HEREDITARY NONPOLYPOSIS COLORECTAL CANCER: COMPREHENSION OF A CANCER RISK IN CONJUNCTION WITH A GENETIC RISK

ZANDRé BRUWER
BRWZAN001

SUBMITTED TO THE UNIVERSITY OF CAPE TOWN
in partial fulfilment of the requirements for the degree

MSC (MED) GENETIC COUNSELLING

Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN

15 August 2007

Supervisor: Dr Merle Futter

Co-supervisors: Assoc. Prof. Jacquie Greenberg
Lauraine Vivian

Principal Investigator: Prof. Rajkumar Ramesar

Division of Human Genetics
Department of Clinical Laboratory Medicine
University of Cape Town

The copyright of this thesis vests in the author. No quotation from it or information derived from it is to be published without full acknowledgement of the source. The thesis is to be used for private study or non-commercial research purposes only.

Published by the University of Cape Town (UCT) in terms of the non-exclusive license granted to UCT by the author.

University of Cape Town

DECLARATION

I, Zandré Bruwer, hereby declare that the work on which this dissertation is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I empower the university to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Signature:. Signed by candidate

15 August 2007

ABSTRACT

Hereditary nonpolyposis colorectal cancer (HNPCC) is an inherited predisposition to early onset colorectal and endometrial cancer, caused by mutations in DNA mismatch repair genes. It is the most common form of hereditary colorectal cancer (CRC) and has a worldwide prevalence of 1 in 3 000 persons. As the mortality and morbidity related to HNPCC is decreased through surveillance for CRC, it can be beneficial for an individual to know if they are likely to develop an HNPCC-related cancer. Once a disease-causing mutation has been identified in an affected individual, predictive testing can be offered to first-degree relatives to refine their risk.

The purpose of this study was to explore the level of understanding of the predictive test result and subsequent impact of testing for a predisposition to HNPCC. Using a qualitative research design, in-depth interviews were conducted with ten individuals (all mutation-positive and asymptomatic for CRC) subsequent to the disclosure of their predictive test result. The use of personal interviews could construct rich descriptions of the circumstances faced by these individuals, following their predictive testing for HNPCC.

Study results showed a good level of knowledge and understanding related to HNPCC. The results also illustrated that knowledge derived from personal experience often took precedence over the information received during counselling. This was especially evident in relation to the perceived risk for CRC. Furthermore, predictive testing for HNPCC did not seem to induce any significant psychological problems for the participants. In addition, the emerging data is promising with regard to the health-related behaviour.

Limited literature is available internationally and non-existent in South Africa, on the individual's understanding and impact of predictive testing, for HNPCC. This study provides a useful framework for further research, together with potential implications for genetic counselling. Recommendations, to improve the counselling process and genetic services in the predictive testing programme, are made.

ACKNOWLEDGEMENTS

My sincerest thanks to those that helped me complete this study. Your contribution, guidance and support during this time was invaluable:

- The participants, for sharing their experiences and personal information with me;
- Prof. Rajkumar Ramesar, Head of the Division of Human Genetics and principle investigator of the research project;
- Dr Merle Futter, my supervisor;
- Prof. Jacquie Greenberg and Lauraine Vivian, my co-supervisors;
- Sr Elize Pietersen and Sr Ursula Algar, genetic nurses involved in the predictive testing programme.

I would additionally like to thank and acknowledge:

- The University of Cape Town: Senior Entrance Merit Scholarship.

TABLE OF CONTENTS

PAGE

LIST OF FIGURES AND TABLES

PAGE

FIGURE NUMBER

TABLE NUMBER

LIST OF ABBREVIATIONS

CRC	Colorectal Cancer
CSM	Common Sense Model of Self-Regulation
DNA	Deoxyribonucleic Acid
EXO1	Exonuclease 1
FAP	Familial Adenomatous Polyposis
GSH	Groote Schuur Hospital
hMLH1	Human MutL Homologue 1
hMLH3	Human MutL Homologue 3
hMSH2	Human MutS Homologue 2
hMSH6	Human MutS Homologue 6
hPMS1	Human Postmeiotic Segregation 1
hPMS2	Human Postmeiotic Segregation 2
HNPCC	Hereditary Nonpolyposis Colorectal Cancer
ICG-HNPCC	International Collaborative Group on HNPCC
InSiGHT	International Society for Gastrointestinal Hereditary Tumour
MMR	Mismatch Repair
SA	South Africa
UCT	University of Cape Town
UK	United Kingdom
US	United States of America

GLOSSARY

Adenoma: A benign tumour that develops from epithelial tissue.

Autosomal dominant inheritance: The expression of a gene in the heterozygous state, located on an autosome.

Colonoscopy: A medical procedure, which permits the visual examination of the entire colon, using an illuminated flexible endoscope.

Colectomy: Surgical removal of part or all of the colon.

DNA: The genetic material of a cell, which allows for the transmission of genetic information from one generation to the next.

Gene: A sequence of DNA that codes for a particular protein.

Germline mutation: A heritable mutation in the lineage of germ cells. These mutations are transmitted to offspring.

HNPCC: An autosomal dominant cancer syndrome characterised by early-onset colorectal cancer with an absence or limited number of colonic polyps, usually occurring in the proximal colon. There is also a predisposition to other extracolonic cancers.

Ileorectal anastomosis: Surgery involving the removal of the colon, which leaves the rectum intact by attaching the ileum to the rectum.

Mutation: An alteration in the DNA sequence or chromosome structure, damaging the function of a gene and may be disease-causing.

Polyp: A mucousal protuberance into the lumen of the colon.

Predictive testing: A form of genetic testing which is capable of identifying the presence of a mutation in a gene prior to the individual developing any symptoms of the disease. The detection of the genetic mutation does not necessarily mean the individual will definitely develop the disorder.

Predisposition: Having a greater than average risk of developing a disease as a result of an inherited gene mutation.

Prophylactic surgery: Surgery performed before a particular phenotype manifests itself in the individual.

Sigmoidoscopy: A medical procedure involving the examination of the rectum and the lower portion of the colon (sigmoid colon) through an illuminated sigmoidoscope.

Tumour: An abnormal mass of tissue resulting from excessive cell division. This may be benign (non-cancerous) or malignant (cancerous).

(The terms in the glossary have been adapted from Jorde et al 2006 and Naussbaum et al 2004).

DEFINITIONS

In this dissertation the following terms are defined as:

"Asymptomatic" refers to the fact that the individuals in this study have no clinical history of colorectal cancer

"Cancer" refers specifically to that of an HNPCC-related cancer, unless stated otherwise

"Estimated risk" refers to the lifetime risk for colorectal cancer, expressed as a percentage

"Genetic testing" refers to predictive genetic testing, unless specified otherwise

"Mutation-positive" refers to individuals who have received their predictive test result, which confirms that they carry the gene mutation predisposing to HNPCC

"Perceived risk" refers to the individual's personal perception of the risk of developing colorectal cancer

"Test" refers specifically to the predictive test.

CHAPTER 1: INTRODUCTION

CHAPTER ONE

1.1 INTRODUCTION

One of the most commonly occurring cancers in western countries is colorectal cancer (CRC), with a worldwide incidence exceeding one million cases and mortality of over half a million (Hampel et al 2005). In South Africa (SA), CRC is the third most common cancer in females and fourth in males. According to the Cancer Association of South Africa (CANSA), the risk of developing CRC amongst South Africans is 1 in 91 for males and 1 in 134 for females.

Genetic alterations contribute to the development of all colorectal malignancies. In the majority of these cases the mutations are acquired and CRC occurs sporadically, usually in individuals over the age of 50 years, without the presence of a family history (Schulmann et al 2002). In approximately 5-15% of patients, a family history is apparent, and a subset of these patients carry germline mutations that play a central role in the aetiology of their disease (Abdel-Rahman et al 2006; Hampel et al 2005). Inherited forms of cancer include a group of distinct syndromes, in which germline mutations result in an autosomal dominant disorder with a predilection for CRC (Strate and Syngal 2005). These include familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC), amongst others. HNPCC is the most common form of hereditary CRC, and will form the focus of this review (Devlin et al 2005).

HNPCC is an autosomal dominant inherited cancer syndrome, predisposing individuals who carry the mutated gene, to a high risk (80-85%) of colorectal and endometrial cancer. This syndrome is caused by germline mutations in DNA mismatch-repair genes (Schulmann et al 2002). The international prevalence of HNPCC is 1 in 3000 persons (Young 2001). To date, despite considerable effort, the incidence or prevalence statistics for HNPCC, in SA, have not been published.

The diagnosis of an inherited form of CRC in a family raises many questions for family members relating to their own health status. First-degree relatives of an individual with HNPCC have a 50% risk of inheriting the mutation and are advised to follow increased surveillance recommendations. The Division of Human Genetics at the University of Cape

Town initiated research into HNPCC in 1988, and services providing predictive genetic testing have been available since 1994 (The genetic testing protocol and policy guidelines are included in Appendix V, and further details are available from the Division of Human Genetics' website at http://www.uct.ac.za/depts/genetics/). Predictive testing can identify the underlying mutations that result in the predisposition to HNPCC, and mutation-carrying individuals can be advised to engage in appropriate risk-management strategies. For individuals who are tested and have not inherited the mutation, the intensive medical surveillance and anxiety about the increased risk for developing CRC is removed (Claes et al 2004).

Predictive testing is offered to at-risk, asymptomatic family members in whom the familial mutation in an affected relative has been identified. All candidates for the predictive test receive non-directive genetic counselling prior to the test. During this session, information concerning HNPCC and its heritability, cancer risks, predictive testing and options for prevention and early detection are discussed. The pre-test counselling provides information to facilitate an informed autonomous decision regarding the uptake of genetic testing. If testing is requested the result is given in a post-test counselling session, during which issues relating to the interpretation, screening recommendations based on the test result, and the psychological and social impact on the individual and family are addressed. Following the disclosure of the test result, psychological and medical follow-up is offered appropriate to the mutation status of the individual.

Genetic testing for cancer predisposition can have a profound effect on the individual and family, both practically and emotionally. Insight into the individual's understanding of the predictive test in HNPCC is needed because of its potential impact on distress and health-related behaviour (Claes et al 2005). A limited number of international studies have reported on the psychosocial impact of genetic counselling and testing (Gritz et al 2005; Meiser et al 2004; Keller et al 2002), but to date, no research in SA has been published on this aspect in terms of the individual's understanding and impact of their predictive test result. There is thus a need to address the local situation given the possible differences between this country and those developed countries, from which published data are available.

1.2 AIM

The aim of this study was to investigate the:

- level of understanding of a genetic predisposition to cancer following predictive testing for HNPCC in a cohort of asymptomatic mutation-positive individuals;
- investigate the motivations for predictive testing; and the
- subsequent impact on the individual.

1.3 OBJECTIVES:

- To establish the sociodemographics of the study population;
- To investigate the level of understanding of the predictive genetic test;
- To explore the individual's perceived risk of developing CRC; and
- To investigate the impact of genetic testing for HNPCC on the individual

1.4 ORGANISATION OF THE STUDY

Chapter Two presents an overview of current literature on HNPCC.

Chapter Three discusses the methodology design and outlines the entire research process. The steps involved in selecting participants are described and the validity and reliability/trustworthiness of the measurement instrument is discussed. A description of the data collection and analysis is provided while addressing ethical principles.

Chapter Four presents and discusses the results of the research study.

Chapter Five summarizes the main findings in the conclusion of the study.

Chapter Six identifies aspects to improve the genetic counselling service.

CHAPTER 2: LITERATURE REVIEW

CHAPTER TWO

2.1 INTRODUCTION

The literature review will present an overview of HNPCC, including clinical and molecular diagnosis, management and surveillance recommendations. Cancer in general has negative connotations and the psychosocial impact of genetic counselling and predictive testing for individuals at risk for HNPCC will also be reviewed. Literature searches were performed using terms such as "genetic testing," "predictive testing," "genetic counselling and testing," "genetic susceptibility testing" and "testing for cancer susceptibility" on Pubmed, ScienceDirect, Ebscohost and CancerLit for research on genetic testing for familial cancers, with specific reference to HNPCC. No published studies were found on the experience of genetic testing in terms of the psychological impact and understanding of the predictive test result for HNPCC in SA.

2.2 HEREDITARY NONPOLYPOSIS COLORECTAL CANCER (HNPCC)

2.2.1 Characteristics of HNPCC

HNPCC, also termed Lynch syndrome, was originally called cancer family syndrome. The history of HNPCC dates back to 1913 when Aldred Warthin described his observations of a cancer prone family (Warthin 1913). It was first delineated as a hereditary cancer syndrome in 1966 following the identification of two further families by Henry Lynch (Anwar et al 2000; Lynch and Krush 1971). HNPCC is the most common form of hereditary colorectal cancer accounting for estimates as high as 5% of all CRCs, although population-based studies reflect estimates closer to that of 1-2% (Young 2001; Salovaara et al 2000; Lynch and Smyrk 1996; Stephenson et al 1991). HNPCC is an inherited autosomal dominant condition resulting from mutations in one of several DNA mismatch repair (MMR) genes. A mutation in the MMR gene leads to the accumulation of cell mutations, which greatly increase the likelihood of malignant transformation and cancer (Naussbaum et al 2004; Korf 2000). These mutations confer a lifetime risk of 80-85% of developing CRC and an elevated risk for several other extracolonic cancers, of which endometrial cancer is the most common (Lynch and de la Chapelle 2003). Offspring and first-degree relatives of patients with HNPCC have a 50% chance of inheriting the gene defect. At-risk individuals are advised to follow regular clinical surveillance recommendations, with screening programmes being life-

long, once started (Vasen et al 2005). Through regular colorectal surveillance, polyps can be removed before they progress to cancer or the cancer can be detected at an early stage when still treatable (Yu et al 2003; Lynch et al 1996).

2.2.2 Diagnostic criteria

Prior to the identification of causative genes in the 1990's, the diagnosis of HNPCC was exclusively based on the evaluation of clinical findings together with pedigree analysis (Lynch et al 1998). The diagnosis is considered in young patients (mean age 44 years) with CRC, patients with multiple primary colonic cancers, or when a family clustering of either colorectal or endometrial cancer is observed (Lynch and de la Chapelle 2003). The features which typify HNPCC are provided in Figure 2.1.

Familial clustering of colorectal and/or endometrial cancer
Associated cancers*
Development of cancer at an early age
Development of multiple cancers
Features of colorectal cancer:
- predilection for proximal colon
- improved survival as compared to sporadic cancer
- multiple colorectal cancers
- increased proportion of mucinous tumours, poorly differentiated tumours, and tumours with marked lymphocytic infiltration and lymphoid aggregation at the tumour margin

Features of colorectal adenoma:
- the numbers vary from one to a few
- increased proportion of adenomas with a villous growth pattern
- a high degree of dysplasia
- probably rapid progression from adenoma to carcinoma

High frequency of microsatellite instability
Immunohistochemistry: loss of gene protein expression
Germ-line mutation in MMR genes

* ovary, stomach, small bowel, hepatobiliary tract, ureter/renal pelvis and brain

Figure 2.1 ICG - HNPCC Definition of Hereditary Nonpolyposis Colorectal Cancer (Vasen et al 1999).

2.2.3 Clinical presentation

HNPCC is a cancer predisposition syndrome without any clear clinical signs preceding cancer development except for colorectal adenomas (Jarvinen 2003). Difficulties in

diagnosing HNPCC arise due to the lack of a characteristic phenotype and several attempts have been made to define the clinical criteria for diagnosis. Diagnostic criteria (Table 2.1) for HNPCC were initiated by the International Collaborative Group on HNPCC (ICG-HNPCC) in 1990 and later revised to include extracolonic cancers (Vasen et al 1999; Vasen et al 1991). Essentially, criteria have been developed to identify patients, who are most likely to benefit from genetic testing, which is central to making an accurate clinical diagnosis.

TABLE 2.1: Diagnostic criteria for HNPCC as defined by the International Collaborative Group on HNPCC (Adapted from Vasen 1999; InSiGHT Database).

Classic criteria (Amsterdam I-Vasen et al 1991)

- At least three relatives affected with CRC;
- One of the affected should be a first degree relative of the other two affected individuals;
- At least one of the CRC cases should be identified before the age of 50 years;
- FAP should be excluded; and
- Tumours should be verified by pathology

(all criteria need to be present)

Revised criteria (Amsterdam II-Vasen et al 1999)

- At least three affected relatives should be affected with HNPCC related cancer, including CRC, cancer of the endometrium, small bowel, ureter, or renal pelvis;
- One of the affected individuals should be a first-degree relative of the other two affected individuals;
- At least two successive generations should include affected family members;
- At least one of the CRC cases should be diagnosed before the age of 50 years;
- FAP should be excluded; and
- Tumours should be verified by pathology

(All the preceding criteria should be included)

2.2.4 Molecular genetics

HNPCC is caused by mutations in MMR genes. The MMR genes encode for a family of proteins that recognise, excise and correct mismatches occurring during DNA replication (Yu et al 2003). The MMR gene can remain functional when one allele is compromised, which occurs when the defect is inherited. However, following an acquired defect in the

remaining allele, the MMR system is less capable of repairing DNA mismatch errors (Anwar et al 2000). A mutation in the MMR gene leads to the accumulation of cell mutations, which gather errors at a rate of 30-1000 times that of a normal cell, increasing the likelihood of malignant transformation and cancer (Yu et al 2003; Naussbaum et al 2004; Korf 2000; Lynch et al 1998).

Although seven genes have been associated with HNPCC (*hMSH2*, *hMLH1*, *hMSH6*, *hPMS1*, *hPMS2*, *hMLH3* and *EXO1*), mutations in three of these (*hMLH1*, *hMSH2* and *hMSH6*) are currently considered to predominantly cause HNPCC (Robinson et al 2007; Abdel-Rahman et al 2006; Jarvinen 2003; Miyaki at al 1997; Lindblom et al 1993; Peltomaki et al 1993). Germline mutations of *hMLH1* and *hMSH2* account for approximately 90% of all HNPCC cases (Shulmann et al 2002). Phenotypic variation exists between genotypes, with *hMLH1* associated with a lower risk of extracolonic cancers than *hMSH2* (Yu et al 2003). *hMSH6* mutations are associated with a later onset of disease, higher incidence of endometrial cancer and lower incidence of CRC (Abdel-Rahman et al 2006; Yu et al 2003).

2.2.5 Risk of different cancers in HNPCC

HNPCC is predominantly characterised by a high risk of early-onset (mean age of onset 20 years earlier than that for sporadic) cancer in the colon (Abdel-Rahman et al 2006; Lynch and Lynch 2000), with a higher lifetime risk for CRC in males (69%) than females (52%) (Hampel et al 2005). Individuals who have inherited germline mutations have an additional increased risk for extracolonic tumours. These include endometrial, stomach, ovary, small bowel, brain and hepatobiliary and urinary tracts (Lynch et al 1998; Vasen et al 1999; Mecklin and Jarvinen 1991). Of these cancers, endometrial cancer is the most common cancer after colorectal, with 30-50% of females affected by the age of 70 years (Strate and Syngal 2005). The overall prognosis for HNPCC-related CRC is suggested to be better when compared to non-hereditary (sporadic) CRC (Watson et al 1998).

2.2.6 Early detection and prevention of HNPCC

Interval surveillance for colorectal, endometrial (women) and possibly other HNPCC-related malignancies are recommended for patients with strong clinical evidence or a definitive molecular diagnosis of HNPCC (Lynch and de la Chapelle 2003). CRCs occur proximal to the splenic flexure, with one third of the cancers occurring in the caecum, thereby mandating full colonoscopy rather than flexible sigmoidoscopy (Lynch and Lynch 2000).

Surveillance studies have established that HNPCC adenomas are more aggressive and undergo an accelerated malignant transformation when compared to sporadic adenomas (Yu et al 2003). More frequent colonoscopic surveillance is thus justified for individuals at risk of HNPCC than in the general population (Yu et al 2003; Lynch et al 1996).

In HNPCC the cancer incidence rises significantly after the age of 20-25 years (Jarvinen 2003). The ICG-HNPCC proposes that the surveillance of the colon be initiated when the patient is 25 years old, or 5 years prior to the onset in the youngest affected family member, and should be repeated every 1-3 years. In SA screening is recommended biennially until 30 years of age and annually thereafter, with polyps being removed when seen on colonoscopy (Goldberg et al 1998). Extracolonic investigation, especially surveillance of endometrium and ovary, is also indicated, though endometrial and ovarian cancer surveillance is less well established than that of CRC (Strate and Syngal 2005; Lynch and de la Chapelle 2003). In addition, screening for cancers that have occurred in other family members is a reasonable precaution to be considered (Strate and Syngal 2005).

A 15-year follow-up study of 252 patients found that colonoscopic surveillance and the removal of polyps reduced CRC by more than 50%. Mortality from CRC in patients at-risk and among mutation-positive individuals could also be shown to be reduced by approximately 65% (Jarvinen et al 2000). Benefits of surveillance are further supported by a study of the cost-effective analysis of CRC for mutation-positive individuals. The costs of surveillance when compared to costs involved without a surveillance strategy were found to be less. In addition to this, it was further concluded that CRC surveillance increases life expectancy by seven years (Vasen et al 1998).

2.2.7 Surgery

If a mutation-positive individual develops CRC, consideration is given to surgical treatment. In affected patients with CRC, a subtotal colectomy is usually favoured over total colectomy. However, these patients are still at risk and require lifelong endoscopic surveillance of their rectal segment. Mutation-positive, asymptomatic individuals also have the option of prophylactic subtotal colectomy (Lynch and Smyrk 1996). Prophylactic total colectomy offers little benefit over partial colectomy and is generally not recommended (Syngal et al 1998). However, it may be considered in mutation-positive individuals, where poor compliance of screening, difficult or early-onset adenomas and presentation of debilitating

anxiety is apparent (Strate and Syngal 2005; Vasen and Morreau 2002). Prophylactic removal of uterus and ovaries can be considered following childbearing years (Schulmann et al 2002).

2.2.8 Chemoprevention

Currently, pharmacologic agents are not a substitute for routine screening or management strategies. Although such agents have been shown to reduce adenoma development and progression in patients with FAP or sporadic cancer, no data illustrates any benefit for HNPCC specifically (Abdel-Rahman et al 2006; Strate and Syngal 2005). Trials are underway evaluating the efficiency of celecoxib, aspirin and resistant starch on adenoma prevention in carriers of HNPCC (Yu et al 2003).

The recognition of a genetic cause of cancer is important. For patients, treatment for hereditary cancer may differ from that of sporadic disease and individuals with an increased risk should adhere to periodic screening. Cancer-screening recommendations are based on the patient's risk of developing cancer and offered to at-risk and mutation-positive individuals. Genetic testing for HNPCC is available to distinguish between individuals with a mutation, who require surveillance, and those without a mutation, who do not require the intensive surveillence. The ability to identify mutation-positive individuals prior to the development of malignancy has made the provision of detailed information and psychosocial guidance prerequisites for genetic testing (Vasen and Morraeu 2002).

2.3 GENETIC COUNSELLING AND GENETIC TESTING FOR HNPCC

2.3.1 Genetic counselling

Previous definitions for genetic counselling have been considered too cumbersome and lacking in acknowledging the counselling elements (Biesecker and Peters 2001). A current definition is given by the National Society of Genetic Counsellors and describes genetic counselling as a process of aiding individuals in understanding and adapting to medical, psychological and familial implications of genetic contributions to disease (Resta et al 2006). The fundamental principles include:

- Assessing the chance of disease occurrence or recurrence based on the family and medical history

- Facilitating patient education in terms of the genetics, testing options, management, prevention, ongoing research and available resources
- Counselling of clients to enable an informed decision concerning their choices and adaptation to the risk or condition (Resta et al 2006).

The expansion of genetic counselling into cancer genetics is most probably due to a strong public interest and to the medical advances leading to the early detection or prevention of cancer in individuals at a high hereditary risk (Bennet et al 2003). While it is based on the general principles of genetic counselling, it differs significantly with respect to medical and psychological impact, the levels of risk that result from the genetic factors and the efficiency of surveillance and prophylactic measures (Weil 2000). Additionally, cancer-screening recommendations are provided in a directive manner, a departure from the traditional philosophy of non-directive genetic counselling (Bennet et al 2003).

The recent identification of gene mutations involved in hereditary cancers has led to the increase in use of DNA testing in the management of familial cancer disorders and genetic testing for cancer susceptibility is available for some families with a history of cancer (Strate and Syngal 2005; de Wert 1998).

2.3.2 Genetic testing

Genetic testing includes two aspects: diagnostic and predictive testing. Diagnostic testing refers to testing for a genetic mutation in an affected individual. It is very similar to conventional medical diagnostic testing, as both involve the provision of definitive results on the patient's existing condition. Although the information may have implications for the future, it largely reflects the patient's present health status. The term, predictive genetic testing, refers to the examination of genetic material with the aim of providing future health related information about the individual at a suspected high-risk (Evans et al 2001). The concept of predictive genetic testing and its consequences, to identify individuals who are predisposed to a disease that has not yet developed, is a difficult one. Furthermore the uncertainty about whether or not the condition will develop, when it will appear and how severely it will manifest itself adds to the complexity of predictive testing (Aktan-Collan et al 2001; Chapman and Burn 1999).

Due to the complexities associated with genetic testing, in addition to its effects on the patient together with the implications for the family, pre and post-test genetic counselling is integral to the genetic testing process (Ensenauer et al 2005).

In HNPCC, genetic testing starts with an affected individual who has been diagnosed with an HNPCC-related cancer. If a mutation is identified in a MMR gene (diagnostic genetic testing), predictive genetic testing can be offered to the individual's family members, as they are at-risk of carrying the mutation. Testing negative for a known mutation indicates that the individual is not at an increased cancer risk. However, if genetic testing does not identify a mutation in an affected individual, the results are uninformative and all members of such families are advised to adhere to high-risk surveillance recommendations. For these families, genetic testing does not help determine which relatives may or may not be at an increased risk for developing HNPCC-related cancers.

2.3.3 Ethical aspects of genetic testing

The literature states that the provision of conditional information given in relation to future illness is not strictly defined (Chapman and Burn 1999). However, the general principles of medical ethics: autonomy, beneficence, nonmaleficence, justice and confidentiality outline the importance of informed consent prior to genetic testing (Beuchamp and Childress 2001). The principle of the right to choose whether or not to proceed with testing requires adequate and sufficient information to be given to the patient to allow for an informed independent decision. The principles of doing good and not harm require the informed consent to disclose all benefits, limitations as well as possible risks of the testing. Justice and confidentiality relate to the nondisclosure of the individual's genetic information to third parties (Ensenauer et al 2005; de Wert 1998). Genetic counselling and predictive testing should, where possible, be undertaken by those with experience to ensure that these issues of confidentiality and information provision are explained within the consent process (Vasen et al 2005). To request or decline testing is ultimately the patient's choice. The benefits and risks must be considered in terms of their personal and family history to ensure that a decision compatible to the counselee's beliefs, values and priorities, can be made (Ensenauer et al 2005).

The appropriate age for predictive testing is assessed on the age of expression of the disease. If medical benefits of testing are not apparent in childhood, testing is postponed until such an age when the child reaches adulthood and is able to make an informed decision for

her/himself. In the context of HNPCC, predictive testing is usually only offered to individuals over the age of 18 years.

Genetic information does not only concern the individual's genetic identity, however it is also significant to family members as it reflects their disease probability. A duty to warn family members following the diagnosis of a familial cancer also needs to be discussed with the individual receiving counselling and testing (Jarvinen 2003). Legal precedent has implied that individuals are responsible for the dissemination of their own medical information. However, the general agreement is that if the individual is unwilling to disclose his/her result in view of the implications for other family members, the harm caused by the failure of disclosure may outweigh the harm resulting from disclosure (Ensenauer et al 2005; National Society of Genetic Counsellors Position Statement).

2.4 Motivation for predictive testing in individuals from high-risk families

Individuals have been found to display several motives for requesting predictive testing. Claes et al (2004) assessed the motivation of 19 mutation-positive and 21 mutation-negative individuals with self-report questionnaires, following predictive testing. This Belgium study found the most important motives to be: early detection of cancer, the knowledge of their children's risk and the opportunity to reduce uncertainty. Similar findings were reported for American patients in a study by Esplen et al (2001), where primary motivations included wanting to know if more screening tests were needed, obtaining information on the risk to offspring and certainty about their own risk.

Knowing one's genetic risk, for the hereditary cancer, can facilitate early detection and prevention of the cancer (Marteau and Lerman 2001). However negative psychological sequelae may develop, particularly among individuals who learn that they are personally at an increased risk for developing disease or passing on cancer predisposing genes to their offspring (Lerman et al 1998). The amount of literature on the emotional reaction relating to genetic counselling and testing has only recently started to increase, with focus on cancer-related worry often used as an outcome variable in such studies (Watson et al 2005; Hopwood et al 1998).

2.5 Impact of genetic counselling and genetic testing

For genetic counselling to be considered effective, it should improve an individual's accuracy concerning the perceived likelihood of developing cancer and his/her knowledge of the disease genetics, with no adverse emotional impact (Braithwaite et al 2006). The distress and health-beliefs before and after genetic counselling for families at risk for HNPCC were investigated by Keller et al (2002) in a German study of 65 counsellees. Their results suggest that the individual's distress and worries related to HNPCC can be decreased by comprehensive counselling, whereby information conveying the benefits of early detection is addressed. Keller et al (2002) also found that by helping the counsellees absorb the information in the context of their personal cancer experience, the threatening aspects of HNPCC-related distress appeared to be reduced.

It is important that cancer-specific distress is reduced with genetic counselling as depressive symptoms may have an impact on genetic test acceptance (Lerman et al 1998). Keller et al (2002) recommended promoting an individual's sense of control and confidence in the effectiveness of early detection as a measure to reduce the perceived threat associated with HNPCC-related cancers.

Persons at risk for HNPCC are advised to have regular colorectal screening, and studies have shown that this reduces morbidity and mortality from CRC (Jarvinen et al 2000; Vasen et al 1998; Jarvinen et al 1995). The adherence to such advice prior to genetic testing is suboptimal. In order to optimise surveillance practices, screening is targeted at those individuals identified as mutation carriers, following predictive testing. Ideally, knowing ones genetic status allows for focused screening and medical management of these mutation-positive individuals (Aktan-Collan et al 2001). Hadley et al (2004) assessed the impact of genetic counselling and testing on the use of and adherence to screening recommendations in 56 asymptomatic at-risk individuals from American families known to carry a HNPCC mutation. At a follow-up of 12 months, it was demonstrated that genetic counselling and testing did influence adherence to screening guidelines. Recommended guidelines included increased screening for mutation-positive individuals and discharge from intensive screening, for those testing negative. The study found that 87% of mutation-negative individuals adhered to recommended guidelines, as compared to only 65% of mutation-positive individuals. However, a slight increase (41 to 53%) of colonoscopic surveillance was found among mutation-positive individuals following the genetic testing. Wagner et al (2005) evaluated the use of regular colonoscopies in 94 asymptomatic mutation-positive

individuals in the long term (average follow-up time 3.5 years), and found genetic testing largely improved screening compliance. Prior to genetic testing 31% of these individuals had regular colonoscopies, following the testing this increased to 88%.

Liljegren et al (2004) investigated the psychological aspects related to genetic counselling and the influence of a Swedish surveillance programme in at-risk individuals. They found that the high-risk group of asymptomatic mutation-positive individuals, while compliant with surveillance programmes, underestimated their personal risk of developing cancer. Aktan-Collan et al (2001) studied 268 participants in a Finnish population to investigate the comprehension of their cancer risk, following predictive testing for HNPCC. The study was based on questionnaires completed three times during the procedure, including, the time prior to the first counselling session, one month and one year after test disclosure. The authors noted that nearly all the respondents correctly recalled whether or not they had inherited the mutation predisposing them to cancer. However, for mutation-negative individuals the recall of their post-test risk of developing cancer was understood more often than for mutation-positive individuals. Following the questionnaire, one-year post-test, 90% of mutation-negative individuals could correctly state their risk compared to only 36% of those who were mutation-positive. Amongst those with a mutation, misunderstanding was more common among the elderly and the less educated. Interestingly, the mutation-positive individuals who understood their result were significantly more worried about their risk of developing CRC than those mutation-positive individuals who did not understand the test result correctly. Contrastingly, this was just the opposite in the mutation-negative group.

2.5.1 Risk perception

Individuals may misinterpret risk figures by placing different emphasis on the numbers presented to them. The manner in which individuals interpret their particular risk of developing cancer will depend on their life experience, their attitude to life in general and their personality type (White and Mackay 1999). The response to risk information will also depend on how they perceive the illness, together with the test and its results.

Risk is a numerical concept, and usually defined in terms of probability. Determining the probability that an individual is carrying an inherited mutation is only part of the risk assessment (Eiser 1998). The other probability is the likelihood of the mutation-positive individual developing cancer by a given age (Neuhausen 1999). Decisions based on risk

information involve the individual's own interpretation of what they are told by the expert (Eiser 1998).

Understanding how an individual perceives his or her risk of developing cancer is complex. One such aspect is the individual's experience with cancer. This may lead to certain knowledge on the disease, which could contribute to risk perception regarding cancer (d'Agincourt-Canning 2005). Observing the impact of cancer on another person makes the disease and its meaning more real and often leads to a personal reflection about an individual's own risk of developing or passing on cancer (Murphy 1999). It has been recognised that individuals with an affected parent perceive cancer risks as higher than those without an affected parent (van Oostrom et al 2006). As for many common diseases, having a family history is the strongest predictor of lifetime risk, and perceptions of personal risk have been found to be exaggerated in individuals with a family history. A study by Keenan et al (2003) found that women with a family history of breast cancer used their individual experiences as a reference point in evaluating and interpreting their own cancer risk. Woman relied more on these experiences than on statistical probability to interpret their genetic risk and guide decisions for health-related management. Similar findings were reported for CRC in a study conducted by McAllister (2002) who found that the participant's understanding of cancer risk appeared to result from experiences of and interpretation of their family history rather than the actual pattern of cancer within the family.

2.5.2 Psychosocial aspects of genetic testing

Meiser et al (2004) investigated the psychological impact of predictive genetic testing for HNPCC in 114 individuals, 32 of whom were mutation-positive and 82 mutation-negative. Only individuals who had never had a CRC or any of the cancers associated with HNPCC were included in this Australian study. The data illustrated that predictive testing amongst those who were mutation-negative led to psychological benefits and that no adverse psychological outcomes were found amongst mutation-positive individuals, one-year post-test results. This was in keeping with the findings from a study performed in the United States (US) in which 155 participants were also followed-up over a year period subsequent to their involvement in a genetic testing programme.

Gritz et al (2005) reported on the long-term psychological responses following genetic testing for HNPCC among American individuals with and without a personal history of cancer. Among cancer-affected participants, no increase in distress, regardless of mutation

status, was found in response to their genetic test results. Asymptomatic mutation-positive individuals however, did experience an increase in anxiety and depression immediately after the disclosure of their test result. This was found to decrease over the one-year period. Additionally it was also found that the perceived risk of developing CRC among mutation-positive asymptomatic participants was raised following the test results and remained elevated during the observation period. Gritz et al (2005) found those individuals with higher levels of baseline distress (prior to testing), lower quality of life, and fewer social support systems to be at risk for increased short and long-term distress.

Claes et al (2004) studied the short-term psychological impact of predictive testing for HNPCC in 40 individuals and found the distress level to be within normal ranges one month after test disclosure. The distress remained the same over the pre and post-test period for mutation-positive and negative individuals, while a decline was noted for mutation-negative individuals following their results. Further investigation into the impact of predictive testing for HNPCC was conducted by Claes et al (2005), in a clinic-based genetic testing programme. This study evaluated the illness representation, distress and health-related behaviour in 72 individuals (36 were mutation-positive and 36 mutation-negative). Distress levels were higher in mutation-positive individuals than mutation-negative, with the level of cancer-related distress shown to be low to moderate, however this decreased from pre to post-test in both groups. Findings further revealed that 53% of mutation-positive and 20% of the mutation-negative individuals reported at least one disadvantage with knowing their test result. The main disadvantage for mutation-positive subjects was the need for regular screening and the psychological burden. For mutation-negative subjects, it was the reaction of their relatives when disclosing a favourable result.

An individual's perception of disease can have an important impact on both their emotional response and health-related behaviour. Claes et al (2005) reported on such health-related behaviour in their study. Twenty-seven out of the thirty-six mutation-positive participants had a colonoscopy within the first year following their test disclosure. Three did not have a colonoscopy but were younger than 25 years, and not strictly due for examination, and six had had a colonocopy prior to testing. The authors concluded that all the mutation-positive individuals were thus adherent to the recommendations of the screening procedure if accounting for a maximum interval period of two years. None of the mutation-negative individuals had a colonoscopy within the first year, however about a third intended to have one in the future. This is in accordance with findings from Bleiker et al (2003) who found

some mutation-negative individuals to be concerned regarding the discharge from colonoscopies.

As further long-term information on the psychological impact of predictive testing was needed to fully assess such programmes, Collins et al (2007) conducted a three-year follow-up study of Australian participants. The study included 19 mutation-positive and 54 mutation-negative individuals. Psychological measures were used, consisting of baseline assessment and follow-up periods of 2 weeks, 4 months, 1 year, and three years after test disclosure. As had been previously reported, an increase in mean cancer distress could be shown in mutation-positive individuals at two weeks. This returned to normal baseline in 12 months (Collins et al 2007). The authors found that this level was maintained over the three-year period. Mutation-negative individuals illustrated a sustained decrease after testing. All mutation-positive and 7% of the mutation-negative group had had a colonoscopy by the end of the three-year period.

2.5.3 Illness representation

An individual's representation of illness is defined as a dynamic entity shaped from a variety of sources, which are important when considering reactions to health threats. These may develop from direct experience of the illness and associated medical care, a family or friend's experience, and ideas relating to cultural beliefs (Shiloh 2006; Leventhal et al 2003).

Theories concerning the response of an individual, to the potential of developing a life-threatening illness and the reasoning behind the resultant health behaviour, are relevant to research relating to genetic testing (Gooding et al 2006). An investigation into the psychosocial aspect of genetic testing is crucial in the examination of individuals utilising genetic testing and their response to the genetic results. Gooding et al (2006) argue that theories that focus on stress and coping provide useful frameworks for studying genetic testing for adult-onset disease risk. One such theory is Leventhal's Common Sense model of Self-regulation (CSM), which highlights the importance of both a cognitive and emotional involvement in reacting to a health-threat (Leventhal et al 2003). This model posits that an individual's personal understanding of an illness, determines their coping response, health behaviour and psychological well-being (Leventhal et al 2003). The relevance of such a model was noted by Shiloh (2006) in terms of specific recommendations that need to be undertaken prior to genetic testing. In light of the client being viewed as an active

information processor rather than a passive receiver of given information, the following recommendations were made:

- To examine the understanding of genetics and heredity, in general, prior to any educational attempt being made in the session
- To explore specific representations that clients have concerning the particular genetic condition before trying to modify their knowledge and reactions
- To investigate the former experiences with genetic conditions using a personalised approach that would help facilitate the individual's meaning of the experience
- To clarify the role of self-representations and coping behaviours involved in the response to these threats and direct counselling in dealing with these issues
- To evaluate the costs and benefits of the client's misconception before trying to change them
- To consider the interaction of a cognitive and emotional aspect as predictors of coping with genetic conditions and risk

Predictive genetic testing provides a very specialised type of genetic information. Insight into the potential impact of this information for individual's undertaking predictive testing for HNPCC is crucial due to the possible effect on distress and health-related behaviour (Claes et al 2004). This review highlights a few of these aspects that may have an impact on participants involved in these programmes. The literature included provides perspectives from developed countries such as the United Kingdom, US and Australia, and it will be interesting to compare how this relates to developing countries such as SA.

CHAPTER 3: METHODOLOGY

CHAPTER THREE

3.1 INTRODUCTION

This chapter describes the research design in detail. Sections addressed include participant selection and description, instrumentation, data collection and analysis and the identified limitations and strengths of the research methodology.

3.2 RESEARCH DESIGN

A qualitative approach by means of a descriptive exploratory design were utilised for this study.

Qualitative research offers the opportunity of providing insight into an individual's actions, beliefs, thoughts and perceptions that quantitative methods alone cannot (McMillan and Schumacher 2001). This type of research has been particularly suited to understanding the "how" and "why" questions with the goal of attaining an insider's view of the group under study. An insider's view may explain how people perceive and react to a given health problem and what interventions, if any, are most likely to be successful (Ulin et al 2005; Holloway and Wheeler 1996). Qualitative methods are orientated towards discovery and process; illustrate a high validity, less concerned with generalisability, and more interested in obtaining a deeper meaning of the research problem in its unique context (Ulin et al 2005).

Interviews were used to provide the participants with the opportunity to describe their experiences to the researcher. Popay (1992) states that the qualitative inquiry "explores the meaning people attach to their experiences and identifies and describes the social structures and processes that shape these meanings."

The primary purpose of the study was to build rich descriptions of the circumstances that confront individuals following predictive testing for HNPCC. This is relatively unexplored in the literature, and thus a descriptive and exploratory study design was incorporated. The main purpose of a descriptive study is the acquisition of comprehensive and exact information about a particular fact, in light of providing new information on that specific event or incident (Giacomini and Cook 2000; Neuman 1999). The exploratory study tries to

identify or discover important categories of meaning in poorly understood phenomena and it is usually conducted in new areas of inquiry (Marshall and Rossman 1999).

The study focuses on the gathering of information from each participant, at one point in time. As it is a cross-sectional design, it does not capture changes over time as with a longitudinal study (McMillan and Schumacher 2001). Although this method lacks comparability over time, it is a less costly method used by researchers with limited resources, time and money (McMillan and Schumacher 2001), as is the case in the present study.

3.3 PARTICIPANTS

3.3.1 Sample size determination and selection

Qualitative sampling consists of small sampling units studied in depth. The use of large samples does not enhance the research, but rather lacks the depth and richness of a smaller group, as the specific responses of the participants and their meanings may be lost (Holloway and Wheeler 1996).

More than 400 families have been recruited into the South African HNPCC research programme. Disease-causing mutations have been identified in 30 of these families, 19 of which are currently involved in the predictive testing programme. The majority of these individuals live in the Western and Northern Cape Provinces. For the purpose of this study 12 mutation-positive individuals from the Western Cape, who met the inclusion criteria (see 3.3.3.1 below), were identified by the genetic nurse involved in the Colorectal Cancer Unit. These individuals were approached and those who volunteered were included in the study.

3.3.2 Sampling method

Convenience and purposive sampling was utilised in this qualitative study. Convenience sampling facilitates the selection of participants that are accessible to the researcher, permitting for time and distance limitations of the research project. Purposive sampling was chosen to select "information rich" cases to allow the researcher to identify particular types of cases for in-depth investigation (Neuman 1999; McMillan and Schumacher 2001). Furthermore purposive sampling is used when a few cases are studied in depth to yield insight into particular phenomena being investigating (McMillan and Schumacher 2001).

The sample group of 12 participants were chosen on the grounds of their mutation status rather than randomly selected from the predictive testing programme. The sample size was already limited due to time constraints, and only mutation-positive individuals were selected. As a general consideration when selecting sample size, the more heterogeneous the population, the larger the required sample size, it was thus a further consideration to limit the number of variables being studied (Rossouw 2003).

3.3.3 Eligibility criteria

3.3.3.1 Inclusion criteria

- Individuals over the age of 18, who have received their HNPCC predictive genetic test results and are mutation-positive;
- Individuals consenting to be interviewed and tape-recorded by the researcher;
- Individuals accessible for a personal interview and within a 100 km radius of the University of Cape Town.

3.3.3.2 Exclusion criteria

- Individuals who have received their predictive test results and are mutation-negative;
- Individuals who have developed CRC.

3.4 MEASUREMENT INSTRUMENTATION/OUTCOMES

3.4.1 Data collection

In-depth semi-structured interviews together with the researcher's observations were used to gather information for the study (Appendix III and IV). The majority of the interviews took place in the participants' homes and were tape-recorded.

Qualitative interviews provide the participants with the opportunity to describe their experiences in detail and to give their perspectives and interpretations of these experiences (Holloway 2005). A semi-structured interview schedule was used to collect similar types of data from all the informants in addition to allowing for the exploration of the participants' feelings, thoughts and perceptions. Such interviews establish an exchange between the

interviewer and respondent whereby a structure, without compromising the open exchange, is created (Ulin et al 2005). Furthermore it allows for control over the interview so that the purpose of the study can be achieved and the research topic explored (Holloway and Wheeler 1996).

The majority of questions in the interview guide were open-ended to encourage free responses from the participants without the limitation of categories. Closed-ended questions were used to obtain the demographic information. Neutral probes were included to clarify responses if they were incomplete or misunderstood. Any non-verbal cues including the participant's facial expression, gestures or reactions that were present during the interview were noted. These were included in field notes, which were completed following the interview session, such that it did not take place in front of the participant.

Questions included in the interview schedule were generated from the literature and discussion with the genetic nurses. The section on cancer knowledge was adapted from de Vries et al (2004) and Collins et al (2000). Questions from Aktan-Collan (2001) were incorporated amongst the other questions into the sections on personal understanding and the recall of cancer risk and subjective risk perception. The question relating to factors influencing the decision on the up-take of the genetic test, included in the section relating to the motivation for participation in the predictive testing programme, was adapted from Claes et al (2004).

The validity of the interview schedule was reviewed by the colorectal cancer genetic nurse and the research supervisors, to ensure that the items were comprehensive and the sequencing was appropriate. The interview schedule, information sheet and consent form were available in English and Afrikaans. As the researcher is fluent in both languages, the interview was conducted in the language of the participant's choice, depending on their preference. Interviews did not differ in content for each interviewee. However the time of each depended on the individual response and ranged from 40 minutes to just under one and a half hours.

3.4.2 *Research setting*

The researcher requested that the interviews take place in the homes of the participants. Holloway and Wheeler (1996) suggest that the individual is more likely to be comfortable and less inconvenienced in their home, when asked to talk about issues, which they might find sensitive. Furthermore a dialogue with a person in their natural surrounding will reveal gradations of meaning from which their perspectives and definitions are continually shaped (Marshall and Rossman 1999). By interviewing the participants in their home environment, the researcher could see the setting, and better observe the family interaction and behaviour. For those participants where it was not convenient to be seen in their homes, interviews were conducted in a private venue of their choice. Five subjects, including the two pilot interviewees, elected to be seen in a private room at their local clinic.

3.5 PROCEDURE

The genetic nurse involved in the Colorectal Cancer Unit at Groote Schuur Hospital (GSH) contacted the potential participants and informed them of the study. Consenting individuals were then contacted by the researcher to arrange the interview times and venues.

3.5.1 Piloting

A pilot study was carried out on two of the participants to refine the structure of the interview schedule and to identify any changes needed to improve the clarity and format. Questions were tested for difficulty of comprehension and to ensure that answers elicited the type of information envisaged (Roussow 2003). Following each interview the researcher asked the interviewees for their critical analysis on any confusing categories or any other aspects of the schedule, which could be considered insightful (Roussow 2003). Several questions were adapted to eliminate the ambiguous nature and to aid the clarity of the interview schedule. Subsequent to these corrections, the shedule was rechecked by the researcher's supervisors. The information used in the pilot study was not included in the study. However, in addition to serving as a pre-test of the interview schedule, it provided an estimate of the amount of time required to complete the interview with a mean time of approximately one hour.

3.5.2 Recruitment

Study participants were drawn from a group of individuals willing to share knowledge and experience related to the research topic (Ulin et al 2005). Individuals were selected on the basis of having undergone experiences about which the researcher wanted to gain information. Potential participants meeting the inclusion criteria, accessible and likely to be willing to participate, were selected from the HNPCC database by the genetic nurse familiar with these individuals. As far as possible, individuals representative of a generalised broad base in terms of socio-economic status, education level and ethnic background were chosen and contacted via telephone by the genetic nurse, and invited to participate in the study. She then, with the permission of the individual, provided the contact details to the researcher. The researcher invited the first twelve consenting participants to participate in the study. The interview times and venues were subsequently arranged to suit the subject.

3.5.3 Data collection

Tape-recorded interviews allowed the researcher to capture the participants' words without having to write down what was being said, which would have interfered with the researcher's engagement with the participants. Each tape was dated and labeled with a code and the participants' names were kept separate from the tapes and interview schedules, to which only the researcher had access. Reassurance was provided to the participants that the information discussed would be kept confidential apart from the possibility of being published in a scientific journal where names would not be used.

Each interview took place in a private venue of the participant's choice. The researcher conducted each interview personally during the months of March and April 2007. Some of the questions in the interview schedule may have revisited sensitive issues and individuals were given the option of further counselling following the interview, to address any distress caused by talking about their experiences. None of the interviews exceeded an hour and a half and the need for a second interview was not requested by any of the participants.

It is acknowledged that, before analysis of the data can take place, the researcher must preserve the words of the individuals they have interviewed as accurately as possible (Holloway and Wheeler 1996). Therefore, the transcription of the recorded interviews allowed for a greater efficiency of the data analysis (Marshall and Rossman 1999).

Following the recording of the interview, the schedule was transcribed by an official university transcriber (in either English or Afrikaans), in preparation for the data analysis.

3.6 DATA ANALYSIS

The method of analysis used was based on the constant comparative method of Glaser and Strauss (1967). Content analysis was used to organise the data collected from the interviews in a manner that facilitated the identification of emerging concepts and themes. Although several topics had been predetermined based on the structure of the interview schedule, themes within these topics and their relatedness to one another could emerge from the interview rather than hypotheses being created, a priori.

Data analysis facilitates the process of bringing order, structure and interpretation to the mass of collected information (Roussow 2003; Holloway and Wheeler 1996). The researcher recorded the interviews to preserve the data and meanings on tape, which allowed for the analysis to be completed subsequent to the interviews. As the analysis was done following the communication process, the data could be analysed without influencing the communicator in any way (Roussow 2003).

Once the recordings were transcribed, the coding of the data, which fragments the interviews into separate categories, allowed for the raw data to be processed (Rubin and Rubin 1995). The coding was then discussed with the researcher's supervisors before further analysis took place. Breaking the material down into manageable sections allowed for the constant comparing and contrasting of categories to identify patterns of meaning (Holloway 1997). The transcripts were read through several times, and the content elicited was compared with the earlier collected data. Each category reflected a concept being analysed to describe the participants' understanding and impact of the predictive testing programme. The interviewee's responses where then grouped into categories of similar ideas and concepts. These categories were then explored to identify any further significant themes, recurring ideas and patterns of belief (Holloway 1997). The data was then compared with the available literature.

3.7 TRUSTWORTHINESS AND VALIDITY

Lincoln and Guba (1985) suggest that the fundamental criterion for a qualitative report is trustworthiness and that the criteria for judging qualitative data include credibility, dependability, confirmability and transferability (Ulin et al 2005). By ensuring the trustworthiness and thus validity of the study it ensures that an appropriate meaning is derived from the specific deductions made, following data analysis.

3.7.1 Credibility focuses on the confidence in the truth of the findings of the study and the provision of an accurate understanding of the context (Ulin et al 2005). This study utilised peer debriefing in an attempt to ensure credibility. The researcher regularly met with her neutral co-supervisor to analyse and interpret her data.

3.7.2 Dependability: According to Holloway (1997), for the study to be dependable it should illustrate consistent and accurate findings. A detailed description of the research method is thus given to ensure the decision trail is clear, process is consistent and results are dependable (Holloway 1997).

3.7.3 Confirmability: The attempt of the researcher to maintain the distinction between her personal values and those of the participant's, ensure that the findings are the result of the research and not the biases or subjectivity of the researcher. The researcher mechanically recorded the data to enhance the validity by providing an accurate and complete record (McMillan and Schumacher 2001). Additionally, the genetic nurse and qualitative researcher reviewed the interview guide to ensure that questions were easily understood and applicable to the participants.

3.7.4 Transferability relates to the conclusions of the study and their transferability to other contexts. The goal of transferability is to produce data which can be applied to other contexts if samples are selected to represent viewpoints and experiences that reflect key issues in the research problem (Ulin et al 2005). The use of comprehensive descriptions will enable peers and or readers to decide if the findings described may be transferred to another context or participant group.

To further certify that the findings of the qualitative study represent reality, the content analysis was verified by the research supervisors to ensure minimal research bias in the interpretation and categorisation of the data. The use of the pilot study together with the supervisors' comments on the validity of the interview schedule ensured further trustworthiness (Holloway and Wheeler 1996; McMillan and Schumacher 2001).

3.8 ASSUMPTIONS

The researcher assumed that each participant answered questions as honestly as possible and expressed a true reflection of their experience.

3.9 LIMITATIONS AND STRENGTHS OF THE STUDY

3.9.1 Limitations of the study

- Time constraints due to the course design. As in-depth interviews produced a rich source of data, it was necessary to restrict participation in the study to a small sample size. By using this approach the intention is not to make generalisations, and findings are only valid for populations with similar characteristics;
- The use of a cross-sectional design meant that changes to the participant's understanding and impact of the predictive test could not be assessed over time. It is possible that certain views could change following further contact with the clinical/genetic team;
- Selection bias: individuals who chose to participate may be unrepresentative of the target population;
- The researcher is aware that her counselling skills are limited and that a sufficient rapport facilitating the full disclosure of sensitive information may not have been established. The participants may also have provided answers, which they thought, may have been appropriate rather than that of their true attitudes (Holloway 1997);
- As the interview schedule was based on the literature, counsellor's opinion and input from the genetic nurse and supervisors, the questions may have missed relevant points from the participant's perspectives;
- Minimal international literature and absence of South African literature implies that a limited amount of data is available for comparison purposes.

3.9.2 Strengths of the study

- The researcher was not part of the clinical/genetic team known to the individuals involved in the predictive testing programme. The individuals were thus probably more likely to speak honestly and openly about their experiences;
- Each interview was conducted personally by the researcher in a venue of the participant's choice and in a language that they were familiar and comfortable with;
- Certain questions used were from other validated studies which increased the trustworthiness of the study;
- The use of a semi-structured interview enabled the researcher to focus on issues salient to the participants. Open-ended questions facilitated responses that were not limited to pre-set categories. Furthermore, clarification could be sought and allowed the researcher to explore or probe issues of interest;
- By tape-recording the interviews, the exact words of the participants were captured, and the researcher could provide her full attention to what the participant was saying;
- Research bias: The researcher was conscious of her own assumptions and recorded her experiences and thoughts during each interview, to try and overcome any potential bias associated with her subjectivity on the information obtained.

3.10 ETHICAL CONSIDERATIONS

The research project maintained the ethical principles of participant autonomy, anonymity, confidentiality and respect. Approval was obtained from the Department of Research and the Institution of Research and Ethics, of the Faculty of Health Sciences at UCT, prior to the study (REC REF: 427/2006).

The genetic nurse involved in the initial contact of the selected participants explained the purpose of the research and participants were in no way coerced or persuaded into taking part in the study. The participants were assured that they could withdraw at any time without jeopardising any medical services that are available to them or their families at the clinic or hospital. Every possible avenue for protecting the anonymity of participants was taken, and a coding system was used to facilitate this. The researcher ensured the participants that the names and the information provided to her during the interview would be kept confidential. Access to the identification information would be limited to the researcher only.

All participants were 18 years and older, and legally competent to sign consent. Written consent was obtained prior to the interviews, from all participants except for one individual who was illiterate, where verbal consent was given. The participants were informed that the session would be tape-recorded for which consent was also obtained (Appendix I and II). The audiotapes were kept in a locked filing cabinet that only the researcher had access to, and the tapes were destroyed as soon as the transcription process was complete.

3.11 RISK BENEFIT

The risk to participants was the discussion of emotional issues and personal concerns related to their perception of cancer. The researcher was sensitive to the emotional state of the individuals and ensured that confidentiality and anonymity was maintained following the disclosure of information in the interview. Participants had the opportunity of a second session with the researcher to clarify any questions or address emotional concerns, which had evoked anxiety. With their permission, the researcher could additionally schedule a session with an experienced genetic counsellor. None of the participants felt they required a second session with either the researcher or genetic counsellor.

The presentation of the analysis, findings and discussion are intermixed in Chapter Four. This is customary in qualitative research (McMillan and Schumacher 2001) and subtitles are included to connotate the different findings. This facilitates the description and prevents unnecessary repetition of information, which distinct chapters for each component would require.

CHAPTER 4: ANALYSIS, RESULTS AND DISCUSSION

CHAPTER FOUR

4.1 INTRODUCTION

This chapter provides information on the sociodemographic and socioeconomic backgrounds of the participants. The data obtained from each interview are presented and discussed in sections and compared to the available literature, where applicable. A total of ten interviews were conducted and transcribed for the data analysis.

The data-analysis involved the coding of various sections and identification of categories and themes, as described in the research methodology. Direct quotes are included from the participants' interviews to provide the reader with a greater insight into the information and to enhance the validity of the identified themes. If a participant's response required translation from Afrikaans to English, it has been indicated, after the quote.

To ensure confidentiality and anonymity, participants (P) are replaced by coding numerals.

4.2 SOCIODEMOGRAPHIC DATA

Participants ranged in age from 24 to 55 years. The majority of participants were females and of mixed ancestry. The sociodemographic and socio-economic information for the ten individuals is presented in Table 4.1

Table 4.1: Sociodemographic and socioeconomic information for participants (n=10).

P	Gender	Age	Marital status	Level of education	Employment status	Occupation
1	Male	49	Single	Grade 12	Full-time	Information Technology
2	Female	32	Single	Grade 12	Full-time	Administration
3	Female	24	Single	Grade 12	Full-time	Human Resources
4	Female	49	Married	Grade 12	Full-time	Bookkeeping
5	Female	50	Single	Grade 5	Full-time	Cleaner
6	Female	24	Single	Grade 11	Unemployed	N/A
7	Female	24	Married	Grade 10	Full-time	Seamstress in clothing factory
8	Female	44	Married	No schooling	Full-time	Domestic worker
9	Male	24	Single	Grade 11	Full-time	Labourer
10	Female	55	Divorced	Grade 12	Full-time	Nurse

The level of education was high among most of the participants. In South Africa, formal schooling comprises of 12 years of primary and secondary education. High school ends at Grade 12, otherwise known as standard ten or matric. Half of the participants had matriculated and three had a tertiary education. Of the participants who had completed secondary school, four of the five had taken biology as one of their main subjects. Only P5 and P8 did not complete primary school (seven years of schooling) and for P8, the school had been inaccessible, as she had grown up on a farm away from the rural town.

The ten participants reported a range of monthly household incomes, and all except for one (P6), had a full-time job. According to Statistics South Africa (2004), the average annual income per household for Cape Town is R 87 811 (R 7 317 per month). Seven of the participants had an income below this amount and the most disadvantaged participant had a household income of R1 600 or less to support five people. Thus the socioeconomic status for the participants in this study was relatively low (Table 4.2), with the exception of P1 and P4 who were also the only participants who could afford medical insurance.

Table 4.2: Number of individuals dependent on the monthly income (n=10).

Participant No.	Household income/month (indicated by an income bracket)	No. of people supported by income
1	R 25 601 - R51 200	3
2	R1 601 - R3 200	4
3	R6 401 - R12 800	3
4	R 25 601 - R51 200	6
5	R801 - R1 600	5
6	N/A†	N/A*
7	R1 600 - R3 200	5
8	R 3 201 - R 6 400	5
9	R3 201 - R 6 400	6
10	R3 201 - R6 400	3

†P6 did not know the household income/month; she was unemployed at the time of the study and not earning an income. *The residence provided boarding for 17 individuals, none of whom were related to P6.

4.2.1 Family history of cancer

The feature that differentiates genetic disorders from other illnesses is the implications for other family members (Murphy 1999). The majority of counselees are aware of genetic testing due to having a family member with cancer, and thus upon initiating counselling may already have strong emotions relating to their experience within their own family (Weil 2000).

Part of each interview focused on obtaining information relating to the participant's family history of HNPCC. Data were gathered on the number of and relationship to relatives with an HNPCC-related cancer. This was obtained from the HNPCC database in the Division of Human Genetics at UCT, and questions from Section A of the interview schedule. Table 4.3 illustrates a few of the important aspects relating to the HNPCC-related cancer in the family, and comments made by the participants are included in the text.

Table 4.3: Experience of cancer in the family and involvement in a genetic testing programme (n=10).

	INFORMATION RELATING TO THE PARENT OF THE PARTICIPANT			INFORMATION RELATING TO THE PARTICIPANT	
P	**Affected parent (CRC)**	**Parent tested for MMR mutation predisposing to HNPCC**	**Parent died due to cancer**	**Realised that they were at risk for CRC**	**No. of children involved in predictive testing programme**
1	Mother	Yes	Yes	As teenager, due to grandmother's cancer	N/A
2	Father	Yes	Yes	With father's involvement in programme	Too young*
3	Father	Yes	No	Related to father's cancer and own involvement in programme	N/A
4	Mother	Yes	No	Mother's enrolment in programme and contact with genetic team	1 child tested 2 too young*
5	Father	Yes	Yes	With testing	2 children not tested
6	No	Yes	No	When approached for testing	Too young*
7	Father	Yes	Yes	Due to father's involvement in programme	Too young*
8	Mother	No	Yes	When mom and sister had cancer	1 child tested 1 not tested 1 too young*
9	Father	Yes	No	Related to father's cancer and involvement in programme	N/A
10	Mother	Yes	Yes	When mother had been diagnosed and involved in programme	1 child tested 1 too young*

* Predictive testing is only offered to individuals over the age of 18 years. The age limit has been set at 18 as it reflects the age when an individual legally becomes an adult in SA.

When asked about the time when they had realised that they were at risk for CRC, eight of the ten participants stated that it had been as a result of the diagnosis of a parent's HNPCC-related cancer and/ or a family member's involvement in the genetic testing programme. P5 and P6 had only realised the risk factor subsequent to their own involvement in predictive testing. P1 recalled that this had been around the age of 13 years. His grandmother had had cancer, and he realised that due to the family history, he was also at risk. For the other participants, the realisation had been much later, from an age of 19 years and older. All the participants, excluding P6, had grown up with an affected parent. The mother of P6 was unaffected, however she had a maternal grandmother (now deceased) and maternal uncle who were affected.

Predictive testing is only possible following the identification of a mutation in an affected family member. For all the participants with an affected parent, the disease-causing mutation had been identified in the respective affected parent. The mother of P8 had passed away prior to any genetic testing and her older affected siblings had been tested. P1, P2, P5, P7, P8 and P10 had lost a parent as a result of the cancer. Although it had not been directly asked, many of the participants volunteered the status or the suspected mutation status of their siblings and extended family. Many of the participants' children had also consented to be tested for the familial CRC predisposing mutation (of those eligible for predictive testing; only P5's two children and P8's one child had not entered the programme. Table 4.3, page 37).

4.3 GENETIC TESTING

4.3.1 Motivation for predictive genetic testing

Participants were asked to rate seven statements according to the extent that it had influenced their decision to have a predictive genetic test. The accumulated responses of the ten participants are presented in Table 4.4

Table 4.4: Participants' motivation for predictive testing (n=10).

MOTIVATION STATEMENT	NOT AT ALL	SOMEWHAT	VERY MUCH	NOT APPLICABLE
1. To learn about my children's risk			6	4
2. To reduce my risk of developing cancer	1	1	8	
3. To plan for the future	1	2	7	
4. To help research			10	
5. To be certain about my risk		2	8	
6. To make decisions about having children		2	3	5
7. Marital decisions	2	1	1	6
8. Doctor recommended it	2	4	4	
9. Family members urged me to take test	4	2	4	
10.Worried about abnormal stools/health related concerns	7	1	2	

The decision to have a genetic test was strongly influenced by the fact that the participants were concerned about their children's risk. All the participants who had children of their own viewed this as an important factor in their decision-making.

P8 stated that the most essential reason for testing was for her children's benefit and to be able to explain to them about predictive testing and the future surveillance required. P4 commented:

" ... the main thing was that we felt if we could prevent anything happening to our kids, we could stop it, because the more you know about a thing, the more likely you are to prevent it or find ways of preventing it and that was a big deal for us".

For the majority of participants, future planning (7/10), reducing their risk of developing an HNPCC-related cancer (7/10), gaining certainty (8/10) and aiding research (10/10) rated as further key motivating factors. P1 was the only participant that viewed these items (2, 3, 5 in Table 4.4) to have "no", or "very little effect" on his decision-making. The only factor that strongly motivated him to have the genetic test was to aid research. P1 felt that he was already going for regular surveillance (colonoscopy) prior to testing, and thus did not see the

need to know his mutation status. He expressed that he felt the benefit of the research would not be for him, but rather for other people.

" ... I was already going for check-ups and that sort of thing so you know, whether the blood test were going to reveal - I was already being tested anyway, so as far as I was concerned I was at the end of it anyway. Whatever benefits came out of the research stuff would not necessarily benefit myself but it may benefit other people... "

Eight of the ten participants did not express any health-related concerns, prior to the testing, to have strongly influenced their decision. However P3 was very worried about her health although, when asked if she was experiencing any symptoms, she commented that she had no physical symptoms. For P9, the health concerns were one of the factors that had played a large role in his decision-making concerning the uptake of the test. When asked if he had been apprehensive about any health concerns prior to the testing, P9 responded:

"No not actually, but some days, I don't know if I was imagining it, but I felt like my bowel action was somehow different" (translated).

The participant also added that it was important for him to know his status. He reported that he had been extremely anxious due to the uncertainty. P9 recalled an experience prior to his involvement in the predictive testing programme where he felt not knowing was making him physically ill.

"... when I tried to stand-up, I felt ill all of a sudden and then I thought, this is where I could have known already. So it's about my health, that I need to know where I stand" (translated).

4.4 LEVEL OF UNDERSTANDING OF THE TEST RESULTS

Participants were questioned about their understanding of the genetic test. Their responses are summarised in Table 4.5

Table 4.5: Participants' knowledge of cancer genetics (n=10).

P	Knew that they had tested positive for the gene predisposing to CRC	Risk of developing CRC (estimated and perceived risks)	Genetic test can tell you if you have cancer	Difference between genetic test (GT) and colonoscopy (C)	Additional factors affecting personal risk perception
1	Yes	80% - will get it unless pass away before the onset	"Can not tell you if you have cancer, but can provide risks"	(GT)-"is about the risk factor". (C) – "identifies polyps".	Family history and number of affected family members
2	Yes	80% - prevent it by a healthy lifestyle	Yes	"Require GT to see if you have the gene or not", (C) "identifies changes to colon wall".	Test only
3	Yes	80% - but views it as a definite	No	(GT)- "can see if you are predisposed to bowel cancer". (C) – "checks that the regeneration and cells working normally".	Family history
4	Yes	50% - feels she will not get cancer	"Not a cancer test. Can provide you with the possibility"	(GT) – "blood test". (C) – "is a visual thing".	Only test

P	Knew that they had tested positive for the gene predisposing to CRC	Risk of developing CRC (estimated and perceived risks)	Genetic test can tell you if you have cancer	Difference between genetic test (GT) and colonoscopy (C)	Additional factors affecting personal risk perception
5	No*	50%	Yes	GT – "tells you if you are a carrier". (C)- "tells you if you are fine".	Only test
6	Yes	50%	Yes	(GT) – "looks for gene". (C) – "identifies anything in the colon".	Only test
7	Yes	50%	Yes	(GT) – "have gene or not". (C) – "can see if the colon is OK".	Family history
8	Yes	50% - will get cancer, 100% chance	"No- shows you if you have the gene or not"	(GT) – "looks for gene". (C) – "looks for cancer in colon".	Family and age is near that of other affected family members
9	Yes	80% - feels this has been reduced as colonoscopy showed no polyps	Yes	(GT) – "looks for cancer gene". (C) – "identifies lesions in colon wall".	Family history
10	Yes	50% - but will develop it	Yes	(GT) – "see if cancer/TB/other problems". (C) – "can identify gene, if have the gene must have an operation".	Family history

* The participant did recall her positive test result; however this was at a later stage of the interview.

All the participants in the study could recall their approximate dates of counselling and result-giving session, as well as the geneticist who had been involved in delivering the results. For the majority of individuals, the person who had created the awareness of the availability of a predictive test had been the nurse or doctor involved in the programme. Only P3 and P6 had initially heard about the possibility of a predictive test through a family member, which in this case had been the affected father and aunt, respectively.

Upon being asked if there were any additional factors (independent of the genetic test result) that they had felt may have increased their risk, six participants (P1, P3, P7 - P10) viewed their family history as a factor. P1 mentioned the number of affected individuals in his family, in addition to the family history. P8 indicated that being of similar age to the onset of the affected family members was a further indication that she was at high-risk for the CRC.

All the participants correctly stated that they were mutation-positive. When asked how the predictive test was conducted, all of them accurately recalled that it had been a blood test. One of the specific aims of the research was to investigate the understanding of the predictive test. The ten participants demonstrated different levels of understanding and responses ranging from a very basic to a high comprehension. Questions relating to the genetic test in terms of: risk of developing CRC with a mutation-positive result; if the genetic test was capable of detecting cancer or not; and the difference between the genetic test and a colonoscopy are presented in Table 4.5 (page 41).

All the participants could explain that their mutation-positive result had placed them at an increased risk for developing CRC. However, only seven participants (P1-P4, P7-P9) realised that being mutation-positive implied that their risk of developing cancer was consequently higher than the general population. P5 and P10 thought it was the same, and P6 did not know. The estimated risk expressed by the participants, differed among the group. P1, P2, P3 and P9 recalled an 80% risk. However, P9 who identified his risk to be 80%, felt that after having a colonoscopy showing no polyps, this could be reduced.

P4, P5, P6, P7, P8 and P10 quoted 50%, as the estimated lifetime risk of developing CRC. However P4 felt she had a positive outlook and did not intend developing cancer. P1, P3, P8 and P10 added that they felt that they would definitely develop cancer. P1 further expressed that, even though he knew his risk was not a 100%, he viewed it as that.

"... the risk is there, and the risk is that I will get it at some point. I would say it's a 100% chance, unless I pass away before I get it".

Six of the participants (P2, P5-P7, P8 and P9) incorrectly stated that the genetic test could provide information on whether or not a person had cancer or could identify cancer in the body. However, all the participants, except for P10, could correctly explain what type of information the genetic test could provide, when they were asked the question relating to their understanding of the genetic test as compared to the colonoscopy. When P10 was asked about the genetic test she commented:

"It can tell you if you have cancer or not, and in which part of your body it may be, and if they find a growth they must remove it, and the quicker they remove it the better it will be for me..."

P10 was asked about the colonoscopy and if both tests were necessary:

"It can tell you if there is a gene, or if there is not a gene, and you have to go for the operation or you don't have to go for the operation. It can also tell you about the colon of the gene itself, if there is a fault in the colon, and as I said, you will have to go for an operation or you won't have to".

She also added:

"I can't think there is a difference between the two tests (between the genetic test and the colonoscopy), *they also went in with the scope at that time".*

Interestingly, P10 was a nurse and it was surprising to see that she was the participant that illustrated the greatest confusion and had difficulty in distinguishing between the genetic test and the colonoscopy.

Further questions relating to the participants' knowledge of cancer genetics are provided in Table 4.6

Table 4.6: Frequency of responses in each category (n=10).

Question	Knew the answer	Did not know	% of correct answers
1. Colon cancer is always inherited	5	5	50%
2. Everyone with the gene causing CRC will develop CRC	4	6	40%
3. A person who does not have the gene for CRC is less likely to develop it than someone with the gene	5	5	50%
4. There is more than one gene that can cause CRC	1	9	10%
5. Colonoscopy (the inside of the bowel is viewed with a special tube) is very likely to detect CRC if present	10	-	100%
6. In a family where the gene causing CRC has been found, those without the gene have the same risk of CRC as the general population	7	3	70%
7. If a person looks like (or has the same personality) as a family member who developed CRC, they are likely to have inherited the same gene as that person	8	2	80%
8. The increased risk of cancer can be passed on to your children	9	1	90%
9. Half of your genes are from your mother and the other half from your father	7	3	70%
10. If a person has the gene, the chance of developing CRC may be reduced with regular check-ups (colonoscopy)	8	2	80%
11. If you have a healthy lifestyle you are less likely to develop CRC	7	3	70%
12. If there is something wrong with your genes you will notice this (you will feel a difference in your body)	9	1	90%
Mean level of knowledge	**67%**		

The percentage of individuals correctly answering each of the 12 items ranged between 10% (item 4) and 100% (item 5). The total scores for each participant across the group ranged between 50% (6/12) for P8 to 92% (11/12) for P10, with the average total score calculated at 67%. Most participants responded correctly to items 5 (100%) and 10 (80%), which assessed the knowledge on surveillance measures. Items 1 to 4 assessed awareness of sporadic CRC and the knowledge of incomplete penetrance of the gene mutations, which was answered incorrectly by the majority of participants. Few participants knew that there was more than one gene predisposing to CRC. By contrast, the knowledge relating to inheritance was high, as reflected by item 8 (90%) and 9 (70%).

4.4.1 Discussion of understanding of predictive test and perceived risk

4.4.1.1 Reasons for taking the test

The findings of this study were similar to those of Claes et al (2004) and Esplen et al (2001), who found key motivation factors to include: early detection of cancer, concern for children's risk and reduction of uncertainty. Esplen et al (2001) suggested that pursuing testing to gain certainty about the children's risk might be linked to feelings of guilt or anticipated feelings associated with passing on the illness to their offspring.

A desire to further research has also been highlighted in the literature (Esplen et al 2001). This may be related to the close relationship with the medical professionals and the continuous follow-up and contact, although recommendation by a doctor did not significantly increase test uptake. Family and marital planning did not appear to play a major role in predictive testing for HNPCC, and may have been related to the fact that for the majority, decisions regarding this aspect of their lives had already been made prior to testing.

4.4.1.2 Level of understanding and perceived risk

The estimated lifetime risks were assessed and six of the ten individuals underestimated their cancer risk as being only 50% or less, which in this context, referred to the very high cancer risk without regular surveillance. Aktan-Collan et al (2001) found the level of misunderstanding amongst mutation-positive individuals, to be high, especially among the elderly and less educated. In contrast, this study reflected a range, not limited to a specific age group or education level, for those individuals underestimating their CRC risk. None of the individuals reported a perceived risk at the same level as that communicated to them during counselling. This has also been demonstrated by other studies (Domanska et al 2007; Aktan-Collan et al 2001).

Possible explanations for the underestimated lifetime risks expressed, may include a reflection of a coping mechanism such as denial or risk minimisation. Another consideration could be the difficulty in expressing a high but not an inevitable risk in percentages, which may result in the simplification of the risk into the possible outcomes – either it will or it won't happen. Weil (2000) states that, when faced with a critical decision about uncertain outcomes, counselees commonly transform numerical risk into a binary form. Although all

the subjects had correctly recalled their mutation status, the understanding of the test result seemed to be complex.

A review on risk communication in genetic testing for cancer suggested that the individual's perception of the personal risks of cancer, are resistant to education and counselling (Croyle and Lerman 1999). Findings by Hopwood et al (1998) have suggested that previous experiences of cancer, within the family, shape the individual's belief of how threatening the disease is. Additionally, McAllister (2002) found these experiences were used as a reference point in interpreting personal risk, in her study of predictive genetic testing. Therefore it is likely that the experience and knowledge of hereditary cancer plays an important role in the individual's interpretation regarding cancer-risk information provided to them during counselling. For 60% (6/10) of the participants in this cohort, family history was noted as an additional factor (independent of their actual risk), influencing their perceived cancer risk. The majority recalled that affected family members had passed away as a result of CRC, and were likely to have built up personal beliefs surrounding this. Many of the participants believed the cancer to be inevitable and the illness and or death of other family members added to this risk perception. These findings support other studies indicating that lived experiences and family history affect how individuals construct perceptions of personal cancer risk (d'Agincourt-Canning 2005; McAllister 2002). According to d'Agincourt-Canning (2005), perceptions of cancer risk depend more on emotional well-being and life experiences rather than the numerical risks. This should be an important consideration for those involved in managing these individuals, and highlights the significance of probing more deeply into the individual's experiential knowledge.

For P1, an individual with a tertiary level education and a good comprehension of the genetic test and results, an 80% lifetime risk was still viewed as a certainty that he would develop CRC. P1 stated that his experience of his family's HNPCC-related cancer and realisation of a personal risk had been at a young age (13 years). In addition to being aware of his family history at an early age, he drew on the experiences of affected family members (grandmother and his mother) to construct knowledge on the cancer and the course that it may take on his own life. Van Oostrom et al (2006) confirms that individuals with an affected parent tend to perceive cancer risks as higher than those without, and the highest level of cancer distress and risk perception occur in individuals with a parental cancer experienced during their childhood.

4.4.1.3 Cancer related knowledge

The average knowledge score among the ten participants was 67%. The knowledge scores recorded by other studies in cohorts of individuals at risk for breast cancer (Meiser et al 2001; Lerman et al 1996) and CRC (Collins et al 2000) have illustrated an increase in knowledge scores post-test counselling as compared to pre-test counselling. This study only investigated the HNPCC-related cancer knowledge among the participants at one point in time and could not be directly compared. It can be noted that the scores reflected a good knowledge of colonoscopic surveillance, but only moderate levels of recall about the genetic aspects of colon cancer. The data presented in this study showed that the level of knowledge was related to the education level and less convincingly to the socioeconomic status. As with other studies, education was found to be associated with knowledge score, and a higher education could be assumed to facilitate a better understanding (Collins et al 2000). This finding suggests that individuals with lower levels of education may benefit from additional counselling to improve their genetic knowledge levels.

4.5 IMPACT OF GENETIC TESTING ON THE INDIVIDUAL

Participants were asked questions relating to their experience following the test disclosure. The responses are summarised in Table 4.7

Table 4.7: Summary of the participant's experience at the time of the predictive test results (n=10).

P	Year result given and time since test result	Suspected result prior to testing	Emotional reaction to test result	Shared result with family
1	2003 - 4 years	Due to the family history of cancer, felt that there was a strong possibility of testing positive.	Had expected it, so was prepared.	Yes - Family is the support system for each other.
2	2002 - 5 years	Expected to test negative.	Very upsetting. Having to tell the parents was worse for her than receiving the positive test result.	Yes – "Can't hide such a thing away from your family". Very close to her family.
3	2003 – 4 years	Was uncertain- " I was open to anything".	Discouraged and sad. Had pictured other family members who had died as a result of the cancer.	Yes - Only certain members that they were close to.
4	2003 – 4 years	"I didn't really affect me one way or the other".	Not too concerned-had a positive outlook on life.	Yes - Open family and discuss everything.
5	2006 – 1 year	Felt certain of testing positive.	Disappointed and sad. Immediately thought of her children and worried about who would look after them if anything happened to her.	No - Only with partner (boyfriend).

P	Year result given and time since test result	Suspected result prior to testing	Emotional reaction to test result	Shared result with family
6	2004 – 3 years	P6 felt that she would test negative. "I felt I would not be a carrier".	" I didn't feel like myself".	Yes - Only with her mother.
7	2004 – 3 years	Suspected that she would test positive.	I felt normal- I was the eldest so I knew I had to have it".	Yes - Only with mother, husband and aunt.
8	2004 – 3 years	Knew she would test positive as a result of previous health concerns (unrelated health problems).	Had felt like the end of the world, then realised she had to live with it. Worried and concerned, but accepted it.	Yes – "Shared result with whole family as they have a right to know, as they are family".
9	2004 – 3 years	Had a feeling he would test positive.	Was not good news, but didn't feel bad about it. Had a feeling prior to the time, was not stressed or worried.	Yes - Shared with family and friends as felt a sense of relief by telling them.
10	2002 – 5 years	Uncertain.	Very emotional. Difficult to understand as had led a healthy lifestyle.	Yes - Shared with mother and sister. Felt that if something were to happen to her, they had to know what the cause was.

P2 and P6 were the only participants who expected to test negative prior to receiving their predictive test results. When P2 was asked about how she had felt when a positive test result was given, she commented:

"... it was difficult to hear. What was even more devastating was telling the parents, with a father that was sitting there, knowing that he could possibly have given it to his child. That was the worst" (translated).

P10 also commented on sensing her mother's guilt when she disclosed the test result to her family. Projection describes a defence mechanism whereby a person attributes their own unwanted or undesirable emotions onto another person (Weil 2000; Djurdjinovik 1998). It is possible that feelings relating to the guilt of passing on the condition may be something that was projected onto the parent's experience in both these cases. These assumptions may reflect the emotions currently being experienced by the participants, relating to their own guilt.

For P5, one of the participants who had felt certain that she would test positive, it was still a shock to receive confirmation of an unfavourable result. She had actually hoped that her expectation would be proven wrong. When asked how she felt following the outcome, she responded as follows:

"I was very disappointed. Actually I was more saddened. I thought, my gosh, my children are still so young, if I had to die, what would happen to them" (translated).

P10 stated that it had been very emotional for her to receive the result; she had felt that her life would end at that moment. She commented:

"It was very difficult when I heard; I asked them, why... I don't smoke, I don't drink, why do I have it in me then and some of my sisters don't have it. It was a shock, because I make sure that I lead a healthy lifestyle, why do I have it?"

Further comments made by the participant included:

"I felt extremely upset.... I cried and cried... I asked myself time and time again, I thought, my life ends here, but afterwards I sat down and prayed and felt my life would not end here. There are so many people with cancer who still live a long life, and if my cancer is so bad, I have the gene, I know that now, if it is then so bad, I will accept it if I require an operation...

but if they do find something and I require an operation, will I ever wake up again and those thoughts scare me".

For P10 it was the fear of a future surgery that consumed her thoughts, not only the increased risk of cancer. Several times during the interview, she recollected how terrified she was by the thought of surgery.

Nine of the ten participants had shared their test result with their family, or selected family members who they were especially close to. The majority stated that they viewed their family as a support base and were open about such issues with them as they were close to one another. P10 and P7 voiced similar reasons as to why they had shared this with certain of their family members. P7 commented:

"They must know, my mom, my husband and my auntie, because when I die, then they will know what caused it" (translated).

Only P5 had not shared her result with her family. Many of her siblings had passed away and of those that were still alive she did not feel close to or that she could trust them.

In this study, participants were additionally asked a range of questions relating to their perception of controllability over developing cancer and subsequent surveillance measures undertaken. Selected responses are presented in Table 4.8 (page 53) and Table 4.9 (page 55).

Table 4.8: Perception of the predisposition to cancer (n=10).

	INFORMATION RELATING TO CANCER PERCEPTION		
P	Control over risk of developing cancer	If were to develop cancer when would it be	Cope with the development of cancer
1	No control unless medical solution becomes available in future	Not relative to specific age	Yes
2	Can lower chance by a healthy lifestyle	"Older you get, greater risk". In 40s as family got it then	Yes – "Won't be shocked if I get it"
3	Yes – by going for regular check-ups and colonoscopies	30s - family got it then	Yes - If develop it will catch it early
4	Yes – healthy lifestyle, regular check-ups and pick it up early	50s - family developed it around this age	Yes - Cope well as has a lot of support
5	*	No specific age	*
6	Yes – with prayer	No specific age	Yes - Cope through faith
7	Yes – colonoscopies	No specific age	Had not thought about it
8	Yes – with faith	"I am now 44 and susceptible when you reach that age"	Yes - Has to live with it
9	Yes - colonoscopies	*	Yes - Prepared himself
10	No	*	*

* Did not know or did not answer the question directly

The age at which close family members were diagnosed with an HNPCC-related cancer acquired particular salience for many of the participants. Four of the participants were convinced that if they were to develop cancer it would be near the age of their affected family members. P3's comment illustrates that her concern and sense of vulnerability increased as she neared the age of the cancer development in her family.

"... if I look at my sister, she developed it when she was very young. She developed it in her early 30's and I wonder... and my dad was in his late 50's, so why did my dad have it at 50 and she in her 30's, and I think she had a stressful life and I wonder if that is part of it happening quicker than...I have this in my mind that at 30 I must really start worrying!"

P4 felt that the possibility of developing cancer would also be age-related:

"If it had to occur, probably round about now is when it would happen. I turn 50 next year, and if it's going to happen it will probably happen within the next few years, as the majority of my mother's side of the family developed it roughly between 45 and 50"(translated).

The other participants gave no specific age, while P9 and P10 did not know.

P7 was the sole participant to state that, if she ever developed cancer, she did not think she would survive it. She was extremely afraid and revealed that she had no control over preventing it. P1 and P10 responded that they had no control over whether or not they would develop cancer, however P1 did feel he would survive it while P10 did not know if she would survive it or not, and was terrified by the thought of cancer. Support from family, faith and catching it early, were commented on as respective reasons for facilitating the coping process.

Table 4.9: Compliance with colonoscopic surveillance following genetic test result (n=10).

P	Colonoscopy within year of test result disclosure	Number of colonoscopies attended	Recommended colonoscopic surveillance (subsequent to test results)†	Compliance (%)*
1	Involved in surveillance prior to testing	3	4	75
2	Yes	2[a]	3	67
3	No	1	1	100
4	Yes	6	6	100
5	Yes	2	2	100
6	Yes	2	2	100
7	Yes	2	2	100
8	Yes	3[b]	4	75
9	Yes	2	2	100
10	Involved in surveillance prior to testing	6	6	100

† Recommended surveillance was calculated for each individual participant. The date of result disclosure (according to the genetic test report) and recommended age-related colonoscopic frequency was taken into account.
* Compliance was calculated by dividing the attended number of colonoscopies by the recommended number of colonoscopies. [a] Unable to attend scheduled colonoscopy as a result of an unassociated medical complication. [b]At the time of the study the scheduled colonoscopy date for the current year was still outstanding.

Eight of the participants had never had a colonoscopy prior to genetic testing. Within the year following disclosure, nine of the ten proceeded to have a colonoscopy and the one participant who did not, was younger than 25 years (colonoscopies not strictly recommended before this age). The majority of participants (7/10) were adherent to the recommended screening guidelines, except P1, P2 and P8. However P1 had been unable to receive a colonoscopy as a result of the travelling nature of his job at the time; P2, an unrelated medical complication; and P8 was still scheduled to have a colonoscopy (at a stage later than the completion of this study). Therefore all the participants could theoretically be shown to follow the screening recommendations.

4.5.1 Discussion of the impact of genetic testing on the individual

4.5.1.1 Satisfaction with the decision

All the participants were satisfied about their decision to go for predictive testing. They were asked to consider whether or not they felt they had made the right decision, and if given the opportunity to go back in time, would have made a similar decision. All participants (10/10) felt they would have retaken the test. Regret of being tested was not expressed by any of the participants. Furthermore, they all viewed the genetic test as reliable and trusted the result completely.

4.5.1.2 Psychosocial impact

One of the main concerns associated with offering predictive testing, is the potentially adverse emotional impact on the individual. Counselling is aimed at having a positive impact on reducing distress and studies have found the adverse psychological outcome among individuals receiving their test results, to be minimal (Claes et al 2005; Wagner 2005; Claes et al 2004). The literature on the impact of predictive testing and counselling has highlighted that depression, anxiety, and cancer worry scores were within normal ranges and there were no long-term adverse psychological outcomes (Gritz et al 2005; Meiser et al 2004; Aktan-Collan et al 2001). Collins et al (2007) confirmed these findings, following assessment of these outcomes over a period of three years. The value of this finding has important implications for individuals considering predictive testing, as participants can be reassured that no adverse psychological outcomes have been observed among those testing mutation-positive (Meiser et al 2004).

However, mean results can often obscure the individual reactions (Claes et al 2004) and these individual reactions may vary greatly (Chapman and Burn 1999). The use of a qualitative format including interviews and open-ended questions was a strength of this study, as responses were not limited to psychometric measurements. Questions relating to the individual's general distress at the time of result disclosure and concern about the prospect of developing cancer were included in the interview. Sixty percent (6/10) of the participants expressed emotions relating to shock and distress post-test result disclosure. However a general reflection of being able to cope with a cancer predisposition, and survive cancer if it were to develop, was observed among the majority (7/10) of individuals.

Open communication among family members is generally associated with more effective coping and greater emotional support (Weil 2000). For many of the participants, support was another essential component of their coping process. Nine of the ten participants communicated their mutation status to their family, and expressed this as one of their reasons for the disclosure. A further source of support identified by the participants included being involved in a predictive testing programme. For P5, the only participant who stated that she did not trust her family or communicate with them about the family cancer, this was a central source of support.

4.5.1.3 Cancer surveillance

Predictive testing is valuable in the management of HNPCC, as it facilitates targeted screening of high-risk individuals (Stanley et al 2000; Jarvinen et al 2000). An individual's perception of disease may not only have an influence on emotional reactions and coping response, but additionally on their health-related behaviour (Leventhal et al 2003). In the present study, 70% (7/10) of the participants perceived that they had some control over their increased risk of CRC, (four out of the seven viewed this as a result of regular screening). As suggested by other studies, the focus on the benefits of regular screening probably fosters the participant's ability to cope with the genetic test result and predisposition to CRC (Keller et al 2002; McAllister 2002). This is further supported by the overwhelming confidence illustrated by the participants in the effectiveness of the surveillance programme. All (10/10) of the participants believed the colonoscopy was capable of detecting CRC and eight of the ten, believed that it could reduce their chance of CRC (Table 4.6, page 45).

An important finding of this study was the high compliance rate (7/10 participants adhered to surveillance recommendations and 10/10 were involved in colonoscopic screening practices). Noteworthy, is the fact that this held true for individual's representative of poor education levels, low socio-economic status, those underestimating CRC risk and individuals with a poor understanding of the genetic test and implications thereof. However, these individuals are faced with the necessity of adherence to this health-related behaviour for a long period of time. Long-term follow-up of the cancer screening in these individuals will be needed to see whether the high uptake remains. This was also a recommendation arising from Kruger's (2005) work. She investigated the factors affecting non-adherence and adherence to surveillance guidelines for mutation-positive individuals in rural areas of the Northern and Western Cape Provinces in SA.

The conclusion is presented in the next chapter.

CHAPTER 5: CONCLUSION

CHAPTER FIVE

5.1 CONCLUSION

One of the central features of genetic counselling is to enable the comprehension of an individual's risk for a disorder and facilitate the understanding of options for dealing with this risk (Resta et al 2006; Weil 2000). In the context of HNPCC, genetic counselling can be considered effective if it results in an improved accuracy of perceived risk, knowledge of the disease, genetics and adherence to recommended screening, without causing undue anxiety (Braithwaite et al 2006).

The main aim of this study was to provide insight into the level of understanding of the individual's genetic predisposition to CRC, following predictive testing for HNPCC. This included investigating the subsequent impact on the individual, specifically in terms of: the risk perception, psychological effect and adherence to screening recommendations. The use of qualitative in-depth interviews allowed the participants to discuss their beliefs and emotions, relating to their experience of the predictive testing, in a way that quantitative research could not. Such an insider's view, obtained through the use of personal interviews with the participants, was suited to the provision of information on the understanding and impact of the predictive test result.

Predictive testing has far-reaching implications, not only for the individual but also for the rest of the family (Evers-Kierbooms et al 2000). This was particularly evident, as one of the main motivations for the uptake of the predictive test, among the participants, was to obtain knowledge of their children's risks. Additionally, the experience of an HNPCC-related cancer in the participant's family appeared to have a significant role in the individual's interpretation of information. The emotional representation of the disease, influenced by the individual's personal experience and perceptions of cancer in the family, rather than the given information seemed to affect the perceived risk of the participants.

Further findings of this study indicate that the majority of individuals illustrated a misunderstanding of their CRC risk, particularly an underestimation. However, the perceived risk among the individuals was high and some viewed the possibility of developing an HNPCC-related cancer, as a definite. The discrepancy between the recall of estimated risks

provided and perceived risk, most likely reflects the process of binary reasoning. As participants were already involved in the screening programme, a further consideration could be linked to the high efficacy of the colonoscopy in terms of CRC prevention. Noteworthy, is the fact that none of the individuals involved in the study reported a perceived risk at the same level as that communicated to them during counselling. Therefore attributing a great deal of time and effort into providing accurate risk figures may be time misspent (Mackay and Ponder 1997).

Perceptions of perceived risk have previously been suggested to be relatively resistant to educational efforts (Croyle and Lerman 1999) and largely been shown to be unique to each individual. Risk comprehension among participants is critical to decision-making about risk management. Incorrect perception is acceptable, as long as these individuals continue to participate in the screening programmes; and are aware of the reason for the prevention procedure.

As predictive testing can have an impact not only on health-related behaviour but also on distress levels (Claes et al 2005), this aspect was additionally investigated. The small sample in this study did not reveal any significant psychological problems as a consequence of the predictive test result. However, the interview data indicated some individually different problems in addition to the concern over being at an increased risk, such as the fear of the possibility of future surgery.

It is not easy to convey the information that predictive testing represents in a way that facilitates the recipient's understanding and relevance thereof. While such testing has considerable potential for accurate risk assessment and appropriate targeting of screening and preventative strategies, it remains at best, predictive. This study suggests that a good level of understanding and knowledge related to hereditary cancer can be demonstrated for the majority of the participants (mean level of knowledge of the ten participants was 67%). Particularly evident was the insight of how to prevent CRC and the effectiveness of colonoscopies. This may be associated with the high adherence rate to screening recommendations.

It is important to realise that the time following result disclosure varied across the sample (a range of 1-5 years) and the continual contact with the clinical/genetic team over this period

may have influenced the level of knowledge and understanding. While this should be interpreted with caution, it does support the importance of having a person trained in dealing with genetic information as part of the clinical team. Furthermore, it could reflect the benefits of such constant revisiting of information. This however, did not appear to influence the participant's risk perception in this study.

CHAPTER 6: RECOMMENDATIONS

CHAPTER SIX

6.1 RECOMMENDATIONS

6.1.1 Recommendations identified through the study:

The small sample size of only ten individuals is a major limitation and the results reflect very individualised experiences, which cannot be generalised. However the study provides a useful framework for further research, together with potential implications for genetic counselling in the predictive testing programme. Recommendations obtained from the findings include:

- Many of the participants believed the HNPCC-related cancer to be inevitable and the sensitivity of this response should strengthen the argument for continued support to these individuals;
- Vulnerable individuals may include those participants with a parental cancer diagnosed during their childhood and the highest levels of anxiety could be suggested to occur at a time nearing the age of the affected parent's diagnosis. An effort should be made to identify subjects where this may be the case, and psychological support should be more actively offered. As family history plays such an important role in risk perception it may be a useful tool in enabling identification of individuals at risk for adverse psychological consequences;
- A deeper exploration into the personal experience of cancer in relatives. To understand the perspective and background of the individual participant, investigation into how the cancer is represented in the individual's mind and the related anxiety and concern, may be required. Beliefs and attitudes may not simply be corrected through the provision of facts alone, and educational approaches may not be enough to correct misperceptions. d'Agincourt-Canning (2005) suggests that counselling strategies, which expand upon the lived experiences and knowledge of the disease may enhance effective communication of genetic risk.

6.1.2 Recommendations from the participant's perspective:

At the end of each interview, the participants were given the opportunity to comment on or provide their opinion of the predictive testing programme. The feedback relating to the

participant's experience of the counselling received during the programme was especially positive. Regular follow-up in terms of reminders to attend screening practices and a support system was highlighted by the participants. Further recommendations from the participants included:

- The provision of more written material with the focus on practical issues specifically how to live a healthy lifestyle;
- To be informed of emerging therapies and treatment options and to receive feedback on future research;
- More aggressive pursuit of family members who were not adherent to screening recommendations (although this may be controversial to apply and unethical).

6.2 RECOMMENDATIONS FOR FUTURE RESEARCH

It will be of value to consider the following suggested projects:

- The study focused on individuals who had already received their test results, and their interpretation may have been subjected to potential recall bias and influenced by the knowledge of their test result. A prospective study design, with a larger sample number and assessment over a number of time points could be beneficial in further exploration of these preliminary findings;
- Include participants representative of the rest of SA. This study only investigated individuals from urban areas and experiences from rural areas would be required for comparison purposes;
- The underestimation of the HNPCC-related CRC risk did not influence screening behaviour negatively, however there is a need for further follow-up of screening behaviour over the long-term, given its role in CRC prevention;
- The impact of previous experiences of cancer in the family appears to be an important moderating factor that needs a greater consideration in future investigations;
- The family are often the messengers of information relating to predictive testing. Two of the participants received such information from their family prior to any contact with the clinical/genetic team. It would be important to investigate the

understanding and accuracy with which information is conveyed within the familial setting.

REFERENCES

Abdel-Rahman WM, Mecklin JP, Peltomäki P (2006) The genetics of HNPCC: Application to diagnosis and screening. Oncol Haemotol 58(3): 208-220

Aktan-Collan K (2001) Predictive genetic testing and counselling for hereditary non-polyposis colorectal cancer (HNPCC): A Prospective follow-up study of acceptance and psychosocial consequences. Doctoral thesis. University of Helsinki. Helsinki

Aktan-Collan K, Haukkala A, Mecklin JP, Uutela A, Kaariainen H (2001) Comprehension of cancer risk one and 12 months after predictive genetic testing for hereditary non-polyposis colorectal cancer. J Med Genet 38: 787-792

Anwar S, Hall C, White J, Deakin M, Farrell W, Elder JB (2000) Hereditary non-polyposis colorectal cancer: An updated review. Eur J Surg Oncol 26(7): 635-645

Bennett RL, Hampel HL, Mandell JB, Marks JH (2003) Genetic counsellors: Translating genomic science into clinical practice. J Clin Invest 112: 1274-1279

Beuchamp TL and Childress JF (2001) Principles of biomedical ethics. 5th edn. Oxford University Press: New York

Biesecker BB and Peters KF (2001) Process studies in genetic counselling: Peering into the black box. Am J Med Genet 106: 191-198

Bleiker EM, Menko FH, Taal BG, Kluijt I, Wever LD, Gerritsma MA et al (2003) Experience of discharge from colonoscopy of mutation negative HNPCC family members. J Med Genet 40: e55

Braithwaite D, Emery J, Walter F, Prevost T, Sutton S (2006) Psychological impact of genetic counselling for familial cancer: A systematic review and meta-analysis. Familial Cancer 5: 61-75

CANSA Registry (Colorectal cancer: numbers and Incidence). Available at: http://www.cansa.org.za/Research/registry1997_colorectal.asp Last accessed: March 2007

Chapman PD and Burn J (1999) Genetic predictive testing for bowel cancer predisposition: The impact on the individual. Cytogenet Cell Genet 86: 118-124

Claes E, Denayer L, Evers-Kiebooms G, Boogaerts A, Legius E (2004) Predictive testing for hereditary non-polypois colorectal cancer: Motivation, illness representation and short-term psychological impact. Patient Edu Counsel 55: 265-274

Claes E, Denayer L, Evers-Kiebooms G, Boogaerts A, Philippe K, Tejpar S et al (2005) Predictive testing for hereditary nonpolyposis colorectal cancer: Subjective perception regarding colorectal and endometrial cancer, distress, and health-related behaviour at one year post-test. Genet Test 9(1): 54-65

Collins V, Halliday J, Warren R, Williamson R (2000) Assessment of education and counselling offered by a familial colorectal cancer clinic. Clin Genet 57:48-55

Collins V, Meiser B, Ukoumunne OC, Gaff C, St John JD, Halliday JL (2007) The impact of predictive genetic testing for hereditary nonpolyposis colorectal cancer: Three years after testing. Genet Med 9(5): 290-297

Croyle RT and Lerman C (1999) Risk communication in genetic testing for cancer susceptibility. Monogr Natl Cancer Inst 25: 59-66

d'Agincourt-Canning L (2005) The effect of experiental knowledge on construction of risk perception in hereditary breast/ovarian cancer. J Genet Couns 14(1): 55-69

de Wert G (1998) Ethics of predictive DNA-testing for hereditary breast and ovarian cancer. Patient Educ Couns 35: 43-52

Devlin LA, Price JH, Morrison PJ (2005) Hereditary non-polyposis colon cancer. Ulster Med J 74(1): 14-21

de Vries H, Mesters I, van der Steeg H, Honing C (2005) The general public's information needs and perceptions regarding hereditary cancer: An application of the integrated change model. Patient Educ Couns 56:154-165

Division of Human Genetics (Faculty of Health Sciences) Available at: http://www.uct.ac.za/depts/genetics/ Last accessed: June 2007

Djurdjinovic L (1998) Psychosocial counselling. In: Baker DL, Schutte JL, Uhlmann WR (Eds) A guide to genetic counselling. Wiley-Liss: New York

Domanska K, Nilbert M, Soller M, Silfverberg B, Carlsson C (2007) Discrepancies between estimated and perceived risk of cancer among individuals with hereditary nonpolyposis colorectal cancer. Genet Test 11(2): 183-186

Eiser RJ (1998) Communication and interpretation of risk. Br Med Bull 54(4): 779-790

Ensenauer RE, Michels VV, Reinke SS (2005) Genetic testing: Practical, ethical, and counselling considerations. Mayo Clin Proc 80(1): 63-73

Esplen MJ, Madlensky L, Butler K, McKinnon, Bapat B, Wong J et al (2001) Motivations and psychosocial impact of genetic testing for HNPCC. Am J Med Genet 103: 9-15

Evans JP, Skrzynia C, Burke W (2001) The complexities of predictive genetic testing. BMJ 322: 1052- 1056

Evers-Kierbooms G, Welkenhuysen M, Claes E, Decruyenaere M, Denayer L (2000) The psychological complexity of predictive testing for late onset neurogenetic diseases and hereditary cancers: Implications for multidisciplinary counselling and for genetic education. Soc Sci Med 51: 831-841

Giacomini MK and Cook DJ (2000) User's guides to the medical literature. XXIII. Qualitative research in health care. Are the results of the study valid?. JAMA 284: 357-362

Glazer B and Strauss A (1967) The discovery of grounded theory. Aldine: Chicago

Goldberg PA, Madden MV, Haocopos C, Felix R, Westbrook C, Ramesar RS (1998) In a resource-poor country, mutation identification has the potential to reduce the cost of family management for hereditary nonploy posis colorectal cancer. Dis Colon Rectum 41: 1250-1255

Gooding HC, Organista K, Burack J, Biesecker BB (2006) Genetic susceptibility testing from a stress and coping perspective. Soc Sci Med 62: 1880-1890

Gritz ER, Peterson SK, Vernon SW, Marani SK, Baile WF, Watts BG et al (2005) Psychological impact of genetic testing for hereditary nonpolyposis colorectal cancer. J Clin Oncol 23(9): 1902-1910

Hadley DW, Jenkins JF, Dimond E, de Carvelho M, Kirsch I, Palmer CG (2004) Colon cancer screening practices after genetic counselling and testing for hereditary nonpolyposis colorectal cancer. J Clin Oncol 22: 39-44

Hampel H, Stephens J, Pukkala E, Sankila R, Aaltonen LA, Mecklin JP, de la Chapelle A (2005) Cancer risk in hereditary nonpolyposis colorectal cancer syndrome: Later age of onset. Gastroenterology 129: 415-421

Holloway I and Wheeler S (1996) Qualitative research for nurses. Blackwell Science: Oxford

Holloway I (1997) Basic concepts for qualitative research. Blackwell Science: Oxford

Holloway I (2005) Qualitative research in health care. University Press McGraw Hill: New York

Hopwood P, Keeling F, Long A, Evans G, Howell A (1998) Psychosocial support needs for woman at a high genetic risk of breast cancer: Some preliminary indicators. Psychooncol 7: 401-412

InSiGHT Database. Available at: http://www.insight-group.org/ Last accessed: June 2007

Jarvinen HJ, Mecklin JP, Sistonen P (1995) Screening reduces colorectal cancer rate in hereditary nonpolyposis colorectal (HNPCC) families. Gastroenterology 108: 1405-1411

Jarvinen HJ, Aarnio M, Mustonen H, Aktan-Collan K, Aaltonen LA, Peltomaki P et al (2000) Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. Gastroenterology 118: 829-834

Jarvinen HJ (2003) Genetic testing for polyposis: Practical and ethical aspects. BMJ 52: 19-22

Jorde LB, Carey JC, Bamshad MJ, White RL (2006) Medical genetics. 3rd edn. Mosby: Philadelphia

Keenan R, Audern-Jones A, Eeles R (2002) Family story and the use of heuristics: Woman from suspected hereditary breast and ovarian cancer families. Soc Health Illn 25: 838-865

Keller M, Jost R, Mastromarino Haunstetter C, Kienle P, Knaebel HP, Gebert J et al (2002) Comprehensive genetic counselling for families at risk for HNPCC: Impact on distress and perceptions. Genet Test 6(4): 291-302

Korf BR (2000) Human Genetics: A problem based approach. 2nd Edn. Blackwell Science Ltd: Oxford

Kruger BJ (2005) Hereditary nonpolyposis colorectal cancer: Factors contributing to adherence and non-adherence to surveillance for mutation carriers in rural areas of the northern and western cape. MSc dissertation. University of Cape Town. South Africa

Lerman C, Narod S, Schulman K, Hughes C, Gomez-Caminero A, Bonney G et al (1996) *BRCA1* testing in families with hereditary breast - ovarian cancer. A prospective study of patient decision making and outcomes. JAMA 275(24): 1885-1892.

Lerman C, Highers C, Lemon SJ, Main D, Snyder C, Durham C et al (1998) What you don't know can hurt you: Adverse psychological effects in members of BRCA2 linked families who decline genetic testing. J Clin Oncol 16: 1650-1654

Leventhal H, Brissette I, Leventhal EA (2003) The common-sense model of self-regulation of health and illness. In: Cameron LD, Leventhal H (Eds) The self-regulation of health and illness behaviour. Routledge: London

Liljegren A, Lindgren G, Brandberg Y, Rotstein S, Nilsson T, Jaramillo E et al (2004) Individuals with an increased risk of colorectal cancer: Perceived benefits and psychological aspects of surveillance by means of regular colonoscopies. J Clin Oncol 22: 1736-1742

Lincoln YS and Guba EG (1985) Naturalistic inquiry. Sage: California

Lindblom A, Tannergard P, Werelius B, Nordensjöld M (1993) Genetic mapping of a second locus predisposing to hereditary non-polyposis colon cancer. Nat Genet 5: 279-282

Lynch HT and Krush AJ (1971) Cancer family "G" revisited: 1895-1970. Cancer 6(27): 1505-1511

Lynch HT and Smyrk T (1996) Hereditary Nonpolyposis Colorectal Cancer (Lynch Syndrome). Cancer 78: 1149-67

Lynch HT, Smyrk T, Lynch JF (1996) Overview of natural history, pathology, molecular genetics and management of HNPCC (Lynch Syndrome). Int J Cancer 69: 38-43

Lynch HT, Smyrk T and Lynch JF (1998) Molecular genetics and clinical-pathological features of hereditary nonpolyposis colorectal carcinoma (Lynch Syndrome). Oncol 55: (2) 103-108

Lynch HT and Lynch JF (2000) Hereditary Nonplyposis Colorectal Cancer. Oncol 18: 305-313

Lynch HT and de la Chapelle A (2003) Hereditary colorectal cancer. NEJM 348: 919-932

Mackay J and Ponder BA (1997) The management of inherited breast cancer. In: Bonnadonna G, Hortogagyl G, Gianni AM (Eds) Textbook of breast cancer: A clinical guide to therapy. Martin Dunitz: London

Marshall C and Rossman GB (1999) Designing qualitative research. 3rd Edn. Sage: California

Marteau TM and Lerman C (2001) Genetic risk and behavioural change. BMJ 322: 1056-1059

Mecklin JP and Jarvinen HJ (1991) Tumour spectrum in cancer family syndrome (Hereditary nonpolyposis colorectal cancer). Cancer 68: 1109-1112

Meiser B, Collins V, Warren R, Gaff C, St John DJ, Young MA (2004) Psychological impact of genetic testing for hereditary non-polyposis colorectal cancer. Clin Genet 66: 502-511

Meiser B, Butow P, Barratt A, Gattas M, Gaff C, Haan E et al (2001) risk perceptions and knowledge of breast cancer genetics in women at increased risk of developing hereditary breast cancer. Psychol Health 16: 297-311

McAllister M (2002) Predictive genetic testing and beyond: A theory of engagement. J Health Psychol 7(5): 491-508

McMillan JH and Schumacher S (2001) Research in education: A conceptual introduction. 5th Ed. Longman: New York

Miyaki M, Konishi M, Tanaka K, Kikuchi-Yanoshita R, Muraoka M, Yasuno M et al (1997) Germline mutations of MSH6 as the cause of hereditary nonpolyposis colorectal cancer. Nat Genet 17: 271-272

Murphy AE (1999) Dealing with the uncertainty of developing a cancer. Eur J Cancer Care 8(4): 233-237

National Society of Genetic Counselors Position Statement. Confidentiality of test results. Available at: www.nsgc.org/about/position.asp#confidenoftest Last accessed: April 2007

Naussbaum RL, McInnes RR, Willard HF (2004) Thompson and Thompson: Genetics in medicine. 6th edn. W.B. Saunders Company: New York

Neuhausen SL (1999) Ethnic differences in Cancer Risk Resulting from Genetic Variation. Cancer supp 86: 2575-2582

Neuman WL (1999) Dimensions of research: Social research methods in qualitative and quantitative approaches. 4th edn. Allyn and Bacon: Massachusetts

Peltomäki P, Aaltonen L, Sistonen P, Pylkkanen L, Mecklin J, Jarvinen H et al (1993) Genetic mapping of a locus predisposing to human colorectal cancer. Science 260: 810-812

Popay J (1992) "My health is alright, but I'm just tired all the time": woman's experience of ill-health. In: Roberts H (Eds) Women's health matters. Routledge: London

Resta R, Biesecker BB, Bennett RL, Blum S, Hahn SE, Strecker MN (2006) A new definition of genetic counselling: National society of genetic counselors' task force report. J Genet Couns 15(2): 77-83

Robinson KL, Liu T, Vandrovcova J, Halvarsson B, Clendenning M, Frebourg T (2007) Lynch syndrome (Hereditary nonpolyposis colorectal cancer) diagnostics. J Natl Cancer Inst. 99(4): 291-299

Rossouw D (2003) Intellectual tools: Skills for the human sciences. 2nd edn. Van Schaik: Pretoria

Rubin HJ and Rubin IS (1995) Qualitative interviewing: The art of hearing data. Sage: London

Salovaara R, Loukola A, Kristo P, Kaariainen H, Eskelinen M, Harkonen N et al (2000) Population based molecular detection of hereditary nonpolyposis colorectal cancer. J Clin Oncol 18: 2193-2200

Schulmann K, Reiser M, Schmiegel W (2002) Colonic cancer and polyps. Best Pract Res Clin Gastroenterology 16: 1 91-114

Shiloh S (2006) Illness representations, self-regulation, and genetic counselling: a theoretical review. J Genet Couns 15(5): 325-337

Stanley AJ, Gaff CL, Aittomaki, Fabre LC, Macrae FA, John J (2000) Value of predictive testing in management of hereditary non-polyposis colorectal cancer (HNPCC) Med J Aust 172: 313-316

Statistics South Africa. http://www.statssa.gov.za/ Last accessed: July 2007

Strate LL and Syngal S (2005) Hereditary colorectal syndromes. Canc Causes Contr 16: 201-213

Stephenson BM, Finan JP, Gascoyne J, Garbett F, Murday VA, Bishop DT (1991) Frequency of familial colorectal cancer. Br J Surg 78: 1162-1166

Syngal S, Weeks JC, Schrag D, Garber JE, Kuntz KM (1998) Benefits of colonoscopic surveillance and prophylactic colectomy in mutation carriers for hereditary nonpolyposis colorectal cancer. Ann Intern Med 129: 787-796

Ulin PR, Robinson ET, Tolley EE (2005) Qualitative methods in public health: A field guide for applied research. Jossey-Bass: San Fransico

Van Oostrom I, Meijers-Heijboer HM, Duivenvoorden HJ, Brocker-Vriends A, Van Asperen CJ, Sijmons RH at al (2006) Experience of parental cancer in childhood is a risk factor for psychological distress during genetic cancer susceptibility testing. Ann Oncol 17(7): 1090-1095

Vasen HF, Mecklin JP, Meera Khan P, Lynch HT (1991) The International Collaborative Group on Hereditary Non-Polyposis Colorectal Cancer (ICG-HNPCC). Dis Colon Rectum 34: 424-425

Vasen HF, van Ballegooijen M, Buskens E, Kleibeuker JK, Taal BG, Griffioen et al (1998) A cost-effectiveness analysis of colorectal screening of hereditary nonploypposis colorectal carcinoma gene carriers. Cancer 82: 1632-1637

Vasen HF, Watson P, Mecklin JP, Lynch HT (1999) New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative Group on HNPCC. Gastroenterology 116: 1453-1456

Vasen HF and Morreau H (2002) Familial and hereditary colorectal cancer with emphasis on the hereditary non-polyposis colorectal cancer syndrome. Curr Diagn Pathol 8(4): 241-248

Vasen HF, Burn J, Sheridan E, Houlston RS, Douglas (2005) Management of hereditary non-polyposis colorectal cancer In: Lalloo F, Kerr B, Friedman JM, Evans DG (Eds) Risk assessment and management in cancer genetics. Oxford Univeristy Press: New York

Wagner A, van Kessel I, Kriege MG, Tops CM, Wijnen JT, Vasen HF et al (2005) Long term follow-up of HNPCC gene mutation carriers: Compliance with screening and satisfaction with counselling and screening procedures. Familial Cancer 4:295-300

Warthin AS (1913) Hereditary with reference to carcinoma: as shown by the study of the cases examined in the pathological laboratory of the University of Michigan, 1895-1913. Arch Intern Med 12: 546-555

Watson P, Lin KM, Rodriguez-Bigas MA, Smyrk T, Lemon S, Shashidharan M et al (1998) Colorectal carcinoma survival among hereditary nonpolyposis colorectal carcinoma family members. Cancer 83: 259-266

Watson M, Kash KM, Homewood J, Ebbs S, Murday V, Eeles R (2005) Does genetic counselling have any impact on management of breast cancer risk?. Genet Test 9(2): 167-174

Weil J (2000) Psychosocial genetic counseling. The counselee as individual. Oxford University Press: New York

White E and Mackay J (1999) A critical evaluation of the process of cancer genetic counselling: From research-based investigation to clinical diagnosis. Eur J Oncol Nursing 3(2): 96-101

Young ID (2001) Medical Genetics. Oxford University Press: New York

Yu HA, Lin KM, Ota DM, Lynch HT (2003) Hereditary nonploypsis colorectal cancer: Preventative management. Cancer Treat Rev 29(6): 461-470

APPENDICES

M.Sc in Genetic Counselling Research Project

HEREDITARY NONPOLYPOSIS COLORECTAL CANCER: COMPREHENSION OF A CANCER RISK IN CONJUNCTION WITH A GENETIC RISK.

INFORMATION AND CONSENT FORM

STATEMENT BY PARTICIPANT

I, ... Living at (address)

.....

confirm that:

1. I have been invited to participate in the above research project, which has been initiated through the Division of Human Genetics, University of Cape Town because I have received my predictive genetic test results and am currently involved in the HNPCC predictive testing programme.

2.1 I understand that the objective of this study is to investigate:

- the level of understanding of a genetic predisposition to cancer following predictive testing for HNPCC;
- the subsequent impact on the individual.

2.2 I understand that the interview will take place in my home or at another venue of my choice and that it may take one or two visits of up to two hours each.

2.3 I am aware that this is a once off procedure that will be implemented in 2007 at a time convenient to me.

2.4 I understand that some of the questions may make me angry or sad, but the risks to me from the study are minimal. The researcher will refer me to a genetic counsellor if necessary. She will show me respect, acceptance and empathy during the interview.

3.1 I have been assured that all the information will be handled confidentially. Information may be used for a thesis, publications in scientific journals and at presentations at professional congresses, but names will not be included.

3.2 I understand that the interview will be tape recorded so that the researcher does not have to write too much during the interview. The tape will be stored in a safe place until the research has been written up and will then be destroyed immediately. The data stored on the computer will have a numerical code only and my name does not appear anywhere.

4.1 I have been assured that the recorded and transcribed information discussed at the meeting will only be made available to the researcher's supervisors with my study code number and that they do not know that it refers to my name.

5. I have not been persuaded to consent to taking part in the study and I have been informed that I my refuse to participate in this project, that I may stop participating at any stage, and that such refusal or stoppage will not in any way negatively affect my future access to medical and genetic services to which I am entitled.

6. ..... has explained the information of the study to me in English/Afrikaans. I am proficient in that language and my questions have been answered satisfactorily.

7. I understand that there will be no medical benefits to me from this study.

8. I have been assured that participation in this project will not lead to additional costs for me and I will not benefit from it financially.

I hereby declare that I voluntarily agree to participate in the above research study

Signed at:
(address) ..... on ...../...../2007

....
Participant's signature Witness

I hereby declare that I agree to have my interview audiotape recorded

Signed at:
(address) ..... on ...../...../2007

....
Participant's signature Witness

IMPORTANT INFORMATION

Dear participant,

Thank-you very much for your participation in this study. If you have any questions about the research concerning:

1. problems due to the research, or
2. questions relating to the information about the project

you can contact me or Prof. Greenberg on:

Zandre Bruwer (021) 406 6373
E-mail: zbruwer@cormack.uct.ac.za

Prof Jacquie Greenberg (021) 406 6299

If you have any questions relating to your right as a participant, contact Prof. Marc Blockman, the chairman of the ethics committee of the University of Cape Town on (021) 406 6492.

M.Sc in Genetiese Berading Navorsingsprojek

HEREDITARY NONPOLYPOSIS COLORECTAL CANCER: COMPREHENSION OF A CANCER RISK IN CONJUNCTION WITH A GENETIC RISK.

INLIGTING EN TOESTEMMING VORM

VERKLAARING DEUR DEELNEMER

Ek, ...,

(adres) .....

bevestig dat:

1. Ek is uitgenooi om aan die bogenoemde navorsings projek wat deur die Divisie van Mensgenetika, Universiteit van Kaapstad geinisieer is, deel te neem aangesien ek my voorspellings toets resultate ontvang het en tydens betrokke is in die HNPCC voorspellings toets program.

2.1. Ek verstaan die doel van hierdie projek is om die volgende te ondersoek:

- Hoe 'n persoon die voorspellings toets resultate verstaan en;
- die impak daarvan op die individie;

2.2. Ek verstaan dat die onderhoud of by my huis of by 'n ander plek van my keuse sal plaasvind en dat dit een of twee besoeke van twee ure elk behels.

2.3. Ek is bewus dat dit 'n eenmalige ondersoek is wat in 2007 sal plaasvind op 'n tyd wat vir my en my gesin gerieflik is.

2.4. Ek verstaan dat van die vra my hartseer of ongelukkig mag maak, maar dat die risiko's van die studie minimaal is. Die navorser sal my na 'n genetiese raadgewer verwys indien nodig. Sy sal my met respek, aanvaarding en empatie behandel geduurende die onderhoud.

3.1. Ek is verseker dat alle inligting vertroulik behandel sal word. Inligting mag vir 'n tesis, publikasies in wetenskaplike tydskrifte en aanbiedings by professionele kongresse gebruik word, maar name sal nie ingesluit word nie.

3.2. Ek verstaan dat die onderhoud op band opgeneem sal word sodat die navorser nie te veel hoef te skryf geduurende die onderhoud nie. Die band sal in 'n kluis gestoor word tot dat die navorsing opgeskryf is en sal daarna dadelik vernietig word. Die band en die data op die rekenaar sal slegs 'n numeriese kode op hê en my naam sal nie daarop verskyn nie.

4. Ek is verseker dat die inligting wat opgeneem en getranskribeer is slegs aan die navorser se mentor bekend gemaak sal word, maar dit sal slegs my numeriese studie kode bevat en my naam sal nie daarop verskyn nie.

5. Ek is nie oorreed om aan die die projek deel te neem nie en ek is bewus dat ek mag weier om deel te neem, en ek kan op enige staduim besluit om te onttrek. My onttrekking sal op geen manier my huidige of toekomstige toegang tot die mediese of genetiese dienste, waarop ek geregtig, is beïnvloed nie.

6. ..... het die inligting van die projek in Engels/Afrikaans aan my verduidelik. Ek is vlot is hierdie taal en my vra is ten volle beantwoord.

7. Ek verstaan dat daar geen mediese voordele vir my sal wees as gevolg van hierdie projek nie.

8. Ek is verseker dat my deelname aan hierdie projek nie tot enige additionele koste vir my familie sal lei nie en dat ek nie finansieel gaan baat daarby nie.

EK VERKLAAR HIERMEE DAT EK VRYWILLIG AAN DIE BOGENOEMDE NAVORSINGS PROJEK DEELNEEM

Geteken te:
(Adres) ..... op 2007

....
Deelnemer se handtekening Getuie

EK VERKLAAR HIERMEE DAT EK MY ONDERHOUD OP BAND OPGENEEM MAG WORD

Geteken te:
(Adres) ..... op 2007

....
Deelnemer se handtekening Getuie

BELANRIKE INLIGTING

Geagte deelnemer,

Baie dankie vir u deelname aan hierdie studie. As U geduurende die verloop van die navorsing enige vra het aangande:

1. probleme as gevolg van die navorsing, of
2. vrae aangaande inligting oor die projek

kontak my of Prof. Greenberg gerus op die volgende telefoon nommers:

Zandre Bruwer (021) 406-6373
Email: zbruwer@cormack.uct.ac.za

Prof Jacquie Greenberg: (021) 406-6299

As u enige vrae het in verband met u reg as 'n deelnemer, kontak Prof. Marc Blockman, die Voorsitter van die Etiese Hersiening Komitee van die Universiteit van Kaapstad by (021) 406-6492.

INTERVIEW SCHEDULE - English version

Participant number: □□

Section A: Assessment and update of pedigree information

The pedigree together with section A will be used in answering the following questions:

Is all the information on the pedigree still correct?

1. Do you have any children of your own (blood relatives)?

□ No
□ Yes

If yes please indicate the gender and age

1st Child: Age: _____
Boy? □
Girl? □

2nd Child: Age: _____
Boy? □
Girl? □

3rd Child: Age: _____
Boy? □
Girl? □

4th Child: Age: _____
Boy? □
Girl? □

.....

2. How many brothers do you have?

_____

3. How many sisters do you have?

_____

4. How many of your brothers have had cancer? (who you are aware of)

_____

5. How many of your sisters have had cancer? (who you are aware of)

_____

6. To your knowledge have any of your brothers passed away from cancer?

_____

7. To your knowledge have any of your sisters passed away from cancer?

_____

8. Did one of your parents have cancer?

- ☐ Yes
- ☐ No

9. When was the first time that you realised that cancer was in your family (how old were you)?

10. How old were you when you realised you were at risk for colon cancer (had a chance of developing the colon cancer)?

_____

11. When was your first recruitment session (information and blood taking session) with the genetic team?

12. Has your blood been tested for the gene that causes colon cancer in your family?

- ☐ Yes
- ☐ No (go to question 14)
- ☐ I don't know (go to question 14)

IF YES TO QUESTION 12 - When did you receive your result for this genetic test?

13. Do you have the gene that causes colon cancer in your family?

- ☐ Yes
- ☐ No (go to question 15)
- ☐ I don't know (go to question 15)

14. IF NO OR I DON'T KNOW TO QUESTION 12: The researcher will explain that the participant did have the test at a certain date and explore their reasons for not understanding this. The genetic status will be discussed with the individual in a supportive way.

15. IF NO OR I DON'T KNOW TO QUESTION 13: The researcher will explore the participants reasoning for their answer. The researcher will inform the participant of their genetic status in a supportive manner.

The researcher will refer the participant for re-counselling following the interview.

16. Can you recall who gave you this result?

17. Where was this result given to you?

18. Do you remember the day that you received this genetic test result? Can you recall it in much detail?

Section B: Sociodemographic Information

19. What is your date of birth?

☐☐ Day ☐☐ month ☐☐☐☐ year

20. Are you male or female?

☐ Male ☐ Female

21. Until which grade/standard did you complete school?

☐ Grade 12 (matric/standard 10)

☐ Grade 11 (standard 9)

☐ Grade 10 (standard 8)

☐ Grade 9 (standard 7)

☐ Grade 8 (standard 6)

☐ Grade 7 (standard 5)

☐ Other – please provide standard/grade

22. Did you have biology at school?

☐ Yes ☐ No

If yes, until which grade/standard? .....
If yes, how do you rate your knowledge? .....

23. Do you use any resources to read up on current health issues

☐ Internet

☐ Books

☐ Newspaper

☐ Magazines

☐ Discuss with family members

☐ Other

24. What is the highest level of education you have obtained since leaving school?

Please indicate the specific type if relevant.

☐ No post-school ☐ Diploma (beyond standard 10)

☐ Trade/Apprentice ☐ Bachelors degree

☐ Certificate from college ☐ Postgraduate degree / degree

☐ Other.....

25. Do you belong to a specific religious denomination?

.....

26. Has your religion played a major role in coping with your genetic test results?

Many factors influence the way we live our life. What would you consider is the most important factor that guides your life and helps you make decisions?

27. Do you work?

☐ Yes ☐ No

If yes to the question, what kind of work do you do?

.....

Is the work;

- ☐ Self-employed
- ☐ Full-time employed
- ☐ Part-time employed/ Casual

If no to the question, are you:

- ☐ Unemployed
- ☐ Permanently unable to work
- ☐ Retired or pensioner
- ☐ Other

28. How many people live with you in the house where you stay? Are they all blood relatives?

29. Do you talk to them about the colon cancer that occurs in the family? Is there any particular person with whom you talk more frequently?

30. What is your current household income per month?

- ☐ No income
- ☐ Disability grant (what type..... how much R .....)
- ☐ R1 - R400
- ☐ R401 - R800
- ☐ R801 - R1600
- ☐ R1601 - R3200
- ☐ R3201- R6400
- ☐ R6401 - R12 800
- ☐ R12 801 - R25 600
- ☐ R25 601 - R51 200
- ☐ R52 201 - R102 400
- ☐ R102 401 - R204 800
- ☐ More than R 204 801

31. How many people contribute to the household income?

32. How many people are dependent on these incomes?

33. What is your present marital status?

☐ Married/ Partner ☐ Single

☐ Separated/Divorced ☐ Widowed

☐ Never married

Section C: Knowledge on Cancer (Adapted from Collins et al 2000a and De Vries et al 2004)

34. Please select the most appropriate answer to the statement.....

	True	False	Don't know
Colon cancer is always inherited – if a person develops colon cancer, they always have a family history of colon cancer			
Everyone who has the gene causing colon cancer will develop colon cancer			
A person who does not have the gene for colon cancer is less likely to develop cancer than someone with the gene			
There is more than one gene that can cause colon cancer			
Colonoscopy (the inside of the bowel is viewed with a special tube) is very likely to detect colon cancer if it is present			
Faecal occult blood testing (a test which tests for blood in the stool) is very likely to detect bowel cancer if it is present			
In a family where the gene causing colon cancer has been found, those WITHOUT the gene have the same risk for getting colon cancer as the general population			
If a person looks like (or has the same personality) a family member who developed cancer, they are likely to have inherited the same gene as that person			

35. Please mark each question as being true or false

	True	False	Don't Know
• The increased risk of cancer can be passed on to your children	☐	☐	☐
• Everyone with the gene causing colon cancer, will develop colon cancer	☐	☐	☐
• 50% of a persons genes are the same as the genes of their parents	☐	☐	☐
• If a person has the gene causing colon cancer, the chance of developing the cancer that other family members may have can be reduced with regular check ups (colonoscopy)	☐	☐	☐
• If you have a healthy lifestyle you are less likely to develop colon cancer	☐	☐	☐

- If there is something wrong with your genes then you will notice this (you will feel a difference in your body) ☐ ☐ ☐

---

36. Which of the following may influence whether a person gets cancer?

	No Influence	A little Influence	A lot of influence	Don't know
Personality	☐	☐	☐	☐
Stress	☐	☐	☐	☐
Environmental pollution	☐	☐	☐	☐
The gene	☐	☐	☐	☐
Lifestyle or habits	☐	☐	☐	☐
Bad luck	☐	☐	☐	☐

Section D: Personal understanding of genetic test for cancer

37. Who provided you with the information that a genetic test was available, to test for the gene that causes an increased risk for colon cancer? (Nurse/ family member)

38. Whose idea was it for you to have a genetic test?

☐ My own idea
☐ Other family member
☐ General practitioner
☐ Specialist
☐ Family bowel clinic
☐ Other _____

39. Can this genetic test tell you if you have the gene that may cause you to have an increased chance of developing the colon cancer?

40. Can this genetic test tell you if you have cancer or not?

41. How is this predictive test done?

☐ **Physical examination**
☐ **Blood test to identify the gene**
☐ **Colonoscopy**

42. How long has it been since you have received your genetic test results?

43. When you went for your genetic test, did you think you would test positive for the gene? (Before you had received your test results)

44. Describe how you feel about the fact that the test showed that you have the gene causing you to have an increased risk for cancer?

45. What happened to these feelings or emotions since the test results?

46. Have you shared this test result with anyone?

- ☐ No
- ☐ Yes (whom?)

.....

47. When did you share the result (How long after you received the test result)?

48. Why did you share this result with them?

49. How have they responded to you sharing this information (their reaction)?

50. Explain how the result has affected your life medically

51. When last has someone from the genetic team spoken to you? What was it about?

52. How much contact have you had with the clinical/genetic team following your result giving?

- ☐ Once
- ☐ Twice
- ☐ Few times
- ☐ None

Section E: Recall of cancer risk and subjective risk perception

53. Do YOU think you are at an increased risk for colon cancer? (reasons besides the test)

54. What is your risk (chance) of developing colon cancer after the genetic testing?

- ☐ I am at 80% risk of developing colon cancer
- ☐ I am at 50% risk of developing colon cancer
- ☐ I have been told that I have colon cancer (100% risk)
- ☐ I am at less than 50% risk of developing colon cancer
- ☐ I am at no risk

55. Do you think you have control over your risk of developing colon cancer?

56. How will you try and prevent the cancer from developing?

57. Are you worried about your risk (the chance) of developing colorectal cancer?

- ☐ **Very worried**
- ☐ **Slightly worried**

□ **Not at all worried**

58. Have you thought about how you will cope if you develop cancer?

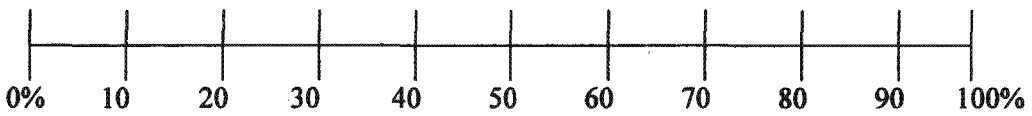
59. If you were to develop colon cancer, do you think that it would develop at a specific age?

If yes, why then.....

60. Do you think the chance that you will develop cancer is bigger or smaller in comparison with someone else of the same age and same sex (not from your family)?

61. Please rate your chances of getting colon cancer on a scale from 0 to 100, where 0 = a 0% or no chance and 100 = a 100% chance, meaning that you will definitely get it.

Please make a mark on one of the vertical lines to indicate your chances, given your current situation. In your opinion, what number from 0 to 100 reflects your chances of getting bowel cancer?



Section F: Motivations for participating in a predictive testing programme

Please select the most appropriate answer to

62. My decision to have a genetic test was influenced by wanting .....

	Not at all	Somewhat	Very much	Not applicable
To learn about my children's risk				
To reduce my risk of developing cancer				
To plan for the future				
To help research				
To be certain about my risk				
To make decisions about having children				
Marital decisions				
Doctor recommended it				
Family members urged me to take test				
Worried about abnormal stools/health related concerns				

(Adapted from Claes et al 2004)

63. Try to remember the situation when you made your decision about the test. Were there any other factors that caused you to take the test?

.....
.....

64. Why did you not want to take the test?

.....
.....

65. Are you satisfied with your decision to take the test?

66. How reliable do you think the test is?

67. Now that you know the result, would you have taken the test in the first place?

Section G: Health-related behaviour

68. Which day hospital do you go to when you feel sick?

69. Which hospital do you go to if your health worries relate to your concerns of developing colon cancer?

70. Do you have a medical aid?

☐ Yes
☐ No

71. Have you ever had a colonoscopy?

☐ Yes (How many?)
☐ No
☐ I don't know

72. When was your last colonoscopy?

73. What can a colonoscopy tell you?

74. What is the difference between a colonoscopy and a predictive test?

75. Why do you need both of these tests?

76. Why do you go for colonoscopies?

77. Did you have a genetic test prior to the colonoscopy?

- ☐ Yes
- ☐ No

78. Did you have a colonoscopy prior to your genetic test?

- ☐ Yes
- ☐ No

Section H: Perceived severity (adapted from Aktan-Collan 2001)

79. If you developed colon cancer, do you think you would survive it?

80. Are you afraid that you may have cancer?

81. What does your future look like?

Section I: Opinions of counselling

82. What is your general opinion about the counselling protocol?

83. Did you consider the pre-test counselling useful?

- ☐ Very
- ☐ Fairly
- ☐ Slightly
- ☐ Not at all

84. Have you had post test counselling?

- ☐ Yes
- ☐ No

85. Do you have any further comments or suggestions?

The researcher thanks the participant for their time in allowing her to do the interview.

Support and educational input requiring re-counselling will be offered if emotional concerns or clarity on facts are needed.

ONDERHOUD SKEDULE - Afrikaans wergawe

Ondernemer nommer: ☐☐

Seksie A: Familie geskiedenis

Die familie geskeidenis en seksie A se antwoorde sal gebruik word om die volgende vra te beantwoord:

1. Het u enige kinders?

☐ Ja
☐ Nee

1ste kind: Ouderdom: _____
Seun? ☐
Dogter? ☐

2de kind: Ouderdom: _____
Seun? ☐
Dogter? ☐

3de kind: Ouderdom: _____
Seun? ☐
Dogter? ☐

4de kind: Ouderdom: _____
Seun? ☐
Dogter? ☐

.....

2. Hoeveel broers het u?

_____

3. Hoeveel sisters het u?

_____

4. Hoeveel van u broers het al kanker gehad? (Wat u van weet)

_____

5. Hoeveel van u sisters het al kanker gehad? (Wat u van weet)

_____

6. Sover u weet, hoeveel van u broers het gesterf van dikderm kanker?

_____

7. Sover u weet, hoeveel van u sisters het gesterf van dikderm kanker?

_____

8. Het een van u ouers kanker gehad ?

☐ Ja
☐ Nee

9. Wanneer het u vir die eerste keer bewus geword daarvan dat dikderm kanker in die familie is (hoe oud was u)?

10. Hoe oud was u toe u agterkom dat u 'n risiko het vir dikderm kanker (kans het om dikderm kanker te ontwikkel)?

_____

11. Wanneer was u eerste sessie (inligting en bloed neem) met die genetiese span?

12. Is u blood al getoets vir die geen wat dikderm kanker in u familie veroorsaak?

☐ Ja
☐ Nee (gaan na vraag 14 toe)
☐ Ek weet nie (gaan na vraag 14 toe)

INDIEN JA NA VRAAG 12 - Wanneer het u die resultate gekry?

13. Het u die geen wat dikderm kanker veroorsaak in u familie?

☐ Ja
☐ Nee (gaan na vraag 15 toe)
☐ Ek weet nie (gaan na vraag 15 toe)

14. INDIEN NEE OF EK WEET NIE VIR VRAAG 12: Die navorser sal verduidelik dat die deelnemer reeds getoets is en sal die redes verduidelik waarom hy/sy dit nie verstaan nie. Dit sal op 'n ondersteunende wyse gedoen word. Die navorser sal die deelnemer verder op 'n ondersteunende wyse inlig oor sy/haar genetiese status.

15. INDIEN NEE OF EK WEET NIE VIR VRAAG 13: Die navorser sal die rede verduidelik waarom die deelnemer die antwoord gegee het. Die navorser sal die deelnemer verder op 'n ondersteunende wyse inlig oor sy/haar genetiese status.

Die navorser sal die deelnemer verwys vir genetiese berading na die onderhoud

16. Wie het vir u jou resultate gegee (persoon)?

17. Waar het u hierdie resultate gekry (plek-huis of hospitaal)?

18. Kan jy die dag goed onthou? En beskryf?

Afdeling B: Sosiodemografiese Inligting

19. Wat is u geboortedatum?

☐☐ Dag ☐☐ maand ☐☐☐☐ jaar

20. Is u manlik of vroulik?

☐ Man ☐ Vrou

21. Wat is die hoogste graad/standerd wat u op skool voltooi het?

☐ Graad 12 (matriek/standerd 10)

☐ Graad 11 (standerd 9)

☐ Graad 10 (standerd 8)

☐ Graad 9 (standerd 7)

☐ Graad 8 (standerd 6)

☐ Graad 7 (standerd 5)

☐ Ander – dui asseblief aan .....

22. Het u biologie op skool gehad?

☐ Ja ☐ Nee

Indien ja, tot watter standerd .....
Indien ja, hoe beskou u jou kennis daarvan? .....

23. Gebruik u enige hulp bronne om oor huidige gesondsheids kwessies op te lees?

☐ Internet

☐ Boeke

☐ Koerant

☐ Tydskrifte

☐ Bespreek met ander familie lede

☐ Ander

24. Wat is die hoogste kwalifikasie wat u na skool gekry het?

☐ Geen ☐ Diploma (na Graad 12)

☐ Ambag ☐ Bacculureurs graad

☐ Kollege sertifikaat ☐ Na-graadse diploma/ - graad

☐ Ander.....

25. Behoort u aan enige godsdiens verband?

.....

26. Speel u geloof 'n groot rol in die manier waarop u, u toets resultate hanteer?

Baie faktore beïnvloed die manier waarop ons ons lewe lei? Wat beskou u as die faktor wat u help om besluite te neem?

27. Werk u?

☐ Ja ☐ Nee

Indien ja, watter tipe werk?

.....

Is die werk;

- ☐ U eie besigheid
- ☐ Voltydse werk
- ☐ Deeltydse werk

Indien nee, is u:

- ☐ Werkloos
- ☐ Kan permanent nie werk nie
- ☐ Afgetree of pensionaris
- ☐ Ander

28. Is al die mense wat saam met jou bly in die huis bloedfamilie? Hoeveel mense bly in die huis?

29. Praat julle oor die familie siekte (kanker) met mekaar? Is daar iemand wat jy meer gereeld mee praat?

30. Wat is u huidige huishoudelike inkomste per maand?

- ☐ Geen inkomste
- ☐ Ongeskikheids toelaag (Tipe..... bedrag R .....)
- ☐ R1 - R400
- ☐ R401 - R800
- ☐ R801 - R1600
- ☐ R1601 - R3200
- ☐ R3201- R6400
- ☐ R6401 - R12 800
- ☐ R12 801 - R25 600
- ☐ R25 601 - R51 200
- ☐ R52 201 - R102 400
- ☐ R102 401 - R204 800
- ☐ Meer as R 204 801

31. Hoeveel mense dra by tot die huishoudelike inkomste?

32. Hoeveel mense is afhanklik op hierdie inkomste?

33. Is u getroud?

☐ Getroud/woon saam ☐ Enkellopend

☐ Geskei ☐ Weduwee/wewenaar

☐ Nooit getroud nie

Seksie C: Kennis oor kanker (Aangepas van Collins et al 2000a en De Vries et al 2004)

34.Selekteer asseblief die mees gepaste aantwoord vir die stelling.....

	Waar	Onwaar	Weet nie
Dikderm kanker is altyd oorerflik-daar moet 'n familie geskeidenis van kanker wees vir die persoon om kanker te ontwikkel			
Almal wat 'n geen het vir oorerflike dikderm kanker sal dikderm kanker kry			
'n Persoon wat NIE die geen vir dikderm kanker het nie, het 'n kleiner kans om kanker te ontwikkel as iemand met die geen			
Daar is meer as een geen wat dikderm kanker veroorsaak			
Kolonoskopie (kyk na die binnekant van die derm met 'n spesiale buis) sal heel moontelik dikderm kanker optel as dit teenwoordig is			
'n Okkultebloed-stoelgangtoets ('n toets wat onsigbare bloed in die stoelgang aandui) sal heel moontelik dikderm kanker optel as dit teenwoordig is			
In 'n familie waar die geen vir oorerflike dikderm kanker gevind is, het die mense SONDER die geen dieselfde risiko om dikderm kanker te ontwikkel as die algemene populasie			
As 'n persoon soos 'n familie lid wat dikderm kanker gehad het lyk (of dieselfde tipe persoonlikheid het) het hulle moontelik dieselfde geen as daardie persoon			

35. Merk asseblief die vraag as waar of onwaar	**Waar**	**Onwaar**	**Weet Nie**
• Die verhoogde risiko vir kanker kan oorgedra word tot u kinders	☐	☐	☐
• Almal wat die dikderm geen het, sal dikderm kanker ontwikkel	☐	☐	☐
• As a seun soos sy pa lyk, is dit moontelik dat hy dieselfde siekte/toestand as sy pa sal ontwikkel	☐	☐	☐
• 50% van 'n persoon se gene is dieselfde as hulle ouers se gene	☐	☐	☐
• As 'n persoon die geen het vir kanker, is dit moontelik om die			

kans te verminder met gereelde ondersoeke (kolonoskopie)	☐	☐	☐
• As jy 'n gesonde lewe lui, is die kans minder dat jy oorerflike kanker sal ontwikkel	☐	☐	☐
• As daar iets verkeerd is met jou gene sal jy dit kan agterkom (jy sal 'n verskil voel in jou liggaam)			

36. Watter van die volgende mag dalk beinvloed of 'n persoon kanker ontwikkel of nie?

	Geen invloed	Klein Invloed	Baie Invloed	Weet nie
Persoonlikheid	☐	☐	☐	☐
Stress	☐	☐	☐	☐
Omgevings besoedeling	☐	☐	☐	☐
Die gene	☐	☐	☐	☐
Lewenstyl of gewoontes	☐	☐	☐	☐
Ongeluk (Bad luck)	☐	☐	☐	☐

Seksie D: Begrip van genetiese toets vir dikderm kanker

37.Wie het vir u ingelig oor die feit dat 'n bloed toets vir die geen wat dikderm kanker veroorsaak beskikbaar is? (Het een van die sisters of familie lede vir jou ingelig)?

38. Wie se idëa was dit dat u getoets moet word (bloedtoets/genetiese toets)?

- ☐ My eie
- ☐ Ander familie lid
- ☐ Dokter
- ☐ Spesialis
- ☐ Familie dikderm kliniek
- ☐ Ander _____

39. Kan hierdie genetiese toets vir u sê of u die geen dra wat veroorsaak dat u 'n verhoogte risiko vir dikderm kanker het?

40. Kan hierdie genetiese toets vir kanker toets?

41. Hoe is hierdie voorspellings toets vir HNPCC gedoen?

- ☐ **Ondersoek**
- ☐ **Bloed toets vir die geen**
- ☐ **Kolonoskopie**

42. Hoe lank sedert u die toets resultate ontvang het (genetiese toets)?

43. Toe u vir die genetiese toets gegaan het, het u gedink u sal positief toets vir die geen (voor die resultate gegee is)?

44. Kan u vir my beskryf hoe u voel oor die feit dat u die geen het wat vir 'n mens 'n verhoogde risiko vir dikderm kanker gee?

45. Wat het gebeur met hierdie gevoelings of emosies sedert u die resultaat gekry het?

46. Het u die resultaat met enige iemand gedeel?

- ☐ Nee
- ☐ Ja (met wie?)

.....

47. Wanneer het u die resultaat met hulle gedeel (Hoe lank na u die resultaat gekry het)?

48. Wat was u rede dat u die resultaat met hulle gedeel het?

49. Hoe het hulle gereageer op hierdie inligting (hulle reaksie)?

50. Verduidelik hoe die resultaat u lewe beïnvloed het op n mediese vlak?

51. Wanneer laas het iemand van die genetiese span met u gepraat? Waaroor was dit?

52. Hoeveel kontak het u al gehad met die genetiese/kliniese span na dat u die resultate ontvang het?

- ☐ Een keer
- ☐ Twee keer
- ☐ Baie
- ☐ Geen

Seksie E: Begrip van kanker risiko en kanker persepsie

53. Dink u, u het 'n verhoogde risiko vir dikderm kanker? (enige redes behalwe die toets resultate)

54. Wat is u risiko om dikderm kanker te ontwikkel na die toetsing?

- ☐ Ek het 'n 80% risiko om dikderm kanker te ontwikkel
- ☐ Ek het 'n 50% risiko om dikderm kanker te ontwikkel
- ☐ Dit is vir my gesê dat ek dikderm kanker het (100% risk)
- ☐ Ek het 'n miner as 50% kans om dikderm kanker te ontwikkel
- ☐ Ek het geen risiko nie

55. Dink u, u het beheer oor die kans om dikderm kanker te ontwikkel?

56. Hoe sal u die ontwikkeling van die kanker probeer stop?

57. Is u bekommered oor u huidige risiko om dikderm kanker te ontwikkel?

- o **Baie bekommered**
- o **Effens bekommered**
- o **Glad nie bekommered**

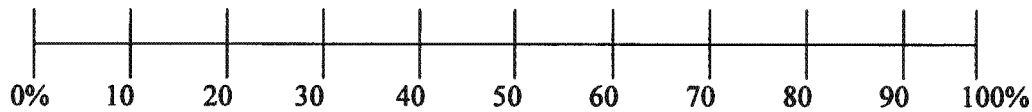
58. Het u al gedink hoe u die situasie sal hanteer as u kanker ontwikkel?

59. As u dikderm kanker sou ontwikkel, dink u dit sou op 'n spesifike ouderdom gebeur?

As ja, hoekom dan.....

60. Dink u die kans dat u dikderm kanker ontwikkel is grooter of kleiner as iemand van dieselfde geslag en ouderdom (nie van jou familie nie)?

61. Dui asseblief u kans om dermkanker te kry aan op 'n skaal van 0 tot 100, waar 0 = 'n 0% of geen kans en 100 = 'n 100% kans, bedoelende dat jy dit beslis sal kry. Merk asseblief die horisontale lyn om jou kans op dermkanker aan te dui. Volgens jou opinie, watter nommer van 0 tot 100 weerspieël jou kanse om dermkanker te kry?



Seksie F: Motiveering vir die onderneeming in die voorspellings programme

Kies asseblief die aantwword wat die beste pas

62. My besluit om die voorspellings toets te neem is .....

	Glad nie	Effens	Baie	Nie van toepassing
Om oor my kinders se risiko te leer				
Om my risiko van dikderm kanker te verminder				
Om vir die toekoms te beplan				
Om navorsing te bevorder				
Om seker te wees oor my risiko				
Om 'n besluit te kan neem oor gesinsbeplanning en te besluit of ek kinders wil hê of nie				
Huweliks besluite				
Dokter het dit aanbeveel				
My gesin het my gevra om die toets te neem				
Bekommered oor abnormale stoolgang/ gesondheids kwale				

(Aangepas van Claes et al 2004)

63. Probeer om te onthou hoe u gevoel het toe u oor die toets moes besluit. Wat was nog vir u belangrik toe u besluit het om die toets te neem ?

.....
.....

64. Hoekom wou u nie die toets neem nie?

.....
.....

65. Is u tevrede met die besluit om die toets te neem? (genetiese toets)

66. Hoe betroubaar beskou u die toets? (genetiese toets)

67. As jy weer moes besluit, sou jy weer vir die genetiese toets gaan, nou dat jy die resultate weet?

Seksie G: Gesondheids opdrag

68. Na watter dag-hospitaal gaan u na toe wanneer u siek word?

69. Is dit dieselfde hospital as die een waar jy gaan vir jou gesondheids kwessies vir dikderm kanker?

70. Het u mediesefonds?

☐ Ja
☐ Nee

71. Het u al ooit 'n kolonoskopie gehad?

☐ Ja (Hoeveel?)
☐ Nee
☐ Ek weet nie

72. Wanneer was u laaste kolonoskopie?

73. Wat kan 'n kolonoskopie vir 'n mens vertel?

74. Hoe verskil 'n kolonoskopie en 'n voorspellings toets van mekaar?

75. Hoekom is altwee toetse nodig?

76. Hoekom gaan u vir 'n kolonoskopie?

77. Het u 'n genetiese toets voor die kolonoskopie gehad?

☐ Ja
☐ Nee

78. Het u 'n kolonoskopie voor u genetiese toets gehad?

☐ Ja
☐ Nee

Seksie H: Voorsienbare ernstigheidsgraad (aangepas van Aktan-Collan 2001)

79. Indien u dikderm kanker ontwikkel, sou u dit oorleef?

80. Is u bang dat u dalk kanker het?

81. Hoe lyk u toekoms?

Seksie I: Opinie oor berading

82. Hoe behulpsaam beskou u die ondersteuningsdiens/beradingsdiens?

83. Het u die berading voor die genetiese toets breikbaar gevind?

☐ Baie
☐ Min of meer
☐ Effens
☐ Glad nie

84. Het u al raadgewing ontvang na die toets resultate?

☐ Ja
☐ Nee

85. Het u enige verdere stellings of vra?

Die navorser bedank die deelnemer vir hulle onderneming in die onderhoud

Die navorser sal die deelnemer verwys vir genetiese berading indien ondersteuning en opvoedkundige insette nodig is.

DIVISION OF HUMAN GENETICS

Faculty of Health Sciences · University of Cape Town

GENETIC TESTING

Genetic testing is an examination of the DNA (basic material of hereditary) of an individual. Results of these tests may disprove or confirm a suspected fault or change (mutation) in the DNA. Genetic testing of DNA is performed on a blood sample collected from an individual.

Predictive genetic testing is a means of knowing one's genetic status with regard to a particular condition. To undergo a predictive genetic test implies that one is forewarned about one's risk of developing a particular disorder before the signs and symptoms of that condition manifest it in an individual.

HNPCC is a dominant inherited disorder with the result that all family members of an affected individual (first degree relative) are at 50% risk of developing cancer at an early age. Predictive genetic test for HNPCC is a relatively recent option available to individuals at risk for having inherited the gene for HNPCC. This test allows an individual a chance of knowing whether he / she has the mutation. Knowledge of one's genetic status, with regard to HNPCC, allows the individual to make informed decisions about commencing preventative screening for cancer.

To take the test is a very serious decision. Therefore, it is important that subjects are well informed and understand the programme and procedures of predictive genetic testing that are necessary before finally getting the result. If after careful consideration, you decide to take the test, you will be requested to come to the Department of Human Genetics on at least 2 occasions to see the geneticist involved in running the programme. Arrangements can be made to link you with the clinical team for screening if needed.

PROGRAMME FOR PREDICTIVE TESTING - HNPCC

1. Telephonic contact with family members re interest in predictive genetic testing. Setting up date(s) for meeting with geneticist.

2. **1st Meeting with geneticists:** (Group session) Information and implication of predictive genetic testing.

The outcome of this meeting can be:

- You need time to assimilate what you have heard. The registered nurses will make contact with you within a week to discuss your decision.
- You have opted to know your genetic status on HNPCC -- 1st Blood samples collected, with informed consent.

3. **2nd Meeting with geneticist:**

- Those who have opted to know their genetic status during the 1st meeting: meet individually with the geneticist and receive their genetic information. They have the opportunity of asking further questions pertinent to their specific situation. A second blood sample will be collected for confirmatory analysis. Contact numbers of the support team will be given. Plan of action with regard to preventative screening will be discussed. Appointments (support team + screening) can be arranged.
- Those who have decided to know their genetic status subsequent to the 1st meeting: meet individually with geneticist to clear up any uncertainties. Meet with registered nurse to take 1st blood specimen.

4. **3rd Meeting with geneticist:**

- Those who have opted to know their genetic status during the 2nd meeting: meet individually with the geneticist and receive their genetic information. They have the opportunity of asking further questions pertinent to their specific situation. A second blood sample will be collected for confirmatory analysis. Contact numbers of the support team will be given. Plan of action with regard to preventative screening will be discussed. Appointments (support team + screening) can be arranged.

GENERAL INFORMATION ON THE HNPCC PREDICTIVE GENETIC TESTING PROGRAMME

1. We strongly recommend that you inform your family doctor of your decision to undertake the test. If you do not have a family doctor we recommend you find one.

As part of the policy of this programme, we believe that the on-going medical care and support your doctor is able to give is very important to you and your family. A letter will be sent to your doctor (with your permission) to inform him/her about the programme after the 2 / 3rd meeting.

2. Support is essential and we therefore strongly advise that you choose a family member or a trusted friend to accompany you to all the meetings. (optional)

3. The final results will be given to you approximately 1 month after your blood samples have been taken and will be strictly confidential. No results will be given to you by telephone. With your permission your family doctor will be contacted and written to regarding the results.

4. If at any stage in the programme you decide you do not wish to continue, the decision is entirely yours. Your decision will in no way prejudice our relationship with you or your family. We will be happy to continue to offer you the support and help you need, within our capabilities.

5. Reactions to predictive genetic testing might vary widely. Some people who might have the predisposing genetic defect may suffer a sense of shock and grief however well they may have been prepared beforehand. People whose test is negative may feel relief but at the same time suffer guilt and anxiety. A health care professional will be available to discuss any questions / problems you might encounter after entering into the HNPCC predictive genetic testing programme.

6. No children under the age of 18 will be included in the HNPCC predictive genetic test programme.

7. Those individuals who carry the mutation for HNPCC will be counselled with regard to best practice regarding regular colonoscopic and other relevant screenings for cancer – in private or provincial settings.

8. Cost for the research leading to the finding of the genetic defect predisposing to colorectal cancer has been borne by the Division of Human Genetics. The (confirmation of diagnosis / predictive) laboratory test is available to members in families where the pre-genetic defect has been detected at an approximate cost of R596.40, which is generally payable through a medical aid scheme. Testing will not be denied to individuals who are unable to afford the cost.