

# Horizon Scanning Series

## The Future of Precision Medicine in Australia

### *Indigenous Health*

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#### **Suggested Citation**

Kowal, E, Watt, E, Weyrich, L, Kelaher, M, Tobler, R (2017). The Future of Precision Medicine in Australia: Indigenous Health. Input paper for the Horizon Scanning Project “The Future of Precision Medicine in Australia” on behalf of the Australian Council of Learned Academies, [www.acola.org.au](http://www.acola.org.au).

# Indigenous health

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## 1. Introduction

Aboriginal and Torres Strait Islander (henceforth Indigenous) peoples of Australia are the most disadvantaged group in Australian society. With respect to health, the “gap” between Indigenous and non-Indigenous outcomes is well documented. The life expectancy of Indigenous people at birth is 5-10 years lower than the general population (Cooke *et al.*, 2007; The Australian Institute of Health and Welfare, 2016), primarily because they suffer from high rates of chronic disease and at younger ages than other Australians. Indigenous Australians are 3-5 times more likely suffer from diabetes, 2.5 times more likely to have respiratory problems and 1.9 times more likely to die from chronic heart disease, which helps explain why the standardised death rate for Indigenous Australians is twice that of non-Indigenous Australians (Australian Bureau of Statistics 2013). This alarming disparity can be largely explained by many historical and sociological factors. Indigenous people are on average more likely suffer from racism and social exclusion and less likely to live near and utilise health services. Drug and alcohol misuse, smoking, low educational attainment, high unemployment, poor housing and poor nutrition are also common in Indigenous communities (Paradies, Harris and Anderson, 2008).

Australian governments have committed to reduce the health and social disadvantage experienced by the nation’s First Peoples. Investments in precision medicine are unlikely to benefit Indigenous Australians unless specific efforts are made to engage Indigenous people, families and communities and enhance Indigenous access to health care. Further, efforts to engage Indigenous people and enhance access are unlikely to succeed unless Indigenous people are given the opportunity to directly shape these measures. While addressing these socio-economic disparities is undoubtedly the most important step towards closing the “gap”, government initiatives aimed at improving Indigenous Australian health by correcting socioeconomic factors (for example, ‘Close the Gap’) largely failed to rectify Indigenous health disparities (Conifer *et al.*, 2017). Genomics and precision medicine may be a part of the solution to addressing Indigenous health inequalities, if Indigenous people are involved in their implementation.

Twenty-first century biomedicine has started to unravel the complex interactions between genomic and environmental factors that underlie all biological functions. An enhanced understanding of genomics has allowed for better prediction, detection, and treatment of certain cancers, rare diseases and many other conditions. However, Indigenous Australians are unlikely to benefit from these advances in the absence of reference data about genome variation in Indigenous populations. The role of genomics in Indigenous health cannot be understood solely from research on populations of European origin. Information on -omic’ variation (including genomic, epigenomic, metabolomic, microbiomic, and proteomic variation) in Indigenous communities is also needed (Moltke *et al.*, 2014). Without research data on population genetic variation and associations with health and disease in Indigenous communities, the potential for precision medicine to contribute to addressing Indigenous health inequalities will remain unclear. The lack of inclusion of Indigenous Australians in genome research is part of a global pattern. A 2016 study found that 80 per cent of the participants in Genome Wide Association Studies worldwide are European, while only 0.05 per cent of those classified are Indigenous (Popejoy and Fullerton, 2016). Even within these measures

Indigenous Australians are underrepresented relative to Indigenous groups in other countries (Kowal *et al.*, 2012).

Research with Indigenous communities in Australia using genome-wide association scans has so far analysed mutations associated with diabetes, rheumatic heart disease, and a cancer cluster, with research on genomic associations with end-stage renal disease still underway (Busfield *et al.*, 2002; Anderson *et al.*, 2015; McWhirter, Nicol and Savulescu, 2015). The small number and scope of these existing studies mean that any clinical translation is some time away. There is also great interest, but not yet any research, on the role of epigenetics in transgenerational transmission of disease risk related to experiences of trauma (Kowal, 2016) and the microbiome in noncommunicable diseases, such as obesity, diabetes, and cardiovascular disease.

If Indigenous Australians continue to be excluded from the research that leads to advances in precision medicine, then any health benefits that accrue from precision medicine may actually widen the health disadvantage. To avoid this scenario, it is critical that efforts are made to engage Indigenous people, families, and communities in precision medicine. The National Aboriginal and Torres Strait Islander Health Plan 2013-2023 includes four principles to support health equity by 2031: health equality, community engagement, partnerships and accountability. Genomics and precision medicine can play a part in this vision, but only if specific efforts are made to include Indigenous people. McWhirter and colleagues (2015) recommend the following steps to allow Indigenous people to benefit equitably from precision medicine:

1. ensure diversity of participants by implementing appropriate protocols at the study design stage;
2. target diseases that disproportionately affect disadvantaged groups;
3. prioritise capacity building to promote Indigenous leadership across research professions;
4. develop resources for consenting patients or participants from different cultural and linguistic backgrounds; and
5. integrate awareness of issues relating to Indigenous people into the governance structures, formal reviews, data collection protocols and analytical pipelines of health services and research projects (McWhirter, Nicol and Savulescu, 2015).

These principles and step make it clear that Indigenous people must be central to any efforts to making precision medicine inclusive, not least in order to ensure that Indigenous approaches to decision making and governance are adhered to. The final part of the chapter addresses options for Indigenous governance of and participation in precision medicine.

In addition to issues of Indigenous governance, attention should be paid to the distinct cultural beliefs and historical experiences of Indigenous Australians. These will influence the engagement of Aboriginal and Torres Strait Islanders in the field and ensure that benefits are broadly accessible, not restricted to the “privileged few” (Popejoy and Fullerton, 2016).

## 2. Cultural values

Indigenous Australians have unique and diverse cultural viewpoints. Although difficult to generalise given the diversity of Indigenous peoples, there are two primary ways that genomics and precision medicine may clash with Indigenous belief systems.

Firstly, genomic accounts of population structure may challenge Indigenous peoples’ understanding of their origins and relatedness. Historically, Indigenous Australians conceive of themselves as products of a process known in English as “the Dreaming” – the ongoing mythic work of creator ancestors. There is a potential conflict between this view and the mainstream scientific view that the

ancestors of contemporary Indigenous Australians are descended from the first modern humans to leave Africa, reaching the continent of Sahul up to 65,000 years ago. Based on their own deep-time creation myths, many Native Americans have challenged scientific views that their ancestors crossed the Bering Strait 15,000 to 45,000 years ago. In Australia, however, Indigenous attitudes towards genetic accounts of their history have been more favourable (Kowal, 2012), perhaps in part because research has bolstered Indigenous claims to remarkably ancient connections to country (Malaspina *et al.*, 2016; Tobler *et al.*, 2017).

The second way in which genetic research may challenge Indigenous views relates to traditional ideas about the spiritual significance of biological specimens. The different ways that geneticists and Indigenous peoples may conceive of bio-specimens and genomics has led to public disputes between Native Americans and scientists in the US, Canada and Brazil (National Centre for Indigenous Genomics, 2017). Blood has immense metaphoric value in many indigenous communities across the world, including Indigenous Australia (Copeman, 2009; Carsten, 2013). This may deter Indigenous people from participating in the genomic research that is required if they are to benefit from precision medicine. It is impossible to make firm conclusions, however, because of the absence of empirical research on this issue. In the single paper of relevance here, Indigenous participants in a Darwin-based study on diabetes risk who consented to long-term storage of their blood samples tended to come from older non-smokers with some non-Indigenous grandparents, whose consent forms were administered by Indigenous staff members (Cunningham and Dunbar 2007 see also (Sahota, 2014)). This suggests that trust in the researchers and research institutions is crucial to encourage the participation of Indigenous Australians in genomic research and precision medicine.

### 3. Historical issues

Indigenous peoples' experiences of dispossession, marginalization, and oppression have led many to distrust Western institutions and mainstream Australian society in general. Scientific institutions may be particularly suspect as past researchers have appropriated artefacts, information, and bio-specimens without consultation, consent, or compensation and have used this information to develop systems of racial classification that validated attempts to exclude Indigenous people from mainstream Australian society, or at other times and places, biologically absorb them into the White majority (see for example, Anderson 2002, Douglas and Chesterman 2008).

Genetics has featured in this history of mistrust. An important example was the Human Genome Diversity Project (HGDP) in the mid-1990s which sought to collect samples from Indigenous groups around the world. Australia did not participate in the Project and Mick Gooda, who was then the Aboriginal and Torres Strait Islander Social Justice Commissioner, raised concerns about the "Vampire Project". He noted in particular the possibility of "the cultural, political and social complexity of Indigenous identity and Aboriginal rights being reduced to an arbitrary genetic test" (Human Rights and Equal Opportunity Commission 1996). Aboriginal scholars have also raised concerns that genetics research could revive old ideas about their biological difference from – and inferiority relative to – the White majority (Hook, 2009). However, as the Darwin study cited above suggests, it is possible to engage Indigenous people in biomedical studies with free and informed consent, if a rigorous community engagement strategy is developed and maintained (Sharp and Foster, 2002; Couzos *et al.*, 2005; Arbour and Cook, 2006). As Chapter **Error! Reference source not found.** suggests, engagement efforts around precision medicine need to be capable of accommodating diverse interests and beliefs, to ensure both the viability of the field and the safeguarding of Indigenous (and other patient' and citizen') interests.

#### 4. Access to health services

Even if these cultural and historical barriers are overcome, equitable access to precision medicine requires equitable access to health services. Indigenous Australians lack access to health care services, particularly specialist services (Gruen *et al.*, 2001). Despite having a higher incidence of many genetically determined conditions that may benefit from precision medicine (Condon *et al.*, 2009; Hoy *et al.*, 2012), including some cancers, renal disease, and neurodegenerative conditions such as Machado Joseph Disease, Indigenous people are under-represented in patient populations of genetic services (for example, by approximately two-thirds in the NT). This is in spite of evidence of a demand for these services (Garvey and Bernardes, 2012). Australia must close the gap of health care access more widely, if precision medicine is also to contribute to closing the health gap.

#### 5. Options for indigenous engagement and ownership

Australian researchers and health care providers have an obligation to engage Indigenous people in any research or health care that seeks to benefit their communities. The relevant Indigenous people or community should be provided with the resources necessary to shape these efforts according to their own governance and decision-making processes. One example of this occurring at a national scale is the National Centre for Indigenous Genomics at the Australian National University (Kowal, Easteal and Gooda 2016). Indigenous engagement and control of research is facilitated through an Indigenous-majority Governance Board, an Indigenous Collection Access Committee, an identified Indigenous Engagement Officer position, and Indigenous members of the Advisory Board, including Indigenous community representatives. While most precision medicine initiatives will have a broader scope than Indigenous people alone, and therefore may not involve Indigenous governance on this scale, the National Centre for Indigenous Genomics offers practical examples of Indigenous governance that other projects can draw on.

Ensuring that advances in genomics and precision medicine narrow, and not widen, the gaps of health disadvantage is an ethical issue. However, there is also much to gain practically from including Aboriginal and Torres Strait Islander Australians in advanced health care. Measures taken to engage Indigenous communities may lead to innovations that have wider relevance. For example, as a result of engaging with Maori communities and elders, the Christchurch Tissue Bank in New Zealand offers their participants the option of having their sample disposed of with a Maori blessing or karakia when it is no longer required for research. This option is taken up by many non-Indigenous biobank participants as well (Morrin *et al.*, 2005). The dynamic consent practices proposed by the National Centre for Indigenous Genomics are another example of innovative practice with potential for wider application (National Centre for Indigenous Genomics 2017). The dynamic consent model allows biobank participants to be informed of how their samples are being used for, with the option of opting out of particular projects while maintaining participation in the biobank (Kaye *et al.*, 2015). In this way, the inclusion of Indigenous Australian in genomics and precision medicine can have wider impacts on the practice of 21<sup>st</sup> century Australian biomedicine.

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