South Australian Clinical Genomics Plan 2022

March 2019

Government of South Australia

SA Health

Introduction

Genes are packaged in chromosomes, made of deoxyribonucleic acid (DNA). A genome is an organism's complete DNA, including all of its genes. We all have approximately 20,000 genes. Variations in about 1% of these cause the differences that make us unique. Each gene is made up of a collection of nucleotide bases. While individual genes may be defective through one or more base changes and cause disease, interactions between different genes may also cause disease.

While genetics refers to the study of individual genes and their roles in inheritance, genomics aims at the collective characterization and quantification of all of an organism's genes. Genes direct the production of proteins which make up body structures such as organs and tissues, as well as control chemical reactions and carry signals between cells. Genomics involves the technical and bioinformatics ability to sequence and analyse the function and structure of multiple genes.

Since the structure of DNA was uncovered over 60 years ago, our understanding of the relationships between genes and disease has grown enormously. In 2003 the entire base sequence of the human genome was published. This major breakthrough was an enormous and hugely expensive undertaking with the technology available at the time. Since then there has been an explosion in gene sequencing technology enabling rapid and relatively inexpensive genome sequencing for people, making genomic testing widely available.

Advances in genomics have triggered a revolution in understanding of even the most complex biological systems in health and disease.

It is now time that South Australia (SA) looks to the future and develops a plan for what needs to be done to use clinical genomics and affiliated services to benefit the health of South Australians through better disease prevention, earlier diagnosis and better targeted treatment, while managing the associated risks and social, legal and ethical issues.

To achieve this, it is proposed to establish the SA Clinical Genomics Advisory Group. This group will be chaired by the SA Chief Medical Officer under the auspices of the Chief Executive, Department for Health and Wellbeing in collaboration with the consumer groups, Local Health Networks, SA Pathology, the private sector, SA's universities and other stakeholders.

Why is clinical genomics important?

Many human diseases can be caused by single gene changes that are inherited (e.g. cystic fibrosis) or occur through mutations as cells divide (e.g. cancers). In addition, changes in genes can predispose to a risk of disease, which may occur under certain, but not all circumstances (e.g. predisposition to Alzheimer's Disease).

Clinical genomics is important because it enables better disease prevention, earlier diagnosis and better targeted treatment. By understanding how individual genes and interactions between different genes, and interactions between genes and the environment and lifestyle, either cause disease or prevent disease, better diagnostic tests can be developed leading to earlier, more accurate and easier diagnosis and treatment. Similarly understanding the interactions between genes and treatments enables the development of highly targeted treatments aimed at the individual genes, and better understanding of why certain treatments might be more or less successful in different people. Using clinical genomics appropriately as part of routine care has potential to reduce the burden of disease through earlier and more precise diagnosis for people with disease, identification of those at risk of future disease, better surveillance and prevention strategies, reduced unnecessary investigation and treatment, reduced toxicity of treatment, and informing the specific treatment which will work best .

These developments and their likely expansion over the next decade have been described as "precision" or "personalised" medicine (Williamson R et al (2018), The Future of Precision Medicine in Australia. Report for the Australian Council of Learned Academies, www.acola.org.au).

It also enables a better understanding of microbial disease outbreaks through sequencing the genomes of microbes that cause disease in people. By determining that the same organism is causing disease in different people, earlier identification and management of infectious outbreaks will mean fewer sick people, less disruption to business and a healthier and more economically vibrant community. In addition, earlier specific identification of which microbe is causing disease in an individual enables quicker and better targeted antimicrobial/antibiotic treatment for that person.

National Health Genomics Policy Framework 2018-2021

The SA Plan builds upon the National Health Genomics Policy Framework 2018-2021, endorsed by the Council of Australian Government Health Council. This Framework went through extensive consultation and is built around 5 key inter-linked and interdependent Priorities and underpinned by 3 Principles and 3 Enablers.

Priorities:

1. Person-centred approach: delivering high quality care for people through a person-centred approach to genomics.

   Rationale: Making sure that people are involved in, and central to, their care is a key component of developing high-quality health care, including health care informed by genomics.

2. Workforce: building a skilled workforce that is literate in genomics.

   Rationale: Upskilling the workforce through increasing capacity and capability in genomics and bioinformatics is necessary to effectively and efficiently support improved health outcomes for the individual and population.

3. Financing: ensuring sustainable and strategic investment in cost-effective genomics.

   Rationale: Australia's investment in genomic research and testing needs to deliver actionable results that lead to people living longer and better lives.

4. Services: maximising quality, safety and clinical utility of genomics in health care.

   Rationale: The use of genomics in health care should be based on the best available knowledge, evidence and research and the outcomes of treatment should be used to help improve care.

5. Data: responsible collection, storage, use and management of genomic data.

   Rationale: The collection and analysis of genomic data is essential to driving improvements in health outcomes for all Australians and providing a pathway to truly personalised health care.

Principles:

1. The application of genomic knowledge is ethically, legally and social responsible and community trust is promoted.
2. Access and equity are promoted for vulnerable populations.
3. The application of genomic knowledge to health care is supported and informed by evidence and research.

Enablers:

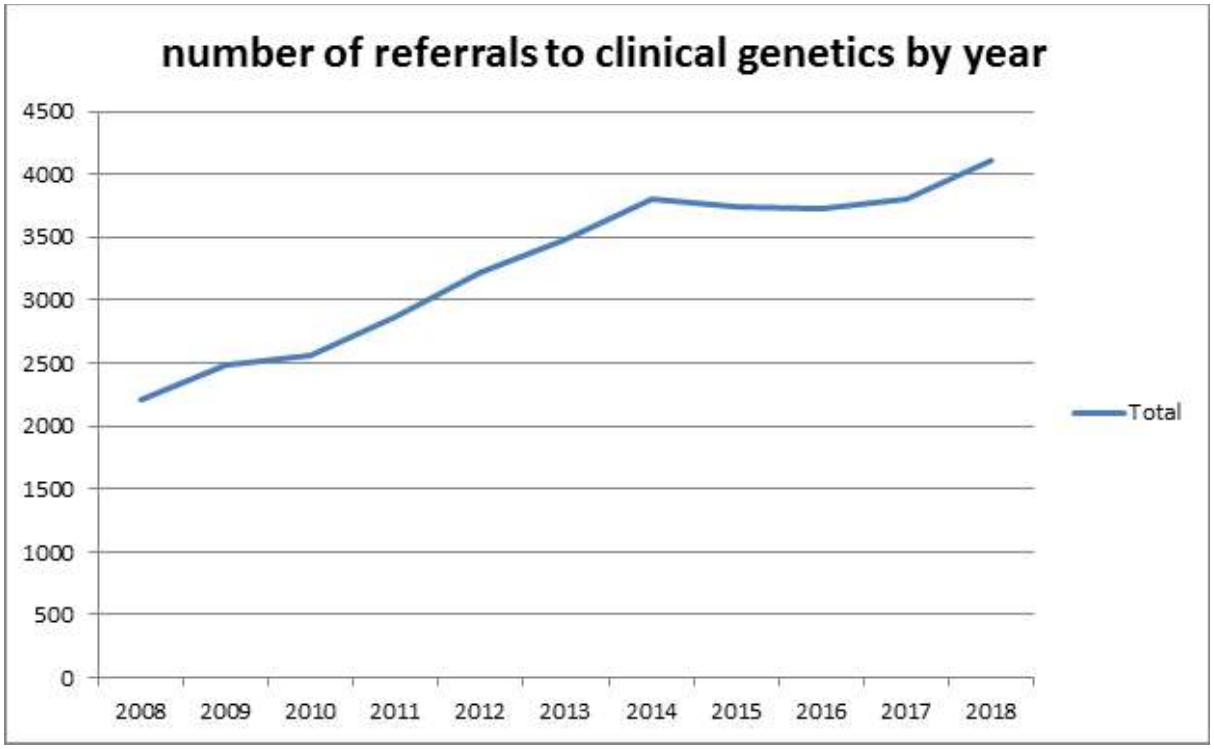
1. Collaborative governance and leadership.
2. Stakeholder engagement.
3. National and international partnerships.

SA has already committed to this Framework. From it, the SA Clinical Genomics Advisory Group (see Appendix 1 for membership) produced this plan which is now for consultation.

How is clinical genomics used in South Australia now?

In SA, clinical genomics is used in a wide variety of clinical services including in the diagnosis and risk assessment of genetic disease in fetuses, babies, children and adults; and in the diagnosis and treatment of cancer and infectious disease.

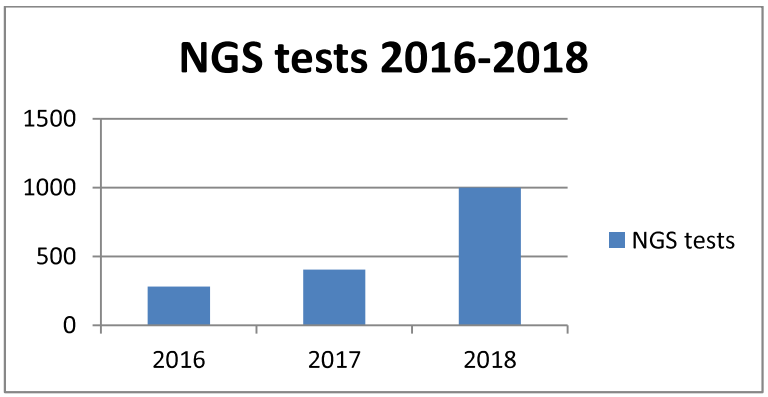
In Australia, both child and adult Clinical Genetics have their own training under the auspices of the Royal Australasian College of Physicians. Specialist Clinical Genetic Services exist at the Women's and Children's Hospital as well as Royal Adelaide Hospital for diagnosis, advice and treatment of inherited and other genetic disorders. There are no other private specialist clinical genetics services in SA. Demand for these services has been rising with a doubling of referrals since 2008.



Other clinical specialties such as neurology, oncology, nephrology, endocrinology and cardiology, also use clinical genomic information to inform diagnosis and treatment.

SA Pathology provides the laboratory service for clinical genomics in SA.

Next generation sequencing (NGS) test volumes have been steadily rising since 2015 with an annual doubling of requests increase over that time. In 2018 SA Pathology performed approximately 1000 next generation sequencing tests.



Microbial genomic testing has also increased substantially following the formation by the Australian public health laboratories of the Communicable Disease Genomic Network (CDGN) in 2015. CDGN is

tasked with planning and coordinating testing methods and data sharing pathways, and standardising the analysis tools used for the detection of outbreaks of infectious diseases. Microbial genomics has been used in South Australia for research and sporadic public health investigations since 2014. In 2018 SA Pathology committed to building the state's genomic public health capacity with the appointment of new staff and a planned development program initially focussing on food borne infections. The value of such programs is illustrated by the demonstration of contaminated mouthwash as the cause of clinical infections in severely ill patients in intensive care as demonstrated in Box 1.

All of these services are underpinned by research programs to help understand and advance the use of clinical genomics in health and disease.

Box 1: Burkholderia cepacia complex (Bcc) are predominantly environmental bacteria but are known to cause of pharmaceutical contamination and infections in immunocompromised patients.

In 2016 Bcc isolates were obtained from blood and tracheal aspirates from 6 ICU patients in a South Australian hospital. An investigation by the hospital's infection and prevention control team noted discoloration of a commercial chlorhexidine mouthwash. Bcc isolates were cultured from all 5 tested bottles from the discolored batch but not from any bottles from 4 other non discoloured batches.

Whole genome sequencing was performed on the patient isolates, the mouth wash isolates and hand basin Bcc isolates from the patient rooms. The analysis revealed a single distinct clone of Bcc. Further, a New South Wales isolate from a similarly discoloured mouthwash bottle from the same batch was also part of this clone (conventional laboratory typing techniques for Bcc would have been unable to confirm the mouth wash as the source of the outbreak).

This investigation led to a nationwide recall of the contaminated mouthwash batch. No further cases were reported.

Reference: Burkholderia lata Infections from Intrinsically Contaminated Chlorhexidine Mouthwash, Australia, 2016. Leong LEX, Lagana D, Carter GP, Wang Q, Smith K, Stinear TP, Shaw D, Sintchenko V, Wesselingh SL, Bastian I, Rogers GB. Emerg Infect Dis. 2018 Nov;24(11):2109-2111. doi: 10.3201/eid2411.171929.

What does South Australia need for 2022?

While SA has excellent expertise in laboratory and clinical genomic services, it is clear that demand is rising and will escalate as new advances in research highlight new areas for health improvement. High quality clinical genomic services of the future need to integrate clinical services, laboratory services, education and research. This means that we must prepare now for what will be needed in the future.

Based on the National Health Genomics Policy Framework 2018-2021, there are many areas we can work on. The National Framework has priority areas for action and these have been edited to suit SA's needs.

1. Person and family-centred approach: delivering high quality care for people through a person and family-centred approach to genomics.

Rationale: Making sure that people and their families are involved in, and central to, their care is a key component of developing high-quality health care, including health care informed by genomics.

1.1 Improve support for individuals, and their families, to make informed choices about genomic testing, and take responsibility for those choices and related risks.

Action: Develop culturally aware resources about clinical genomics for health consumers and health care professionals in SA as part of a SA Clinical Genomics Communications Plan.

1.2 Encourage appropriate referrals for genomic testing, that put the welfare and needs of the individual first, thereby avoiding unnecessary testing.

1.2.1 Developing and promoting clinical practice guidelines (CPGs) and decision support tools for engaging with individuals on their personal context and health goals.

Action: Develop state-wide, agreed CPGs for the use of clinical genomics that are evidence based and available to clinicians and consumers.

1.3 Engage relevant community/patient/carer advocacy organisations and consumers in discussions of the consumer experience, as well as on the ethical, legal and social issues of genomics.

1.3.1 Developing community engagement strategies to promote an understanding of the application and impact of genomic advances in health care, including the gap between testing and treatment options.

Action: Involve consumers in implementing all parts of this plan and establish a Clinical Genomics Consumer Advisory Group reporting to the SA Clinical Genomics Advisory Group.

1.3.2 Exploring how the consumer experience can be captured and measured to inform priorities and establish a baseline.

Action: Incorporate consumer experience of clinical genomics services into existing LHN and DHW consumer/community surveys.

1.4 Promote public awareness and understanding of genomics, including through linguistically and culturally safe and appropriate information resources for targeted consumer groups.

Action: As part of the SA Clinical Genomics Communications Plan (see 1.1) ensure linguistically and culturally safe and appropriate information resources for targeted consumer groups are included.

1.5 Identify barriers to equity of access and develop a state-wide approach to address these, noting that access is multi-dimensional and includes location, cost, availability and appropriateness (including cultural acceptability). This includes, but is not limited to:

- exploring barriers to the uptake of genomic services including the potential for discrimination (life insurance, employment, lifestyle, access to services etc); and
- evaluating the delivery of genomic services in terms of being accessible, appropriate and culturally secure and responsive for Aboriginal and Torres Strait Islander peoples.

Action: Commission this work from the SA Health Translation Centre in collaboration with the Clinical Genomics Consumer Advisory Group.

1.6 Investigate how genomics data can be integrated with SA's electronic health records (EHRs) to improve coordination of care, support better clinician decision-making and facilitate seamless clinical pathways.

Action: Once SA's EHR strategy is decided, ensure clinical genomics is incorporated as a subset of that work.

1.7 Explore the potential to develop integrated person and family-centred care delivered by multi-disciplinary teams, where appropriate, including the sharing of genomic test results that have implications for family members.

Action: Develop state-wide resources for family communication of genomic test results and incorporate person and family-centred care into clinical genomics CPGs (see 1.2.1).

1.8 Identify and promote a standard model of consent that is sufficiently flexible to support a person's understanding of the potential implications of having their genome sequenced, familial aspects and decision-making about any secondary findings, as well as including provision for access by researchers if appropriate.

Action: Ensure a flexible standard model of consent is incorporated into the clinical genomics CPGs (see 1.2.1) that includes legal, ethical and respectful researcher access to data that is consistent with relevant privacy and confidential regulations.

2. Workforce: building a skilled workforce that is literate in genomics.

Rationale: Upskilling the workforce through increasing capacity and capability in genomics and bioinformatics is necessary to effectively and efficiently support improved health outcomes for the individual and population.

2.1 Improve the genomics literacy and capability of the whole health workforce through the development, delivery and ongoing maintenance of appropriate genomic education, training and skills.

Action: Establish a SA Clinical Genomics Education and Workforce Advisory Group reporting to the SA Clinical Genomics Advisory Group.

2.2 Build the capacity for, and promote access to, a skilled and literate genomics workforce, through workforce strategies and planning at the state-wide level.

Action: Under the auspices of the SA Clinical Genomics Education and Workforce Advisory Group (see 2.1) develop relevant workforce strategies and plans and material for the SA Clinical Genomics Communications Plan (see 1.1) regarding SA's capacity for, and access to, a skilled and genomics-literate workforce.

2.3 Facilitate partnerships and networks to promote and support sharing and application of knowledge including regarding impacts on patients and families.

Action: Partnerships and networks to promote and support sharing of knowledge on clinical genomics to be included in the Terms of Reference for the SA Clinical Genomics Advisory Group.

2.4 Investigate the potential for a SA State-wide Clinical genetics Service, with appropriate governance, workforce and training positions for clinical, counselling and laboratory staff.

Action: Investigate the potential for a SA State-wide Clinical Genetics Service, with appropriate governance, workforce and training positions for clinical, counselling and laboratory staff to be included in the Terms of Reference for the SA Clinical Genomics Advisory Group.

3. Financing: ensuring sustainable and strategic investment in cost-effective genomics.

Rationale: Australia's investment in genomic research and testing needs to deliver actionable results that lead to people living longer and better lives.

3.1 Consider genomics in the context of any broader review of health technology assessment to support state-wide consistency.

Action: Determine how clinical genomics should best fit into SA's health technology assessment process.

3.2 Develop partnerships, funding and data sharing approaches for genomics that promote access to safe, efficient and cost-effective services.

Action: Partnerships, funding and data sharing approaches for genomics that promote access to safe, efficient, equitable and cost-effective services to be included in the Terms of Reference for the SA Clinical Genomics Advisory Group.

3.3 Develop a state-wide research agenda for genomics and identify opportunities to link to national research priorities.

Action: Establish a SA Clinical Genomics Research Advisory Group reporting to the SA Clinical Genomics Advisory Group to develop a state-wide genomics related research agenda and monitor and report on state and national clinical genomics research developments.

3.4 Better understand the role of the private industry, and the opportunities for partnerships to support the development and sustainable application of genomic knowledge.

Action: Understanding of the role of the private industry to be included in the Terms of Reference for the SA Clinical Genomics Advisory Group.

3.5 Collaborate across stakeholders to maximise investments and reduce duplication of resources and efforts.

Action: Ensure membership of the SA Clinical Genomics Advisory Group has the appropriate representation to ensure collaboration across boundaries.

4. Services: maximising quality, safety and clinical utility of genomics in health care.

Rationale: The use of genomics in health care should be based on the best available knowledge, evidence and research and the outcomes of treatment should be used to help improve care.

4.1 Review and build on guidelines, regulations and standards to ensure genomic applications:

- are evidence-based;
- nationally consistent (where appropriate);
- demonstrate clinical utility; and
- align with agreed national ethical approaches.

Action: The SA Clinical Genomics Advisory Group will ensure that all CPGs, regulations and standards regarding genomic produced will be evidence-based, consistent with national guidelines, regulations and standards, demonstrate clinical utility and align with agreed national ethical approaches and ensure equity of access to services.

4.2 Strengthen processes to identify, promote, monitor and report best practice in clinical genomics, including storage and appropriate sharing of DNA resources, sharing of data and information, and reporting and communication of genomic test results for patients, families and other clinicians.

Action: Processes to identify, promote, monitor and report best practice in clinical genomics, including storage and appropriate sharing of DNA resources, sharing of data and information, and reporting and communication of genomic test results for patients, families and other clinicians to be included in the Terms of Reference for the SA Clinical Genomics Advisory Group.

4.3 Maximise genomics research opportunities that aim to resolve clinical uncertainty and improve quality and safety.

Action: Maximising genomics research opportunities that aim to resolve clinical uncertainty and improve quality and safety to be included in the Terms of Reference for the SA Clinical Genomics Research Advisory Group (see 3.3).

5. Data: responsible collection, storage, use and management of genomic data.

Rationale: The use of genomic data is essential to driving improvements in health outcomes for all Australians and providing a pathway to truly personalised health care.

5.1 Establish a state-wide genomic data governance framework that aligns with national and international frameworks.

5.1.1 Explore ICT and other infrastructure options for national genomic data collection, storage and sharing

5.1.2 Strengthen public trust of data systems and mechanisms so that people are empowered to engage with genomic interventions in the health system.

Action: Strengthening public trust of SA data systems and mechanisms so that people are empowered to engage with genomic interventions in the health system will be a key focus of the SA Clinical Genomics Communications Plan (see 1.1).

5.2 Promote culturally safe and appropriate genomic and phenotypic data collection and sharing that reflects the ethnic diversity within the Australian population, including for Aboriginal and Torres Strait Islander peoples.

Action: Work with the SA Health Translation Centre to ensure that culturally safe and appropriate genomic and phenotypic data is collected and shared so that all South Australians, Aboriginal and Torres Strait Islander peoples can benefit from genomic knowledge

5.3 Develop state-wide agreed standards for data/DNA/tissue collection, safe storage, data sharing, custodianship, analysis, reporting and privacy requirements that align with national standards.

Action: Work with consumers and interstate colleagues to adapt and or adopt wherever possible national standards for data collection, safe storage, data sharing, custodianship, analysis, reporting and privacy requirements that align with South Australian requirements

5.4 Promote public awareness of the contribution of all research activities, including those funded through private industry, to advancing the application of genomic knowledge to health care.

Action: Promotion of public awareness of the contribution of all research activities, including those funded through private industry, to advancing the application of genomic knowledge to health care to be included in the SA Clinical Genomics Communications Plan (see 1.1).

5.5 Support SA's engagement with national and international genomic alliances to promote shared access to data for research and global harmonisation of data where appropriate.

Action: Engagement with national and international genomic alliances to promote shared access to data for clinical diagnosis, research and global harmonisation of data where appropriate to be included in the Terms of Reference for the SA Clinical Genomics Research Advisory Group (see 3.3).

Next steps

These proposed priorities and actions describe *what* needs to be done. From these detailed work streams and implementation plans will be developed to determine *how* they will be done.

This work will be led by the SA Clinical Genomics Advisory Group in collaboration with the consumer groups, Local Health Networks, SA Pathology, the private sector, SA's universities and other stakeholders.

Appendix 1

The SA Clinical Genomics Advisory Group:

- Professor Paddy Phillips, CMO (Chair)
- Julia Overton, CEO, Health Consumers' Alliance
- Professor Katina D'Onise, Director, Prevention and Population Health, DHW
- A/Professor Janice Fletcher, Clinical Director, Genetics & Molecular Pathology, SA Pathology
- Professor Eric Haan, Clinical Geneticist, Adult Genetics Unit, Central Adelaide LHN (CALHN)
- A/Professor Christopher Barnett, Head, Paediatric and Reproductive Genetics SA Clinical Genetics Service, Women's and Children's Health Network (WCHN)
- Dr Nicholas Smith, Consultant Paediatrics Neurologist, WCHN
- Professor Randall Faull, Senior Consultant in Nephrology, CALHN
- Professor Geoff Higgins, Clinical Director, Microbiology and Infectious Diseases, SA Pathology
- Dr Nicola Poplawski, Clinical Geneticist and Lead Clinician - Cancer Genetics, Adult Genetics Unit, CALHN
- Dr Erin Symonds, Principal Medical Scientist, Bowel Health Service, Southern Adelaide LHN (SALHN)
- Dr Craig Wallington-Beddoe, Haematology Consultant, SALHN
- Dr Damian Clark, Paediatric Neurologist, WCHN
- Paul Monaghan, Chief Financial Officer, WCHN
- Dr Hendrika Meyer, Executive Director Medical services, Country Health SA LHN (CHSALHN)
- Anne Baxendale, Senior Genetic Counsellor, WCHN
- Dr Jacqui Adams, Clinical Director, Cancer Services CHSALHN; Clinical Director, Cancer Services NAHLN

For more information

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Interpreter