Molecular Genetic Testing in New Zealand

A Report from the
National Advisory Committee on Health and Disability
(National Health Committee)

September 2003

NATIONAL HEALTH COMMITTEE
NATIONAL ADVISORY COMMITTEE ON HEALTH AND DISABILITY
HUNGA KAITITIRO I TE HAUORA O TE TANGATA

Incorporating the Public Health Advisory Committee
Te Rōpū Tohutohu I Te Hauora Tūmatanui

First published October 2003

by The National Advisory Committee on Health and Disability
(National Health Committee)

Wellington, New Zealand

ISBN: (Book) 0-478-25335

ISBN: (Internet) 0-478-25336

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FOREWORD

The discovery of the structure of DNA 50 years ago, marked the beginning of a genetic journey that has led us to the decoding of the human genome and the identification of mutations associated with human disease. The rapid development of genetic technologies associated with this new information has the potential to redefine health care as we know it.

Based on international literature, an estimated 40 to 60 percent of New Zealanders will experience a disease with some form of genetic component within their lifetime and genetic technologies have the potential to help many of them. Many jurisdictions throughout the world are working to understand and address the social, legal, ethical and policy challenges presented by new genetic developments.

Genetic testing is an area of considerable and rapid change. It is moving from testing for rare diseases, into also testing for susceptibility to more common diseases that affect large sections of the population, such as cancer and heart disease. In this report, the National Advisory Committee on Health and Disability (National Health Committee, NHC) has identified some risks for New Zealand associated with an expected increase in demand for genetic testing as genetic knowledge develops around these common diseases.

As public awareness grows, greater demands are being put on health systems to provide genetic tests. Clinical Genetic Services in New Zealand are not sufficiently well resourced to meet this increase in demand. The number of clinical geneticists and genetic counsellors falls well short of international standards with no pathways for increasing capacity. Urgent consideration should be given to an appropriately resourced model for the delivery of genetic services in New Zealand.

Primary care practitioners are increasingly being asked for genetic tests by their patients and many feel underprepared for the pressures to order tests. Inappropriate ordering of genetic tests is widespread and where test requests do not go through Genetic Services, there is no scrutiny for inappropriate ordering.

Structures and processes need to be established in order to manage risks in this rapidly changing environment and to ensure equitable access to high quality services. The NHC has identified some of these risks and has made recommendations. It has not attempted to address prenatal or preimplantation genetic testing, pharmacogenetics, population screening, gene patenting, intellectual property or implications for insurance and employment. There is still much to be done!

The committee also notes that there is no one agency in New Zealand taking an overview of health-related genetic technologies and associated service delivery. It believes that the Ministry of Health should take this role.

The committee acknowledges the contribution many people have made to its work on genetic testing and in particular, the advice provided by the Genetic Testing Advisory Group and by those who commented on this report in draft form.

Robert Logan

Chair National Health Committee

EXECUTIVE SUMMARY AND RECOMMENDATIONS

1. Assessment and evaluation of new genetic tests

Internationally, developed countries have recognised the need to formally assess and evaluate new genetic tests, particularly for their analytical and clinical validity and clinical utility. However, work is still in progress and no country has yet developed formal means of assessing new genetic tests for their clinical validity.

The NHC recommends that:

- international developments on the assessment and evaluation of new genetic tests be monitored for their applicability to New Zealand
- an assessment be made of the applicability of the National Health Committee's New Health Intervention Assessment (NHIA) framework to the assessment of genetic technologies and genetic tests
- if the NHIA process is not suitable, then a process and structure be explored for the assessment of clinical validity and utility of new tests while awaiting international developments
- dependent upon a suitable framework being developed, new genetic tests be funded on the basis of their clinical validity and utility
- having developed criteria for assessing the clinical utility and clinical validity of genetic tests, consideration be given to the application of these criteria to other clinical testing
- where new genetic testing is being considered for asymptomatic individuals or populations, the screening criteria developed by the NHC should be applied[2].

2. Quality in genetic testing laboratory and clinical services

Clinical genetic services in New Zealand are in urgent need of increased capacity to ensure equitable access to safe genetic testing and to respond to increasing demand. Workforce shortages urgently need addressing.

A report to the NHC in 1995* recommended a national, coordinated approach to the delivery of genetic testing clinical services. The current regionally-based structure of service delivery makes it difficult to build capacity in response to an expected rapid increase in demand for genetic testing. National coherence is required.

The 1995 report also identified quality criteria for all molecular laboratories that receive public funding. These criteria should be reviewed for currency and implemented where appropriate. To avoid unnecessary duplication and to ensure retention of competencies for low-volume tests, a Scottish consortium of genetic testing laboratories has developed specialisations and rationalised the provision of some more common tests. This model may have applicability in New Zealand.

Existing laboratory quality assurance mechanisms are not adequate to cover genetic testing because of rapidly developing technology.

* Dixon JW, Winship I, Webster DR. 1995. Priorities for genetic services in New Zealand. A report to the National Advisory Committee on Core Health and Disability Support Services

The NHC recommends that:

- the genetics workforce be increased to meet internationally recommended levels
- the provision of genetic services be funded and coordinated nationally, with regional delivery
- the national service be adequately resourced to improve access to safe and effective genetic testing, with pathways identified for increasing capacity as necessary
- clinical genetic services allow for more sub-specialisation and that the specialty areas be complementary and nationally coordinated
- attempts be made to recruit Māori to be a part of the provision of genetic services; service provision needs to reflect the wider cultural diversity in the community where possible
- international models that use a national approach to the delivery of genetic testing laboratory services, including the Scottish consortium model, be investigated for their applicability to New Zealand, including the adoption of reference or designated laboratories for specific tests to avoid unnecessary duplication and ensure maintenance of competency
- quality criteria for molecular and cytogenetic laboratories, as recommended by the 1995 report to the NHC on genetic services, be reviewed for currency and adopted
- the peer review process for genetic testing laboratories be increased in frequency to accommodate rapid changes in genetic technology; a peer review once every two years is recommended
- International Accreditation New Zealand (IANZ) be requested to accredit genetic laboratories against appropriate professional standards, developed by appropriate professional bodies such as the Human Genetics Society of Australasia
- if in the accreditation process, a laboratory's provision of a testing procedure is deemed unsafe, the activities which do not meet quality standards should be suspended until failures have been rectified.

3. Practitioner and consumer issues in genetic testing

The NHC believes that informed consent processes are central to the development of protocols on genetic testing.

Increasing demand for genetic testing raises issues of the adequacy of public and professional knowledge, given that the impact of many types of genetic testing on individuals and families has the potential to be very serious. It is inappropriate for all health practitioners to be expected to order all genetic tests, given the level of knowledge required for adequate informed consent processes.

A survey of GPs commissioned by the NHC confirmed that there is a general lack of knowledge about genetic testing and some clear training needs. Given the expected increase in demand for genetic testing from primary healthcare services, this gap will need to be addressed.

In addition, there is currently unequal access to specialist genetic services, with a shortage of clinical geneticists and an apparent lack of knowledge of their existence by many health professionals.

The NHC recommends that:

- protocols be developed for each test approved for use and, distinguishing between diagnostic, carrier, and prediction or predisposition testing, include:
  - consent protocols
  - when and how each test should be used
  - which practitioner has access to which genetic test, based on education and training
  - the appropriateness of the use of each test for children
  - sensitivity to cultural issues and in particular, to the needs and expectations of Māori as tangata whenua
  - appropriate levels of support in decision-making for those whose decision-making may be compromised, such as those with sensory or intellectual disabilities
- a process be devised for the development of such protocols including involvement from medical geneticists, other health professionals, consumer groups, and disabled people's organisations
- GPs, specialists and medical students have increased access to genetic education; this will feed into any review of the medical curricula
- ways of making information about genetics more accessible to the public be investigated, including information about the limitations of genetic testing.

INTRODUCTION

1.1 Genetic testing – an overview

The Human Genome Project has led to recent rapid advances in information about human genetics and the consequent identification of genetic mutations associated with human diseases. Tests have been developed to diagnose many of the rare single gene disorders and are rapidly being developed to identify susceptibility to more common conditions, such as breast cancer and heart disease. Over time we will see new ways of predicting and preventing ill-health, more targeted and effective use of existing drugs and the development of new gene-based drugs and therapies to treat illness.

The trend towards testing for predisposition to diseases, to which large sections of the community are susceptible, is creating an increase in demand for genetic testing. This has resource implications, but also implications for professional and public knowledge, the way that genetic tests are assessed for effectiveness as they become available, and for the way that genetic testing services are delivered.

There are many challenges associated with genetic knowledge, including:

- the level of scientific knowledge about particular genetic conditions and associated tests is widely variable and changing rapidly
- the level of knowledge about genetics varies among health professionals
- the level of public knowledge varies and this has implications for informed consent
- the configuration of services (for laboratories and clinical services) is affected by structural changes in the health system which are driven by wider considerations than genetic services and testing.

As public awareness grows, greater demands are being put on health systems to provide genetic tests. The increased demand will put further pressure on a discipline where there are already workforce capacity and capability issues. There are too few clinical geneticists and associates (counsellors) in New Zealand by international standards. Primary care practitioners are increasingly being asked for genetic tests by their patients and many feel under prepared for these pressures. Inappropriate ordering of genetic tests is widespread and where test requests do not go through Genetic Services, there is little scrutiny for the appropriateness of testing. (These issues are discussed later in this report.)

Genetic testing does not offer a 'magic bullet'. While it is crucial that health services adapt and develop to meet increased need, it is important that genetics is not overemphasised at the expense of other factors that influence people's health, such as the physical, social and economic environments in which people live.

1.2 Background to this report

This report has been informed by an advisory group established by the National Health Committee, (see Appendix One), by consultation with the sector and by a number of pieces of work either carried out or commissioned by the NHC:

- Dixon JW, Winship I, Webster DR. 1995. Priorities for genetic services in NZ. A report to the National Advisory Committee on Core Health and Disability Support Services.
- Nicholas B. 2001. Literature Scan: Utility and funding of genetic testing. A report for the National Health Committee. September 2001
- Regional Genetic Services. 2001. Description of genetic testing services. A report to the National Health Committee. November 2001

- Sarfati D. 2002. Some practical aspects of genetic testing in New Zealand. A Report to the National Health Committee. March 2002
- Genetic Testing Advisory Group (GTAG). 2002. Genetic Testing. A report to the National Health Committee. November 2002 (see Appendix One for the membership of this group)
- White S, McLeod D. 2003. Genetic Testing: A survey of New Zealand General Practitioners' knowledge and current practice. A report to the National Health Committee. Department of General Practice, Wellington School of Medicine. March 2003.

1.3 Purpose and scope of this document

The rapidly changing genomics environment brings enormous possibilities for the early identification and management of genetic diseases, but also brings risks that will need to be managed. The National Advisory Committee on Health and Disability (National Health Committee, NHC) has identified some of these risks and the possible impact of testing for the susceptibility to disease, and has made recommendations.

The committee has limited its investigations to molecular genetic testing. It has not attempted to address prenatal or preimplantation genetic testing, pharmacogenetics or population screening. The committee acknowledges the importance of these issues, along with intellectual property and social and ethical issues in genetic testing, and the implications for insurance and employment, but has not attempted to explore them in any depth in this document. Some of these issues are being addressed by other agencies (see section 1.5) but there are still gaps. The committee believes these are all important areas of work that need to be addressed in New Zealand.

The NHC has formulated some recommendations based on advice from the Genetic Testing Advisory Group and from consultations with the sector. The Terms of Reference for the Genetic Testing Advisory Group and the definition of genetic testing used for this report is outlined in Appendix One. However, the Genetic Testing Advisory Group strongly believed that it also needed to address structural issues that were outside the Terms of Reference to provide a context for its other recommendations. The committee has extended the brief further as a result of consultations with the sector, which highlighted resourcing and workforce issues.

1.4 Links with other National Health Committee work

This report builds on the 1995 report to the NHC on genetic services (see above) on priorities for genetic testing services and makes links with other relevant NHC work on quality and new health intervention assessment.

1.4.1 Quality

The National Health Committee's dimensions of quality in the provision of a health service are: safety, consumer focus, access, effectiveness, and efficiency. Within this framework, the principles of a quality service for genetic testing would include:

a. genetic tests made available on the basis of their analytical and clinical validity[†]

b. tests carried out to a high technical standard in a cost-effective way

c. tests offered by professionals/clinicians with an appropriate level of expertise for the test under consideration

d. consumers given high quality information in a form that they understand, and supported in making heir choices.

[†] See Appendix Two for definitions of validity

1.4.2 New Health Intervention Assessment

The New Health Intervention Assessment (NHIA) work being done by the National Health Committee, may provide a structure that could be used for assessing genetic technologies for their suitability for public funding. This proposed assessment framework[††] takes a national approach based on a six-stage process of:

a. identifying emerging technologies before they are available for introduction

b. deciding which technologies should undergo further assessment

c. assessment of the safety, efficiency, effectiveness and efficacy of the new technology

d. appraisal of the social and ethical acceptability and appropriateness, including community need, equity and opportunity cost

e. adoption into clinical practice

f. evaluation and ongoing assessment of the new technology following its introduction.[1]

1.4.3 Screening criteria

The National Health Committee has developed criteria to assess screening programmes, to inform decisions about prospective new screening programmes, and to reassess or alter existing programmes to ensure the benefits outweigh the potential for harm.[2] The criteria are (condensed):

- suitability of the condition for screening
- existence of a suitable test
- availability of effective treatment
- high quality evidence that a screening programme is effective in reducing mortality or morbidity
- potential benefits outweigh the potential for harm
- the health care system will be capable of completing the screening pathway
- there is consideration of social and ethical issues
- there is consideration of cost-benefit issues.

These criteria should be used whenever genetic testing is being considered to screen asymptomatic populations or individuals, to ensure that screening tests are safe and effective.

1.5 Links with work by other agencies

There are pieces of work on genetic testing and related fields being conducted in New Zealand. However, we lag behind other similar developed countries in this area. The committee notes that there is no one agency that is taking an overview of health-related genetic technologies and associated service delivery. We believe that the Ministry of Health should undertake this role.

Health-related genetic technologies that have a relationship with the NHC work on genetic testing are outlined below.

1.5.1 Patenting of human DNA

The New Zealand Patents Act 1953 allows for the patenting of human DNA sequences and their biological functions. The Patents Act is currently being reviewed, led by the Ministry of

[††] This framework was proposed within a discussion document released by the NHC in 2002. The NHC is continuing to develop its work on NHIA.

Economic Development. The Ministry of Health has asked that gene patenting is explored further and is assisting in this process.

The Nuffield Council on Bioethics has identified four potential problems associated with the patenting of human DNA:[3]

- 'preventing or hindering development of new or improved medicines and treatments
- limiting access to healthcare by increasing the cost of diagnostic tests and treatment for certain diseases
- exploiting information and materials and inhibiting their free exchange between researchers
- involving parties in extensive and costly legal battles.'

The Nuffield Council rejects arguments that patents on DNA are necessary to stimulate investment in research and development. It cites the example of BRCA1 and BRCA2 genes that indicate susceptibility to breast and ovarian cancer. Myriad Genetics, a privately owned company, was awarded patent rights over mutations of the BRCA1 gene along with tests for detecting these mutations. The company is restricting access to the test by requiring testing to take place in its own laboratories at a substantially higher cost. It is also preventing the use of other tests that have been shown to be more effective in detecting mutations.

The counter argument that patenting encourages innovation, resulting in more genetic technologies, needs further investigation.

1.5.2 Preimplantation genetic diagnosis (PGD)

The Minister of Health has recently given approval in principle to the use of preimplantation genetic diagnosis (PGD) in New Zealand. The Minister has asked the National Ethics Committee on Assisted Human Reproduction (NECAHR) to develop guidelines on its use in treatment and to undertake a consultation

process on those guidelines. There are a number of complex social and ethical issues associated with PGD and these will need to be carefully considered, including:

- the range of tests available
- the decision-making mechanism for determining what tests should be allowed
- the use of PGD in connection with tissue typing
- the use of PGD for sex selection
- the use of PGD for genetic enhancement.

The committee notes that preimplantation genetic diagnosis is not currently available in New Zealand but is expected to be in the near future. It will retain an interest in future developments.

1.5.3 Antenatal and newborn screening

The Ministry of Health's National Screening Unit (NSU) and Clinical Services Directorate are currently exploring the need for more work in the area of antenatal screening, (for Down Syndrome in particular), and of funding and quality monitoring issues associated with the newbornmetabolic screening programme. In the future, the NSU will also examine the public health issues of screening populations with the use of genetic tests.

The committee notes that the social and ethical aspects of antenatal testing, of particular concern to the disability community in New Zealand, have not been formally examined at this time.

2 ASSESSMENT AND EVALUATION OF GENETIC TESTS

2.1 Background to molecular genetic testing[§]

2.1.1 Testing for rare disorders

Currently in New Zealand, most molecular genetic testing is concerned with inherited, fairly rare disorders caused by a single gene or chromosome that results in a specific medical condition such as, cystic fibrosis or muscular dystrophy. More than 9,000 single-gene conditions have now been identified worldwide.

Genetic testing in this context is used to:

- confirm a diagnosis where symptoms already exist *(diagnostic genetic testing)*
- indicate whether someone with a family history of a late-onset disease such as Huntingdon Disease, is likely to develop the disease *(predictive genetic testing)*
- check whether someone is a carrier for a recessive disorder, such as cystic fibrosis *(carrier testing)*
- screen before birth for genetic disorders such as Down Syndrome *(prenatal genetic testing)*.

It is also possible to test an embryo before implantation in the uterus for single-gene disorders *(preimplantation genetic diagnosis)*. This form of genetic testing is not available in New Zealand currently. (See section 1.5.2)

2.1.2 Testing for common disorders

Susceptibility to some common diseases can be caused by a single defective gene. Where there is significant family history, genetic testing can help estimate the chance of healthy family members developing the disease in the future. For example about one in 800 women is thought to have inherited a defect in the BRCA1 gene, which means they have a lifetime risk of developing breast cancer of up to 85 percent and up to 65 percent for ovarian cancer.[4] The women who test positive for this gene *(susceptibility or pre-disposition testing)* may be offered regular mammograms to detect cancer at an early stage, be prescribed a drug, or opt for prophylactic surgery, to reduce the risk. It is likely that more of these familial mutations will be discovered and tests developed for them.

Most of the more common diseases, such as heart disease and diabetes, also have a genetic component. An individual's susceptibility is determined by a combination of genetic, environmental and lifestyle factors. Tests do exist for multifactorial conditions but they have low predictive power and have not been used widely outside research settings (susceptibility or pre-disposition testing). However, genetic knowledge is advancing rapidly and it will soon be possible to identify and test more people for predisposition to a condition.

Between 5 percent and 10 percent of cancers are considered to be attributable to an inherited cancer predisposition. Cancer genetics is a new discipline that is developing rapidly. The ability to identify individuals at high risk has also led to major advances in screening, surveillance and prevention.

More and more genetic tests will come onstream as more genetic mutations are identified. Currently there are no mechanisms for assessing and evaluating new tests for safety or for their effectiveness in improving health outcomes.

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§ Section 2.1 is based on Our Inheritance, Our Future: realising the potential of genetics in the NHS. Department of Health, NHS. June 2003.

2.2 International developments

Internationally, there is a lack of high quality evidence that the use of genetic testing will lead to improvements in health. Most developed countries are grappling with the challenges of validating tests in an environment of rapid change and unpredictability. There is pressure in the United States not to regulate and technical advisory committees are being wound down.[5] This means that the Food and Drug Administration (FDA) is unlikely to provide world leadership as expected, although there are signs that it will take regulatory action in the United States if required.[#]

Other countries, such as the United Kingdom, Canada and Australia, have identified a need to formally assess, evaluate and monitor new genetic technology and are addressing ways of doing this.

A report to the Department of Health in the UK[6] states strongly that a mechanism is needed for the validation of proposed genetic tests before they become accepted for routine use, including whether the test:

- has appropriate sensitivity, specificity and reliability in indicating the presence of the mutation *(analytical validity)*. (In New Zealand this is addressed by the laboratory accreditation process)
- is a good predictor of clinical disorder *(clinical validity)*
- enables a clinical prediction which is useful and valued by the individual, family or professionals concerned *(clinical and social utility)*
- is cost-effective.

Thus, ideally, a genetic test should not be publicly funded and made available for service use until, and unless, its validity and utility have been formally assessed. The assessment process should include analytical and clinical validity and ideally, clinical and social utility.

Once a test is assessed and made available for service use, a subsequent decision is required as to whether it should be publicly funded, and how. However, until appropriate assessment frameworks are developed, it will not be feasible to fund tests on this basis.

The committee acknowledges that although this report is confined to molecular genetic testing, an independent assessment and evaluation process should be in place for all new clinical tests and investigations, rather than being commercially driven.

2.3 Risks in a New Zealand context

In New Zealand, there is currently no coordinated mechanism to develop and evaluate new tests, and no criteria for assessing when they might be ready for service use. Genetic tests are not included in the Laboratory Services Schedule[††] (are ex-schedule) and do not have an advisory body to recommend which tests should be publicly funded.

There are a number of risks associated with this lack of assessment of new genetic tests.

a. An increasing number of new genetic tests are coming onstream with little or no mechanism in place to assess or evaluate their clinical validity and utility.

[#] The FDA has taken recent steps to call a drug company to account for releasing a test that should have gone through a regulatory approval process

[†] A Laboratory Services Schedule exists that lists which clinical tests provided by community laboratories should be publicly funded. A Laboratory Services Advisory Group was established to decide what tests should go on the Schedule. At the time of writing this report, this group was in recess..

b. Knowledge of genetic tests is evolving in parallel with their clinical use, resulting in tests being used while their clinical validity and utility is uncertain.

c. Inappropriate use of genetic testing. For example:

- the ordering of tests that have limited clinical utility and where other diagnostic tests would be more appropriate, eg, testing for haemochromatosis[##]
- health professionals' lack of recognition of the distinction between analytical validity (the ability to identify the presence of a mutation) and clinical validity (the significance of the presence of the mutation for likely clinical outcome)
- the overordering of genetic tests due to lack of suitable processes to support development of clinical expertise outside genetic services.

Analytical validity may be adequately addressed by the accreditation process, involving an audit each year for three years and a peer review in the fourth year. However, given the rapidly advancing nature of genetic testing, a more frequent peer review may be necessary.

There are no formal processes for assessing *clinical* validity. Each laboratory decides what tests to offer. Generally this is based on an evolving knowledge of each test as it is being used and is demand driven. Tests are being used when their clinical validity is uncertain. Clinical geneticists have a greater understanding of the clinical validity of genetic tests than other health professionals, but among medical practitioners and specialists there is variable knowledge. While Genetic Services make sound clinical decisions based on the need to do the test, the quality of the reference laboratory, the cost, and wishes of the patient and whāanau, processes outside of Genetic Services are unlikely to be able to achieve the same level of effectiveness, efficiency and timeliness.

A mechanism is needed for the validation of genetic tests before they become accepted for routine use. New Zealand needs to take an international perspective on validation and will need to work in tandem with international initiatives.

We note that other medical tests and investigations are not formally assessed for their clinical validity in New Zealand and that this is an area that needs addressing.

2.4 Managing the risks

International developments on the assessment and evaluation of new genetic tests are progressing slowly in what is a relatively new field. New Zealand will need to maintain a watching brief and assess any new developments for their applicability to the assessment and evaluation of genetic tests in New Zealand.

Meantime, it is important to ensure that initiatives designed to assess these new developments, are consistent with other initiatives in new technology assessment.

The New Health Intervention Assessment (NHIA) work by the National Health Committee may provide a structure that could be used for assessing tests for their suitability for public funding. The NHC believes that while any framework should be suitable for assessing genetic technologies, particularly tests for more common disorders that may have large resource implications, the committee acknowledges that the NHIA framework is designed to be generic and may not provide adequate detail for the assessment of specific technologies such as genetic testing.

[##] Haemochromatosis is an inheritable disease that results in the excess deposition of iron in the tissues, which may damage organs over a long period

The NHC recommends that:

- international developments on the assessment and evaluation of genetic tests be monitored for their applicability to New Zealand
- an assessment be made of the applicability of the National Health Committee's New Health Intervention Assessment (NHIA) framework to the assessment of genetic technologies and genetic tests
- if the NHIA process is not suitable, then a process and structure be explored for the assessment of clinical validity and utility of new tests while awaiting international developments
- dependent upon a suitable framework being developed, new genetic tests are funded on the basis of their clinical validity and utility
- having developed criteria for assessing the clinical utility and clinical validity of genetic tests, consideration be given to the application of these criteria to other clinical testing
- where new genetic testing is being considered for asymptomatic individuals or populations, the screening criteria developed by the NHC should be applied.[2]

3 QUALITY IN THE DELIVERY OF GENETIC TESTING CLINICAL AND LABORATORY SERVICES

3.1 Genetic testing clinical services

In New Zealand, Genetic Services provides a comprehensive range of services for individuals and families affected by genetic conditions. These services include education and information, family history documentation and assessment, clinical assessment and diagnosis and patient management. These are all supported by genetic counsellors (genetic associates) in the context of the social and ethical implications of genetic testing.

There are two regional contracts for the provision of clinical genetic services, one for the Northern region administered by Auckland DHB and one for the Central and Southern region administered by Capital and Coast DHB.

3.1.1 Risks in a New Zealand context

With the anticipated growth in the demand for genetic testing, the challenge will be to strategically plan for services equipped to meet this demand. A regionally based and inadequately funded service, which we currently have in New Zealand, makes it difficult to build capacity. A national coordination of clinical testing services that are regionally delivered would provide the coherence necessary to ensure effective service delivery. However, such a service needs to be adequately resourced and staffed to reflect this rapidly growing area of health care.

3.1.2 Managing the risks

The 1995 report to the NHC on genetic services recommended a nationally coordinated and funded service that is regionally delivered. Although there is some interaction between the two regional services (Northern and Central/Southern), the service is not nationally coordinated.

A national approach to the delivery of genetic services would address some of the issues associated with the assessment and evaluation of genetic tests. National coordination would ensure a cooperative approach, which would develop processes to ensure that there are appropriate responses to a rapidly changing field. Adequate national funding would facilitate prioritisation. A national service would lead to national consistency.

A UK NHS report recommends that one clinical genetic service would be sufficient to service a population of between two and five million.[4] This would mean that New Zealand would need only one service. This does not mean that it would centralise to one building, but move towards a nationally funded and coordinated service with regional service delivery and outreach to other parts of the country. This model would be based on the principle of moving professionals rather than patients.

Currently, Genetic Services are configured on a regional basis and although the communication and cooperation between the services is increasing, the services were developed in the market-driven political philosophies of the 1990s, which encouraged competition between services rather than cooperation. If the regional services were brought under a national umbrella, the services could be rationalised to provide a more cost-effective delivery.

3.2 Workforce issues

3.2.1 Capacity

Currently in New Zealand, the capacity of the genetics workforce does not meet internationally recommended levels. Considering that the demand for genetic services is predicted to grow very

quickly, there is an urgent need to address genetics workforce issues. The committee considers that many of the recommendations in this document depend upon clinical genetics expertise for their implementation, and that workforce capacity must be addressed with some urgency.

There are currently 3.7FTE[§§] medical geneticists working in New Zealand and six New Zealand medical genetics trainees in Australasia. If some of the trainees were retained, New Zealand would be close to meeting WHO recommended levels for medical geneticists (ie, one per 500,000 population). They would need to be supported by the trebling of genetic counsellors This would amount to a total of at least 8FTE clinical geneticists and 16 genetic counsellors.

However, other countries such as the United Kingdom are putting a major emphasis on genetics and resourcing it well. It is likely that New Zealand will lose at least some of the new trainee geneticists to these countries unless something is done to retain them. Training needs to be followed up by availability of jobs. Currently there are no pathways for expanding the genetics workforce even though the signals are strong that the need for genetic testing services will accelerate very quickly. Unless there are sufficient trained clinical geneticists and genetic associates, there will continue to be inequitable access to safe genetic testing and this inequity will grow.

It is also important that the genetics workforce reflects the diversity in the community it serves wherever possible and that particular efforts are made to recruit Māori.

3.2.2 Specialisation

In an environment where the technology is changing rapidly, it is increasingly difficult for a clinical geneticist to maintain competence across the full range of genetic conditions. A national approach would include clinical geneticists with sub-specialisations, rather than generalists. Clinical geneticists could be complemented by specialists in other fields, trained in the clinical genetics that had application to that particular field. For example, an oncologist would be trained in clinical genetics associated with cancer.

Common conditions such as cancer may require more than one genetic specialist in the field, ideally with some geographical spread. Rare conditions would need only one genetic specialist, with strong connections with peers in Australia. It may be appropriate for some geneticists to specialise in more than one area, particularly for rare conditions.

The NHC recommends that:

- the genetics workforce be increased to meet internationally recommended levels
- the provision of clinical genetic services be funded and coordinated nationally, with regional delivery
- the national service be adequately resourced to improve access to safe and effective genetic testing, with pathways identified for increasing capacity as necessary
- clinical genetic services allow for more sub-specialisation and that the specialty areas be complementary and nationally co-ordinated
- attempts be made to recruit Māori to be a part of the provision of genetic services; service provision needs to reflect the wider cultural diversity in the community where possible.

[§§] FTE = full time equivalents

3.3 Current arrangements for ordering and carrying out genetic tests

There is widespread use of genetic testing in New Zealand, largely by medical specialists. Molecular genetic tests are ordered largely by clinical geneticists, but also by general practitioners, paediatricians, physicians, obstetricians and neurologists. Predictive and predisposition or presymptomatic tests are used to assess the future likelihood of developing a genetic disorder prior to the onset of signs or symptoms in a family setting. This latter group of tests is most likely to be undertaken within a clinical genetic service. Likewise, carrier testing for the "silent" carriers of autosomal or x-linked recessive disorders is mainly done by geneticists.

The majority of tests carried out in New Zealand are for diagnosing single gene disorders and for identifying carriers. These conditions are relatively rare in the population. It is difficult to quantify the impact that testing for the predisposition to more common conditions, preimplantation and other prenatal testing, and pharmacogenetic testing may have on laboratory services. However, the impact has the potential to be large and New Zealand needs a more coordinated approach to ensure a quality response to the expected increase in demand.

Routine genetic testing is carried out in public hospitals while research-focused genetic testing is done in university laboratories. Community laboratories do not currently do genetic testing because genetic tests are not on the Laboratory Services Schedule.

Although most genetic tests used in New Zealand are developed overseas, there are some developed here, mainly in research laboratories. There is little funding available for this type of research and development, and no formal mechanisms for the newly developed test to be assessed, evaluated and translated into clinical practice.

3.4 Genetic testing laboratories

3.4.1 Risks in a New Zealand context

An increase in demand for genetic testing will highlight quality issues that already exist around genetic testing laboratories. Some of these risks include:

a. existing quality assurance mechanisms being inadequate to cover genetic testing because of the rapidly developing technology. Current accreditation processes may not be sufficient to pick up poor practice. The IANZ assessment of laboratory process and compliance with quality procedures, will not pick up inappropriate testing, outdated methodology or inappropriate reporting. These failures would only be picked up in the four-yearly peer review.

b. laboratories carrying out tests that have not been assessed for their clinical validity or clinical utility. (See Section 2).

c. laboratories doing low-volume tests (eg, for rare diseases) may not be carrying out a sufficient number to retain competency.

d. research laboratories are not required to be IANZ accredited and although they have a different function from clinical laboratories, they often do provide limited clinical testing (research testing) when specific tests cannot be performed in an accredited laboratory. Research laboratories may need to be used in exceptional circumstances but may not have quality assurance programmes in place.

Current criteria and mechanisms for assuring quality in genetic testing laboratories are no different from those for general diagnostic laboratories. Internationally the model is to treat genetic testing laboratories in the same way as other medical laboratories. The NHC agrees with this general position, but considers that the rapid rate of change in genetic testing technologies may require a more frequent peer-review process.

3.4.2 Accreditation of genetic testing laboratories

The IANZ accreditation process of medical laboratories includes:

- assessment of the laboratory's quality management system
- assessment of the qualifications and continuing competence of the professionals working in the laboratory
- assessment of the laboratory's competence for specific tests against specified methods
- a requirement to participate in internal and external quality assurance programmes relevant to the specific tests carried out within the laboratory, an assessment of the number of tests carried out and whether that number is adequate to maintain competence.

The current IANZ system of accreditation involves a full assessment every year. An annual internal audit is conducted. Every fourth year the full assessment is accompanied by a peer review, which checks that scientists are appropriately trained, that changes in workload and staffing levels are accounted for, and that methodology is appropriate and up-to-date. Given the rapid advances in genetic technology, the peer review should be conducted more frequently.

The accreditation process covers issues of competence and for cytogenetics laboratories, IANZ uses a professional standard (eg, a standard developed by the Human Genetics Society of Australasia, HGSA) as a guideline if a request is made.

If a laboratory receives public funding for any test, the laboratory must be accredited. IANZ is moving towards accrediting laboratories for individual tests. However, tests cannot be accredited before they are put into use. This means that laboratories may be performing tests, which have not been accredited, for some months before accreditation takes place. Theoretically this raises the issue of how quality can be assured while the laboratory is carrying out the unaccredited test. In practice, if the laboratory has been accredited for many other tests, there is high probability that it will perform new tests well. However, there are risks inherent in that assumption.

3.4.3 Managing the risks

It is important that a genetic testing service should be underpinned by a laboratory service of high quality and cost-effectiveness. As part of its quality control, the National Health Service Executive in the UK has developed some core values and principles for genetic laboratory services:

> "laboratory services for genetics should be accessible, equitable, efficient, effective and responsive to the needs of patients and their families. They should be of high quality and sensitive to issues of confidentiality and consent"[6]

A high quality genetic testing laboratory will have the ability to:

- receive and store the specimens as necessary to support the analysis process appropriately and accurately
- carry out the analysis of specimens to identify the genetic status of a person
- accurately report the results to a referrer within an acceptable turnaround time
- explain the results to the referrer
- support the process of informed choice and consent.

A report to the National Health Committee in 1995 identified quality criteria for all genetic testing laboratories that receive public funding:[7]

- accreditation by an approved external provider
- Human Genetics Society of Australasia accredited staff
- identified reference laboratories for all tests provided
- participation in a quality assurance programme
- ongoing audit of test performance and results communication
- demonstrated liaison protocols for the communication of results in a timely and appropriate fashion
- performance on an annual basis of a minimum number of analyses of a given test.
- meet professional guidelines for molecular genetics laboratories such as those developed by the HGSA
- set in place payment arrangements for other laboratories to ensure prompt payment; this is necessary to ensure ongoing access to tests provided by other laboratories such as those overseas.

The report recommended criteria for molecular and cytogenetic laboratories. The NHC believes that these criteria should be reviewed for currency and adopted.

A national approach to the delivery of genetic testing may result in particular laboratories specialising in particular tests, particularly for low-volume tests. This would ensure retention of competency for the less commonly ordered tests.

The 1995 report to the NHC on genetic services also recommended that "designated" or reference laboratories be identified which would specialise in particular tests to ensure "maximal experience and expertise" for low volume tests. Access would be through a clinical geneticist or other tertiary specialist. The report also recommended a minimum of 400 to 1000 samples per laboratory per year to maintain expertise and ensure a wide range of tests available.

The Scottish consortium model, where particular tests are allocated to individual laboratories, could be appropriate for New Zealand. To avoid unnecessary duplication and to ensure the retention of competency for low-volume tests, the consortium has developed specialisations and has rationalised the provision of some more common tests. This means that laboratories develop specialised competencies and the risk of quality failures is much reduced.

The NHC recommends that:

- international models that use a national approach to the delivery of genetic testing services, including the Scottish consortium model, be investigated for their applicability to New Zealand, including the adoption of reference or designated laboratories for specific tests to avoid unnecessary duplication and ensure maintenance of competency
- quality criteria for molecular and cytogenetic laboratories, as recommended by the 1995 report to the NHC on genetic services, should be reviewed for currency and adopted
- the peer review process for genetic testing laboratories be increased in frequency to accommodate rapid changes in genetic technology; a peer review once every two years is recommended
- IANZ be requested to accredit genetic laboratories against appropriate professional standards, developed by appropriate professional bodies such as the Human Genetics Society of Australasia
- if in the accreditation process, a laboratory's provision of a testing procedure is deemed unsafe, the activities which do not meet quality standards should be suspended until failures have been rectified.

4 PRACTITIONER AND CONSUMER ISSUES IN GENETIC TESTING

4.1 Summary of risks

- There is a potential for greatly increased public demand for a range of genetic tests with increased public and practitioner knowledge and confidence in genetic testing for common conditions; this increased demand has begun to occur in New Zealand and is expected to grow rapidly
- Inadequate delivery of genetic testing services due to:
  a. underresourcing
  b. shortage of specialist clinical geneticists and genetic associates
  c. patients accessing specific genetic tests from health professionals outside clinical genetics services, some of whom may have a limited knowledge of genetics, the complexities of genetic testing, and its implications
  d. insufficient support for health professionals outside clinical genetics services as the technology develops
  e. the variable ability of health professionals to deliver culturally appropriate services and services which meet the needs of people with disabilities in the area of genetic testing
- The limited ability to deliver equitable (specialist and other) genetic services of a consistent quality across the country.

4.2 Practitioner issues

Medical specialists and general practitioners will have a critical role in meeting the increasing demand for genetic testing.[8] Indications are that there is variable knowledge of, and competency in, genetic testing issues among health professionals. This has implications for the appropriateness of the ordering of genetic tests and for informed consent processes.

In New Zealand, a significant proportion of genetic tests are ordered by non-geneticists, including primary care practitioners and medical specialists, particularly in paediatrics, oncology, haematology, obstetrics and neurology. Specialists from different disciplines will order different genetic tests although there are variations within specialist groups. For example, a paediatrician who specialises in dysmorphology[***] is more likely to order genetic tests than other paediatricians. Specialist filters could be developed to address the potential for over-ordering or ordering inappropriately. Medical specialists with a particular interest in genetics could be the contact point for other specialists in the field. Criteria or protocols for clinicians could be developed to guide them in the ordering of tests.

Informal communication with genetic laboratories showed that the majority of referrals for genetic tests come from general practitioners and that most of these referrals are to confirm diagnoses of conditions such as Factor V Leiden[†††] and haemochromatosis.

In 2003 the NHC commissioned a survey of 600 general practitioners to find out current practice and training needs. (See Appendix Four for the executive summary). The results confirmed that many GPs have little experience or knowledge of less common genetic conditions and lack of confidence to know when to refer or to whom. Most of the respondents felt that they needed to know more about genetic testing to feel adequately equipped to deal with increasing public demand.

[***] Dysmorphology – the study of human birth defects.

[†††] Factor V Leiden – the most common hereditary blood coagulation disorder.

The NHC believes that there is an urgent need to develop protocols to assist practitioners to assess when and how different tests should be used. Protocols would address which practitioners are most appropriate to order which tests. For example, those tests with the most significant effects on the individual and family (such as Huntingdon disease) should only be available to clinical geneticists with support from genetic counsellors. Protocols would also address over-ordering of tests which have an alternative method of clinical diagnosis that could be more cost-effective, such as for haemochromatosis.

4.3 Managing the risks

Protocol development would address the inappropriate ordering of genetic tests and lack of confidence of primary healthcare practitioners to provide adequate information and to know when to refer. The committee would favour this approach over regulation. It is mindful of the implications of protocol development on an already underresourced workforce since clinical geneticists would need to be fully engaged with this process. It is therefore necessary to increase workforce capacity to allow for these processes to be developed.

It is important that the public has access to sources of information other than those through their medical practitioner and that these sources cover the limitations of genetic testing, especially where tests are used to predict the risk of developing an inherited condition.

4.4 Informed consent

The principles of informed consent are similar throughout all health and disability services and, in the context of being offered a test, cover the client's need to understand:

- that they have a choice whether or not they take the test (freedom from coercion)
- the purpose of the test which is available to them and what it involves
- the potential benefits, risks and degree of uncertainty of the test, including any implications for other family/whānau members
- what will happen to any information/samples collected.[9]

Where genetic testing is concerned, there may be very wide ranging implications for the individual and their families and this must be reflected in informed consent processes.

Underpinning the principles of informed consent[§§§] is the wider concept of informed choice. A skilled practitioner will ensure that the person has accurate information to allow them to weigh up the risks and benefits according to the client's own values and to make a decision based on these. Access to information is fundamental to the level of understanding required to make an informed choice. Particular attention must be given to appropriate methods of communication and support in decision-making for those with conditions that may impede their access to information, (eg, deafness, blindness or level of literacy); or impede their understanding (eg, those for whom English is not their first language or those with an intellectual disability).

4.5 Informed consent in genetic testing

For genetic testing, the level of complexity of the informed consent process will reflect the degree of complexity of the information, the seriousness of the condition being investigated, and the wider implications for the individual and their families. This variation in the complexity of the process is also reflected in the range of genetic conditions that can be tested for, from those which are easily treatable, to those where there is no treatment, with far-reaching implications

[§§§] See Appendix Three for the general principles of informed consent

for the individual and their families. For example, some genetic tests are used to assist routine diagnosis and have the same choice and consent issues as general medical diagnostic tests. However, tests that are used to predict the probability of a condition developing in the future, or which have reproductive implications (eg, carrier tests), have additional complexities that need to be reflected in the consent process.

Some tests may provide a degree of confidence about a diagnosis (diagnostic test) and others may indicate the probability of developing a condition in later life (susceptibility or predisposition test) or the probability of a condition being passed on to the next generation (carrier test). But interpreting the results of genetic tests is not always straightforward. All results need to be interpreted in conjunction with clinical information. Some genetic tests are very sensitive and specific, eg, chromosome analysis for Down syndrome. Some diagnostic genetic tests may not give much information about the severity of the condition because the condition has variable expression. For instance, finding a mutation for a late onset disorder may give no indication of age of onset of the problem, its severity, or even whether it will definitely occur at all within a normal life span, eg, BRCA1 mutation and breast cancer.

Like other medical tests, genetic tests may have: a direct effect on the whole family; implications for employment, insurance and family planning; uncertain outcomes; positive impacts of closure; risks of psychological harm; a lack of therapeutic options. These effects may be more severe for genetic than other tests.

All of these factors emphasise the need for quality informed consent processes, based on health professionals having a sound understanding of genetic testing and its implications.[10] A survey of GPs in New Zealand, commissioned by the NHC in 2002, indicated a limited knowledge of genetics and the associated terminology and procedures[****].[11] Many GPs showed a lack of confidence in the area of genetics and genetic testing and indicated that they would be interested in refresher courses and other training. This indicates that there is variable confidence amongst GPs who may not be adequately equipped to provide accurate information for informed choice or interpretation of test results.

4.5.1 Cultural issues in informed consent for genetic testing

For Maori, *whakapapa* and *iratangata* are two concepts that refer to the human genome, the first referring to what is contained on the genome and the second referring to the actual genome, containing the life force. *Whakapapa* is an important spiritual value that is central to Māori identity. It incorporates genealogical succession and tribal histories and therefore includes the concept of genetic material being passed from one generation to another. Some Māori are concerned that genetic technology may change *whakapapa*. On the other hand, there are also Māori families that have happily sought help from genetic testing services.[12] Cultural attitudes towards *whakapapa* and individual versus collective guardianship of genetic material may vary from *iwi* to *iwi*. The service needs to be sensitive to this diversity.

Issues relating to the storage, disposal and further use of samples have particular significance to Māori, and consent procedures must take account of Māori customary practices and beliefs about the body, health and wellbeing.[13]

It is essential that all people being offered tests are given full and appropriate information and choices about how tissue samples are being stored, for how long and what they will be used for. If the sample needs to be transported to another country for testing, individuals and *whānau* need to know, as it may be culturally inappropriate to send body parts/samples offshore.

**** See Appendix Four for the executive summary of this report. The full version is available on www.nhc.govt.nz

4.5.2 Genetic testing and children – issues of informed consent

Where children are concerned, issues of consent add further complexity to an already complex topic. Guidelines on Consent in Child and Youth Health state that in general terms, consent must be freely given by a person competent to do so, and that children and young people should be involved and informed in decisions affecting them, at a level appropriate to their maturity and understanding, regardless of their capacity to consent.[14]

However, the guidelines go on to say that the best interests of the child should be the primary concern and for genetic testing this should be the bottom line. It is not in the child's best interests, for example, for a healthy child to be tested for a genetic condition for which there is no effective intervention and one that may (or may not) present in later life.

There may be tensions between the child's rights and the parents' need to know especially if there is already a child in the family with a genetic condition. Parents have the legal right to consent on behalf of their child for genetic tests to be carried out. It is therefore crucial that the health professional/counsellor is equipped to explore with the parents, the implications of testing the child. However, health professionals may choose not to offer the test or refuse to order it if they believe it to be not in the best interests of the child and may take legal advice on a case-by-case basis.

Many adults choose not to be tested for late-onset conditions and testing in childhood eliminates the possibility of future autonomous choice, risking stigma and discrimination.[15] The American Academy of Pediatrics believes that genetic testing of children and adolescents to predict late-onset disorders is inappropriate when the genetic information has not been shown to reduce morbidity or mortality through interventions initiated in childhood. Parents must be fully informed of the potential for harm including psychological damage, stigmatisation and discrimination. The NHC concurs with this view.

Although predictive genetic testing is not generally advocated for children, exceptions include disorders with potential paediatric onset and/or benefit of intervention in childhood. Familial adenomatous polyposis†††† fits this category and testing of a child if one parent is affected, can produce good outcomes for the child because there is an effective preventive intervention.

The NHC recommends that:

- protocols be developed for each test approved for use and, distinguishing between diagnostic, carrier, and prediction or predisposition testing, include:
  - consent protocols
  - when and how each test should be used
  - which practitioner has access to which genetic test, based on education and training
  - the appropriateness of the use of each test for children
  - sensitivity to cultural issues and in particular, to the needs and expectations of Māori as tangata whenua
  - appropriate levels of support in decision-making for those whose decision-making may be compromised, such as those with intellectual or sensory disabilities

†††† Familial adenomatous polyposis is an inheritable disease where polyps with a high malignant potential form on tissue lining the mucous membrane of the intestine

- a process be devised for the development of such protocols including involvement from medical geneticists, other health professionals, consumer groups, and people with disabilities where appropriate
- GPs, specialists and medical students have increased access to genetic education; this will feed into any review of the medical curricula
- ways of making information about genetics more accessible to the public be investigated, including information about the limitations of genetic testing.

GLOSSARY

Analytical validity	Indicates how well a test measures the property it is designed to measure
Clinical validity	The accuracy of the test in diagnosing or predicting the risk of a health condition – measured by sensitivity, specificity and predictive value
Clinical utility	Whether the clinical prediction enabled by the test is useful for preventing a disease or designing its effective treatment
Cytogenetics	The study of human chromosomes in health and disease
Genotype	The genetic makeup of a person

Genetic tests

- diagnostic testing – testing genetic material to confirm a diagnosis where symptoms already exist
- carrier testing – tests that identify whether or not an asymptomatic individual carries the gene for a condition which could be passed to the next generation.
- predictive testing – tests that predict whether or not a condition will develop in the future, eg, Huntingdon disease
- predisposition / susceptibility testing – tests that assess the level of future risk of developing a particular condition, eg, breast cancer
- prenatal genetic testing – testing before birth for a particular condition
- preimplantation testing – testing the pre-implanted embryo for a particular condition

Germline DNA	A sequence of DNA that comes from the eggs or sperm and is passed on to sequence offspring.
Human Genome project	An international research project to map each human gene and to completely sequence human DNA.
Pharmacogenetics particular	The study of genes which can determine how an individual responds to a therapeutic drug
Phenotype	The physical expression of a genetic makeup
Recessive gene	In order for a recessive gene to express itself, it needs to be present on both strands of the chromosome
Single gene disorders	Disorders which are governed by a single gene (others may be governed by several genes in a sequence)
Social utility	The value of test result to the individual or family, whether or not there is a change in clinical outcome.
X-linked gene	A gene linked to the X chromosome
$BRCA_1$ and $BRCA_2$ mutations	Genes that are associated with mutations that indicate a susceptibility to breast and ovarian cancer

APPENDIX ONE

Membership of the Genetic Testing Advisory Group (GTAG)

The GTAG was specifically established by the NHC to advise it on genetic testing issues. The group was comprised of Philip Pigou (Chair and Manager SISSAL), Dr Teuila Percival (NHC project sponsor and paediatrician), Assoc. Prof. Ingrid Winship (clinical geneticist), Dr Alexa Kidd (clinical geneticist), Dr Dianne Webster (National Testing Centre), John Forman (consumer, Exec. Director of NZ Organisation for Rare Diseases), Waiora Port (PhD student), Dr Bridget Robinson (oncologist), Assoc. Prof Don Love (molecular geneticist), Dr Margaret Croxson (RCPA), Dr Roderick Mulgan (RNZCGP), Dr Barbara Nicholas (Ministry of Health advisor). The NHC provided secretariat support for this group (Barbara Langford and Dr Keri Ratima).

The group's deliberations covered the period from April to November 2002. Terms of Reference for the Genetic Testing Advisory Group are outlined below. The committee acknowledges the hard work of this group and thanks members for their valuable guidance.

Terms of Reference – Genetic Testing Advisory Group

Background

The National Health Committee acknowledges the expected increase in demand for genetic testing, as the emphasis of human genetics moves from rare, single gene disorders to the more common diseases to which large sections of the community are susceptible, such as cancer, diabetes and Alzheimer's disease. This trend has resource implications, but also implications for the way that genetic tests are assessed for safety and effectiveness as they become available, and general access issues.

The NHC commissioned two pieces of work in 2001 in order to identify possible priority areas for future work. As a result, the committee resolved to focus in the first instance, on four particular areas of genetic testing for its advice to the Minister of Health:

1. the validation of genetic tests
2. quality / accreditation issues associated with genetic testing laboratories
3. which practitioners should order which genetic tests
4. issues of informed consent.

The Genetic Testing Advisory Group is established for this project to advise the National Health Committee on what issues to raise with the Minister of Health. The NHC will hold the findings of the advisory group in high regard, but may not necessarily accept all of the advice given.

Scope of the genetic testing project:

A working definition for the purposes of this NHC project is:

Genetic testing is testing for variations in germline DNA sequences and chromosomal material, which are predictive of significant health effects.

- *This is a working definition, intended to set the boundaries of the issues for the NHC genetic testing project.*
- *It specifically excludes:*

  - *tests for phenotype confirmation, eg, clinical examination, tissue confirmation, biochemical tests, radiology, post-mortem examination*
  - *identity testing and acquired changes in a person's DNA.*
  - *prenatal and preimplantation genetic testing*
- *It covers genetic testing that is diagnostic of a particular disease or condition as well as predictive genetic testing carried out prior to the appearance of clinical signs of the disease or condition.*
- *It refers to testing for germline changes in the individual.*

It may be relevant both to the individuals being tested and their wider family and offspring.

Role of the Genetic Testing Advisory Group

The Genetic Testing Advisory Group will advise the NHC on:

- systems in New Zealand for:
  - ensuring the safety and validity of genetic tests
  - oversight of quality assurance in genetic testing laboratories
  - the ordering and referrals for genetic tests
  - issues of informed consent.
- appropriate criteria, guidelines and processes for:
  - validating new tests
  - oversight responsibilities for quality assurance in genetic testing laboratories
  - ordering and referral of tests – which practitioners should order which tests
  - informed consent.
- which organisations and individuals to consult with prior to advising the Minister of Health.

The work programme of the GTAG will be supported by the NHC secretariat.

The group will report to the NHC through the project sponsor(s) and when appropriate, directly to the committee.

APPENDIX TWO

Definitions of validity and utility

Analytical validity – an indicator of how well a test measures the property or characteristic it is intended to measure. In a DNA-based test, an analytically valid test would be positive when the particular gene mutation is present (analytical sensitivity) and negative when the gene mutation is absent (analytical specificity).

Clinical validity – the accuracy of the test in diagnosing or predicting the risk for a health condition. It is measured by the sensitivity, specificity and predictive value of the test for a given health condition.

Validation can also include:

Clinical utility – whether the clinical prediction enabled by the test is useful for preventing a disease or its effective treatment

Social utility – the value of the information to the individual and their family, whether or not there is a change in the clinical outcome.

APPENDIX THREE

The principles of informed consent

Informed consent is a process, not a single event. In the context of testing for a condition (diagnostic test) or susceptibility to a condition (susceptibility or predisposition test), the whole process involves:

- Pre-test counselling which leads to informed choices
- Informed consent which leads to acceptance or rejection of the test and may include consent for storage and/or use of tissue or genetic information in research
- Post-test counselling, if the test has been consented to, which involves the giving of test results and their implications.

What should the informed consent process include?

Guidelines on informed consent for cancer susceptibility testing have been developed by the Task Force on Informed Consent, part of the National Institute of Health-run Cancer Genetics Studies Consortium. Its recommendations included:[9]

- Informed consent should be seen as part of a process
- Participants should be given time to consider their decision
- Participants experiences, beliefs and attitudes should be elicited prior to the consent process, including the individual's perceived risk of the disease
- A variety of educational formats should be employed, eg, face-to-face, written information, video etc
- Specific information should be given on:
  - Purpose of the test
  - Practical aspects of the test including type of test, time for results, results that may be obtained, the name of a contact person for questions or concerns, and information on how results will be communicated
  - Issues around the interpretation of results and potential uncertainties

  - Prevention and treatment options
  - Psychological and social implications for the individual and their family
  - Confidentiality arrangements
  - Alternatives to testing including the option NOT to test
- Informed consent to be provided in writing, and on a form which participants find easy to understand
- Post-test counselling should always occur, regardless of the result of the test.

However, it is acknowledged that not all of these recommendations would apply in all situations. For example, informed consent processes may vary according to the seriousness of the condition (diagnostic test), the predicted outcomes for the individual (predisposition tests) and whether there is a research component to the testing.

APPENDIX FOUR

Executive summary – Genetic Testing: a survey of New Zealand GPs' knowledge

Genetic testing technology has rapidly advanced and become more widely available in New Zealand. However, demand currently exceeds the ability to supply genetic testing services and an expected further increase in demand will put more pressure on a service already underresourced. It is therefore expected that general practitioners (GPs) will have an increasingly important role in meeting future demand in the area of genetic testing in New Zealand, particularly for the more common conditions.

This report was commissioned by the National Health Committee (NHC) to find out about the current practice and training needs of GPs in relation to genetic testing in New Zealand. A postal questionnaire was sent to a national, random sample of 600 GPs. The questionnaire included questions about current practice, access to genetic services and three case vignettes (breast cancer, cystic fibrosis and Huntington disease) to assess GPs' knowledge. There was also an open question for general comments at the end of the questionnaire. Responses were received from 328 (56%) of the 586 eligible GPs. Responding GPs did not differ from non-responding GPs in terms of demographic variables.

The results of the survey confirm that GPs have little experience with less common genetic conditions. While genetic conditions are not rare overall in the population, the number of patients an individual GP will see in their practice is small, particularly with respect to the less common conditions. While many responding GPs had ordered a genetic test for haemochromatosis in the last 12 months, most had never ordered or referred patients with Huntington disease or myotonic dystrophy. Nevertheless as the number and availability of genetic tests increases GPs will need to know when to refer patients, the conditions they should be referring and to be able to discuss the tests themselves and the results of the tests with their patients. Most of the GPs who responded to this survey felt they needed to know more about genetic testing in order to fill this role.

Responses to the survey and the qualitative comments indicate a lack of knowledge and need for updating/training in the field of genetic testing. This limited knowledge of genetics and the appropriate terminology and procedures was demonstrated by responses to all three scenarios included in the survey. In both the breast cancer and Huntington disease scenarios GPs reported needing further information before they would feel confident discussing the results of genetic tests with their patients.

Good patient specific information is currently being provided by Genetic Services to GPs who have referred patients to Genetic Services. However, many respondents did not feel that Genetic Services were accessible to them and a number of GPs also felt there were barriers to access for patients, such as cost and waiting time. The extent to which these barriers are real or just perceived as barriers by GPs who are unfamiliar with Genetic Services is unclear and should be explored further.

What is clear though is that a substantial number of New Zealand GPs are not sure how to access genetic advice for their patients and some reported not knowing how to contact Genetic Services in their locality. This lack of knowledge about how to contact Genetic Services is likely to reflect a lack of contact with Genetic Services.

The challenge is to provide accessible information to GPs about genetic testing. In particular information about referral – which conditions are appropriate to refer to Genetic Services and when referral should occur. At the level of provision of health services waiting time, cost and distance to travel to services are already identified as barriers for patients. With increasing demand for access it is important to reduce barriers to access for patients as much as possible.

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