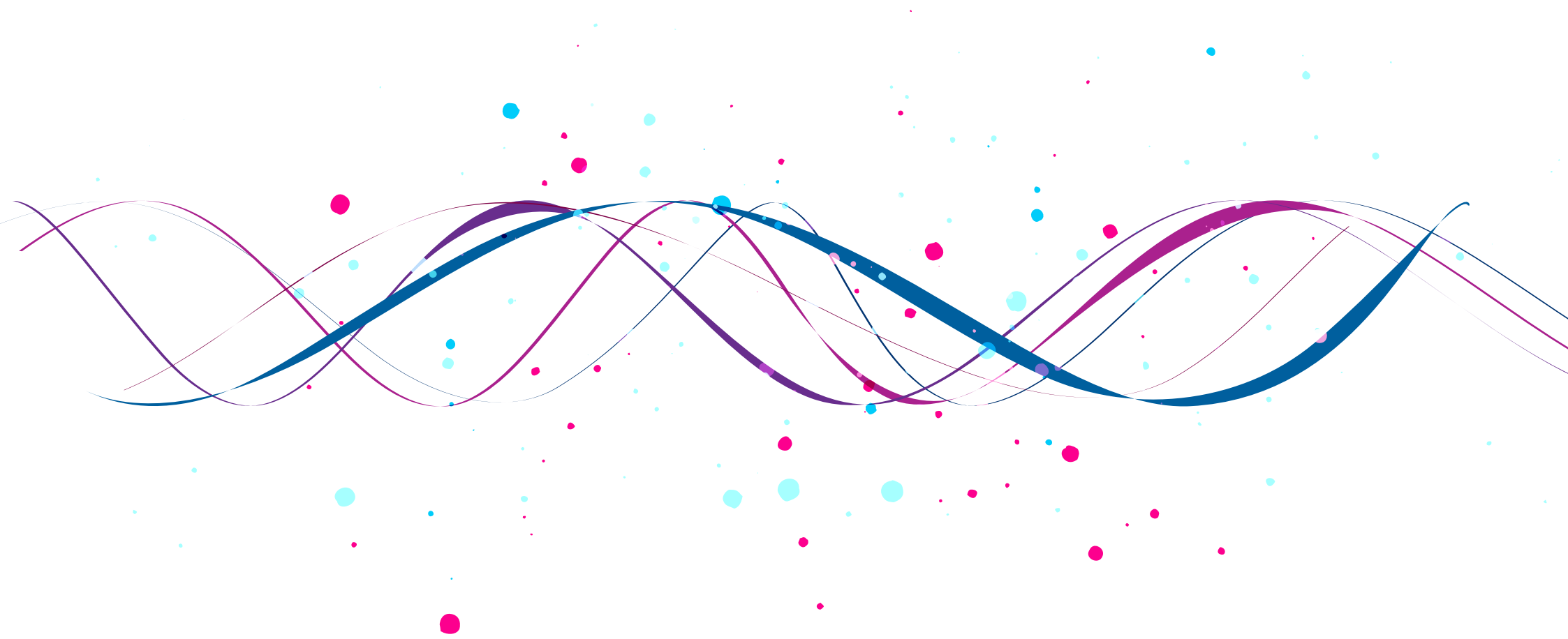
Government of **Western Australia**
Department of **Health**

WA Genomics Strategy 2022–2032

Towards precision medicine and precision public health



Acknowledgements

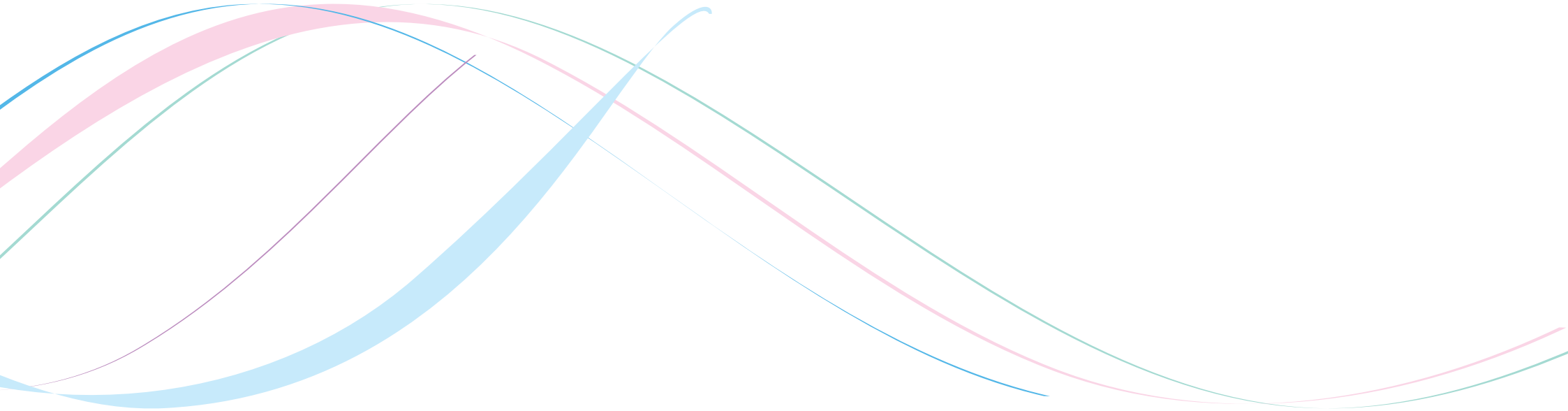
The *WA Genomics Strategy 2022–2032: Towards precision medicine and precision public health* arose from extensive consultation with numerous individuals and organisations.

WA Department of Health sincerely thanks all contributors for their time and feedback.

It also particularly acknowledges the significant contributions of the members of the WA Genomics Strategy Advisory Committee (listed below) for their valuable input and endorsement of the Strategy.

WA Genomics Strategy Advisory Committee

Dr. Benhur Amanuel	PathWest
Mr. Adrian Bautista	PathWest
Dr. Gareth Baynam	North Metropolitan Health Service
Prof. John Beilby	PathWest
Mr. Kane Blackman	Rare Voices Australia
Mr Senkham Boutdara	WA Department of Health
Dr. Karen Carpenter	PathWest
Dr. Aron Chakera	North Metropolitan Health Service
Dr. Fred Chen	East Metropolitan Health Service
Ms. Ronda Clarke	Aboriginal Health Council of WA
Prof. Jan Dickinson	North Metropolitan Health Service
Ms. Rebecca D'Souza	North Metropolitan Health Service
Dr. Carolyn Grove	PathWest and North Metropolitan Health Service
Mr. Francois Joubert	Health Support Services
Ms. Sue Kiely	Child and Adolescent Health Service
Dr. Deepan Krishnasivam	North Metropolitan Health Service
Prof. Nigel Laing	Harry Perkins Institute for Medical Research
Prof. Michael Millward	University of Western Australia
Dr. Philip Montgomery	WA Country Health Service
Dr. Kristen Nowak	WA Department of Health
Dr. Gemma Ossolinski	WA Primary Health Alliance
Dr. Michael O'Sullivan	Child and Adolescent Health Service
Ms. Peta O'Sullivan	WA Department of Health
Dr. Nicholas Pachter	North Metropolitan Health Service
Prof. Gerald Watts	East Metropolitan Health Service
Dr. Marianne Wood	Aboriginal Health Council of WA
Ms. Belinda Whitworth	South Metropolitan Health Service
Ms. Janet Zagari	North Metropolitan Health Service



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Minister's foreword

It is with great pleasure that I present the *WA Genomics Strategy 2022–2032: Towards precision medicine and precision public health* (the Strategy). This inaugural Strategy outlines key outcomes for the next decade to ensure the Western Australian community achieves optimal health outcomes through the timely and sustainable adoption of genomics into our healthcare system.

Following a rapid period of development, genomic technologies are enabling a much more detailed understanding of the link between our genes and our health and are transforming how we prevent, diagnose, treat and predict disease. Genomic technologies are now efficient, accurate and cost-effective enough to be integrated into standard care across a wide range of health specialities, including critical care.

As such, genomics is a core driving force behind precision medicine and precision public health. These 2 emerging fields promise to improve individual and population health by replacing a one-size-fits-all approach with targeted methods to improve the quality and affordability of health care by maximising benefit and reducing harm.

From the early months of 2020, 'genomics' became a term familiar to many Western Australians. This is because genomics has been integral to our state's response to the COVID-19 pandemic, assisting local testing and contact tracing efforts to detect the DNA code of the SARS-CoV-2 virus. Genomic sequencing has been able to determine precise variations in the viral code, critically informing the management of community outbreaks. Genomic technology has also been a vital tool guiding the development and evaluation of COVID-19 vaccines around the world.

Despite the recent increase in community awareness, genomics is certainly not new to WA. The WA health system has a strong track record of implementing innovative genomic health care, underpinned by research and robust evidence. Prominent examples include precisely diagnosing rare and complex conditions, guiding targeted treatments for certain cancers, and preventing adverse drug reactions, as explored in vignettes throughout the Strategy. Local yet internationally renowned clinicians, scientists and researchers have formed strong foundations for us to build upon.

Now, with the launch of this Strategy, we have a framework for safeguarding WA's unique strengths. In addition to leveraging past successes, we will ensure we have the right infrastructure and resources to appropriately expand our capacity and capability in genomics to deliver equitable and high value health care.

Safety and quality will also continue to be essential so that genomics-enabled healthcare delivery is responsible, accountable and transparent, with the recognition that genomics has unique ethical, legal and social considerations. Strong partnerships with consumers, health professionals and the community will be fostered to build trust and empower stakeholders through the co-design and co-production of genomic health services, research and innovation projects.

I acknowledge the many dedicated and motivated people who have contributed towards the development of this important Strategy, as well as expressing a commitment to work together towards the realisation of its shared vision. Agile and responsive health care enabled by genomics is key to preparing our world-class health system to address the current problems of today and the emerging issues of tomorrow.

I look forward to the positive impact the implementation of this Strategy will deliver for the WA community and the role it will have in enhancing our reputation as a world leader in precision medicine and precision public health.

Hon Amber-Jade Sanderson MLA
Minister for Health; Mental Health

Executive summary

Over the past couple of decades, major advances in genomics have significantly expanded the understanding of genetics and genomics in health and disease. This growing body of knowledge has accelerated progress towards more tailored and precise approaches in health care, underpinning the development of new tests, treatments and interventions.

The multitude of genomic applications available today is transforming the way we deliver healthcare services, with huge potential to optimise health outcomes for people and populations. A broad array of genomic tests can be used to decipher the DNA code of many genes at once, or even all human genes at the same time. The generated data can then be analysed and interpreted for a range of health-related applications, including diagnosing disease, informing prognosis, matching patients to suitable therapies and/or clinical trials, making informed predictions of the risk of developing or passing on a genetic disease, as well as for the management and surveillance of infectious disease outbreaks [1].

The swift pace of developments in genomics has led to the need for a systematic and strategic approach to its current and future applications in the WA health system. Additionally, the predictive capability, familial implications, longevity and uniqueness of genomic data present multiple ethical, legal and social issues [2] which need to be suitably considered and managed. For the state to access the enormous potential benefits for patients, the health system and the broader community, it was thus necessary to develop the first strategy for implementing genomics into the WA health system.

The *WA Genomics Strategy 2022–2032: Towards precision medicine and precision public health* outlines an ambitious vision to benefit all Western Australians through timely and appropriate translation of genomics. To achieve this vision, the Strategy identifies 5 strategic priority areas, each with an accompanying goal:

1. **Person and family-centredness** – to ensure consumers, carers, families, and communities are at the heart of how genomic healthcare is designed, delivered and evaluated.
2. **Genomic healthcare services** – to achieve the optimal integration of genomic knowledge in the WA health system to deliver high value care that is timely, equitable and safe.
3. **Workforce, education and training** – to develop a sustainable health workforce that has appropriate capacity, agility and the necessary education and training to deliver genomic healthcare services.
4. **Digital health and data** – to establish digital health and data solutions, protocols and standards needed to optimise the delivery of responsible genomic health care.
5. **Research and innovation** – to have a health system that values and supports the creation and translation of genomics research and innovation.

Each priority area is accompanied by a set of key outcomes that will serve to direct stakeholder efforts over the next 10 years. It is envisaged that implementation of the Strategy will be broken into 3 implementation phases, each with an implementation plan and actions mapped to the Strategy's key outcomes.

The Strategy is the embodiment of extensive stakeholder consultation and consensus. Its development has been guided by representatives from the WA health system, consumers, researchers and subject matter experts. It represents an exciting and momentous step for WA: an inaugural systemwide policy to bring the state's current strengths and assets to the forefront and maximise stakeholder efforts. The Strategy also reflects the WA health system's desire and intent to keep pace with evidence-based developments and growth in demand, so as to deliver high value health care amidst a climate of finite resources [3].

Strategy snapshot

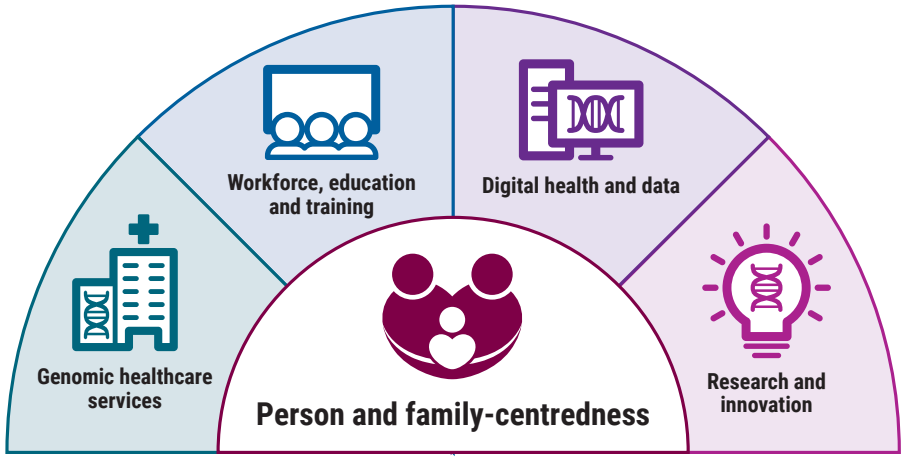
Vision

To ensure all Western Australians benefit from the timely and appropriate translation of genomics, enabling precision medicine and precision public health.

Aim

To coordinate and maximise stakeholder efforts to enable efficient, effective, ethical and equitable translation of genomics knowledge into the WA health system.

Priorities



Enablers of success

- Sustainable investment
- Meaningful partnerships and collaboration
- Senior leadership and support
- Accountability, roles and responsibilities

Underlying principles

- The application of genomic knowledge to health care is equitable and is informed by scientific evidence and the diverse needs of consumers, families and the community.
- Investment in genomic services and applications is strategically prioritised based on their value to consumers, services and the WA health system.
- Consumers, families and the community are empowered to make decisions about the application of genomic knowledge in their health care.
- Trust in the use of genomics in health care is promoted through adherence to quality and safety standards and compliance with privacy and confidentiality policies.

Introduction

Introduction

Genomics in relation to human health

Genes and genetic variation

Deoxyribonucleic acid (DNA) is a molecule that provides the information needed to build and maintain living organisms. Genes, the functional components of the DNA sequence that contain the operational instructions for all cells, are part of the genome.

Variation occurs across genomes. In humans, genomic variation contributes to characteristics such as hair and eye colour. Other variations, depending on their location in the genome, can influence a person's health. A change as small as a single DNA letter (nucleotide) in a human genome may cause a genetic disease by interrupting the body's normal development, while a change in a microbial genome may make a pathogen more infectious.

Understanding genes and inheritance in the context of medicine

The study of genomes encompasses the inheritance of genes, their structure and function, as well as how the genes contained in the genome interact with each other and with the environment. Knowledge gained from the study of human and microbial genomes can be used to enhance the provision of medicine and health care at an individual and population level.

In this document, the term 'genomics' is used to refer to the analysis of single genes (genetics), chromosomes, as well as groups of genes or all genes in a genome. Genomics is enabled by DNA testing technologies to detect variation in the DNA sequence. DNA testing is not new to health care; however, it has undergone rapid and significant transformation over the past couple of decades, enabling the testing of multiple genes simultaneously, or even sequencing of entire genomes (known as genomic sequencing).

Genomics in the healthcare sector

As knowledge and technology advances, the widespread utility of genomics in health care is becoming increasingly apparent. There has been a large reduction in the cost of genomic sequencing and increasing demand for genomics to be used in clinical and public health settings. The growing transformative potential for genomics, and the ability to apply the technology to health across the human lifespan (Appendix 2), holds vast promise for consumer, family and population benefits as well as economic savings.

Genomics can provide earlier and more accurate diagnostic, prognostic and risk prediction information, provision of personalised interventions including medicines, tailored treatment plans, better-informed family planning options and disease prevention, and avoidance of inappropriate or unnecessary treatments and procedures (and their side effects) [1]. Additionally, infectious disease management can harness microbial genomics to identify, track and manage disease outbreaks, and describe how pathogens evolve [4].

Some exemplars where genomics has benefitted Western Australians can be explored by interacting with Figures 1 and 2.

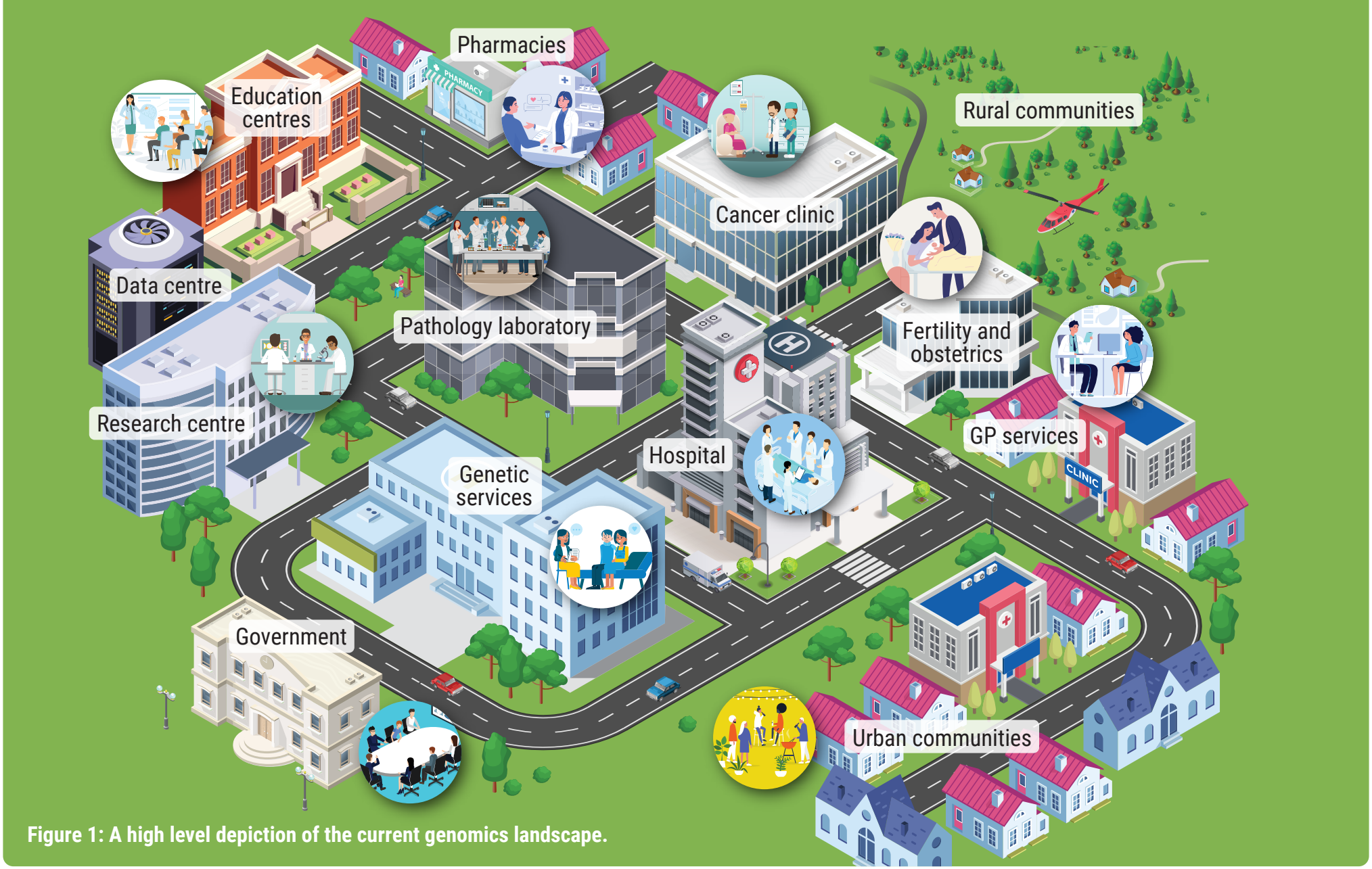


Figure 1: A high level depiction of the current genomics landscape.

Given the rapid pace of development, the genomics landscape is continually evolving. The different services, setting and stakeholders collaborate and work synergistically and multiple features may contribute to the delivery of a health genomic service. The features of the landscape are described on the next page. Vignettes demonstrating examples of the utility and importance of genomics in the WA healthcare can be reached by clicking on certain locations.

Features of the genomics landscape

Cancer clinic: Identifies causative gene mutations to inform cancer treatment.

Data centre: Stores genomic information for medical and research purposes.

Education centres: Increase genomic literacy and effective implementation of sustainable health genomics.

Fertility and obstetrics: Offer services such as pre-implantation and prenatal genetic testing, newborn bloodspot screening.

Genetic service: Interprets outcomes of medical tests and provides genetic counselling.

Government: Provides leadership, coordination and directions for implementing sustainable health genomics.

GP services: Have general practitioners who issue genetic testing requests when appropriate.

Hospital: Uses outcomes of genomic testing to information patient treatment and care.

Pathology laboratory: Performs genomic laboratory tests for medical and research purposes.

Pharmacies: Use pharmacogenomics to identify genetic variations that influence drug metabolism to inform drug options and dosages.

Research centre: Identifies new knowledge that can be translated into clinical use.

Figure 2: Hospital interior.

Genomics – a foundation for precision medicine and precision public health

Precision medicine and precision public health have great potential to fundamentally shift health care from a system aimed at improving outcomes for the 'average' consumer, towards having a more precise and personalised approach at both the individual and population level [5].

Internationally, many countries are formulating policy and investing in research and implementation programmes aimed to support the development of these fields. The WA Government has identified precision medicine and precision public health as an emerging opportunity, as highlighted in the endorsed *Sustainable Health Review Final Report* (see Appendix 3 for further information on the policy context for the Strategy).

Much of the initial momentum around precision medicine was catalysed by the evolution of DNA technologies. The concept of precision public health was then developed to reflect the contemporary, holistic concepts of health and wellbeing, and to mitigate the potential of an increasing focus on precision medicine exacerbating health disparities within populations [6].

Precision medicine and precision public health approaches tailor preventative, management and therapeutic approaches to individuals or populations using knowledge of the variation of multiple parameters. In addition to genomics, these parameters include health risk, health and wellbeing outcomes, physiology, responses to the environment, sociodemographic, cultural and/or lifestyle factors and surrounding context.

Although genomic technologies have to date made significant contributions towards precision medicine and precision public health, it is the combination of a range of technologies that will enable the realisation of the full potential of these approaches to health care [5]. Therefore, other technologies such as various '-omics' (e.g. transcriptomics, proteomics, metabolomics), big data, digital informatics and geospatial will continue to emerge as having important roles along with genomics in the future of precision medicine and precision public health.

Proven and emerging examples of genomics-enabled precision medicine and precision public health

In cancer, genomic testing or 'molecular profiling' is increasingly being used as a diagnostic, prognostic and biomarker tool, to guide optimal treatment and identify potential new drug targets [7]. As the number of druggable gene targets and predictive biomarkers is increasing, the demand for routine molecular profiling of cancers is growing.

In the rare diseases field, the ability is growing for genomics to provide more timely diagnosis through the identification of causative variants of a disease, helping to end what is often a long diagnostic journey as well as guide treatment options and family planning. Precision medicine is assisting the development of new medications and treatment options [8]. In certain circumstances, this information has been useful for the diagnosis and treatment of other conditions influenced or caused by the same underlying biological pathways, including some common diseases [9].

In public health, genomic sequencing is providing more detailed pathogen identification while reducing the reliance on other diagnostic methods that can be time-consuming and costly. This information is underpinning more efficient investigation and management of outbreaks, prediction of antimicrobial resistance and development of new therapeutics and vaccines [4]. The utility of genomics has been clearly demonstrated during the COVID-19 pandemic [10], and is anticipated to have a critical ongoing role in pandemic preparedness and outbreak management.

Over the next decade, the significant investment in genomics research around the world will generate new evidence and opportunities to incorporate genomics into health care. For example, expanding the role of genomics in preventative population-based screening programs seems highly likely with the advances already occurring. Genomic testing provides the possibility for newborn bloodspot screening programs to increase the number of appropriate conditions screened for, to reduce or avoid harm in early life or improve long-term outcomes due to early detection [11]. Reproductive genomic screening can support parents to make informed choices regarding family planning [12]. Adult population-based screening for selected high-evidence genetic conditions (e.g. hereditary cancers, familial hypercholesterolemia), would facilitate the identification of individuals at increased risk of developing these diseases, to support targeted risk-based monitoring and personalised preventative approaches [13].

The field of pharmacogenomics has considerable potential to enable more accurate prescribing of medications to individuals, reducing the trial and error approach to drug choice and dosing. Integrating pharmacogenomics into health systems has promise for enabling individuals to have medicines that are more appropriate and safer for them, whilst avoiding wastage of money and time on treatments that are ineffective and possibly even harmful [14].

There are and will be many other applications of genomics for precision medicine and precision public health. The challenge will be to ensure that the WA health system has the processes, expertise and infrastructure to continually evaluate genomic advances and ensure that they are implemented into the WA healthcare system in a timely manner prioritising ethics, equity of access and financial responsibility.

Why is a strategy needed?

All Western Australians should be able to access and benefit from genomics-enabled precision medicine and precision public health. However, the WA health system presently lacks a statewide, strategic approach to the delivery of genomic health care. Consequently, genomic services have developed in an ad hoc manner, resulting in variable and fragmented genomic health care across the health system. In the absence of a cohesive approach, genomic services will not be delivered as equitably, efficiently and effectively as possible.

These issues have been compounded by the rapid advancement of genomics, which continues to provide new tests, therapies, and interventions that enhance health care and improve health outcomes. Strategic oversight and new approaches are needed to enable timely integration of genomic technologies into the health system when there is robust evidence of health utility, safety and cost-effectiveness. This integration should ensure the greatest benefit to consumers while minimising potential harms, including over-diagnosis and over treatment, data misuse, discrimination and stigmatisation. Community engagement and support to ensure public trust and confidence will be of paramount importance [15].

A systemwide strategy is thus imperative to guide the efficient, effective, ethical and equitable translation of genomic knowledge into the WA health system.

About the *WA Genomics Strategy 2022–2032: Towards precision medicine and precision public health*

The *WA Genomics Strategy 2022–2032: Towards precision medicine and precision public health* (the Strategy) presents a shared vision for all stakeholders. It outlines strategic priority areas and key outcomes to guide the efficient, effective, ethical and equitable translation of genomics into the health system, and valuably contribute towards the delivery of precision medicine and precision public health. It aims to achieve this by safeguarding current progress, building on local strengths and outlining the way forward for enhanced health service delivery to achieve the best possible outcomes for all Western Australians through genomics.

Scope

The Strategy focuses on the application of genomic knowledge and services to enable precision medicine and precision public health approaches, as well as the associated health outcomes and policy implications.

All uses of genomics for precision medicine and precision public health purposes are within the remit of the Strategy. This includes genetic and genomic tests (i.e. tests that focus on a single gene and those that focus on multiple genes at the same time), and interventions (delivered at an individual or population level) or therapies utilising genomic knowledge (e.g. gene therapies, gene editing, vaccines). While genomics alone will not sufficiently deliver precision medicine and precision public health, other contributing technologies are outside the scope of the Strategy.

The Strategy has been developed primarily for use by the WA health system over the next decade. As such, its focus is on genomic activities that occur within or are facilitated by the WA Department of Health and health service providers (HSPs). However, it is recognised that there are many existing and potential partners outside the WA health system important to supporting the development and optimal application of genomics for the benefit of the WA population. Collaboration and engagement with these partners will therefore be an ongoing objective.

Strategy development process

The WA Department of Health developed the Strategy with the guidance of the Advisory Committee. This Committee comprised representatives from the WA Department of Health and HSPs, and subject matter experts (including consumers) across a range of fields relevant to genomics. Stakeholders had opportunities to provide input during the development of the Strategy, as well as feedback directly on the draft Strategy through an open public consultation process. A range of methods were used to consult stakeholders, including face-to-face and telephone interviews and online surveys. Over 120 stakeholders were engaged, including health consumers and advocates, clinical geneticists, genetic counsellors, medical specialists primarily trained in areas other than genetics, primary healthcare specialists, laboratory scientists, medical researchers, policy makers, and clinical service planners.

Current health-related genomic services in WA

Most genomic healthcare services in the state are provided through the WA health system. These services are delivered by a range of health professionals, although a great proportion of these are provided by the single statewide service providers for clinical genetics and pathology, Genetic Services of WA (GSWA) and PathWest Laboratory Medicine WA (PathWest), respectively. A small number of genomic services for health care are also provided in the private sector, including primary health. A more detailed breakdown of WA's genomic services can be found in Appendix 4.

The vision for genomic health care in WA

Vision

To ensure all Western Australians benefit from the timely and appropriate translation of genomics, enabling precision medicine and precision public health.

Aim

To coordinate and maximise stakeholder efforts to enable efficient, effective, ethical and equitable translation of genomics knowledge into the WA health system.

Underlying principles

To achieve the vision of the Strategy, the implementation of the strategic initiatives will need to be underpinned by the strong principles outlined below.

Principle 1: The application of genomic knowledge to health care is equitable and informed by scientific evidence and the diverse needs of consumers, carers, families and the community.

Principle 2: Investment in genomic services and applications is strategically prioritised based on their value to consumers, services and the WA health system.

Principle 3: Individuals, families and the broader population are empowered to make decisions about the application of genomics in their health care.

Principle 4: Trust in the use of genomics in health care is promoted through adherence to quality and safety standards and compliance with privacy and confidentiality policies.

Enablers of success

To guide the successful implementation of the Strategy, 4 enablers have been identified as critical building blocks:

1. Sustainable investment.
2. Senior leadership and support.
3. Meaningful partnership and collaboration.
4. Accountability, roles and responsibilities.

Sustainable investment

The current funding models have not kept pace with the rapidly evolving advances, nor the rising demands and expectations relating to the delivery of genomic services in the WA health system. When operating within the context of finite health resources, a strategic approach to funding and investment for genomics is critical to delivering high value care whilst minimising wastage and reducing burden on the WA health system.

Funding and investment in genomic healthcare must be reliable yet offer flexibility. Sustainable investment linked to transparent and timely translation of genomic knowledge into the WA health system.

Therefore, investment and disinvestment processes should underpin and secure long-term transformation, yet also allow short-term opportunities to ensure the WA health system can suitably take advantage of emerging opportunities. A way of achieving this is via upfront investments, where a significant contribution goes towards funding an initiative that shows promise at being able to produce high returns over the longer term.

Decisions need to be determined based on the needs of the population and evidence gained through rigorous processes such as health technology assessments. This builds assurance and trust that the genomic applications being funded are indeed appropriate, and of the highest quality and benefit to the WA population, whilst supporting ongoing safety, quality and cost-effectiveness.

There is a need to raise the profile and clearly articulate the health utility and cost saving potential of genomics among health system decision-makers to ensure that genomics is recognised as a priority for investment. Key main areas for genomics that would benefit greatly from upfront investment opportunities are workforce, infrastructure and data management.

Senior leadership and support

Leadership and support are critical to the success of the Strategy. The System Manager and HSPs have a clear leadership role in lifting WA's standing as a world leader in the emerging fields of precision medicine and precision public health. It is important that leadership at the senior executive levels is ongoing, engaged, recognises the value of genomics and encourages the translation of benefits into the health system. There is a responsibility to ensure that high quality and fit-for-purpose genomic healthcare services become widely and equitably accessible to all Western Australians. This includes providing support to guide the safe and appropriate application of genomics within their respective services and influencing the organisational culture to adapt to new ways of working.

Meaningful partnerships and collaboration

Partnerships and collaborations are necessary for maximising outcomes and reducing duplication of efforts in the translation of genomic research and advances into health care to benefit all Western Australians. It is imperative that collaboration exists at the state, national and international levels. Building partnerships that are meaningful and collaborative will be aided via active dialogues enabling all parties to have their voices heard. Commitment to the implementation of the Strategy across all levels and the breadth of stakeholders will be key to its success.

There are already many valuable partnerships and collaborations relating to the use of genomics in health care that exist involving Western Australians. Purposeful efforts will be made to continue to develop and expand partnerships with a diverse range of stakeholders including:

- health consumers, their carers, family members and the broader community
- HSPs
- primary healthcare providers
- Aboriginal Community Controlled Health Services
- private healthcare providers
- mental health providers
- private industry and philanthropists
- education institutions
- researchers
- diagnostic service providers
- non-government organisations and patient support organisations
- government organisations and policy makers.

Accountability, roles and responsibilities

Clear roles and responsibilities for all stakeholders involved in the delivery of genomic services in health care in WA are paramount to ensuring accountability is upheld and outcomes are achieved in unity. Measurable performance indicators and reporting mechanisms will support effective implementation of the Strategy and support the WA health system to remain accountable for the delivery of high quality genomic services that are fit for purpose and provide value to all Western Australians.

Strategic priorities

Priority 1: Person and family-centredness

Goal 1: To ensure consumers, carers, families and communities are at the heart of how genomic healthcare is designed, delivered and evaluated.

The WA health system is committed to a person-centred approach to health care for all Western Australians [3]. The needs and preferences of consumers will be consciously placed at the core of the use of genomics in health care. Consumers will be equal partners in the co-creation of genomic services and policies, as well as their individual genomic-related health care [16].

The partnership approach will be extended beyond the person receiving health care to include family members and carers. These people play an integral role in providing care and support for individuals with health conditions. The familial nature of genomic information means that a family-centred approach is particularly important for health care involving genomics. A growing amount of evidence links a person and family-centred approach to improved health care quality and better health outcomes, including improved safety, cost-effectiveness, and consumer, family and staff satisfaction [17].

A person and family-centred approach will be embedded in all aspects of the delivery of health services involving genomics, including pathology services, medical services, the management of genomic data, and genomic-related research. The focus will be on listening to consumers, enabling information exchange, facilitating choices and sharing decision-making, so that individual and family needs, goals and preferences are met as part of a collaborative approach, while also supporting safer and more effective care. In doing so, genomic providers will respect the ethnic, cultural and socio-economic diversity of consumers and families.

Person and family-centred approach to genomic health care

Consumers will be able to partner with the providers of their genomic health care to ensure that care and support is coordinated and personalised to reflect their values, needs and preferences. Individuals receiving genomic health care, along with their carers and families, will be treated with dignity, compassion and respect. People will be supported to develop the knowledge, skills and confidence they need to make informed decisions about their genomic health care. An essential component to this will be the provision of appropriate pre and post-test genetic counselling, including obtaining informed consent. The choice to undergo genomic testing will be discussed in a safe and effective manner with consumers and their families to empower them to make informed decisions. There will be a balanced approach to genomic testing, whereby choosing not to have a test is deemed a valid and acceptable option and this is built into consent and healthcare service models. In addition, post-test genetic counselling will recognise the potential mental health implications of receiving genomic test information (particularly predictive test results) and will provide appropriate support.

As genomic testing is increasingly taking place outside of specialist clinical genetic services, standard frameworks for appropriate genetic counselling will need to be designed and promoted [18]. These will emphasise consumer choice models, taking into consideration variations in healthcare context.

When a person undergoes genomic testing, the resulting information obtained about them may have implications for family members in terms of their genomic risk of disease. This creates the need to consider intra-familial communication of genomic risk information. Family members may also need to be involved and undergo testing to clarify the likely consequence of findings and to aid interpretation of inconclusive test results (e.g. newly discovered DNA variants).

Communicating with families about genomic information can be a difficult matter, as the process is grounded in the broader context of existing family relationships and how families function and communicate, as well as cultural and individual beliefs. Finding the right balance between an individual's privacy and confidentiality of their genomic information, and what is in the best interest of family members is an ongoing ethical and social challenge for health professionals [19].

Consumers and their families will be supported to understand and manage genomic information, and decisions about how their genomic information is used and shared will be made in alignment with their wishes and in accordance with legal and regulatory requirements.

Vignette 1

A comprehensive paediatric hereditary cancer surveillance service

Li-Fraumeni syndrome (LFS) is a devastating hereditary cancer predisposition syndrome, associated with a high risk of cancer early in life, starting in infancy. Children with LFS have a 40 per cent chance of developing cancer by age 40 and a lifetime risk of cancer close to 90 per cent [20].

Hereditary cancer predisposition syndromes (HCPS) overall, represent 10 to 15 per cent of childhood cancers, all of which have a high risk of early onset and of arising in multiple organs or developing more than once over a lifetime [21]. The early detection of cancers using regular clinical review and medical imaging helps to reduce the morbidity and mortality of children with HCPS and minimises their need to undergo aggressive treatments.

In 2018, Department of General Paediatrics and Oncology at the Perth Children's Hospital collaborated with Genetic Services of Western Australia (GSWA) to establish a Paediatric Surveillance Clinic for HCPS. The clinic predominantly sees children and adolescents with or at 50 per cent risk of LFS, but also manages patients who have other gene mutations associated with increased cancer risk such as Von Hippel-Lindau syndrome and Gorlin syndrome.

The clinic offers a holistic patient and family orientated service with a multidisciplinary team consisting of a general paediatrician, paediatric nurse, paediatric oncologist, genetic counsellor and clinical geneticist. The clinic attempts to use toys, play and humour to reduce anxiety associated with clinic visits, particularly for younger patients and their families.

Predictive genomic testing is essential for diagnosing children with HCPS. These children (many of whom have LFS) are referred to the Paediatric Surveillance Clinic where they receive regular cancer screening. Undiagnosed children known to be at risk of HCPS – such as those with an affected parent – are also eligible to attend the clinic and are offered regular clinical examinations until a genetic diagnosis is confirmed.

There are many reasons why families postpone genetic testing for their children, including parental illness, grief and coping with the certainty or risk of their children having cancer. The clinic therefore addresses the individual needs of families with at-risk children. This person- and family-centred approach benefits the HCPS community.

Return to Figure 1

Co-creation of genomic healthcare services and policies

Recommendation 4 of the *Sustainable Health Review Final Report* [3] includes a commitment to new approaches to support citizen and community partnership in the design, delivery and evaluation of sustainable health and social care services and reported outcomes. Genomics presents several scientific, clinical, ethical, legal and social issues and challenges [2]. Given the complexities of genomics there is a clear need to ensure consumer and community voices are surfaced, shared and acted on. Consumer perspectives will shape genomic health care through the co-creation of relevant policies, services, supports and systems.

Co-creation and public engagement approaches will be tailored to the needs and preferences of different communities where appropriate, in ways that build trust and sustain community confidence. Facilitating partnerships and high levels of participation among harder to reach groups is essential to ensure that a representative sample of community voices are included.

For Aboriginal people, community is of critical importance. The concept of community engenders a sense of belonging, encompassing cultural, emotional and social ties and is intrinsically linked to the cultural rights and sense of identity of Aboriginal people [22]. Engagement with Aboriginal people will focus on developing partnerships with Aboriginal communities to ensure that the cultural rights, beliefs and values of Aboriginal people are respected.

Improving health literacy

Ensuring that the community has adequate health literacy is relevant across the breadth of health service provision. Yet the degree of literacy of consumers for genomics is particularly pertinent as the nature of genomic information and associated issues can potentially be complex and controversial. As such, how people respond to genomic information, such as genomic susceptibility to disease is likely to be affected by their levels of health literacy.

Despite the community becoming increasingly exposed to genomics, research suggests that in general the community's understanding of underlying genomic concepts is limited [23]. Improving genomic literacy and understanding among stakeholders including consumers will empower them to be genuine partners in shared decision-making and the co-production of genomic health services, programs and policies.

The provision of credible information resources and tools, increased transparency of information on service quality and support to navigate complex systems will ensure consumers have access to evidence-based, up-to-date, impartial information on the application of genomics in health care. Educational resources and programs will be tailored to meet the needs and preferences of different groups and communities, including priority populations.

Key outcomes

- Strong leadership and commitment to a person and family-centred culture for genomic health care.
- Consumers are active partners in decision-making around the use of genomics in their health care.
- Consumers and communities are equal partners in the co-creation of services, policies and research that reflect their needs, values and preferences, in line with ethical, legal and professional standards.
- The consumer experience of genomic health care is understood and optimised, including individual and family outcomes related to the use of genomic testing.
- Equity of access to value-based genomic services is championed, including for priority populations such as Aboriginal people, people from culturally and linguistically diverse backgrounds, and people living in rural and remote communities.
- Standardised, culturally appropriate, voluntary and informed consent processes, with effective support and counselling around intra-familial communication pre- and post-test are offered to all those considering genomic testing.
- Improved consumer knowledge, health literacy and capability for informed decision-making about the use of genomics in their health care.
- Increased public awareness and understanding about potential benefits, risks and limitations of individual and population-based genomic health care.

Priority 2: Genomic healthcare services

Goal 2: To achieve the optimal integration of genomic knowledge in the WA health system to deliver high value care that is timely, equitable and safe.

Major advances in the field of genomics over the past decade have expanded its applicability to standard care for a range of medical disciplines and have provided opportunities to revolutionise medicine and public health. Given the rapid growth in this field, there is a pressing need for a collaborative and coordinated approach to health service planning, capacity building and investment to support the equitable integration of new genomic advancements into the WA health system in a timely manner. Genomic services and programs will be appropriate, innovative and high value to meet the needs of individuals, families and the population in a safe and ethical way.

Designing and implementing contemporary models of care

Realising the full promise of genomics, including the delivery of precision medicine and precision public health, will rely on its broader adoption and appropriate use in mainstream health care [24]. This will require the introduction of a coordinated approach between statewide pathology and clinical genomic services and other providers of health services, to grow genomic capacity across the WA health system. New and innovative service models will be needed to ensure that genomic advancements can be incorporated into the WA health system in a safe and equitable manner to bring the greatest benefit to Western Australians close to where they live.

Maintaining statewide service models for genomic health care

The rationale for maintaining statewide service models include the size of population relative to the state's vast geographical size, the small, specialised genomic healthcare workforce within WA, and the specialised nature of pathology and clinical genomic services. PathWest and GSWA's statewide arrangements aim to support the efficient use of limited resources, ease and equity of access, and consistent delivery of quality services across the state. Their advantages include being central resources for information and expertise about the relationships between genomics and health conditions, as well as a means for timelier translation of new genomic technologies, knowledge and processes into clinical and public health pathways to deliver high value care and improve outcomes. PathWest and GSWA have well-established statewide workflows and strong links with national and international services and networks, which are essential to support genomic innovation and translation into the WA health system.

There has been increasing demand for services and expert advice from PathWest and GSWA by health professionals and consumers from across WA. Appropriate governance arrangements are required to ensure these services can manage this demand in a timely manner and provide equitable, high value care. Purposeful and adaptive service planning, sustainable and fit-for- purpose funding models, and upfront investment in capacity building and resources are also necessary to ensure equity of access to these statewide services. To meet the needs of people living in rural and remote areas, new and innovative models of service delivery will need to be explored. In addition, there will need to be consideration of how the diverse needs of consumers across various ethnic, social and cultural groups can be met.

Vignette 2

Genetic diagnosis points to life-saving treatment for young lung disease patient

From her first year of life, Miss C was battling severe lung disease and showing minimal response to numerous different treatments. Miss C's condition was deteriorating so quickly that her doctors were considering a lung transplant for her. Before the lung transplant workup, her doctors decided to run a genetic test, which revealed that she had a primary immune deficiency called STING-associated vasculopathy with onset in infancy (SAVI). SAVI is a condition that manifests in excessive inflammation throughout the body, particularly in the skin, blood vessels and lungs, damaging the cells and tissues [25].

Since learning that Miss C has SAVI, her doctors have been able to find a more suitable treatment (ruxolitinib) to target the underlying cause of her deteriorating lungs. On this new treatment, Miss C's lung function and quality of life have improved significantly.

At 6 years of age and having caught up in growth, Miss C is now able to attend school and increase her level of physical activity. Her improved response to treatment has also meant she now needs less supplementary oxygen and has not needed another emergency hospitalisation.

Based on Miss C's genetic test, plans for a lung transplant have been abandoned because such transplants can be life-threatening for people with SAVI. Although Miss C's long-term prognosis remains unclear given SAVI is a relatively recently described disease, her journey highlights the life-changing potential of a diagnosis.

Return to Figure 1

Genomics in mainstream health care

Beyond the specialised statewide genomic services, it is important that opportunities are created to improve the sustainability of other successful models of care and explore how these could be expanded across the WA health system to help meet growing demand and ensure genomic services are sustainable. This includes the integration of genomics into mainstream health care, as well as the use of digital technologies to maximise service availability.

Early learnings have shown that different specialties require different ways of integrating genomics depending on existing clinical and public health pathways and the types of diseases their patients have. As such, the optimal integration of genomics into the WA health system will require flexible and tailored approaches that are appropriate to each specialty area, while also being evidence-based and responsive to advancements in genomic knowledge and technology.

To facilitate this expansion of services into mainstream health care, the specialised statewide services will need to form strong partnerships with all HSPs to better understand and address their various needs for specialist services and expertise. They should also provide advice, education and training to mainstream healthcare providers to aid in clinical and public health decision making, expand multidisciplinary genomic clinics, upskill specialists across the health system, and support the integration of genomic technologies into healthcare pathways across different specialties. Engagement with private, primary and community care providers will also be needed to facilitate appropriate referrals to genomic services.

Into the future, appropriate oversight from the System Manager and quality assurance processes will be essential to maximise quality, safety and utility of genomic health care. Guidelines and standards for healthcare delivery and clear processes for requesting and conducting genomic tests will ensure that

genomics is based on the best available knowledge, evidence, and research, and will help to reduce variation across the WA health system.

Expediated and simplified decision-making mechanisms

Rigorous assessment mechanisms, including health technology assessments (HTAs), are a means through which new health services, technologies and treatments are evaluated for safety and cost-effectiveness to inform investment (or disinvestment) decisions in the health system [26]. These processes serve an important purpose to ensure publicly funded health care is safe, effective and fiscally sustainable in the longer term.

HTAs and other decision-making mechanisms are inherently and rightly time consuming. They are therefore challenged by the rapid pace and nature of developments in the application of genomics in health care, which hinders the timely translation of technological and medical advancements. The use of genomics in the delivery of health care also presents unique complexities. For example, additional challenges for existing evaluation mechanisms are created by the volume of data generated that is not directly relevant to a clinical investigation, and the potential predictive nature of genomic results with respect to risk of diseases and familial implications.

Ensuring the timely, but appropriate, integration of genomics into the WA health system will require exploration of ways to modify, simplify and expediate decision-making mechanisms for assessing the clinical and public health need, validity and utility of new developments in genomics. Such mechanisms must also strategically prioritise the translation of genomic developments into the WA health system and should be linked to sustainable funding models.

There is no standardised or nationally consistent approach to HTAs in Australia. Decisions can be made at the national, state or territory, and in some cases the local hospital level. In 2017, the WA health system devolved responsibility for the majority of HTAs to HSPs [27]. Central management of these functions, such as the nationally cohesive approach to HTAs proposed in the National Health Reform Agreement, would be beneficial to reduce duplication of effort, lower clinical variability, and improve consistency in advice and the decisions reached. This would also support more timely and cost-efficient evaluations of rapidly evolving technologies like genomics – an important consideration given limited health resources.

A fit-for-purpose funding system for integrating genomics

Improved implementation of genomics into the WA health system will require a fit-for-purpose funding model with the ability to respond in a timely way to the introduction of evidence-based, effective new technologies and innovations in delivering health care. The *Sustainable Health Review Final Report* describes a need to introduce new funding methods that shift away from funding health services based on the historical volume of services they provide to a more flexible funding approach based on population health needs and outcomes. It is important to recognise the factors unique to genomics that introduce funding complexities to enable development of more appropriate models for effectively funding existing and emerging genomic applications. In addition, upfront investment in critical components such as infrastructure and workforce are essential to support capacity building and delivery of high value care. This will have additional benefits including presenting WA as an attractive hub for building partnerships with experts from interstate or internationally.

Key outcomes

- Increased capacity and capability of the WA health system, in collaboration with external health providers as appropriate, to deliver timely, equitable, accessible and high value genomic healthcare services.
- Referral, assessment and management pathways, standards and policies that aid the optimal, safe and equitable delivery of genomic healthcare services including provision of health information and advice where appropriate.
- Partnerships and networks to promote and support sharing of health-related genomic knowledge and reduce duplication of effort.
- Innovative and adaptive service delivery models that support the sustainable and equitable integration of genomics into mainstream health care.
- Mechanisms for the timely and evidence-based assessment of genomic tests, technologies, models of service delivery and therapies, as well as prioritisation of their translation into the WA health system.

Priority 3: Workforce, education and training

Goal 3: To develop a sustainable health workforce with the appropriate capacity, agility and necessary education and training to deliver genomic healthcare services.

The rapid development of genomics presents a major workforce development challenge for the WA health system. Efficiently and sustainably implementing genomic advances will require a coordinated effort and investment to develop, attract and retain the required specialised genomic workforce as well as increase the genomic literacy across the broader healthcare workforce. Both local and national approaches to workforce development are necessary. Collaboration and partnerships with the governments of the Australian Commonwealth, states and territories, as well as the relevant medical and nursing colleges and educational institutions will be formed and developed. These will be harnessed to design and implement workforce development strategies and initiatives that are responsive and flexible to the rapidly expanding application of genomics to health care.

Specialised genomic workforce

The appropriate delivery of genomic health care requires a specialised workforce. This workforce comprises clinical geneticists, genetic counsellors, molecular pathologists, bioinformaticians and medical and/or laboratory scientists working collaboratively and often as part of broader multidisciplinary teams with other health professionals. Presently in WA, the demand for genomic services exceeds workforce capacity and capability, which has placed pressure on the existing small and highly specialised workforce. This challenge is not unique to the WA health system but is also experienced in many other jurisdictions and is influenced by several overlapping challenges [30].

Workforce modelling and planning, as well as service level redesign, will be regularly undertaken to ensure that health professionals with specialised genomic knowledge can sustainably deliver high-quality care that meets the increasing demand. This planning will consider the training needs of the workforce and identify adequate pathways to train and upskill health professionals in the delivery of genomics. Examples of these include innovative on-the-job training opportunities, increasing the number of training positions available to health professionals (including apprenticeships and fellowships), and better defining roles and responsibilities in a way that helps to support career pathways in genomics.

Currently there is a critical shortage of some specialist genomic professionals, such as bioinformaticians, a role pivotal to establishing and developing new systems to analyse and interpret genomic data [31]. Targeted strategies to build, attract and retain an adequate number of genomic specialists will help place WA at the forefront of delivering precision medicine and precision public health. For example, a review of remuneration arrangements and recognition of specialist genomic professions through national accreditation will support further workforce development initiatives for key professions.

Vignette 3

First in the nation to offer genetic testing for FH

Familial hypercholesterolaemia (FH) is a genetic disorder that reduces the body's ability to clear low-density lipoprotein (LDL, or bad) cholesterol from the blood. Excessive buildup of LDL cholesterol can cause narrowing and hardening of the arteries. Undiagnosed and untreated individuals with FH have a 20-fold increase in the risk of heart disease – males have a 50 per cent risk and females have a 30 per cent risk of suffering from heart attack or stroke by the ages of 50 and 60 years, respectively [28].

It is estimated that one in 250 to 300 Australians has FH [29].

In 2010, Professor Gerald F Watts, a Professor of Cardiometabolic and Internal Medicine, established Australia's first multidisciplinary cardio-metabolic service (CMS) to provide treatment and advice on the care of people living with FH and other lipid disorders.

Based at Royal Perth Hospital, the CMS was the first place in Australia to offer a diagnostic genetic test for FH. Because FH runs in families, the CMS cascade screens family member of individuals who have tested positive to FH. This is to see if the family members also have the condition. The CMS effectively provides early detection and prevention of heart disease and heart attacks.

It has also provided training to clinical nurse specialists, nurse practitioners, general practitioners and consultants, contributing to clinical workforce development across WA's public and private sectors and the establishment of a new clinical service in paediatric lipidology at Perth Children's Hospital, headed by Dr Andrew Martin.

The CMS also facilitated the development of the National FH Registry, curated by Dr Jing Pang, which enabled health economic evaluations on FH care. These evaluations were integral to informing the Medicare Benefits Schedule (MBS) Item 73352 for genetic testing for FH – a milestone achievement because it was the first MBS item number for an inherited heart disease.

The CMS continues to advocate for new testing paradigms to enable even greater identification and management of FH, such as through universal child screening and reverse child-parent cascade screening. The CMS is actively involved in testing new biologics directed at novel targets (PCSK9 and ANGPTL3) for advancing the treatment of hypercholesterolaemia and improving cardiovascular outcomes and quality of life of patients with FH.

Return to Figure 1

Building a multi-professional genomic literate workforce

More broadly, the appropriate translation of genomics into mainstream service delivery will be reliant on the involvement of a wide range of health professionals across clinical and public health subspecialties. Therefore, having a skilled and genomic-literate multi-professional workforce (e.g. medical specialists, general practitioners, nurses, midwives, occupational therapists, pharmacists, public health practitioners) with genomics understanding and the competence and confidence to appropriately deliver and communicate genomics is essential to the provision of high-quality services and improved health outcomes for consumers [32].

Workforce needs assessments can be important to assess current knowledge and competency across all levels of the workforce and understand their requirement for tailored education and training. An increasing need for a wide range of genomic tests (including those for screening purposes) and therapeutics across a range of clinical disciplines and public health and prevention programs necessitates adaptive approaches to manage this demand. These include upskilling health professionals to perform different tasks and adopting decision support tools and technologies. This will involve ongoing education training and upskilling of health professionals to achieve competency in aspects of genomic health care relevant to their role, for example, achieving competency in pre- and post-test counselling to ensure there is informed consent and decision-making by consumers.

This will be further supported by clinical pathways, standards or guidelines that assist the multi- professional workforce to deliver consistency in health care, provide advice on how and where to seek expertise and how to interpret and communicate genomic results. Efforts to support ongoing education, training and upskilling must also consider health professionals working in regional and remote areas of WA. To ensure equal opportunity for these health professionals in the journey of integration of genomics into mainstream care, multiple approaches such as online learning, virtual multidisciplinary clinics and connection to communities of practice are required. The WA health system will also need to be cognisant of the interface between genomic services in the private, public and not-for-profit sectors and consider cross-sector training and education requirements, as well as working arrangements, to strive towards consumers having equitable and seamless access to services and support.

Key outcomes

- Regular workforce modelling and planning, by utilising existing research and collecting additional data as necessary to determine the workforce capacity needed in WA and inform investment decisions, particularly in areas where there are critical workforce shortages.
- Mechanisms to grow the genomic workforce and attract and retain genomic healthcare professionals in WA.
- Collaboration with stakeholders from WA and other jurisdictions, including educational institutions to foster a sustainable, approach to meet WA's genomic education and training needs.
- A range of mechanisms, including innovative digital training approaches, to improve the genomic literacy and capability of the multi-professional health workforce, including competency required to deliver person and family-centred genomic services and facilitate informed decision-making about genomics.

Priority 4: Digital health and data

Goal 4: To establish digital health and data solutions, protocols and standards needed to optimise the delivery of responsible genomic health care.

Advances in data analytics and bioinformatics, as well as wider digital health technologies are driving a revolution that can help deliver the promise of precision medicine and precision public health [33]. The successful integration of genomic technologies into the WA health system is dependent on the state's ability to address several unique challenges relating to genomic data management and digital and technological infrastructure capability. One of these is that genomic sequencing involves the generation of large amounts of raw data compared to other health data.

Genomic data

The potential of data and digital innovation to improve healthcare efficiency and transform health care has been highlighted in the *Sustainable Health Review Final Report* under Enduring Strategy 6 'Invest in digital healthcare and use data wisely'. This potential extends to genomic data and the successful integration of genomics into the WA health system is reliant on being able to appropriately create, securely store, manage and analyse these data. There need to be appropriate governance processes and standards to ensure privacy and security of genomic data are maintained. It is also essential that adequate consent processes exist, considering how genomic data are unique with respect to predictive capability, familial implications, longevity and ability to identify both individuals and families.

Some uses of genomics are dependent on long-term storage of data, as well as the possibility to link with other health data in a format that can be readily accessed and analysed. For example, stored genomic data can be re-analysed as new health discoveries are made and disease-causing genetic variants are uncovered. National and global cooperation and appropriate sharing of genomic data can also be vitally important in achieving a diagnosis, informing appropriate treatment or conducting research, especially for rare genetic conditions and cancers. Similarly, sharing knowledge of variations in microbial genomes across jurisdictions can assist with detecting the source of infections and tracking infectious outbreaks.

To optimise the use of genomic data in supporting effective healthcare decision making we need consistency in how genomic data are captured, shared, stored and protected across all parts of the WA health system. Development of genomic data protocols for the WA health system must consider relevant national and international frameworks and standards, as well as community expectations and legal and regulatory requirements, to ensure public trust and confidence in the use of genomic data in health care.

New computational approaches, such as those offered through artificial intelligence, hold great promise in addressing some of the current challenges in the management and analysis of genomic data, including automation of quality control processes, more timely processing of sequences and genome interpretation [35]. These techniques are worthwhile exploring as more evidence on their applicability and effectiveness comes to light.

Vignette 4

Mackenzie's Mission

Healthy couples planning a pregnancy can unknowingly be carriers of serious genetic conditions capable of being passed on to their children. Due to the way these conditions are inherited there is seldom a known family history of the condition.

For families of children diagnosed with a severe genetic condition, the diagnosis can be devastating. Such was the case for Rachael and Jonathan Casella whose daughter Mackenzie was diagnosed with spinal muscular atrophy (SMA) and passed away at just 7 months of age. SMA is an autosomal recessive disorder that progressively destroys a child's nerve cells, causing muscle weakness and wasting [34].

In May 2018, the Australian Government invested $20 million of the Genomics Health Futures Mission to a research study, called Mackenzie's Mission, on reproductive carrier screening for genetic conditions including SMA, fragile X syndrome and cystic fibrosis. Reproductive carrier screening is a form of genetic testing done before or in early pregnancy to identify a couple's risk of having a child born with a recessive X-linked genetic condition. Depending on the results of the test, a couple may wish to seek genetic counselling and support to make informed decisions in relation to their reproductive choices. Mackenzie's Mission aimed to screen up to 10,000 Australian couples for 1,300 genes associated with around 750 serious genetic conditions that occur in childhood and have a significant impact on life expectancy and/or quality of life.

Professor Nigel Laing AO, an internationally acclaimed genetics researcher, was one of 3 Co-Leads of Mackenzie's Mission and the Principal Investigator of the WA arm of the study. The WA arm provided reproductive carrier screening for selected WA couples since late 2019 and extended this service to Queensland and South Australian couples between late 2019 and early 2022. Professor Laing previously led the WA Preconception Carrier Screening Project, which screened more than 200 couples for 476 genes and significantly shaped Mackenzie's Mission. Outcomes from Mackenzie's Mission will help inform the feasibility of providing reproductive carrier screening as a routine service to all Australian couples wishing to access it.

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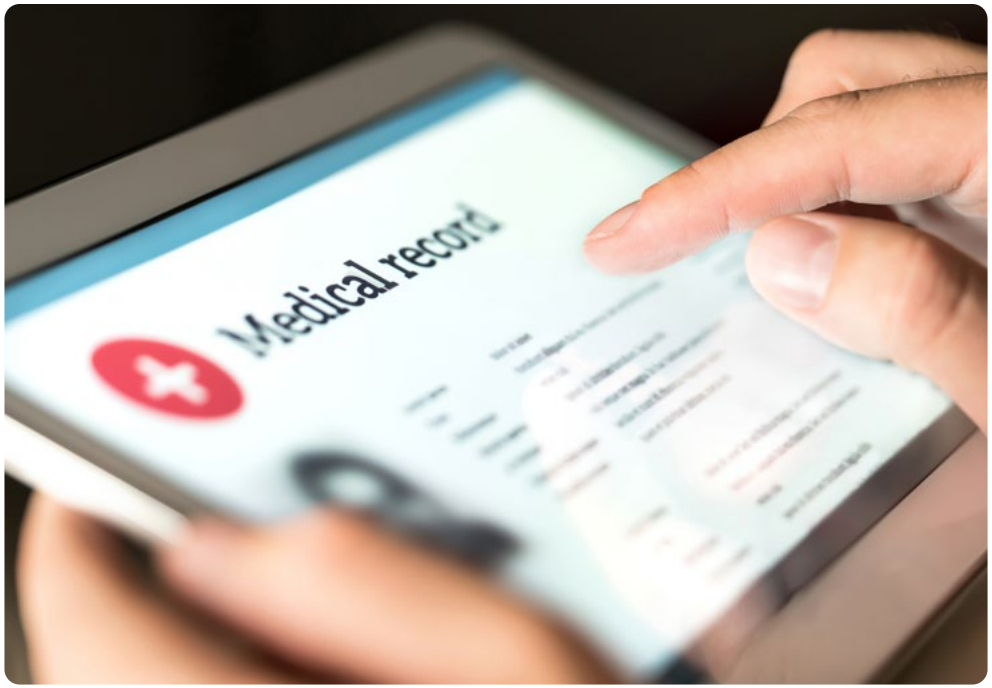
Privacy and trust

The extent to which genomics is successfully applied across the WA health system is influenced by public trust and participation. Fostering public trust and willingness to engage with genomic health care and research relies on preserving individual privacy. The vast amount of genomic data that can be created increases the risk of privacy breaches and data misuse. Consumers must be confident that their data are safe and being used appropriately and responsibly. Privacy and security must be imbedded in all data processes and there must be transparency about how data are used.

For example, consultation with Aboriginal people and co-design of data policies and consent processes with Aboriginal communities will be integral to building trust and ensuring equity of access to genomic healthcare services for these communities. In the past, some genomic initiatives have jeopardised the cultural and intellectual property of Aboriginal people, resulting in these communities having some mistrust regarding genomic testing [36]. Upholding Aboriginal data sovereignty, establishing culturally appropriate informed consent processes, ensuring there is transparency with respect to ownership and uses of genomic data, and communicating the health benefits of genomic testing must be central to the development of genomic initiatives in WA and be in keeping with the important cultural significance of genomic data to Aboriginal people.



Digital health and innovation

Through the *WA Health Digital Strategy 2020–2030* (Digital Strategy), WA has committed to a range of strategies and initiatives intended to progress the state towards its vision of a digitally-enabled health system. A key initiative of the digital strategy is investment in the development of statewide Electronic Medical Record (EMR) functionality. This initiative brings the opportunity to improve health care by providing a single source of truth that will reduce unnecessary duplicate testing, reduce variation in care, as well as provide decision-support tools to aid in healthcare decision-making. If WA is to lead in the application of genomics to health care, as is recognised in the Digital Strategy, then it is incumbent upon the WA health system to consider how genomic data could be incorporated into or interface with the EMR.

Approaches to genomic data storage and analysis (within or interfacing with the EMR) would benefit from decision-support tools to assist in the provision of genomic health care. For example, alerts to prompt clinicians when a consumer may benefit from a certain pharmacogenomic test or to notify healthcare providers when a genomic test warrants changes to medication or management. Additionally, incorporation of support tools within the EMR could help improve upon current processes for ordering genomic tests, by requiring provision of phenotypic information as part of the ordering process. Adoption of these tools would also have the added benefit of helping to educate the health workforce regarding genomic applications to health care.

Some of the initiatives proposed by the Digital Strategy may also improve genomic health care through enabling introduction or leveraging of digital models of care, such as virtual consultations and telehealth services. These will be particularly beneficial in the Western Australian context given the dispersion of the state's population over a large geographic area.

Successful adoption of these approaches could help reduce the burden of travel on consumers from regional and remote areas and improve equity of access to genomic services, which are currently predominantly located within the metropolitan area.

Key outcomes

- Adoption of digital solutions that enable the appropriate integration of genomics into health care, including the capture, access and transfer of phenotypic information and the analysis and interpretation of genomic data.
- Implementation and regular review of policies and standards for how genomic data should be effectively and efficiently recorded, shared, stored, and protected, which align with evolving community expectations, legal and regulatory requirements, and international standards.
- Culturally secure and appropriate collection, storage and sharing of genomic and phenotypic data reflecting the ethnic diversity of the Western Australian population.
- Exploration of emerging areas such as digital health records, machine learning and artificial intelligence, and consideration of best practice models for their integration into genomic health care.
- Investigation of opportunities for utilising genomic data to enhance cohort identification for designing healthcare services, interventions, treatments, clinical trials and research.
- Contribution towards the National Approach to Genomic Information Management.

Priority 5: Research and innovation

Goal 5: To have a health system that values and supports the creation and translation of genomic research and innovation.

There is an increasing body of evidence demonstrating a range of benefits to clinical and public health practice that arise from the translation of genomic research and innovation. These include faster and more accurate diagnoses, and the ability to tailor health care for consumers, families and populations to maximise benefits. Multiple research groups in WA have successfully delivered local, national and international genomic research and innovation projects relating to health care. Some notable examples are included throughout this Strategy document as vignettes.

Interface between health care and research and innovation

Cross-sector collaborations between health consumers, health professionals, researchers and innovators are critical to achieving timely, safe, equitable and effective translation of positive genomic research and innovation outcomes across the WA health system. A coordinated systemwide approach is required along with an organisational culture that values collaboration across multiple disciplines. This is anticipated to improve the interface between research, innovation and health service delivery by creating a 'translation loop', where benefits are delivered across 3 domains (Figure 3).

Firstly, the consumer can benefit from increased dialogue and a deeper understanding about genomic health care including consent, diagnosis, prognosis and treatment. Meanwhile, they contribute to improvements in how these processes are designed and delivered and are partners in determining research needs through co-creation processes. Next, the health professional can provide insights from the healthcare setting particularly about existing aspects of services in need of improvement as well as feasible ways new discoveries could be incorporated into service delivery. Thirdly, health system administrators and policy makers can determine systemwide barriers and enablers and identify whether system-level changes are required to implement new knowledge. Lastly, research and innovation can be accelerated by the insights gained through collaboration, and then new knowledge created can be translated to health administrators and policy makers, health professionals and consumers, thereby completing the loop. Recognising and enhancing the translation loop is anticipated to prove useful across many areas, such as understanding the functional impact of the growing number of genomic variants of uncertain significance on health and disease.

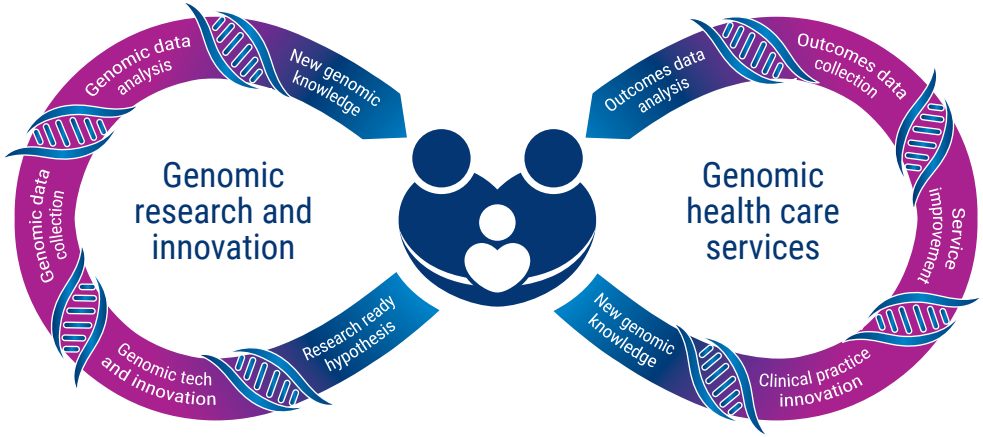


Figure 3: The 'translation loop'

The relationship between human genomic research and genomic health care. Figure adapted from: Green et al, (2020) Strategic vision for improving human health at The Forefront of Genomics, Nature, 586(7831):683-692.

Vignette 5

WA's participation in Australian Genomics Flagship programs

In 2016, the Australian Genomics Health Alliance (Australian Genomics) was launched through a National Health and Medical Research Council grant to evaluate the implications and impact of offering genomic testing to thousands of Australians with a rare disease or cancer. Additional funding through philanthropic donations and the Genomics Health Futures Mission also help support Australian Genomics to deliver its projects.

Under its Cancer and Rare Disease Flagships, Australian Genomics researched the impact on workforce and education, piloted national approaches to data capture and analysis, and the economic, policy, regulatory and ethical implications of genomics in Australian health care. Australian Genomics has strategically built a large, inclusive, national multidisciplinary genomic network, connected to international genomic initiatives.

WA health system staff members from multiple HSPs including specialists, researchers and laboratory scientists participated in or led various Flagship projects. These resulted in capacity and capability building in genomic healthcare delivery for the WA health system and benefits to local patients. Genomic testing capabilities for the Flagships were provided by PathWest or interstate laboratories.

Australian Genomics Flagships included those with a focus on primary immune deficiencies, early-onset autoimmunity and auto inflammatory diseases, inherited kidney diseases, mitochondrial diseases, neurodevelopmental disability (including encephalopathies, brain malformations, leukodystrophies and intellectual disabilities), neuromuscular disorders, acute care, inherited cardiovascular disorders, interstitial and diffuse lung disease, and somatic cancers.

Return to Figure 1

Maximising opportunities and support for innovation are key to ensuring WA becomes a destination of choice for genomics, precision medicine and precision public health. This can help bring newer technologies and industry involvement to the state to further progress research and innovation, as well as attract and retain a high calibre workforce to advance the translation of genomics-enabled precision medicine and precision public health across the WA health system. One way of maximising research and innovation opportunities is to build better pathways for professionals from all disciplines, and at all levels, to participate in projects. This could be through postgraduate opportunities or training positions, mentorships for budding researchers and innovators, and back-filling of healthcare duties to increase the capacity of health professionals to partake in more projects. It is also imperative to increase access, capacity and capability of local DNA sequencing and bioinformatics.

Progress in this area will support local researchers and innovators to be strong candidates for research and innovation grants such as those offered through the WA Future Health Research and Innovation (FHRI) Fund and the Australian Genomics Health Futures Mission.

Consumer-informed research and innovation

Research and innovation for genomic health care should be informed by the needs and priorities that matter most to the people of WA. To achieve this, health consumers need to have a certain level of genomic literacy through access to educational material and opportunities and have an awareness of the possible applications of genomic innovations in health care. Increased opportunities for health consumers to be involved in genomic research and innovation projects, including clinical trials, and empowering them to contribute to the co-creation process will enhance the translational loop described above.

Diversity in research

Historically, genomic research has largely focused on populations of European descent, and this has resulted in an ethnic bias in most large genomic datasets and the subsequent bioinformatic tools used in health care [37]. Yet promoting genomic research in diverse populations is particularly relevant for heterogenous societies like WA. Ensuring diversity and inclusion of people participating in genomic research programs is key to adequately representing human genetic variation. This has several benefits for improving consumer outcomes as it can lead to greater understanding of complex genomics, such as which gene mutations and/or what frequency of gene variants predispose certain population groups to a disease. It also has potential to result in diagnoses, prognoses, therapies and new drug discoveries that are more accurate and effective for different population groups.

Additionally, it will be important to ensure cultural and social diversity is valued and reflected in key decisions relating to genomic research and innovation. This will include increasing Aboriginal cultural awareness training and an adherence to data sovereignty principles, which are imperative when collaborating with Aboriginal people in the utilisation of their biological samples and the information gained from them.

Key outcomes

- Translational genomic research and innovation projects are informed by the needs of consumers, carers, families, the community and the WA health system.
- Empowered health consumers are involved in genomic healthcare research and innovation projects.
- Diversity is valued and encouraged in the genomic healthcare research and innovation sectors.
- An organisational culture that provides opportunities and encourages health professionals and medical scientists to collaborate in translational research and innovation projects in genomic health care.
- Local, national and international partnerships and networks inform and conduct translational research and innovation projects in genomic health care to bring benefits to Western Australians.
- Strengthened ability for WA to be a leader in innovation and research for genomic health care.

Conclusion and next steps

Conclusion and next steps

This Strategy has been developed as a living document to unite stakeholders involved in the delivery and/or utilisation of genomic services in the WA health system. It provides a shared vision and 5 strategic priority areas to streamline investment of resources to achieve the optimal application of genomics across the WA health system. This is premised on a belief that more outcomes may be achieved to benefit all Western Australians by working collaboratively and cohesively, rather than in silos.

It is important to note that a strategy document on its own cannot deliver its vision. Rather, it must be implemented appropriately and effectively to ensure that its well-intended outcomes are achieved and sustained. The essential steps to achieving the vision include establishing governance arrangements, developing and carrying out implementation plans, and building on a culture of accountability.

Governance

Strong stewardship and governance are essential to achieving a coordinated approach to the delivery of the Strategy. The WA Genomics Strategy Implementation Committee (the Implementation Committee), will be established to oversee and guide the implementation of the Strategy. The Implementation Committee will bring together key leaders and stakeholders from across WA including representatives from HSPs, other subject matter experts and health consumers with lived experience. The Implementation Committee will facilitate and support partnerships and initiatives to progress the priorities outlined in the previous section. The Implementation Committee will also provide ongoing monitoring, review and evaluation of the Strategy. In addition to this, working groups are likely to be formed to guide the implementation of specific projects as required.

Implementation and evaluation

The Strategy provides a guide to achieving the optimal application of genomics to delivering precision medicine and precision public health. Given the rapid pace at which new evidence emerges and technology advances in genomic health care, an agile approach to implementation (including planning, evaluation and monitoring) will be required.

The Strategy will be implemented through a series of short-, medium- and long-term horizons. However, it is anticipated that some larger projects and initiatives will span 2 or more phases of implementation. Implementation plans will be a key tool for measuring the success of the Strategy. An evaluation of each implementation plan will be undertaken to help inform the development of the next implementation plan. The benefits of these are 2-fold as they will also serve as mid-point evaluations determining the success of the Strategy.

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Appendices

Appendix 1 – Glossary of terms

Bioinformatician: A specialist who uses computer science, data analysis and mathematics to study large data sets, such raw genomic data, to solve complex biological (i.e. health) issues.

Chromosome: DNA is packaged into long, thread-like structures called chromosomes. Humans have 46 chromosomes, which can be arranged into 23 pairs, with one chromosome from each pair inherited from each biological parent. Of the chromosome pairs, 22 are autosomes, which appear the same for males and females. The remaining pair of chromosomes are sex chromosomes, which determine biological sex.

Consumers: People who utilise services within the health system.

Deoxyribonucleic acid (DNA): A chemical polymer that provides the information needed to build and maintain living organisms. In humans, the complete set of the DNA sequence is called the human genome.

Gene: The functional components of the DNA sequence that contain the operational instructions for all cells in the human body. Genes code for molecules that influence the expression of a person's characteristics. Changes in the DNA code of a gene can potentially result in a person having a health condition.

Genetics: The study of the functions and composition of individual genes.

Genetic test: A test whereby DNA material is extracted from cells and analysed in a laboratory for changes to chromosomes, genes, RNA and/or proteins.

Genomics: The examination of genes and how they interact with each other and the environment. Differs from genetics, which is focused on analysing single genes.

Genomic testing/sequencing: Testing for variants in many genes, specific regions of the genome, or the entire genome sequence at one time. Genomic testing can detect changes in many genes at once using a gene panel, in the exome (i.e. sections of the genome that contain the instructions for proteins) using whole exome sequencing, or throughout the entire genome using whole genome sequencing.

Mutation: a variation in the DNA code, which can be causative of disease.

Nucleotide: The chemical 'letters' (nucleotides) that make up the DNA sequence, of which there are 4 – adenine (A), guanine (G), thymine (T) and cytosine (C).

Person-centred care: Focuses on the delivery of quality healthcare while respecting a person's values, needs, wants and goals.

Pharmacogenomics: The study of how the human genome affects an individual's response to different drugs.

Value-based health care: Delivers the best outcomes for consumers and the best value for the health system.

Appendix 2 – Current and emerging application of genomic tests across the life cycle

Type of test	Description
Diagnostic	Test to investigate the cause of disease. Follows onset of symptoms, a clinical or public health discovery or a positive screening test.
Microorganism	Testing of microorganisms that impact human health. Used to understand and trace infection, outbreaks and antimicrobial resistance. Emerging applications include investigation of human microbiomes and influence on immunity, drug interactions and disease expression.
Newborn bloodspot screening	Screening of newborns to identify infants at increased risk of one of many rare and serious genomic conditions to enable early intervention.
Pharmacogenomics	Screening for genomic variants that influence drug metabolism to inform drug choice and dosage.
Predictive/ pre-symptomatic	A test to establish whether an asymptomatic at-risk individual has predisposition to disease development.

Type of test	Description
Preimplantation genetic testing	Screening or diagnosing of embryos to determine those without a specific genomic variant or a chromosomal abnormality for subsequent use in vitro fertilisation (IVF).
Prenatal testing	Screening or diagnosing of a fetus during pregnancy for specific genomic variants or a chromosomal abnormality to inform reproductive choice, preparedness and/or early intervention.
Prognostic	Identifies gene variant/s to predict disease progression, severity and outcomes and guide and monitor therapeutic interventions.
Reproductive carrier screening	Testing to determine the carrier status of couples planning a pregnancy or in pregnancy to inform reproductive choice, preparedness and/or early intervention.
Posthumous	Molecular autopsies to identify cause of sudden unexplained death, including in utero death.

Table adapted from: Bilkey et al, (2019) Genomic Testing for Human Health and Disease Across the Life Cycle: Applications and Ethical, Legal, and Social Challenges, *Frontiers in Public Health*, 7:40.

Appendix 3 – Genomic health care in the context of current health policies

A growing number of countries are formulating policies to support the development of genomics and the adoption of more precision approaches to health care. In Australia, the application of genomics to health care has received national recognition at the highest levels, evidenced by the release of the *Australian National Health Genomics Policy Framework 2018–2021* (National Policy Framework) [38] endorsed by the Council of Australian Governments Health Council, and the allocation of $500 million over 10 years to the Australian Government's Medical Research Future Fund's Genomics Health Futures Mission [39].

The National Policy Framework has provided a shared direction and commitment between all governments in Australia to consistently and strategically integrate genomics into the Australian health system. The WA Government committed to supporting implementation of this framework. The strategy aims to build on and aligns with the National Policy Framework, while taking into consideration local context and needs and advances and changes that have occurred since the National Policy Framework was released.

Several Australian jurisdictions have developed genomics-related strategies and service plans [40-43], either prior to or after the release of the National Policy Framework, which set out goals and/or recommendations for the integration of genomics into their health systems. These documents have informed the development of this Strategy and where appropriate, it has been aligned with these documents to ensure harmonisation of the national policy context.

In WA, several policies have been developed that embrace the promise of genomics and/or precision health. These include the *Sustainable Health Review Final Report*, which under Enduring Strategy 8 prioritises an 'enhanced reputation as a world leader in the emerging field of precision medicine and [precision] public health that includes new data/digital, informatics, genomics, phenomics and geo-spatial technologies, and their application to health'. In this Strategy the wording has been slightly changed to be 'precision medicine and precision public health' to provide greater clarity to the reader and better convey the intention of the SHR recommendation.

In addition to Enduring Strategy 8, there is also strong alignment to Recommendation 4 'commit to new approaches to support citizen and community partnership in the design, delivery and evaluation of sustainable health and social care services and reported outcomes,' Recommendation 16 'establish a systemwide high value health care partnership with consumers, clinicians and researchers to reduce clinical variation and ensure only treatments with a strong evidenc e base and value are funded,' and Recommendation 26 'build capability in workforce planning and formally partner with universities, vocational training institutes and professional colleges to shape the skills and curriculum to develop the health and social care workforce of the future.'

Additionally, elements of the Strategy closely align to the *Sustainable Health Review*'s themes of:

- increased spending on prevention and public health
- investing during the first 1,000 days of life
- person-centred, equitable, seamless access, promoting systemwide strategies such as clinical care standards
- pursuing opportunities to maximise the use of Medicare Benefits Schedule (MBS) funding for specialist outpatient services
- digital healthcare that will support sustainability is patient-centred, and supports health literacy and the whole of a person's health journey
- capitalising on predictive analytics, big data
- developing a coordinated approach to assessing and implementing new and existing equipment, procedures, medications and technologies
- drive implementation of standardised care pathways to maximise value to patients and communities, and reduce healthcare variation and waste
- a systemwide approach to improvement and innovation.

Additionally genomic data are mentioned as an example of an area for investment for analytic and diagnostic capability within the critical success factors for implementation.

Priority 2 of the *WA Cancer Plan 2020–2025* [44] also singles out genomics in its strategy to 'develop and implement statewide genomic sequencing capability to inform treatment.' The plan recognises that 'as advances in personalised medicine are made there will be increasing opportunities to tailor interventions to better target specific high-risk groups such as those with inherited or rare cancers. The area of personalised medicine is changing rapidly'. It also states that 'there is an urgent need to implement genomic profiling of tumours into routine patient care, develop key policy frameworks to govern the introduction of this initiative, monitor changes in practice and support the necessary upskilling of the workforce.'

Genomics-enabled precision medicine and precision public health are also of relevance to the *WA Health Digital Strategy 2020–2030* (Digital Strategy) [45] strategic themes 3 (optimised performance), 5 (enhanced public health) and 6 (embedded innovation and research), particularly as the utility and demand for precision medicine and precision public health and their related technologies are anticipated to grow over the life of the Digital Strategy.

Other important plans and frameworks that the Strategy aligns with are the *State Public Health Plan for Western Australia 2019–2024* [46], the *WA Aboriginal Health and Wellbeing Framework 2015–2030* [47], the *Newborn Bloodspot Screening National Policy Framework* [48], the *National Microbial Genomics Framework 2019–22* [49], the *National Strategic Action Plan for Rare Diseases* [50], and the *WA Rare Diseases Strategic Framework 2015–2018* [51]. Elements of this Strategy will work synergistically with these WA and national policies.

Appendix 4 – Current health-related genomic services in WA

Statewide service providers

GSWA is the only public provider of clinical genetics in WA, operating a statewide service through a network of metropolitan and regional outreach clinics to provide a comprehensive diagnostic and confidential counselling service. GSWA assists health consumers with the diagnosis and management of their genetic condition, testing for predisposition to inherited cancers, and prenatal diagnosis and carrier screening to assist with family planning. These services are provided by clinical geneticists and genetic counsellors who work closely with molecular and cytogenetic laboratories and other associated disciplines such as diagnostic imaging and obstetrics.

PathWest is the other statewide genomic healthcare service provider, being WA's only public provider of pathology services. PathWest delivers a broad range of genomic services to public hospitals, general practitioners as well as certain other health professionals working in the private sector in WA. Services offered include diagnostics, predictive testing, tumour profiling, carrier screening and prenatal testing for high-risk pregnancies. Decisions regarding which tests PathWest provides are made by their senior staff in collaboration with specialist clinicians and scientists. These decisions are based on a multitude of factors including national and international evidence-based guidelines and practice, healthcare demand, evidence of health utility, available resourcing and funding avenues.

Other genomic service providers

There has been a growing role of health professionals (from medical specialties other than clinical genetics) across all HSPs in the application of genomics to inform diagnosis and treatment, as well as in administering emerging therapies. The establishment of multidisciplinary genomic clinics and integration into mainstream services are 2 approaches that have facilitated the increasing uptake of genomics.

Most multidisciplinary genomic clinics in WA have emerged informally, due to strong partnerships between GSWA, and/or PathWest and selective clinical specialties. In many instances, they have been enabled through research projects. These clinics apply a collaborative approach to managing complex medical conditions and involve a range of experts from the different aspects of healthcare delivery (e.g. medical consultant, clinical geneticist, genetic counsellor, laboratory scientist). As a result, these clinics have improved consumer outcomes, provided education and upskilling opportunities for the health professionals involved, and increased the cost-effectiveness of health services. As examples, multidisciplinary genomic clinics in cardiology and nephrology have been working well in WA.

Other medical specialties have integrated genomics as part of routine health care without the involvement of a clinical geneticist or genetic counsellor. In these circumstances, the treating health professional has full oversight of the genomic care pathway of the health consumer. This has often been enabled by the health professional upskilling in genomics and developing networks across medicine, diagnostic laboratories and research to aid in the diagnosis, management and treatment of genetic conditions. This has occurred either in the presence or absence of defined standards, guidelines and oversight. Examples of speciality areas that have successfully integrated genomics as part of routine care in WA are haematology and neuromuscular disorders.

Providers outside of the WA health system

Health professionals in the WA health system are most likely to request their genomic tests through PathWest. However, if PathWest does not provide a certain test that is deemed most appropriate for the health consumer, PathWest can facilitate DNA samples being sent away to an accredited laboratory interstate or overseas for this test to be conducted. Alternatively, some health professionals order tests direct from laboratories interstate or overseas. This is facilitated by their own networks or through research projects.

In the primary healthcare sector, general practitioners are becoming increasingly involved in genomic testing. In many cases they refer health consumers suspected of having a genetic disease to the relevant medical specialist or GSWA. However, there are occasions where they will order tests directly. These are mostly non-invasive prenatal tests or single gene tests that are available through the Medicare Benefits Schedule.

Appendix 5 – Vignettes

Vignette 6: Solving WA's most confounding medical mysteries

GSWA's Undiagnosed Diseases Program (UDP) is an innovative program that is helping to diagnose children (up to 16 years) and adolescents (16 to 25 years) with complex and long-standing health conditions.

The program brings together a clinical geneticist, genetic counsellor, care coordinator and panel of medical experts from various clinical specialties to undertake a comprehensive diagnostic work-up of each patient, including genomic sequencing where appropriate. The formula is helping solve WA's most challenging medical mysteries.

Master J, an autistic 7 year old with a multisystem disorder that affects his skin, heart, kidneys and joints, is one of many children to have benefitted from the UDP, which is the first program of its kind to be integrated into clinical care. With no clear clinical pathway to manage his condition, Master J and his family had lived with uncertainty every day.

Through the UDP, Master J was diagnosed with Myhre Syndrome, a rare genetic condition associated with progressive skin thickening, limited joint movement and fibrosis (scarring) of the heart and lungs. The syndrome is also characterised by an unusually aggressive scarring response to surgery and other invasive medical procedures [52].

Master J's quality of life has improved significantly since his diagnosis because it has enabled him to receive best practice medical care personalised to his condition. His doctors now understand why previous surgery for his finger mobility was of limited success and they can also minimise invasive procedures he has in the future to prevent excessive scarring.

Master J has been able to cease expensive inappropriate (biologic) therapy and commence on a safe, inexpensive and readily available drug (Losartan) that has been repurposed for his condition, as has an interstate child with the same condition. A diagnosis has enabled Master J's parents to connect with other families in similar situations, lessening their feelings of isolation and uncertainty.

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Vignette 7: Cutting-edge DNA sequencing speeds up donor-recipient matching

Scientists at the PathWest Immunology Laboratory at Fiona Stanley Hospital are using cutting- edge DNA sequencing technology to significantly improve donor-recipient matching for bone marrow and organ transplants.

The sequencing focuses a group of genes in a region of the genome known as the human leukocyte antigen (HLA) complex. Proteins produced by the HLA complex serve as markers that are used by the body's immune system to detect foreign invaders such as viruses – but they can also detect foreign tissue. Close matching of HLA markers between a recipient and donor is important to minimise the chances of a transplant being rejected.

High-resolution DNA sequencing used by PathWest enables HLA markers to be examined in greater detail than previous methods, providing clinicians with more information to guide donor- recipient matching. This helps prevent unknown mismatches and improve clinical outcomes for transplant recipients.

Timeliness is of critical importance to support the viability of transplant organs. High-resolution DNA sequencing increases the rate at which samples can be processed, allowing more HLA sequencing to be achieved in a shorter amount of time. This has reduced the turnaround time for matching donor and recipients to just 4 hours. Innovative use of DNA sequencing demonstrates how genomic technologies can improve patient health outcomes and enable more efficient healthcare delivery.

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Vignette 8: Statewide comprehensive genomic testing to expedite excellence in treatment of WA cancer patients

Advances in genomic technology, in combination with medical research, has transformed understanding of cancer development and progression. As a direct result of this, treatment strategies are becoming increasingly tailored to the genomic profile of the cancer. This means patients are being treated according to the genomics of their disease – not solely on the cancer type or its anatomical location.

The number of genomic biomarkers being recognised as clinically important for each cancer type is also growing rapidly, making it necessary to have a more comprehensive analysis of cancer specimens in order to determine the optimal treatment strategy, and ultimately improve patient survival. In WA, the Molecular Anatomical Pathology Laboratory at PathWest is the publicly-funded accredited laboratory that performs genomic testing on cancer specimens for diagnostic, prognostic and treatment purposes.

A collaborative WA team driven by Professor Benhur Amanuel as the molecular lead and Professor Michael Millward as the clinical lead has been working in close conjunction with the Molecular Anatomical Pathology laboratory. This team has been focused on the translation of genomics into the clinical setting and providing cancer patients with the most up-to-date and effective treatments by investigating the very latest technologies and monitoring clinical needs and research findings as they emerge.

In 2017, a research translation project funded by the Department of Health was commenced to investigate the feasibility of comprehensive genomic testing of cancer specimens for 6 high-priority cancer types within WA. The pilot study established and optimised the workflow for integrating comprehensive testing into the clinical setting, with regular Molecular Tumour Board meetings having a significant role in interpreting the complex genomic results and translating them into meaningful recommendations accessible to referring clinicians and consumers.

The project also demonstrated clear benefits for cancer patients, including refinement of diagnosis, identification of alternative treatment strategies, avoidance of treatments unlikely to be effective or that would

cause harm, and alignment with clinical trials that could enable early access to novel therapeutic agents and reduce cancer burden.

Beginning in February 2020, PathWest and Linear Clinical Research collaborated to set up the WA node of the Australian Genomic Cancer Medicine Programme – Molecular Oncology Screening and Treatment (MoST) – which aims to offer comprehensive genomic testing to patients with rare and uncommon cancers and match them to clinical trials coordinated by the NHMRC Clinical Trial Centre.

The next area of focus is to expand the availability of this comprehensive genomic testing to all WA cancer patients. Of the 45,000 cancer specimens currently received per year by PathWest, fewer than 10 per cent undergo a comprehensive genomic test. The ultimate goal is to offer genomics as a first-line test to replace the many tests of single or small numbers of genes that are currently carried out on different platforms. This should not only maximise efficiency and cost-effectiveness, but also ensure early patient treatment.

Based on previous developments from screening colorectal cancer patients for Lynch syndrome, similar workflows are being established for other hereditary cancers such as breast, prostate, ovarian and pancreatic. These workflows will include both the genomic testing of tumours and normal tissue or blood tests at the time of diagnosis. Identifying individuals who are at higher risk of a hereditary cancer syndrome at their time of diagnosis could significantly alter their surgical and medical management plan, improving their outcomes. Additionally, the ability to then test first-degree relatives for the same inherited cancer-causing genetic variant, enabling early preventative action, could amplify the benefit of the initial genetic diagnosis.

The creation of comprehensive genomic testing pathways aligns with objectives of the current 4 year, Australian Government-funded WA Precision Oncology Program, as well as the *WA Cancer Plan 2020–2025* to enhance statewide genomic sequencing capability in WA. Such pathways will also enable WA cancer patients to access equitable, person-centred and more seamless genomic testing than is currently offered.

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Vignette 9: A blood test for early detection and monitoring of melanoma

More than 13,000 Australians are diagnosed with melanoma each year. One in 10 patients will be diagnosed at a stage when the melanoma has already spread to other parts of their body, significantly reducing their chance of survival [53].

Early detection and routine monitoring are key to improving melanoma survival rates. Current methods to detect melanoma, however, are opportunistic (e.g. self-examination) while diagnosis and monitoring require further observation through invasive tissue biopsies and scans that expose patients to high levels of radiation.

The Melanoma Research Group at Edith Cowan University's Strategic Research Centre for Precision Health (led by Associate Professor Elin Gray, and previously by Professor Mel Ziman) investigates how melanoma spreads and why certain tumours respond to current treatments while others are treatment resistant. The group's world-leading research shows promising results for non-invasive blood tests (or liquid biopsies) to enable earlier detection of melanoma and less invasive methods for monitoring disease progression. These blood tests measure tumour cells, mutant DNA, and other circulating biomarkers in the patient's blood.

As well as overcoming the need for painful tissue biopsies or exposure to harmful levels of radiation, the blood tests allow for more frequent monitoring of patients, giving doctors a more accurate picture of their patient's health and enabling them to predict patients who are at higher risk of metastasis and relapse.

The blood tests are also an alternative means of monitoring patients in rural areas with limited access to health services.

Other advantages of these blood tests are that they can offer information about a patient's response to drug therapies – enabling a more tailored treatment plan to reduce the risk of adverse side effects – and be used as a screening tool to detect melanoma as soon as it develops, enabling early treatment and a greater chance of survival.

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Vignette 10: Neurogenetic diseases: causes and therapies

Research integrating with clinical care

The Neurogenetics Clinic at Royal Perth Hospital facilitates genomic testing for patients suspected of having an inherited neurological or neuromuscular (neurogenetic) disease to diagnose and inform the management of their condition.

Because many disease-causing genetic variants remain undiscovered, not all patients receive a diagnosis following initial genomic testing.

Consultant neurologist and Clinical Professor Phillipa Lamont, PathWest medical scientist Dr Mark Davis and Harry Perkins Institute of Medical Research genetics researchers Professor Nigel Laing AO and Dr Gina Ravenscroft are at the forefront of addressing this challenge.

Collaborative efforts between Royal Perth Hospital, PathWest and the Harry Perkins Institute have led to the discovery of new disease-causing genes and variants that have provided much needed answers for WA patients and their families. Their strong working relationship led to the development of a neuromuscular gene panel (available at PathWest) that is ordered by clinicians throughout Australia and internationally. The panel significantly improved the rate of genetic diagnoses for neuromuscular conditions and has demonstrated cost-effectiveness for diagnosing muscle diseases in children. Professor Laing and Clinical Professor Lamont also led the Australian Genomics Health Alliance Flagship Neuromuscular Disorders, which further solidified WA as a leader in neuromuscular disease expertise and innovation.

Clinical Professor Lamont, Dr Davis, Professor Laing and Dr Ravenscroft continue to collaborate on neurogenetic diseases. Their multidisciplinary integrated approach to clinical care, diagnostics and research demonstrates how 3 distinct fields can work synergistically to improve patient outcomes.

Genetic therapies

Murdoch University professors Steve Wilton and Sue Fletcher are pioneers in the development and use of antisense oligonucleotides (synthetic nucleic acids) to treat genetic diseases such as Duchenne muscular dystrophy (DMD). In DMD, the disease results from mutations in the gene coding for the dystrophin protein that is essential for stabilising muscle fibres. These mutations prevent production of the dystrophin protein, meaning the patients have no functional dystrophin protein in their bodies. Over time this leads to weakness and wastage of muscle. The disease is ultimately fatal [54].

Professors Wilton and Fletcher's treatment resulted from Professor Wilton's discovery that some patients with DMD have small amounts of the dystrophin protein in their muscles due to low levels of natural exon skipping – essentially, these are rare mistakes in gene transcript expression. Exon skipping is a process whereby faulty coding instructions in the DNA, and then primary transcript, are skipped by the cellular machinery during gene message maturation, enabling a functional but shorter protein to be produced.

Professors Wilton and Fletcher used this knowledge to develop a 'gene patch' which specifically induces skipping of the 51st exon in the dystrophin gene message. The United States Food and Drug Administration expedited approval of the gene patch, which is licensed through the University of Western Australia to Sarepta Therapeutics. The gene patch enables a shorter dystrophin protein to be created. It is effective in about 13 per cent of cases, reducing the severity of the individual's DMD.

The 2013 Eureka Prize for Medical Research Translation was among many accolades Professors Wilton and Fletcher received for their invention.

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Vignette 11: Genomic testing uncovers new pathways for managing blood cancers

Over the past several years, haematologists at PathWest have used genomic tools to diagnose, treat and monitor blood cancers. The use of genomics in this clinical area has become so extensive that it is now considered part of the routine care they provide to patients. It has had a profound impact on disease prognoses, provision of targeted and personalised treatments, avoidance of ineffective therapies (and their side effects) and patient's quality of life.

Genomic applications in haematology range from simple molecular tests to complex next generation sequencing. A simple molecular test can be used to confirm BCR:ABL in most chronic myeloid leukaemia patients, a gene mutation that causes cancer cells to grow and divide out of control.

Next generation sequencing can detect distinct changes in a patient's DNA code that can lead to acute myeloid leukaemia or another rare disease.

These tools help haematologists identify therapies to improve disease prognoses. Regular monitoring of molecular levels through blood tests thereafter can enable early detection of remission or relapse, enabling further tailoring of treatment to improve symptoms and patient outcomes.

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Vignette 12: Innovative approach to treat retinitis pigmentosa

A WA ophthalmologist's discovery of the gene responsible for a WA family's rare form of Retinitis Pigmentosa (RP) has led to the development of a new 'precision approach' to treating the debilitating eye condition.

RP is an inherited eye condition caused by mutations in any of more than 80 different genes. RP causes cells in the retina (the light-sensitive part of the eye) to degenerate slowly and progressively, leading to severe vision impairment or complete loss of sight [55].

With help from the Australian Inherited Retinal Disease Registry (AIRDR), Professor Fred Chen was able to identify the gene responsible for the WA family's form of RP (RP11). The breakthrough enabled him and fellow researcher Professor Sue Fletcher to collaborate on an approach to treating the family's condition by targeting its underlying cause. Professor Fletcher is renowned for her pioneering work in antisense oligonucleotide therapies for conditions including Duchenne muscular dystrophy.

The pair continues to collaborate to develop the antisense oligonucleotide therapy and plan to commence clinical trials in 2022. The researchers' goal is to develop additional drugs to treat other forms of inherited blindness.

About the AIRDR

The AIRDR, which was key to Professor Chen's discovery, is a national resource designed to advance research translation and the treatment and management of inherited retinal diseases, including RP. It is available to approved researchers interested in discovering more about the varied genetic causes of inherited retinal disease.

The AIRDR collects DNA from consenting patients across Australia and analyses their DNA to characterise the specific genetic cause of their condition, including identification of known causative mutations in more than 250 genes. Approximately 300 to 400 samples are received by the AIRDR each year.

Under Professor Chen's leadership, the AIRDR, Genetic Services of WA and PathWest have worked closely together as an ocular genetics multidisciplinary team providing a service for WA patients with genetic eye diseases.

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Vignette 13: Pharmacogenomic testing for personalised life-saving drugs

It is estimated that around 250,000 hospitalisations annually are due to medication-related problems, costing the Australian Government $1.4 billion per year – the equivalent to 15 per cent of total Pharmaceutical Benefits Scheme (PBS) expenditure. Fifty per cent of the harm caused by medication problems is thought to be preventable [56]. Pharmacogenomics – the study of how a person's genes can affect their response to certain drugs – presents an opportunity to reduce medication-related problems. This field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications and doses that are tailored to an individual's genetic makeup and how their body reacts or metabolises the drug, thereby ensuring maximum efficacy with minimal adverse effects.

Predicting adverse drug reactions in HIV patients

The introduction of highly active antiretroviral therapy for human immunodeficiency virus (HIV) infection has transformed the condition from what was previously considered a death sentence to that of a manageable chronic condition.

Drugs used to treat HIV infection are highly efficacious and therefore prescribed widely. However, a small percentage of patients taking these drugs (4 to 8 per cent) will develop hypersensitivity. This usually occurs within the first 6 weeks of commencing therapy. Drug hypersensitivity reactions (most notably associated with Abacavir and Nevirapine therapy) include fever, rash, gastrointestinal tract symptoms and respiratory symptoms. With continued dosing, these can become severe and potentially life-threatening.

In 2002, a WA research group led by Dr Simon Mallal used genetic testing to confirm an association between the HLA-B*5701 allele and hypersensitivity to Abacavir. The group found that HIV patients who carry the HLA-B*5701 allele were at increased risk of an adverse reaction to Abacavir and so should avoid this drug in their treatment plan. Prior to this discovery, it was difficult to know which HIV patients would go on to experience drug hypersensitivity reactions until they had occurred. Dr Mallal championed the clinical translation of prospective genetic screening of HLA-B*5701 in WA and around the world for Abacavir-naïve patients. This dramatically reduced the risk of developing Abacavir-related hypersensitivity reactions.

Drug treatment-resistant mental health disorders

Across Australia, one in 7 people will experience depression in their lifetime. For those who require medication to alleviate their symptoms, the current process for finding the right one is a matter of trial and error. Some people spend years switching from one medication to the next in search for something that works. However, WA researchers as part of Australia's first non-biased double-blinded, randomised-control trial lead by clinical geneticist Dr Kathy Wu (NSW) are hoping to change this. The AustraLIan trial of GeNotype-guided pharmacothErapy for Depression (ALIGNED) study could revolutionise how medications to treat mental health disorders are prescribed, remove the guessing game, reduce unpleasant side effects of medication and improve quality of life.

Professor Sean Hood, a psychiatrist with the North Metropolitan Health Service and University of WA, is steering the WA arm of this investigation that will determine whether the first antidepressant drug treatment a patient receives (first-line medication) will produce better outcomes if the prescription is guided by the patient's genetic makeup.

Working in conjunction with Meeting for Minds, this project involves people with lived experience of mental illness as research partners, so that those who stand to gain the most from the benefits of this research are involved as respected contributors. Funding is being provided through the Australian Government's Medical Research Future Fund.

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