Introduction

This position statement refers to pre-symptomatic and predictive genetic testing in relation to children and young people who have a family history of a heritable condition but who do not have symptoms or signs of the condition. Neonatal screening is not considered in this document nor is carrier testing in minors which is the subject of a separate position statement.

The term ‘pre-symptomatic testing’ applies if a person with a specific mutated gene is almost certain to develop the condition during their lifetime (if they live a normal lifespan). Familial adenomatous polyposis (FAP), Huntington disease, and autosomal dominant spinocerebellar ataxia are examples of conditions to which this term applies. The term ‘predictive testing’ is used where a person with the mutated gene has an inherited predisposition to develop the condition i.e. is at increased risk but may never develop the condition unless other factors are present. These include other gene(s) and/or environmental factors. Testing for mutations in the BRCA1 and BRCA2 genes (familial breast cancer) and the MLH1, MSH2, MSH6 and PMS2 genes (Lynch syndrome) are examples of predictive testing.

For the purposes of this document, the term young person/people refers to those under 18 years of age, 18 years being the legal age of majority throughout Australasia.

Pre-symptomatic and predictive testing for people of any age raises complex issues for individuals and families. It differs from diagnostic testing in that psychosocial sequelae may occur far into the future, not only for the individual being tested but also for other family members whose genetic status may be revealed in the process. These issues and guidance in providing pre-symptomatic and predictive testing are addressed in more detail in the HGSA guidelines for Pre-symptomatic and Predictive Testing for Genetic Disorders.¹
In relation to pre-symptomatic and predictive testing in children and young people for adult-onset disorders, the issue of cognitive and psychosocial maturity is of key importance to the young person’s ability to understand genetic concepts and make informed decisions. The decisions they make might have long term consequences for psychological health, social circumstances, relationships, employment and insurance. These issues have been carefully considered in the development of this position statement and the rationale that follows.

**Background**

**Evidence from research with adults undergoing pre-symptomatic or predictive testing**

Pre-symptomatic genetic testing has been available for Huntington disease (HD) for longer than any other adult-onset genetic condition. While risk factors for psychological sequelae have been identified, few adverse events have been described. Two long-term follow up studies found significant reductions in distress compared to baseline for both non-carriers and carriers. However, about 50% of the original cohorts were lost to follow up, and neither study performed an analysis of participation bias; consequently it is not known whether those lost to follow up differed systematically from those who were retained. A third long-term follow up study, on the other hand, assessed participation bias and found that carriers who were lost to follow up reported more distress pre-testing, compared with retained carriers, which means that post-test distress amongst carriers may have been underestimated. Another longer term follow-up study showed that a significant minority of mutation negative individuals did not cope well with their result, reinforcing the importance of psychosocial support for both mutation positive and mutation negative individuals.

One issue with all long term follow-up studies in HD is that none have compared psychopathology in mutation positive individuals who have had predictive testing with a matched cohort who are mutation positive but unaware of their genetic status. Ascribing psychopathology to knowledge of mutation positive status may not be correct at least in some individuals since it is becoming increasingly apparent that mutation positive individuals can experience impacts of disease for many years prior to formal diagnosis. Thus psychopathology identified in mutation positive individuals many years after predictive testing may at least in part be due to the disease itself and not a reaction to knowledge of mutation positive status.

There is evidence that individuals who choose to be tested tend to be psychologically robust, thus self-select for a favourable response to testing, which suggests that findings of studies on the psychological impact of genetic testing for HD may not be generalisable to the population of individuals at risk of HD at large. Moreover, by their very nature, cohort studies are based on average group responses, meaning that the minority of participants with adverse outcomes may not be adequately described. However, adverse outcomes have been documented in the context of pre-symptomatic genetic testing for Huntington disease including hospitalisation for psychological distress.

A substantial body of literature has also become available on the psychological impact of predictive genetic testing for hereditary breast/ovarian cancer susceptibility. Most studies on the psychological impact of genetic testing for cancer susceptibility amongst individuals who have
never been affected by cancer demonstrate that mutation negative individuals derive significant psychological benefits from genetic testing, while few adverse effects have been observed amongst those mutation positive.12

**Evidence from research related to children/young people undergoing pre-symptomatic and predictive genetic testing**

There is little empirical evidence available on the impact of pre-symptomatic or predictive genetic testing amongst children/young people where no prevention/treatment is available in childhood (e.g. testing for HD or hereditary breast/ovarian cancer).

An international survey of clinical geneticists in 2003 reported 49 cases of pre-symptomatic or predictive testing in young people for conditions which generally have onset in adulthood and for which no medical benefit of testing exists.13 The most common condition tested for was HD. In 22 cases (45%), the young person tested was immature (defined as under the age of 14 years). Results were disclosed to only two immature young people and in three cases parents experienced anxiety related to how they would pass on information to their mutation positive child. In 27 cases (55%), the young person tested was classified as mature (see note below*). Results were disclosed to 26 mature young people and it was reported that two individuals experienced a minor negative psychological impact. Consistent follow-up did not take place and findings represent the minimum frequency of adverse events. The majority of respondents agreed with existing guidelines but many believed each case must be considered individually.

(*Note that this article uses the words immature/mature with reference to age, not cognitive or psychosocial maturity).

A study reported in-depth interviews with eight young adults who had undergone pre-symptomatic testing for HD between the ages of 17 and 25 years.14 Although not all participants were minors at the time of their test, this research is an indication of young peoples’ experiences of waiting to be tested and then undergoing testing. Findings indicated that many of these young people had been living with the assumption that they were mutation positive prior to their test and several were engaging in high levels of risk behaviour. For some, the uncertainty about their genetic status was distressing and a barrier that prevented them from moving forward in life. Testing alleviated these barriers in some cases and facilitated positive behavioural changes. All of the young people who took part in the study had actively sought testing themselves. It is also possible that those who agreed to be interviewed for this study were those who were coping best.

A qualitative study detailed interviews with nine young people who had predictive testing for adult onset disorders prior to 18 years of age. Six of these young people were mutation positive and no major harms from the genetic test result were identified.15 The major harms identified by the young people were a result of the prolonged process they were generally required to undergo prior to testing taking place. None of the young people regretted undergoing testing. The young people in this study also all actively sought testing themselves.

The literature on the psychosocial impact of pre-symptomatic genetic testing for FAP provides a useful context relevant to the issues being considered here, although there are preventative measures available in FAP. Young people are routinely tested for FAP as a consequence of the preventative measures available, but debate still exists about the way in which this is performed,
particularly in relation to developmentally appropriate care. Several studies have examined the short to medium-term impact of undergoing pre-symptomatic genetic testing for FAP in children and adults. While it appears that the majority of children and adults are not adversely affected by pre-symptomatic genetic testing for FAP, there is evidence that some individuals experience clinically significant levels of psychological morbidity after testing. Codori et al. conducted a large prospective study of the impact of genetic testing for hereditary colorectal cancer in 48 children aged 10-16 years, during the first five years after testing. Overall no evidence was found that genetic testing had a negative impact on psychological outcomes. However, subgroups of children were demonstrated to have experienced negative outcomes.

Position Statement

The interests of the young person, the parents and the family need to be considered in relation to pre-symptomatic and predictive testing of a young person. The benefits and harms should be categorised into short and long-term medical, psychosocial and reproductive issues. Ultimately, the best interests of the young person must prevail, and it is important that the health professional be an advocate for the young person during the genetic counselling process.

Conditions for which there is potential medical benefit in the immediate future

Pre-symptomatic and predictive testing should be offered to children and young people for conditions in which the result is likely to be of direct medical benefit to the young person through surveillance, use of prevention strategies, or other medical interventions in the immediate future, eg. FAP, or in the situation where the result may be used for decisions by the young person regarding reproductive options including prenatal diagnosis and preimplantation genetic diagnosis.

Conditions for which there is no medical benefit in the immediate future

The HGSA recommends that pre-symptomatic and predictive testing for adult onset conditions should not be undertaken for young people who lack the maturity to appreciate the implications of the test and thus are unable to provide informed consent, either at their own request or at the request of parents/guardians, where:

- There are no treatment(s) that are proven to alter the natural history of the condition and knowledge of genetic status provides no medical benefit in the immediate future, such as Huntington disease (HD) and autosomal dominant spinocerebellar ataxia; or
- Potential medical benefits do not occur until adulthood, such as hereditary breast/ovarian cancer and Lynch syndrome.

The HGSA does not recommend a specific age to differentiate between those whose request for testing should be supported, and those whose request should be declined or deferred. Rather, each request requires individual assessment. In this circumstance, the cognitive and psychosocial maturity of the young person is a crucial consideration with regard to the young person’s ability to make an informed decision (see Sections 3, 4). Potential benefits of a mutation negative result need to be considered alongside the perceived benefits and potential harms of a mutation positive result, in the knowledge that either outcome is possible and irreversible. The decision to offer
testing must also take into account the relevant jurisdictional laws which enable or prohibit a minor to consent to their own medical management.

Potential health benefits

a) Testing for a condition that always has its onset before adolescence.

Where a condition has been identified in a child, parents sometimes request testing for an asymptomatic at-risk sibling. They may see benefits in knowing if the sibling is pre-symptomatic such as planning for future management of the child in mid-childhood and adolescence; and for decisions that impact on the family as a unit, such as further reproductive decisions, housing modifications for disabled children, balancing needs of abled and disabled children, wills and financial provisions. Where the condition is always expected to have its onset at an age when the asymptomatic minor is too young to be involved in the decision to be tested (e.g.: Duchenne muscular dystrophy, metachromatic leukodystrophy) the decision about testing should be that of the parents after appropriate genetic counselling.

b) Testing where the condition can have its onset at an age when the asymptomatic minor is too young to be involved in the decision to be tested, or in adolescence or adulthood.

In such circumstances (e.g. Friedreich ataxia), caution is advised and the child or young person’s best interests must be paramount (see Section 4). In this situation, HGSA recommends that testing is not undertaken until minors are of an age where they can be involved in the decision regarding testing, as is the recommendation for predictive testing for adult onset conditions. It is also important that if minors are tested prior to an age at which they are able to provide fully informed consent, their participation, understanding and involvement is sought and maximised in developmentally appropriate ways.

Rationale/Justification

Age of consent, competence and maturity
Legal models used to determine competence to consent in Australia generally entail a fixed age rule, or an assessment of whether the young person has ‘sufficient intelligence and maturity to understand fully what is proposed’. Accepted ages of consent vary in different jurisdictions and for different purposes. In Australia, eighteen years is regarded as a suitable age for voting and there are restrictions on selling alcohol to people under the age of 18. Generally 16 years is the age at which it is legal to engage in sexual relations, but this varies in jurisdictions with regard to age, gender and circumstances. In relation to consenting to medical treatment, for individuals 16 years and over, their own consent is usually sufficient. For a child under 14 years, consent of a parent is generally necessary. Acceptance of consent by a minor is qualified by their ability to understand the seriousness of the issue, its nature and possible consequences. The health practitioner must decide on a case-by-case basis whether a young person has sufficient understanding, intelligence and maturity of judgment to consent, taking into account not only their age but also the seriousness of the issue in question. The Medicare system in Australia recognises young people’s capacities to seek medical care and consent to medical procedures.
independently from their parents. Young people in Australia can access their own, separate Medicare card from the age of 15 years.\(^{19}\)

Young people can be broadly divided into **immature** young people who do not have the cognitive capacity and psychosocial maturity to participate at any level in the decision to have a pre-symptomatic or predictive test and **mature** young people who have such capacity. The process of an individual transitioning from being an immature young person to a mature young person, able to make fully informed decisions regarding pre-symptomatic or predictive testing is gradual and therefore requires full psychosocial assessment to determine.

**Autonomy**

The principle of autonomy relates to a person's right to make or exercise a self-determining choice without coercion. Pre-symptomatic and predictive testing in children and young people who cannot yet make a mature decision about testing removes the possibility for them to make an autonomous decision as an adult. It is for this reason that it is recommended that pre-symptomatic and predictive testing be limited to individuals assessed to have sufficient maturity to make an informed decision about testing.

The concept of autonomy includes the principle that a person’s autonomous actions should not infringe on the autonomous actions of others. As with pre-symptomatic and predictive testing of an adult, testing of a young person may reveal the genetic status of other family members and therefore needs to be considered.

**Non-Maleficence**

Pre-symptomatic and predictive testing of children and young people may result in immediate or long-term harm. Potential harms that might arise from predictive testing include:\(^{22}\)

- increased risk of harmful psychological sequelae including depression, anxiety or suicide
- disclosure of the test result to others, resulting in loss of privacy
- discrimination and loss of options directly arising from pre-symptomatic and predictive testing results, eg in employment and life insurance
- stigmatisation in the family or community, with reduced opportunities for education, marriage, employment or reproduction
- negative alterations of parenting as the result of knowing the child's genetic status
- potentially negative impact on the extended family dynamics as a result of clarification of genetic risk status

There is also emerging evidence of harm from not allowing mature minors testing when the minor wishes to be tested.\(^{14,15}\)

**Beneficence**

Potential benefits of testing a young person include:\(^{22}\)

- removal of uncertainty about genetic status, positive or negative, that can result in reduced anxiety for some young people
• a mutation negative result meaning the young person knows he/she will not develop the genetic condition
• ability to plan for the future including reproductive decisions for those who are mutation positive as well as career and lifestyle choices

Justice

Justice requires that these principles be applied consistently so that like cases are treated alike, such as where a young person under the age of 18 has been assessed as having an equivalent level of psychosocial maturity and cognitive capacity for decision-making as a person over 18 years.

Pre-symptomatic and predictive testing in mature young people for conditions where there is no medical benefit

If pre-symptomatic or predictive testing is being considered for mature young people for conditions for which there is no medical benefit in childhood, for example, HD or BRCA mutation, health professionals should be mindful of jurisdictional legal requirements or policies on minor’s consent to medical treatment.

It is strongly recommended that testing be arranged through a clinical genetics service, in conjunction with an adolescent psychologist or psychiatrist who ideally has experience in pre-symptomatic or predictive testing. In order to undertake a thorough psychosocial assessment, some of the key aspects to consider will include the young person’s: general maturity, competence to understand what is involved, capacity to make an informed choice, reasoning ability and appreciation of the impact of pre-symptomatic and predictive testing, home setting, engagement with peers, family and school, activities and risk behaviours, and mental health. This approach would generally involve several consultations. A useful model for basic psychosocial assessment in adolescents is known as the HEADSS approach.23

Literature is also emerging about how to engage adolescents effectively in the clinical genetics setting for those with limited experience working with young people.24

Where pre-symptomatic and predictive testing in a mature young person is undertaken, it is imperative that appropriate psychosocial follow-up occurs particularly where a mutation positive result is given, but also where a mutation negative result is given as research indicates that young people receiving mutation negative results can also struggle to incorporate this information into their identity.14,15 Follow-up is also important as young people’s cognitive capacities and social circumstances often change significantly during the adolescent and young adult years, in which case they might require different types of information and support. Such a test should only be considered if requested by the young person and not a third party such as a parent. Careful consideration needs to be given to the best interests of the young person as there may be a potential conflict of interest between the parent and child.

HGSA Guidelines on Pre-symptomatic and Predictive Testing for Genetic Disorders
All predictive testing should be undertaken in accordance with HGSA Guidelines, *Pre-symptomatic and Predictive Testing for Genetic Disorders*, giving particular consideration to the following:

- Genetic testing may identify other family members at risk. The individual (or parents/guardians) should be advised of this possibility before testing starts and be encouraged to decide how such information would be handled.
- Pre-symptomatic or predictive testing should not be used to resolve conflict within a family or between family members and other concerned parties in areas pertaining to custody, social welfare or the young person’s future education.
- A child or young person may not be able to exercise free choice in the face of strong parental opinions or parental discord.
- Pre-symptomatic or predictive testing should not be used to determine a child or young person’s suitability for adoption or foster care.
- Pre-symptomatic or predictive testing should not be used as a means for altering a child or young person’s social circumstances.
- Children and young people may be made vulnerable to discrimination on the basis of pre-symptomatic or predictive testing results. This includes eligibility for insurance and employment. Where the potential for discrimination exists, the young person, parents and professionals involved should be advised of this.
- Health professionals should be mindful that prenatal testing for an adult onset genetic condition is a de-facto predictive test in childhood and is to be considered in that light.
- Pre-symptomatic or predictive testing results should only be made available to a young person and those for whom appropriate permission has been granted.
- An asymptomatic young person’s DNA should not be collected and stored for research or for possible future use by the young person or the family where the young person is of an age that the condition could manifest in the future. Collection is acceptable if there is certainty that the young person is unaffected by the condition for gene discovery research. An example is research into a condition that clinical manifestation is always present by a particular age.
- New consent should be obtained for a person’s DNA to be used for any other purposes.

**General information**

Parents should be encouraged to make their child aware, at an appropriate age, of the genetic condition in the family and the implications, and for the child to be reared with this knowledge. Being able to discuss this information within the family, at different stages of maturity, will ultimately enable the child to have a better understanding of the outcome of testing (if performed in childhood), or to make a more informed choice about pre-symptomatic or predictive genetic testing.

Genetic counselling assists the family and the individual in making informed decisions based on an understanding of the process and implications of predictive genetic testing. Genetic counselling should be provided by appropriately trained health professionals who are familiar with the genetic conditions for which these tests are available. They should be working in a clinical genetics setting, and be certified by an appropriate professional body. They should also have knowledge and experience of the psychosocial issues arising from genetic testing, and ideally have experience working with children.
Counselling should be provided using the language and terminology that can be best understood by the young person and parents. The young person should be seen alone for at least part of each counselling session. Interpreters should be used as required. Follow-up counselling should be available from appropriate professionals.

Parents should be encouraged to view the outcome of the pre-symptomatic or predictive testing in terms of the benefit to the individual rather than in terms of the benefit to others. In the event of a dispute between the young person and parents regarding pre-symptomatic or predictive genetic testing, the counsellor should act as an advocate for the young person. However, resolution of such a dispute should recognise that the young person is part of a family, with counselling focussing on the family and young person together and separately.

Referral for further counselling from an appropriate health professional (eg. psychiatrist, family therapist, social worker or psychologist) may be appropriate. Pre-symptomatic and predictive genetic testing for adult onset conditions should not be performed without the at-risk person’s knowledge and participation in the counselling process. When pre-symptomatic or predictive testing is medically indicated in young children, decisions will necessarily be made by parents/guardians alone (e.g. when testing a baby for their risk of retinoblastoma from a mutation in the RB1 gene).

References

15. Mand C, Gillam L, Duncan RE, Delatycki MB. "It was the missing piece": adolescent experiences of predictive genetic testing for adult-onset conditions. Genetics in medicine : official journal of the American College of Medical Genetics 2013.