Position Statement

Pre-symptomatic testing in children and young adults

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.

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 and MSH2 genes (hereditary non-polyposis colon cancer) are examples of predictive testing.

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

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".

Pre-symptomatic testing in children and young adults
2008PS02
February 2008
In relation to pre-symptomatic and predictive testing in children and young people, for adult-onset disorders, the issue of intellectual and psychosocial maturity is of key importance in the young person’s ability to fully understand difficult genetic concepts and make informed decisions. The decisions they make at that time may 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.

**Position Statement**

**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\(^2,3\), or in the situation where the result may be used for decisions by the young person regarding prenatal 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 under the age of 18, either at their own request or at the request of parents/guardians, where:

- conditions are presently untreatable 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 hereditary non-polyposis colorectal cancer (HNPCC)

**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.

Such circumstances should be managed on a case-by-case basis. 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), extreme 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 done until the minor is of an age that they can be involved in the decision regarding testing, as is the recommendation for predictive testing for adult onset conditions.

c) When a young person close to the age of 18 requests testing for an adult onset condition.

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 negative result need to be considered alongside the perceived benefits and potential consequences of a positive result, in the knowledge that either outcome is possible and irreversible. The HGSA recommends that management of these issues should be through counselling and that testing be delayed until the young person is 18 years old to allow for increased maturity. Health professionals skilled in the area of pre-symptomatic and predictive testing can help parents, children and young people manage uncertainty and anxiety associated with the delay of testing until adulthood.
Rationale/Justification

These recommendations are based on concerns related to the child or young person’s autonomy, confidentiality and potential harm; and evidence discussed below that indicates that maturity of judgment in decision-making may not be sufficiently developed in young people to appreciate the long-term consequences of pre-symptomatic or predictive testing. The recommendations are consistent with International Guidelines on pre-symptomatic testing for Huntington disease.

Age of consent, competence and maturity

There are a number of models to determine legal competence to consent that include singly or in combination, concepts of: fixed age, understanding the nature and possible consequences of the treatment and the type of treatment.

Accepted ages of consent vary in different jurisdictions and for different purposes. Generally, 18 years is the age at which young people are recognised by society as adults in areas of decision-making requiring maturity of judgement. Hence, 18 is regarded as a suitable age for voting and there are restrictions on selling alcohol to people under the age of 18. Most jurisdictions accept 17 years as the maximum age of treatment as a child for criminal responsibility, except in Queensland where the maximum age is 16 years. 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, sex 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 necessary. Acceptance of consent by a 16 year old 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.

However, most rulings on age of consent for medical treatment for minors have been made in contexts that differ from pre-symptomatic and predictive testing for adult onset conditions. They apply to situations that will affect the young person immediately, i.e. medical tests, treatments or contraception, overlapping rights of the adolescent and the parents, and refusals of medical treatments where refusals are considered not to be in the best interests of the young person.

By contrast, in pre-symptomatic and predictive testing, the adolescent and/or parents may request a test that some health practitioners may consider not to be in the young person's best interest.

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. Clearly the change from an individual being an immature adolescent to being of sufficient maturity to make a
fully informed decision regarding pre-symptomatic or predictive testing is gradual. Models for assessing cognitive and psychosocial factors involved in decision-making eg Steinberg and Cauffman\(^8\) and Cauffman and Steinberg\(^9\) show that maturity in decision-making continues to develop into early adulthood, but also that there are significant individual differences within each adolescent age.

There is discord between the HGSA’s recommendation against pre-symptomatic and predictive testing in people under the age of 18 and the acceptance by some jurisdictions, and some health professionals, of 16 years as the age when young people are capable of providing their own consent to medical treatment.

Some have challenged the view that pre-symptomatic and predictive testing under the age of 18 years should be restricted\(^10,11\), suggesting that there may be other benefits for the individual and the family that have not previously been considered. These include preparing children for their future health issues, empowering parents, avoiding professional paternalism, and avoiding uncertainty for parents and child.

Of paramount importance is that the child’s or young person’s best interests are served.

**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 of making 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 aged 18 years or older unless there is a clear and immediate medical benefit to the child or young person.

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.

**Non-Maleficence**

Pre-symptomatic and predictive testing of children and young people may result in immediate or long-term harm for the person. Potential harms that can arise from predictive testing include:

- increased risk of harmful psychological sequelae including depression and 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 and community, with reduced opportunities for education, marriage, employment and reproduction
- alteration 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

**Beneficence**

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.

**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.

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

The HGSA recommends that testing be delayed until the young person is 18 years old to allow for increased maturity. However, if in exceptional circumstances pre-symptomatic or predictive testing is being considered for mature young people for conditions for which there is no medical benefit, extreme caution is advised.

Health professionals should be mindful of jurisdictional legal requirements or policies on minor’s consent to medical treatment.

Pre-symptomatic and predictive testing should be undertaken on a case-by-case basis and exceptional cause should be demonstrated as to why the young person should have the test.

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 assess the young person’s psychological state the following should be considered: general maturity, competence in understanding what is involved, capacity to make an informed choice, reasoning ability and appreciation of the impact of pre-symptomatic and predictive testing (see Appendix 1). This approach would involve several consultations.

Where pre-symptomatic and predictive testing in a mature young person is done, it is imperative that appropriate psychosocial follow-up occurs particularly where a gene positive result is given. Finally, 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.
All predictive testing should be undertaken in accordance with HGSA Guidelines, *Pre-symptomatic and Predictive Testing for Genetic Disorders*¹, 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. A person’s DNA should only be collected for reasons directly relating to, and necessary for, their healthcare and treatment. New consent should be obtained for a person’s DNA to be used for any other purposes.

Further background information/evidence from research

**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 condition¹². While risk factors for psychological sequelae have been identified, few adverse events have been described¹²,¹³. Two recent long-term follow up studies found significant reductions in distress compared to baseline for both non-carriers and carriers¹⁴,¹⁵. 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\(^{16}\). There is also 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\(^{12,13}\). Moreover, by their very nature, cohort studies are based on average group responses, which means that the minority of participants with adverse outcomes may not be adequately described. However, case reports are available that document adverse outcomes in the context of pre-symptomatic genetic testing for Huntington disease\(^{17,18,19}\).

A substantial body of literature has also become available on the psychological impact of predictive genetic testing for hereditary breast/ovarian cancer susceptibility\(^{20}\), and the findings have been reviewed recently in several review articles\(^{13,20,21}\). Most studies on the psychological impact of genetic testing for cancer susceptibility amongst individuals who have never been affected by cancer demonstrate that non-carriers derive significant psychological benefits from genetic testing, while no adverse effects have been observed amongst carriers\(^{13,19,22,23}\).

**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 testing is not generally accepted or recommended (e.g. Huntington disease or hereditary breast/ovarian cancer).

An international survey of clinical geneticists 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\(^{3}\). The most common condition tested for was Huntington disease. 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 clinically significant anxiety related to how they would pass on information to their gene 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 psychological impact. Consistent follow-up did not take place and findings represent the minimum frequency of adverse events. The majority of respondents agree with existing guidelines but many believe each case must be considered individually. (*Note that this article uses the words immature/mature with reference to age, not cognitive or psychosocial maturity).

The literature on the psychosocial impact of pre-symptomatic genetic testing for FAP provides a useful context relevant to the issues being considered, although there are preventative measures available in FAP. Several studies have examined the short to medium-term impact of undergoing pre-symptomatic genetic testing for FAP in children and adults\(^{24,25}\). 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.\(^{23}\) 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. Children who were found to carry the gene mutation, and who had an affected mother or a sibling who was also found to carry a gene mutation, experienced significant increases in depression.

**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. Interpreters should be used as required. Follow-up counselling, when indicated, 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 (i.e. a mutation in the RB1 gene).
Appendix 1

Criteria for assessing maturity, competence and capacity of young people to consent to predictive testing for adult onset conditions where there is no medical benefit

Assessment would include but not be limited to:

Firstly, an assessment of general maturity based on:
   a. Speech
   b. Personality
   c. Sense of self as an individual versus self as part of a family or other social group
   d. Age appropriate scholastic progress
   e. General functioning in peer relationships
   f. General functioning in response to stressors

Secondly, assessments of developmental capabilities related to competence to make this specific type of decision:

1. Understanding
   a. The facts / concrete information associated with the condition and test processes
   b. Consequences of results
   c. Probability / risk concepts

2. Capacity to make a free choice
   a. Exploration of family functioning / communication
   b. Recognition of coercive influences / direct pressure from others
   c. Evidence of appropriate socialisation, autonomous functioning and independence which is consistent over time

3. Reasoning
   a. Ability to articulate personal reasons for requesting predictive test
   b. Appropriate rationalisation
   c. Ability to give hypothetical weighting to probable outcomes
   d. Ability to perform a cost / benefit analysis for both testing and not testing

4. Appreciation of impact
   a. Abstract concept appreciation
   b. Ability to understand and anticipate a future with either a negative or positive result (both short-term and long-term consequences.)
References


