

PRECISION MEDICINE

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At a glance

- Precision medicine allows healthcare to be finely tuned to each individual. Properly implemented, it has the potential to shift the focus of the health system from the treatment of illness to the protection of health.
- It is enabled by recent advances in genomics, data analysis and availability, and artificial intelligence.
- Australia is well placed to benefit from precision medicine. Our healthcare system is admired internationally, our medical research is of high standard, and recent investments in the sector aim to create highly-skilled jobs, stimulate economic growth, and close gaps of health disadvantage.
- Public trust will be earned and maintained by ensuring security of data and quality of care, and by initiating community discussion about the benefits and the ethical and social implications of precision medicine.



INTRODUCTION

Every one of the nearly 8 billion people living on planet Earth is unique, a one-off combination of our genes and our personal history. What if our healthcare could be tailored to our individual needs, preventing disease, or responding with the best possible treatment, at the optimal dose, first time?

The concept of precision (or personalised) medicine isn't new.¹ What is new is the array of technologies emerging to enable it, and the scale at which these technologies can be provided.

Progress in **genomics** has seen the cost of a human genome sequence fall from over \$100 million at the turn of the millennium to \$1,000 today. This downward trajectory appears to be continuing (**Figure 1**).

Progress in **computing** allows massive datasets to be mined for insights into the relationships between genes, environmental factors and health.

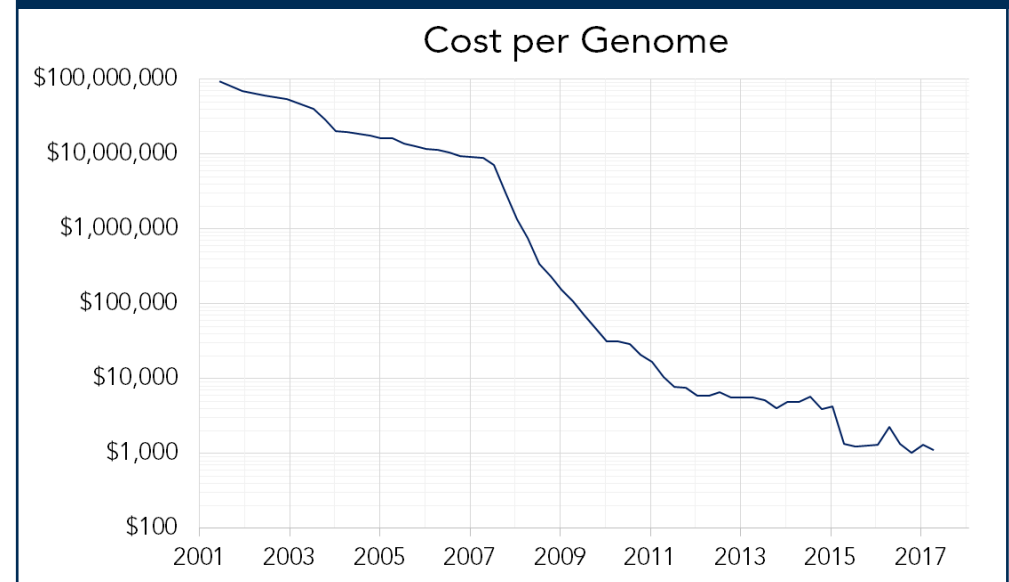
Progress in **connectivity** can enable the records generated through all our interactions with medical professionals to follow the patient over a lifespan, providing each doctor with a comprehensive picture of our individual health profiles.

Progress in **artificial intelligence** overcomes the cost and human capacity barriers to delivering custom-made medicine on a population scale.

The challenge for Australia is to harness these technologies for the benefit of every patient, ensuring that Australian healthcare – and Australian life expectancies – remain amongst the best in the world. That reputation for quality provides a strong foundation for attracting clinical trials, commercialising Australian technologies and building high-skill jobs.

This paper summarises the findings of '*The Future of Precision Medicine in Australia*', a horizon scanning report commissioned by the Commonwealth Science Council and published by the Australian Council of Learned Academies (ACOLA) in 2018.

Figure 1: Advances in genomics are driving down the cost of genome sequencing (US dollars).²



THE 2030 GOAL

The signature achievement of the twentieth century was the spread of expert healthcare – from a luxury only affordable for the elite, to an expectation of every Australian. To work affordably at that scale, access to healthcare is targeted at those in greatest need, and usually after symptoms appear. Community population screening is based on crude risk indicators such as age and weight, and the treatment that most commonly works is tried first, although it may prove to be unsafe or ineffective for an individual patient.

The great promise of the twenty-first century is the transition from universal standard care to universal precision care (Table 1).

	Now	2030
Health system	<ul style="list-style-type: none">• Reactive, treats the sick.• 'Average care' for the 'average' patient.	<ul style="list-style-type: none">• Predictive, preserves health.• Customised care for each individual.
Prevention	<ul style="list-style-type: none">• Large population screening based on coarse risk indicators: age, weight and cholesterol level.• Intervention when symptoms are present and advanced.	<ul style="list-style-type: none">• Genetic screening done early in life to provide individual risk profiles.• Early intervention before symptoms appear in individuals, reducing risk of disease and improving chances of recovery.
Treatment	<ul style="list-style-type: none">• The <i>most common</i> treatment is provided first.• Not always the safest or most effective.	<ul style="list-style-type: none">• The <i>right</i> treatment is provided first.• Personalised treatments maximise efficacy, avoid side-effects and are cost-effective.

Table 1: Health care today versus the precision medicine ideal

From reactive to preventive

Most medical problems are due to a combination of genes and environment. As research progresses, doctors will have access to an ever-expanding library of gene markers and life experiences linked to specific conditions, whether rare diseases (Box 1), or common chronic conditions. Precision medicine will help the healthcare sector to develop improved early intervention strategies and focus prevention efforts on at-risk groups, sparing the cost and trauma of treating people who are unlikely to develop a disease.

Dementia, for example, is the second leading cause of death in Australia.³ It is degenerative, irreversible and incurable. The most common form of dementia is Alzheimer's disease. Several genes have been identified that appear to increase risk with age.⁴ Researchers believe that early intervention for those at high risk will be the most promising way to postpone onset, improve quality of life and ultimately beat the disease.⁵ Genomic research enables asymptomatic individuals who are at high risk to be recruited for clinical trials to accelerate the discovery of effective therapies.

Box 1: Rare diseases

Around 7,000 rare diseases are recognised today, collectively affecting more than 300 million people.⁶ This means that about one in 25 people will suffer from a 'rare' disease. Fewer than five percent of these illnesses can currently be cured.

Leigh Syndrome is a 'textbook' rare disease that affects one in 40,000 newborns globally.⁷ It is a severe neurological condition that typically results in death in two to three years. World-leading research at the Murdoch Children's Research Institute in Melbourne is opening new paths to diagnosis and treatment. By sequencing the genome of a young boy with the condition, researchers were able to identify an extremely rare mutation that was responsible for his symptoms.

The effects of this specific mutation can be treated with high doses of two commonly available vitamins, and the boy is now a happy five year old. Genetic screening of his family members identified one of his siblings as a carrier of the mutation, who is now receiving preventative treatment and has avoided the disease.

First time, every time

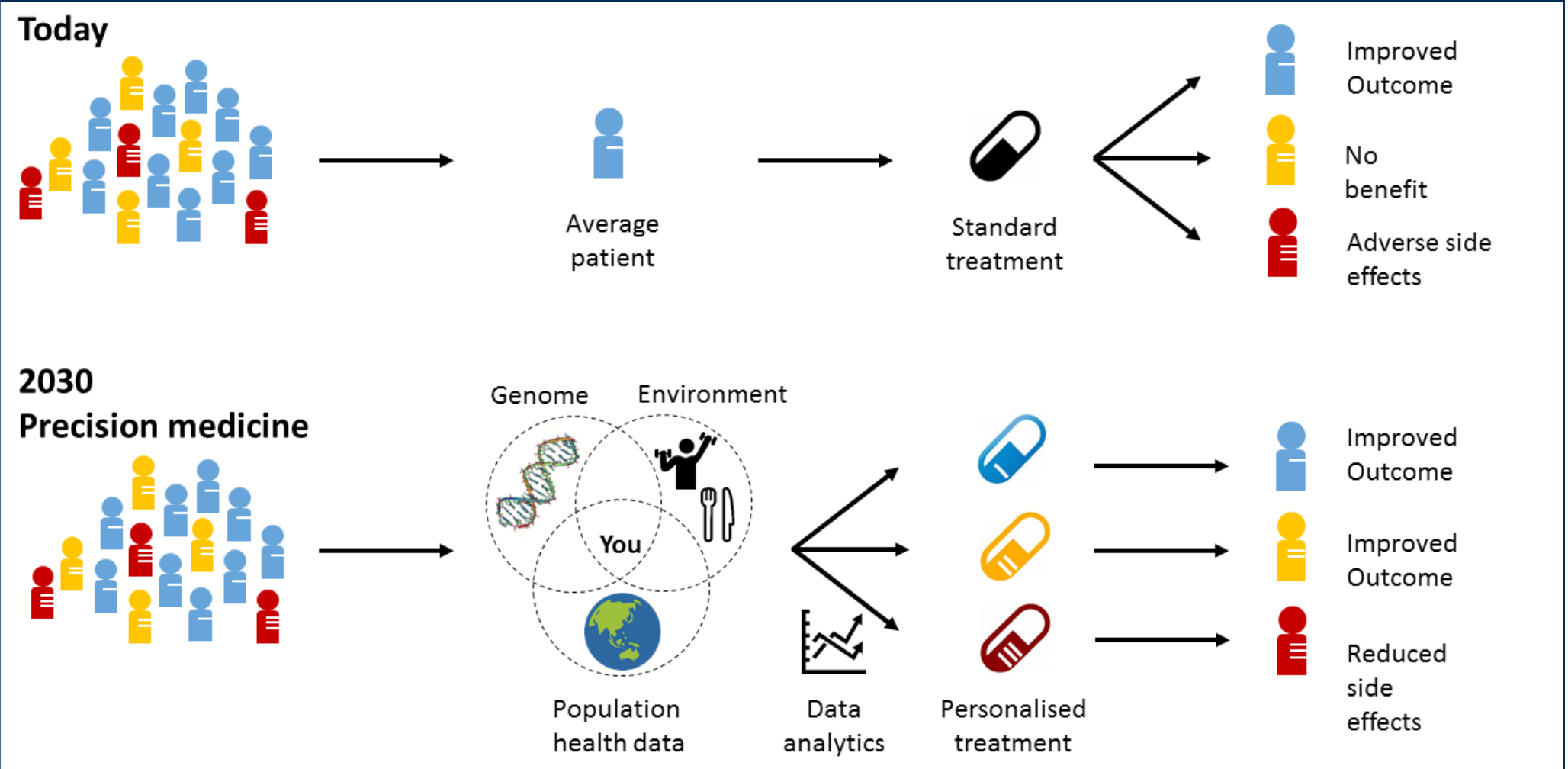
Today the management of conditions such as cancer involves a long, complex process of monitoring and evaluation. The 'trial and error' approach can consume precious time, and burdens patients with treatments that have no effect, or worse, have debilitating side effects.

Over time, advances in precision medicine will equip doctors to match patients to treatments that provide maximum efficacy and minimise debilitating side effects (**Figure 2**).

The Peter MacCallum Cancer Centre in Melbourne, for example, has demonstrated the potential for genetic testing in the treatment of tumours. In a recent example, a 56 year old woman was diagnosed with advanced lung cancer that continued to develop despite her undergoing radiotherapy, chemotherapy and surgery. A tumour biopsy revealed a mutation of the ALK (anaplastic lymphoma kinase) gene. This mutation is seen in four percent of lung cancers.⁸ Once identified, this condition can be treated by drugs that are designed to specifically inhibit activity of the ALK gene.⁹ One such drug is Ceritinib, which was prescribed to the woman as part of the study. After several months her tumour began to shrink and her symptoms improved.



Figure 2: Precision medicine builds on participation from the population. An individual has their genomic and environmental health data collected. This is analysed against population-wide records, allowing doctors to identify preventative treatments customised to benefit each individual.



AUSTRALIA'S OPPORTUNITY

Precision medicine is a funding priority across the world, with the US, UK, China and other nations making significant commitments over the last five years.^{10,11,12,13} National precision medicine strategies seek to accelerate the discovery of disease markers and therapies; prepare the healthcare sector to implement new treatment models cost-effectively at scale; and open pathways to investment in biomedical research.

Australia is a well-established player in the medical genetics field. In 1967, Professor David Danks ensured that Australia was one of the first countries to set up a clinical genetics research unit, based at Melbourne's Royal Children's Hospital, and supported by the National Health and Medical Research Council (NHMRC).¹⁴

Today, Australia is recognised as a global and regional hub for biomedical innovation.

More than 1,000 clinical trials commence in Australia every year across a broad spectrum of medical fields including oncology, central nervous system, infectious disease, metabolic disorders and cardiovascular diseases. Medicines and vaccines are Australia's largest manufactured export, supported by a reputation for quality products and robust regulation.¹⁵

These strengths, coupled with a world-class healthcare system, have ensured that life expectancies in Australia are amongst the highest in the world, and continue to rise.¹⁶

In 2018, Innovation and Science Australia (ISA) identified "using genomics and precision medicine to help Australia become the healthiest country on Earth"

as an ideal National Mission to catalyse activity around an audacious goal.¹⁷

Some of the building blocks are already in place, including

- the National Health Genomics Policy Framework, a scaffold to integrate the technology in an efficient, effective, ethical and equitable way across jurisdictions;¹⁸
- the Australian Genomics Health Alliance, a collaboration of 80 organisations including research institutions and clinical service providers;¹⁹
- the Commonwealth Government's announcement of a \$500 million, 10 year commitment to a *Genomics Health Futures Mission* in the 2018 Budget, following from the recommendation of ISA and informed by the ACOLA horizon scanning report.¹⁷



Australia's capacity for clinical trials will help increase the scale and sophistication of our medical research and development sector, and help researchers to tailor precision medicine approaches to the needs of an ethnically and culturally diverse population.

The \$50 million Australian Genomic Cancer Medicine Program, for example, is a clinical trial program involving eight major cancer centres and three leading research institutes.²⁰ 5,000 patients with rare cancers and advanced stage cancers will have their cancer genome individually sequenced, to improve our understanding of the genetic basis of these conditions and to trial cutting-edge immunotherapies targeted to the patient's specific cancer profile.²¹

A clinically-accredited and commercial-ready genome profiling platform is now being developed by the Garvan Institute of Medical Research, GenomeOne and Illumina. The platform will include a tumour profiling test and a national patient matching system for clinical trials. It aims to provide competitively priced and rapid local testing, helping to establish the viability of precision medicine approaches in best practice care.²²

We note that research supporting precision medicine is not an investment in isolation. It will also be relevant in fields as diverse as agriculture, environmental science, sports medicine and defence industries.

CHALLENGES

The emergence of precision medicine is transforming relationships between patients, clinicians, and industry. Its impact will rest upon its reception in the community.

Data and Privacy

Public awareness of data and privacy issues is growing and is particularly sensitive in the health sector.

There are many benefits that flow to patients individually from consolidating their medical data, including improved coordination of their medical care. Analysis of large-scale, de-identified data will also benefit the community by enabling research that was hitherto impossible or prohibitively labour-intensive.

The community will only have confidence in the use of their data if privacy is guaranteed. Every Australian should have ultimate control over the purposes to which their health data is put.

Maximising the pool of willing and informed participants contributing their data for research relies on responsible data custodianship, in line with community expectations. Governments and the medical community must continue to lead a public conversation explaining the benefits that flow to patients, individually and collectively, and informing all healthcare consumers about their rights and the protections in place.

Equity

Governments will need to ensure equal access to precision medicine for all patients, including groups such as Aboriginal and Torres Strait Islander Australians, individuals living in rural communities, and individuals at high risk of specific diseases, to help close gaps of health disadvantage. Understanding the interactions between genetic and environmental factors relies on large data sets from people who are healthy as well as those who are unwell, so it is important that data collection is comprehensive to enable researchers and clinicians to provide optimal care.

It is also conceivable that genomics, lifestyle and other data collected for healthcare could be used in unexpected ways to disadvantage an individual.

For example, under decades-old Australian legislation, life insurance applicants are required to disclose all relevant health information, including genetic test results done for reasons other than clinical purposes, such as for research or genealogy. Other countries have introduced laws to ensure that employment and life insurance are not unfairly denied to anyone due to such data profiles. Australia can learn from the experience of these jurisdictions in seeking to ensure that precision medicine does not come at unfair personal cost.

Health economics

Over time, precision medicine has the potential to shift the balance of health care spending from expensive lifetime management of chronic conditions to more cost-effective early intervention. By pinpointing the treatment most likely to succeed, it can cut expenditure on unnecessary tests and procedures.

This transition will challenge traditional models for both allocating resources in the healthcare sector and incentivising investment in medical research. Is there, for example, enough incentive for industry to develop expensive treatments that effectively and precisely cure a small number of patients? Governments and industry need to consider how to share risks for drug development, maximise patient access, involve those affected and their families, and ensure value for money across the healthcare sector.

Australia is not alone – these are global issues. However, as in other fields, Australia is highly respected internationally and can play a leading role in finding solutions that work at home and abroad.

CONCLUSION

Precision medicine has the potential to boost the years of active, healthy living that Australians enjoy, whilst opening new opportunities for Australian research to benefit the world. Its promise rests on our community-wide commitment to access, equity and innovation.

About the Authors

Dr Alan Finkel is Australia's Chief Scientist. Dr Adam Wright and Dr Shafique Pineda are from the Office of the Chief Scientist. Professor Robert Williamson is an Honorary Senior Principal Fellow at the University of Melbourne, and chaired the ACOLA expert working group for the ACOLA horizon scanning report "The Future of Precision Medicine in Australia".

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