Genetic Testing and Genomics in Medicine

2020

1. Preamble

1.1 Genomics (the study of an individual's genetic material and the influences of environmental and other factors) and genetics (the study of individual genes and associated inherited conditions and traits) is one of the most rapidly evolving areas of medicine. New developments in genetic and genomic testing have the capacity to rapidly transform health care in Australia potentially providing more cost-effective treatments and improving patient outcomes;[1] for example, by improving diagnostic accuracy for many conditions and allowing doctors to develop more patient-specific preventive and targeted interventions.[i]

1.2 Considering the potential health benefits of genetic and genomic advances, these technologies should be incorporated into everyday health care. Equitable and efficient access to safe, evidence-based, genetic and genomic testing services throughout Australia is vital but requires appropriate infrastructure and a genomic literate workforce.

1.3 In addition, the ethical, economic and social issues associated with genetic and genomic testing must be addressed to remove any barriers and disincentives and allow equitable access to these services.

1.4 This position statement outlines ways to improve access to genetic and genomic testing services throughout Australia.[2]

2. Genetic information and genetic testing

2.1 There are certain features of some types of genetic information that distinguish it from other (non-genetic) health information. For example, genetic information can be relevant to non-heritable (also known as non-familial) conditions and/or heritable (also known as familial) conditions and can potentially predict an individual's risk of developing certain conditions or health problems in the future.

2.2 Somatic genetic testing involves testing a specific tissue for variants that have occurred after birth and are known to be associated with disease of that tissue. Somatic genetic tests can confirm a precise disease diagnosis and provide prognostic and therapeutic information that leads to targeted treatment for specific variants.[ii]

2.3 Genetic testing for heritable conditions, also known as germline genetic testing, differs from somatic genetic testing in that it can reveal information relevant to heritable conditions or those involving multiple genes. Germline genetic testing can reveal information about the genetic status of a person's genetic relatives (even if the genetic relatives have not been tested).[iii] This type of genetic information is often referred to as 'shared genetic information' and may be used

[1] Genetic testing may be undertaken for a variety of reasons such as paternity testing, ancestry determination, forensic and health care issues. This position statement focuses on genetic testing for health care issues.
[2] For the purposes of this position statement, 'genetic testing' will refer to both genetic and genomic testing unless otherwise specified.

to assist individuals and their genetic relatives identify both risks and relevant interventions to prevent or reduce the morbidity of a heritable condition. Testing positive for a particular variant does not necessarily equate to being affected by that condition.

2.4 Predictive genetic tests can determine if an asymptomatic person with a family history of a particular disorder has inherited the relevant variant. If the variant is present, the person has an increased chance of developing the disorder; however, not everyone who carries a mutation will develop the condition and it can be difficult to predict accurately the age of onset of the condition, its rate of progression, severity, life expectancy or even whether the person will ever develop the condition.[iii] Other factors play a role in disease development including environment, lifestyle, complex interactions between inherited genes, spontaneous variants occurring during life and chance.[iii] The benefit of predictive genetic information is that an individual with a higher risk of developing a particular condition can undertake lifestyle changes (such as routine screening) that can reduce the chance or severity of disease development.

2.5 In addition to diagnostic and predictive tests, genetic testing is used in a number of other clinical contexts; for example,

- pre-symptomatic genetic tests determine if a person with a family history but no symptoms of a specific condition has inherited the relevant mutation. If the mutation is present, the person is at increased risk of developing the condition;[iii]
- pharmacogenomic tests may help determine whether an individual's genomics are likely to affect their response to a particular medication or treatment, allowing individualisation of care;[iv]
- carrier tests determine if an individual carries a particular heritable mutation (or mutations) that, if also inherited with another pathogenic variant, may affect the health of future offspring (reproductive carrier screening);
- pre-implantation genetic diagnostic tests determine if an embryo carries a mutation for a particular genetic condition;[v]
- tests in pregnancy can estimate the probability that a fetus carries a genetic condition (antenatal screening) or confirm a diagnosis of a genetic condition (antenatal diagnosis).[v]

2.6 Different genetic tests have different requirements for consent and the protection of personal genetic information. Somatic genetic tests can be treated the same as other medical tests;[ii] however, genetic tests that reveal shared, pre-symptomatic and/or predictive genetic information - or have reproductive implications - require careful discussion and consideration prior to testing (as outlined below).

3. Consent to genetic testing and the protection of personal genetic information

3.1 Genetic testing should only be undertaken with the patient's explicit consent (or, for patients who lack decision-making capacity, the explicit consent of the appropriate substitute decision-maker). As with any medical test, it is essential to ensure individuals are fully informed of the potential risks and benefits of genetic testing.[3]

3.2 In certain circumstances, pre-test and post-test genetic counselling should be provided. Genetic counselling aims to help individuals, couples and families understand and adapt to the medical,

[3] For guidance on patient consent, refer to the AMA *Guidelines on Maintaining Clear Sexual Boundaries Between Doctors and Patients and the Conduct of Patient Examinations 2019* and the AMA *Ethical Guidelines for Doctors on Disclosing Medical Records to Third Parties 2015.*

psychological, familial and reproductive implications of the genetic contribution to specific health conditions.[4] Examples where pre-test and post-test counselling is essential include:

- where an individual is considering undertaking pre-symptomatic or predictive genetic testing for a significant heritable disorder;
- where a parent(s) is considering having their child undertake pre-symptomatic or predictive genetic testing for a significant heritable disorder;
- where a couple are considering testing their fetus for a genetic abnormality or a significant heritable disorder.

3.3 In general, children should only undergo pre-symptomatic or predictive genetic testing when the resulting information will be used to manage their health in the immediate future; otherwise, testing should wait until the child has reached an age where they can consent on their own behalf.[iii, vi]

3.4 An individual has the right to withdraw from genetic testing and to require that their sample be destroyed at any time before the genetic test results are relayed to them.

3.5 Unless required by law, there should be no compulsion or coercion of any person to undertake a genetic test.

3.6 Genetic information unrelated to the reason for testing may be revealed by modern genetic testing technologies. Each laboratory and clinical service should have a policy that defines how this information should be managed. Appropriate disclosure and referral for counselling should occur, where indicated. As information on the genome and disease grows, it is likely that information considered unremarkable today could prove significant in the future.

3.7 Patients and clinicians should be aware that genetic information can be stored. Clinicians and pathologists will need to develop systems for management of this information.

3.8 In general, genetic information acquired in the context of the doctor-patient relationship should not be disclosed to a third party without the patient's specific and, where possible, written consent.[5] This not only includes genetic test results but also whether a person has undertaken a genetic test or sought genetic counselling.

3.9 Genetic testing for heritable conditions poses particular challenges to confidentiality. Genetic information relevant to the individual who has been tested may have implications for the health of their close genetic relatives. In the case of a positive test result the individual tested should be encouraged to discuss the test results with their close genetic relatives. In situations where a patient does not provide consent, privacy legislation allows a doctor, in exceptional circumstances, to use or disclose a patient's genetic information where there is reasonable belief that doing so is necessary to lessen or prevent a serious threat to the life, health or safety of their genetic relatives.[6] It is important to consider, however, that family member(s) who have not undertaken genetic testing may not want to know their own genetic status or have their genetic status known to others.

[4] As defined by the Australasian Society of Genetic Counsellors. Definition of Genetic Counselling. https://www.hgsa.org.au/asgc/definition-of-genetic-counselling

[5] As with any personal health information, there may be an exception to patient consent if authorised or required by law.

[6] For further information on the disclosure of genetic information to genetic relatives, refer to the National Health and Medical Research Council. *Use and disclosure of genetic information to a patient's genetic relatives under Section 95AA of the Privacy Act 1988 (Cth). Guidelines for health practitioners in the private sector.* Commonwealth of Australia. 2014.

3.10 Genetic information about a deceased individual might have implications for the health, confidentiality and privacy of living genetic relatives; however, there are special ethical and legal issues that arise in relation to the disclosure of the deceased individual's genetic information to a third party. Genetic information about a deceased person might be subject to legal duties of confidentiality. Unless required by law, consent should normally be sought from the executor or appointed administrator for genotyping the stored identifiable tissue of a deceased individual.

4. Genetic discrimination and the protection of personal genetic information

4.1 It is essential that genetic discrimination be prohibited.

4.2 Attendant with the benefits of genetic testing comes the possibility of genetic discrimination where an individual, their family members or community perceive they are being treated unjustly or unfairly by a third party (such as a life insurer or employer) based on their real or perceived genetic status.[vii]

4.3 The fear of genetic discrimination may deter some individuals from undertaking clinically indicated genetic testing (or participate in genetic research) that could benefit their health. For example, a person may forego a clinically indicated genetic test that determines their risk for developing a particular type of cancer because they fear a third party such as a life or travel insurer may deny them insurance or increase their premiums due to their genetic risk.

4.4 A patient's genetic status should never be used to limit their access to medical care.

5. Direct-to-Consumer (DTC) Genetic Tests

5.1 DTC genetic tests are offered on a commercial basis directly to consumers and without referral or consultation with a doctor or other health care professional.[viii]

5.2 DTC tests for health matters are particularly problematic as the individual might receive test results that are inaccurate, contradictory, misleading and, taken out of context, may be open to misinterpretation.[viii]

5.3 In the context of providing health care, genetic testing should only be undertaken with a referral from a doctor as there is no consistent oversight of DTC genetic testing services internationally and some countries may exert little or no regulatory control over DTC tests.[7,viii]

5.4 Further, a doctor can discuss the risks, benefits and appropriateness of genetic testing with patients, interpret the test results and, if appropriate, provide or refer the patient for pre-test and/or post-test counselling.

5.5 Patients considering using a DTC genetic test should discuss the risks, benefits and appropriateness of DTC genetic testing with their doctor first. If a patient has already undertaken a DTC genetic test, they should be encouraged to discuss the test results with their doctor.

5.6 Doctors require adequate and ongoing education and training in facilitating informed patient choice regarding DTC genetic testing. Doctors should be able to discuss the risks of DTC genetic

[7] Overseas DTC genetic testing services may not follow the standards that Australian laboratories are required to follow. The AMA supports the current system of accreditation (NATA/RCPA) as an essential part of ensuring quality standards across the industry.

testing for patients seeking information about them and support those patients who have already undertaken DTC genetic testing in the use and interpretation of test results.

5.7 Public awareness campaigns and educational resources should be targeted at consumers to highlight the potential risks of DTC genetic testing.

6. Increasing access to genetic testing services throughout Australia

6.1 There should be a national approach to the provision and regulation of genetic testing to ensure equitable and efficient access to safe, evidence-based genetic testing services throughout Australia.

6.2 Genetic testing and associated counselling in health care requires a multidisciplinary approach with a range of health professionals and community support groups. There should be a sufficient health care workforce to support the use of genetic testing in mainstream health care as well as appropriate infrastructure to ensure that individuals have access to genetic testing, relevant health care professionals, pathology services, specialist genetic services and counselling services regardless of where they live.

6.3 In particular, there should be appropriate workforce planning and investment in training and development to ensure an ongoing high-quality genetic pathology-related workforce.

6.4 Geographical and economic access to pathology services should provide safe, affordable and timely access to quality genetic testing for all patients in Australia. The current balance and mix of public and private services ensure Australia has a diversity of pathology providers with different areas of expertise that can provide a wide range of services. Neither the public nor private sectors have sufficient capacity to meet demand alone. To ensure equitable and affordable patient access, genetic testing services should be available from public and private pathology providers.[ix]

6.5 Every doctor will need sufficient knowledge and understanding of the principles of human genetics and their application to a wide variety of clinical settings.[x] All doctors should continue their education and training in genetic issues throughout their career, recognising that this is a rapidly moving field. Education and training should include the clinical, ethical, legal and social implications of genetic testing, skills in genetic counselling and innovations in genetic testing including the expansion and implication of direct-to-consumer genetic testing.

6.6 There should be a national approach to raising public awareness of the risks and benefits of genetic testing including promoting reasonable expectations of the benefits of genetic testing as well as the shared nature of genetic information.

6.7 Wherever possible, genetic testing should be performed in Australia. This will ensure that data from the Australian population, particularly for indigenous peoples, is available to assist with variant interpretation.

6.8 Genetic support groups and related community organisations play an important role in the community. They promote the interests and well-being of those affected by genetic conditions and provide information, resource materials and other support services to affected individuals and their families as well as to health care professionals. Genetic support groups reflect the cultural sensitivities associated with many genetic conditions and the role of these groups should be promoted and respected.

7. Research

7.1 Ongoing research into genetic testing and genomic medicine is required in order to better understand how genes work and their impact on health, leading to the development of new and improved clinical genetic testing.

7.2 Genetic research should be conducted under appropriate ethical and regulatory guidelines in secure environments according to recognised national and international standards.

8. Gene and genetic patents

8.1 The AMA supports the current legislation that prohibits the patenting of human genes.

8.2 The holding of patents should not infringe the principle that the human genome is the common heritage of humanity.

8.3 The holding of patents should not present an obstacle to the diagnosis, prevention, management and treatment of disease.

9. Genetic selection

9.1 The AMA condemns the practice of eugenics.

9.2 Genetic testing of embryos created through IVF (*in vitro* fertilisation) is undertaken to screen for or diagnose unspecified or specified genetic or chromosomal abnormalities prior to embryo transfer. Embryos identified with an abnormality can then be excluded from transfer.[v] In the absence of effective therapy, genetic testing of pre-implantation embryos or of a fetus should be restricted to potentially fatal or seriously and permanently disabling diseases.

9.3 Genetic selection should not be undertaken on the basis of sex unless it is to reduce the risk of transmission of a sex-dependent condition or disease that would severely limit the person's quality of life.[xi]

10. Genome editing

10.1 Genome editing involves removing, inserting or replacing DNA in a genome. These techniques can be used to correct mutations that cause disease or to introduce new mutations to alter gene function in order to prevent or treat disease.[xii]

10.2 The two major types of gene editing are somatic genome editing and germline genome editing. Somatic genome editing is undertaken on cells that cannot contribute to gamete formation and thus cannot be passed on from the individual to their offspring. Germline genome editing occurs in a germ cell or embryo and results in changes that could be passed on from the individual to their offspring.[xii]

10.3 Somatic genome editing for research purposes may be acceptable so long as such research is in accordance with relevant Australian research guidelines, regulations and legislation.

10.4 Germline genome editing is a rapidly advancing field; however, it requires further scientific, ethical and social consideration as the potential risks to the health of future generations is unclear at this time. Germline genome editing for the purposes of reproduction should be prohibited at this time.[xii] Should germline gene editing become legal in the future, it should be highly regulated.

10.5 Germline gene editing for research purposes (and not for reproduction) may be acceptable so long as such research is in accordance with relevant Australian research guidelines, regulations and legislation.[8]

[i] National Health & Medical Research Council (NH&MRC). Health Advice. Genomics. (https://www.nhmrc.gov.au/health-advice/genomics)

[8] For example, the *Research Involving Human Embryos Act 2002* and the *Prohibition of Human Cloning for Reproduction Act 2002*.

[ii] National Health & Medical Research Council. *Medical Genetic Testing: Information for Health Professionals.* April 2010.
[iii] Human Genetics Society of Australasia. *Guideline. Pre-symptomatic and Predictive Testing for Genetic Disorders* (2014GD02). March 2014.
[iv] National Health & Medical Research Council. *Personalised Medicine and Genetics.* NHMRC REF #G4. November 2013.
[v] The Royal Australian and New Zealand College of Obstetricians and Gynaecologists. *Prenatal Screening and Diagnostic Testing for Fetal Chromosomal and Genetic Conditions.* July 2018.
[vi] Human Genetics Society of Australasia. *Guideline. Pre-symptomatic and Predictive Testing for Children and Young Adults.* (2013PS03). August 2014.
[vii] National Health & Medical Research Council. *Genetic Discrimination*. NHMRC REF#G1. November 2013.
[viii] National Health & Medical Research Council. *Discussing Direct-to-Consumer Genetic DNA Testing with Patients. A Short Guide for Health Professionals.* NHMRC REF#G7. December 2013.
[ix] Australian Medical Association*. Position Statement on Pathology 2019*.
[x] Human Genetics Society of Australasia. *Core capabilities in genetics for medical graduates.* 18 August 2018.
[xi] National Health and Medical Research Council. *Ethical guidelines on the use of assisted reproductive technology in clinical practice and research.* 2017.
[xii] American Society of Human Genetics. *Position Statement. Human Germline Genome Editing*. The American Journal of Human Genetics 101: 1-10. 2017. Position Statement endorsed by Human Genetics Society of Australasia.