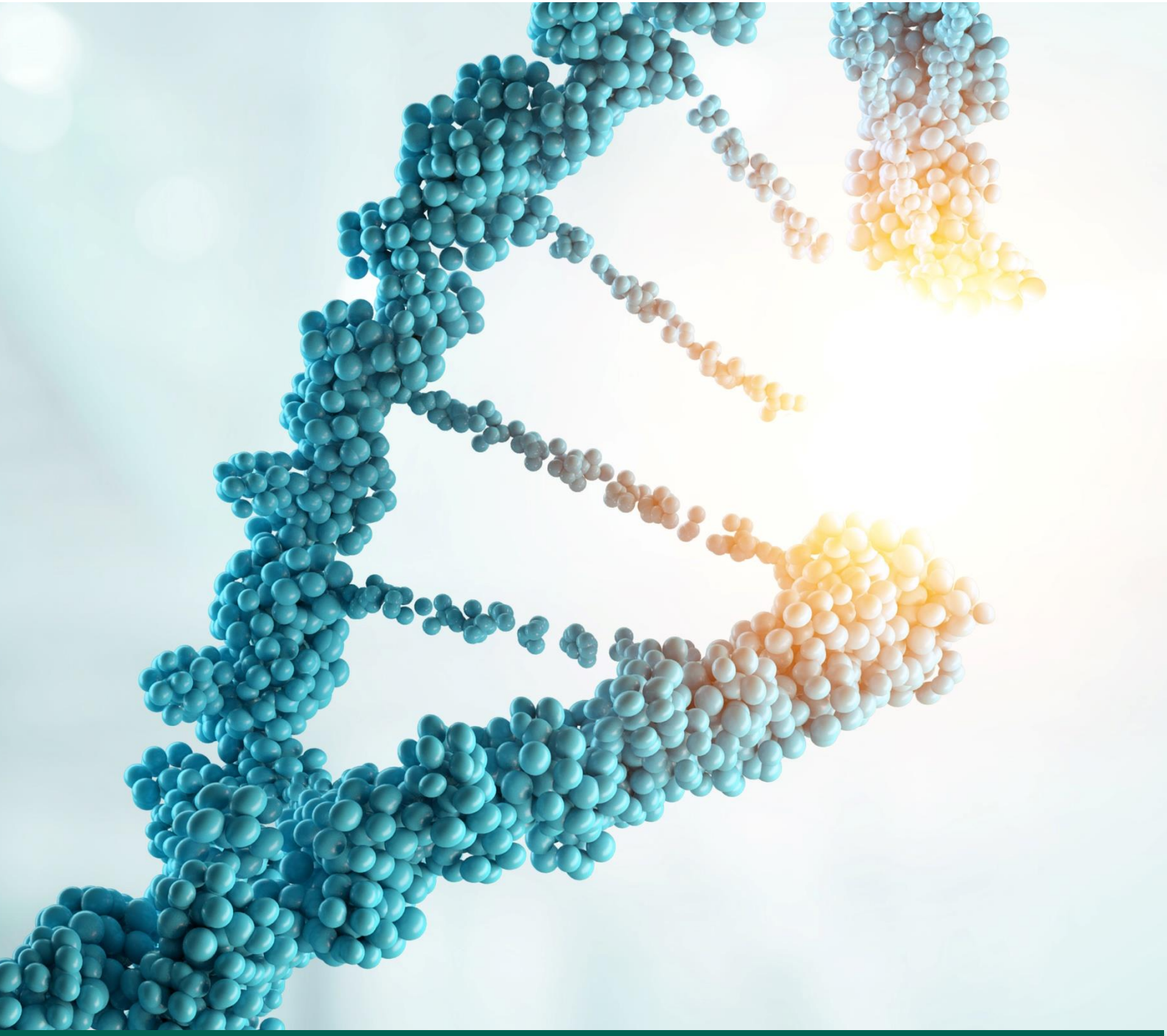


National Strategy for Accelerating Genetic and Genomic Medicine in Ireland

Draft version 5, Working Draft not for further circulation

Contents

Foreword by Stephen Donnelly, Minister for Health, Ireland

Placeholder.

Foreword by Dr Colm Henry, Chief Clinical Officer, HSE

Genomics has already demonstrated that it can contribute to improved patient outcomes globally by offering the best in predictive, preventive, and personalised care. In Ireland, much has been done to advance genetics and genomics over recent years, with pockets of excellence across clinical, laboratory, and bioinformatics specialities throughout the country. This includes, but is not limited to, St James's University Hospital's Cancer Genetics Service, the Mater Misericordiae University Hospital's Family Heart Screening Clinic, the National Maternity Hospital's Perinatal Genomics Service and Children's Health Ireland's Department of Clinical Genetics.

As we look to build on these advancements and accelerate the development of a nationally led genetic and genomic service in Ireland, we will continue to ensure that patient and public involvement is core to all that we do. Initially our focus will include enhancing specific areas of opportunity for patient benefit, such as perinatal genetics and the childhood rapid assessment approach, as well as establishing a national governance structure to strengthen and focus delivery of the service.

Large-scale service developments like this take time, planning, and a singular vision, and I would like to acknowledge the significant hard work and dedication of the members of the National Genetics and Genomics Strategy Steering Group and Working Groups who have collaborated with diverse stakeholders across Ireland to set out the vision and the way forward in this National Strategy. A testament to the work achieved to date is the commitment made to genomics with the €2.7million in funding secured for the implementation of this strategy in 2023.

This funding will enable the Health Service Executive to initiate implementation across the key areas of focus set out in this document and accelerate the establishment of a nationally led genetic and genomic service for Ireland that will improve patient outcomes, drive down the cost of care, and fuel the translation of scientific innovation and discovery into clinical practice.

INSERT SIGNATURE

Foreword by Dr Mark Bale, Chair

The increased accessibility of DNA sequencing, and the undeniable clinical value of genetic and genomic information, means that Ireland needs a comprehensive strategy for genetics and genomics that efficiently scales to meet patient needs.

Ireland's first National Strategy for Accelerating Genetic and Genomic Medicine in Ireland builds on previous reviews of the development of clinical and laboratory services to use the power of genetic knowledge to diagnose and treat disease. Our work has reinforced the previous assessments about the excellent work of clinicians, laboratory scientists, and researchers who are active in global research and advances in genetic and genomic medicine in Ireland. But we have also heard challenges due to limited capacity for genetic testing and a small clinical workforce relative to demand.

What we heard most strongly during the development of this strategy was the impact on patients and families of not being able to access timely genetic diagnoses, either because of a long waiting period or because specialist services were not available outside of major cities, especially Dublin. In setting out the new plans for the genetic and genomic service, we have put patients and families at the heart of this National Strategy. We intend for new services to be person-centred and for patients to be empowered and supported to navigate some of the complexities around genetic and genomic testing.

The new national office for genetics and genomics will have patient voices at the centre of discussions on new services and on the ethical and societal issues associated with the availability of new genetic and genomic opportunities. We are also delighted to have initial funding for additional clinical geneticists, genetic counsellors, and genetics resource associates. This will help improve the coordination of care, especially for families with rare and complex conditions who require the services of many specialists.

Of equal priority is the role of the national office to support the improvement of laboratory services, bioinformatics, and secure data storage. Senior expert leadership will be put in place to ensure that the strategy for genetics and genomics is integrated and closely aligned with the other key national programmes such as the National Cancer Control Programme (NCCP), the National Women and Infants Health Programme (NWIHP), and the National Rare Diseases Office (NRDO). They will be able to make an important contribution to the main priorities recently outlined in the WHO Science Council report to:

'Identify and overcome the practical issues that impede the implementation of genomics through local planning, financing, training of essential personnel, and the provision of instruments, materials, and computational infrastructure '.

Another key element of this National Strategy is a closer alignment with the academic and commercial scientific community. The improvement of Ireland's genetics and genomics service can be boosted by the ability to rapidly adopt the results of genomic research. In return for carefully controlled access to genetic information from Irish patients and families who consent, it is possible to improve the diagnosis of rare conditions and offer access to new, ground-breaking therapies in clinical trials.

Successful partnerships between patients, their clinicians, and researchers need to be transparent and enjoy the support of the wider community and policy makers. The development of this National Strategy has been informed by the active engagement and participation of each of those groups, along with policy, civil society, and industry stakeholders.

It is encouraging that a separate Citizen's Jury process of the Irish Platform for Patient Organisations, Science, and Industry (IPPOSI) that ran in parallel during the strategy development period returned a verdict in October 2022 that closely mirrored the key priorities of this National Strategy with respect to patient and public involvement, appropriate use, national partnerships, data security, and the importance of consent.

It has been an enormous privilege to chair the National Genetics and Genomics Strategy Steering Group that has overseen the development of this strategy. I have been amazed at the speed and quality of the responses to the initial requests for information, with over 100 experts feeding into the process. It has been a pleasure to work with the staff at the Health Service Executive (HSE) and Department of Health (DOH) in a process that was ably managed by the former's Strategic Programmes Office.

We aim to begin the important work of implementing this National Strategy from early 2023 and continue to enhance genetics and genomics in Ireland.

INSERT SIGNATURE

Executive Summary

Our genes hold powerful information that can be used to help diagnose conditions, guide more effective treatments, and predict our risk for disease, helping to improve patient outcomes and overall population health and wellbeing. Genomic medicine harnesses this power and is enabling a paradigm shift from a disease-oriented 'one-size-fits-all' healthcare approach to one that is more personalised, predictive, preventative, data-driven, and cost-effective.

To date, Ireland has made some progress in developing its genetic and genomic services, with pockets of excellence evident throughout the country. However, to fully realise the benefits of genetics and genomics, there is an urgent need to mainstream them so that they can become an integral part of our routine care delivery. A coordinated national genetics and genomics service is required to optimise patient outcomes and patient/citizen experience while advancing research, innovation, and discovery in this fast-moving field.

In early 2022, the Health Service Executive (HSE) Office of the Chief Clinical Officer established a National Genetics and Genomics Strategy Steering Group and four Working Groups to drive the collaborative and inclusive development of Ireland's first National Strategy for Genetics and Genomics. Over 100 experts, a number of patient representatives, the Department of Health (DOH), and other key stakeholders contributed to the work. Patient and public involvement was at the heart of the strategy's co-creation. Patients and professionals have contributed reflections on their current experiences and vision and expectations for the future of genetics and genomics in Ireland; these appear throughout the document.

In alignment with Sláintecare, this National Strategy outlines our approach for developing a sustainable patient and family centred genetics and genomics service that can be accessed equitably across the country and across the lifespan of patients. The service is to be supported by strong governance, a skilled workforce, pioneering research and innovation, and trusted partnerships.

The strategic areas of focus for the development of the genetics and genomics service are mapped in the strategy to five interconnected priority themes: Coordinating a National Approach, Ensuring PPI and Partnerships, Building the Workforce for the Future, Enhancing Clinical Services, and Strengthening Infrastructures.

Coordinating a national approach to genetics and genomics

To ensure the equitable delivery of an efficient, effective, and safe genetics and genomics service in alignment with Sláintecare vision, there is a need for a coordinated national approach underpinned by appropriate policy and legislation. The national office for genetics and genomics will be established to provide oversight of all aspects of genetic and genomic clinical and research activities. The national office will engage with key stakeholders to ensure that any requirements to address policy and legislative gaps are addressed. The national office will also be responsible for driving the five-year implementation plan that will follow this strategy.

Ensuring Patient and Public Involvement (PPI) and Partnerships

Patient and public involvement has been at the heart of development of this strategy and will remain the cornerstone of clinical service, research, and policy and legislative developments as we implement this strategy in a timely fashion. Fundamental to this is increasing awareness of and literacy in genetics and genomics among the public and patients. By empowering patients and the public, we will ensure that the development of the future consent process for genetics and genomics is reflective of their values and perspectives while ensuring alignment with best practice.

Building the genetics and genomics workforce for the future

A modern genetics and genomics service needs a fit-for-purpose and agile workforce to meet current demands and support future developments in genetics and genomics. A robust workforce plan will support the recruitment, retention, education, and career development of the current specialised workforce, which includes genetic counsellors and clinical scientists, as well as the future genetics and genomics workforce. Staff will be supported and have the opportunities to develop specialised knowledge and skills in genetics and genomics to confidently use in their everyday practice.

Enhancing genetic and genomic clinical services

To realise the potential of personalised medicine for the benefit of patients, there is a need to continue the transition of genetics and genomics into routine service delivery and support the timely use of effective, evidence-based genetic and genomic tests. This will enable the development of locally integrated multidisciplinary patient and family centred diagnostic and care pathways. Fundamental to this is defining and measuring quality in genetic and genomic service delivery.

Strengthening infrastructures to drive advances in genetics and genomics

Harnessing the power of genetic and genomic technologies for improved patient outcomes requires a supporting infrastructure to collect, test, store, process, and analyse samples for both patient care and ongoing research applications. To strengthen data infrastructure in Ireland, existing genetic and genomic data capacity and capability will be reviewed and there will be continued work toward the establishment of a secure, scalable, and accessible data and analytical infrastructure to support clinical service delivery, bioinformatics, data access, and research. To build upon our existing infrastructure and skilled workforce, we will create a Laboratory and Bioinformatics Partnership Network supported by the establishment of a National Centre for Excellence in Genomic Testing and Bioinformatics.

A future-proofed genetic and genomic infrastructure network requires an enabling research ecosystem. This ecosystem will be enhanced by collaboration and partnership both nationally and internationally to ensure the translation of technological advancements and knowledge into improved outcomes for patients and their families. This approach will enable Ireland to be a key contributor in advancing research, innovation, and discovery in genetics and genomics on the global stage.

Conclusion

As we progress into implementation of this strategy in 2023 and beyond, we now have a path forward for improving outcomes for patients and their families and establishing Ireland as a leader in the area of genetics and genomics. Continued collaboration between all stakeholders will be key to realising our shared vision of the establishment of a nationally led genetics and genomics service for Ireland.

Genetics: The study of genes, genetic variation, and heredity in living organisms.

Genomic medicine: The use of genomic information and technologies to determine disease risk and predisposition, diagnosis and prognosis, and the selection and prioritisation of therapeutic options.

Personalised medicine: Medicine targeted towards an individual or group of individuals, which uses knowledge of genetic, environmental and lifestyle factors to determine suitable methods of prevention,

Key Strategic Areas of Focus

1. A national office for genetics and genomics will be established in 2023 under the governance of the HSE and will provide oversight and a standardised approach to the delivery of the genetics and genomics service as outlined in the National Strategy for Accelerating Genetic and Genomic Medicine in Ireland.

2. The Department of Health will engage with stakeholders across the clinical, academic, research, and non-profit sector to identify gaps in Irish policy and legislation. This engagement, in conjunction with wider public consultation, will be used to inform future legislative and policy action.

3. A national education and communication programme will be developed and implemented to raise awareness of genetics and genomics and increase genetic and genomic literacy amongst patients and the public.

4. Building and maintaining public trust and engagement will ensure sustainability and impact positively on service, research, and policy developments. Meaningful partnerships with the public will be established to ensure that the public and patient voice is at the heart of implementation of the strategy and in the design and development of any new services or initiatives.

5. There will be a national approach to ensure that standardised guidance on consent for genetic and genomic clinical and research purposes, is harmonised and developed in line with relevant guidelines and legislation.

6. A National Genetics and Genomics Workforce Plan will be developed in 2023 to support the recruitment, retention, education, and career development of the current and future genetics and genomics workforce.

7. A suite of measures that ensure the delivery of safe, high-quality care will be developed, and processes will be implemented to monitor performance against agreed targets to drive quality improvement.

8 Locally integrated multidisciplinary patient and family centred care pathways will support the continued transition of genetic and genomics into mainstream healthcare by building on existing services, collaborative networks, and expertise to enhance service delivery i a manner that is efficient, equitable, and in accordance with the Sláintecare vision.

9 Equitable, timely, and evidence-based availability of genetic and genomic tests and technologies in clinical practice will be improved through a coordinated and standardised national approach including the development of a National Test Directory.

10 The national office will work with services to enhance existing laboratory infrastructure and informatics services to promote the development and use of innovative technologies for testing, sample tracking, and reporting.

11 A National Centre of Excellence in Genomic Testing and Bioinformatics will be established as a single entity which will sit under the governance of the HSE.

12 The national office will review existing genetic and genomic data capacity and capability and work toward the establishment of a secure, scalable, and accessible data and analytical infrastructure to support clinical service delivery, bioinformatics, data access, and research.

13 Engagement, collaboration, and partnership with international organisations, industry, government, and academic partners will be key to enhancing Ireland's research ecosystems. Procedures, processes, and guidelines will be developed to support the translation of advances in genetics and genomics into current and future clinical practice

Section 1
Introduction

1.1 Introduction

Genetics is the study of inherited features, and genomics is the study of all of a person's genes (their genome). Genomic medicine is the use of genetic and genomic information and technologies to determine disease risk and predisposition, diagnosis and prognosis, and the selection and prioritisation of therapeutic options – thus improving clinical care and health outcomes.

Genomic medicine is enabling a paradigm shift from a disease-oriented 'one-size-fits-all approach' in healthcare to an approach that is more personalised, predictive, preventative, data-driven, and cost-effective. The large amount of genomic data generated from clinical and research activities can be harnessed to improve patient outcomes. Since the publication of the human genome sequence 20 years ago, the volume and availability of genomic data has grown exponentially, and this has led to significant benefits for patients and populations. Some of these examples in cancer, rare diseases, foetal medicine, chronic diseases, infectious diseases, and pharmacogenetics are set out below.

To date, Ireland has made a degree of progress in developing genetic and genomic services, with pockets of excellence throughout the country. However, there is a need to mainstream genetic and genomic services so that they become part of routine care delivery. There is more that we can do, set out later in this document, to enable a coordinated national genetic and genomic service that can harness the power of genetic and genomic data, alongside research and innovation, to inform clinical decision making and advance personalised medicine in Ireland.

Genomics and personalised medicine

The development of advanced bioinformatics tools for the analysis of genomic data is enabling a shift to personalised medicine. Personalised medicine is a fast-growing medical approach that takes into account a patient's individual variables including their genetics, and in some cases their lifestyle, as well as other environmental factors. A more comprehensive understanding of disease-causing factors provides:

- Earlier, faster, and more accurate diagnoses
- Optimised outcomes through targeted treatments and reduced adverse effects, which may also be more cost effective
- Early detection of patients at risk for a disease or condition, allowing time to implement preventative measures to halt or slow down development of a disease or condition

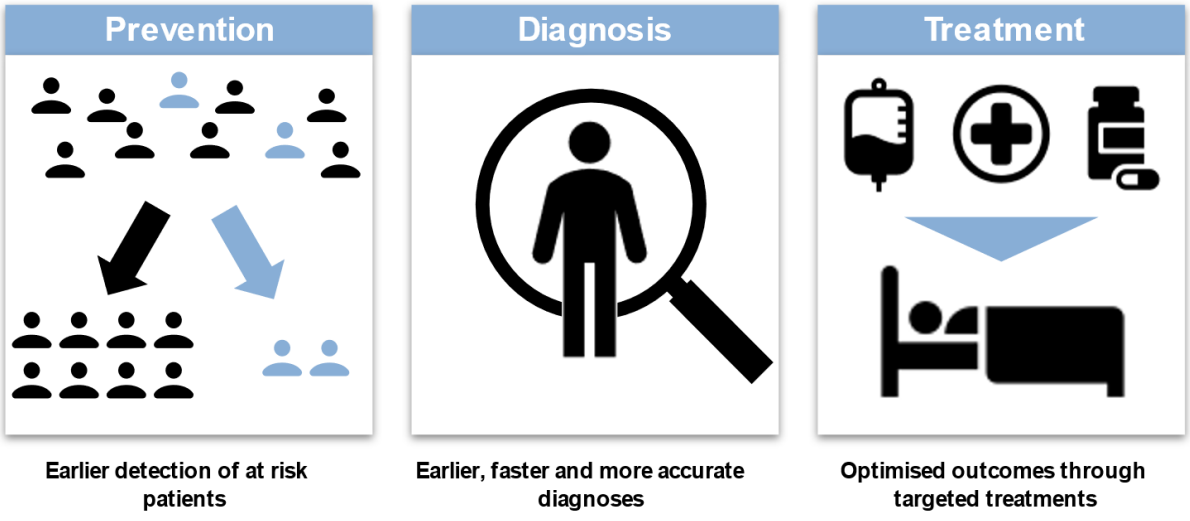


Figure 1: Personalised medicine drives significant benefits for patients

As technology has improved, the cost of genetic testing and storage and the interpretation of results has reduced. Advances in technology and affordability will continue to support the mainstreaming of genetics and genomics in healthcare systems and increase access to testing for our population.

Potential of genetics and genomics to transform the delivery of healthcare

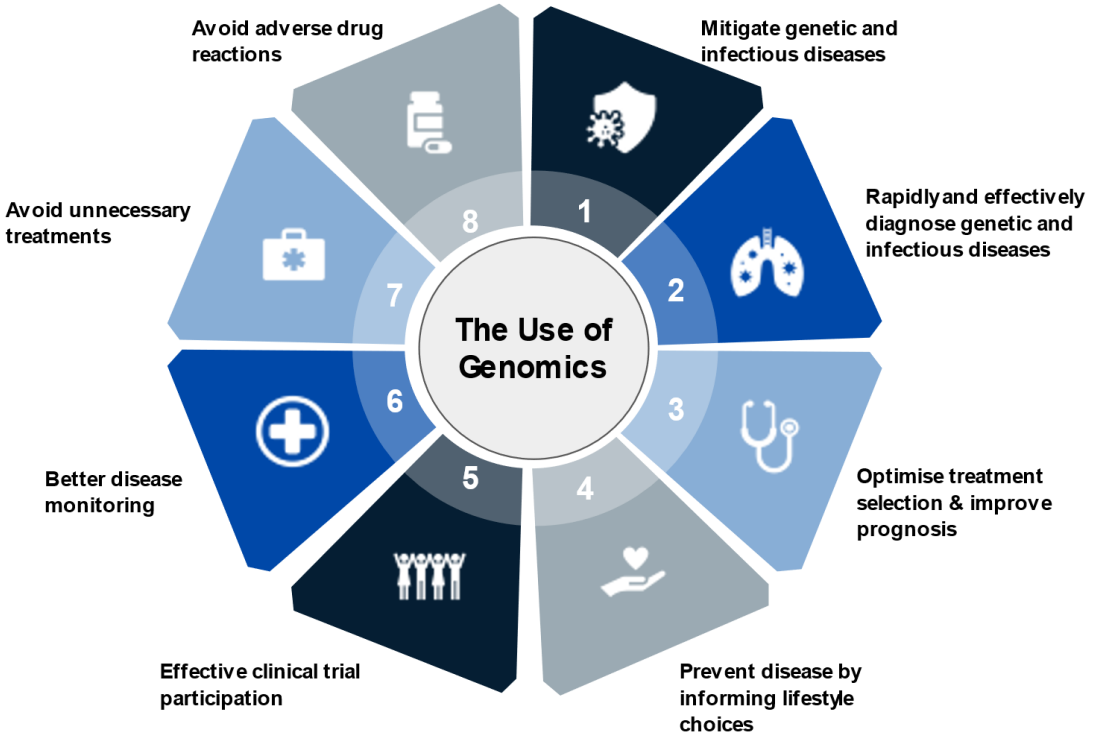


Figure 2: Potential of genetics and genomics to transform the delivery of healthcare

Cancer

The National Cancer Strategy 2017-2026 aims to meet the needs of cancer patients in Ireland for the next decade. Personalised medicine in cancer has evolved at a significant rate over the last decade. Molecular diagnostics are now routinely incorporated into clinical decision making. The use of genetic and genomic analytical techniques allows a much more detailed analysis of the genomic make-up of a tumour and can provide insights into how an individual's cancer has developed, assist in monitoring clinical progress, and inform a likely response to treatment. This opens up new treatment opportunities, new targets for drug development, and the potential for improved patient outcomes.

It is estimated that inherited gene variants are responsible for between 5–10% of cancers. The identification of such cancer predisposition allows for the implementation of risk-reduction measures, such as prophylactic surgery and chemoprevention, and surveillance to ensure early detection. In this way, genetic testing and provision of comprehensive downstream services can effectively reduce both cancer incidence and cancer mortality.

Rare diseases and undiagnosed rare conditions

Rare diseases tend to be complex, chronic, and multi-systemic. In many cases, patients require follow-up care with management from multiple medical specialists and health and social care professionals, which necessitates a high level of integrated care and service coordination between hospital, community, social, and primary care services. It is estimated that 300,000 people in Ireland are living with over 6,000 known rare diseases[1].

The use of genomics has improved rates of diagnosis for patients with rare disease and reduced the 'diagnostic odyssey', or the extended length of time it can take for a patient

to receive a diagnosis. However, there continues to be a large number of patients with rare diseases who remain undiagnosed for years and experience unique challenges in accessing appropriate care and support as a result. International studies show that for 25% of those who receive a genetic diagnosis, there was immediate clinical actionability. In the diagnosis of rare diseases, there is a clear economic and personal benefit in early genome sequencing[2].

Foetal medicine

One of the frontiers of the genomic revolution is foetal medicine, which encompasses diagnosis of foetal anomalies and the assessment of foetal conditions such as structural, genetic, and growth disorders. A diagnosis can inform:

- Management decisions, including where and how to deliver the baby
- Possible treatments that may be offered in the antenatal or postnatal period
- The development of future in-utero foetal therapies
- Palliative care decisions, potentially reducing invasive diagnostic testing in the postnatal period
- Family planning

Chronic diseases

Genomic data can provide more targeted insight into chronic disease management, supporting a preventative approach which reduces disease burden and improves population health. Treatment of chronic diseases which can be enhanced by genetic and genomic medicine include those affecting the cardiovascular, respiratory, endocrine, and neurological systems. For example, economic data from the UK and US suggests that approximately 3% of the total health budget (equating to approximately €600 million for Ireland) goes toward managing heart failure alone. A 2–5% drop in incidence of heart failure may lead to additional savings of €12–30 million per year[3].

Infectious diseases

The COVID-19 pandemic has shown the critically important role genetics and genomics play in monitoring and controlling infectious diseases. Whole genome sequencing (WGS) of the SARS-CoV-2 genome and the access of data across the global community was unprecedented during the pandemic and essential in informing the public health response. Understanding the genetic structure of the virus was critical to diagnosing and monitoring cases and outbreaks, tracking variants, and facilitating the development of vaccines and therapeutics. Genomic research is finding that our genes influence our resistance or susceptibility to certain infectious agents, including SARS-CoV-2, as well as the severity of disease experienced.

Pharmacogenetics

Pharmacogenetics is the study of how an individual's entire genetic makeup determines the body's response to drugs. Genome-guided prescribing can help to:

- Avoid severe and life-threatening adverse reactions to pharmaceuticals
- Determine which drug is likely to be effective for a given patient
- Determine what dose should be given to maximise the therapeutic benefit and minimise side effects
- Increase patients' compliance with treatment by targeting the right patient with the right drug
- Improve patients' quality of life
- Reduce the time, cost, and failure rate of pharmaceutical clinical trials

References:

1. Health Service Executive (2022). National Rare Diseases Office: What is a rare disease? Retrieved from /www.hse.ie/eng/services/list/5/rarediseases/#:~:text=There%20are%20more%20than%206000,Ireland%20have%20a%20rare%20disease
2. Smedley, D., *et al. (*2021). 100,000 Genomes Pilot on Rare-Disease Diagnosis in Health Care — Preliminary Report. Retrieved from www.nejm.org/doi/full/10.1056/NEJMoa2035790
3. Heart Failure National Clinical Programme (2022). Clinical Design and Innovation. Retrieved from https://www.hse.ie/eng/about/who/cspd/ncps/national-heart-programme/heart-failure/

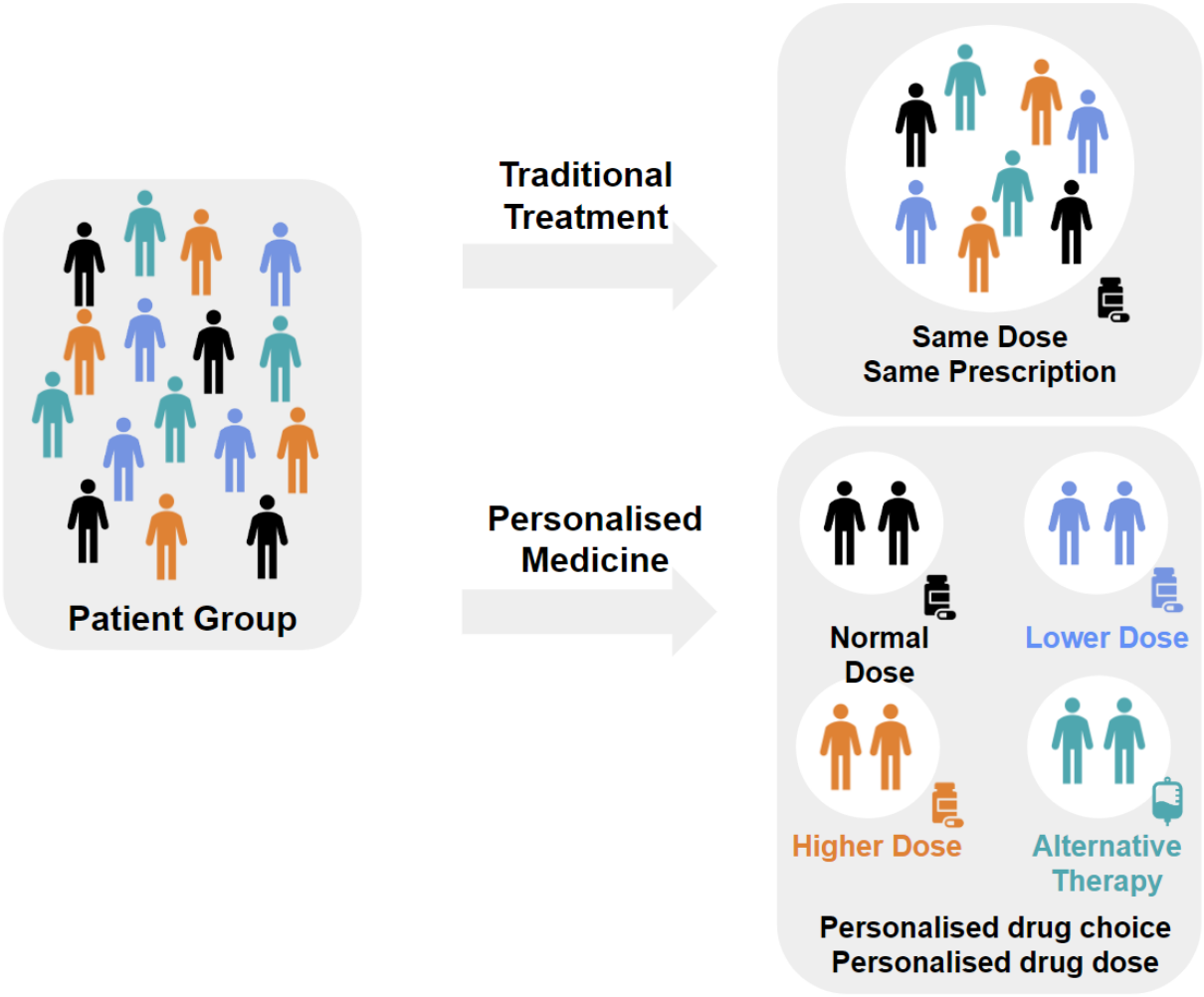


Figure 3: How personalised medicine can benefit patients

1.2 Current Situation in Ireland

Over the last number of years, advances in the delivery of genetic and genomic services in Ireland have progressed, and the support this strategy has received builds upon previous government commitments to expand this area in the health service. The Programme for Government, for example, made a commitment to establish a National Genetics and Genomics Medicine Network, a development that will be facilitated by this strategy.

Clinical genetics is an established medical subspecialty with excellence number of examples of good practice existing throughout the country. However, there is broad consensus from the stakeholders involved in developing this National Strategy that we can accelerate and improve our genetics and genomics service in Ireland through:

- Improving equity and access to genetic testing, services, and support
- Building and enhancing the genetics and genomics workforce of the future
- Bolstering genetic and genomic literacy
- Developing our services to harness the rapid advances that are occurring in genetics and genomics
- Developing a national coordinated approach to genetic and genomic testing
- Coordinating and enhancing collaboration between research and clinicians for the benefit of patients
- Leveraging our recognised leadership in biomedical, molecular, and translational research to further harness the power of genomic data and research to inform clinical decision making

Laboratory capacity has been developed in Ireland to support a level of genetic and genomic testing. Currently, a volume of patient samples is sent overseas for testing.

A national programme for genetics and genomics will provide the opportunity to create more efficient services for patients and support an effective use of healthcare resources.

Coordination and integration between clinical and research genetics and genomics is critical to the provision of a high-quality service. This strategy provides the opportunity to move our genetics and genomics service forward at pace, in alignment with existing programmes, national strategies, and models of care (e.g. National Cancer Control Programme [NCCP], National Women and Infants Health Programme [NWIHP], National Rare Diseases Office [NRDO]) for the benefit of our population.

My point of view: hope for the future of genetics and genomics in Ireland

Our son was born in December 2013 by emergency C-section due to extreme stress in utero and being small for dates. Immediately after birth he was treated in the NICU for a multitude of different abnormalities. It quickly became clear that all symptoms were leading to a congenital or inherent disorder.

James spent most of his first three years of life in hospital under the care of several multidisciplinary teams. During this time James underwent two unrelated bone marrow transplants to treat his neutropenia.

Throughout his time in hospital and up until the age of six, James was undiagnosed. Under the care of Haematology, James had several genetic tests done. All were inconclusive and gave us no answers as to what we were dealing with.

In August 2019 we finally got the phone call to tell us that a gene mutation had been found, that it was de novo, and that James was the only child in Ireland with this genetic anomaly.

Being someone with a rare disease is like driving your car in the dark with no headlights. You never know what's coming next because there are so many unknowns, and without the proper supports it is a very lonely and isolating place.

With the work being done at present, the future of the genetics and genomics service in Ireland looks bright. My hopes for patients and families when the strategy is implemented are:

- That we have easier access to genetic services in Ireland such as genetic counselling, increased access to fertility treatments, and a reduction in test waiting times
- That our centres will have nurse specialists for patients with rare diseases to support and guide them through the process, and that our GPs carry a level of knowledge of the genetic process so they can care for patients in those early days

James is doing exceptionally well; he has the most wonderful zest for life and lives it to the max. I'm truly honoured to be his mother, and we are all so proud of him. Because of his story and many others like him, genetics and genomics in Ireland is changing — and changing for the better

Karen Morgan,
Patient Representative

Section 2
Vision and Approach to Development

2.1 Vision for Genetics and Genomics in Ireland

Our vision for Irish genetics and genomics is to develop a patient and family centred service that aligns with the values of Sláintecare through its focus on equity of access and enhanced patient outcomes. This service will cover the patient lifespan and be available across the Regional Health Areas. It will be supported by a strong governance system, a skilled workforce, innovative research, and trusted partnerships.

This future of the genetics and genomics service is described across six key strands in the graphic below. The development of this strategy and its implementation over the next five years, and beyond, is a key step in delivering on this vision.

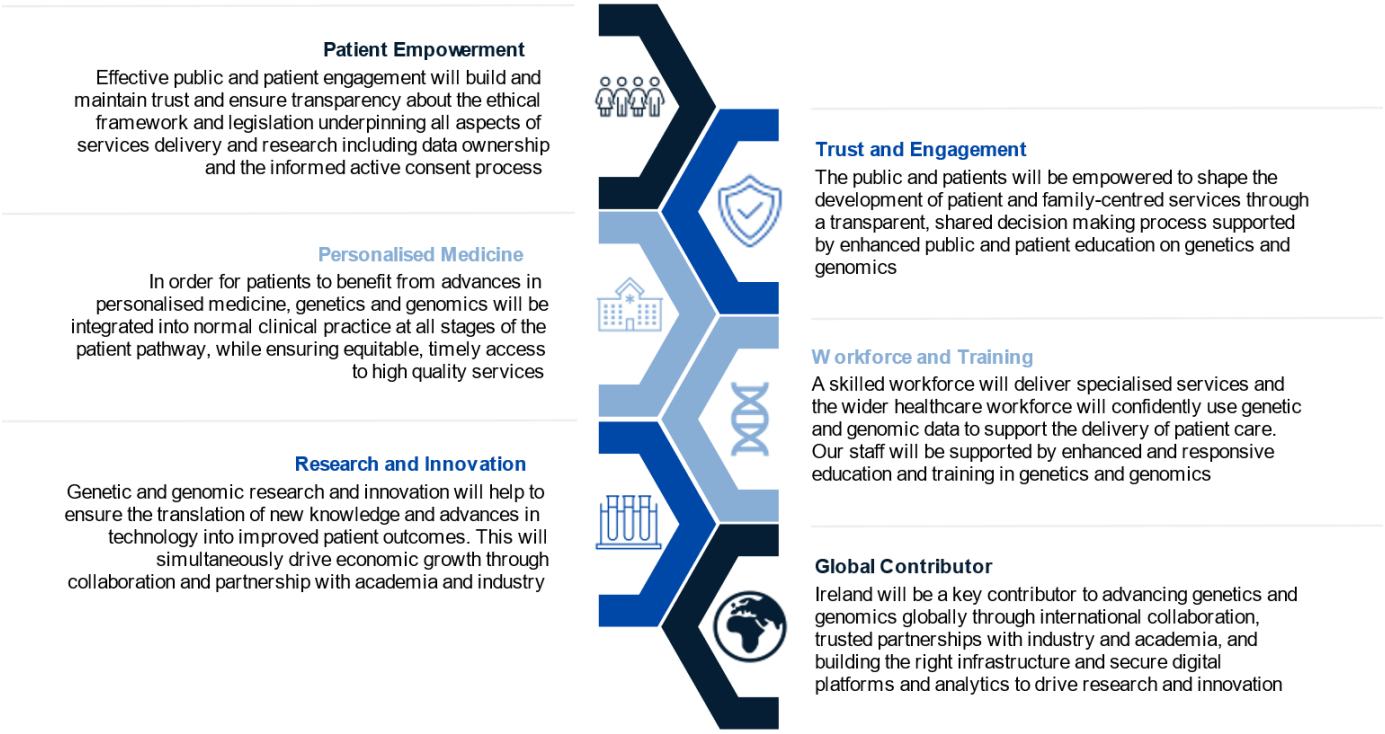


Figure 4. The vision for genetics and genomics in Ireland

The guiding principles

Figure 5: The guiding principles of the National Strategy for Accelerating Genetic and Genomic Medicine in Ireland.

The eight key guiding principles that underpin the strategy are:

- **Patient and family centred**: Services will be delivered in an integrated patient and family centred manner.
- **Responsive:** Given the speed at which the fields of genetics and genomics are progressing, we will remain agile and adaptable to advances in scientific knowledge and tools and their clinical and research application.
- **Ethically grounded:** The use of personal data will meet the highest ethical principles for clinical practice and research and reflect the voice of the citizens of Ireland.
- **Trusted:** Effective governance will ensure that genetic and genomic clinical services and research are delivered in a manner that fosters trust and builds public and patient confidence in genetic and genomic medicine
- **Empowering:** Patients and their families will be empowered to make informed decisions about the use of genetic and genomic tests and health data in the delivery of their care.
- **Inclusive and accessible:** Clinical genetics and genomics and research will be equitable, inclusive, accessible, responsive, and respectful of diversity in society.
- **Evidence-based and cost effective:** The translation of advances in genetics and genomics into healthcare services will be evidence-based and in the best interest of our patients, while remaining cost effective and reducing waste.
- **Collaborative:** To advance knowledge and fuel innovation in genetics and genomics, we will work collaboratively both nationally and internationally for the benefit of patients

2.2 Approach to the Development of the National Strategy for Accelerating Genetic and Genomic Medicine in Ireland

Approach to strategy development

In April 2022, the Health Service Executive (HSE) Chief Clinical Officer, through the leadership of the Strategic Programmes Office, commenced work on the development of a National Strategy for Genetics and Genomics in Ireland. A Steering Group of national experts, patients, patient advocates, professional societies, representatives from the Department of Health (DOH), and researchers was established and chaired by an independent chair, Dr Mark Bale.

The National Genetics and Genomics Strategy Steering Group met monthly over the course of the development of the strategy, with a number of additional Extraordinary Meetings for urgent key decisions.

On recommendation from the Steering Group, four Working Groups to facilitate the strategy development were established: Workforce and Collaboration, Clinical Practice and Innovation, Data and Infrastructure, and Policy, Communication and Engagement.

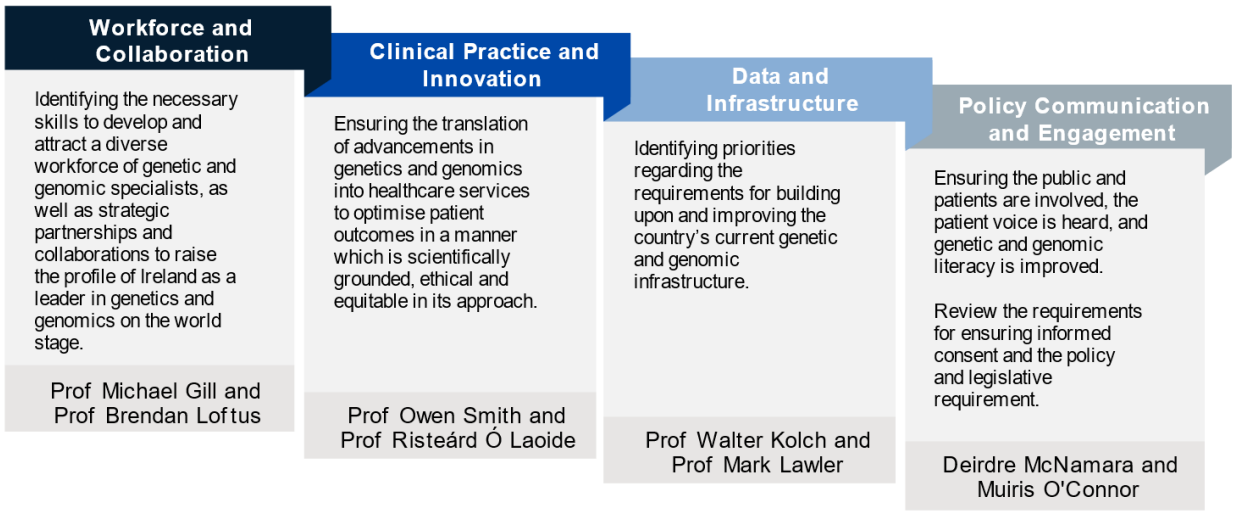


Figure 6: Working Group areas of focus

More than 100 experts and 11 patient representatives across the Steering Group and four Working Groups directly contributed to the development of the National Strategy. Initial proposed recommendations were presented by the Working Groups to the Steering Group in early July 2022. These recommendations were then further discussed and refined by the individual Working Groups before being presented to the larger collective of Working Group and Steering Group members for a collaborative working meeting at a Town Hall event on September 30th, 2022. The drafting process of the present document from October through November 2022 was likewise a cooperative effort between the Strategic Programmes Office, the Steering Group, and Working Group members with input from key external stakeholders.

Public and patient involvement and other stakeholder engagement

To ensure public and patient voices shaped this National Strategy, continuous and meaningful stakeholder engagement took place throughout the development process. Patients actively participated in the Steering Group and were represented across each Working Group. Additionally, a series of public engagement events took place, and feedback tools were employed to ensure there were multiple opportunities for public engagement and feedback.

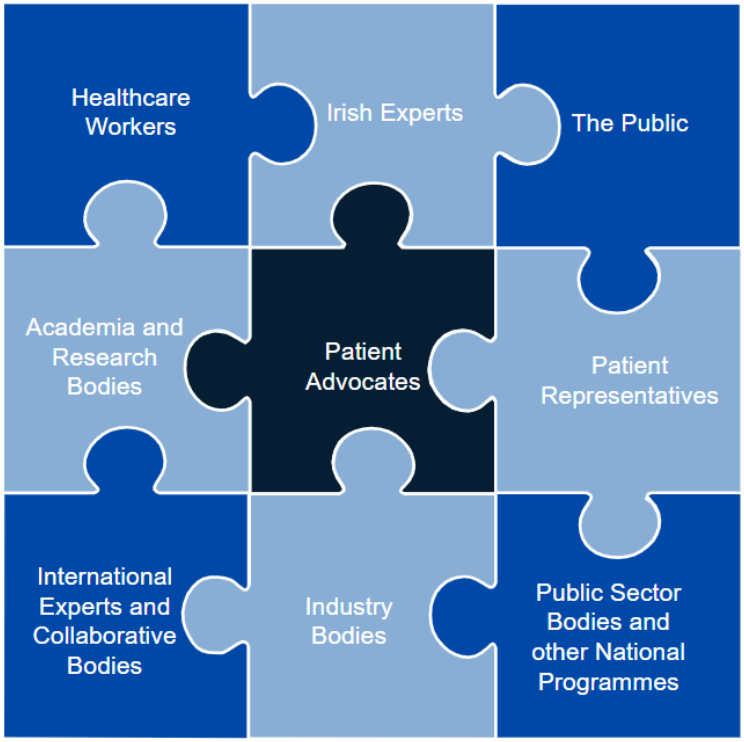


Figure 7: Stakeholders engaged during Strategy Development

Patient and public involvement was supported in a number of ways

In order to ensure that patient representatives were equal partners in the strategy development process, patient representatives participated as members of the Steering Group and Working Groups. The Policy, Communications and Engagement working Group created a network of more than 90 patient advocacy and research advocacy groups that were invited to participate in a series of webinars designed to share information on the strategy development process, gather information related to patient experience and concerns, and discuss patient recommendations to the strategy.

Separately, the Irish Platform for Patient Organisations, Science and Industry (IPPOSI), supported by the PPI Ignite programme at the Royal College of Surgeons in Ireland (RCSI), the Health Research Board (HRB), and grants from two IPPOSI industry members (Pfizer and Roche), carried out a comprehensive Citizens Jury process on the Future Use of Genomics in Ireland. As such, IPPOSI was a valued touchpoint for information on the views and concerns of the public throughout the strategy development. The report on the Citizen's Jury verdict was published in October 2022, and IPPOSI and jury members presented its findings to Steering Group members to inform the development of this strategy. The Jury's recommendations, which focused on the importance of patient safeguards, data protection, and health literacy, are evident in the strategic priorities put forth in this strategy.

Healthcare professionals occupying key roles in areas related to genetics and genomics in Ireland also supported the development of the strategy as members of the Steering Group

and leaders of certain Working Groups and subgroups (e.g. National Working Group to Inform the Strategic Direction of Laboratory Medicine). A larger cohort of healthcare professionals (nearly 200) from around Ireland and working within community, clinical and laboratory settings were also able to provide feedback into the strategy by participating in a series of online forums.

In addition, a Healthcare Worker Engagement Survey was distributed to raise awareness of the strategy development among the broader workforce and seek feedback related to the perception of importance and feasibility of the various strategic priorities identified during the development of the strategy. A total of 196 healthcare workers responded, and the information from this survey will support implementation planning for the National Strategy.

Other forms of stakeholder engagement included attendance, and in some instances presentations, at a number of key conferences in October 2022, including the Irish Society of Human Genetics Annual Conference, the HSE National Clinical Programmes Conferences Day, the NHS Genomics Healthcare Summit, and the Maturity Level Model workshop in Lisbon, which is part of the Beyond One Million Genomes (B1MG) project.

In line with the objectives outlined in Ireland's Shared Island Initiative, initial meetings were held between members of the Steering Group and representatives from Genomics Northern Ireland to share information and promote collaboration.

Certain Working Groups also engaged with international colleagues including NHS England and DATA-CAN, the UK's Health data Research Hub for Cancer, to leverage lessons learned; for example, the Data and Infrastructure Working Groups liaised with Scottish laboratories to inform the necessary bioinformatics requirements for laboratories.

Partnerships with the wider clinical, academic, and industry research communities will be key to improving service delivery, enhancing bioinformatics and data science to increase diagnostic and clinically actionable findings from genomics testing, and informing on the causes of disease and the development of new treatments. As such, a certain degree of early engagement with industry was undertaken as a part of the development of the strategy.

In collaboration with DOH, The Department of Further and Higher Education, Research, Innovation and Science (DFHERIS), Enterprise Ireland, and the Industrial development Agency (IDA), key industry stakeholders were identified, and a survey of these stakeholders was conducted. Some common themes revealed through the survey in relation to Ireland's current capabilities in the genetic and genomic industry include research and academic strengths, strong pharmaceutical and technology presence, a large single-provider health system, and highly trained experts both medical and academic.

The industries which participated in this questionnaire showed a high level of interest in providing services to support the implementation of public genetic and genomic services, such as data storage and security systems, sequencing solutions and community integrated ecosystem platforms to enable functionality.

The feedback, queries, and learnings from all of the above-described engagements with the public, patients, healthcare workers, and other key stakeholders were incorporated into the recommendations and throughout this strategy.

Broad stakeholder engagement and patient and public involvement (PPI) will remain a core focus throughout the implementation of the National Strategy and the delivery of Ireland's genetics and genomics service.

Section 3

Strategic Areas of Focus and the Way Forward

3.1 Coordinating a National Approach to Genetics and Genomics

3.1.1 Establishment of the National Office for Genetics and Genomics

1. A national office for genetics and genomics will be established in 2023 under the governance of the HSE and will provide oversight and a standardised approach to the delivery of the genetics and genomics service as outlined in the National Strategy for Accelerating Genetic and Genomic Medicine in Ireland.

Throughout the development of this National Strategy, there has been overwhelming support to establish a national office to lead strategy implementation, strengthen governance, and drive forward our ambitions for genetics and genomics in Ireland and the benefits they can deliver for our patients.

National Office

The national office for genetics and genomics will be part of the HSE and will:

- Establish national governance processes and professional leadership
- Drive the implementation of the strategy and the collaboration to expand genetic and genomic service delivery
- Work with relevant stakeholders to agree a prioritised approach to the enhancement of genetics and genomics
- Deliver service improvements in the short term through the implementation of the funding commitment in the National Service Plan 2023 to address urgent service deficiencies
- Lead on longer-term continuous service development

The office will be led by a national director, and the leadership team will also include expertise in clinical genetics and genomics, bioinformatics, and laboratory science. The establishment of the national office will be a priority for 2023.

Overview of genetics and genomics service infrastructure

As is the case in other countries, the national service will be supported by external boards and committees. The DOH and the HSE will continue to work together to ensure its implementation. Once established, the national office, as part of the HSE, will work closely with the new Regional Health Areas (RHAs) to provide a seamless care pathway for patients to access specialised national services.

As seen in other countries, the development of a national service needs to be underpinned by the principles of trust and transparency.

A robust governance structure is critical to upholding these values and successfully implementing the strategy. The design and development of appropriate governance structures will be a core focus of the first implementation plan. This will include, but will not be limited to, supporting areas such as clinical practice and data management, research and innovation, and ethics. We expect that over time these governance structures will continue to evolve to ensure they are fit for purpose and in line with international best practice.

3.1.2 Policy and legislative requirements

2. The Department of Health will engage with stakeholders across the clinical, academic, research, and non-profit sector to identify gaps in Irish policy and legislation. This engagement, in conjunction with wider public consultation, will be used to inform future legislative and policy action.

Increasing Ireland's genetics and genomics capacity has the potential to deliver wide-ranging benefits across the healthcare sector. These aims align with the vision of Sláintecare: right care, right time, right place. Harnessing the full potential of genetics and genomics will require a multi-pronged agenda encompassing scientific, clinical, ethical, legal, and social progress.

An important consideration for our future work is the blurred boundary between research and clinical services. Increasingly, research participants are identified in the clinic and have their genome sequenced in the research setting, which generates research findings used to inform their clinical care in real time. It is important, therefore, that any future legislative and policy developments enable the integration of research with clinical care.

The current Irish genetics and genomics system has a wide range of different actors and responsibilities. Collaboration will be necessary between government departments (DOH, DETE, and DFHERIS) and agencies (HSE, HRB, Science Foundation Ireland [SFI], the Industrial Development Agency [IDA], and Enterprise Ireland) as well as industry, academia, and non-profit organisations. At the centre of this will be patient and public engagement.

Findings from the recent IPPOSI Citizen's Jury highlighted the benefits of genetic and genomic advances in healthcare, but stressed the public desire for legislative safeguards, particularly in relation to patient data. Responding to these concerns requires an appropriate framework for ethical conduct of clinical genomic practice, informed patient consent, and strong data protection.

Data protection

Ireland has several legislative safeguards in place related to the use and retention of personal data. While a number of these have stemmed from changes at a European level, in the health research space the safeguards put in place have supplemented the European standards and offer a deeper layer of protection to Irish Citizens. These foundations will provide the base for a broader legislative framework underpinning Ireland's genetic and genomic landscape.

The EU's General Data Protection Regulation (GDPR) set out extensive obligations that data controllers and processors must follow in relation to data retention and processing. The purpose of the regulation is to promote the use of personal data for the benefit of the common good, while also respecting individuals' fundamental rights. GDPR regulations are set out in Irish law under the Data Protection Act 2018.

The Health Research Regulations 2018, which were made under the 2018 Data Protection Act, set out mandatory suitable and specific safeguards that apply to the processing of personal data for the purposes of health research. These regulations make explicit consent the default position for processing personal data and require that all research conducted in Ireland, where data is being used, be approved by a research ethics committee. In instances where explicit consent for the use of personal data cannot be obtained, approval can be applied for through the Health

Research Consent Declaration Committee (HRCDC).

The DOH is currently drafting a Health Information Bill. Among its provisions, the bill will establish a National Health Information Authority to provide strategic national leadership and better governance of health information as well as support the use of health information for care, treatment and wider health service purposes (including health research). It will allow for the use of the Personal Public Service Number (PPSN) as the primary health identifier to organise, link, and match health information. These new measures will facilitate a greater level of clarity, consistency, and certainty in relation to the processing of genetic and genomic data.

Ethical review processes and structures

Ireland has made significant advances in its national research ethics ecosystem. As a result, ministerial-appointed National Research Ethics Committees (NRECs) have been established in the areas of clinical trials, medical devices, and in-vitro diagnostics. The National Office for Research Ethics Committees is responsible for coordinating the work of each NREC and promoting national guidance in ethical approval processes to local committees. These developments have established a coordinated national approach to health-research ethical decisions, which can be expanded to encompass new areas as required.

Considerations for the road ahead

Biological samples

While Ireland has made significant process in the area of personal data, there is still work to be done in relation to the regulation of biological samples. Further regulation is needed around the storage governance and use of biological samples. Considerations in this area should include, for example, the regulation of repositories and biobanks, multinational studies using Irish samples, etc. As these regulations are developed, there are several best practices that can be used to ensure standards are upheld as Irish legislation is developed.

International best practice guides and legislation

There is a large body of guidance that now exists internationally which can inform policy and legislative developments. Ireland is committed to learning from best practice. As part of this, we have entered the Digital Europe Programme, the Horizon Europe Partnership on Rare Diseases, and the Horizon Europe Partnership for Personalised Medicine.

In May 2022, the European Commission published the proposal for a regulation on the European Health Data Space (EHDS). The current proposal is to establish a set of rules and infrastructures to support the primary and secondary use of health data, as well as to develop a European governance framework. This strategy and subsequent implementation plans will respond positively to this agenda.

The way forward

While Ireland has come a long way in establishing a legislative framework in key areas supporting genetics and genomics, it is important to acknowledge that there is still work to do.

To ensure Ireland stays connected to evolving international best practice, Ireland has joined Europe's flagship 1+Million Genomes Initiative (1+MG). This will link us with pan-European clinical and research infrastructure. With the establishment of the national office for genetics and genomics, the DOH, HSE, and relevant stakeholder groups will work closely to ensure genetic and genomic regulations remain responsive to current developments. This work will involve patient and public engagement to ensure Irish legislation meets the needs of the people it is designed to protect.

The effort to review and develop legislation should be seen as dynamic, covering the life of this strategy and beyond as Ireland continues to expand its genetic and genomic capabilities.

3.2 Ensuring Patient and Public Involvement (PPI) and Partnership

3.2.1 Patient and public awareness of and literacy in genetics and genomics

3. A national education and communication programme will be developed and implemented to raise awareness of genetics and genomics and increase genetic and genomic literacy amongst patients and the public.

Fundamental to the successful implementation of the National Strategy for Accelerating Genetic and Genomic Medicine in Ireland is continued PPI and partnership. Therefore, it is important that we continue to raise public awareness of genetics and genomics, improve genetic and genomic health literacy, and increase support mechanisms for patient involvement in strategy implementation. These actions will help build public trust and commitment for advancing the genetics and genomics service.

In recent years, there has been a rapid growth in public awareness of genetics and genomics due to advances in its integration into clinical practice, particularly in the management of cancer and rare diseases. There has also been an increase in global and national sequencing initiatives and in the use of genomics for monitoring new variants of COVID-19.

A key learning globally from the COVID-19 pandemic and the roll out of vaccines and therapeutics was the importance of addressing potential public and patient concerns early to ensure that misinformation is countered, that any failings from the past are acknowledged, and that trust is fostered and maintained. Information needs to be provided in a transparent, accessible, and open manner from credible, trustworthy sources.

In countries where genetic and genomic services are less well-developed, public awareness of the relationship between genomics and health and the potential and limitations therein remains low.

Genetic and genomic literacy is a component of public and patient health literacy and requires additional basic understanding of biology, inheritance as the cause of hereditary diseases, and the concept of appropriate use of genetic data to improve the care of the person, their family, and others with similar conditions. Improved public and patient literacy are crucial to improving individual and population-level health and fostering a safe and transparent environment which allows the healthcare benefits of genetics and genomics – and its implications for personalised medicine – to be realised.

The way forward

The national office will include a dedicated genetics and genomics communications officer or coordinator to support the development of the national genetics and genomics education and communication programme.

Healthcare professionals, patients, and advocacy groups will be consulted to agree targeted information for communication to the public and defined patient groups.

Regular monitoring and evaluation of the impact of communications will be carried out on an ongoing basis through appropriate channels.

3.2.2 PPI in shaping services, research, and policy developments

4. Building and maintaining public trust and engagement will ensure sustainability and impact positively on service, research, and policy developments. Meaningful partnerships with the public will be established to ensure that the public and patient voice is at the heart of implementation of the strategy and in the design and development of any new services or initiatives.

A critical aspect of responsible genetic and genomic practice is PPI in shaping services, research, and policy co-creation. Partnering with patients is defined in the HSE Quality Improvement Framework as 'services that are respectful and responsive to individual's needs and values and partners with them in designing and delivering that care'.

PPI in genetic and genomic research is key to the successful implementation of this National Strategy. The Global Alliance for Genomics and Health (GA4GH) has developed a framework for involving and engaging participants, patients, and the public in genomics research and health implementation. The four key components of this are fairness, context, heterogeneity, and recognising tensions and conflict.

The development of the present strategy for Ireland has been undertaken in partnership with patients and the public. Patients and the public will continue to be active partners throughout the implementation of this strategy. This will include participating in shared decision making in the planning, implementation and evaluation of genetic and genomic services and research.

The way forward

The national office will support the public and patients to be active partners, participating in shared decision making in the planning, implementation, and evaluation of new services and research. PPI will be enabled and embedded in fit-for-purpose national genetic and genomic governance structures, including key national groups. Due consideration will be given to utilising existing PPI structures already in place such as the PPI Ignite Programme.

My point of view: my cancer diagnosis and treatment

Diagnosed with breast cancer in 2017, I received outstanding care from my entire oncology team and will never be able to thank them sufficiently for what they did for me. My treatment pathway included a wide excision lumpectomy, 16 rounds of chemotherapy, 17 rounds of Herceptin over 51 weeks and 20 fractions of radiotherapy over 20 days.

Genetic testing was not available to me at diagnosis. Upon diagnosis I requested a referral for genetic test. I progressed through treatment, lumpectomy, and into chemotherapy, and had yet to receive an appointment. I called regularly and offered to travel at short notice.

I count myself extremely lucky that I persevered; too many people drop out due to difficulty in referral and extremely long wait lists. Nearly nine months after my initial referral, in January 2018, I got a call to attend a cancellation appointment. I postponed my radiotherapy session and travelled to the appointment with my husband. I then waited a further four months to receive my BRCA2 diagnosis.

The confirmation of BRCA2 meant that the best course of action for me was a bilateral mastectomy and a bilateral salpingo-oophorectomy.

Once I received the news of the gene mutation, I had to navigate this path of risk-reducing surgeries. I researched and sought out a surgeon myself. There was no cross-discipline genetic service available to me to support my journey.

I believe, without genetics forming part of our treatment pathways, we are over-treating, which brings additional angst to patients and increases costs nationally.

I would like to see an urgency in establishing a robust genetics service which is accessible across the country, founded on international best practice. In my view, genetic counsellors must be available and embedded in clinical centres of excellence and testing must be efficient (my sample took 6 weeks before it was even received by the lab overseas). I would also like to see support for extended families of patients.

I would implore that we consider genetics and genomics as an investment to avoid some diagnosis completely through patients opting for risk reducing surgeries, to enable early diagnosis through access to screening, and to ensure treatment can be tailored and informed with genetic data.

Margaret Cuddigan
Patient Representative

3.2.3 Ethical considerations and the consent process

5. There will be a national approach to ensure that standardised guidance on consent for genetic and genomic clinical and research purposes, is harmonised and developed in line with relevant guidelines and legislation.

Consent, the giving of permission or agreement for a treatment, investigation, receipt, or use of a service or participation in research and testing, is a fundamental component of good, ethical medical practice. Prior to next-generation sequencing, the traditional genetic counselling approach to single-gene testing was similar to the consent process for medical tests or interventions.

However, there are additional considerations to ensure suitable consent is obtained and maintained in the context of genetic and genomic sequencing, particularly as there may be significant implications in both clinical and research settings. Various different models of consent for clinical and/or research purposes have been developed, including: explicit; layered; broad; dynamic; and hybrid approach models. There are additional considerations around vulnerable groups, including children, which need to be taken into account as approaches to consent are implemented.

In 2020, the HSE published its updated *National Consent Policy*. This guidance relates to informed consent for medical treatments and interventions. The HSE *National Consent for Research Policy* is currently under development.

The way forward

Guidance on, and an associated approach to, consent for genetic and genomic clinical and research purposes will be developed in line with the HSE National Consent Policy and the HSE National Consent for Research Policy (currently in development) and in alignment with Part 4, Appendix 1 of the Disability Act 2005, the Data Protection Act 20189, Health Research Regulations 2018 and 2021, the Assisted Decision Making Act 2015, and the Health Information and Patient Safety Bill, which is currently under development. This will help to ensure good governance of all aspects of consent, confidentiality, research, and data use in relation to genetics and genomics.

3.3 Building the Genetics and Genomics Workforce for the Future

3.3.1 The multidisciplinary workforce

6. A National Genetics and Genomics Workforce Plan will be developed in 2023 to support the recruitment, retention, education, and career development of the current and future genetics and genomics workforce.

Advances in genetics and genomics have led to demand that has exceeded workforce growth. Technological advances in genetic testing and the expanded use of genetic and genomic data in clinical practice and health research have increased the imperative for a highly skilled and expanded workforce. International studies have demonstrated that critical shortages in properly trained and informed healthcare workers to deliver genomic and genetic services are likely to contribute to a significant delay in adoption into patient pathways. Expansion of services, innovations in technology, and establishment of collaborative networks and governance structures are dependent on a scalable workforce.

A multi-pronged approach will be required to ensure Ireland can expand its workforce sufficiently. This will include the development of career pathways and training opportunities in genetics and genomics for both specialists and non-specialists. Alignment with the RHAs to ensure trained staff are recruited and supported across the Irish healthcare system will be essential.

Although there is currently no detailed workforce plan aligned to international best practice, it is generally acknowledged that current workforce numbers are insufficient to meet present demand and support future service development in genetics and genomics. The 2019 HSE report *Review of the Clinical Genetics Medical Workforce in Ireland* highlighted the undersupply of doctors in clinical genetics compared to services in other countries.

A National Working Group to Inform the Strategic Direction of Laboratory Medicine was recently formed. This laboratory medicine Working Group is tasked with producing a series of recommendations on how to enhance laboratory services and staff training needs. The outcome of these findings will help inform new directions in this area. There is a need to support the development of genomic education and training resources to enable the upskilling and development of the multidisciplinary workforce to secure a genomics workforce of the future.

The way forward

A national genetics and genomics workforce plan will be developed by the national office in 2023 in alignment with the broader HSE and DOH workforce plans to enable the implementation of the National Strategy and build on previous work such as the HSE's 2019 Review of the Clinical Genetics Medical Workforce in Ireland*. The national office will support the recruitment, retention, education, and career development of the current and future genetics and genomics workforce.*

My point of view: my career pathway in genetic counselling

I discovered genetics in school, a subject that combined two of my loves: maths and biology. During school, I spent Saturday's volunteering in what is now Laura Lynn's children's hospice. I learned that caring for a child with physical and intellectual disabilities could be rewarding and tiring, joyful and sad. These children were away from their families because the supports were not there for them to live at home.

I went on to study genetics in Trinity College Dublin. In my final year, we had a course of lectures on genetic counselling. I knew then the career I wanted to pursue. A new Master's course had just begun in Manchester. After Trinity, I worked for a year in Marino School in Bray. The children I was teaching all had genetic conditions, and none of the families had access to genetic counselling here.

Following my Masters, I joined the team at the National Centre for Clinical Genetics in 1999. The service had just started, and we all wanted to make a difference. However, the service was to struggle as there was no overall direction, no strategy, no national plan. I moved in 2016 to work in the NRDO. As a genetic counsellor, I found it frustrating that no national listing of clinical expertise had existed for referral purposes. The NRDO is responsible for cataloguing all clinical expertise and runs an information line to signpost families and healthcare professionals.

Through the years I have met some amazing families and inspiring clinicians. I have been part of numerous working groups and have just stepped down as Chair of the Irish Society of Human Genetics. I am delighted to see the Government funding the implementation of this strategy and I look forward to fully supporting its implementation.

Jacqueline Turner,
Genetic Counsellor

3.3.2 Promotion of talent development and career pathways

To realise the full potential of utilising genetics and genomics, a specialised, modern, well equipped, and sustainable workforce is key. Fundamental to this is the development of structured career pathways in genetics and genomics, the opportunity to participate in research, and access to accredited training programmes.

There are a number of challenges which will need to be addressed to attract and develop talent in genetic and genomics, particularly given the global shortage of professionals skilled in the latter. As an example, a genetic counsellor requires a Clinical Master's degree and registration with an accredited body. However, there are currently no Masters of Genetic Counselling degrees available in the Republic of Ireland. In addition, there are no accredited training programmes in the Republic of Ireland for specialised genetics and genomics laboratory and bioinformatics roles, although the Irish Association of Clinical Scientists is currently developing a training programme in Clinical Bioinformatics.

However, there are also opportunities here in Ireland, for example the SFI Centre for Research Training in Genomics Data Science is currently training over 100 Ph.D. data scientists, which will likely impact positively on the availability of a highly skilled genomic data scientist workforce in the future in Ireland.

The way forward

The national office, through collaboration with relevant government and national bodies and institutions, will determine the 'as is' of current education and training opportunities in genetics and genomics in Ireland and identify training and education gaps. This will include engagement with:

- *The Department of Education (DOE)*
- *DFHERIS*
- *Higher Education Authority (HEA)*
- *Quality and Qualifications Ireland (QQI)*
- *SOLAS, the State further education and training agency*
- *Education and Training Boards Ireland (ETBI)*

In addition, there will be steps taken to ensure that all genetic and genomic professional roles are recognised by the appropriate bodies. The national office will also support the recognition of genetic counsellors and scientists by CORU, a regulator for a variety of health and social care professionals.

Work will be progressed with relevant bodies to establish training pathways, accredited training programmes, and educational support for specialised staff, as well as to integrate genetics and genomics into the general curricula for all healthcare professionals.

My point of view: my career pathway as a clinical scientist

I can pinpoint the start of my interest in genetics to a lecture at the National University of Ireland, Galway over 20 years ago whereby a professor outlined various genetic diseases and the link between certain traits and changes in a person's genetic make-up.

Following my studies, I worked at the University of Melbourne, Australia with world-renowned specialists in the fields of epilepsy genetics. While there, I learned about the clinical implications of genetic testing and the positive impact a genetic diagnosis can have for patients and their families, including clinical management, prognosis, and treatment.

One particular memory that has stayed with me is of a mother learning the genetic diagnosis of her young daughter who had severe epilepsy and developmental delay. Although the diagnosis was not easy to hear, the relief from the mother was apparent. I remember her stating that she had spent years worrying as to whether something she had done while pregnant caused her daughter's illness, and she was relieved to learn that it was instead due to 'bad luck'.

Since returning to Ireland, I helped develop the epilepsy gene panel in Ireland and I am currently the Chief Clinical Scientist at a new purpose-built laboratory for genetic testing. I lead the diagnostic team performing germline genetic testing for Irish patients.

Although my role is not patient-facing, the patient is always at the forefront of my work, and through multidisciplinary meetings, the impact of our work and genetic diagnoses is further realised. This impact continues to drive my interest and love of the profession and is always at the centre of any discussions I have with people not familiar with the field of genetics. As my career progresses, I would like to see genetic testing becoming an integral part of the clinical work-up for patients in Ireland.

Dr Sinéad Howard,
Chief Clinical Scientist

3.3.3 Improving genetic and genomic literacy of the healthcare workforce

We know that there is a wide spectrum of understanding, knowledge, and expertise across the healthcare workforce. Those with limited exposure to genomics in their daily practice require a level of knowledge that differs considerably from the knowledge required by sub-specialties in genetics and genomics.

Examples of competency frameworks from other countries that are worthy of further investigation include:

- Europe – Competency Framework through The European Board of Medical Genetics
- Australia – *InGeNA Precision Medicine Workforce Competency Framework*
- Spain – *Competency Framework in Personalized Precision Medicine for Healthcare Professionals*
- UK – *Facilitating Genomic Testing: A Competency Framework*

Increasing genetic and genomic literacy across the healthcare workforce will help release the untapped potential for innovation and expanded provision of the genetics and genomics service within the current healthcare system. This requires a stratified, flexible, and dynamic approach.

Equally, it is important for policy makers and healthcare managers to have an awareness of and level of understanding about genetics and genomics.

In parallel, there is a need to nurture future talent in genetics and genomics to secure the workforce of the future. Pursuing a career in genomics usually requires early exposure to and interest in science, technology, engineering, and mathematics (STEM) education. Therefore, our educational system needs to provide early exposure to age-appropriate educational genomic resources, including raising awareness of the opportunities to apply IT and data science skills to improve the care of patients. This will help to improve public genetic and genomic literacy but also ensure that children and young adults are given the opportunity to develop the skills and expertise required to become part of an exciting and evolving paradigm shift in the delivery of healthcare.

The way forward

Accessible information, resources, and educational and training packages will be developed for healthcare professionals, policy makers, and healthcare managers to increase genetic and genomic awareness and literacy.

The national office will support professional bodies and second and third-level education organisations to promote career development and career pathways in genetic and genomic medicine.

Collaboration with existing international education providers such as Health Education England, the National Institutes for Health, and the European Society for Human Genetics will help support the development of training and educational material.

3.4 Enhancing Genetic and Genomic Clinical Services

3.4.1 Performance delivery and measurement of safe, high-quality patient and family centred care

7. A suite of measures that ensure the delivery of safe, high-quality care will be developed, and processes will be implemented to monitor performance against agreed targets to drive quality improvement.

Clinical applications of genetics and genomics have accelerated at pace in the past decade and are now impacting clinical practice across the lifespan of patients. A strategic, holistic, and cooperative approach is needed to ensure the successful integration of a safe, high-quality genetics and genomics service into routine clinical practice in a patient and family centred manner.

Genetic and genomic testing involves not only a laboratory testing component, but also upstream and downstream services including information provision, genetic counselling, multidisciplinary interpretation of test results, and clinical decision making.

Good clinical practice in genetics and genomics, including access to necessary upstream and downstream services, should be consistent across the country and delivered in a manner which reflects the vision of Sláintecare. This will be facilitated through the national office, working with RHAs to ensure the effective delivery of a national service at a local level. Such an approach will help to ensure that services are delivered in an equitable, evidence-based manner and that all patients have access to the same high-quality care.

Fundamental to the delivery of safe patient and family centred care is defining and measuring the structures, processes, and outcomes required for a quality genetics and genomics service.

Measures should be developed to enable the public, service users, and healthcare providers alike to have reliable information of current and desired standards in genetic and genomic services and to effectively monitor the performance of services. The following diagram illustrates examples under the three dimensions of quality in which performance can be measured.

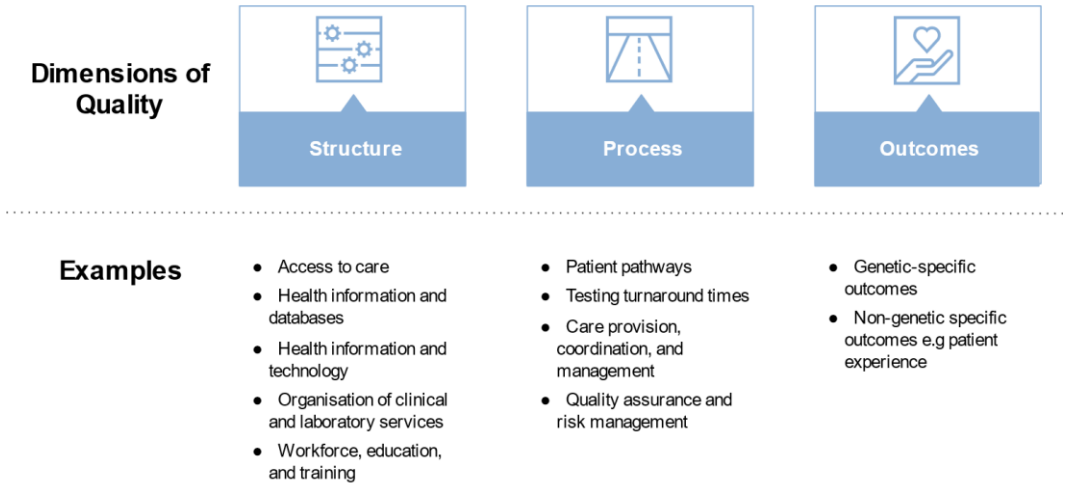


Figure 8: The three dimensions of quality in which performance can be measured

3.4.2 Integration of genetics and genomics into mainstream healthcare

8. Locally integrated multidisciplinary patient and family centred care pathways will support the continued transition of genetic and genomics into mainstream healthcare by building on existing services, collaborative networks, and expertise to enhance service delivery in a manner that is efficient, equitable, and in accordance with the Sláintecare vision.

Genetic and genomic health information increasingly informs routine clinical care and treatment and is relevant to a broad range of healthcare providers. The changing landscape of genetics and genomics requires patient and family centred clinical pathways to continually adapt and evolve. Comprehensive services and referral pathways are required to address the needs of all patients and ensure they receive the right care, at the right time, and as close to home as possible.

Mainstreaming genetics and genomics

'Mainstreaming' is making genetic and genomic services a part of normal, routine care delivery. This requires non-genetic specialty multidisciplinary teams to develop the expertise necessary to integrate genetics and genomics into their patient and family centred integrated clinical care pathways.

In Ireland, many specialties have already developed integrated local multidisciplinary care pathways for the delivery of genetic and genomic services within their specialty and have established collaborative networks.

The way forward

Over the next five years, to enable the mainstreaming of genetics and genomics, clinical specialties will be supported to develop expertise and expand their sub-specialisation in genetics and genomics within their speciality remit, with appropriate and timely access to testing and specialist genetics services as required. In addition, there needs to be scientific and bioinformatics expertise and resources to support clinical service delivery.

The designation and enhancement of an integrated genetic and genomic network will align to national clinical programmes and models of care, including the NCCP, NWIHP, the NRDO and other relevant subspecialty models of care.

As the service develops, there will be a continued need for specialised genetic services to:

- Establish the necessary tertiary referral pathways for complex cases outside of the remit of sub-specialities
- Support those providing genetic and genomic clinical services within their speciality
- Provide leadership and guidance on the development of integrated care pathways
- Drive innovation, research, knowledge transfer, and education into clinical practice.

The way forward

PPI will be central to clinical service development to ensure that services are patient and family centred.

Various genetic and genomic services and referral pathways for primary, secondary, and tertiary care will address the range of patient ages including reproductive decision making, neonatal, paediatric, and adolescent and young adult care.

Clinical governance structures and national standardised policies, procedures, protocols, and guidelines (PPPGs), in accordance with best available evidence, will support the development of these pathways.

Genetic counsellors

The genetic counselling workforce needed to deliver timely access to genomic care is currently under-resourced in Ireland compared to international standards. Genetic counsellors will be central to the mainstreaming of genetic and genomic services. They will play a fundamental role in supporting both specialist clinical genetic services and local integrated multidisciplinary teams delivering timely access to genetic and genomic services within the remit of their specialty.

The way forward

Strengthening local access to genetic counselling will be a priority in the development of patient pathways and referral pathways and is reflected in the commitment made for funding in 2023.

Care coordination

Coordination of care that requires the input of a range of different healthcare professionals is recognised as a challenge for patients and families affected by rare diseases, undiagnosed conditions, and other complex care needs. Improving the patient experience in accessing genetic and genomic services is recognised as a key contributor to the delivery of a high-quality service.

The way forward

A priority in 2023 will be the development of a patient navigator/coordinator role – a genomics resource associate – to help patients and families navigate clinical pathways and access post-diagnosis support.

Building links between clinical practice and research

Ireland will continue to expand infrastructure designed to build links between clinical practice and research. In the area of rare diseases, Ireland is now a member of 18 European Reference Networks which support clinical services delivery including diagnostics, research, and education according to the recommendations of the European Commission 2011 Cross Border Care Directive (Directive 2011/24/EU). Since 2007, Ireland has been involved in 29 EU cancer research projects funded through the EU Framework Programmes, coordinating ten of these projects and including a further 43 Irish partners. For further information on these developments, please see *Section 3.5.5 Driving Innovation and Research* of this document

The way forward

To enhance care delivery, research, and further development of care pathways, there will be increased support for enhanced links between clinical practice and research.

My point of view: modern approaches to cancer treatment

The traditional management of cancer was based on a reaction to symptoms. A patient presents with a problem, pain, bleeding, or a new swelling. Investigations lead to diagnosis, a diagnosis to treatment. We know, however, that by the time cancer is detectable by symptoms, it is often advanced and difficult to treat, sometimes incurable.

Modern approaches to cancer treatment, particularly the most common cancers, is to try to detect cancer early before it becomes symptomatic. The hope is that early detection will result in better survival. We do this by screening large sections of a given population based primarily on the most basic of discriminators: age and gender. But these discriminators are blunt instruments, particularly in the battle against cancer in younger adults. What if we had the tools to tell who was at high risk of developing cancer, especially at a young age?

Genetic testing provides those tools. The genetic variants responsible for many cancers in young people – breast, ovarian, endometrial and colorectal – are known and can be identified through a simple blood test or saliva sample. The hereditary patterns of these genetic variants are equally well known. By testing cancer patients and their close relatives, we can tell who is at high risk to develop cancer in the future. Who would not love to be able to predict the future? To prevent cancer before it occurs? Genetic testing gives us the power to identify high-risk cohorts, initiate high-intensity screening, and stop cancer in its tracks.

Over the last number of years, in the hospital I work, we have offered genetic testing via a mainstreaming pathway to all colorectal cancer patients and their close relatives. We now know the prevalence of the most common colorectal cancer syndrome (Lynch Syndrome) in the catchment and can offer high-intensity screening to affected relatives. If this is achievable in one catchment, it is achievable nationwide. It is my firm belief that national mainstreaming of genetic testing is an essential next step in our battle against cancer. If we can achieve this, we will revolutionise cancer care in Ireland.

Mr Rory Kennelly,
Colorectal Surgeon

My point of view: a physician working in cardiogenetics

My primary interest has always been the prevention of sudden cardiac death (SCD). In 2021, the National Ambulance Service attempted to resuscitate 2,906 cardiac arrest victims, of whom only 6.4% (178) survived. And 118 of the total number who had a true cardiac arrest were under 35.

Some 30–40% of these SCD victims will have an underlying genetic abnormality, and their first-degree relatives will have a 50% chance of carrying the same abnormality and be at increased risk of cardiac arrest. Some of us carry these abnormal gene variants that put us at risk of such an event without knowing it. Identification of young people at risk should begin in the families already visited by such a tragic event.

For many years, we have sent blood samples with delays of more than two years out of the country for genetic analysis. In April 2022, after three years of preliminary work, the lab where I work was fully accredited for performing cardiac gene panels focused on abnormalities found on examination of cardiac arrest victims, survivors, and patients with inherited cardiac conditions.

The lab is currently analysing more than 200 samples per year with turnaround times for such analyses of ten to 12 weeks, allowing us through multidisciplinary team meetings between cardiologists, geneticists, nurses, scientists and genetics counsellors to make a precise diagnosis in many of the affected individuals and identify other family members at risk in a timely fashion. We can then, when appropriate, offer them protection from cardiac arrest with lifestyle changes, medications, or (if they are at high risk) with an implantable cardiac defibrillator to prevent a second tragedy in an already traumatised family.

In addition, we are creating a national Inherited Cardiac Conditions Registry with the aim of one day reaching a 'diagnostic horizon' where we have identified all affected families in Ireland through a network of linked Inherited Cardiac Conditions Clinics throughout the country offering family heart screening and risk assessment to those among us who have lost a loved one to SCD and should not lose another.

Prof. Joseph Galvin,
Consultant Cardiologist

3.4.3 Promoting evidence-based, equitable, and timely access to genetic and genomic tests

9. Equitable, timely, and evidence-based availability of genetic and genomic tests and technologies in clinical practice will be improved through a coordinated and standardised national approach including the development of a National Test Directory.

Standardised approach to testing

To support clinical specialties and ensure the right patient gets the right test at the right time, many countries have developed national test directories for genetics and genomics. The use of a national test directory helps ensure:

- Equity of access for eligible patients to the full range of clinically appropriate genomic tests which meet the needs and prevalence of conditions in the population
- A standardised approach to testing is adopted, including defining which laboratories specific tests should be sent to
- Effective gatekeeping is embedded so that the correct test is ordered to answer the clinical query, duplication and delays in diagnoses or management are avoided, and waste is minimised
- Processes are in place to introduce new genomic testing in the future in line with the latest research and evidence

The way forward

A comprehensive national test directory will be developed to enable appropriate and equitable testing. There will be leadership and oversight on the use of existing, novel, and emerging genetic and genomic tests and technologies in routine clinical practice. Through collaborative processes with clinical, laboratory, and bioinformatics services, recommendations will be made to the HSE on whether genomic tests and technologies should be made available as part of best practice healthcare delivery.

Variant assessment

Clinical interpretation of deoxyribonucleic acid (DNA) sequence variants is a critical step in reporting clinical genetic testing results. The challenge is the identification of variants which are of clinical significance. Currently in Ireland, many medical specialties have established multidisciplinary variant assessment teams which use international recommendations and guidelines for variant calling.

The way forward

To further advance knowledge in genetics and genomics, there will be national oversight and further strengthening of clinical specialities and disease-specific networks to enable collaboration, advance knowledge, assist in the interpretation of variants, and support validation of panels.

Evaluation framework for testing

A reliable evaluation framework is required to support the continued progression of genetics and genomics into routine care delivery in a timely and equitable manner so that patients can benefit from technological advances. In addition, any tests or technologies being used in clinical practice need to be evaluated to ensure they are effective in the clinical setting and that they remain relevant, up to date, and in line with international best practice.

The way forward

A standardised evaluation framework to facilitate informed decision making on the analytical validity; clinical validity; and ethical, legal, and social implications of incorporating new tests and technologies into clinical practice will be developed. This will build on the established processes already in place to evaluate new tests and technologies, such as those used by the NCCP Molecular Diagnostics framework, and proceed in partnership and collaboration with existing agencies and evidence from international partners. The national office will work closely

with local laboratories and the National Centre of Excellence in Genomic Testing and Bioinformatics (as outlined in Section 3.5) to monitor test usage and effectiveness. As advances in genetics and genomics are proceeding at pace, these processes will support the rapid evaluation and uptake of innovations in testing and technology into clinical practice, in line with the best available emerging evidence.

.

My point of view: ovarian cancer and genetic testing

Ovarian cancer provides a powerful example of the value to integrating routine genetic testing into cancer care. When women are diagnosed with ovarian cancer, they are offered genetic testing. For some women a BRCA1/2 pathogenic variant (or mutation) is the reason that they unfortunately developed ovarian cancer. Finding out they have a BRCA pathogenic variant is difficult for a patient and her family. However, it gives us key information for a woman's own cancer care and opportunity to reduce future cancer risk.

We now know that women who have a BRCA-associated ovarian cancer have better prognosis. We can also use this information to predict the potential for response to therapy, both chemotherapy and new drugs, such as poly ADP ribose polymerase (PARP) inhibitors. PARP inhibitors have been revolutionary for women with BRCA associated ovarian cancer, doubling the number of women who are disease free five years after their diagnosis. We hope that some of these women will be cured of their ovarian cancer, and that is a huge breakthrough.

We also have the opportunity to intervene in their future cancer risk through intensive breast cancer surveillance. Critically, we have huge opportunity for their families. Genetic testing can identify family members who have increased cancer risk and initiate management strategies.

We can utilise genetic testing to achieve our goals in cancer control nationally. Genetic testing can help to reduce the burden of cancer in our population through prevention and early detection. We can also reduce the burden of cancer care through targeted therapy approaches.

We have made huge progress which has led to expansion in the role and demand for genetic testing in cancer care. It is fantastic to see the opportunity to put infrastructure in place to deliver equitable and timely access to genetic testing for our population in Ireland.

Dr Karen A Cadoo
Consultant Cancer Geneticist and Medical Oncologist

3.5 Strengthening Infrastructures to Drive Advances in Genetics and Genomics

3.5.1 Laboratory and bioinformatics services

Key to success in harnessing the power of genetic and genomic testing for improved patient outcomes lies in the supporting infrastructure to collect, test, store, process, and analyse samples and data for patient diagnoses, prognostic and predictive testing, and ongoing research applications.

Ensuring robust and resourced clinical services with equitable and timely access for patients and families is critical. The successful integration of genetics and genomics into mainstream healthcare delivery, while supporting innovation and research for the benefit of patients, is dependent on our ability to address challenges across several areas:

- Developing a future-proof, scalable national model for genetic and genomic testing, bioinformatics, and data management
- Ensuring we have a robust, safe, and secure infrastructure for data
- Enhancing the current laboratory network to ensure we have a fit-for-purpose laboratory and testing infrastructure, ensuring use of the most up-to-date technologies
- Building a sustainable biobank network for research use

The National Working Group to Inform the Strategic Direction of Laboratory Medicine

Due to changes in population health and rising levels of chronic diseases, it is imperative that an agile laboratory service exists to support emerging healthcare needs. In March 2022, a National Working Group to Inform the Strategic Direction of Laboratory Medicine was established. The overarching purpose of this laboratory medicine Working Group was to create a strategic, integrated approach to developing laboratory services, in turn enabling and enhancing healthcare reform. The end objective for the laboratory medicine Working Group is to develop and table a paper that will inform the development and direction of future strategy, in addition to a subsequent implementation plan.

The paper will firstly analyse and describe the current services being delivered in acute hospital laboratories across Ireland. This gap analysis will assist in identifying not only the key short-term challenges faced by laboratories, but also the requirements over the medium-to-long term. In addition, the Working Group will also review key advances in technological and scientific practices.

The laboratory medicine Working Group and those responsible for developing the present National Strategy have worked collaboratively to ensure alignment.

3.5.2 Enhancing the current laboratory network

10. The national office will work with services to enhance existing laboratory infrastructure and informatics services to promote the development and use of innovative technologies for testing, sample tracking, and reporting.

Genetic and genomic tests are usually performed on whole blood, saliva, or tissue samples for a variety of clinical indications. Robust sample-tracking and data-tracking systems that follow the patient profile, in accordance with GDPR, are needed to support testing and sample processing. It is essential that all analytical results from genetic and genomic testing are communicated to the referring clinician in an understandable and interpretable manner in a clinically meaningful timeframe.

Implementation of national guidelines for genetic and genomic test results reporting and IT systems for rigorous sample tracking are key to an efficient and effective service.

The way forward

An interoperable end-to-end genetic and genomic samples-tracking and associated data-tracking system will be required to enable the tracking of tests from sample collection through to the issuance of the final report to clinicians. The national office will work with services to develop a standardised electronic sample tracking and lab report for all genetic and genomic tests. This template should be incorporated into Laboratory Information Systems commonly in use.

Laboratories should be accredited and specifically designed and resourced to accommodate the expected number of tests/samples to be received, and they should be future proofed to accommodate further innovations in sequencing or analytical technologies and techniques. Accreditation standards may be developed by national professional bodies, clinical programmes, or collaborative working groups.

In Ireland, the infrastructure and skills required to perform genetic and genomic tests are available in a number of laboratories throughout the country, and a select number of laboratories are providing small panel sequencing (<50 genes). Accreditation is monitored by the Irish National Accreditation Board (INAB). However, existing capacity may not be fully utilised in some laboratories due to current testing referral pathways. In addition, given the significant volume of testing that is performed overseas, there are capacity limitations, the full extent of which is unknown.

The way forward

A comprehensive capacity and demand analysis will be required to establish the current baseline in terms of specific genetic and genomic capability, capacity, and technology used and to enable the modernisation and harmonisation of laboratory services across the country. In addition, a review of existing services should include consideration of the optimal configuration of adult haemato-oncology cytogenetics, paediatric cancer cytogenetics, and constitutional cytogenetics in line with international best practice.

Next-generation sequencing panels

Gene panels assess multiple potential genetic causes of suspected disorders in parallel, which reduces the cost and time of diagnostic testing. Next-generation sequencing (NGS) is a high-throughput method capable of sequencing many DNA strands at once. The expansion of NGS panels has been identified as a key priority for the delivery of cancer and rare disease services, and there is now a requirement to expand these to more comprehensive (>400 genes) gene panels.

The national office will support the development and validation of NGS gene panels for the more prevalent rare diseases presentations in Ireland in collaboration with

the NRDO and other relevant clinical programmes such as the NCCP. In addition, local laboratories should have the opportunity for further enhancement of adult somatic genomic testing services, for example, NGS panels, cell-free DNA (cfDNA), and single-gene testing according to local and national clinical service guidelines.

Given the fast-evolving nature of genetic and genomic testing technologies, laboratory services should remain agile and responsive to technological advances which may necessitate changes to current agreed testing techniques and processes.

The provision of high-quality patient testing requires fit-for-purpose external quality assessments that continuously develop with the pace of change. This requires alignment with international consensus and best practice to assure consistency in the quality of genetic and genomic testing available.

The way forward

The national office will develop guidelines to outline that all tests should be performed to the highest quality performance standards, using approved technologies in appropriately accredited laboratories, processed by a suitably trained and skilled workforce, and with results delivered in a clinically meaningful timeframe.

The national office will also support further engagement in international quality assurance (QA) schemes for genomic and genetic services.

Service level agreements (SLAs) related to turnaround time and other quality metrics will need to be established with contracted parties.

3.5.3 A future-proof, scalable national model for genetic and genomic testing, bioinformatics, and data management

11. A National Centre of Excellence in Genomic Testing and Bioinformatics will be established as a single entity which will sit under the governance of the HSE.

There is a need to ensure we have a future-proofed, scalable national model for genetic and genomic testing, bioinformatics, and data management. The recommended model builds upon our existing infrastructure, workforce, and expertise to deliver an equitable, accessible, effective, and cost-efficient national genetic and genomic testing, bioinformatics, and data management service.

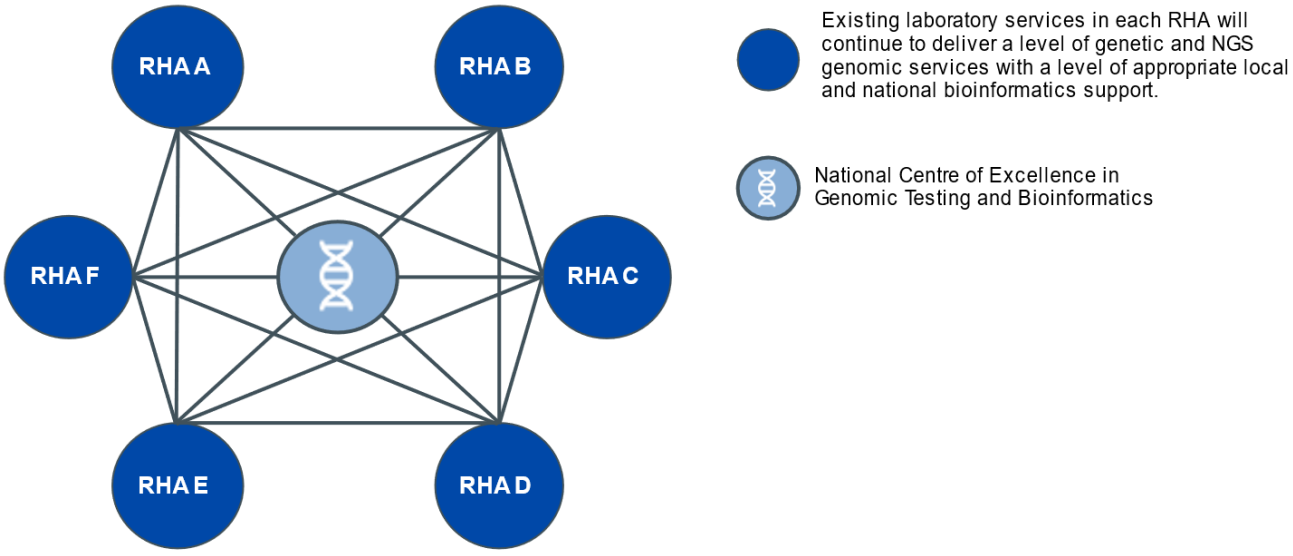


Figure 9: High-level overview of the proposed Laboratory and Bioinformatics Partnership Network

The way forward

The National Centre of Excellence in Genomic Testing and Bioinformatics *will be established as a single entity which will report to the national office, which itself will be under the governance of the HSE. This National Centre will be responsible for the safe and secure collation, analysis, curation, storage, and enabling of access to the data of the national genetics and genomics database. The centre will harness the potential of new technological innovations to improve patient outcomes.*

Existing laboratory services in each RHA will continue to deliver a level of genetic and NGS genomic services with a level of appropriate local and national bioinformatics support. Together, they will form a **Laboratory and Bioinformatics Partnership Network.**

Laboratory and Bioinformatic Partnership Network: *The National Centre of Excellence in Genomic Testing and Bioinformatics will work in collaboration with existing services (along with the national office) to develop national standardised operating procedures to support local and national service delivery. Services will be developed and delivered in compliance with all relevant legislation, including but not limited to IVDR and GDPR.*

3.5.4 Genetic and genomic data management

12. The national office will review existing genetic and genomic data capacity and capability and work toward the establishment of a secure, scalable, and accessible data and analytical infrastructure to support clinical service delivery, bioinformatics, data access, and research.

To harness the power of genetics, a robust and modern approach to the generation, processing, and analysis of and access to patient data is essential. Access to appropriate patient data is necessary for diagnosing diseases and conditions and also for the development, validation, and interpretation of clinical tests. The storage and access of the large amounts of data from genomic tests requires a robust and modern solution to data storage. This requires laboratories to use interoperable standards and the integration of other essential data sources such as clinical data from health records.

Generation and collection of genomic and associated clinical and research data

Genetic and phenotypic data are generated and accessed from a variety of sources including:

- Biobanks
- Disease registries
- Patient data systems
- Lifestyle and environmental data

The way forward

The digital footprint of genetic and genomic data can be very large and inter-connected. We will work towards an integrated system to ensure interoperability with existing and new data sources and adherence to informed consent processes. In addition, as data is pooled from different data sources, there is a need for a unique universal patient identifier.

Data storage and security, data processing and analysis

As genetic and genomic tests have evolved from solely the interrogation of single genes, the complexity of data analysis and interpretation has increased in tandem.

Genomic information requires three specialist infrastructure components:

- High-performance computing hardware for data processing
- High-capacity networks for data access
- Large volumes of data storage capacity

For a country the size of Ireland, this might require the secure primary and backup storage of petabytes (thousands of gigabytes) of data from patients and research participants, with compute capacity for the subsequent analysis. The implementation of such an infrastructure will be complex and will require national collaboration from multiple stakeholders.

It is anticipated that, as innovations in technology related to the analysis and use of genomic data increase at a rapid pace, so too will the requirements for a suitable data infrastructure, such as a national genetic and genomic database. The term ‘database’ is used here in a generic sense and includes different types of data storage and management systems, such as data repositories, data warehouses, data lakes, etc. Currently, Ireland has some well-established centres of research; however, there is a lack of storage and standardisation at the national level which is required to ensure a consistent approach to data storage and access.

The way forward

To enable active collaboration with national and international clinical, academic, and commercial partners for patient diagnoses and research, a scalable, secure, and sustainable facility to access and host large amounts of data (genomic and metadata) will be considered as part of the EU Genomic Data Infrastructure Project.

Data utilisation and downstream analysis and access of data

Data access across laboratories and hospitals is also essential to support accurate and reliable diagnoses. Through enabling access to previously collected reference data, variants of uncertain significance (VUS) can be explored and resolved more rapidly, which may reduce the time to obtaining an accurate diagnosis and treatment plan for patients. However, enabling access to personal data requires robust governance and processes to protect patient privacy and other rights.

Data access between clinicians, researchers, and others has also long been a key characteristic in the genetic and genomic research field to promote disease prevention and treatment and support innovations in technology.

The way forward:

Initially, the national office will review the existing data generation, storage, processing, and analytical capacity and capabilities available locally to develop an approach to standardisation at a national level.

Following this, and building on the work of the Genomic Data Infrastructure Project (see section 3.5.5), a key priority will be the establishment of a national genetic and genomic database (including data storage, processing, and analysis platforms) that is robust and agile to adapt to future innovations and technological advances in genetics and genomics.

My point of view: cancer genomic data can save lives

Cancer is the most common genetic disease. Changes in DNA that are harmful disrupt important genes and normal cell function. For example, disruption of genes that are involved in DNA repair or cell growth can increase the risk of cancer. Some harmful DNA variations are inherited; for example, 55%–72% of women who inherit a harmful variant in the DNA repair BRCA1 gene will develop breast cancer by the time they are 70–80 years of age.

However, most DNA variations that cause cancer are not inherited. Instead, DNA is damaged during normal wear and tear as we age. Our environment can also expose us to DNA damage. For example, DNA in skin cells can get damaged when we get sunburnt, lung cells can get damaged by smoking or pollution, or viruses like HPV can disrupt DNA and increase the risk of cervical cancer. When DNA is damaged, our cells misread the DNA instruction manual. In many cases, the immune system can clear these damaged cells, but sometimes they fail, and cancer develops.

I am a cancer computational biologist. Genetics provides vast quantities of data, and cancer computational biologists use bioinformatics, a mix of statistics, data science and machine learning, to study cancer at the molecular level. We analyse genetic data to identify variations in DNA that are inherited (germline) or environmental (somatic) that increase or reduce the risk of cancer. We examine the immune and normal cells around cancer to study how cancer progresses and spreads. We analyse tens of thousands of molecular data points from many hundreds of patients to learn genetics and genomics patterns that predict response to treatment, so we can identify patients who may benefit from less, more, or different therapy.

We are making astounding progress; cancer research is completely different to ten or 20 years ago. With the internet, communication leaped from letter and fax to iPhone and email. The changes in cancer research are equally dramatic. Ten years ago, our genomic maps of cancer tissue were akin to a drawing with a fuzzy blob for each city, whereas we now have street-view detail. We can measure the genetic and genomic profile of each individual cell in a piece of tissue. This incredible technology was unimaginable even five years ago.

With that data, we are powered to create computer models of cell-to-cell dynamics in cancer and can use advanced machine learning methods to understand and predict the role of each cell. We can design treatments that precisely treat cancer and minimise side effects. Data is empowering next generation medicine, and those of us working in data science and computational biology are leading in the challenge. I am so incredibly excited by the discoveries we can make to help cancer patients in the next ten years. Data will help save lives.

Prof. Aedín Culhane,
Professor of Cancer Genomics

Disease registries and minimum datasets

Disease registries are organised systems that use observational study methods to collect clinical and other types of data to evaluate and record outcomes related to a particular disease or condition. Accessible and complete disease registries can support enhanced clinical practices as well as provide an invaluable tool to the research community in developing novel therapies and technologies that ultimately improve patient outcomes.

In Ireland, at present:

- We have a National Cancer Registry
- We have a renal transplant registry
- We are in the early stages of building up a national chronic disease registry.
- There are specialties that, through their established networks and efforts, have locally developed registries for specific diseases.
- We participate in European Reference Networks [h] that also contribute to the establishment of registries for rare diseases on an international level

The way forward

The national office will work with other relevant national programmes and bodies to support work to define the requirements for a national dataset, including disease registries.

Electronic health records

International approaches to mobilising or scaling a fit-for-purpose national genetics and genomics service typically utilise a robust approach to electronic health records (EHRs). A national EHR has been identified as a key transformative capability requirement for the future delivery of healthcare and is the cornerstone of the *eHealth Strategy for Ireland* and Sláintecare.

The way forward

The national office, in collaboration with the office of the HSE Chief Information Officer (CIO), will review the current capacity in terms of existing databases and IT infrastructure and identify opportunities for the integration of genetic and genomic data with existing systems in the short term and with the national EHR in the medium-to-long term.

Expertise in digital health and information technology architecture will be built into the national office to enable collaboration with eHealth Ireland in creating and implementing a genetic and genomic IT plan. This plan will facilitate the procurement of a new genetics and genomics information system, integrated into other national solutions such as the Individual Health Identifier (IHI) and the EHR, to ensure that digital and data solutions within the health system support the appropriate integration of genomics into healthcare and empower patients to access their own health and genomic information.

Useful links:
www.ncri.ie/
www.hiqa.ie/areas-we-work/health-information/data-collections/national-renal-transplant-registry
www.hse.ie/eng/services/list/1/schemes/cross-border-directive/ern

3.5.5 Driving Research and Innovation

13. Engagement, collaboration, and partnership with international organisations, industry, government, and academic partners will be key to enhancing Ireland's research ecosystems. Procedures, processes, and guidelines will be developed to support the translation of advances in genetics and genomics into current and future clinical practice.

Integration of genetic and genomic data is a rapidly evolving field; therefore, to remain cutting edge, it needs to be connected with the research domain. There are numerous exemplary models in Ireland where partnerships and collaboration between clinical practice and research are already enhancing services and have contributed extensively to the global published literature. There are a number of key strategic documents in relation to progressing research and innovation in Ireland, these include but are not limited to:

- *Impact 2030: Ireland's Research and Innovation Strategy,* which prioritises building on Ireland's reputation as a location for research excellence and impact and highlights the need to strengthen our support for all-island, EU, and global research collaboration.
- *Creating Our Future: Expert Committee Report, April 2022,* which provided an opportunity for the public to submit their ideas about how research can create a better future for all, highlighting the importance of PPI in research and development. This strategy will support and help progress this ambition.
- *Health Research Board Strategy 2021–2025: Health Research – Making an Impact,* which has a specific action to take a leading role to convene stakeholders to progress the design, development, and implementation of national shared, high-cost research infrastructures, including in the areas of biobanking and genomic research.

Collaboration

An impactful research ecosystem facilitates research that positively impacts the public and provides value for money by enabling collaboration and partnership across:

- International entities: Engagement in international collaboration lowers the risk of duplication of efforts, accelerates the pace of discovery and translation, and provides opportunities to leverage learnings from the experiences of other countries. Areas that benefit from international collaborations in genetic and genomic medicine include evidence generation, advances in technologies, workforce development, pharmacogenomics, variant interpretation, and policy and regulatory issues including economic evaluation.
  Some examples of Ireland's involvement in international collaborations include:

  The European 1+MG Initiative: Aims to enable secure access to genomics and the corresponding clinical data across Europe for better research, personalised healthcare, and health policy-making. This initiative is a commitment of 23 European countries to give cross-border access to a million sequenced genomes by 2022. Ireland joined the 1+MG as a member during the development of this National Strategy.

  The Genomic Data Infrastructure (GDI): Project developing the data infrastructure to deliver the vision of the 1+MG Initiative to enable secure access to human genetic data across national borders, in order to improve research and clinical practice. Ireland is a participant in GDI.

  The European Reference Networks (ERNs): Virtual networks involving healthcare providers across Europe that aim to facilitate discussion on complex or rare diseases and conditions that

require highly specialised treatment, thus concentrating knowledge and resources. Ireland has joined 18 ERNs on various rare diseases.

The 2023 European Commission EU4Health ERN Integration Joint Action: Adopted as a response to the COVID-19 pandemic and to reinforce crisis preparedness in the EU, this joint action supports the enhancement of ERNs by contributing to the effective integration of ERNs in national health systems.

Horizon Europe European Partnership on Rare Diseases and European Partnership for Personalised Medicine: Research partnerships to foster collaboration between leading national bodies supporting research and development in these areas. The overall goal of this programme is to bring the EC and private and public partners together to address some key challenges through research and innovation initiatives.

Horizon Europe Mission on Cancer: Will fund a portfolio of activities aimed at addressing the burden of cancer on society and accelerating research and innovation in the cancer domain.

- Industry and academia: The development of trusted partnerships between industry, academia, and national genetic and genomic programmes across the globe has demonstrated the value of co-creation and knowledge transfer by ensuring all stakeholders are working towards a common goal in a coordinated manner.

- Clinical research: The implementation of genomic medicine is complex and no one sector is capable of advancing it in isolation. There has been substantial investment in this area by DOH and HRB. Continued investment in genetics and genomics and the establishment of strategic partnerships for clinical research will increase the opportunities for patients in Ireland to be offered access to the latest diagnostics, therapies, and interventions, as many of these new therapies will be designed for specific genetic causes of disease, both in an investigator-initiated and industry-led context.

The way forward

The national office will support and facilitate partnerships with the public and patients and the wider clinical, academic, and industry research communities to inform improved service delivery. Research and development priorities will focus on known service needs, clinical challenges, and relevant patient risk groups. This will support the establishment of targeted, accessible, evidence-based patient pathways in alignment with Sláintecare. Industry and academic partnerships will be established to enable access to clinical trials, increase the number of investigator-initiated clinical trials, and enable access to consented datasets for research use.

My point of view: retinal genomics in Ireland

In 2012, the All Island Inherited Retinal Degeneration Project (Target 5000) was commenced. The purpose was to identify all patients with inherited retinal degeneration (IRD) in Ireland, phenotype and genotype those affected, and create a major natural history study for patients with IRD. Initially conceived as a research project between an academic centre and patient organisations, the clinical potential was realised early on.

There are now nearly 2,000 patients of an estimated total of 3,000 under the T5000 umbrella. Research grade testing has been completed on nearly 1500 of those patients. We have now been able to accelerate the clinical genomics programme from this and introduce more rapid testing (in absence of core funding) and develop the clinical genetics team to support and guide the ophthalmic management of these patients.

Our adult patients have now seen a reduction in wait time for a clinical diagnosis and, crucially, the wait time for a genetic diagnosis has reduced from about six years to less than six months with a globally leading resolution rate of more than 73%. The HSE is now supporting the initiative with a further genetic counsellor and geneticist appointment. The paediatric arm of the project has seen the wait time reduce from three years to less than 3 months (resolution rate: more than 80%).

By coordinating the expertise we had, along with targeted philanthropic funding, a new care standard was set and now is being modelled in other countries. We are now full members of the ERN for Rare Eye Disease (ERN-EYE), facilitating access to expertise across Europe.

Crucially, we embedded the necessary clinical and psychological supports for our patients and created a bespoke Patient Care Plan (soon to be adopted by the ERN-EYE and Irish Rare Diseases Office). We are now set to offer gene therapy (approved and in clinical trial) for Irish retinal patients for the first time in Ireland via the Ophthalmic Precision Medicine Centre and to repatriate genomic testing.

As part of this National Strategy, we hope to extend our care pathways to IRD patients with multisystem disease (e.g. Stickler's and Usher's Syndrome). We wish to learn from other examples of best practice and share our own learnings with other subspecialist groups.

Prof. David Keegan,
Clinical Professor of Ophthalmology and Retina

Research in genetics and genomics

The impact of genetics and genomics in improving human health has been fuelled by discoveries in clinical research, which has enabled the development of novel therapies and changes to medical practice.

Central to decisions related to genetic and genomic data access in clinical settings are two key objectives:

- Advancing research by maximising data accessibility and use, and
- Minimising risks to the privacy of participants.

In order to meet both of these criteria, controlled access is often adopted. This is when conditions or criteria are placed on the access, use, and reuse of data and each of these conditions are placed equally on all requesters.

The way forward

Genetic and genomic research and innovation will be strengthened through the establishment of a framework for engaging clinical practice with research to ensure the successful translation of research into improved patient outcomes.

Building a sustainable biobank network

Biobank networking and harmonisation is key to ensure meaningful collaborative research and overcome heterogeneity.

In Ireland, the scale of biobanking activity has increased in recent years. There are now a number of biobanks established which are linked to academic institutions, research authorities, charities, private industries, and public and private hospitals. In addition, the National Biobank Working Group was established and has made progress towards improved understanding of the reshaping of the biobank landscape in Ireland.

Much can also be learned from the mobilisation of the National Irish COVID-19 Biobank (NICB). The NICB has worked to ensure that COVID-19 samples and associated clinical data are collected in a coordinated and harmonised manner, and that researchers can access this material using a mechanism that complies with safety, quality, and other international best practices and standards.

The way forward

To drive innovation and research, the creation of a network of existing and future biobanks will be explored. Individual biobanks in the network will remain under existing local governance structures with relevant data access and SLAs in place.

Requirements for a 'FAIR' integrated IT healthcare ecosystem

Advances in genetics and genomics need to take place within the broader requirement to build a FAIR – Findable, Accessible, Interoperable and Reusable – integrated healthcare IT ecosystem that supports clinical service delivery, research, and innovation. The FAIR data principles were developed and endorsed by researchers, publishers, funding agencies, and industry partners in 2016 and are designed to enhance the value of all digital resources.

Interoperability requirements

Like all data intensive healthcare services, interoperability of systems in genetics and genomics allows access to data and tools across and the health service. Information that is coded using consistent, common representations in line with international standards will help ensure interoperability.

The way forward

Clinical information will be coded using consistent, common representations in line with international standards to ensure interoperability.

Funding in genetics and genomics research

A number of state and semi-state agencies exist with the responsibility for funding scientific and clinical research and engaging with industry partners to encourage investment in research and fuel innovation in the area of genetics and genomics in Ireland. These include the HRB, SFI, the Irish Research Council (IRC) and other state bodies such as Enterprise Ireland and the IDA. It is essential that research and innovation in genetics and genomics is encouraged with a focus on known service needs, clinical challenges, and relevant patient risk groups.

The way forward

The national office will work with stakeholders to identify and enable current and potential international collaborations which can be leveraged to support the objectives of this National Strategy.

My point of view: a genetic diagnosis can help identify novel and precise treatments for epilepsy

Seizures are brief electrical storms in the brain that present in different ways, including altered awareness and involuntary muscle movement. Epilepsy is characterised by recurrent, unprovoked seizures. In 1994, researchers first showed that changes in our DNA can cause epilepsy. Since then, researchers have discovered hundreds of genes that can cause many different types of rare epilepsies. This has translated to the clinic, where researchers now help doctors identify the genetic cause of a particular individuals' epilepsy, should one exist.

Our work at the SFI FutureNeuro Centre, with specific hospitals, identified a group of people with a genetic form of epilepsy caused by changes in two related genes: DEPDC5 and NPRL3. Most had very frequent seizures, despite treatment with many different medicines. Uncontrolled seizures can cause severe injuries and, very rarely, death.

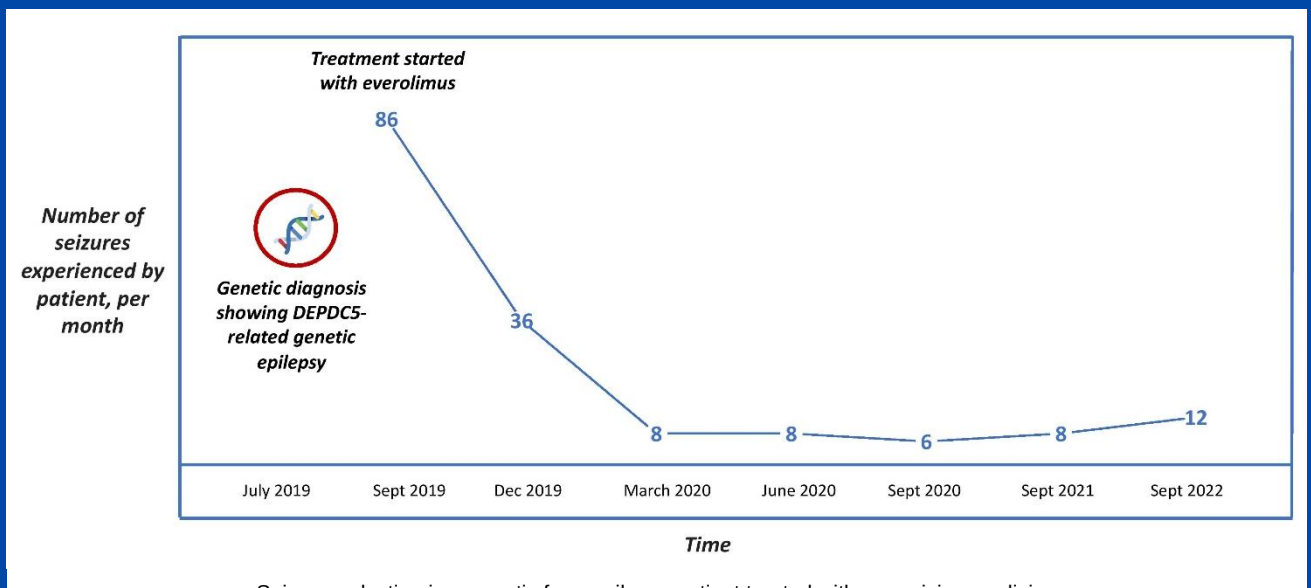
Precision medicine strives to tailor treatment to the unique characteristics of patients, including their DNA. We identified a treatment (everolimus) that targets the precise molecular pathway involved in DEPDC5-related and NPRL3-related epilepsy. Transplant and cancer doctors have many years of experience using this drug. We treated these patients with everolimus, and remarkable benefits have been observed. One man, with seizures since childhood, had been experiencing approximately 100 seizures per month. Now, after treatment with everolimus, he reports around ten seizures per month (see figure below) with significant improvements in his quality of life.

This research highlights the profound impact genomic diagnostics and precision therapeutics can have on patient outcomes. There are many other examples, including genetic forms of epilepsy that can be treated through changes in diet. Unfortunately, today in Ireland most people with identifiable genetic disease remain undiagnosed.

A national, research-engaged programme for genetics and genomics in Ireland can help these people receive the treatment they need, now and in the future.

Prof. Norman Delahunty,
Professor of Neurology

.



Seizure reduction in a genetic form epilepsy patient treated with a precision medicine

Innovation and economic growth

The new paradigm of healthcare brings opportunities for economic growth and international collaboration. Ireland has a diverse range of clinical disease characteristics and therefore has the potential to seize the opportunity to take a leadership position in making use of the economic benefit of genomics. Key to this will be the development, attraction, and retention of scientific talent.

The Irish economy requires ongoing expansion of scientific and technological research and development to continue to grow our capacity for innovation. Particularly important is leveraging science and innovation to give rise to new, fast-growing, advanced industries that spark economic growth and improved standards of living. Substantial Irish economic activity, supporting a volume of high-paying jobs across the nation, can be generated from the performance of genetic and genomic research, the development and manufacturing of commercial genomic technologies, the broad range of diagnostics products and therapeutics on the market that are derived from genomic knowledge, and the associated healthcare services that are delivered.

When considering the total economic impact of genetics and genomics, it is also important to note that the increased use of genetics and genomics in healthcare has the potential to reduce disease and disease burden, streamline diagnoses, eliminate ineffective treatments, and help to return patients to good health and wellbeing faster. These clear gains for patients and their families also have the indirect benefit of increasing the healthy adult workforce. In addition, there is an indirect impact on the workforce in the reduction of parental and carer leave due to improvements in the ‘diagnostic odyssey’ patients and families currently experience.

Section 4
Conclusion

4.1 Moving Ireland's Shared Vision for Genetics and Genomics Forward

This National Strategy for Accelerating Genetic and Genomic Medicine in Ireland outlines a way forward for the genetics and genomics service in Ireland.

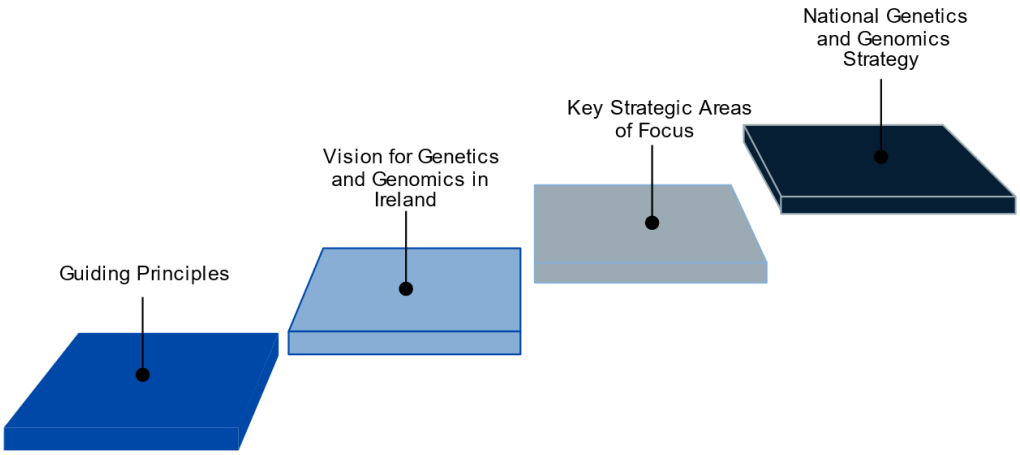


Figure 10: The foundations for progressing towards a shared vision

The way forward requires a comprehensive approach that has been summarised across the following five themes and will guide our development of genetic and genomic services in Ireland:

- Coordinating a National Approach to Genetics and Genomics
- Ensuring Patient and Public Involvement (PPI) and Partnerships
- Building the Genetics and Genomics Workforce for the Future
- Enhancing Genetic and Genomic Clinical Services
- Strengthening Infrastructures to Drive Advances in Genetics and Genomics

The first step in progressing this national strategy will be the development of a detailed implementation plan and timeline for delivery while taking into account planned service developments in the health service. The implementation plan will set out the actions, deliverables, and responsibilities to progress this strategy's implementation. It will define short, medium, and long term goals that can be initiated and implemented within the strategy lifecycle while working towards the achievement of the longer term vision.

The initial funding of €2.7 million will be directed towards the establishment of the new national office with the associated recruitment of roles, as well as towards addressing gaps in the frontline workforce in relation to clinical geneticists, genetic counsellors, and genetic resource associates.

As we accelerate the establishment of a nationally led genetics and genomics service for Ireland over the next five years and beyond, this strategy will be used to guide our path ahead. Patients and families have been placed at the heart of this strategy, and centring them will remain a key part of implementation.

Appendix 1: Glossary of abbreviations

Abbreviation	Definition
1+MG	1+ Million Genomes Initiative
B1MG	Beyond One Million Genomes Project
cfDNA	Cell-free DNA
CHI	Children's Health Ireland
CIO	Chief Information Officer
CPT2	Carnitine Palmitoyltransferase 2
DETE	Department of Enterprise, Trade and Employment
DFHERIS	Department of Further and Higher Education, Research, Innovation and Science
DHA	Digital Health Authority
DNA	Deoxyribonucleic Acid
DOH	Department of Health
EHDS	European Health Data Space
EHR	Electronic Health Record
ERN	European Reference Network
EU	European Union
FAIR	Findable, Accessible, Interoperable and Reusable
GA4GH	Global Alliance for Genomics and Health
GDI	Genomic Data Infrastructure
GDPR	General Data Protection Regulation
GP	General Practitioner
HRB	Health Research Board
HRCDC	Health Research Consent Declaration Committee
HRRs	Health Research Regulations
HSE	Health Service Executive
ICD-10	International Classification of Diseases, 10th Revision
IDA	Industrial Development Agency
InGeNA	Industry Genomics Network Alliance
IHI	Individual Health Identifier
INAB	Irish National Accreditation Board

IPPOSI	Irish Platform for Patient Organisations, Science & Industry
IRC	Irish Research Council
IRD	Genomics Data Infrastructure
ISHG	Irish Society of Human Genetics
IVDR	In Vitro Diagnostic Regulation
NCCP	National Cancer Control Programme
NCRI	National Cancer Registry Ireland
NGS	Next-Generation Sequencing
NHS	National Health Service
NICB	National Irish COVID 19 Biobank
NICU	Neonatal Intensive Care Unit
NRDO	National Rare Disease Office
NREC	National Research Ethics Committee
NWIHP	National Women's and Infants Health Programme
PKU	Phenylketonuria
PPI	Patient and Public Involvement
PPPGs	Policies, Procedures, Protocols and Guidelines
PPSN	Personal Public Service Number
QA	Quality Assurance
QQI	Quality and Qualification Ireland
RCSI PPI	Royal College of Surgeons Ireland Patient and Public Involvement Network
RHAs	Regional Health Areas
SCD	Sudden Cardiac Death
SFI	Science Foundation Ireland
SLAs	Service Level Agreements
STEM	Science, technology, engineering, and mathematics
VUS	Variant of Uncertain Significance
WGS	Whole Genome Sequencing
WHO	World Health Organization

Appendix 2: Glossary of key terms

Key term	Definition
Analytical Validity	Analytical validity refers to how well the test predicts the presence or absence of a particular gene or genetic change.
Biobank	A physical or virtual entity for the collection, handling, storage, preservation, retrieval, and distribution of biological samples and their associated data for current and/or future research purposes.
Bioinformatics	The use of algorithms and software to analyse biological data. A bioinformatician is a person who develops data algorithms and specialised software to analyse biological data, such as DNA or RNA sequences.
Bone Marrow Transplant	A procedure in which a patient receives healthy stem cells (blood-forming cells) to replace their own stem cells that have been destroyed by treatment with radiation or high doses of chemotherapy. The healthy stem cells may come from the bone marrow of the patient or from a related or unrelated donor.
Carnitine Palmitoyl transferase 2 (CPT2)	The CPT2 gene provides instructions for making an enzyme called carnitine palmitoyl transferase 2. This enzyme is essential for fatty acid oxidation, a multistep process that breaks down (metabolises) fats and converts them into energy.
cell-free DNA (cfDNA)	A laboratory method that involves analysing free DNA contained within a biological sample, most often to look for genomic variants associated with a hereditary or genetic disorder. For example, prenatal cell-free DNA testing is a non-invasive method used during pregnancy that examines the foetal DNA that is naturally present in the maternal bloodstream. Cell-free DNA testing is also used for the detection and characterization of some cancers and to monitor cancer therapy.
Chemoprevention	The use of certain drugs or other substances to help lower a person's risk of developing cancer or keep it from coming back. For example, tamoxifen and raloxifene are drugs that may be used to prevent certain types of breast cancer in women who are at high risk of developing the disease.
Clinical Validity	Clinical validity refers to how well the genetic variant being analysed is related to the presence, absence, or risk of a specific disease.
CORU	A multi profession health regulator. CORU was set up under the Health and Social Care Professionals Act 2005 (as amended). It is made up of the Health and Social Care Professionals Council and the Registration Boards, one for each profession named in this Act.
Cross-Discipline Genetic Service	A multi-disciplinary approach to promote engagement, inform decision making and support clinicians and patients is increasingly advocated to realise the potential of genome-scale sequencing in the clinic for patient benefit.
Data Controllers	The data controller determines the purposes for which and the means by which personal data is processed. For example, Employees processing personal data within your organisation do so to fulfil your tasks as data controller.
Data Processors	The data processor processes personal data only on behalf of the controller. The data processor is usually a third party external to the company.
Database	A collection of data that is stored in a computer and can easily be used and added to. A

	genetic database is one or more sets of genetic data (genes, gene products, variants, phenotypes) stored together with software to enable users to retrieve genetic data, add genetic data and extract information from the data. Genetic databases are repositories of organised data that are a resource for understanding how organisms' function.
Deoxyribonucleic acid (DNA)	The chemical that contains, or 'encodes', genetic information. DNA is made up of four different chemical bases.
Diagnostic Odyssey	A term used in genetics and genomics to describe the often-long period of time it can take for a patient to receive a diagnosis for their condition.
eHealth Ireland	eHealth Ireland was established by the HSE and focuses on the digitisation of health services and processes so that the data for the right patient is available in the right place and at the right time to ensure safe and efficient provision of care services. eHealth offers a significant opportunity and is fundamental to providing new and integrated models of care.
Gene	A segment of DNA that that contains the biological instructions for the production of a polypeptide chain, usually a specific protein or component of a protein.
Gene Panel Test	A laboratory test in which many genes are studied in a sample of tissue. For example, multiple-gene panel tests help find mutations (changes) in certain genes that may increase a person's risk of a disease such as cancer.
Genetics	The study of genes, genetic variation, and heredity in living organisms.
Genome	The complete set of genetic information in an organism.
Genomic Medicine	Genomic medicine (or healthcare) is the use of genomic information and technologies to determine disease risk and predisposition, diagnosis and prognosis, and the selection and prioritisation of therapeutic options.
Genomics	The application of genome-based knowledge through the study of genes and other genetic information, their functions, and interrelationships for the benefit of human health.
Germline Testing	Evaluates for inherited mutations (otherwise known as pathogenic or likely pathogenic variants) that are found in virtually all cells of the body and are derived from the fundamental DNA of an individual.
Harmonisation	The act of making systems or laws the same or similar in different companies, countries, etc., so that they can work together more easily. For example from a laboratory context, harmonisation is a fundamental aspect of quality and its main goal is to provide a better patient outcome producing comparable laboratory information regardless of the origins of the data.
Herceptin	A drug used alone or with other drugs to treat certain types of breast cancer, stomach cancer, and gastroesophageal junction cancer.
HSE Quality Improvement Framework	This Framework has been developed by the HSE to influence and guide people's thinking, planning and delivery of care in the healthcare services. It is firmly orientated towards quality, safety and to improve patient experience and outcomes. The Framework provides a strategic approach to improving quality whether at the front-line, management, board or national level.

Inherited condition	A condition caused by a genetic variant that has been passed down from parent to child.
Lumpectomy	Surgery to remove cancer or other abnormal tissue from the breast and some normal tissue around it, but not the breast itself. Some lymph nodes under the arm may be removed for biopsy.
Mainstreaming	A process where genetic/ genomic testing is offered to a patient with a goal of providing streamlined pathways and tailored treatment for the individual.
Mastectomy	Surgery to remove part or all of the breast. There are different types of mastectomy that differ in the amount of tissue and lymph nodes removed.
Metadata	A set of data that describes and gives information about other data.
Molecular Diagnostics	The process of taking DNA or RNA, the unique genetic code found in our cells, and analysing the sequences for red flags that can pinpoint the potential emergence of a specific disease.
National Test Directory for Genetics and Genomics	A directory that specifies which genomic tests are commissioned, the technology by which they are available and the patients who will be eligible to access each test.
Neutropenia	Neutropenia is when the level of neutrophil white blood cells are low. When the neutrophil levels are low, you are more at risk of infection, because white blood cells help the body fight infection.
Next-Generation Sequencing	A high-throughput method used to determine a portion of the nucleotide sequence of an individual's genome. This technique utilises DNA sequencing technologies that are capable of processing multiple DNA sequences in parallel. Also called massively parallel sequencing and NGS.
Personalised medicine	Medicine targeted towards an individual or group of individuals, which uses knowledge of genetic, environmental and lifestyle factors to determine suitable methods of prevention, diagnosis, and treatment of disease.
Pharmacogenomics	The use of genetic and genomic information to tailor pharmaceutical treatment to an individual.
Phenotype	An organism's observable physical and biochemical characteristics directly influenced by the genotype (genetic factor) and/or environment. In humans, this is often the observed signs and symptoms of a condition.
Phenylketonuria (PKU)	A rare but potentially serious inherited disorder. PKU causes the amino acid phenylalanine to build up in the blood and brain. This can lead to brain damage. About 1 in 4,500 babies born in Ireland has PKU. With early diagnosis and treatment most go on to live healthy lives.
PPI Ignite Network	The PPI Ignite Network promotes excellence and inspires innovation in public and patient involvement (PPI) in health and social care research in Ireland.
Precision medicine	The application of emergent technologies to better manage patients' health and to target therapies to achieve the best outcomes in the

	management of a patient's disease or predisposition to disease.
Quality and Qualification Ireland (QQI)	QQI is the state agency responsible for the external quality assurance of further and higher education and training in Ireland.
Rare Disease	There are now considered to be at least 6,000 rare diseases (diseases affecting less than 5/10,000 individuals) affecting approximately 6% of the population.
Ribonucleic acid (RNA)	Chemically like DNA but a single-stranded molecule. RNA is made up of four chemical bases.
Salpingo-Oophorectomy	Surgical removal of the fallopian tubes and ovaries.
Screening	The process of identifying healthy people who may have an increased chance of a disease or condition.
Sequencing	A technique used in laboratories to determine the order of bases in DNA.
Single-gene testing	Single gene tests look for changes in only one gene. Single gene testing is done when your doctor believes you or your child have symptoms of a specific condition or syndrome. Some examples of this are Duchene muscular dystrophy or sickle cell disease. Single gene testing is also used when there is a known genetic mutation in a family.
SOLAS	SOLAS is a state agency which was established in 2013 under the Further Education and Training Act as an agency of the Department of Further and Higher Education, Research, Innovation and Science. SOLAS is guided by the Further Education and Training (FET) Strategy 2020-2024 and the SOLAS Corporate Plan.
Somatic Genomic Testing	Looks for changes in the genes of cancer cells. The results are used to plan treatment, including the use of targeted therapy and immunotherapy.
Variant	A variant is an alteration in the most common DNA/RNA nucleotide sequence. Variants are defined based on the type of DNA/RNA error. The term variant can be used to describe an alteration that may be benign, pathogenic, or of unknown significance. Variants may be germline or somatic.
Variant Calling	Variant calling is the process by which variants are identified from sequence data.
Variant of Uncertain Significance (VUS)	Variant of Uncertain Significance (VUS) is a genetic change that the laboratory cannot interpret. VUS cannot be categorised as potentially disease causing or harmless because the meaning of this type of genetic change is not yet known.
Whole Genome Sequencing (WGS)	A type of genetic sequencing that has the potential to sequence every DNA base in a genome.

Appendix 3. The Development of a National Genetics and Genomics Database in Ireland

A national genetic and genomic database is required to store genomic information safely and securely, analogous to the storage of medical data in an individual's clinical record. The term 'database' is used here in a generic sense and includes different types of data storage and management systems, such as data repositories, data warehouses, data lakes, etc.

Such a system is especially important for genomics, as many people with a genetic condition will not immediately achieve a positive diagnosis, despite an appropriate test being conducted. As the research community steadily improves our understanding of the human genetic and genomic causes of disease, the rate of positive genetic diagnosis will steadily improve. Thus, a national genetic and genomic database will enable a reanalysis and reinterpretation of a 'negative' result in several months or years, which eventually can lead to a positive diagnosis.

By enabling the analysis of this data by the research community, under safe and controlled systems that retain the privacy and rights of the data subject, it is possible to identify novel genetic causes, modifiers of disease, which in turn will increase the value of genetics and genomics in clinical practice, thus having a positive impact on patients and citizens.

For these reasons, a safe and secure national genetic and genomic database has the potential to bring great benefit to the population of Ireland and beyond. Inclusion in the database would be voluntary in accordance with national and EU legislation and policy as outlined in section 3.1.2.

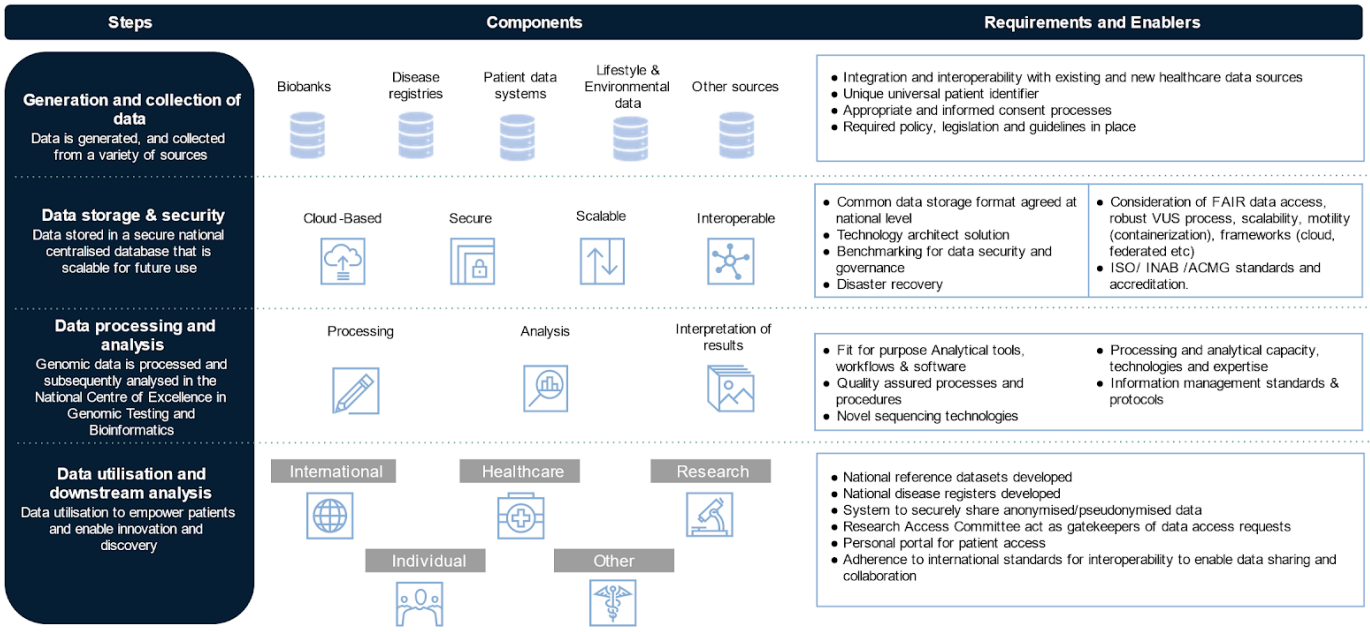


Figure 11. Illustrates how genomic data could be generated, stored, processed, and utilised in a national database.

Appendix 4: National Genetics and Genomics Strategy Steering Group Membership

Membership of the National Genetics and Genomics Strategy Steering Group	
Chair	Dr Mark Bale
Chief Clinical Officer (CCO)	Dr Colm Henry
Director of Strategic Programmes, Office of the CCO	Deirdre McNamara
National Director National Cancer Control Programme	Professor Risteárd Ó Laoide
Acute Operations	Professor Mary Day
Academic Lead, NCHG	Professor Owen Smith
Assistant Director National Cancer Control Programme	Dr Caitriona McCarthy
Royal College of Physicians in Ireland	Professor Andrew Greene
National Clinical Programme, Pathology	Dr Deirdre O'Brien
Clinical Lead, National Rare Diseases Office	Professor Eileen Treacy
Representative from Deans of Medical Schools	Professor Michael Gill
Chief Medical Officer CHI	Dr Allan Goldman
Chief Academic Officer's Network	Professor Timothy Lynch
Department of Health Representative	Muiris O'Connor
Department of Health Representative	Leah Dowdall
Department of Health Representative	Christopher Ryan
National Women and Infants Health Programme	Dr Cliona Murphy
Patient Representative	Karen Morgan
Patient Representative (Aug 2022 – Publication)	Margaret Cuddigan
Patient Representative (May-Sep 2022)	Nikolett Warner
Expert Advisor – Data and Infrastructure	Professor Mark Lawler
Expert Advisor – Workforce and Collaboration	Professor Brendan Loftus
International Expert Advisor	Professor Serena Nik-Zainal
Expert Advisor – Data and Infrastructure	Professor Walter Kolch
Health Research Board	Dr Teresa Maguire
HSE Communications	Fidelma Browne
Clinical Geneticist Representative	Professor Sally–Ann Lynch
GP Representative	Dr Una Kennedy

Appendix 5: Bibliography

1. ACMG (2015). Clinical utility of genetic and genomic services: a position statement of the American College of Medical Genetics and Genomics. Retrieved from https://pubmed.ncbi.nlm.nih.gov/25764213/

2. American Society of Clinical Oncology (2020). What Is Somatic Genetic Testing and How Is It Used in Cancer Treatment?. Retrieved from https://www.cancer.net/blog/2022-03/what-somatic-genomic-testing-and-how-it-used-cancer-treatment#:~:text=Somatic%20genomic%20testing%20looks%20for,of%20targeted%20therapy%20and%20immunotherapy.

3. American Society of Human Genetics (2021). The Economic Impact and Functional Applications of Human Genetics and Genomics. Retrieved from https://www.ashg.org/wp-content/uploads/2021/05/ASHG-TEConomy-Impact-Report-Final.pdf

4. Association for Molecular Pathology (2021). Association for Molecular Pathology Position Statement: Variant Data Sharing. Retrieved from https://www.amp.org/AMP/assets/File/advocacy/AMP_Position_Variant_Data_Sharing_7_29_2021.pdf?pass=90

5. Benjamin, C., *et al.* (2018). Interventions to improve patient access to and utilisation of genetic and genomic counselling services. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6491097/

6. Bowdin, S., *et al.* (2016). Recommendations for the integration of genomics into clinical practice. Retrieved from https://europepmc.org/article/pmc/pmc5557020

7. Brazas, M., *et al.* (2014). A Quick Guide to Genomics and Bioinformatics Training for Clinical and Public Audiences. Retrieved from https://journals.plos.org/ploscompbiol/article?id=10.1371/journal.pcbi.1003510

8. Byrne *et al.* (2018). Insular Celtic population structure and genomic footprints of migration. Retrieved from https://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1007152

9. Cancer Network (2021). Germline Testing in Prostate Cancer: When and Who to Test. Retrieved from https://www.cancernetwork.com/view/journal-germline-testing-in-prostate-cancer-when-and-who-to-test

10. Centers for Disease Control and Prevention (2022). Genomics and Precision Health: Genetic Testing. Retrieved from https://www.cdc.gov/genomics/gtesting/genetic_testing.htm#:~:text=Single%20gene%20testing.,dystrophy%20or%20sickle%20cell%20disease

11. Chu *et al.* (2022). Potentials and challenges of launching the pilot phase of Hong Kong Genome Project. Retrieved from https://jtggjournal.com/article/view/4956

12. Cole, P. (2015). Patentability of Genes: A European Union Perspective. Retrieved from https://docs.google.com/forms/d/e/1FAIpQLSdze5mpoLm8DZzzBsH1k7-TvFCmf--PQIueHPh5l6gUJnR_kA/closedform

13. Collins (2022). Definition of Database. Retrieved from https://www.collinsdictionary.com/dictionary/english/database

14. D'Gama, A., *et al.* (2022). Integrating rapid exome sequencing into NICU clinical care after a pilot research study. Retrieved from https://www.nature.com/articles/s41525-022-00326-9

15. Department of Enterprise, Trade and Employment (2018). Research Priority Areas 2018 to 2023. Retrieved from https://enterprise.gov.ie/en/publications/research-priority-areas-2018-to-2023.html

16. Department of Further and Higher Education, Research, Innovation and Science (2022). Impact 2030: Ireland's Research and Innovation Strategy. Retrieved from https://www.gov.ie/en/publication/27c78-impact-2030-irelands-new-research-and-innovation-strategy/

17. Department of Health (2017). National Cancer Strategy 2017—2026. Retrieved from https://assets.gov.ie/9315/6f1592a09583421baa87de3a7e9cb619.pdf

18. Department of Health (2021). Sláintecare Implementation Strategy and Action Plan 2021 – 2023. Retrieved from https://www.gov.ie/en/publication/6996b-slaintecare-implementation-strategy-and-action-plan-2021-2023/

19. Department of Health and Social Care, UK. (2020). Genome UK: the future of healthcare. Retrieved from https://www.gov.uk/government/publications/genome-uk-the-future-of-healthcare/genome-uk-the-future-of-healthcare

20. Department of Health Australia (2017). Supplementary Information to the National Health Genomics Policy Framework 2018 – 2021. Retrieved from https://www.health.gov.au/sites/default/files/documents/2022/03/national-health-genomics-policy-framework-2018-2021-supplementary-information.pdf

21. Department of Health UK (2017). Annual Report of the Chief Medical Officer 2016: Generation Genome. Retrieved from https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/631043/CMO_annual_report_generation_genome.pdf

22. Department of the Taoiseach (2021). Programme for Government: Our Shared Future. Retrieved from https://www.gov.ie/en/publication/7e05d-programme-for-government-our-shared-future/

23. Dheensa *et al.* (2018). Towards a national genomics medicine service: the challenges facing clinical-research hybrid practices and the case of the 100 000 genomes project. Retrieved from https://jme.bmj.com/content/44/6/397.citation-tools

24. Dugger, SA, Platt, A, and Goldstein, D. (2018). Drug development in the era of precision medicine. Retrieved from https://pubmed.ncbi.nlm.nih.gov/29217837/

25. Edmund, G, Shanmugam, A, and Cavalleri, G. (2022). Revealing the recent demographic history of Europe via haplotype sharing in the UK Biobank. Retrieved from https://www.researchgate.net/publication/361271913

_Revealing_the_recent_demographic_history_of_Europe_via_haplotype_sharing_in_the_UK_Biobank

26. eHealth Ireland (2022). eHealth Ireland. Retrieved from https://www.ehealthireland.ie/

27. European Cancer Patient Coalition (2022). Personalised Medicine: why it matters for patients. Retrieved from https://ecpc.org/tool-box/personalised-medicine/

28. European Commission (2015). Recommendations on cross border genetic testing of rare diseases in the European Union. Retrieved from https://health.ec.europa.eu/publications/recommendation-cross-border-genetic-testing-rare-diseases-european-union_en

29. European Commission (2018). Overview of EU National Legislation on Genomics. Retrieved from https://op.europa.eu/en/publication-detail/-/publication/503c92f7-ff55-11e8-a96d-01aa75ed71a1

30. European Commission (2020). 1+ Million Genomes Roadmap 2020 to 2022. Retrieved from https://digital-strategy.ec.europa.eu/en/library/roadmap-1million-genomes-initiative-now-clearly-illustrated-new-brochure#:~:text=By%20the%20end%20of%202022,threats%2C%20can%20be%20 timely%20 delivered.

31. European Commission (2022). European '1+ Million Genomes' Initiative. Retrieved from https://digital-strategy.ec.europa.eu/en/policies/1-million-genomes

32. European Commission (2022). What is a data controller or a data processor? Retrieved from https://ec.europa.eu/info/law/law-topic/data-protection/reform/rules-business-and-organisations/obligations/controller-processor/what-data-controller-or-data-processor_en

33. European Medicines Agency (2020). Personalised medicine challenges: hype or hope?. Retrieved from https://www.ema.europa.eu/en/documents/presentation/presentation-personalised-medicine-challenges-hype-hope-marisa-papaluca-ema_en.pdf

34. European Molecular Biology Laboratory (2022). Variant identification and analysis. Retrieved from https://www.ebi.ac.uk/training/online/courses/human-genetic-variation-introduction/variant-identification-and-analysis/#:~:text=What%20is%20variant%20calling%3F,creating%20BAM%20or%20CRAM%20files.

35. European Cancer Patient Coalition (2022). Personalised Medicine: why it matters for patients. Retrieved from https://ecpc.org/tool-box/personalised-medicine/

36. Evans, B., *et al.* (2020). How Can Law and Policy Advance Quality in Genomic Analysis and Interpretation for Clinical Care? Retrieved from https://journals.sagepub.com/doi/10.1177/1073110520916995

37. Gaff, C., *et al.* (2017). Preparing for genomic medicine: a real world demonstration of health system change. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5677913/

38. Genetic Counsellor Registration Board (2020). The Genetic Counsellor Role in The United Kingdom. Retrieved from https://gcrb.org.uk/whats-new/2020/august-2020/the-role-of-the-genetic-counsellor/

39. Genomic Medicine Policy (2020). Catalogue of global genomic medicine initiatives. Retrieved from https://www.genomicspolicy.org/catalogue-introduction

40. Genomics England (2019). A major new dialogue has found the public are enthusiastic and optimistic about the potential for genomic medicine but have clear red lines on use of data. Retrieved from https://www.genomicsengland.co.uk/news/public-dialogue-report-published

41. Genomics England (2022). Genomics Research and why it's important. Retrieved from https://files.genomicsengland.co.uk/documents/Patient-Information-Research-V1.4.pdf

42. Gilbert *et al.* (2017). The Irish DNA Atlas: Revealing Fine-Scale Population Structure and History within Ireland. Retrieved from https://www.nature.com/articles/s41598-017-17124-4

43. Ginsburg, G. (2019). A Global Collaborative to Advance Genomic Medicine. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6407494/

44. Global Alliance for Genomics & Health (2021). Pediatric Consent to Genetic Research: Clauses. Retrieved from https://www.ga4gh.org/wp-content/uploads/Pediatric-Consent-to-Genetic-Research_-Clauses-1.pdf

45. Godard, B., *et al.* (2004). Provision of genetic services in Europe: current practices and issues. Retrieved from https://www.nature.com/articles/5201111

46. Green, E., Guyer, M., and National Human Genome Research Institute. (2011). Charting a course for genomic medicine from base pairs to bedside. Retrieved from https://pubmed.ncbi.nlm.nih.gov/21307933/

47. Gunne, E., *et al.* (2022). An estimate of the cumulative paediatric prevalence of rare diseases in Ireland and comment on the literature. Retrieved from https://pubmed.ncbi.nlm.nih.gov/35853949/

48. Hallowell, N., et al. (2019). Moving into the mainstream: healthcare professionals' views of implementing treatment focussed genetic testing in breast cancer care. Retrieved from https://link.springer.com/article/10.1007/s10689-019-00122-y

49. Health Management (2017). Harmonisation of Lab Medicine Across Europe. Retrieved from https://healthmanagement.org/c/healthmanagement/issuearticle/harmonisation-of-lab-medicine-across-europe

50. Hivert, V., *et al.* (2021) IRDiRC: 1000 new rare diseases treatments by 2027, identifying and bringing forward strategic actions. Retrieved from https://rdodjournal.com/article/view/4380

51. Hong Kong Academy of Medicine (2021). Best practice guidelines on genetic and genomic medicine. Retrieved from https://www.hkam.org.hk/sites/default/files/PDFs/HKAM%20GnG%20Guideline.pdf

52. Health Research Board (2021). Strategy 2021–2025: Health research – making an impact. Retrieved from https://www.hrb.ie/fileadmin/2._Plugin_related_files/Publications/2021_publications/2021_Corp/Strategy_2021_2025_Health_research_making_an_impact.pdf

53. HSE (2016). Framework for Improving Quality in our Health Service. Retrieved from https://www.hse.ie/eng/about/who/qid/framework-for-quality-improvement/framework-for-improving-quality-2016.pdf

54. HSE (2022). Heart Failure National Clinical Programme. Retrieved from https://www.hse.ie/eng/about/who/cspd/ncps/national-heart-programme/heart-failure/

55. HSE (2022). Model of Care for Transition from Paediatric to Adult Healthcare Providers in Rare Diseases. Retrieved from https://www.lenus.ie/handle/10147/626908

56. IQN Path, ECPC, and EFPIA. (2021). Unlocking the potential of precision medicine in Europe: Improving cancer care through broader access to quality biomarker testing policy recommendations. Retrieved from https://www.efpia.eu/media/589727/unlocking-the-potential-of-precision-medicine-in-europe.pdf

57. Irish Cancer Society (2021). The Unmet Need in Cancer Genetic Services: conducting an environmental scan of the cancer genetics services in an Irish context underpinned by a mixed method approach. Retrieved from https://www.cancer.ie/sites/default/files/2021-04/Conducting%20an%20environmental%20scan%20of%20the%20cancer%20genetics%20services%20Report%202021.pdf

58. Irish Health Research Forum (2020). Advancing genomics research in Ireland. Retrieved from https://hrci.ie/wp-content/uploads/2021/03/IHRF-2020-Advancing-Genomics-Research.pdf

59. Irish National Accreditation Board (2019). Policy for the accreditation of Whole Genome sequencing (WGS) and Next Generation sequencing (NGS) techniques. Retrieved from https://www.inab.ie/inab-documents/mandatory-policy/policy-for-the-accreditation-of-whole-genome-sequencing-wgs-and-next-generation-sequencing-ngs-techniques.pdf

60. Irish Platform for Patient Organisations, Science & Industry (2022). Citizens' Jury on Future Use of Genomics. Retrieved from https://www.ipposi.ie/2022/02/28/citizens-jury-on-genomics/

61. Julkowska, C., *et al.* (2017). The importance of international collaboration for rare diseases research: a European perspective. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5628265/#:~:text=The%20outcomes%20of%20these%20collaborations,and%20databases%3B%20accelerated%20creation%20of

62. Kerr, K., *et al.* (2022). A Formative Study of the Implementation of Whole Genome Sequencing in Northern Ireland. Retrieved from https://www.mdpi.com/2073-4425/13/7/1104/htm

63. Kirwan, M., *et al*. (2021). What GDPR and the Health Research Regulations (HRRs) mean for Ireland: "explicit consent"—a legal analysis. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7391042/

64. Knoppers, B. (2014). Framework for responsible sharing of genomic and health-related data. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4685158/

65. Kovanda, A, Nyasha Zimani, A, and Borut, P. (2021). How to design a national genomic project—a systematic review of active projects. Retrieved from https://humgenomics.biomedcentral.com/articles/10.1186/s40246-021-00315-6#MOESM2

66. Lawler, M., et al. (2017). Sharing Clinical and Genomic Data on Cancer - The Need for Global Solutions. Retrieved from https://pubmed.ncbi.nlm.nih.gov/28538124/

67. Liu, X., *et al*. (2019). Difficulties and Challenges in the development of precision medicine. Retrieved from https://pubmed.ncbi.nlm.nih.gov/30653655/

68. Lynch, SA., *et al.* (2018). Catalogue of inherited disorders found among the Irish Traveller population. Retrieved from https://pubmed.ncbi.nlm.nih.gov/29358271/

69. Manolio, T, Ward, R, and Ginsburg, G. (2016). Clinical implementation of genomic medicine: the importance of global collaboration. Retrieved from https://www.tandfonline.com/doi/full/10.1080/23808993.2016.1192460

70. Marwaha, S, Knowles, J, and Ashley, E. (2022). A guide for the diagnosis of rare and undiagnosed disease: beyond the exome. Retrieved from https://genomemedicine.biomedcentral.com/articles/10.1186/s13073-022-01026-w

71. Matthijs, G., *et al.* (2016). Guidelines for diagnostic next-generation sequencing. Retrieved from https://pubmed.ncbi.nlm.nih.gov/26508566/

72. Mayo Clinic (2015). Variant of Uncertain Significance. Retrieved from https://mcforms.mayo.edu/mc1100-mc1199/mc1185-82.pdf

73. Mazzucco, W., *et al.* (2017). Current state of genomic policies in healthcare among EU member states: results of a survey of chief medical officers. Retrieved from https://academic.oup.com/eurpub/article/27/5/931/2616592

74. McVeigh, T., *et al.* (2022). A pilot study investigating feasibility of mainstreaming germline BRCA1 and BRCA2 testing in high-risk patients with breast and/or ovarian cancer in three tertiary Cancer Centres in Ireland. Retrieved from https://pubmed.ncbi.nlm.nih.gov/36029389/

75. Mee, B., *et al*. (2021). What GDPR and the Health Research Regulations (HRRs) mean for Ireland: a research perspective. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8049920/

76. Middleton, A., *et al.* (2017). The role of genetic counsellors in genomic healthcare in the United Kingdom: a statement by the Association of Genetic Nurses and Counsellors. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5518913/

77. Milne, R., *et al.* (2019). Trust in genomic data sharing among members of the general public in the UK, USA, Canada and Australia. Retrieved from https://link.springer.com/article/10.1007/s00439-019-02062-0

78. National Cancer Institute (2022). Dictionary of Cancer Terms: Chemoprevention. Retrieved from https://www.cancer.gov/publications/dictionaries/cancer-terms/def/chemoprevention

79. National Clinical Programme for Rare Diseases (2022). Model of Care for Rare Diseases. Retrieved from https://www.lenus.ie/bitstream/handle/10147/626904/model-of-care-for-rare-diseases%20Jly%202020.pdf?sequence=5&isAllowed=y

80. National Human Genome Research Institute (2022). Policy Issues in Genomics: Genome Editing. Retrieved from https://www.genome.gov/about-genomics/policy-issues/what-is-Genome-Editing

81. National Human Genome Research Institute (2022). Cell-Free DNA Testing. Retrieved from https://www.genome.gov/genetics-glossary/Cell-Free-DNA-Testing

82. National Library of Medicine (2022). How can I be sure a genetic test is valid and useful? Retrieved from https://medlineplus.gov/genetics/understanding/testing/validtest/

83. New South Wales Ministry of Health (2017). New South Wales Health: Genomic Strategy. Retrieved from: https://www.health.nsw.gov.au/services/Publications/nsw-health-genomics-strategy.pdf

84. Nicolaus, P. (2019). National Genomic Data Initiatives: A Worldwide Update. Retrieved from https://www.bio-itworld.com/news/2019/08/12/national-genomic-data-initiatives-a-worldwide-update

85. Nunn, J., *et al.* (2019). Public Involvement in Global Genomics Research: A Scoping Review. Retrieved from https://www.frontiersin.org/articles/10.3389/fpubh.2019.00079/full#B20

86. Oncology Nursing Society (2022). Genomics Taxonomy. Retrieved from https://www.ons.org/genomics-taxonomy/variant#:~:text=Variant%20is%20an%20alteration%20in,may%20be%20germline%20or%20somatic.

87. O'Sullivan, L., *et al.* (2022). Harmonising the human biobanking consent process: an Irish experience [version 3; peer review: 2 approved]. Retrieved from https://hrbopenresearch.org/articles/4-96

88. Organisation for Economic Cooperation and Development (2022). Building and sustaining collaborative platforms in genomics and biobanks for health innovation. Retrieved from https://www.oecd-ilibrary.org/science-and-technology/building-and-sustaining-collaborative-platforms-in-genomics-and-biobanks-for-health-innovation_11d960b7-en;jsessionid=u07gAe6mLhYvIMoZf9Y4Jj2SVpwzsGsyflMPi9mM.ip-10-240-5-73

89. Orphanet (2022). What is Orphanet? Retrieved from https://www.orpha.net/consor/cgi-bin/index.php#:~:text=Orphanet%20aims%20to%20provide%20high,health%20and%20research%20information%20systems.

90. Out-of-Hospital Cardiac Arrest Register (2021). National Ambulance Service: OHCAR Report 2021. Retrieved from https://www.nationalambulanceservice.ie/documentrepository/ohcar-report/ohcar-annual-report-2021.pdf

91. Patrinos, D., *et al.* (2022). Sharing and Safeguarding Pediatric Data. Retrieved from https://www.frontiersin.org/articles/10.3389/fgene.2022.872586/full#B33

92. PerMed (2015). Shaping Europe's Vision for Personalised Medicine: Strategic Research and Innovation Agenda. Retrieved from https://www.systemsmedicine.net/wp-content/uploads/2015/07/PerMed_SRIA.pdf

93. PHG Foundation (2011). Genetics and mainstream medicine Service: development and integration. Retrieved from https://www.phgfoundation.org/media/98/download/Genetics%20and%20mainstream%20medicine%20-%20service%20development%20and%20integration.pdf?v=1&inline=1

94. PHG Foundation (2015). Data sharing to support UK clinical genetics and genomics services: workshop report. Retrieved from https://www.phgfoundation.org/media/79/download/Data%20sharing%20to%20support%20UK%20clinical%20genetics%20and%20genomics%20services.pdf?v=1&inline=1

95. PHG Foundation (2018). The GDPR and genomic data. Retrieved from https://www.phgfoundation.org/report/the-gdpr-and-genomic-data

96. PPI Ignite Network (2022). Promoting excellence and inspiring innovation. Retrieved from https://ppinetwork.ie/#:~:text=The%20PPI%20Ignite%20Network%20promotes,social%20care%20research%20in%20Ireland.

97. Public Policy Projects (2022). Bringing the Benefits of Genome Sequencing to the World. Retrieved from https://publicpolicyprojects.com/wp-content/uploads/sites/6/2022/02/PPP-Global-Genomics-Report-122.pdf

98. Quality and Qualifications Ireland (2021). About Us: Our Role. Retrieved from https://www.qqi.ie/about-us/our-role

99. Raspa, M., *et al.* (2021) Barriers and Facilitators to Genetic Service Delivery Models: Scoping Review. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7952239/

100. Raza, S., and Hall, A. (2017). Genomic medicine and data sharing. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5862236/

101. Rehm, H., *et al.* (2021). GA4GH: International policies and standards for data sharing across genomic research and healthcare. Retrieved from https://www.sciencedirect.com/science/article/pii/S2666979X21000367

102. Rigter, Tessel., *et al.* (2014). Developing a framework for implementation of genetic services: learning from examples of testing for monogenic forms of common diseases. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC41594

69/

103. Rindfleisch, T., and Brutlag, D. (1998). Directions for Clinical Research and Genomic Research into the Next Decade. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC61320/

104. Rowe, C., and Wright, C. (2020). Expanded universal carrier screening and its implementation within a publicly funded healthcare service. Retrieved from https://link.springer.com/article/10.1007/s12687-019-00443-6

105. Rumford, M., *et al.* (2020). Oncologist-led BRCA 'mainstreaming' in the ovarian cancer clinic: A study of 255 patients and its impact on their management. Retrieved from https://www.nature.com/articles/s41598-020-60149-5

106. Schully, S., and Khoury, M. (2014). What is translational genomics? An expanded research agenda for improving individual and population health. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4694629/#bb0030

107. Selby, P., et al. (2019). How can clinical research improve European health outcomes in cancer? Retrieved from https://www.sciencedirect.com/science/article/abs/pii/S2213538318300894

108. Seoighe, C. (2021). HRB Open Research: The future of genomics in Ireland. Retrieved from https://blog.hrbopenresearch.org/2021/06/22/the-future-of-genomics-in-ireland/

109. Śliwczynski, A., and Orlewska, E. (2016). Precision medicine for managing chronic diseases. Retrieved from https://pubmed.ncbi.nlm.nih.gov/27535198/

110. Smedley *et al.* (2021). 100,000 Genomes Pilot on Rare-Disease Diagnosis in Health Care — Preliminary Report. Retrieved from https://www.nejm.org/doi/full/10.1056/NEJMoa2035790

111. Smetana, J. and Brož, P. (2022). National Genome Initiatives in Europe and the United Kingdom in the Era of Whole-Genome Sequencing: A Comprehensive Review. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8953625/

112. Snape, K., Wedderburn, S., and Barnwell, J. (2019). The new genomic medicine service and implications for patients. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6752257/

113. SOLAS (2022). About: Who We Are. Retrieved from https://www.solas.ie/

114. Souche, E., *et al.* (2022). Recommendations for whole genome sequencing in diagnostics for rare diseases. Retrieved from https://eprints.whiterose.ac.uk/187457/

115. Springer Nature Limited (2022). Genetic Database. Retrieved from https://www.nature.com/subjects/genetic-databases#:~:text=Definition,extract%20information%20from%20the%20data.

116. Stark, Z., *et al.* (2019). Integrating Genomics into Healthcare: A Global Responsibility. Retrieved from https://www.sciencedirect.com/science/article/pii/S0002929718304221

117. Taylor, J., *et al.* (2019). Implementation of a genomic medicine multi-disciplinary team approach for rare disease in the clinical setting: a prospective exome sequencing case series. Retrieved from https://genomemedicine.biomedcentral.com/articles/10.1186/s13073-019-0651-9

118. The Joint Committee of the Nordic Medical Research Councils (2018). Personalised Medicine in the Nordic Countries. Retrieved from http://norden.diva-portal.org/smash/get/diva2:1347257/FULLTEXT01.pdf

119. Trotman, J., *et al.* (2022). The NHS England 100,000 Genomes Project: feasibility and utility of centralised genome sequencing for children with cancer. Retrieved from https://www.nature.com/articles/s41416-022-01788-5

120. Unim, B., *et al.* (2019). Current Genetic Service Delivery Models for the Provision of Genetic Testing in Europe: A Systematic Review of the Literature. Retrieved from https://www.frontiersin.org/articles/10.3389/fgene.2019.00552/full

121. Wagner, A., et al. (2020). A harmonized meta-knowledgebase of clinical interpretations of somatic genomic variants in cancer. Retrieved from https://www.nature.com/articles/s41588-020-0603-8

122. Wakap, S., *et al.* (2019). Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. Retrieved from https://www.nature.com/articles/s41431-019-0508-0

123. Ward, A., *et al.* (2022). Designing rare disease care pathways in the Republic of Ireland: a co-operative model. Retrieved from https://pubmed.ncbi.nlm.nih.gov/35410222/

124. Wert, G., *et al.* (2020). Opportunistic genomic screening. Recommendations of the European Society of Human Genetics. Retrieved from https://www.nature.com/articles/s41431-020-00758-w#Sec14

125. Wheatstone, P., et al. (2021). DATA-CAN: a co-created cancer data knowledge network to deliver better outcomes and higher societal value. Retrieved from https://blogs.bmj.com/bmj/2021/08/11/data-can-a-co-created-cancer-data-knowledge-network-to-deliver-better-outcomes-and-higher-societal-value/

126. Wilfond, B., and Diekema, D. (2012). Engaging children in genomics research: decoding the meaning of assent in research. Retrieved from https://www.nature.com/articles/gim20129

127. World Economic Forum (2020). Sharing Sensitive Health Data in a Federated Data Consortium Model An Eight-Step Guide. Retrieved from https://www3.weforum.org/docs/WEF_Sharing_Sensitive_Health_Data_2020.pdf

128. World Health Organization (2020). Regulating the unknown: A guide to regulating genomics for health policy makers. Retrieved from https://eurohealthobservatory.who.int/publications/i/regulating-the-unknown-a-guide-to-regulating-genomics-for-health-policy-makers

129. World Health Organizaton (2022). Accelerating access to genomics for global health. Retrieved from https://www.who.int/publications/i/item/9789240052857

130.

131. World Health Organization (2022). Accelerating the use of genomics for global health: A report of the WHO Science Council. Retrieved from https://cdn.who.int/media/docs/default-source/science-division/genomics-report-may-20.pdf?sfvrsn=343ddca4_3

132. Zimani, A., Peterlin, B., and Kovanda, A. (2021). Increasing Genomic Literacy Through National Genomic Projects. Retrieved from https://www.frontiersin.org/articles/10.3389/fgene.2021.693253/full#:~:text=Genomic%20literacy%20is%20defined%20as,this%2C%20a%20basic%20understanding%20of