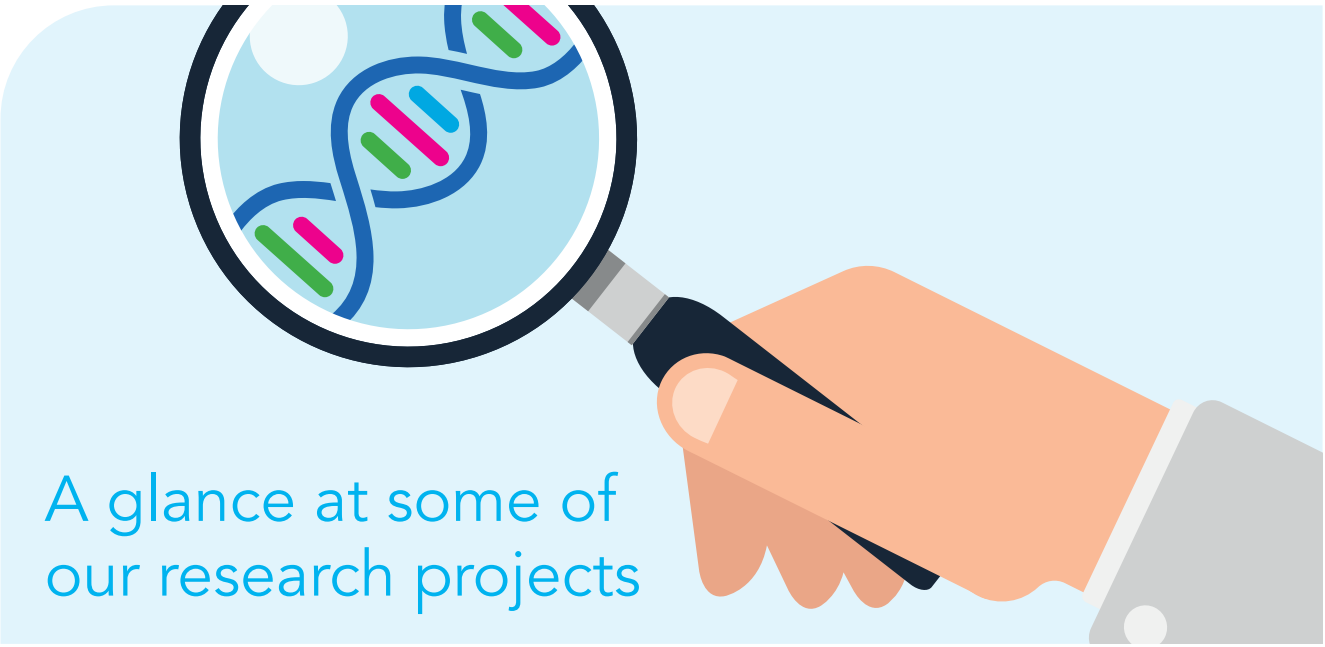
- examine the levels of different genes in blood, enabling an understanding of gene expression in different conditions
- identify variant forms of different genes
- link variants seen in the genome with their likely consequences at a functional level

Proteomics

Proteomics studies the proteins produced by the body's cells. Many genes code for proteins and they have key roles in helping our bodies work.

We are working with researchers from the Charité hospital in Berlin to analyse a set of proteins found in high levels in the same set of participants who are having their transcriptome sequenced.

In addition, we have worked with 2 companies, SomaLogic and Olink, in a pilot to look at low abundance proteins from 500 participants. We're collaborating with the MRC Centre Cambridge to understand if this data can provide diagnostic answers.



A glance at some of our research projects

Whole genome sequencing in rare disease diagnosis[8]

New England Journal of Medicine, November 2021

This study demonstrated the power of WGS for providing diagnoses to rare condition patients. It analysed the genomes of 4,660 early participants in the 100,000 Genomes Project and found that using WGS led to a diagnosis in 25% of them. Of these, 14% would have been missed by conventional non-whole genomic tests.

Liver degeneration caused by mutations in gene TULP3[10]

American Journal of Human Genetics, May 2022

Organ fibrosis is a feature of many common diseases and can lead to a decline in organ function and death. However, its molecular causes are poorly understood. In this analysis of several large groups of individuals with unexplained liver or kidney disease, researchers found 15 patients with variants in the TULP3 gene that cause progressive organ fibrosis. Their work improves our understanding of the condition and facilitates early detection and optimal clinical management.

Analysing mutated genetic signatures in UK cancer patients[9]

Science, April 2022

As cancer develops, patterns of damage and repair cause mutations to accumulate in tumour DNA. These mutational signatures can provide valuable insights into tumour biology and personalised treatments. Researchers analysed the genomes of 12,222 cancer patients in the 100,000 Genomes Project. They examined the significance of previously known and rare new signatures and produced an algorithm that can be used to tailor clinical treatments for cancer patients. These rare signatures can often be detected only in very large sets of data, highlighting the critical importance of resources such as the NGRL.

New diagnoses for patients with rare conditions[11]

Genome Medicine, July 2022

Over 50% of patients with rare conditions live without a precise diagnosis. When DNA gets copied during protein production, non-coding pieces of genetic information get removed; this process is called splicing. Disruption in splicing is a major cause of genetic diseases. Research using data on splicing variation from the 100,000 Genomes Project found a new genetic diagnosis for 6 of its participants that previous routine practices were unable to identify.

Helping to solve the COVID-19 puzzle

We worked in partnership with the GenOMICC consortium – a global collaboration to study genetics in critical illness led by the University of Edinburgh – to better understand the genetic factors contributing to severe COVID-19.

Decoding the puzzle

This study used whole genome sequencing for approximately 15,000 people who had experienced severe COVID-19 symptoms and had been assessed as critically ill. Their genomic data was compared to genomes from a control group including participants from the 100,000 Genomes Project and 15,000 healthy volunteers who had experienced only mild symptoms of COVID-19.

Better patient care

The initial phase of the study used data from approximately half of the recruited severe COVID-19 cases (n=7,500) and from 1,600 participants with mild symptoms. The results were published in Nature in March 2022, and further findings are anticipated in 2023.[12] The study identified 16 new genetic variants associated with severe COVID-19, including some related to blood clotting, immune response and intensity of inflammation. Seven other genetic variations already associated with severe COVID-19 discovered in earlier studies from GenOMICC and the COVID-19 host genetics international consortium were also confirmed.[13,14]

This study was key to helping identify new drug targets, as our findings were shared with the steering committee of the RECOVERY trial, a clinical trial where baricitinib was tested as a potential treatment for COVID-19 and resulted in reduced mortality of patients hospitalised with severe COVID-19.[15]

Difference by diversity

The study matched the demographics of the patients in both groups to reflect data from other studies, which had identified that people from ethnic minority groups are disproportionately affected by COVID-19. Approximately 30% of those in the study were from diverse backgrounds, as were 15% of the mild COVID-19 group.

Future impact

The findings of this study provided a large candidate list of gene targets for developing potential new therapies and drugs as well as a map of genetic variations that could be used to identify individuals at risk of severe COVID-19 and, potentially, other existing and future infectious diseases.

> “All those involved in the study made great efforts to engage with all communities within the UK – including groups that have historically been under-represented in medical studies.”

Dr Rich Scott
Chief Medical Officer, Deputy CEO, **Genomics England**

See page 77 for details of references

Turning science into healthcare, together

Genomics England

Partnerships

Our life sciences partnerships

Industry partnerships are crucial to the success of research supported by Genomics England. The genomic datasets are used to stimulate the life sciences industry, to develop new therapies and technologies that will improve healthcare and to stimulate growth in the UK's life science sector. Through engagement with industry, we aim to improve opportunities of access to new medicines, thereby improving the translational impact of our endeavours, supported by the government and the NHS.

We work with industry through the Discovery Forum

The Discovery Forum provides a platform for collaboration and engagement between Genomics England, industry partners, academia, the NHS and the wider UK genomics landscape. This platform enables us to work together towards transforming research findings into tangible benefits for patients, such as treatments and diagnostics. Ultimately, the Discovery Forum will aid in achieving our vision of improving patient care through groundbreaking genomics research.

Genomics England Discovery Forum 2022

Collaboration between academia and industry

Development of precision treatments for cancer

Bayer joined our Discovery Forum in 2019, enabling access to the National Genomic Research Library's (NGRL) extensive collection of whole genome sequences of tumour samples.

This genomic data was used to:

- generate real-world evidence to support the use of a targeted cancer treatment in patients who have a specific genomic abnormality (fusion protein) present in their cancer
- generate clinically engaging scientific insights in this therapy area

This work supported post-approval research of larotrectinib – a drug which targets abnormal fusion proteins by blocking their action, which can help slow or stop the growth of cancer cells. Larotrectinib can be used across many different types of cancer.

When conventional therapies have been unsuccessful, larotrectinib may offer another treatment option, and can currently be accessed via the Cancer Drug Fund in England. Under this scheme the NHS will fund the drug while more data is collected to demonstrate cost and treatment effectiveness, so that it can be made permanently available.

> "When conventional therapies have been unsuccessful, larotrectinib may offer another treatment option, and can be accessed via the Cancer Drug Fund in England."

Bringing experts together

The collaborative research efforts were supported by a four-way collaboration between us, Bayer, the UK Real World Solutions Team at IQVIA and our academic research community led by John Bridgewater.

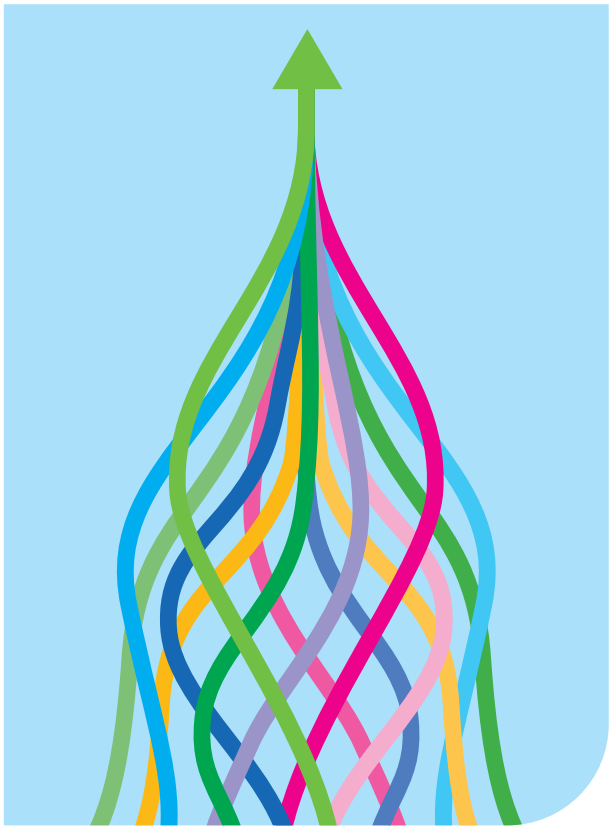
Scientific findings

This study confirmed that the specific fusion protein can be found in different cancers including breast cancer, colorectal cancer, and sarcomas, etc, presenting a potential target for therapeutic treatments developed by Bayer.

The value of our participants' data

As a result of insights generated from this collaboration, evidence was generated to support the use of larotrectinib, the first drug approved in this class, for the treatment of cancer in adult and paediatric patients with the specific fusion protein, from a collaboration with Genomics England.

The collaboration with John Bridgewater enabled the partners to establish clinical insights and to ultimately publish the findings in Cancer Treatment and Research Communications in August 2022.[16]



See page 77 for details of references

Industry partner case study

Boehringer Ingelheim

What it's been like to work with us from Boehringer Ingelheim's perspective

We joined the Discovery Forum 2 years ago to support the company with genomic research in two key areas: oncology and pulmonary fibrosis. This partnership between Genomics England and Boehringer Ingelheim has been flourishing ever since. The bioinformatics consulting team at Genomics England conducted initial research projects to explore somatic mutations to advance knowledge in this field for the oncology research team based in Vienna, Austria; simultaneously, they conducted a preliminary scoping exercise to investigate the genetic basis for progressive fibrosing interstitial lung disease (PF-ILD).

Through engagement with the Genomics England Clinical Interpretation Partnership network, our team at Boehringer Ingelheim were able to work with leading academics in the disease area. We were also able to work with transcriptomics and proteomics providers and analysts to develop groundbreaking multiomic research in this field. The clinical collaboration mechanism made it possible for our team to access untouched samples from a subset of 100,000 participants in the Genomes Project with evidence of PF-ILD. This allowed us to generate new multiomic data and build RNAseq and proteomics on top of the whole genome sequence and clinical data for this cohort.

Furthermore, this study will be assessing similarities and differences in the underlying genetic mechanisms driving this disease and correlating these with people who were found to be severely affected by COVID-19.

These studies demonstrate the breadth of opportunities that are possible when partnering with Genomics England. We anticipate the analysis ahead will reveal new and improved multiomic characterisation and substratification of this disease to support our team in being able to make more accurate diagnoses. This will enable more appropriate recruitment criteria for clinical trials (and the use of novel biomarkers as surrogate endpoints) and enhance research and development in this therapeutic area, allowing Boehringer Ingelheim to move towards creating better personalised treatments for patients with PF-ILD.

"Fibrosis is recognised as one of today's major healthcare challenges and we're committed to advancing therapeutic research and development through large scale genomic studies."

Jan Jensen
Global Head of Computational Biology & Digital Science, SVP, **Boehringer Ingelheim**

"These studies demonstrate the breadth of opportunities that are possible when partnering with Genomics England. We anticipate the analysis ahead to reveal new and improved multiomic characterisation and substratification of this disease to support our team in being able to make more accurate diagnoses."

Industry partner case study

AstraZeneca

Discovery Forum membership applies to an entire company, which, in the case of AstraZeneca, means we can support research and development throughout various departments spread out across different geographies, including the Centre for Genomics Research (CGR), Oncology Translational Medicine and Alexion (Rare Diseases Group).

Our work so far:

- AstraZeneca's CGR has established a powerful target identification dataset in house and has been working closely with our bioinformaticians to establish a parallel workflow in our Research Environment. This enables the 100,000 Genomes Project data to serve as a crucial validation dataset to inform AstraZeneca's drug discovery efforts and permit translation of novel findings to better monitor and understand disease for conditions represented within the NGRL.

- Oncology Translational Medicine has instructed our bioinformatics consulting team to run projects, demonstrating this team's abilities in running outsourced projects on behalf of our partners. These include validating novel whole genome sequencing assays to support assay selection for minimal residual disease testing (to identify residual amounts of circulating tumour DNA – ctDNA – at a high resolution), as well as better characterising the role of structural rearrangements in certain cancer types.

- Alexion identified genetic signatures for yet undiagnosed participants in the 100,000 Genomes Project and returned these through the Diagnostic Discovery pathway to the NHS. Those diagnoses were confirmed, directly impacting participants.

We ran a successful partner workshop with AstraZeneca this year, bringing together representatives from each of these teams with members of the bioinformatics consulting team to identify new opportunities, co-create novel research projects and address any issues with their current research plans. We look forward to growing the partnership even further over the next few years, supporting all key research and development and clinical functions.

"We ran a successful partner workshop with AstraZeneca this year, bringing together representatives from each of these teams with members of the bioinformatics consulting team to identify new opportunities, co-create novel research projects and address any issues with their current research plans."

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Genomics England

Powering genomics through partnerships

New horizons

Investing in genomics research and healthcare

In 2020, the government launched Genome UK, its 10-year genomic healthcare strategy, which set out a vision to become the most advanced genomic healthcare system in the world.[17] In 2022, the government published its latest implementation plan outlining how genomics partners across England, including Genomics England, would take action to implement Genome UK.[18]

The next phase of Genome UK will involve:

£105m Newborn Genomes Programme

A research study delivered in partnership with the NHS to explore the effectiveness of using whole genome sequencing to speed up the diagnosis and treatment of rare genetic conditions in newborns

£22m Diverse Data initiative

To tackle health inequalities in genomic medicine through tailored sequencing of 15,000 participants from ancestrally diverse backgrounds by 2025, as well as extensive community engagement work to build relationships with traditionally excluded groups of people

£26m Cancer 2.0 programme

Delivered in partnership with NHS England and the National Pathology Imaging Co-operative and will evaluate cutting-edge genomic sequencing technology to improve the accuracy and speed of cancer diagnosis and use artificial intelligence to analyse a person's DNA, alongside other information such as routine scans to drive novel research discoveries

Up to £25m for functional genomics

UK Research and Innovation and Medical Research Council funding for a 4-year functional genomics initiative to establish a world-class offer on functional genomics, building on existing infrastructure and UK research expertise

Future of healthcare

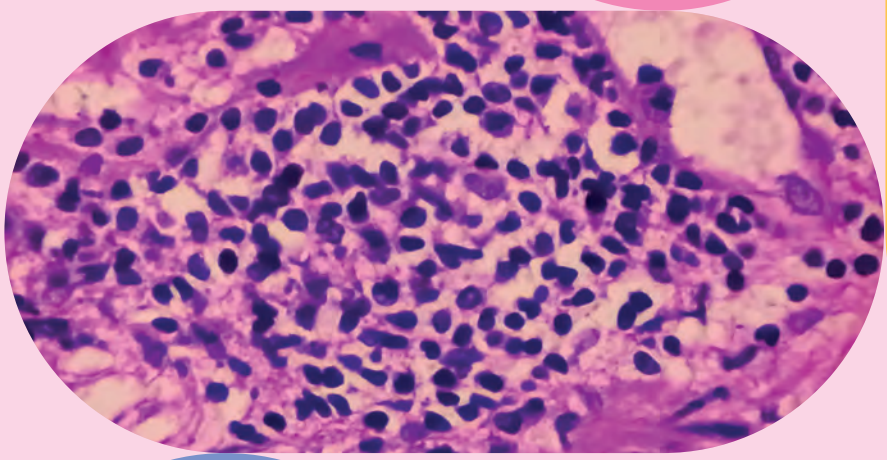
By 2025, the government expects to have made significant progress towards realising the benefits of genomic healthcare. These new initiatives will join existing NHS efforts to use genomic innovations to improve patient care and outcomes.

We're excited to play our part in this genomic revolution.

New horizons:

Cancer 2.0

- Multimodal programme
- Long-read programme



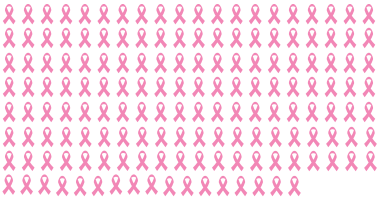
Cancer 2.0

Our Cancer 2.0 programme looks to use two innovative technologies to improve cancer care for NHS patients.

These two technologies are **multimodal data** and **long-read sequencing**.

Over 3m
people are living with cancer in the UK[19]

Around 167k
people died of cancer in 2019[19]



300k+
people are diagnosed with cancer each year[20]

About Cancer 2.0

Collecting and organising over 100,000 medical images (pathology images and radiology images) to unlock new areas of genomic research

Piloting long-read sequencing in 2 of the 7 Genomic Laboratory Hub (GLH) regions of the UK to speed up and create a more comprehensive diagnosis

Building the biggest accessible long-reads cancer data library

Multimodal programme

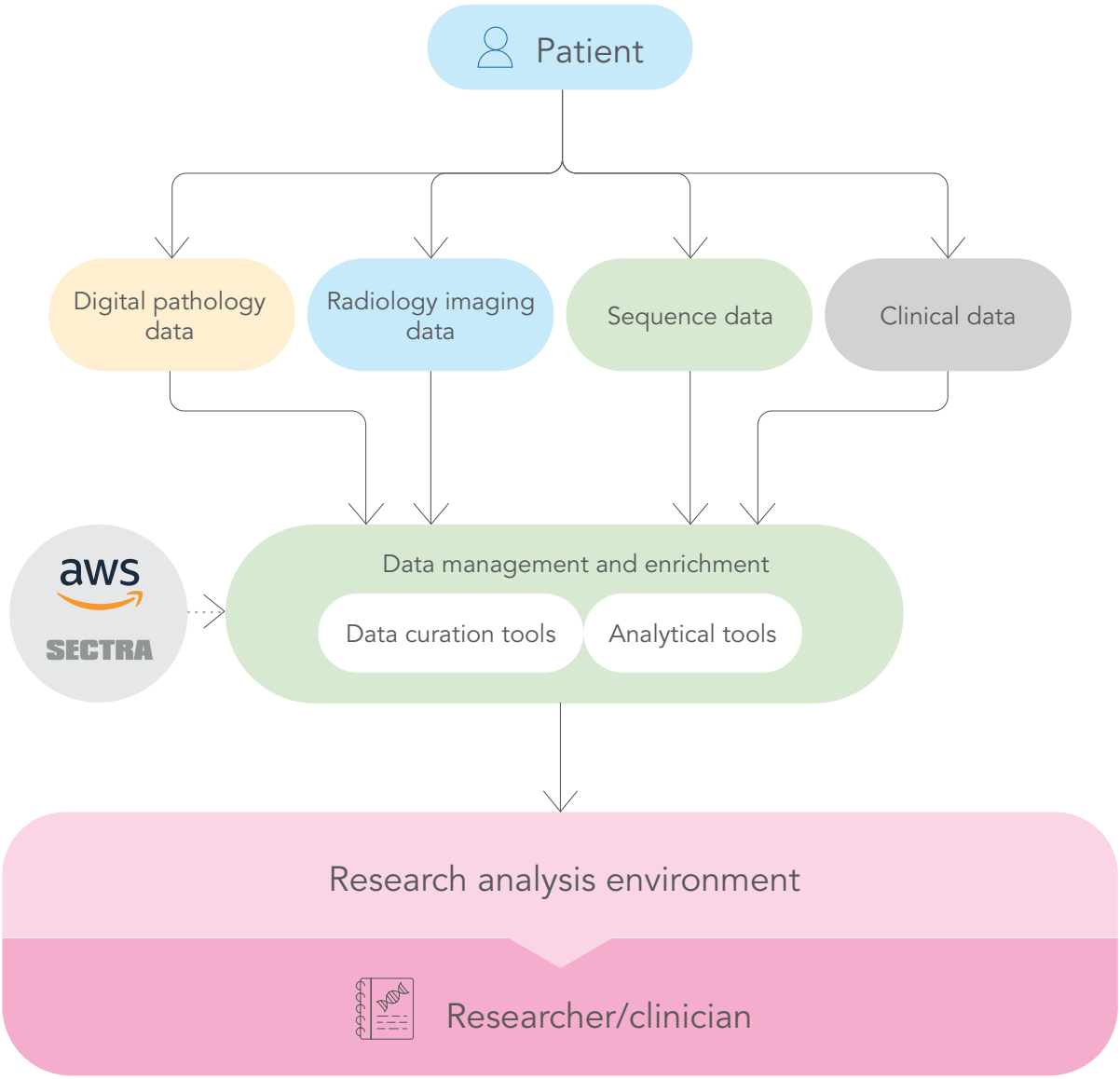
Health data about cancer patients is currently held in many different formats and systems across the NHS. This includes unstructured information (e.g. clinical notes and laboratory tests) and pathology and radiology imaging data (e.g. x-rays, CTs and MRIs).

The multimodal project aims to gather all this data, organise it, structure it and link it to patients' genomic data.

This organised data will sit within our Research Environment, creating the first multimodal Research Environment of its kind.

We believe that providing this digitised, de-identified and annotated data for researchers and clinicians to analyse is a new frontier for genomic research in cancer. It will accelerate research applications and allow us to use machine learning to analyse the data. And it could, one day, allow us to identify genetic mutations from patient imaging alone.

We hope that use of this data in the future could help to predict cancer diagnosis and guide cancer treatment and the prescription of precision medicine for cancer patients.



Progress over 2022

During this year's pilot phase of the project, we established a working architecture and began collecting data.

In close collaboration with over 30 NHS sites, the Participant Panel and internal teams, we have gathered clinical images from more than 15,000 cancer patients.

To digitise these images, we built a partnership with the National Pathology Imaging Co-operative (NPIC); over 60,000 pathology slides and images from across the NHS have already been digitised.

As the data is incredibly complex, we have had to upgrade our technical infrastructure. Sectra – a technology company that offers secure communication and medical imaging systems – worked with us to make their image viewer software available in our Research Environment through Amazon Web Services for the first time.

On the analysis side, insitro, King's College London and the University of Leeds are helping us develop machine learning systems to work with the data.

"We believe this partnership can be an exemplar of future collaborations that unlock the power of high-content data towards improved therapeutics and outcomes."

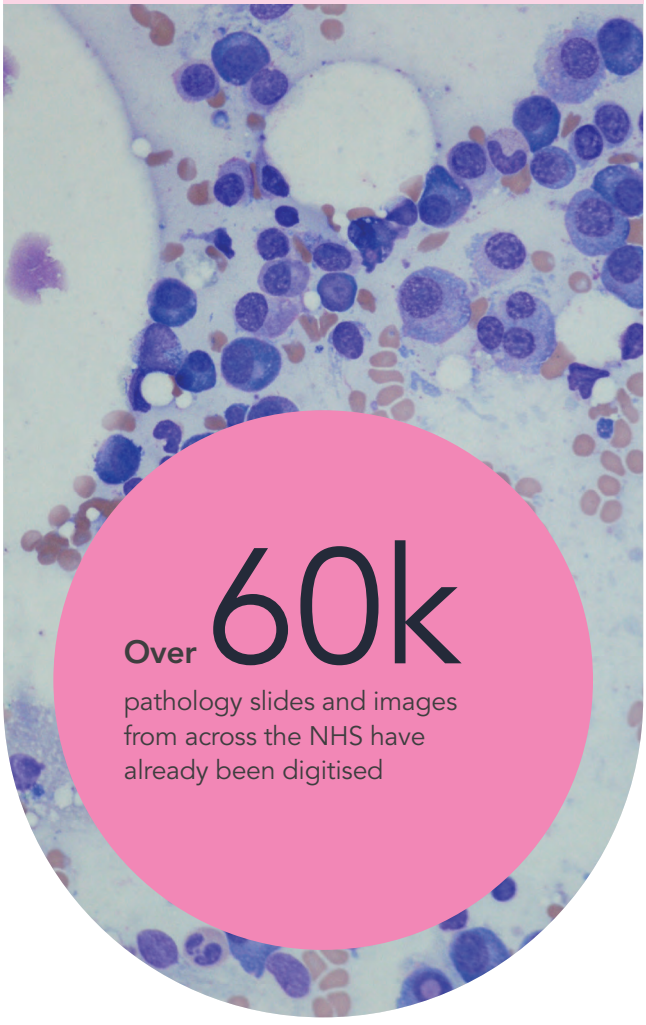
Daphne Koller
CEO and co-founder, **insitro**

2023 and beyond

In 2023, we will shift from set-up to expansion and actual use of the data. Alongside expanding our machine learning capabilities, we will start introducing researchers to the data and working with the research community to explore this data to its fullest.

"At NPIC, we're excited to be working with Genomics England to create the Genome Pathology Imaging Collection, a unique resource of over 300,000 whole slide images that will accelerate genomic discoveries in cancer, as well as building a foundation for multimodal data analysis for the 100,000 Genomes Project."

Darren Treanor
Director and consultant pathologist, **NPIC**



Long-read programme

Understanding how a cancer patient's genome has changed allows us to understand and treat their cancer better.

Currently, the technology we use – called short-read sequencing – looks at short fragments of the genome, one after another. These fragments are then pieced back together into a continuous genome sequence.

However, new long-read technology can look at much longer stretches of the genome, as well as identify changes to the genome that are not readable with short-read sequencing.

Long-read sequencing is portable and quicker, meaning clinicians get more detailed results, faster. In turn, this could lead to better care for cancer patients. We are partnering with 2 of the 7 NHS GLHs to explore how this can be rolled out within the NHS.

The long-read programme is aiming for:

- faster diagnostics – shortening the time from sample taking to results by distributing sequencing machines to diagnostic sites
- more comprehensive data – providing information in one test that currently requires multiple tests
- the right technology – using the best technology for achieving our goals
- equitable access – showing that long-read sequencing can be used across all the GLHs in England for 4 cancer types

Progress over 2022

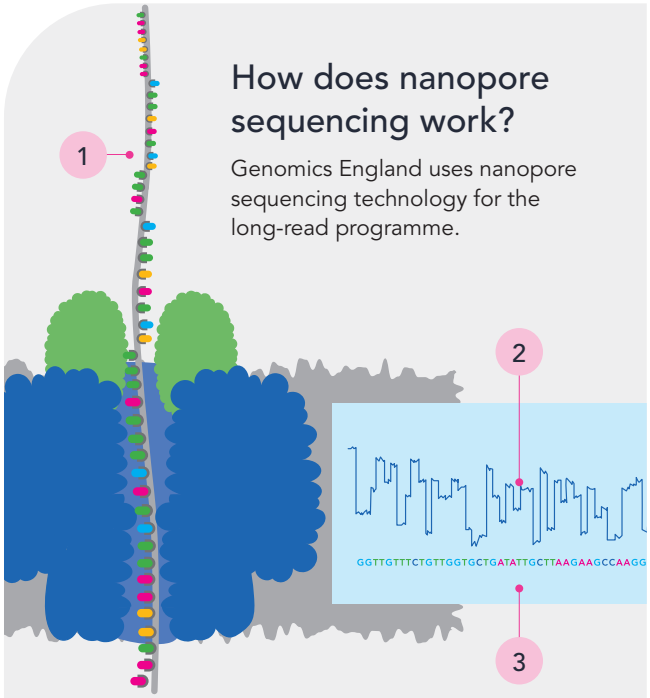
Testing our confidence in the sequencing technology, its chemistry stability and whether it is scalable

Understanding the best methods for acquiring, storing, organising and analysing this data in our infrastructure

Using algorithms designed to test many samples to show that they are as accurate as tests currently used to detect cancer variants

How does nanopore sequencing work?

Genomics England uses nanopore sequencing technology for the long-read programme.



1. A DNA strand is drawn through a nanometre-sized pore in an artificial membrane.
2. An electrical current is passed across the membrane – the current changes depending on what DNA nucleotides are in the pore.
3. Monitoring this current produces data that an algorithm can translate into the DNA sequence.

"I think the really exciting thing about long-read sequencing is we're starting to bring in a new technology, a British technology, that can very quickly get very detailed information about a patient's cancer."

Professor James Brenton
Senior group leader and honorary consultant in medical oncology, **Cancer Research UK, Cambridge Institute**

Partnership with NHS England

We are collaborating with the North-East and Yorkshire and the North Thames GLHs to test and explore how long-reads could work within an NHS clinical laboratory setting.

The following cancers are our focus, as they suit long-read sequencing:

- Acute myeloid leukaemia and acute lymphoblastic leukaemia, which often involve two previously independent genes fused together
- Sarcomas, which often involve alterations to the genome itself as well as changes in the way genes are switched on and off
- Neurological malignancies (such a brain tumours), which often involve changes in the way genes are switched on or off

> "The use of this technology could lead to an increase in the number and speed of cancer patients receiving genomic information to inform their diagnosis or treatment."

NHS Genomic Medicine Strategy

2023 and beyond

With our partner laboratories – North-East and Yorkshire and the North Thames GLHs – we will move from testing to beginning to use long-read sequencing for diagnosis within the NHS.

Together we will explore how best we:

- prepare and sequence long-read cancer samples
- move and store sequencing data between ourselves and the laboratories
- continue to develop analytical algorithms that can identify changes in the genome as well as existing standard of care tests
- make our results available to clinical teams

New horizons:

Diverse Data

Addressing the diversity gap

To date, studies of human genetics have focused largely on populations with European ancestries. This has contributed to a world where genomic healthcare does not necessarily benefit everyone equally.

When genomic datasets are made up of mostly European-ancestry genomes, it can result in the misdiagnosis of genetic conditions and research findings that cannot be widely applied in clinical care. This can further contribute to the mistrust some excluded communities feel about how their genetic data is collected and used.

Our Diverse Data programme aims to address this gap in diversity in genomic research and build towards a world with:

- a new understanding of genes that cause diseases
- new treatments for a more diverse range of populations
- a more accurate reading of a person's risk of developing a specific disease
- the design of tailored clinical care for individuals

To achieve this, we must work across both genomic research and healthcare.

We will be co-creating our research priorities for sickle cell through collaborative workshops, community-based surveys and codesigned priority-setting activities.

Our initial research priorities for 2022 to 2025 are:

- Sickle cell disease
- Improving equity in our services
- Population genetics

Our programmes will support further understanding of:

- basic human biology and its variations, and how certain genes are linked to certain conditions
- diagnosis and development of treatment and care
- new methods that lessen the impact of imbalanced genomic data
- ethical, social and legal implications from the use of genetic data for different populations, to issues like anti-racism and decolonisation

How we will address the gap in data diversity

Research and discovery to understand the data gaps in genomic diversity

How: review, stimulate and conduct research into diversity and its impacts on scientific, clinical and health systems.

Examples of our work so far:

- two reviews into ethical challenges for data diversification in genomics with the Centre for Personalised Medicine (University of Oxford) and Careful Industries
- two commissioned reviews into prevalence and outcome differences by ancestry in cancer and rare diseases in the UK
- a literature review into the different and inconsistent ways in which diversity is defined in genomics
- completion of phase one of analysis into possible ancestry bias in cancer and rare diseases in 100,000 Genomes Project data
- a series of workshops and a review into statistical methods to improve fairness in genomics with University College London, Johns Hopkins University and the Alan Turing Institute (ongoing)

Community and engagement to close the gaps, together

How: work with patient, genomic and data communities to design, develop and implement equity-enhancing strategies.

Examples of our work so far:

- a crowdsourced collection of stories and voices on MindtheGap.health to raise awareness of health data bias
- a co-created list of priorities for future genomics research in sickle cell disease with the Sickle Cell Society and the James Lind Alliance (ongoing)
- a commissioned report by Muslim Census on attitudes toward health and medical research within the Muslim community[21]
- a monthly online webinar – The Genomic Equity Series – which aims to share the latest experiences, projects and research of those working to improve equity in genomic medicine across the world

Sequencing and data to fill the data gaps

How: sequencing whole genomes from minoritised communities – including those of people with sickle cell, neurology, psychiatric conditions and breast cancer as well as those with specific adverse drug reactions – and facilitate better access to data from diverse populations.

Examples of our work so far:

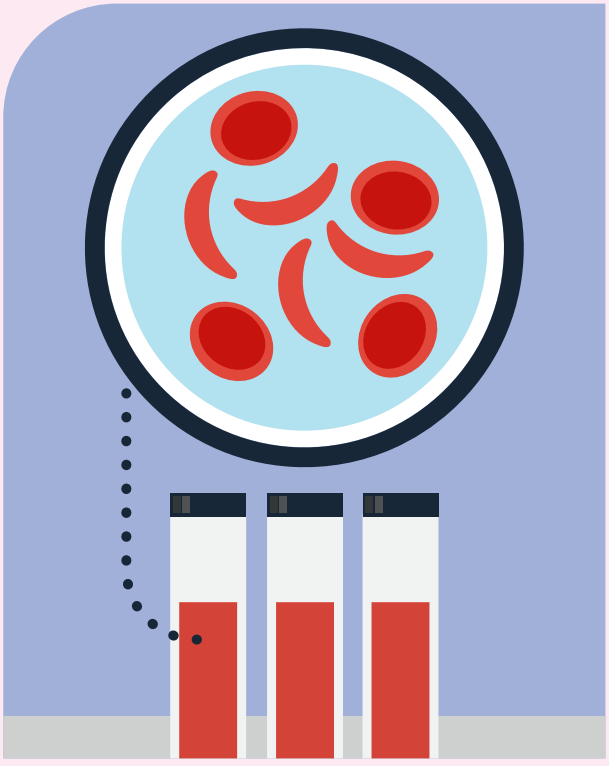
- an open call in 2022 to collaborate with the research community on our data-generation efforts, resulting in improved data quality which can lead to more accurate research findings and better clinical outcomes

Products, tools and behaviours to bridge the data gaps

How: work with clinicians, analysts, researchers, patients and community groups to develop tools and processes to improve research, recruitment and care.

Examples of our work so far:

- a language toolkit to provide a reference guide for discussing race, ethnicity and ancestry, developed with around 40 internal and external experts in the genomics field (ongoing)
- a diversity analysis tool for the 100,000 Genomes Project that creates plots for differences between ethnicities and ancestries in data from participants with rare conditions (ongoing)
- an online community called link23, where the global data and genomics community can find and contribute open-source, equity-enhancing tools, products, resources and handbooks[22]



"It's promising to see Genomics England prioritise sickle cell disease as part of their Diverse Data initiative and we very much look forward to developing a partnership with them to raise the voices of patients, improve research and have a positive impact for the sickle cell community."

John James,
Chief Executive, **Sickle Cell Society**

Diverse Data activities

Innovations to address cancer inequalities event

21 September 2022

Twenty participants from across the scientific ecosystem gathered for a roundtable discussion to identify gaps and opportunities regarding inequalities along the cancer pathway. An open, informal meet-up followed, featuring short talks from Bola Owolabi from NHS England and Ash Rishi from COUCH Health.

Research for genomic equity conference

20 October 2022

We brought together more than 100 people, including researchers in genomics, data, health inequalities and ethics, to share, learn and discuss the opportunities and challenges in making genomics research and practice as equitable as possible.

Ambassador's programme

October 2022

In 2021, we launched a campaign called the National Conversation on Genomics. Its goal is to create a world that understands the benefits and consequences of genomic healthcare so that people can make informed decisions.

Part of this work involves opening two-way dialogue with communities where we know health inequalities exist and that are less engaged – if at all – with the concept of genomic health.

We have partnered with representatives of various communities to use their powers of engagement for good, working with them to develop content and campaigns to drive the National Conversation.

New horizons:

Newborn Genomes Programme

NHS-embedded research study

Our Newborn Genomes Programme is delivering an NHS-embedded research study to explore the benefits, challenges and practicalities of sequencing and analysing newborns' genomes to improve diagnoses and treatments for rare conditions.

Subject to ethics committee approval, we are co-designing and delivering an NHS-embedded research study to explore the benefits, challenges, and practicalities of sequencing and analysing newborns' genomes. As part of this study, 100,000 babies will have their genomes sequenced. The Department of Health and Social Care announced £105 million funding for the programme in December 2022.

The research study has three parts:

Expanded testing
Evaluating the utility and feasibility of screening newborns for a larger number of childhood-onset rare genetic conditions in the NHS, using WGS.

Discovery research
Understanding how babies' genomic data could be used for discovery research, focusing on developing new treatments and diagnostics for NHS patients.

Lifetime genome
Exploring the potential risks, benefits and broader implications of storing a baby's genome over their lifetime.

Research study beginning in 2023

2022 2023 2024 2025

Aiming to find the

9

children born each day in the UK with a rare genetic condition – where early intervention is crucial

To find these children, we'll analyse

100,000+

newborn genomes for a specific set of childhood-onset, actionable conditions

Expecting

1,000

positive results during the study

2022: a year of progress

We have worked with a wide range of groups and experts to design and build key parts of our research study including:

- our model of consent
- principles to underpin decisions about which conditions we should include in the study
- a study to identify the best way to take samples from the babies involved
- our approach to analysis
- a network of healthcare professionals and groups who will be key to delivering the study

Engagement

Our commitment to open communication and meaningful engagement with a wide range of people and organisations has allowed us to incorporate many different views, aspirations and opinions into our work.

Building on our 2021 dialogue with members of the public, we have:

- invited over 35 experts and opinion leaders from academia, clinical practice and research-supporting organisations as well as 50 experts from the life sciences industry to explore diagnostic and long-term research opportunities that could be facilitated by the programme plus strategic priorities with actions to support this
- hosted a series of workshops with members of the public, people with experience of rare conditions and healthcare professionals to co-design guiding principles to identify which conditions, genes and variants – out of the hundreds that could be detected through whole genome sequencing – should be included in the study
- presented at nearly 50 UK and international conferences
- interviewed a diverse group of 115 parents
- consulted with hundreds of clinicians
- held nearly 200 stakeholder meetings with groups including royal colleges, patient and charity organisations, and professional bodies
- commissioned, sponsored and contributed to 5 evening webinars hosted by the Progress Educational Trust to discuss and debate the key aspects of our programme openly[23]

In 2023, we will build on these insights further with public engagement, while continuing to work with parents, clinicians, researchers and members of the public.

Contributing to genomic research

We have invested in and led research that will form the foundations of the programme, as well as provided valuable data and insights to inform the broader genomics research ecosystem.

We have established research studies to find out the best way of taking a sample from a newborn for the purposes of sequencing their genome.

1. The first feasibility study involved 40 adult participants to assess the quality of 5 different sample types.

2. To answer further questions, including on the feasibility of using cord blood to generate whole genome sequences from newborns, we began a second feasibility study called the Baby and Mum Samples Study.

Results from both studies will be reported in 2023.

Contributing to the genomics literature

We commissioned 2 reviews on embedding ethics across the programme:[24]

- An evidence and literature review to examine the ethical dimensions of sequencing newborns' genomes
- An exploration of the regulation and governance of genomic data held over the course of newborns' lifetimes

The team has also contributed to other research literature, including:

- Pichini A and others. Developing a national newborn genomes program: an approach driven by ethics, engagement and co-design. Frontiers in Genetics. 2022 volume 13[25]
- Public Policy Projects. A fairer future: towards a more equitable delivery of care for those with rare diseases and conditions in the UK. 2022[26]
- Bick D and others. Newborn screening by genomic sequencing: opportunities and challenges. International Journal of Neonatal Screening. 2022: volume 8[27]
- Hunter A and others. Public and patient involvement in research to support genome services development in the UK. Journal of Translational Genetics and Genomics. 2023: volume 7[28]

The programme's progress has been bolstered by a dedicated core team, supported by our NHS-led steering group and five expert working groups:

- Conditions
- Education and training
- Ethics
- Evaluation
- Recruitment

"The Newborn Genomes Programme will set firm foundations on which to discover the ways genomics can support babies with a rare genetic condition and treat them before they get sick. The programme is leading the way internationally with the scope of its ambition and is doing so working meaningfully with those who matter most: parents, young people, individuals and groups with experience of rare conditions, healthcare workers, researchers and the public. It is thanks to their generosity of time and spirit that the programme finds itself in such a strong position to begin to address the vital questions it has set about answering – an exciting journey lies ahead."

Sarah-Jane Marsh
Chair, Newborn Genomes Programme NHS Steering Group; former CEO, **Birmingham Women's and Children's NHS Foundation Trust**

"We've established a bespoke process for choosing conditions for our study, designed a consent process for potential participants, and begun to develop our discovery research strategy. This has been achieved through the generous contributions of members of the rare conditions community, healthcare workers, researchers, members of the public, and our working groups. Through their invaluable advice and steers, the programme has been afforded firm foundations for 2023, when we will shift from designing the study to delivering it."

Alice Tuff-Lacey
Programme Lead, **Genomics England**

2023 and beyond

As the programme moves towards recruiting the first families to join the research study, we will invest further in discussion and consultation with the public and participants to ensure that the interests, concerns and opinions of potential participants, healthcare practitioners, members of the public and researchers are embedded as we move from design to delivery. Our progress has been made possible only through the generosity of members of the public, organisations, patients, parents, researchers and healthcare professionals who have and will continue to guide our work.

Owen's story

Resistance to thyroid hormone alpha

Owen, a 9-year-old boy from Ackworth in West Yorkshire, received a diagnosis through the 100,000 Genomes Project after years of uncertainty for him and his family. Our Newborn Genomes Programme aims to transform health journeys like Owen's, ensuring babies with actionable rare genetic conditions get access to appropriate treatments and interventions much earlier.

Owen's parents first became concerned about his health when he was around 6 months old, and he was unable to sit up by himself. As time went on, he also struggled to walk and say his first words.

By the age of 4 and a half, Owen could say just 20 to 30 words. However, the cause of his condition remained a mystery to both doctors and his parents. He had spent years having tests and invasive treatments to understand why he was not growing and was unable to walk unaided or talk properly. These included steroid trials, blood transfusions and growth hormone injections, but none brought his parents closer to any real answer.

A transformational diagnosis

Owen's diagnosis came after he joined the 100,000 Genomes Project. The test, which sequenced his entire genome, identified the genetic change in the THRA gene that stopped his body from responding properly to thyroid hormones. This rare condition has been detected in only 30 people worldwide.

Being diagnosed with the rare genetic condition meant that Owen could finally be put on simple thyroid medication. His condition can be treated with high doses of thyroxine, which he now takes as a daily tablet.

Today, Owen's condition has improved dramatically. His walking and coordination are better, he has grown significantly and his metabolic rate is improving, so he has a lot more energy. He is doing well at school and enjoying life with his friends, and his parents remain hopeful for his future.

Speaking about the diagnosis, Owen's mum Sarah says: "For me, it was transformational. To get that specialist support and information so we could understand what might happen for Owen in the future – it was a gift. I just want Owen to have a full and fulfilled life and as, part of this project, we've found out so much about Owen and he has the best chance now."

How could the Newborn Genomes Programme help children like Owen?

Sadly, in the 5 years waiting for a diagnosis, Owen fell behind with developmental milestones and growth and developed anaemia. Waiting also meant his family went through years of uncertainty while attending continuous medical appointments and while Owen received invasive treatments.

The Newborn Genomes Programme will sequence the genomes of up to 100,000 babies shortly after they are born. The study will aim to find out whether using this technology could speed up diagnoses and interventions for rare conditions that affect babies and young children like Owen.

> "For Owen, it would have avoided unnecessary testing and treatment and would have given him the best chance of reaching his potential by helping his development from an early age. The programme is a great advance in testing that will give families the opportunity to start treatment very early on in their child's life."
>
> **Rob, Owen's dad**

30

people worldwide have been diagnosed with the same rare condition

Owen

Governance

Company structure

Genomics England Board

Partnership Board

Genomics England

Audit and Risk Committee

People Committee

Ethics Advisory Committee

Ensures that ethics are at the heart of everything Genomics England does

Chaired by Nicola Perrin MBE

Access Review Committee

Ensures that those who access the data are appropriate and that access is for authorised purposes

Led by an independent chair

Technology Advisory Group

Focuses on making sure our tech processes are robust and that we resist security threats

Chaired by Andrew Eland

Participant Panel

Puts the participants at the heart of Genomics England's decision making

Led by an independent chair, Jillian Hastings Ward

Science Committee

Makes sure that we follow the science

Chaired by Professor Sir John Bell

Genomics England Clinical Interpretation Partnership (GECIP) Board

Oversees the operation of academic research projects.

Chaired by Professor Eamonn Sheridan

Board of Directors

The Genomics England Board oversees all our activities, ratifies all major decisions and sets the overall strategy for the organisation. Several independent advisory committees report to the board, including the Ethics Advisory Committee, Science Advisory Committee, Data Advisory Committee, Access Review Committee, GECIP Board and Audit Committee.[29]

Chris Wigley
CEO

Baroness Nicola Blackwood
Chair

Dr Vikram Bajaj
Non-Executive Director

Professor Sir John Bell
Non-Executive Director, Chair of Scientific Advisory Committee

Professor Ewan Birney
Non-Executive Director

Professor Matt Brown
Chief Scientific Officer

Roz Campion
Director, Office for Life Sciences

Andrew Eland
Non-Executive Director

Dr Tim Ferris
Non-Executive Director

Dr Annalisa Jenkins
Non-Executive Director

Nicola Perrin MBE
Non-Executive Director

Dr Keith Stewart
Non-Executive Director

Sir Jonathan Symonds CBE
Non-Executive Director

More about our Board's roles, responsibilities and backgrounds at: genomicsengland.co.uk

Executive Leadership Team

The Executive Leadership Team works alongside the Board of Directors to set and influence our strategic direction, while providing leadership both within the organisation and externally, as ambassadors and thought leaders.[30]

Chris Wigley
CEO

Dr Richard Scott
Chief Medical Officer and Deputy CEO

Professor Matt Brown
Chief Scientific Officer

Catherine Byers
Chief Financial and Performance Officer

Jackie Kinsey
Chief People Officer

Nick Maltby
General Counsel, Company Secretary and Data Protection Officer

Parker Moss
Chief Ecosystems and Partnership Officer

Rakhi Rajani
Chief Digital and Strategy Officer

Dr Augusto Rendon
Chief Bioinformatician

Pete Sinden
Chief Information Officer

Chris Schonewald
Chief of Staff and Director of Strategy

More about our Executive Leadership Team's roles, responsibilities and backgrounds at: genomicsengland.co.uk

Participant Panel

The Participant Panel is an independent advisory group made up of volunteers, all of whom have generously donated their genomic and other health data to the National Genomic Research Library (NGRL).

The Participant Panel champion the interests of the participants and keep them at the heart of everything Genomics England does. They hold Genomics England accountable for the safety and security of their data and how it is used, advise on future design and ensure that their lived experiences and expertise are considered in decision-making.

The Participant Panel meet quarterly and invite senior staff from Genomics England and NHS England as well as any external partners to discuss what they are doing with the data held in the NGRL. Between these meetings, Panel members actively engage with all our committees and boards.

Jillian Hastings Ward, Chair, and Rebecca Middleton, Vice-Chair, report directly to the Chair of Genomics England's Board.

Panel members also represent participants at external events and discussions (such as the Festival of Genomics and Nuffield Council on Bioethics workshops) and share the participant perspective on our podcast, The G Word.

Embedding the participant voice into everything we do is critical to driving Genomics England forward.

> "The Participant Panel meet quarterly and invite senior staff from Genomics England and NHS England as well as any external partners to discuss what they are doing with the data held in the NGRL"

See page 10 for Jillian Hastings Ward's review of the key highlights of the Participant Panel's work this year, including contributing to the European Journal of Human Genetics and developing a guide to language and terminology.

Source and application of funding – 2022/23 plan

Where does our funding come from?

Department of Health and Social Care
£84m

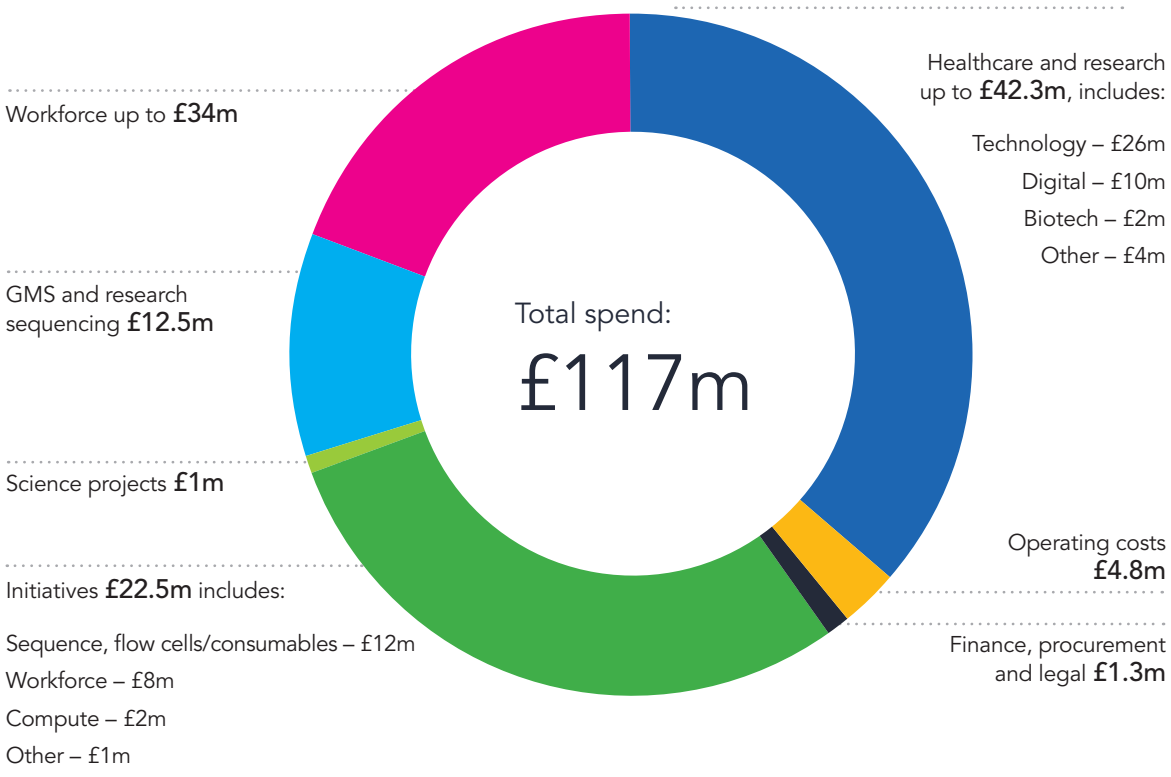
Genomic Medicine Service (GMS) sequencing and infrastructure
£13.3m

Commercial
£3.5m

R&D tax credits
£1.8m

Research cohorts
£1.8m

Where do we spend it?



Our budget-setting process deliberately 'over-programmes' the opening financial plan to account for known and unknown internal and external variables that influence spending and income across a financial year. The final costs incurred as per audited financial statements must not exceed the agreed total funding envelope at the financial year-end.

Closing remarks

Chris Wigley

This report reflects the strong foundations that Genomics England has built to deliver high-quality services for patients and participants, researchers, industry partners and the NHS. This is down to the ambition, talent and drive of our people and our strong collaborations across the genomics ecosystem.

Our public funding allows us to innovate and operate with a degree of impartiality that is fundamental to delivering the best value for patients and participants and the Office for Life Sciences continues to offer strategic support to our aims.

The unique partnership we have with the NHS is invaluable in our continuing drive to make genomic medicine part of routine care. I am grateful to all our NHS colleagues, Dame Professor Sue Hill in particular, for their ongoing collaboration. Our Newborn Genomes Programme, which will begin sequencing soon as an NHS-embedded research study, is a shining example of this approach.

Thanks must also go to all our academic and industry research partners who use the Research Environment, as well as our partners on whom we rely to forge vital links in the chain. We are proud to play our part in a thriving collaboration of expertise and capability.

I am wholeheartedly looking forward to what is to come for Genomics England and our partners in the next financial year and beyond. There is no doubt that there will be more world firsts, innovations and positive outcomes for patients.

Chris Wigley
CEO

Appendix: references

The references and source information included were correct at the time of publication (March 2023)

About Genomics England | From page: 02

1. **Genomics Nation 2022. Highlighting Future Opportunities for the UK Genomics Sector**
   UK Bioindustry Association. 2022
   www.bioindustry.org/policy/strategic-technologies/genomics/genomics-nation-2022.html

2. **Over £175 Million for Cutting-edge Genomics Research**
   GOV.UK. 2022
   www.gov.uk/government/news/over-175-million-for-cutting-edge-genomics-research

Reviews | From page: 07

3. **Guide to Language and Terminology**
   Genomics England. 2022
   files.genomicsengland.co.uk/documents/Genomics-England-Language-Guide.pdf

4. **Research Participants: Critical Friends, Agents for Change**
   Hastings Ward and others. European Journal of Human Genetics. 2022: volume 30, pages 1309–1313
   www.nature.com/articles/s41431-022-01199-3

5. **Accelerating Genomic Medicine in the NHS**
   https://genomicsenglandltd.sharepoint.com/:u:/s/ct/ETc-EXQocVtNnVM7jLY7A2ABV-5WQcblYLf6fKtGTPof2Q?e=JMIoa9

The ecosystem | From page: 30

6. **Genomics Nation 2022. Highlighting Future Opportunities for the UK Genomics Sector**
   UK Bioindustry Association. 2022
   www.bioindustry.org/policy/strategic-technologies/genomics/genomics-nation-2022.html

7. **Accelerating Genomic Medicine in the NHS**
   NHS England. 2022
   www.england.nhs.uk/long-read/accelerating-genomic-medicine-in-the-nhs

Research | From page: 33

8. **100,000 Genomes Pilot on Rare-disease Diagnosis in Health Care – Preliminary Report**
   The 100,000 Genomes Project Pilot Investigators. New England Journal of Medicine. 2021: volume 385, pages 1868-1880
   www.nejm.org/doi/full/10.1056/NEJMoa2035790

9. **Substitution Mutational Signatures in Whole-genome–sequenced Cancers in the UK Population**
   Degasperi A and others. Science. 2022: volume 376
   www.science.org/doi/10.1126/science.abl9283

10. **Progressive Liver, Kidney, and Heart Degeneration in Children and Adults Affected by TULP3 mutations**
    Devane J and others. American Journal of Human Genetics. 2022: volume 109, pages 928-943
    www.cell.com/ajhg/fulltext/S0002-9297(22)00111-2

11. **A Systematic Analysis of Splicing Variants Identifies New Diagnoses in the 100,000 Genomes Project**
Blakes JMA and others. Genome Medicine, 2022: volume 14, article number 79
genomemedicine.biomedcentral.com/articles/10.1186/s13073-022-01087-x

12. **Whole-genome Sequencing Reveals Host Factors Underlying Critical COVID-19**
Kousathanas A and others. Nature. 2022: volume 607, pages 97-103
https://www.nature.com/articles/s41586-022-04576-6

13. **Genetic Mechanisms of Critical Illness in COVID-19**
Pairo-Castineira E and others. Nature. 2020: volume 591, pages 92-98
https://www.nature.com/articles/s41586-020-03065-y

14. **Mapping the Human Genetic Architecture of COVID-19**
COVID-19 Host Genetics Initiative. Nature. 2021: volume 600, pages 472-477
www.nature.com/articles/s41586-021-03767-x

15. **Baricitinib in Patients Admitted to Hospital with COVID-19 (RECOVERY): a Randomised, Controlled, Open-label, Platform Trial and Updated Meta-analysis**
RECOVERY Collaborative Group. The Lancet. 2022: volume 400, pages 359-368
www.thelancet.com/journals/lancet/article/PIIS0140-6736(22)01109-6/fulltext

Partnerships | From page: 44

16. **Prognosis and Oncogenomic Profiling of Patients with Tropomyosin Receptor Kinase Fusion Cancer in the 100,000 Genomes Project**
Bridgewater J and others. Cancer Treatment and Research Communications. 2022: volume 33
www.sciencedirect.com/science/article/pii/S2468294222001149

New horizons | Introduction | Page: 51

17. **Genome UK: the Future of Healthcare**
GOV.UK. 2022
www.gov.uk/government/publications/genome-uk-the-future-of-healthcare/genome-uk-the-future-of-healthcare

18. **Genome UK: 2022 to 2025 Implementation Plan for England**
GOV.UK. 2022
www.gov.uk/government/publications/genome-uk-2022-to-2025-implementation-plan-for-england/genome-uk-2022-to-2025-implementation-plan-for-england

New horizons | Cancer 2.0 | From page: 52

19. **Statistics Fact Sheet**
Macmillan Cancer Support. 2022
www.macmillan.org.uk/dfsmedia/1a6f23537f7f4519bb0cf14c45b2a629/9468-10061/2022-cancer-statistics-factsheet

20. **Cancer Statistics for the UK**
Cancer Research UK. 2023
www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk

New horizons | Diverse Data | From page: 58

21. **Attitudes Toward Health and Medical Research within the Muslim Community**
Muslim Census. 2022
files.genomicsengland.co.uk/documents/Muslim-Census-Genomics-England-Report.pdf

22. **Making Genomic Tools that Work for Everyone**
link23. 2023
www.link23.world/

New horizons | Newborn Genomes Programme | From page: 63

23. **Evening webinars**
Progress Educational Trust. 2023
www.youtube.com/c/ProgressEducationalTrust

24. **Newborn Genomes Programme. Embedding Ethics**
Genomics England. 2023
www.genomicsengland.co.uk/initiatives/newborns/ethics

25. **Developing a National Newborn Genomes Program: an Approach Driven by Ethics, Engagement and Co-Design**
Pichini A and others. Frontiers in Genetics, 2022: volume 13
www.frontiersin.org/articles/10.3389/fgene.2022.866168/full

26. **A Fairer Future. Towards a More Equitable Delivery of Care for Those with Rare Diseases and Conditions in the UK**
Public Policy Projects. 2022
publicpolicyprojects.com/wp-content/uploads/sites/6/2022/07/PPP-Rare-Disease-Report-622.pdf

27. **Newborn Screening by Genomic Sequencing: Opportunities and Challenges**
Bick D and others. International Journal of Neonatal Screening. 2022: volume 8, page 40
www.mdpi.com/2409-515X/8/3/40

28. **Public and Patient Involvement in Research to Support Genome Services Development in the UK**
Hunter A and others. Journal of Translational Genetics and Genomics, 2023: volume 7, pages 17-26
jtggjournal.com/article/view/5425

Governance | From page: 70

29. **Board**
www.genomicsengland.co.uk/about-us/governance?team=board

30. **Executive Leadership Team**
www.genomicsengland.co.uk/about-us/governance?team=leadership-team

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