THE KNOWLEDGE AND ATTITUDES OF FAMILY MEMBERS WHO HAVE RECEIVED PREDICTIVE GENETIC TEST RESULTS FOR HEREDITARY NONPOLYPOSIS COLORECTAL CANCER IN SOUTH AFRICA

by

Ursula Algar

(UCT Student No: Algurs001)

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Supervisors:

Lt. Col. Renee Hill (2 Military Hospital)

Associate Professor Paul Goldberg (University of Cape Town/Groote Schuur Hospital)

DECLARATION

I, Ursula Algar, hereby declare that the work on this dissertation is based on 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.

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ABSTRACT

Introduction

Predictive genetic testing for hereditary nonpolyposis colorectal cancer (HNPCC) has been offered to families with known mutations in South Africa since 1997.

Aim

The aim of this study is to evaluate the benefits and limitations, as perceived by family members, of the current management of inherited colorectal cancer.

Methodology

The research population was made up of six families. The 239 individuals live along the West Coast of South Africa. During a 10- day trip from Cape Town to Port Nolloth, (Map 1.1) (Appendix 10-Itinerary) 119 subjects were contacted. (Flow chart 3.1 explains the attrition in the sampling process).

Sixty four individuals were entered into a cross-sectional descriptive survey using a questionnaire provided by the Victorian Clinical Genetic Services (Australia) (Appendix 3). The entry criteria included individuals; i) from families with HNPCC caused by the inheritance of a *h*MLH1 mutation as a result of a C to T transversion at nucleotide 1528 in exon 13 on chromosome 3p(2;3) and; ii) those who had received predictive genetic test results from Professor R. Ramesar the Professor of Human Genetics, University of Cape Town (Appendix 1 - protocol).

Descriptive and analytical statistics were used to explore the data.

Results

The sociodemographics showed a middle to lower socioeconomic group of single and two parent families, mostly with dependant children, and a low number of high scholastic achievers.

Frequent exposure to cancer, knowledge of genetic risk, and a predictive genetic test were recalled by most of this group. Their retained knowledge of the consequences of HNPCC inheritance and subsequent effects was moderate to low except for the question about colonoscopic surveillance. This showed a high level of insight into how to prevent colon cancer. The majority of this group also had a positive attitude toward predictive genetic testing.

At the time of the study most of the cohort was not experiencing stress about being at-risk for colon cancer but there were those who had experienced stressful events. Most of the subjects with a positive genetic mutation had experienced a stressful event in the last year and these events were mainly caused by death or cancer. Subjects who had both negative and positive genetic mutation results had; i) misunderstood their risk, ii) had low colon cancer knowledge scores, iii) were 'worried' about colonic and extracolonic cancers being detected and iv) had concerns about not coping emotionally with their predictive genetic results. Most of the respondents were coping psychologically at the time of the study and did not have anxiety or depression.

The cohort was confident that the medical team would find, cure and enable survival after a colon cancer was diagnosed. Even though the accuracy of the surveillance worried them, they seemed positive about undergoing the procedure and were eager to decrease the surveillance intervals.

Recommendations

Individuals with both positive and negative genetic results require regular information sessions.

The concepts of preventative colectomy and pre-predictive test screening for depression and coping styles, would require further research before suggestions could be made for their use in a predictive genetic testing protocol.

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For ALL my friends and family for understanding the long silences.

To those who live with a heritable disease

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GLOSSARY

Adenomatous polyp: A premalignant lesion found on the mucosal lining of the colon.

Allele: Alternative form of a gene found at the same locus on homologous chromosomes(4).

APC: Adenomatous polyposis coli gene.

Autosomal dominant inheritance: A dominant trait is one which manifests in a heterozygote and is often possible to trace through many generations(4).

Autosomal inheritance: The pattern of inheritance shown by a disorder or trait, determined by a gene on one of the non-sex chromosomes(4).

Biliary Tract: The collection of ducts that connect the liver and gall bladder to the duodenum (upper small intestine).

BRCA1: Breast cancer Gene 1.

Chemotherapy: Drug therapy to rid the body of cancer cells.

Chromosomes: Thread-like, darkly staining bodies, within the nucleus of the cell, composed of DNA and chromatin, which carry genetic information(4).

Colectomy: Surgical removal of the colon.

Colonoscopy: A medical procedure that enables visualisation of the inner lining of the colon.

Construct: A concept created by researchers for scientific use(5).

Construct validity: The extent to which a research tool measures the concept or variable that the researcher wants it to measure(5).

Content validity: Concerned with sampling adequacy. A judgement whether the content of the questionnaire is representative of all possible questionnaires(5).

Cross-sectional design: A design, where data is collected at one point in

time(6).

Descriptive research: The main objective of this type of research is the accurate portrayal of characteristics of persons, situations or groups and/or the frequency with which certain phenomena occur. The research is also designed to recount, characterise, narrate, describe, or classify observations(5;6).

Descriptive statistics: A process of summarising and synthesising data from a sample(5).

DNA: Deoxyribonucleic acid. The nucleic acid in chromosomes, in which genetic information is coded(4).

Endometrium: Mucosal lining of the uterus.

Exon: Region of a gene which is not excised during transcription forming part of mRNA and therefore specifying part of the primary structure of the gene product(4).

Face Validity: The extent to which the instrument is judged appropriate by an experienced researcher(5).

FAP: Familial adenomatous polyposis.

FOB: Faecal occult blood.

Gene: A part of the DNA molecule of a chromosome, which directs the synthesis of a specific polypeptide chain to create protein(4).

HADS: Hospital Anxiety and Depression Scale.

Heterozygote: A person possessing both an abnormal or mutant allele and a normal allele(4).

Homologous chromosome: Chromosomes which pair during meiosis and contain identical loci(4).

***h*MLH1:** Name of a mismatch repair gene that causes HNPCC (human MutL homologue 1).

***h*MSH2 and *h*MSH6:** Name of a mismatch repair gene that causes HNPCC (human MutS homologue).

***h*PSM1 and *h*PSM1:** Name of a mismatch repair gene that causes HNPCC (human post meiotic segregation).

HNPCC: Hereditary Nonpolyposis Colorectal Cancer.

IES: Impact of Events Scale.

Locus: The site of a gene on a chromosome(4).

Median: It is the middle score that divides a set of scores in two equal parts. The value above and below which 50 per cent of the score lies(6).

Mean: A simple descriptive statistic that is a measure of central tendency computed by adding all values or scores and dividing it by the total number of scores(6).

mRNA: A single stranded molecule complementary to one of the strands of double-stranded DNA which is synthesised during transcription and transmits genetic information in the DNA to the ribosome's for protein synthesis(4).

MBSS: Miller's Behavioural Style Scale.

Mutation: A change in genetic material, either in a single gene, or in a number or structure of the chromosomes(4).

Nucleic acid: Is composed of a long chain of individual molecules called nucleotides(4).

Nucleotide: Each contains a nitrogenous base, pentose sugar and a phosphate group(4).

Ovary: Female reproductive organs in which ova are produced.

Pancreas: Glandular organ that produces hormones and digestive juices.

Penetrance: The proportion of heterozygotes for a dominant gene who

express a trait, even if mildly(4).

Proband: An affected individual (irrespective of sex) through whom a family comes to the attention of an investigator (index case)(4).

Proctocolectomy: Surgical procedure that removes the colon and rectum.

Palliative: A procedure that is not curative but attempts to alleviate symptoms.

Radiotherapy: Use of radiation to rid an area of the body of malignant cells.

Reliability: The extent to which data is consistent, accurate and precise, as well as the extent that procedures yield consistent data(5).

Renal Pelvis: Area of the kidney into which produced urine drains and passes into the ureter.

Research population: The whole group of individuals being researched or those having common characteristics, sometimes called the universe(7).

Response set bias: Factors that interfere with measurement of attitude or answers to questions(5).

STAI: Spielberger State-Trait Anxiety Inventory.

Survey research: Non-experimental research that focuses on obtaining information regarding the activities, beliefs, preferences, and attitudes of people via direct questioning of a sample of respondents(6). A collection of data by questionnaire or interview(5).

Trait: Any detectable phenotype property or characteristic(4).

Transversion: the substitution of one nucleotide for another in an exon, resulting in a mutation.

Ureter: Muscular duct that transports urine from the kidney to the bladder.

X-Linked: Genes carried on the X chromosome(4)

X chromosome: One of the sex chromosomes.

1 CHAPTER 1 - INTRODUCTION

1.1 HNPCC - early history

In about 1895, Dr Alfred Warthin, the Chairman of Pathology at the University of Michigan, identified the earliest hereditary form of cancer. His seamstress predicted that she would die at an early age of either a gastric, colon or uterine cancer as most of her family members had died of these diseases. She died at an early age of endometrial carcinoma(8;9). Dr. Warthin published two articles on this family, one in 1913(10) and the other in 1931(10).

Dr. H.T. Lynch presented a family with inherited colon cancer that was not familial adenomatous polyposis at the 1964 American Society of Human Genetics meeting. Dr. Marjorie Shaw was in the audience. She was a colleague of Dr. Warthin's successor at the University of Michigan, Dr. A.J. French(9). Dr French entrusted Dr. Lynch with Dr Warthin's detailed records and pathology specimens that had been meticulously collected over 30 years. Dr. Lynch re-published this information in 1988(11).

The medical community were sceptical about the possibility of a hereditary form of nonpolyposis cancer in the 1970's to mid 1980's, but more and more evidence was published(9) until in 1989 the 'International Collaborative Group on HNPCC (ICG-HNPCC) was established by a group of interested physicians who drew up uniform diagnostic criteria called 'The Amsterdam Criteria'(12;13) (Table 2.2).

It took until 1993 before a definite genetic mutation was found for HNPCC(9;14;15).

1.2 South African background

In the mid 1980's Dr. Neville Polley worked in Kleinsee. This is a small, remote diamond-mining town on the northwestern coast of South Africa, close to the Namibian border. In casual conversion, Dr. Polley's 23-year-old

gardener complained of cramping abdominal pain. The gardener predicted that he had the same condition that had killed his father. The gardener was correct. He had an obstructing colon cancer(2).

Dr. Polley constructed a family pedigree and when it became obvious that this disorder was inherited, he contacted Dr. M. Madden of the department of Surgery of the University of Cape Town. Dr. Madden arranged a trip with Dr. Goldblatt, from the Department of Human Genetics, to the area. They found a family living in Kommagas with 16 men from three generations who had developed colon cancer and they thought that they were dealing with a X-linked inherited colon cancer(16). Kommagas at the time was a tiny village clustered around a Moravian mission. These people had settled here because it was a perennial source of surface water in a semi-desert environment.

It subsequently became apparent, as more data was collected, that the condition was HNPCC. The initial data was skewed because; i) many of the male family members stayed in the area and worked for the mines whilst their sisters moved away and married men from the surrounding towns and; ii) in HNPCC the penetrance in men is higher than in women (17).

Colonoscopic surveillance had been commenced biennially in 1988. Genetic material was collected for a formal research project to identify the causative mutation in 1991(3).

Professor R. Ramesar identified the causative mutation as a *h*MLH1 genetic mutation (C to T transversion at nucleotide 1528 in exon 13 on chromosome 3p) in 1995(2;3).

This family was the first South African family entered into predictive genetic testing and a colonoscopic surveillance outreach program (Appendix 1). A registered nurse, Christina Harocopos, from the family colorectal cancer unit at St. Marks Hospital, London was recruited to Cape Town to establish a similar program for this family. The local program was established in 1997/1998.

1.3 Personal involvement

In January 1999, I took over the co-ordinating role from Sr. C. Harocopos. By December 2002, nine families had entered predictive genetic testing (Appendix 1) whilst 21 others had known HNPCC mutations (Table 1.1). 12 of these families had the same genetic mutation as the original family but there is as yet no established genealogical connection. To date, six of these families are being actively managed for HNPCC and a total of 414 individuals from these six families have received their predictive genetic test results (Table 3.1 and Flow Chart 3.1).

Table 1.1: HNPCC mutations in the South African cohort as of December 2002

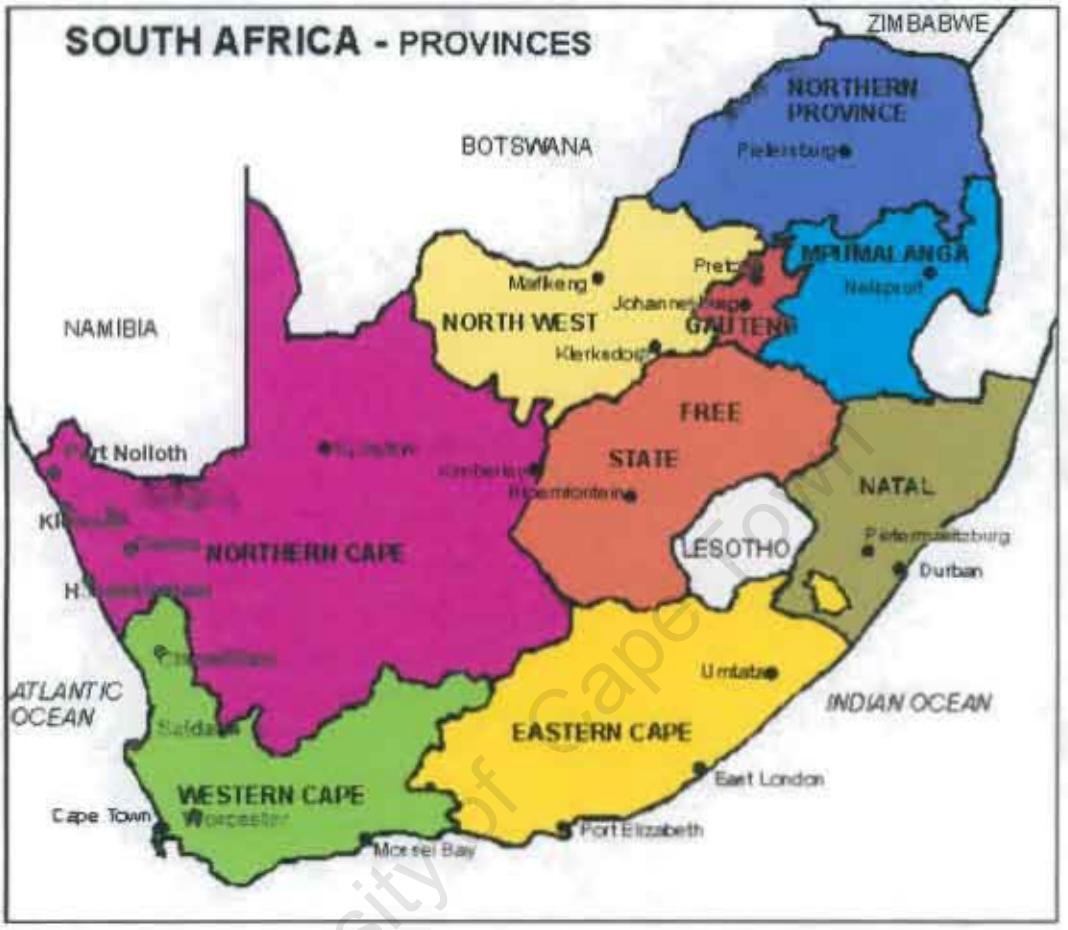
Mutation name	Gene name	Number of Families found to have the mutation	Number of families in Predictive Management
exon 13 (C1528T)	*h*MLH1	13	6
exon 13 (InsT1521)	*h*MLH1	1	-
exon 19 (C152T)	*h*MLH1	1	-
exon 19 (C2152T)	*h*MLH1	1	-
exon 9 (delGTTA731)	*h*MLH1	1	-
exon 6 (G->A 5' DONOR SITE)	*h*MLH1	1	-
exon 6 (C1046G)	*h*MSH2	1	-
exon 15 (DelCTAATTT)	*h*MSH2	1	1
exon 6 (G965A)	*h*MSH2	2	-
exon 7 (delCT1220)	*h*MSH2	5	1
exon 8 (InsGG1340)	*h*MSH2	2	1
exon 9 (A1489G)	*h*MSH2	1	-
Totals	12	30	9

These family members live in a wide variety of environments, mainly the western parts of South Africa (Table 1.2) (Map 1.1). These environs vary from subsistence-living in rural areas, to professional individuals in urban areas.

Table 1.2: Number of individuals and residential areas of those who had a genetic test by December 2002

Residential areas (colour coded with Map 1.1)	Number of individuals from nine different eligible families who have had an *h*MLH1 HNPCC mutation (C125FT in exon 13) predictive genetic test								
Totals	214	44	13	1	21	100	21	16	57
Unknown address	84	6				51	1		8
Cape Town	7	18	13	1	1	26		15	3
Worcester		2			16				
Stellenbosch		2							
Oudshoorn					1				
Wuppertal						11		1	
Clanwilliam						10			
Saldana						2			11
[illegible]	36								
[illegible]	10								27
[illegible]	10								
[illegible]	15								1
[illegible]	2								4
[illegible]	9								1
[illegible]							19		
[illegible]									11
[illegible]									1
[illegible]							2		
[illegible]		3							
Johannesburg		10			3		5		
Maseru		2							
Australia		1							

Map 1.1: Provincial Map of South Africa(18)



These individuals, who had been through the predictive testing program, were thought to be representative enough to guide the future management of families and individuals in this obviously growing field of medical science. With 21 more families who require to be entered into the predictive testing phase of management, this pilot study will guide the future managers of these families with regards to the needs of the family members.

My inspiration for shifting to this relatively new field of nursing came after reading the first chapter of "The Troubled Helix"(19) where patients tell of their soul-searching dilemmas with Hereditary Breast Cancer. I discovered that there are many parallels between this condition and the hereditary form

of colon cancer(20). There are many anecdotes from patients that I manage. Two illustrate the problems these individuals have to face:

- "Mary" is 18 years old. She is the eldest of four children and has had to assume the role of 'Mom' to her younger brothers and sister for the last 8 years because her mother died of metastatic colon cancer at the age of 30. Mary has a 50 percent risk for inheriting her mother's colon cancer. She has been offered a predictive test that will inform her whether she has inherited the same gene. Without knowledge of her result she will always be at a 50 percent risk and will need biannual / annual surveillance colonoscopy. After a traumatic, but normal, colonoscopy at the age of 17 she has, at 18 years of age, consented to having the family specific predictive genetic test. Her result was negative. Mary now knows that she and her children have the same risks of developing colon cancer as the general population.
- One of Mary's uncles, "Aaron", received his predictive genetic test results at the age of 34. He attended colonoscopic surveillance annually. He manifested a precursor lesion for the disease and underwent an uncomplicated colectomy. He died two months after surgery of severe ethanol induced pancreatitis.

I became increasingly interested in knowing what it was like; i) to decide if you wanted this information or not and ii) knowing you were 'THE ONE'. Would Aaron, who died as a result of high alcohol intake, have done so any way? Were these just part of life decisions despite fate?

These were some of the questions going through my mind when I embarked on this research project:

- Was 'troubled', how they felt?
- How does this complex information affect their lives?
- How does knowing this information benefit or limit individuals?

- Will attitudes determine responses to future screening, should it be needed?
- Does the level of education play a role in understanding the complex concepts of genetics?

This growing clinico-genetic service (which involves care of individuals and families with hereditary colon cancer) requires very close ties with an academic clinical complex to maintain high levels of surveillance and treatment as well as continuous counselling for individuals and families. Any surveillance program has both beneficial and detrimental aspects. For this program the benefits are:

- The prevention of death from colon cancer.
- Enabling individuals to make positive life decisions.
- Accurately targeted intervention thereby avoiding unnecessary colonoscopies. This reduces both the costs to the community and risk and unpleasantness to the majority of individuals.

The possible important detrimental aspects include:

- The unpleasantness and risks of repeated colonoscopy.
- The knowledge that a mutation-positive individual is highly likely to develop colon or other related cancers.
- The potential discrimination against family members in terms of employment and insurance opportunities.
- The possible negative psychological consequences of knowing predictive test results.

This research project was aimed at those individuals who had experienced realisation of their own risk of developing colon cancer, being offered predictive genetic testing and having the looming fate of possibly requiring lifetime surveillance. Did they perceive the same benefits and limitations as

the providers of the clinico-genetic service? If not, then the service would need to adapt its philosophy to meet their needs.

1.4 The aim of this study

The aim of this study was to evaluate the benefits and limitations, as perceived by family members, of the current management of inherited colorectal cancer.

1.5 The purpose of this project

Genetic researchers are rapidly finding new disease-causing mutations. The transition from research to clinical service results in a need to provide many more individuals and families with guidance and support from health care workers who are trained to deal with their potential problems(21). In assessing how individuals have coped with knowing a little of their own destiny, this research intends to provide data that will assist in assessing and directing the growing clinico-genetic service to meet the yet unmeasured needs of those unique individuals who have to 'outlive' their fate.

Respondents have received either a positive or negative predictive genetic result to be eligible for the study. These 2 variables will be used to group individual responses in the statistical analysis of the categorical variables grouped into the 4 objectives.

1.6 Objectives

1. To establish the sociodemographics of the study population.
2. To ascertain the knowledge and attitudes of individuals who have had predictive genetic testing for HNPCC, toward genetics, cancer risks, and how to prevent the development of cancer.
3. To measure the effects that the genetic test results have had on the psychological and functional health status of subjects.
4. To evaluate how genetic testing impacts on medical decisions made

by subjects who have received predictive genetic test results.

2 CHAPTER 2 - LITERATURE REVIEW

2.1 Introduction

Colon cancer and the resultant familial risk are briefly explained. The focus is on those autosomal dominant conditions that cause colon cancer particularly HNPCC. Studies of the role of genetics (predictive genetic testing and counselling) and clinical medicine (surveillance and surgery) in the management of these families are highlighted.

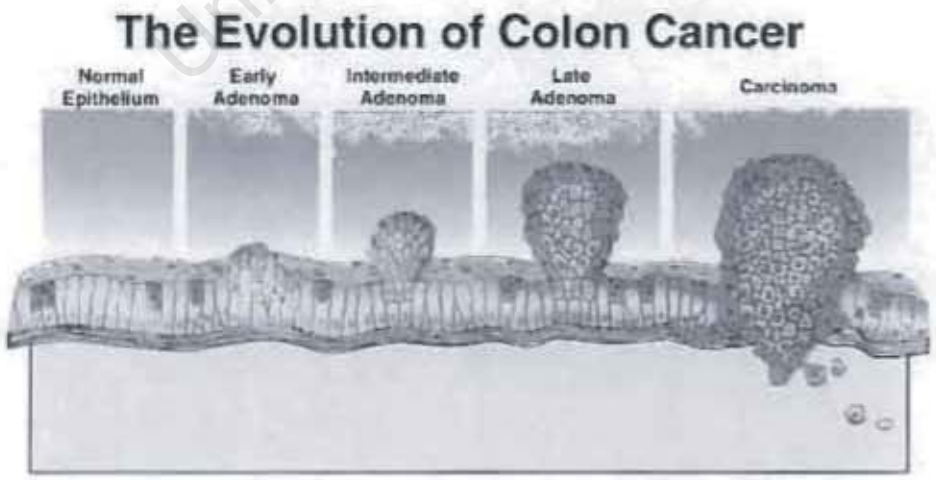
2.2 Colon cancer

2.2.1 Evolution of colon cancer

Cancers are genetic disorders(22), but not necessarily inherited. The term genetic implies that the transformation of a normal cell to a malignant cell is achieved through the step-by-step accumulation of genetic alterations(22).

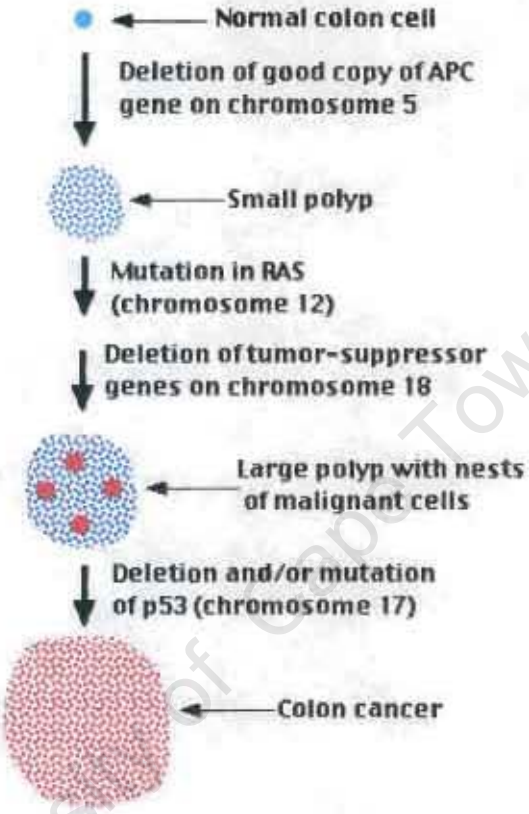
Colon cancer occurs after a series of genetic and pathological steps. Inactivation of the APC, *h*MSH2 or *h*MLH1 genes could cause an adenoma, and with a further accumulation of genetic abnormalities, could result in a carcinoma (Diagram 2.1)(23).

Diagram 2.1: The evolution of colon cancer (24)



Eighty five per cent of colon cancers are as a result of chromosomal instability resulting in alterations in chromosome number (aneuploidy) of chromosomes 5q (APC), 18q, 12 (K-ras), 17p (BAT -26, p53)(25).

Diagram 2.2: Development of colorectal cancer (Vogelstein pathway)(26)



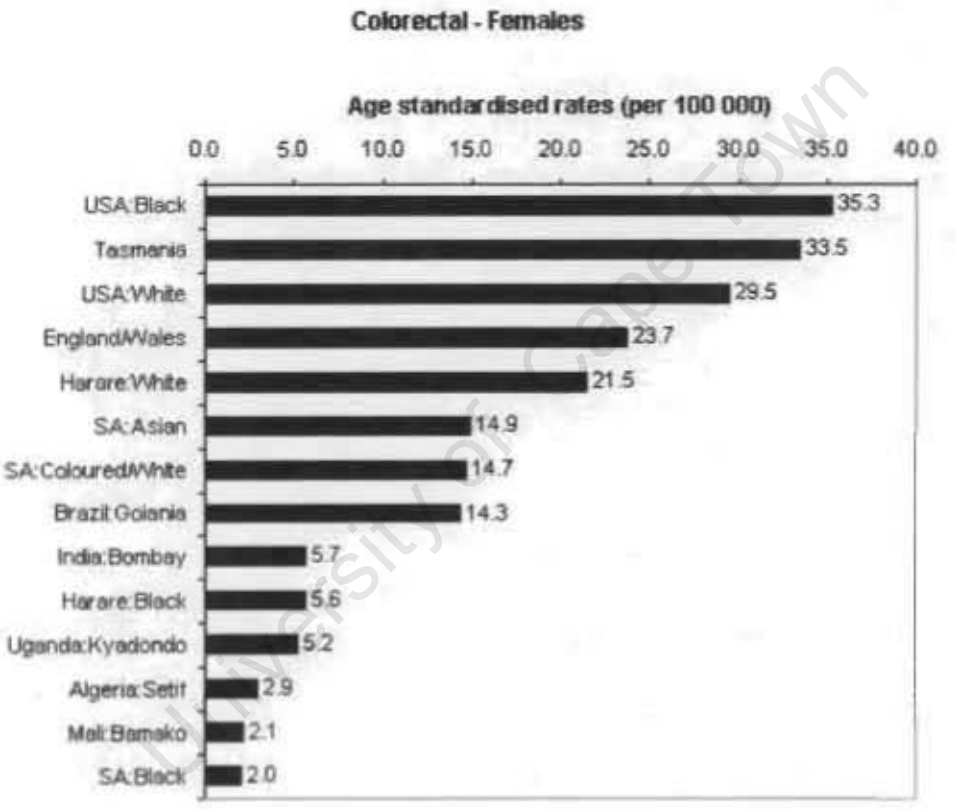
Fifteen per cent of colon cancers are due to events that do not affect the chromosome complement, but accumulate large numbers of DNA repair defects in the cell, resulting in genetic instability(25;27). In the process of cell division, the original DNA is used as a template to replicate a copy, catalysed by an enzyme called DNA polymerase. An error in this process can cause a mismatch in the copy. A gene, called a mismatch repair gene, is meant to detect and repair the error. Any failure in this editing process will cause an increase in the mutation rate in the resultant cells. There are four described mismatch repair proteins namely *h*MLH1, *h*MSH2, *h*MSH6 and *h*PMS2(22).

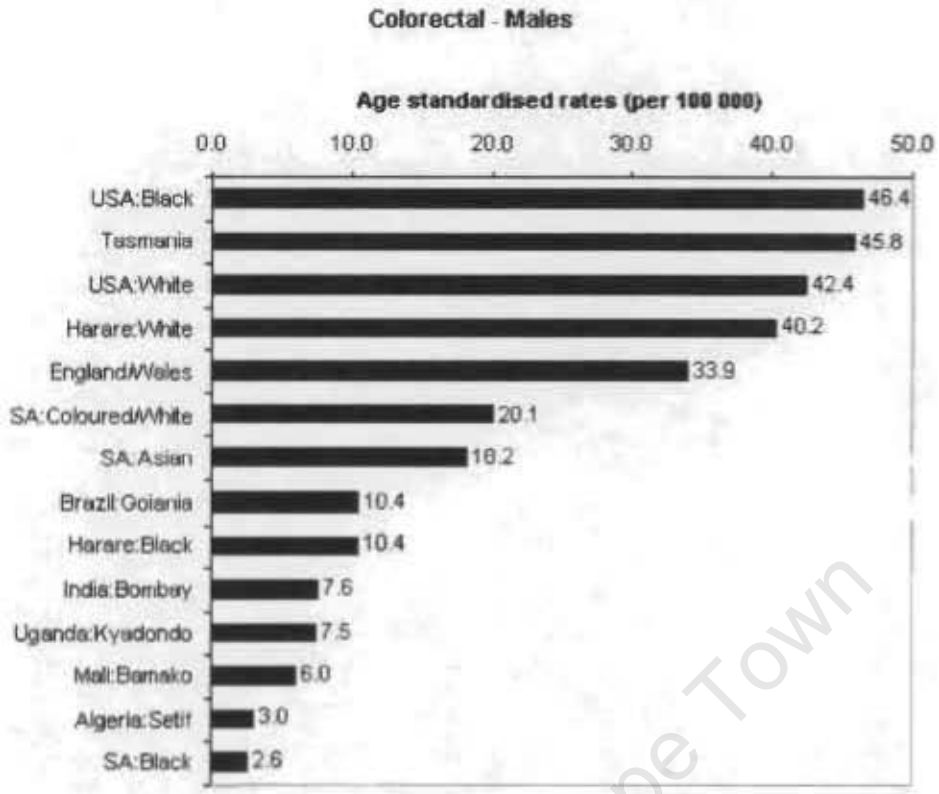
2.2.2 Incidence of colon cancer

Important population differences exist. In the United States all ethnic groups

are affected, but African Americans have the highest prevalence and mortality(28), whilst in South Africa, Asian, Coloured and White females and males have the highest incidence rates. These rates are half of those reported by the United States, Tasmania, England and Wales. South African Black females and males have the lowest rates of colon cancer in relation to any other countries and population groups(29). The risk of developing colorectal cancer in South Africa is 1 in 91 for males and 1 in 134 for females(29).

Figure 2.1: International comparisons of colorectal cancer incidence(29)





(Adapted from Parkin *et al.* 1997)

Ninety percent of colorectal cancers occur in individuals over 50(28;30). Seventy-five percent of these cancers occur sporadically (without risk factors other than age)(28) with a family history being unusual.

Survival for colorectal cancers is directly related to the extent of disease at presentation. The majority of these cancers develop in a pre-existing adenoma(22) or pre-malignant adenomatous polyp(28;30). Thus intervention at an early pathological or pre-malignant stage improves survival(31).

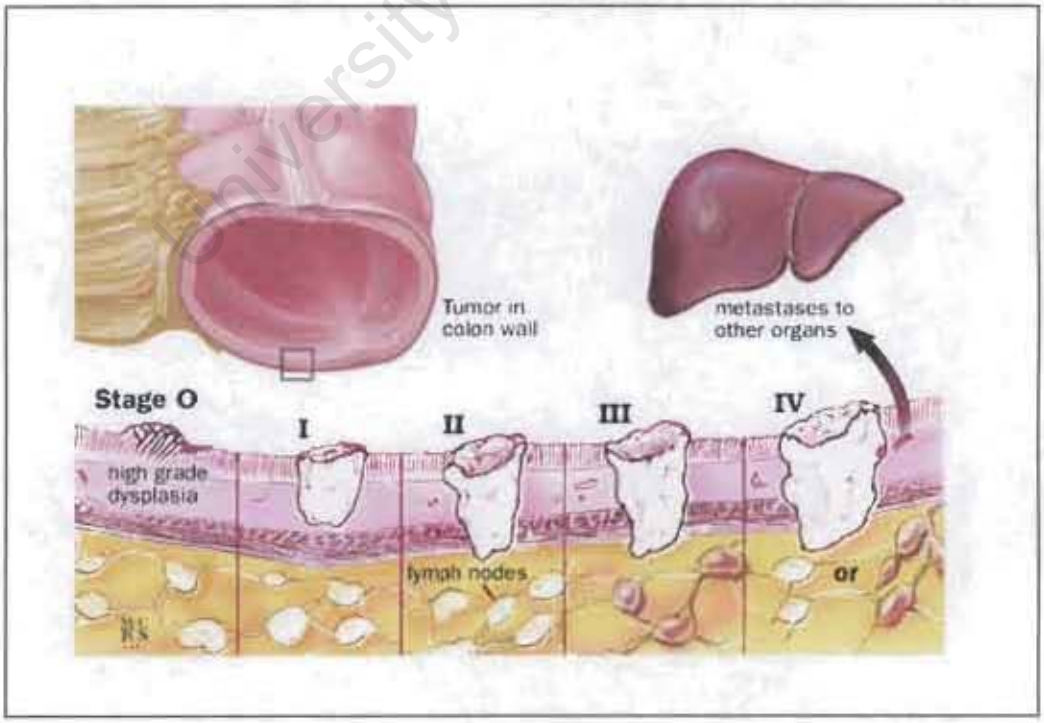
2.2.3 Staging of colon cancer

There are two main staging classifications of colon cancers i.e. the older Dukes or the newer TNM (Tumour, Node, Metastases) classifications (Table2.1) (Figure 2.4)(27).

Table 2.1: Staging of colon cancer(27)

Staging classification	Description	5 year survival
Stage 0	Carcinoma in situ	
Stage I (Duke's A/T1)	Confined to invasion of the sub mucosa	85% to 95%
Stage II (Duke's B/ T2, T3, T4)	T2 Penetrates the muscularis propria	55% to 85 %
	T3 Invasion is through the muscularis propria into the subserosa	20% to 55%
	T4 Direct invasion of other organs	1% to 3%
Stage III (Duke's C/N)	Spread to lymph nodes	38%
Stage IV (Duke's D/ M)	Distant metastases	3%

Figure 2.3: Staging of colon cancer(32)



2.2.4 Treatment of colon cancers

2.2.4.1 Surgery

Surgery is the primary form of treatment for a colon or rectal cancer. Part of the decision to operate depends on the staging.

- Stage 0 can be treated with local removal of the lesion, usually at colonoscopy.
- Stages I, II and III require more extensive surgery depending on the location of the cancer within the colon or rectum. The ability or inability to anastamose the colon adds to the extent of the surgery.
- Colonic surgery in Stage IV (metastatic disease) is usually a palliative procedure to assist with quality of life. A liver resection could also be considered depending on the number of lesions within the liver(27).

2.2.4.2 Chemotherapy

Chemotherapy (fluorouracil, leucovorin and levamisole) is usually indicated to control systemic disease. Stage III disease indicates that lymph nodes were involved at resection and is thus an indication for treatment. Chemotherapy can either be given pre- and/or post-operatively depending on the treatment trial or regimen of the institution.

Stage IV disease indicates not only a direct spread to local organs but also to distant organs, usually the liver. Chemotherapy is usually a palliative form of treatment at this stage(27).

2.2.4.3 Radiotherapy

Radiotherapy is usually used for rectal cancers to reduce the size of the tumour prior to surgery, prevent local recurrence post-operatively or as palliation for inoperable rectal lesions(27).

2.2.5 Familial risk

Ten to thirty per cent of all individuals with a colon cancer have a

for five to ten per cent of all colon cancers(34;36).

2.3.1 Familial adenomatous polyposis (FAP)

Familial adenomatous polyposis (1% of colorectal cancer load) is caused by germline (i.e. in ovum or sperm) mutations in the adenomatous polyposis coli (APC) gene that is located on the long arm (5q21) of chromosome 5. Individuals with this condition develop hundreds of colonic polyps in their late teens. If not treated, these individuals become symptomatic in their twenties, and develop colorectal cancer and if untreated, die at a young age(37;38). At-risk individuals require regular surveillance of the rectum to detect the polyps.

2.3.2 Hereditary Nonpolyposis Colorectal Cancer (HNPCC)

HNPCC (±6 to 10% of colorectal cancer load) is caused by mutations in mismatch repair genes (*h*MLH1 (chromosome 3p), *h*MSH2 (chromosome 2p), *h*MSH6 (chromosome 2p), *h*PMS1 (chromosome 2q) and *h*PMS2 (chromosome 7q))(22;39;40). This condition has no obvious clinical features that differentiate it from sporadic colorectal cancer. It tends to have an early age of onset, has a tendency to form multiple colorectal cancers(15) and special pathological features(15;41) can alert a clinician to its possibility but usually it is only when the family pedigree is studied that the autosomal dominance of the condition becomes apparent(42-44).

Common international criteria (Table 2.2: Amsterdam Criteria) have been set to assist with the clinical identification of HNPCC families (Table 2.2) (12;34;41;45).

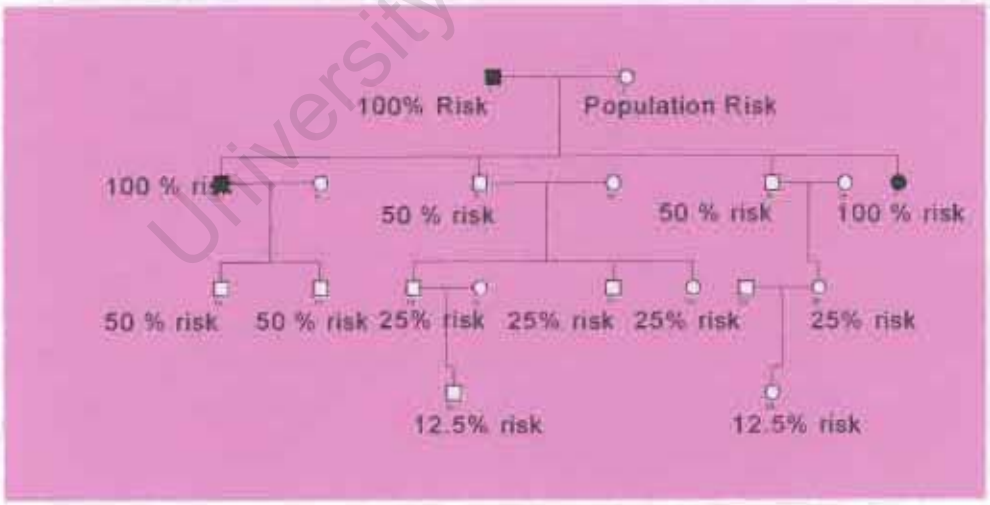
predisposition towards a familial risk. Increased familial risk probably results from a combination of genetic and environmental factors(28).

The genetic factors that formulate inherited susceptibility appear to be more dominant in those that have a predisposition towards a familial risk. The risks for colorectal cancer have been shown to increase threefold by having an affected first-degree relative(33). An affected relative younger than 45 increases this risk to fourfold. The number of affected relatives also raises the risk for first- and second-degree relatives(28;33).

In inherited cancers, the assessment of individual risk begins with the construction of a family pedigree (Diagram 2.3). The risk of the development of cancer can then be determined by analysis of the pedigree, by ascertaining family cancer history (with proven histology) and age of onset of cancer in affected individuals(34). This knowledge can then be used in strategising surveillance programs(33;35).

Figure 2.4: A typical autosomal dominant pedigree showing risk assessment

Key: ○ = unaffected female, □ = unaffected male, ● = affected female, ■ = affected male



2.3 Autosomal dominant conditions

Numerous genes are probably involved in formulating a predisposition to cancer risk, but mutations in some genes are known to cause cancer(28) and definitely result in two autosomal dominant genetic conditions that account

Table 2.2: Amsterdam criteria

The modified Amsterdam criteria for HNPCC:

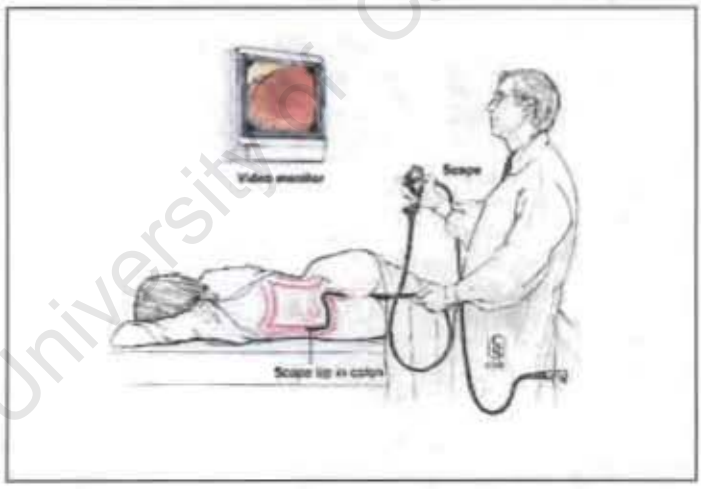
At least three relatives with a HNPCC-associated cancer (colorectal, endometrial, ovary, stomach, hepatobiliary, small bowel, brain, ureter or renal pelvis and skin)

The following criteria should all be present:

- One case a first-degree relative of the other two
- At least two successive generations affected
- At least one case diagnosed before the age of 50
- Exclusion of familial adenomatous polyposis
- Tumours should be verified by pathological examination

The majority of the cancers in this condition occur in the proximal colon(34;41-43) necessitating repeated (annual or biennial) colonoscopic surveillance(9;34).

Figure 2.5: Colonoscopy(46)



This is an invasive and unpleasant intervention requiring expensive equipment and a high level of expertise and extensive colonic preparation. These high-risk individuals are also at-risk for extra-colonic malignancies i.e. endometrium, ovary, small intestine, biliary tract, ureter, renal pelvis, stomach and pancreas. Surveillance of these organs should start at age 30(9;34;47).

2.3.3 Treatment of autosomal dominant conditions

When colonic lesions (adenomatous polyp or cancer) are found in either colorectal cancer or familial adenomatous polyposis high-risk individuals, the management, as with sporadic colon cancers, requires primarily surgical intervention. The procedures will either be a total colectomy with an ileo-rectal anastamosis (Figure 2.7) or a restorative proctocolectomy (Figure 2.8). It has been suggested that prophylactic surgery should be discussed as an option of management with a known gene positive colorectal cancer individual(15;41).

Depending on pathological staging and site of lesion pre and/or post-operative chemo-radiation is offered.

Figure 2.6: Total colectomy and ileorectal anastamosis(48)

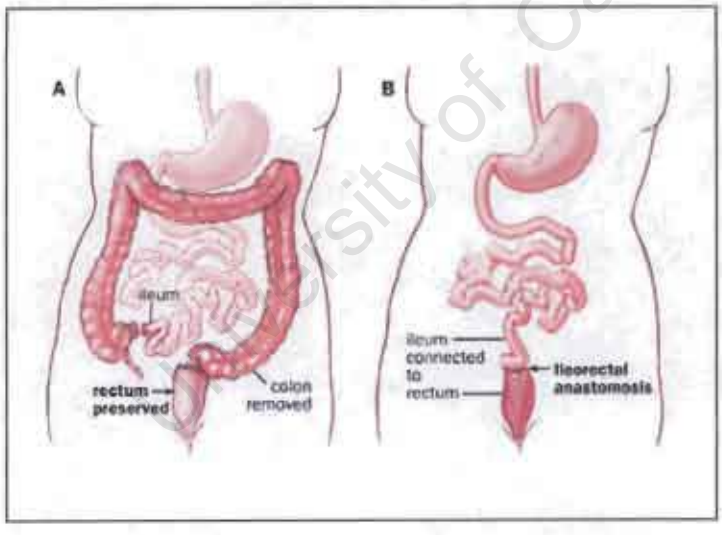
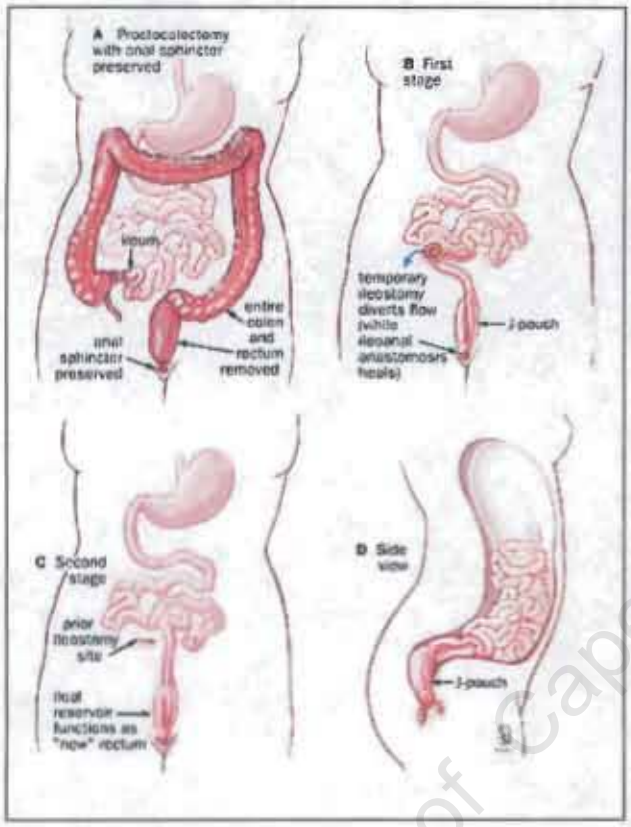


Figure 2.7: Restorative proctocolectomy (49)



2.4 Genetic testing

Should a genetic mutation be found in a proband's blood, then high-risk, consenting, adult relatives can be offered predictive genetic testing. DNA can be extracted from the relatives' blood and 'matched' to that of the probands'. Each direct relative will have a 50% (1 in 2) chance of having inherited the same mutation (autosomal dominance) (Figure 2.5)(2;4;34).

In conjunction with genetic testing, early detection strategies, e.g. surveillance colonoscopies, are vital, since early lesions found at colonoscopy more than halve the risk of colorectal cancer, prevent colorectal cancer deaths and decrease overall mortality by 65% in HNPCC families(28;36).

2.4.1 Pre-predictive genetic testing

The presence of a colon cancer-causing genetic mutation places an individual, or carrier, at an extremely high risk of developing the disease (80 to 85%)(2;47;50). Identification of the causative genetic mutation for colon cancer increases the accuracy of risk assessment(51). A negative genetic mutation result returns the individuals' risk to population level(52) and relieves them of unnecessary surveillance(53).

South African medical decision-makers argue that there are significant health and economic benefits resulting from knowledge of mutation status(3). This benefit is to; i) individual: by improving survival through increased focus on early detection or prevention strategies and; ii) medical economy: by creating a focus on those who are carriers of the causative genetic mutation, at-risk family members are therefore actively encouraged to accept genetic testing. Those that wish to know their predictive genetic test results are entered into a predictive genetic testing program (Appendix 1 - protocol).

The possible psychological risks/distress may include anxiety(54), depression(55), denial and guilt at possibly having passed on the genetic mutation to children(56). They may, on the other hand, experience the benefits of safety in the knowledge that they are reacting positively to their risk(54).

2.4.2 Benefits and Limitations

The decision to accept a predictive genetic test has been studied internationally. Lerman et al(55) redesigned and used a 12 item scale, initially used for psychosocial assessments in predictive testing for Huntington's disease(57). The scale measures perception, benefits and risks of genetic testing in studies that looked at predictors of genetic test utilisation and interest in genetic testing(55;58). To learn about children's risk(20;55;58-62) was the most commonly cited reason for requesting a genetic test. To increase use of screening tests and to take better care of oneself(20;55;59-

62) as well as the desire to participate in research(60) were also important motivators.

The most common perceived limitations to genetic tests were concerns about accuracy(20;58) and the effect on the family(61).

2.4.3 Interest in genetic testing

Interest in genetic testing was studied in populations at high-risk for colon cancer. Results showed that those from a higher socioeconomic background(56;63), who were younger and had first-degree relatives with colon cancer(63) expressed the highest interest and intention to learn their genetic results.

Factors predicting test uptake for colorectal genetic testing have been widely investigated. An increased perception of risk(54;59;61;63;64), a greater perceived confidence in their ability to cope with unfavourable genetic information(59), past experience with testing(54), more cancer thoughts(54;63) and having at least one colonoscopy were predictors of accepting predictive genetic testing.

Factors that were associated with having a high-risk perception and an associated lack of optimism, were, having a family history of colon cancer, poorer health behaviours and higher levels of anxiety(65;66). Rob et al(65) found that those males, who were older and non-white perceived their risks to be lower than their peers which was found to be opposite of true risk.

Barriers to accepting predictive testing were found by Lerman et al(47) to be less formal education, lower socioeconomic group, symptoms of depression especially among women and not having health insurance(58).

Consistent findings by Croyle et al(54) were that individuals process and evaluate risk information very differently when the information is personally relevant. Lerman et al(47) offered genetic testing to a group of clinically and molecularly proven family members at high-risk for HNPCC and only 43%

elected to participate in the counselling and testing program. Results from a recent study by Keller et al showed that although all patients showed a high interest in genetic testing, their attitude toward genetic testing was not a valid predictor of actually accepting genetic results(62).

Spirituality was also investigated and it was found that highly spiritual women were less likely to receive predictive test results than less spiritual women(67).

2.4.4 Psychological and functional health

Anxiety, educational level and coping style seemed to be obvious factors to research but none was found to be associated with an interest in genetic testing (54;61).

Esplen et al(60) looked for psychological distress prior to genetic testing, and found female patients with colorectal cancer had higher levels of event stress than males. Significantly higher levels of anxiety and depression were found in those who were younger than 50 when their colon cancer was diagnosed, or younger than 25 when a close relative was diagnosed. The number of family members with colorectal cancers did not correlate with increased pre-test distress but, additional losses (not cancer related) were associated with pre-test stress and depression(60). Esplen et al(60) also found no difference in the psychological functioning between those that anticipated a negative or positive result.

Most women anticipated a negative psychological impact (increased anxiety, depression and impaired quality of life) if their test was positive for a breast cancer mutation(55). They also felt that they would worry if they had a negative result(55). Depression was the strongest predictor of an anticipated negative impact of genetic testing(55).

2.4.5 Predictive genetic testing

2.4.5.1 Psychological distress

There are few studies that have investigated psychological distress after disclosure of genetic test results for HNPCC. Most have been done before the mutation analysis.

2.4.5.1.1 Depression

Many studies found depression to be linked with potential problems in the predictive genetic testing process. Murakami et al(68) found that a history of depression and not disclosure of genetic test results was a significant predictor of psychological distress. Lerman et al(47) found that females with clinical depression had a fourfold reduction in predictive testing acceptance and that depressed individuals may also delay preventative medical care(47) thus they suggested that depression could be a barrier to genetic testing. They advised that it should be possibly screened for in an individual prior to embarking into a predictive genetic testing program(68).

Balmana et al(20) found that depression rates in subjects undergoing breast cancer genetic testing, and who were found to be non-carriers, were reduced, while in the carriers it remained the same, and increased in those who declined testing. This seems to show that those accepting genetic tests are a select group with a good ability to cope emotionally with the results.

2.4.5.1.2 Stress

According to Atkan-Collan et al(69) the moment of disclosure of mutation status was the most stressful time and thus the time for the greatest need for support. Making the decision and waiting for the results were also times of heightened stress. Esplen et al(60) found that the majority of individuals who tested positive experience moderate stress in the short term, but that it appeared to resolve over time, while those that did not have a disease-causing mutation showed an initial reduction in distress.

Knowledge, experience with the disease and previous experience of surveillance prior to the genetic test disclosure, reduced the level of stress(70). Dorval et al(71) and Bonadona et al(72) found that those who

had cancer, underestimated their distress reactions to disclosure of a positive genetic result. There appears to be a group of individuals who anticipate and experience adjustment difficulties such as anxiety and depression, specifically related to genetic tests(20;60;71). Individuals with characteristics of depression and an avoidance style of coping were associated with heightened stress(47;70).

2.4.5.1.3 Guilt

Dorval et al(71) found that only modest levels of guilt were reported in anticipation of positive or negative results and this remained low after the test disclosure. This was supported by Murakami et al(68) who only found that 12% of his sample had feelings of guilt one month after disclosure.

2.4.5.1.4 Anxiety

Atkan-Collan et al(53) found that a high level of anxiety and worry were caused by misunderstanding a predictive genetic result in mutation-positive and negative individuals. This misunderstanding was associated with a lower pre-test perception of risk in mutation-positive individuals and a higher pre-test risk perception amongst the few mutation-negative individuals who had misunderstood their result.

Women, adolescents, young adults and mutation-positive individuals demonstrated very high levels of anxiety(69;70).

2.4.5.1.5 Coping style

Busjan et al(73) stated that "the psychological processes aimed at diminishing stress are called the coping processes or the things people do to avoid being harmed by life-strains".

According to Miller(74) "when faced with threatening situations, individuals who differ in coping styles diverge in their choices of coping strategy: Monitors, who characteristically seek information and Blunters, who characteristically distract themselves."

Petersson(75) found coping style to be unrelated to demographic variables as well as measures such as anxiety and depression but Phipps and Zinn(76) however found that monitors were more anxious than blunters and that there were significant interactions between coping styles and change in anxiety and depression scores over time, amongst their subjects who were having amniocentesis.

Steptoe and Sullivan's(77) study found that monitors engaged in more vigorous health related information seeking behaviours and were more likely to undergo preventative behaviour than blunters.

2.4.5.2 Impacts on medical decisions

In a study by Codori et al(64), the subjects were unaffected, high-risk first-degree relatives of HNPCC families who had been offered predictive genetic testing. They found an all-or-nothing attitude. Those who accepted regular surveillance because of high risk also accepted genetic testing and vice versa.

Lerman et al(47) found that persons with lower socioeconomic status or alternatively, lack of formal education, had low levels of utilisation of colorectal cancer surveillance.

Myres et al(78) found older females who had a faecal occult blood test in the past were more likely to adhere to surveillance. Men were found to require encouragement and instruction in relation to surveillance. Perceptions of the severity and curability of the disease, worry about having an abnormal screening test, salience and coherence of the screening test, were positively associated with screening. The belief that 'powerful others' could exercise control over health and that the perception of an effective physician-patient relationship, was found to be positively associated to adherence.

This view was shared by Johnson et al(79) who stated that "previous preventative health behaviour, perception of benefit of screening, physician recommendation for screening and knowledge of others with colon cancer"

were factors that increased screening adherence.

Hadley et al(36) also found that the most common reason given for an individuals decision to screen (or not to screen) was that the doctor did (or did not) recommend it.

Johnson et al(79) also suggest that "absence of symptoms or health problems, embarrassment and discomfort of testing, a desire not to know about health problems and increased anxiety" were reasons for avoiding surveillance.

2.4.5.3 Genetic counselling

Genetic counselling attempts to improve early detection and prevention of colon cancer by identifying those at high-risk. Options and recommendations are offered to reduce risk, and psychological support assists with reducing negativity towards preventative screening(79). Johnson et al(79) evaluated the impact of genetic counselling and testing on subsequent colorectal screening behaviour, and found that screening behaviour correlated with the genetic test result. Recommendations were well adhered to by patients who received genetic counselling for positive genetic results(79). Hadley et al(36) found that genetic counselling and testing influenced endoscopic screening appropriately during the 12 months post genetic counselling and testing.

There appears to be a reluctance to cease surveillance after receiving a low-risk result(36;52;80). Hadley et al(81) found an element of hypervigilance amongst young mutation-positive individuals.

2.5 Research instrument

The Victorian Clinical Genetics Services (Australia) modified a questionnaire developed for the investigation of breast cancer(58) for use in HNPCC research.

The Australian instrument (Appendix 2), (used with permission (Appendix 3)) was modified to suit the South African context (Appendix 4) and then translated into Afrikaans and piloted (Appendix 5). Utilising the feedback from the pilot study, the instrument was altered to suit the target group (Appendix 6).

The questionnaire consisted of:

- A sociodemographic section.
- A scale used to measure knowledge about inherited colorectal cancer. This scale was altered by Meiser et al(82) from eleven true-false items used by Lerman et al(58) to a revised nine item version of this measure.
- A scale that measures perception, benefits and risks of genetic testing. Lerman et al(55) redesigned and used a 12 item scale, initially used for psychosocial assessments in predictive testing for Huntington's disease(57). The scale has subsequently been used for studies concerning inherited breast and colon cancer(20;55;58-61).
- A set of six points about family members who had cancer. Petersen et al(66) used a similar set of questions to depict family history and experiences with colon cancer in the family.
- A scale used to measure coping style called the Miller's Behavioural Style Scale (MBSS)(56;74).
- A measure of stress experienced in the previous year(60).
- An impact of Events Scale (IES)(61;83). This scale was devised initially to measure the degree of subjective impact experienced as a result of a specific event(83), but could also be used to measure this impact over a period of time. In this study the stressor was the concern of being at risk for colon cancer.

- A scale called the Hospital Anxiety and Depression Scale (HADS)(84) had been designed specifically for patients with physical illness. According to Snaith(84) and Bjelland et al(85) this scale is only valid if used for screening purposes and cannot give a definitive diagnosis. It has 14 items divided into two subscales, seven for anxiety and seven for depression with somatic items excluded. Only the depression scale was used in this study.
- A short version of the Spielberger State–Trait Anxiety Inventory (STAI)(56;86) which was included as a measure for situational anxiety.
- A measure that asked about perceptions of risk for developing colon cancer(64) which gives a baseline of risk perception to which screening and health behaviour can be compared.
- A medical measurement of risk that utilises family history and colonoscopic surveillance which usually yields adenomatous polyps(42-44;87).
- An enquiry of actual participation in colonoscopic surveillance, their opinions about choices in health related behaviour, beliefs and attitudes about the effectiveness of preventative surveillance, opinions about colon cancer, and the reasons and motivations for accepting or rejecting surveillance(36;79).

2.6 Conclusion

Much has been researched internationally about HNPCC and the predictive and actual effects of genetic testing on high-risk individuals. To date there is no knowledge of the opinions of South African individuals, some of whom had received their results in 1997. The results of this study will be compared with this literature and the resultant discussion will offer recommendations provided by this cohort.

3 CHAPTER 3 - METHODOLOGY

3.1 Introduction

This chapter includes the research design and the steps followed in reaching the final sample. The choice and enhancement of the instrument is explained with evidence provided for its validity and reliability. Data collation and analysis are described with due regard for research and ethical principles.

3.2 Research Design

A cross-sectional descriptive survey approach was selected, as it enabled flexibility and allowed versatility with regards to venue, scale and mode of enquiry(88).

This non-experimental research is termed ex post facto or correlational research. This approach indicates that the research will be conducted after a variation (positive or negative genetic result) in the independent variable (predictive genetic testing) has occurred(6). Correlational research seeks associations between two variables and tries to understand them(7).

3.3 Sample and Setting

3.3.1 Sample:

Up to and including December 31 2002, 173 probands had been recruited to enter the HNPCC, University of Cape Town/Groote Schuur Hospital research program(1) (Research criteria Appendix 7). HNPCC mutations were found in 30 different probands and some extended families of which nine had been entered into the predictive genetic testing program (Table 1.1).

The research population was made up of six out of the nine families (Table 3.1). The individuals who met the criteria were:

1. From families with HNPCC caused by the inheritance of a mutation in the *h*MLH1 gene as a result of a C to T transversion at nucleotide 1528

in exon 13 on chromosome 3p(2;3).

2. Those who had received predictive genetic test results from Professor Raj Ramesar (Professor of Human Genetics, University of Cape Town) (Appendix 1 - Protocol).

Table 3.1: Number of families and individuals eligible for inclusion in the sample

Number of Families	**Number of eligible individuals per family**
1	214 individuals
2	100 individuals
3	57 individuals
4	21 individuals
5	21 individuals
6	1 individual
Total	**414 individuals**

Subjects were excluded for any one of the following reasons:

1. Inability to be contacted;
2. Refusal to participate; or
3. Geographical reasons.

Out of the 414 eligible individuals, 239 were thought to be contactable (Table 3.2).

Table 3.2: List of eligible families and individuals after exclusions

Number of Families	**Number of eligible individuals per family**
1	126
2	71
3	22
4	20
Total	**239**

The 239 individuals live along the West Coast of South Africa. During a 10-day trip from Cape Town to Port Nolloth, (Map 1.1) (Appendix 10-Itinerary) 119 subjects were contacted.

The following flow chart (Flow chart 3.1) was created to explain the attrition in the sampling process.

Levels 1, 2 and 3 in the flow chart are part of the predictive genetic testing program offered through the Division of Human Genetics of the University of Cape Town and Groote Schuur Hospital. The current study commences from level 4 and explains the attrition in the sampling process.

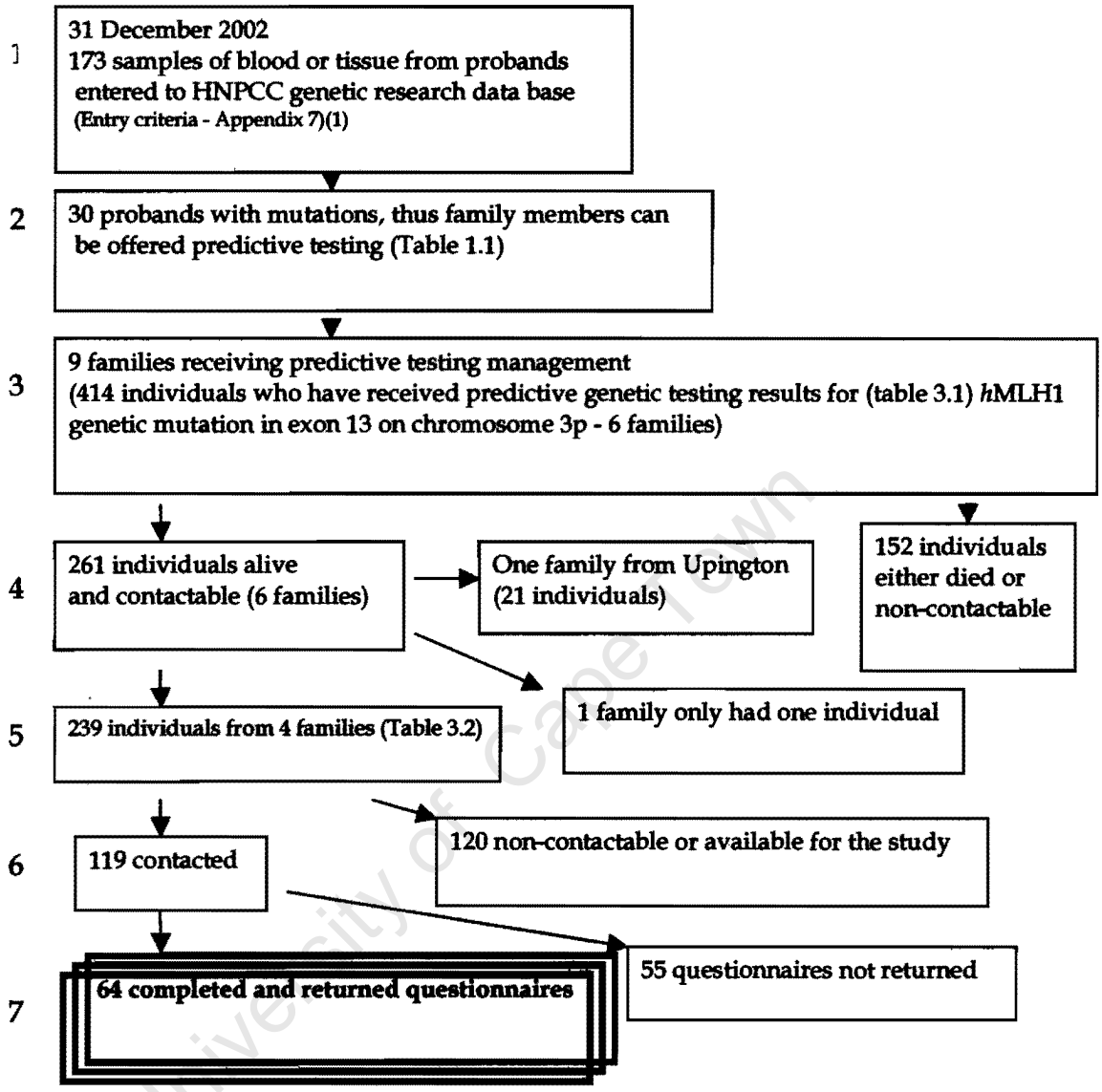


Figure 3.1: Flow diagram of study sample

3.3.2 Sample size

In the current study only 64 individuals were available for data analysis. The response rate for this research project was 50% with a hypothesised proportion of 40% (difference of 10%) the power of the test among 64 individuals was 36%. The ideal sample size with 80% power and 95% confidence interval would have

been n = 194.

3.4 Instrument

3.4.1 Selection and Modification

The Victorian Clinical Genetics Services (Australia) modified a questionnaire developed for the investigation of breast cancer(58) for use in HNPCC research.

The Australian instrument (Appendix 2), (used with permission (Appendix 3)) was modified to suit the South African context (Appendix 4) and then translated into Afrikaans and piloted (Appendix 5). Utilising the feedback from the pilot study, the instrument was altered to suit the target group (Appendix 6).

The changes made to the original instrument included:

- The last paragraph of the instruction sheet was altered to include the fact that a data collector would be available to assist with queries about the questionnaires and collect them on completion (Appendix 4 English and Appendix 5 Afrikaans).
- Addition of questions.
- Deletion of questions.
- Changes to the wording in the English questionnaire, facilitating translation into Afrikaans.

Detailed changes to the final instrument and explanations for the alterations can be found in Appendix 8.

3.4.2 The Final instrument

3.4.2.1 Objective 1: Sociodemographics

(Questions 1 to 10)

Questions 7 to 10 were added to the original questionnaire. The questions and numbering were changed to provide a South African context (Appendices 4, 5 and 6).

The following factors were used to measure and record sociodemographic details:

3.4.2.1.1 Age and gender

(Questions 6 and 9)

The attitude of individuals toward predictive genetic testing could be influenced by these two factors(47;60;63).

3.4.2.1.2 Marital status and children

(Questions 4 and 10)

The support structure and stability within a family can have an influence on an individual's decision-making. Managers of these families find it vital to know how many children are at-risk especially if a parent is positive for a HNPCC mutation or affected with colon cancer(20;55;56;59;63).

3.4.2.1.3 Education

(Questions 2 and 3)

An individual's knowledge and education level has been shown to be influential in creating a barrier to genetic test acceptance. The in/ability to understand genetic concepts, risk, and the basis of knowledge assessment, could contribute to that barrier(20;47).

3.4.2.1.4 Employment and Medical Care

(Questions 1, 8 and 14)

Financial stability, as well as health and insurance choices, influence benefits and

limitations within the predictive testing process(47).

3.4.2.1.5 Faith

(Question 7)

Beliefs and attitudes can have a basis in spirituality and religion and could influence a decision made by an individual or community(67).

3.4.2.1.6 Origins

(Question 5)

In South Africa, places of origin impact on an individual's education and later on, employment status, which in turn would impact on health care provision. Rural origins in South Africa often result in migration of younger family members to urban environs, with family support remaining in rural areas.

3.4.2.2 Objective 2: Knowledge and attitude

(Questions 11, 12, 13 and 15)

An individual's actual and perceived risk would highlight their understanding of information provided in pre- and post-test counselling. The perceived benefits and limitations of predictive genetic testing would also clarify what has been understood(55;58;71).

3.4.2.2.1 Cancer Risk

A six-point question (Question 11) about family and family members who have had cancer was added. The literature review showed that experience with disease was a factor associated with reduced levels of stress(70). Petersen et al(66) used a similar set of questions to depict family history and experience with colon cancer in the family.

Question 12 was altered to test the research subjects' own experience of receiving a predictive genetic test. The original questionnaire was used for subjects who

had not had predictive genetic tests.

Question 13 was added to ask if predictive genetic tests had been done. The reason for this was that question 12 asked "who referred you to having a test?" and question 14 asked "who you go to for clinical help?" For the sake of completion it appeared logical to ask if a result had been given.

3.4.2.2.2 Perceived benefits and limitations of genetic testing

A modified 12 item scale (Question 15) from a previously validated measurement of perceptions of benefits, limitations and risks of genetic testing in breast cancer(55;58), had been adapted and piloted in Australia (See Appendix 3). It was proposed to assess the intention to request genetic testing and acceptance of preventative surveillance strategies, should a predictive genetic result have been positive for an HNPCC causing mutation. It had also been used in other studies to measure benefits and limitations of those undergoing testing for HNPCC(55;58;59;61).

The scale has two sections. The first six statements are concerned with the perceived benefits of predictive genetic testing, and the last six about the limitations.

Two scores, a total benefit and a limitation score, were calculated. Subtracting the total benefit from the total limitation score generated a resultant risk score. The final risk score defined those who felt they had benefited or not from predictive genetic testing.

3.4.2.2.3 Knowledge of colon cancer

A scale used to measure knowledge about inherited breast cancer and BRCA1 testing(58), consisted of 11 true-false items, but Meisner et al(82) used a revised nine-item version of this measure. The revised scale (Questions 16 to 24) was used to measure subjects' knowledge about colon cancer.

One of the nine knowledge scale statements – "Everyone who has a gene for Hereditary Bowel Cancer will get bowel cancer" (Statement 17) - was discussed with the content supervisor. All three responses could have been correct for this cohort. For the purposes of this study, which pertains to families at-risk of inheriting this specific mutation (*h*MLH1 exon 13 C1528T HNPCC mutation), it was decided that the correct response was 'true'.

Another statement from the knowledge scale (Statement 22) – "Faecal occult blood testing will always detect bowel cancer", caused concern. Four other sections in the instrument also contained a question referring to faecal occult blood testing.

Faecal occult blood testing had not been part of the predictive testing program information package given to this research sample. This concern was discussed with the statistician. These questions were not included in the analysis of the research objectives but analysed separately as part of a substantiation of reliability.

3.4.2.3 Objective 3: Psychological and functional health status

3.4.2.3.1 Coping style

According to Miller(74) "when faced with threatening situations, individuals who differ in coping styles diverge in their choices of coping strategy". She defined two coping styles, namely:

1. Monitors who characteristically seek information.
2. Blunters who characteristically distract themselves.

The validated Miller's Behavioural Style Scale (MBSS) (Questions 37 to 40) had been included as it enabled a measurement of coping in threatening situations and possible responses to these(56;74).

This scale asks the subject to imagine four stress-invoking scenarios of an uncontrollable nature i.e. the dentist, a hostage situation, the threat of job loss and a potential aeroplane disaster. Eight statements that offer different ways of dealing with the situation follow each scenario.

Petersson et al(75;89) suggest that three scores can be derived:

1. Total monitoring score;
2. Total blunting score; and
3. Sum score.

The sum score is calculated by subtracting the blunting from the monitoring total. Individual scores above the sum score refer to monitors and those below represent blunters.

3.4.2.3.2 Stress

The majority of individuals testing positive, in a predictive genetic testing program, experience moderate stress in the short term that appears to resolve over time, whilst testing negative shows an initial reduction in stress(60).

The respondents were asked if they had (Question 41a, b, and c):

a) a stressful life event in the last year?;

b) if 'yes', what was the event? (They had a choice of ten events) and

c) were presented with a Likert scale asking how stressful the event was for them on a scale of 0 (not stressful) to 100 (very stressful).

The Impact of Events Scale (IES)(61;83) (Questions 55 to 70) was initially devised to measure the degree of subjective impact experienced as a result of a specific event(83), but could also be used to measure this impact over a period of time. In this study the stressor was the concern of being at-risk of colon cancer.

The scale consists of two major responses intrusion and avoidance. Initially the scale consisted of twenty items. Horowitz(83) revised and published a scale consisting of 15 items (seven intrusion and eight avoidance items). These two subscales were developed and worded to apply to any event. A specific life event examined could then be added to the top of the form.

Scoring applied to the raw data was, 0 = not at all, 1 = rarely, 3 = sometimes 5 = often. The scale provides sub scores:

- Avoidance with a potential range of 0 to 40
- Intrusion with a potential range of 0 to 35
- Total score (sum of the two subscales) with a range of 0 to 75

A score of 40 or more is suggested as a significant stress response(90).

3.4.2.3.3 Depression

Subjects undergoing breast cancer genetic testing showed that depression rates varied depending on genetic results(20). In individuals who were mutation-negative it was reduced, in mutation-positive individuals it remained the same, and increased in those who declined testing(55).

The Hospital Anxiety and Depression Scale (HADS)(84) (Questions 42 to 48) had been designed specifically for patients with physical illness. The scale is reported to be valid if used for screening purposes and it cannot give a definitive diagnosis(84;85). It has 14 items divided into two subscales, seven for anxiety and seven for depression with somatic items excluded. Only the depression scale was used in this study.

Each item has a four point response ranging from 0 to 3, where 0 is no problem and 3 is a high level problem. The individual's total score range is 0 to 21, with scores of 0 to 7 regarded as normal, 8 to 10 suggestive of depression and 11 and

higher as a probable presence of depression.

3.4.2.3.4 Anxiety

Most first-degree relatives of women with breast cancer anticipated a negative psychological impact (increased anxiety, depression and impaired quality of life) if their test was positive(55). They also felt that they would still worry if they had a negative result(55).

The Spielberger State–Trait Anxiety Inventory (STAI-State Short version) (Questions 49 to 54) is included as a measure for situational anxiety(56;86).

Marteau and Bekker(86) developed this shortened version of the Spielberger State–Trait Anxiety Inventory (STAI). The full length STAI consisted of two questionnaires of 20 items each. The STAI-State Short version has six items which according to Marteau(86) provides acceptable levels of reliability and validity and maintains the inventory as sensitive to different degrees of anxiety.

Statements 50, 51 and 54 had optional scores of 1, 2, 3 or 4 and statements 49, 52 and 53 had these scores weighted in reverse. Mitchie et al(91) also used the shortened version(86) but pro–rated the score to be equivalent to the full form of the scale giving a score range of 20 to 80. The scores were multiplied by 3.33 to achieve this. This pro-rated scale had a cut off score of 42 with scores above indicating clinical levels of anxiety.

3.4.2.4 Objective 4: Impacts on medical decisions

3.4.2.4.1 Awareness of risk and medical decisions made

The medical measurement of risk utilises family history and the colonoscopic surveillance yield of adenomatous polyps(42-44;87). Colonoscopic surveillance was found to reduce the incidence of bowel cancer in people at-risk for HNPCC by performing a polypectomy at intervals of one to three years(50;92).

Two measures (Question 25) that asked about risk-perceptions for developing colon cancer (64) gave baseline knowledge of the subjects' risk perception to which screening and health behaviour could be compared.

In a study on attitudes towards a colon cancer gene test, it was found that risk perception was linked to the number of affected relatives, cancer worry and a younger age(66). An increase in risk perception was found to be a predictor of accepting a predictive genetic test(54;59;63).

3.4.2.4.2 Effects of genetic results on beliefs about effectiveness of surveillance methods

Genetic counselling attempts to improve early detection and prevention of colon cancer, by identifying those at high-risk. Surveillance recommendations were found to be well adhered to by patients who received genetic counselling for positive genetic results(36;79).

The subjects' actual participation in colonoscopic surveillance and their opinions about choices in health-related behaviour were ascertained by questions 26, 27 and 28. This data was compared to their genetic mutation status.

The individual's beliefs and attitudes about the effectiveness of preventative surveillance were measured by questions 29 to 36. Their opinions about colon cancer, beliefs about the effectiveness of surveillance methods, and the reasons and motivations for accepting/rejecting surveillance, were accumulated.

Surveillance forms part of the preventative health model(78) that combines sets of factors/variables which could influence an individual's decision to take preventative health action. The following four factors make up a preventative health model:

1. Background factors - sociodemographic information.
2. Representation factors – perceptions with respect to the threat and procedures available to cope with the potential threat.

3. Social influence factors – relationships of individuals with health care professionals and social norms regarding prevention.
4. Program factors – individual, group, or mass communications.

In isolating the representation factors of Myers et al(78), the perceived susceptibility to the threat of disease, severity (Question 29), curability (Question 30) and worry (Questions 30, 31 and 36) about the consequences, which shape an individuals' psychological view of the threat, were measured.

Myers et al(78), from their preventative representation factors, suggest that "individuals engaging in preventative health behaviour, must judge it to be technically effective (Question 34), practically convenient (Question 33), and personally beneficial and actively encouraged by significant others" (Question 35). They call these perceptions salience and coherence.

3.4.3 Translation

The English questionnaire was translated into Afrikaans. The clinic registered nurse in Okiep (town and clinic where much of the Northern Cape HNPCC management and co–ordination occurs) was consulted to make sure that the choice of words was accurate (compared to the English versions) as well as making sure that the vocabulary would be understood.

Once the translated questionnaire was piloted, it was critically scrutinised for appropriateness of responses to questions by the pilot subjects that could have been due to the translation. The pilot subjects made constructive translation suggestions and these were adopted.

3.4.4 Pilot study

The English and the terms used in the questionnaire were adapted to suit the South African context (especially the sociodemographic section) and then

translated into Afrikaans (Appendices 5 and 6). Five Afrikaans questionnaires were used as a pilot study to guide further changes to the measuring tool. The main aim was to create a tool that the subjects would easily understand, retain the original meaning and ensure a reliable measurement.

Five individuals from a HNPCC family with a different mutation (*h*MLH2 with a CT deletion at 1220 on the gene/exon 7) who resided in Cape Town were asked to complete the translated questionnaire. These individuals were of similar ethnic characteristics and economic and educational status to the sample for the main study. They had also received predictive genetic test results during a similar time period.

Five questionnaires were issued (between 17 February 2003 and 7 March 2003) and four were returned.

The data fields were transferred to an excel spreadsheet with each question placed in its own column and each questionnaire in its own row. The translated questionnaire was re-evaluated, with guidance from the pilot respondents comments and responses to the questions.

The statistician assisted with answers to questions about how the data should be captured (Appendix 9). In performing this exercise it became clear that changes to the questionnaire were required. These changes were implemented (Appendix 6 - Final Afrikaans questionnaire)

3.4.5 Validity

3.4.5.1 Face validity

The instrument was chosen for this research because of its face validity, as its variables appeared to fulfil the needs of this construct.

3.4.5.2 Content Validity

Content representativeness(93) was found in the international literature reflecting the measurements of knowledge and attitudes toward predictive genetic testing.

3.4.5.3 Construct Validity

The measurements of individuals' knowledge and attitudes toward predictive genetic testing were divided into four objectives (sociodemographics; knowledge and attitudes; effects of genetic testing on psychological and functional health status; and effects of genetic testing on medical decisions). These objectives in turn were met by various validated scales and inventories(7;93).

3.4.6 Reliability

The instrument for the current study was received with permission from the Victorian Clinical Genetics Services (Australia) (Appendix 3). Their instrument contained 11 well-documented and previously validated scales and inventories. For the purposes of this study the complete questionnaire was modified to suit the South African situation and piloted once for the purposes of maintaining the original meaning of the questions in the translation.

Polit and Beck(7) state that reliability coefficients, that measure internal consistency, are adequate at .70, but desirable at .80 or higher.

Results published by researchers who developed and utilised the scales and measures used in the instrument, were considered to be vital information for proof of stability and internal consistency of the instrument. This is shown in the following examples:

1. Lerman et al(58) found that the twelve item scale for measuring the benefits and limitations of predictive genetic testing to have a high internal consistency of α= .83 and .81 respectively

2. Miller(74), in her article on validating the monitoring and blunting as coping styles, did a test-retest to assess the stability of the subscales. She found the monitoring subscale to be stable with a reliability co-efficient of r =.72 and the blunting subscale r =.75.
3. Marteau and Bekker(86) developed a short form of anxiety inventory. They proved the short version to be reliable and valid, with an internal consistency of α = .82 for the six item scale.
4. Horowitz et al(83) revised the impact of events scale and found the stability of r = .86 and internal consistency of α = .78 for the intrusion scale and α = .82 for the avoidance scale.
5. Bjelland et al(85) looked at the validity of the Hospital Anxiety and Depression scale (HADS) and found the mean internal consistency to be α = .82

The above results show that the instrument had measures that were reliable. To prove its reliability in the current research, the results were assessed by comparing them to those found in the international literature.

The factor used to prove that scores could be produced repeatedly and consistently within the instrument were the questions about faecal occult blood (FOB) testing. These were posed in two different sections (impacts on medical decisions and knowledge and attitude) of the instrument, involving five questions (Questions 22, 26d, 26e, 34 and 35).

The results could substantiate the reliability of the instrument by proving that the majority of the South African subjects should consistently not have been sure of FOB testing.

3.4.7 Data Collation

3.4.7.1 Data Collection

A research assistant was appointed and the eligible sample list created. These individuals were telephonically recruited where possible by the researcher, local clinic nurses, and family members who were asked to assist with recruitment of blood relatives who were not readily contactable.

It became quite clear early in data collection, that it took at least one hour to complete a questionnaire. The majority of subjects took the questionnaire home and completed it without the proposed supervision. The questionnaires were returned a month later when the colonoscopy surveillance team visited the Northern Cape. In the Western Cape the completed questionnaires were either delivered to the research assistant or arrangements were made to collect them.

The questionnaire was supplied in a pre-packaged personally addressed envelope delivered to the relevant person. It was delivered after written informed consent was obtained from the subjects. The following explanation was given to the subjects:

1. The questionnaire should be completed in private.
2. Once the labelled envelope was opened, the envelope should be discarded.
3. To check that one questionnaire and one unlabelled envelope were present in the labelled envelope.
4. Once completed, the questionnaire should be placed and sealed in the unmarked envelope.
5. Maintain the integrity of this envelope and return it to the researcher.

3.4.7.2 Bias

- It was attempted to keep the situational contaminant of the researcher's

presence to a minimum. In order to achieve this, the researcher attempted not to stay in the proximity where the research assistant was engaged with a research subject.

- At all times completion of the questionnaire was voluntary and no pressure was exerted on the subjects to participate.
- A table was created comparing the profiles of the respondents and the non-respondents (Table 3.3).
- Finally, in order to identify a bias by positive-tested respondents, a comparison was made of the responses of the research individuals whose genetic test results had been either positive or negative for the *h*MLH1 (exon 13 C1528T) HNPCC mutation(94).

3.5 Ethics

3.5.1 Risks/Benefits

The subjects who voluntarily assisted with this study had been involved with the genetic research service since the mid 1980's. The essence of this research project was to obtain an honest answer about how the clinico-genetic service and surveillance program had impacted on the lives of the subjects.

This research project would reflect personal and collective attitudes and opinions of the research sample. Future and current service providers could be informed with knowledge that could predict psychological trauma to an individual at high risk. Their predictive testing and surveillance management could be altered accordingly. Changes to the current management protocol (Appendix 1 - Protocol) could be guided by the recommendations of this small descriptive study, which serves as a pilot to further research

3.5.2 Voluntary participation and anonymity

The researcher and research assistant created an awareness of confidentiality by initially creating trust with ensuring that time was spent explaining the purpose and voluntary-ness of the study.

Maintaining total anonymity was not possible as the cohort was well known to the researcher. Every respondent was therefore given assurance (verbally and in writing on the information sheet) that his or her individual identity would remain anonymous and protected.

3.5.3 Informed consent

An English consent form and information sheet were created and translated into Afrikaans. These were incorporated into the English and Afrikaans questionnaire packages (Appendices 4, 5, and 6).

All participants were 18 years and older, thus legally competent to participate in the research and sign their own consent. Written informed consent was obtained from all subjects. It was made clear that they could withdraw at any time and that choice of participation would not affect future medical treatment.

3.5.4 Autonomy and privacy

Autonomy is difficult to maintain when decisions involve families. In the interests of time management, respondents were permitted to take the sealed questionnaires home and return them within one month. The justification was that the principle of autonomy, as well as the maintenance of confidentiality and privacy would be improved. Social pressure and stigma could be minimised in this way.

3.5.5 Confidentiality

The information sheet and consent form did not require identifying information and identification codes were allocated. To prevent researcher bias, the data

collector maintained a strict numbering system for the completed questionnaires. Reassurance was provided that information supplied in the questionnaires would be kept separate from identifying information. Access to identifying information would be restricted to the researcher only.

The double envelope system was another attempt at providing confidentiality. A predictive genetic result is very confidential information. Family members and clinic staff from small towns know each other well and are usually very supportive of each other. It was made clear that even though the envelope had a name on it, the participation of individuals was not dependant on predictive genetic test results. In essence this meant that although the member was participating in the research, it did not imply that they were mutation-positive.

Once a questionnaire was completed, the subject was instructed to seal it in the return address envelope. This was strictly adhered to by all the subjects. The envelopes were opened later by the researcher and filed according to allocation codes for data collation and analysis. All these questionnaires were safely stored.

To maintain ethical integrity, the data initially used to identify and contact the individuals was collated and analysed separately from the UCT Human Genetics database, thus preventing any links to the current service and individuals in their care. The data was kept in the strictest confidence. All the final results do not identify any of the subjects.

The study proposal was submitted and approved by the Research Ethics Committee of the University of Cape Town (Reference number 334/2001 - Appendix 11).

3.6 Analysis

Predictive genetic test results are confidential. These results formed the basis of

this study and were integral in selection criteria. Including this vital information was essential as it would shed light on whether the result itself was possibly responsible for an individuals' response. Maintaining confidentiality was thus vital. The results were transferred to a spreadsheet and aligned with the appropriate allocation code, thus no individual details were integrated into the data.

3.6.1 Statistics

The statistician advised that all unanswered questions be included in all frequencies. Descriptive and analytical statistics were used to explore the data from the study population. All data was assumed to be nonparametric because of the non-normal distribution of scores. Frequencies, percentages, measures of central tendency and dispersion were produced (median and upper and lower quartiles (q1 q3)).

3.6.2 Summary of analysis

- STATA(95) was used to create descriptive statistics from the raw research data captured on a spreadsheet (Microsoft Excel (Microsoft office XP 2003)).
- The descriptive data was presented in Microsoft Word.
- This descriptive data was grouped into the described scales or inventories and placed back onto a spreadsheet (Microsoft Excel (Microsoft office XP 2003)).
- Microsoft Excel was then used to rearrange the descriptive nominal data to produce collective results and graphical descriptions.
- 2x2 pivot tables were created in Microsoft Excel (Microsoft office XP 2003) with the grouped nominal data.

- The data from the 2x2 tables was analysed by STATA(95) in search of statistically significant associations between descriptive variables within the four objectives. Chi^2 or Fisher exact (when any of the four frequencies was below 5% in the 2x2 table) non-parametric statistical tests were used. A result of $p = 0.05$ and below(5) was considered to be significant.
- StatSoft Statistica 6(96) computer program was used when comparing two independent samples. The Mann Whitney U non-parametric test was used.

3.6.3 Data analysis

The analysis was arranged according to the research objectives:

Objective 1: To establish the sociodemographics of the study population (Questions 1 to 10)

Age (Question 6), number of children (Question 11) and number of relatives with cancer were nominal variables and the rest of the data was categorical.

The categorical data needed to be converted into a nominal form thus enabling statistical analysis and associations to be made e.g. categorical results of positive or negative predictive genetic tests were then converted to nominal data with positive = 1 and negative = 0.

Questions 1 to 9 excluding question 6 were single questions (employment, education, marital status, origins, gender, faith and medical aid) and each had its own nominal conversion list.

Question 6, age, was a nominal variable.

Question 10 was a set of questions about children, number and ages. A simple nominal list was created for Yes and No. The other information was used in the descriptive statistics.

Objective 2: To ascertain the knowledge and attitudes of individuals, who have had predictive genetic testing for HNPCC, toward genetics, cancer risks, and how to prevent development of cancer (Questions 11, 12, 13, 15 and 16 to 24).

Question 11 consisted of eight questions (related to cancer exposure) with nominal variables. These were combined to show how many respondents had affected first-degree relatives.

Questions 12, 13 and 14 were single questions (own experience of genetic testing) with a choice of responses. These responses were used descriptively and then regrouped to create nominal data.

Question 15 was a 12-item scale. Data was grouped into responses i.e. benefits and limitations. The respondents answered not at all, somewhat and very much or not applicable (in some cases) to the 12 statements. The frequencies were tabulated and very much and somewhat were converted to percentages and added together to give an overall percentage for both the benefit and limitation questions. These results were used descriptively

The original responses in the raw data for the two responses was converted to nominal data with not at all and not applicable = 0 and somewhat and very much = 1. Two scores (one benefit and one limitation) per respondent were generated. The limitation score was subtracted from the benefit score with a resultant individual risk score.

Questions 16 to 24 were a nine-item knowledge scale. Results were grouped into correct and incorrect answers. This data was used descriptively per question. A resultant score out of eight (excluding the question about faecal occult blood testing) per respondent was used to compare with related factors.

Objective 3: To measure the effects that the genetic test results have had on the psychological and functional health status of subjects (coping style (Questions 37

to 40), stress (Question 41a, b, and c) (Questions 55 to 70), depression (Questions 42 to 48), anxiety (Questions 49 to 54).

Questions 37 to 40 made up a validated MBSS scale. The data was grouped according to the responses (coping style) and lists of scores were established that were described. A sum score list was created and used as a nominal list.

Question 41 had three components, which were used descriptively

Questions 42 to 48 make up a seven-item scale (HADS). The raw data consisted of possible scores of 0, 1, 2 and 3 per question. The scoring in questions 44, 45 and 46 was reversed to score 3, 2, 1 and 0. The sum of each individual score could range from 0 to 21 with below eight considered normal, ≥ eight suggestive of depression or ≥ 11 indicating the probable presence of depression. Descriptive data was derived as well as a nominal list created, after placing results above or below a level stated in the literature.

Questions 49 to 54 were a six-item scale (STAI). By adding the numbers allocated (1, 2, 3 or 4) per question, a score was obtained per respondent. A nominal list was created of the scores above or below a level stated in the literature.

Questions 55 to 70 were a 15-point scale (IES). The responses were divided into intrusion and avoidance subscales and descriptive scores were derived. A total nominal list score was created, after placing results above or below a level stated in the literature.

Objective 4: To evaluate how genetic testing impacts on medical decisions made by subjects who have received predictive genetic test results (Questions 25 26, 27, 28, and 29 to 36).

Question 25 was two similar questions (opinion about colon cancer risk) answered in different ways. Both were used descriptively and statistically compared to genetic results.

Question 26 consisted of five questions (surveillance opinions). These were used descriptively and statistically compared to genetic results.

Questions 27, 28a and 28b, and 29 to 36 were questions (colon cancer and surveillance) with a choice of responses. These were used descriptively and statistically compared to genetic results.

Graphs were constructed utilising this data (Results Chapter 4).

3.7 Conclusion

This chapter described in detail the research design, sample size and selection as well as the data collection process. The method of data analysis was outlined in this chapter. The results are discussed further in Chapter 4. Recommendations were made for changes to the current clinico-genetic service as well as possible further research opportunities in Chapter 5.

4 CHAPTER 4 - RESULTS

4.1 Introduction

The analysis of the data is arranged into four sections each representing an objective i.e.:

1. Sociodemographics
2. Knowledge and attitudes
3. The effects that the genetic test results have had on psychological and functional health status
4. How genetic testing impacts on medical decisions

4.2 Analysis

Profile of the research sample

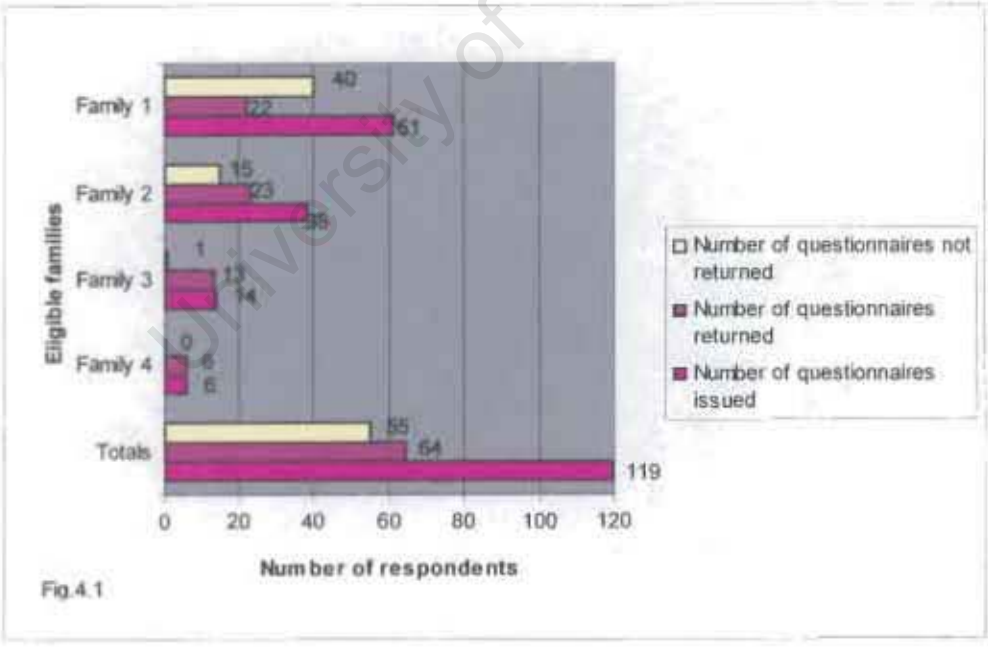


Figure 4.1: Questionnaire response from the four families in the final research sample

Questionnaires were issued to 119 individuals from four different families with HNPCC. It took approximately two months (29 July 2003 to 6 October 2003) to collect the questionnaires. The response rate was 64(54%) respondents and 55(45%) non-respondents (Figure 4.1).

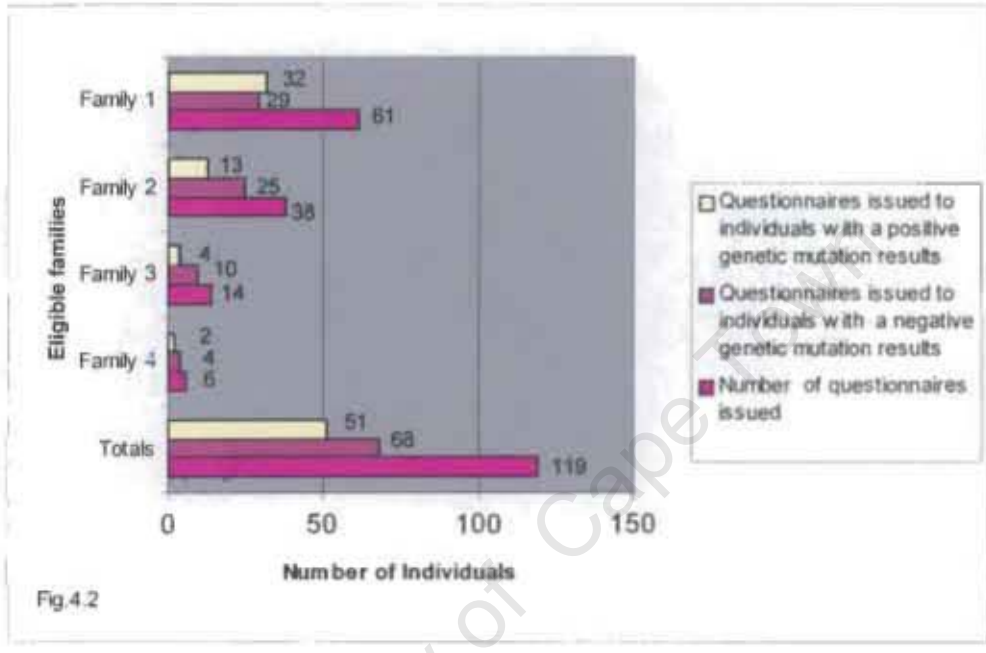


Figure 4.2: The genetic mutation status of individuals who made up the final research sample from the four families to whom questionnaires were issued

The genetic mutation status of the 64/119 respondents revealed that 31(48%) were mutation-positive and 33(52%) were mutation-negative (Figure 4.2).

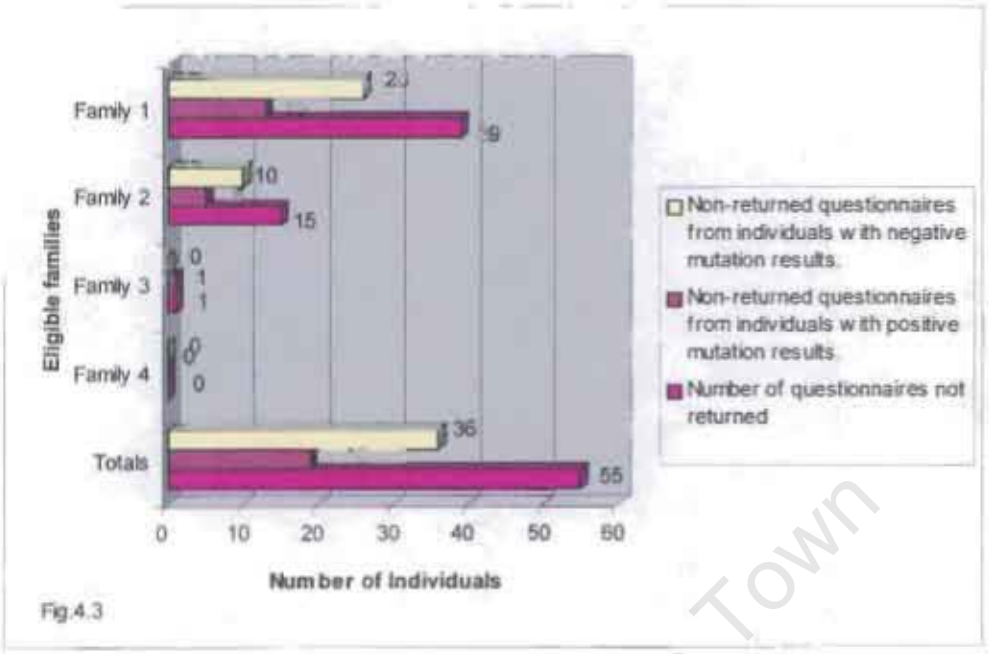


Figure 4.3: The genetic mutation status of individuals from the four families that did not return questionnaires (non-respondents)

The non-respondents were from three different families with 19(35%) who were mutation-positive and 36(65%) who were mutation-negative (Figure 4.3). These genetic results were given between 1997 and 2002.

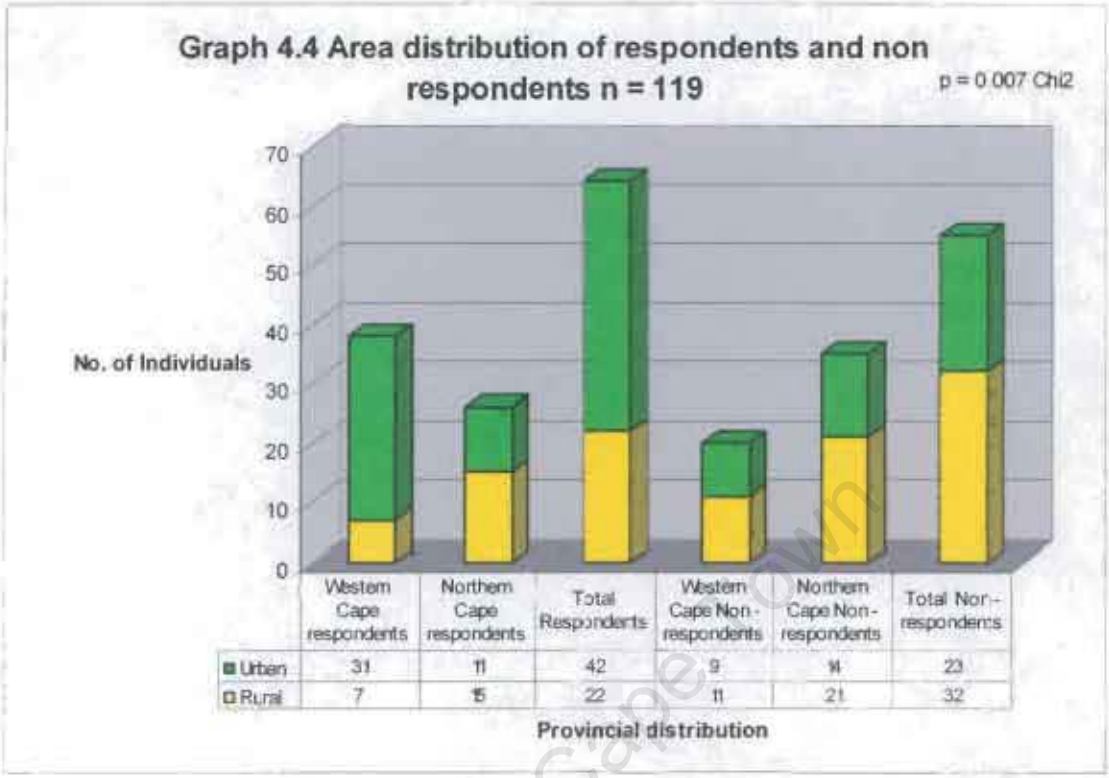


Figure 4.4: The residential areas of respondent and non-respondents

The area distribution of the non-respondents (Figure 4.4) showed that the majority came from the Northern Cape 35(54%) with 32(58%) from rural areas.

The majority, 42(66%), of respondents came from urban areas and 31 of them were from the Western Cape ($p < 0.002$ Fisher exact).

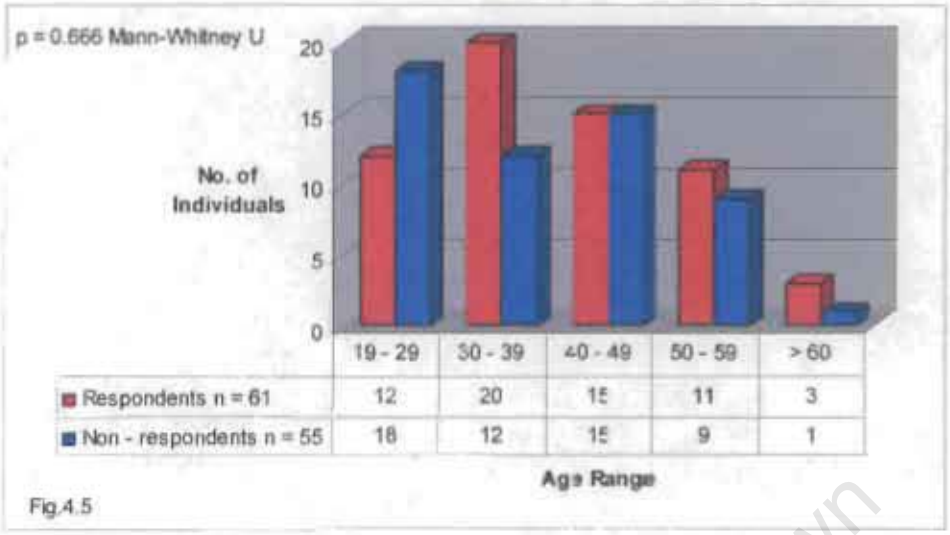


Figure 4.5: A comparison of the age-ranges of respondents and non-respondents

Although the age of respondents was similar to non-respondents (median 38 v 36 years (upper and lower quartiles q1-q3 31-49 v 28-47), there was a trend towards a greater proportion of respondents in the fourth decade of life, and non-respondents in the third decade of life (Figure 4.5).

4.2.1 Sociodemographics of the study population

4.2.1.1 Gender

Gender (n = 64).

The respondent group consisted of 40(63%) females and 24(37%) males (Figures 4.7 and 4.9).

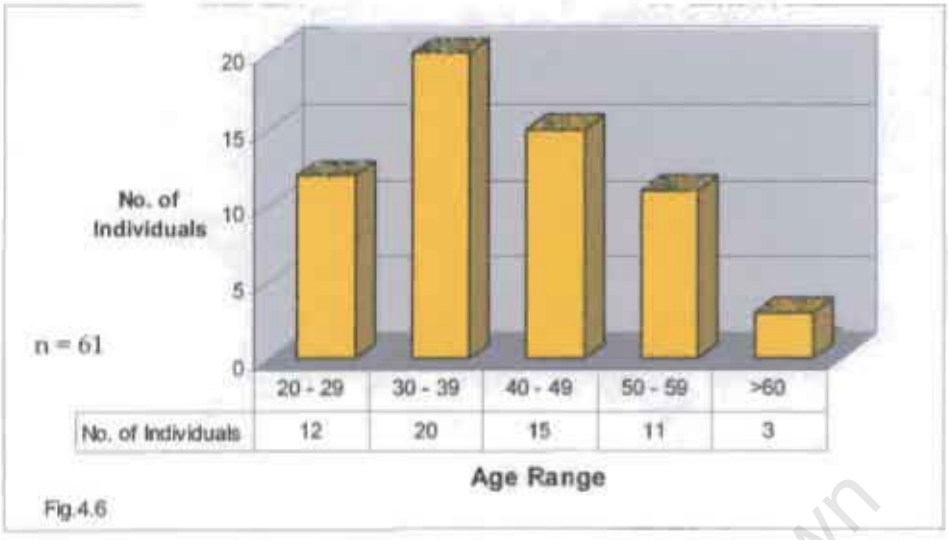


Figure 4.6: The age range of the respondents

The median age was 38, q1-q3 31-49 (Figure 4.6).

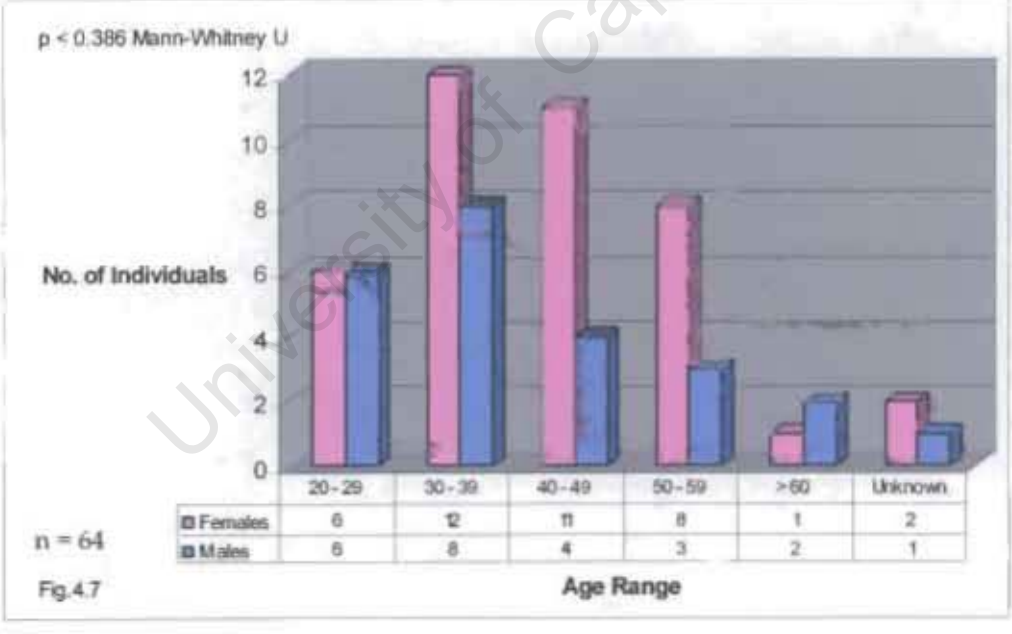


Figure 4.7: The age range and gender of the respondents

The age and gender distribution of the research subjects showed an even distribution of males and females across the age spectrum (20 to 59) (Figure 4.7). 46(72%) of the 64 respondents were in the 30 to 59 year range.

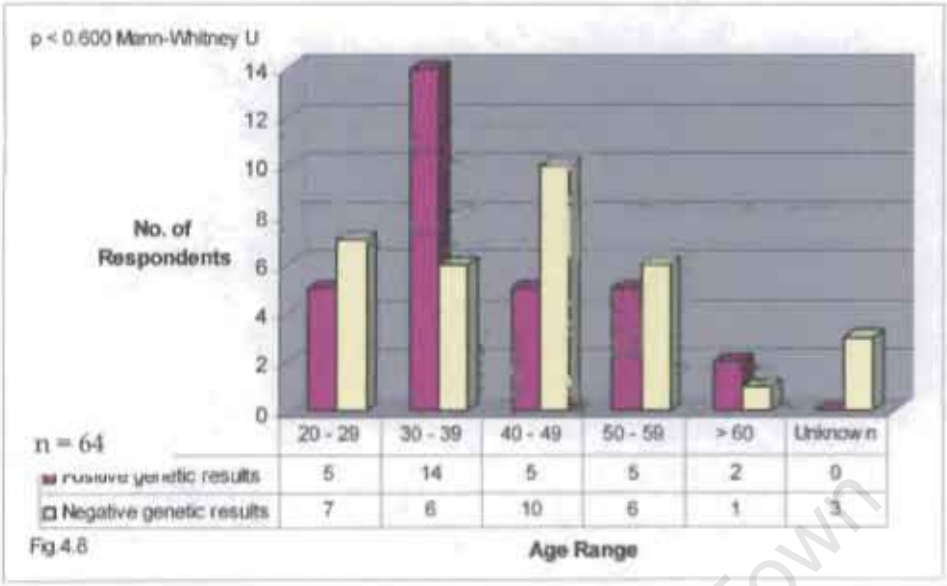


Figure 4.8: The age range and genetic mutation results of respondents

There were 14(45%) of the 31 mutation-positive respondents who were in the fourth decade of life, while ten of the 33(30%) mutation-negative respondents were in the fifth decade of life (Figure 4.8).

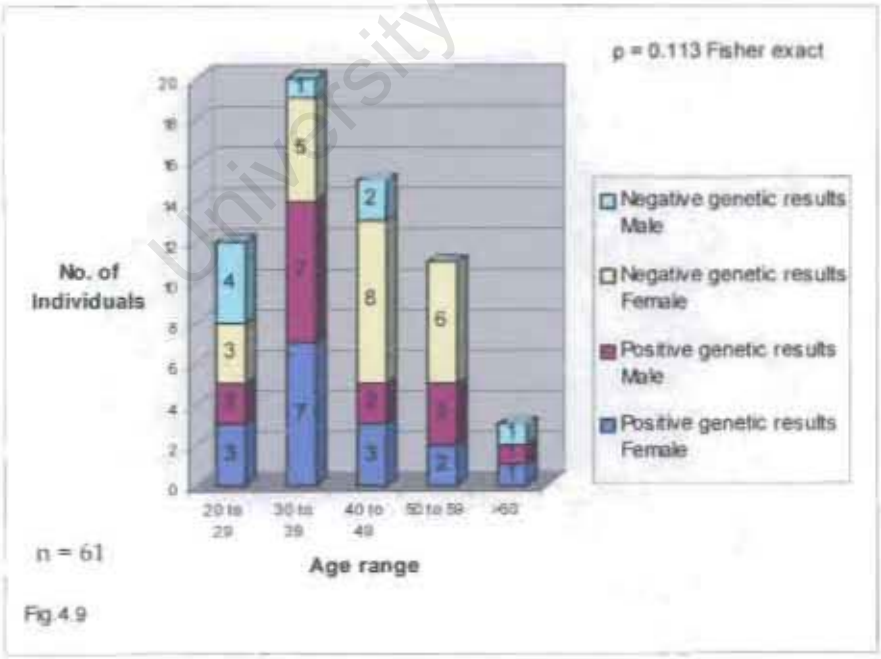


Figure 4.9: Age, gender and genetic mutation results

Those that had positive genetic results were 15(62%) of the 24 males and 16 (40%) of the 40 females.

Those that had negative genetic results were 8(33%) of the 24 males and 22(55%) of the 40 females (Figure 4.9).

4.2.1.2 Origins

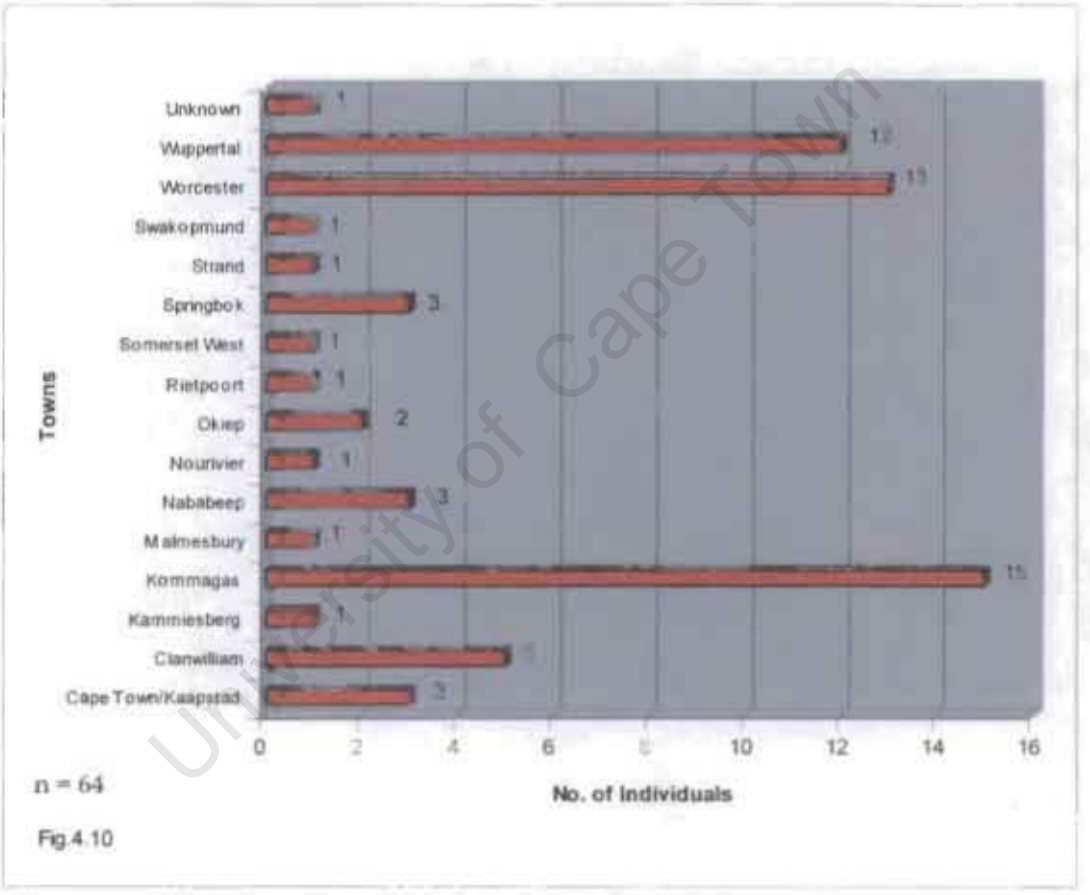


Figure 4.10: Places of birth of the respondents

The majority of the respondents 36(56%) were born in the Western Cape and 26(40%) were born in the Northern Cape. One individual was born in Namibia and the other did not document the place of birth.

Two thirds of the respondents were born in Kommagas 15(23%), Wuppertal 12(19%) and Worcester 13(20%). Kommagas (Northern Cape) and Wuppertal (Western Cape) are rural villages, while Worcester is a large town in the Western Cape (Map1.1).

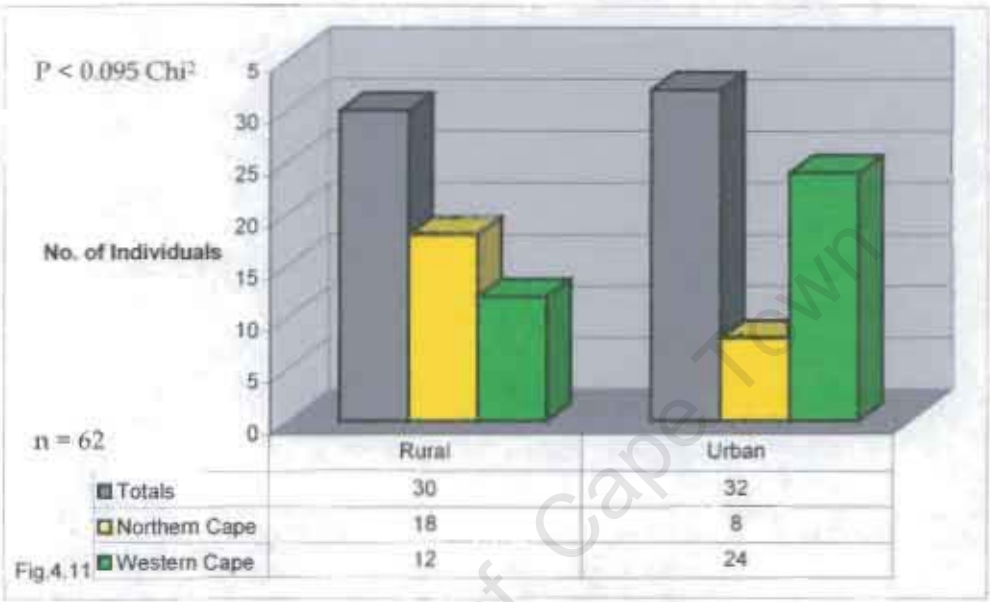


Figure 4.11: Rural and urban places of birth of respondents

Half of the respondents were born in rural areas and the remainder in urban areas (two unknown) (Table 4.1) (Figure 4.11).

Table 4.1: Comparison of rural and urban places of birth

Northern Cape Rural	Number of Respondents
Kammiesberg	1
Kommagas	15
Rietpoort	1
Nourivier	1
Totals	**18**

Northern Cape Urban	Number of Respondents
Nababeep	3
Okiep	2
Springbok	3
Totals	**8**

Western Cape Rural	Number of Respondents
Wuppertal	12
Totals	**12**

Western Cape Urban	Number of Respondents
Cape Town	3
Clanwilliam	5
Malmesbury	1
Somerset West	1
Strand	1
Worcester	13
Totals	**24**

4.2.1.3 Faith

The majority of the respondents 62(97%) reported that they had a strong faith.

4.2.1.4 Education status

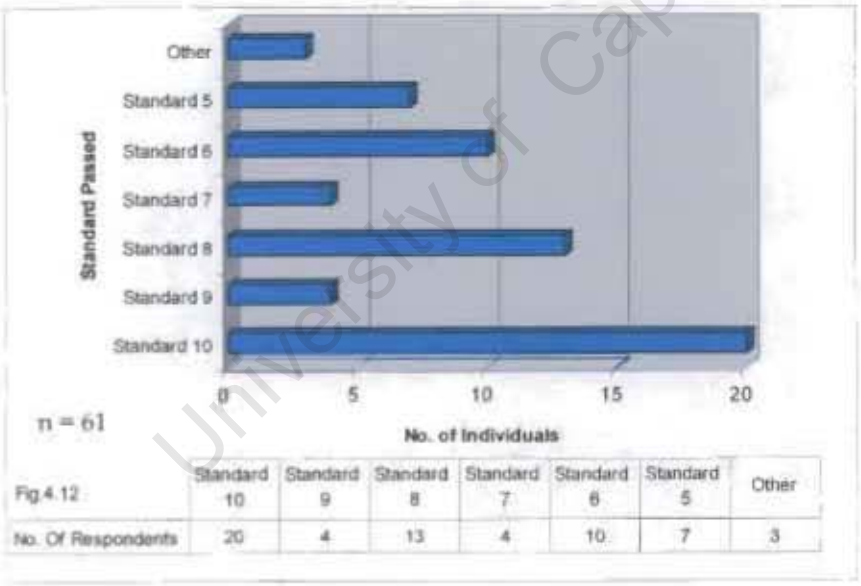


Fig 4.12	Standard 10	Standard 9	Standard 8	Standard 7	Standard 6	Standard 5	Other
No. Of Respondents	20	4	13	4	10	7	3

Figure: 4.12: School education of respondents

School education ends at Grade 12 (Standard 10 or matric) and 20(33%) achieved a matric certificate (Figure 4.12). Of those that matriculated, 17 studied further (Figure 4.13).

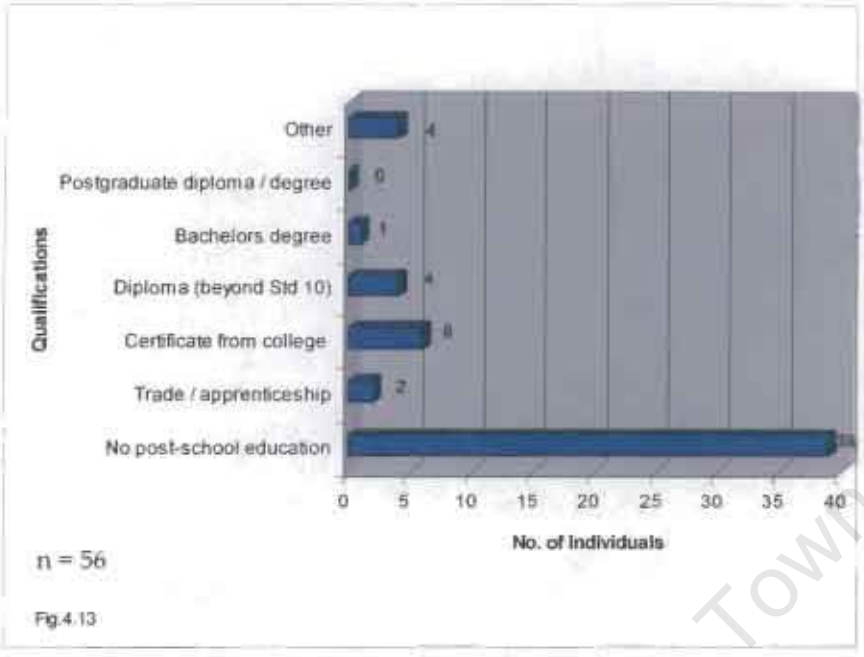


Figure 4.13: Post school education of respondents

4.2.1.5 Marital status

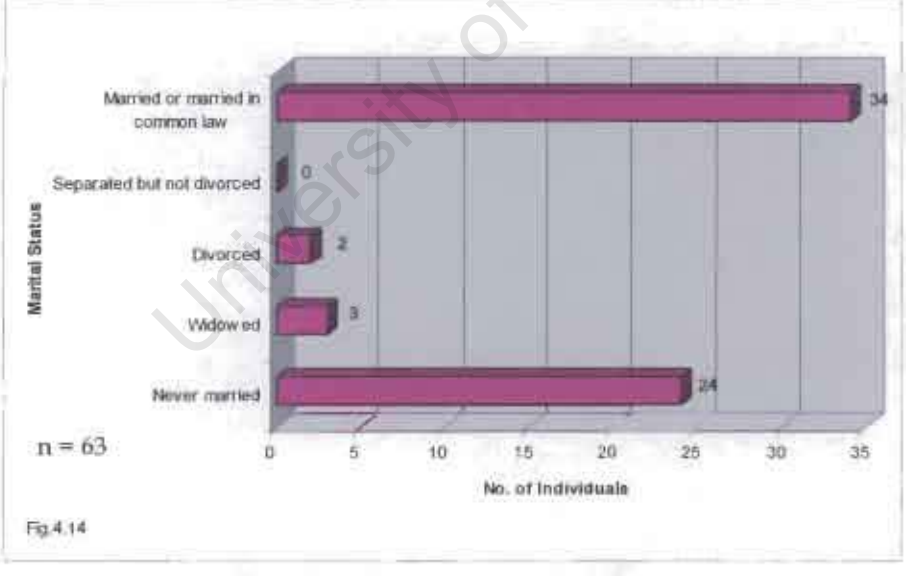


Figure 4.14: Marital status of the respondents

Half of the respondents had partners 34(54%): 2(3%) were divorced, 3(5%) had a deceased partner and 24(38%) had never married (Figure 4.14).

4.2.1.6 Employment status

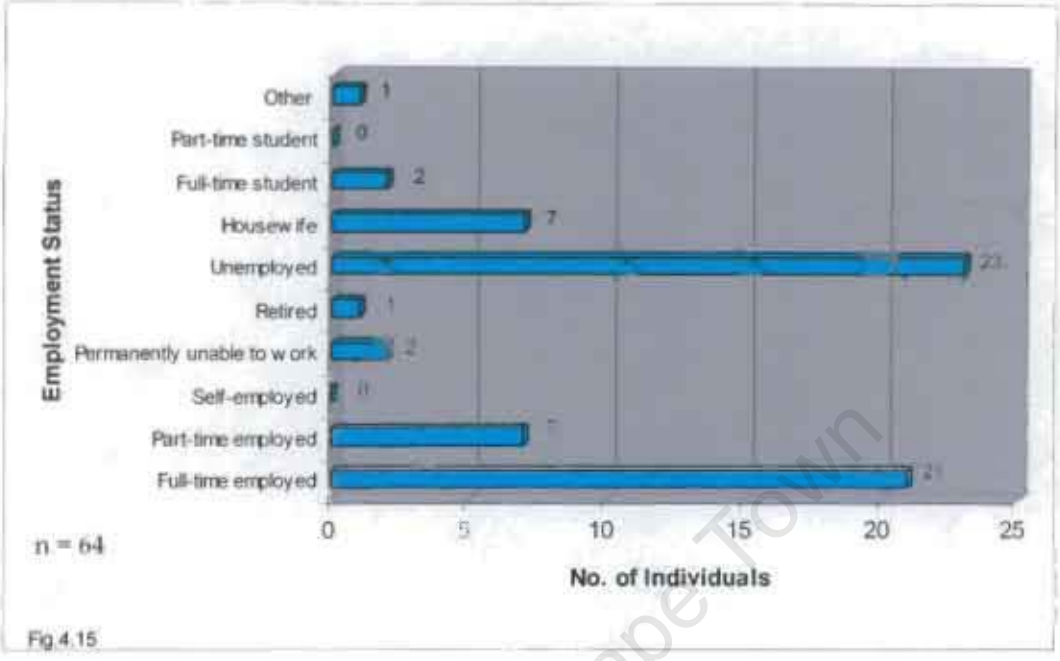


Figure 4.15: Employment status of the respondents

Half of the respondents had no personal income 33(52%). 7(10%) of these were housewives, 2(3%) were full-time students and 23(36%) were unemployed. One third had full-time employment 21(33%). Seven were employed part time (11%), 2(3%) were unfit for work and 1 was retired (Figure 4.14).

4.2.1.7 Gender, employment, marital status and education

Some form of income was available to 31(48%) subjects, 23(74%) of these individuals were females and 8(26%) were males. More than half (23) of the 40 females worked, however only 8 of the 24 males worked. Of those that were employed, 24 of 39 had no post-school education and 6 of 17 had post-school education. Of the working females, 10 had no partners and 12 had partners. One working woman did not state whether she had a partner or not. Two working males had no partners, while 6 had partners.

4.2.1.8 Medical Aid

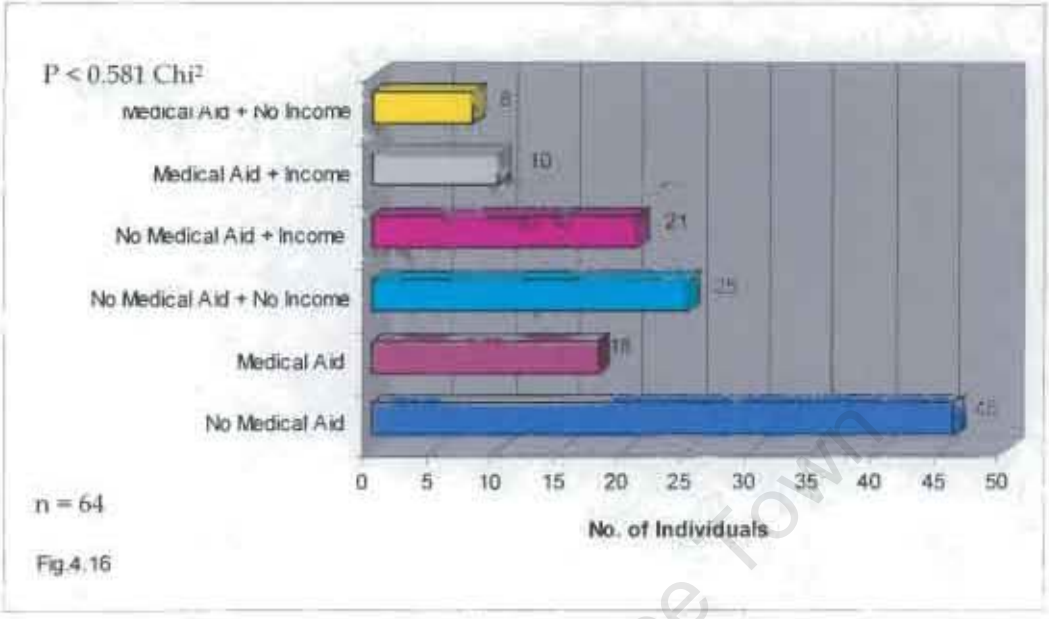


Figure 4.16: Medical aid/insurance and income status of respondents

The majority, 46(72%), of the respondents did not have any form of medical aid and just over half (25) also had no income. Of the 18(28%) respondents who had a medical aid, 10 were employed (Figure 4.15).

4.2.1.9 Children

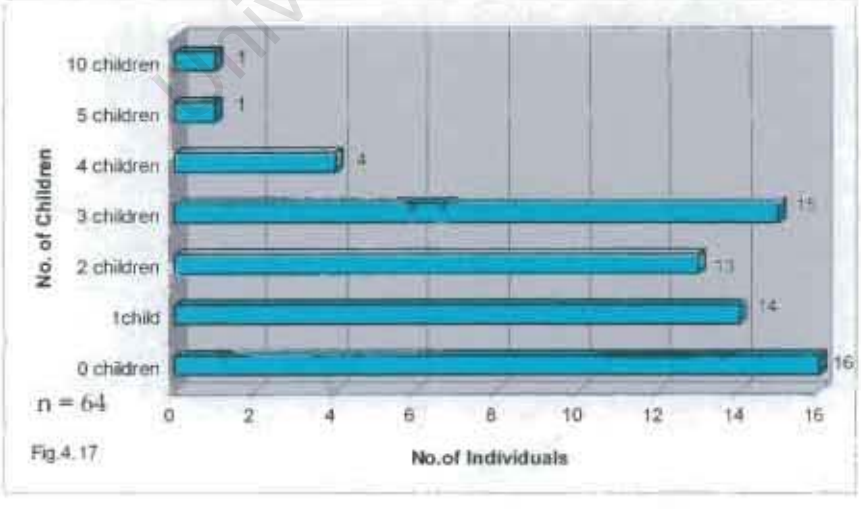


Figure 4.17: Number of children per respondent

The majority of respondents, 48(75%), had children, while 16(25%) did not. Male children accounted for 52%(61/117), while females made up 48%(57/117). Most 58(90%) respondents had 0 to 3 children per family (Figure 4.17) and 24(38%) were two parent families with children (Figure 4.18) while 21(33%) were single parent families.

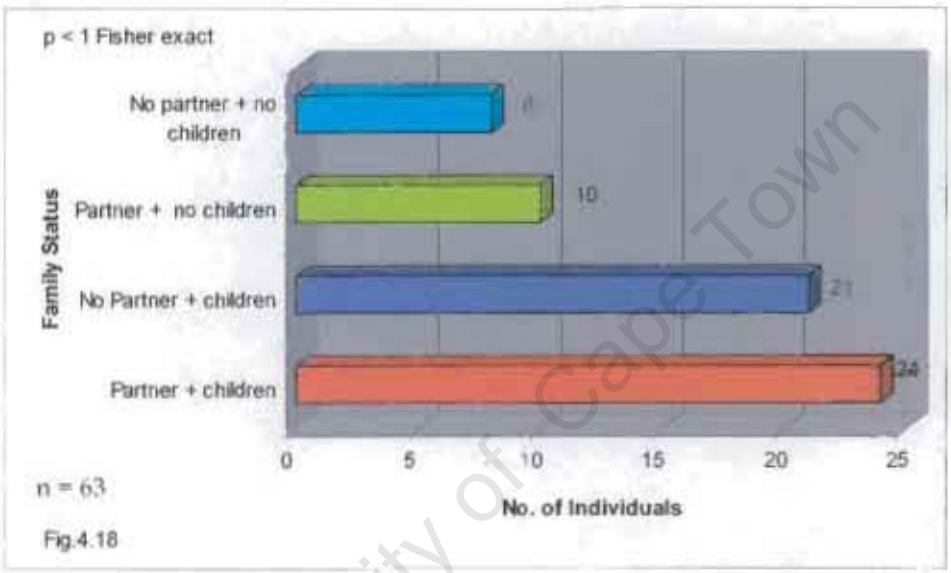


Figure 4.18: Respondents family status

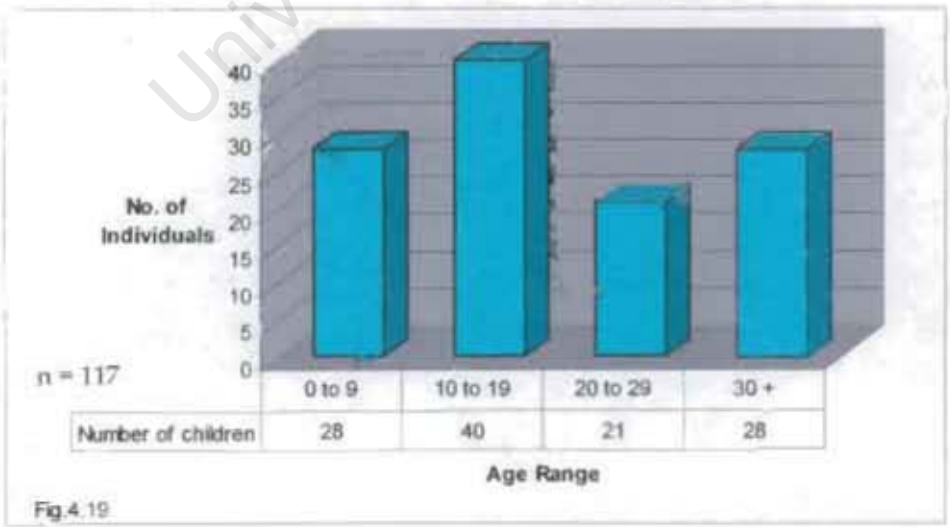


Figure 4.19: Age distribution of respondents' children

More than half, 58%(68 of the 117), of the children were below the age of 20 (Figure 4.19).

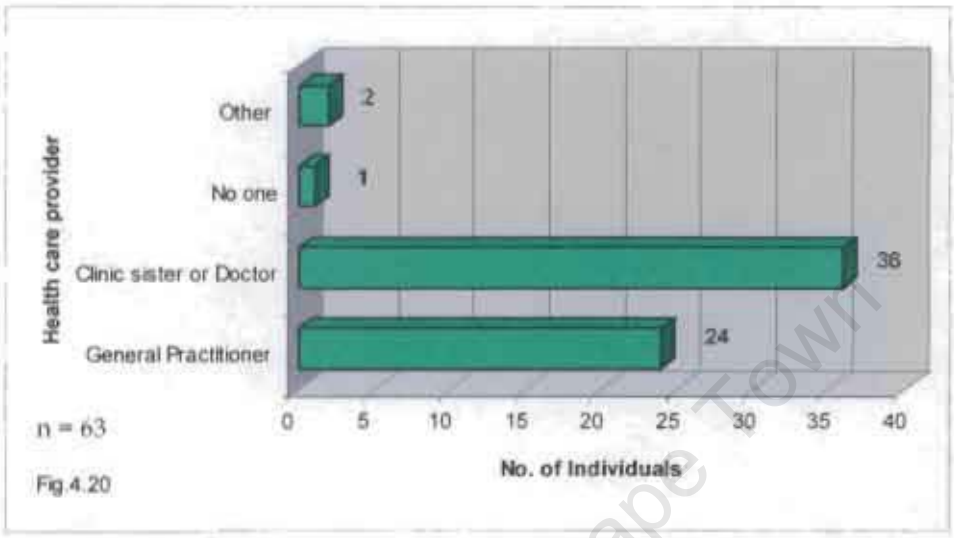


Figure 4.20: Respondents choice of primary health care

The local government funded clinic was used by 36(56%) respondents while 24 used a private general practitioner for their primary health care needs (Figure 4.20).

4.2.2 Knowledge and attitudes

4.2.2.1 Cancer Risks

All 64 research subjects had received predictive genetic test results. 62 of these results were delivered between 1997 and 2002 (For two subjects the date was unknown).

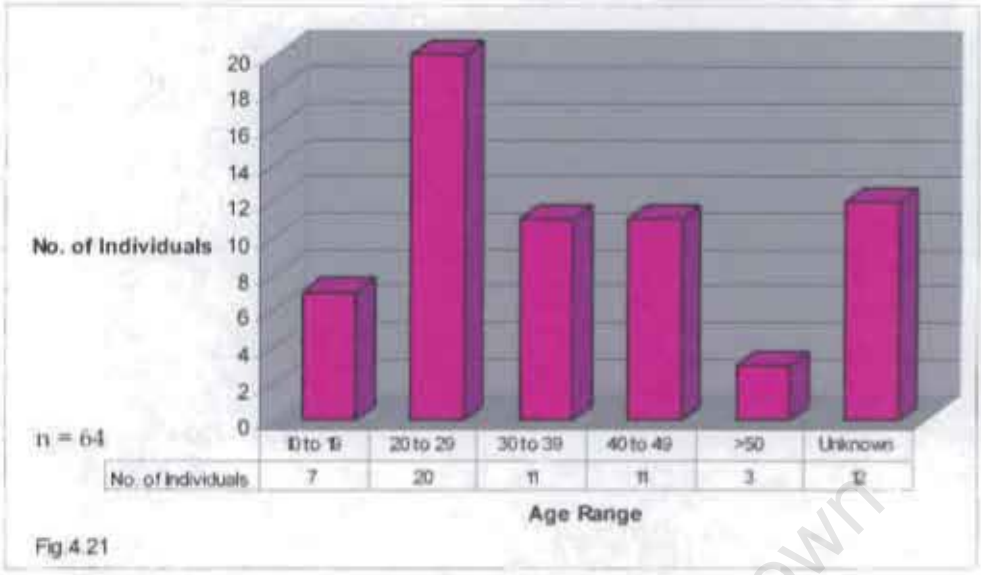


Figure 4.21: The age at which respondents realised they were at-risk for HNPCC

Respondents realised that they were at-risk for HNPCC between the ages of 12 and 70, (Median = 29 yrs, q1-q3 21 - 40). A third, 20(31%) of the subjects realised this risk between the ages of 20 and 29 but 25(39%) were over 30 when they first became aware of this risk (Figure 4.21).

All respondents had met the entry criteria but 10 of 63(16%) respondents maintained they had not had a predictive genetic blood test and a further four were not sure. Six of the 14 (who responded that they had not had a predictive genetic result) are mutation-positive.

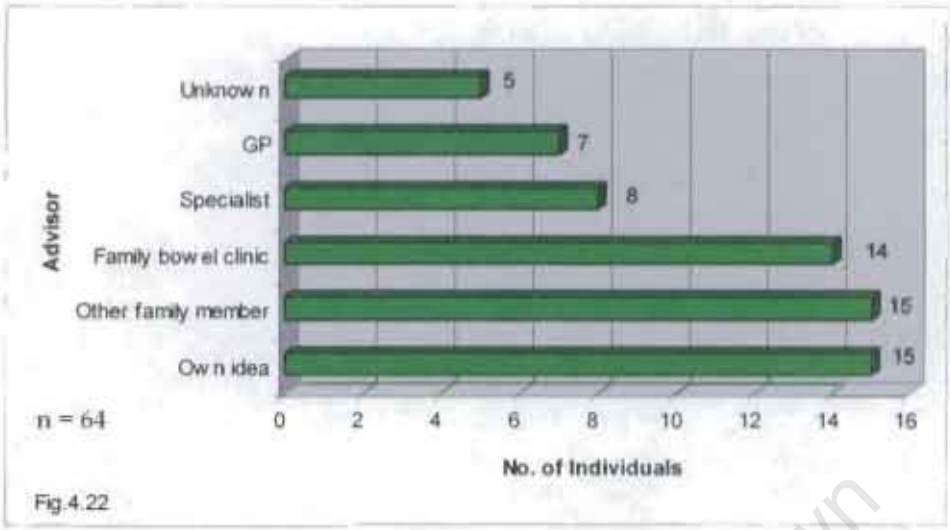


Figure 4.22: The person who had advised the respondent to have a predictive genetic test

Of those who said they had not had or were unsure if they had had a predictive genetic test, 13 answered this question (Figure 4.22). Four of the 49 who agreed that they had results did not answer. One individual did not answer either question and had a negative genetic mutation (Graph 4.22).

4.2.2.2 Exposure to Cancer.

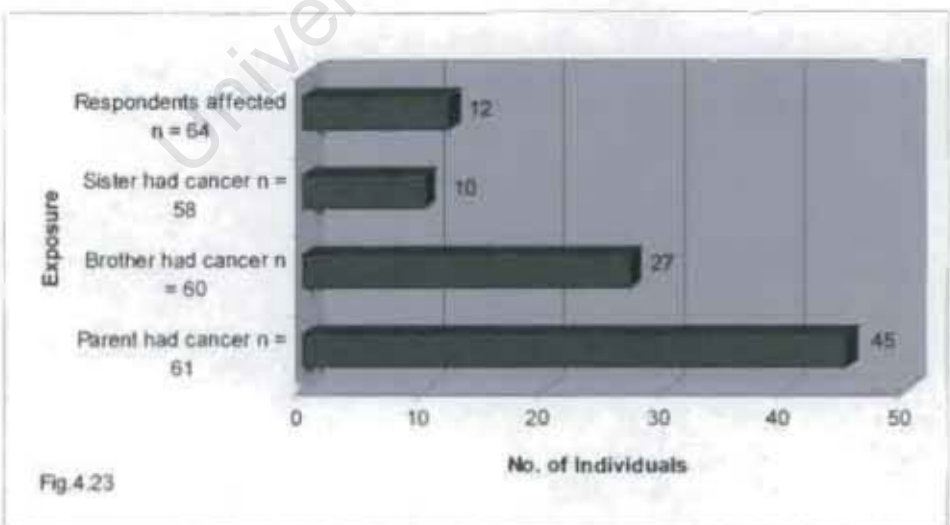


Figure 4.23: The respondents' exposure to cancer

Of the 12(19%) respondents who had a cancer themselves, 10 had colon cancer and two (who had negative HNPCC genetic tests) had breast cancer.

Of the respondents with close relatives with cancer, 27 of 60(45%) respondents who answered this question had a brother and 10 of 58(17%) had a sister who had a cancer. 45 of 61 respondents (74%) had a parent who had a cancer (Figure 4.23)

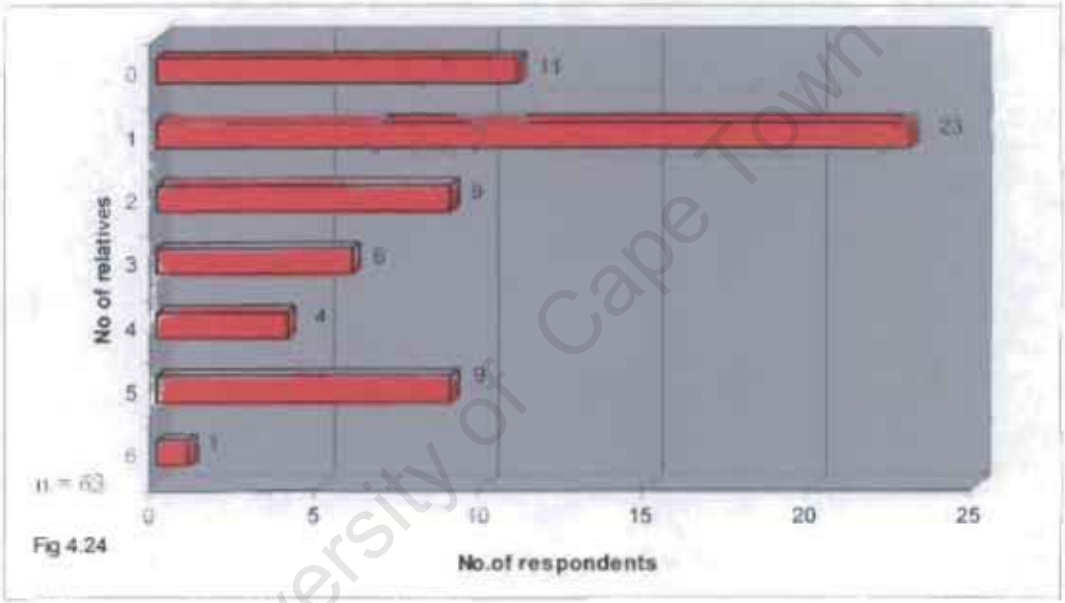


Figure 4.24: Number of respondents with first-degree relatives with cancer

One of the 64 respondents did not answer the questions concerning relatives with cancer. 52(83%) reported at least one first-degree relative who had a cancer. 11 reported that they had no first-degree relatives who had developed cancer (Figure 4.24).

4.2.2.3 Perceived benefits and limitations of genetic testing

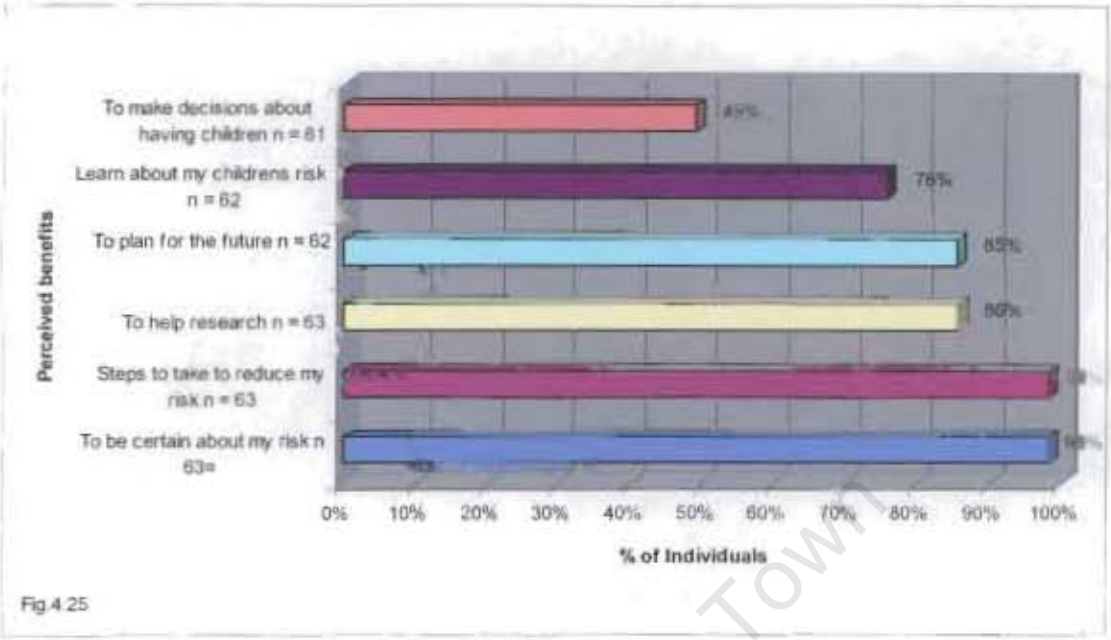


Figure 4.25: The percentages of responses to the six questions on the perceived benefits of predictive genetic testing

The respondents perceived risk reduction and knowledge of their own risk of cancer as the most important benefits of genetic testing (Figure 4.25).

In half the respondents, genetic testing influenced decisions to have children (18 respondents had a negative genetic mutation result and 12 had a positive result).

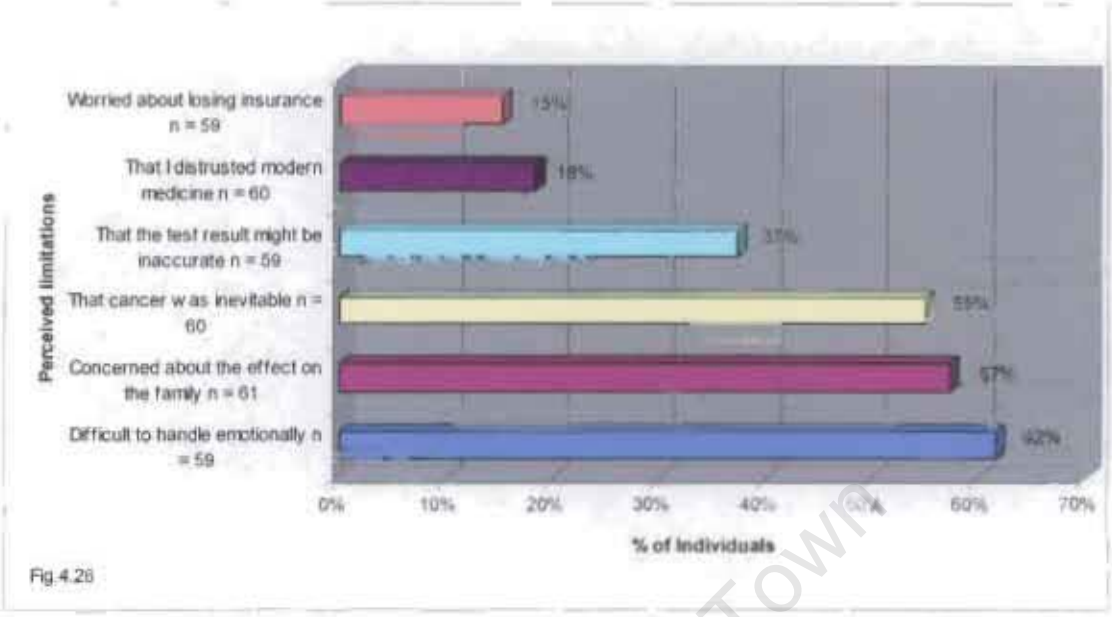


Figure 4.26: The percentages of responses to the six questions on the perceived limitations of predictive genetic testing

More than half the respondents were concerned about the effect of predictive testing on themselves (14 respondents had a positive genetic mutation result and 23 had negative results) and their family (15 respondents had a positive genetic mutation result and 18 had negative results) (Figure 4.26).

4.2.2.4 Risk score

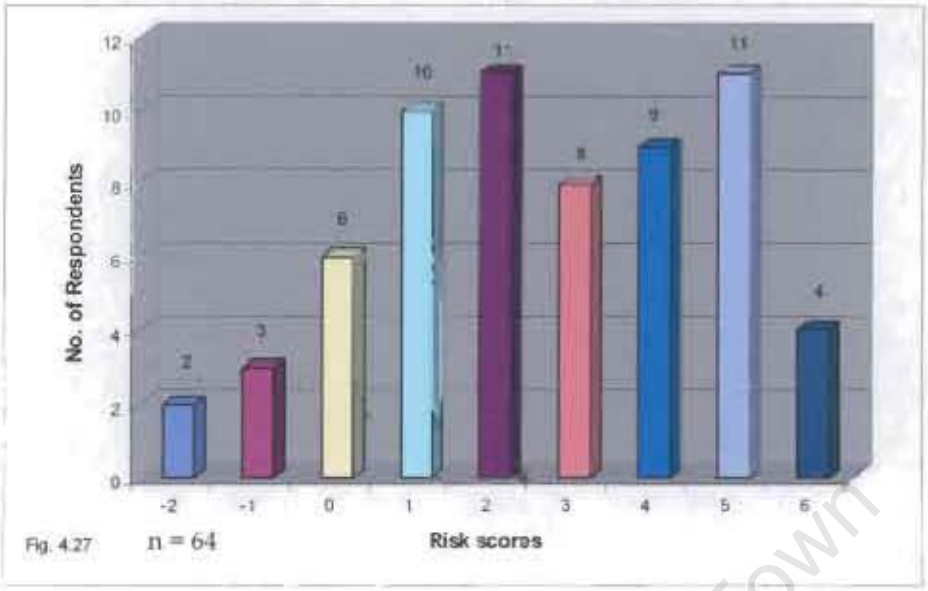


Figure: 4.27: The risk scores of the respondents

The median risk score was 3, q1-q3 1 - 4.

Five (8%) respondents perceived that predictive genetic testing was harmful (Figure 4.27). Three of these individuals had a negative predictive genetic test result (Figure 4.28).

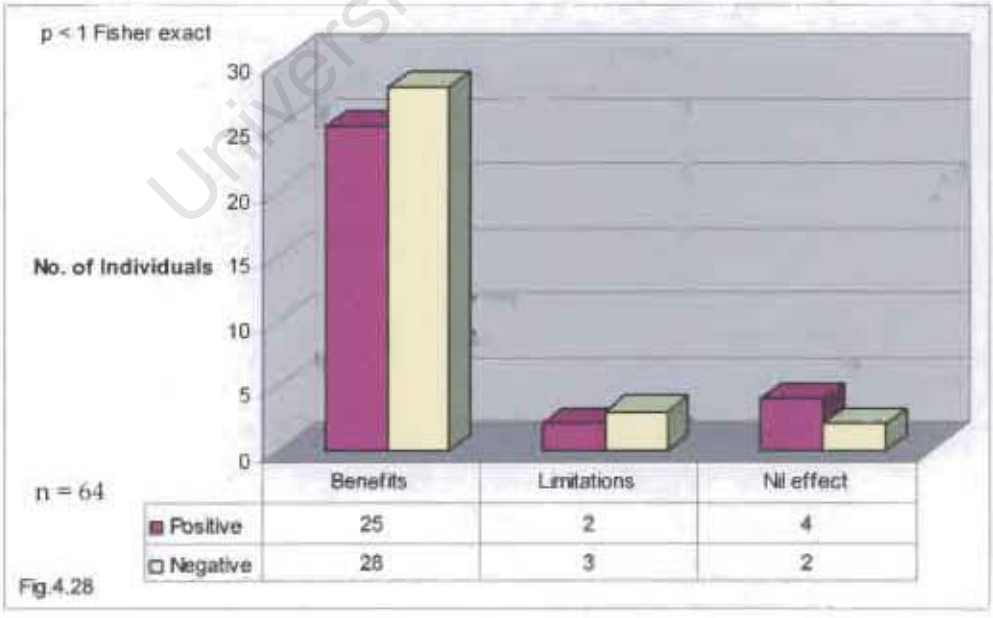


Figure 4.28: Utilising the risk score as the resultant perceived benefit and limitation to compare with respondents' genetic mutation results

Equal numbers of respondents with positive genetic mutation results, 27(42%) and negative results, 26(40%), felt they had benefited from receiving their predictive genetic result (Figure 4.28).

4.2.2.5 Knowledge of bowel cancer

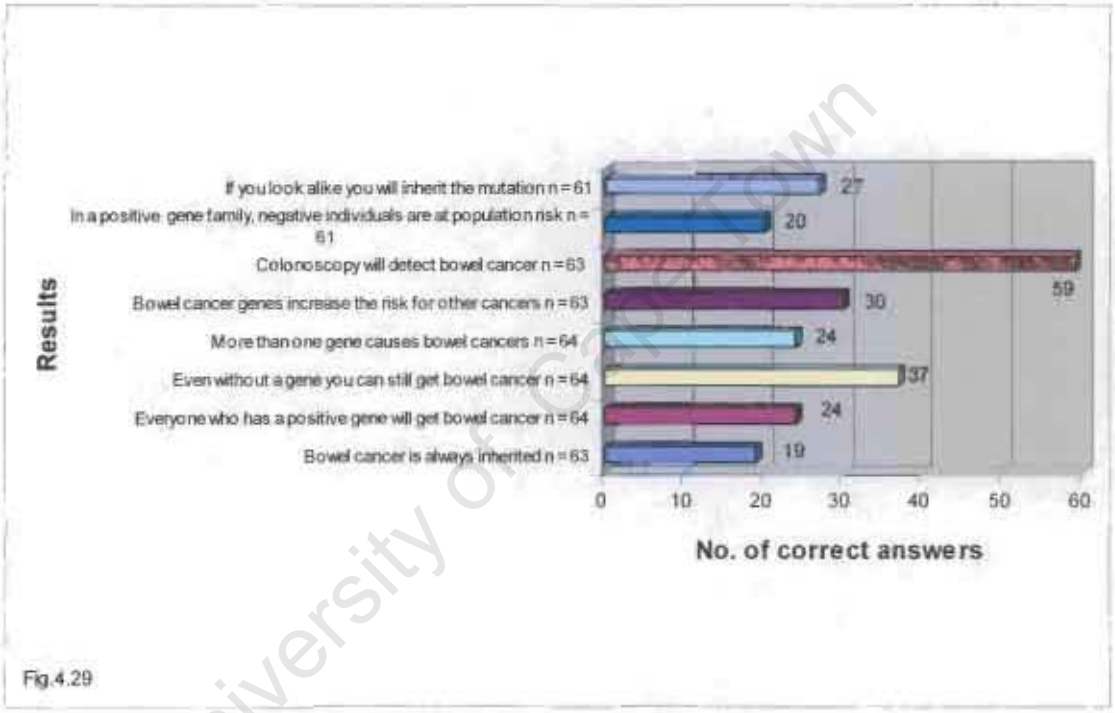


Figure 4.29: Percentages of correct responses to eight questions ascertaining respondents' knowledge of HNPCC

Most respondents, 59(94%), believed that colonoscopy would detect a colon cancer (Figure 4.29).

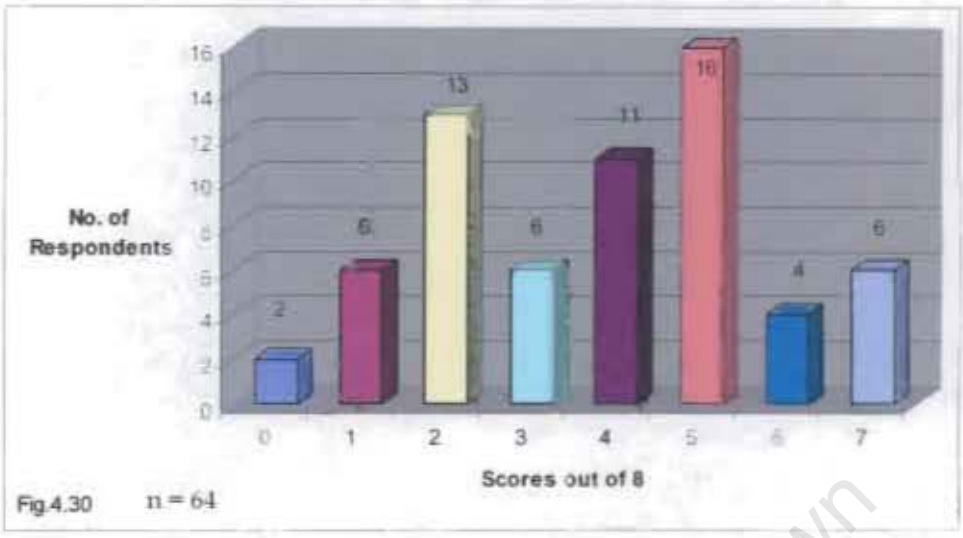


Figure 4.30: The distribution of respondents' scores, out of eight, to the HNPCC knowledge-questions

The median score was 4, q1-q3 2 - 5. Sixteen (25%) respondents scored 5/8, and 10 scored higher (6 and 7/8). Thirty eight (59%) respondents scored between 0 and 4/8 (Figure 4.30).

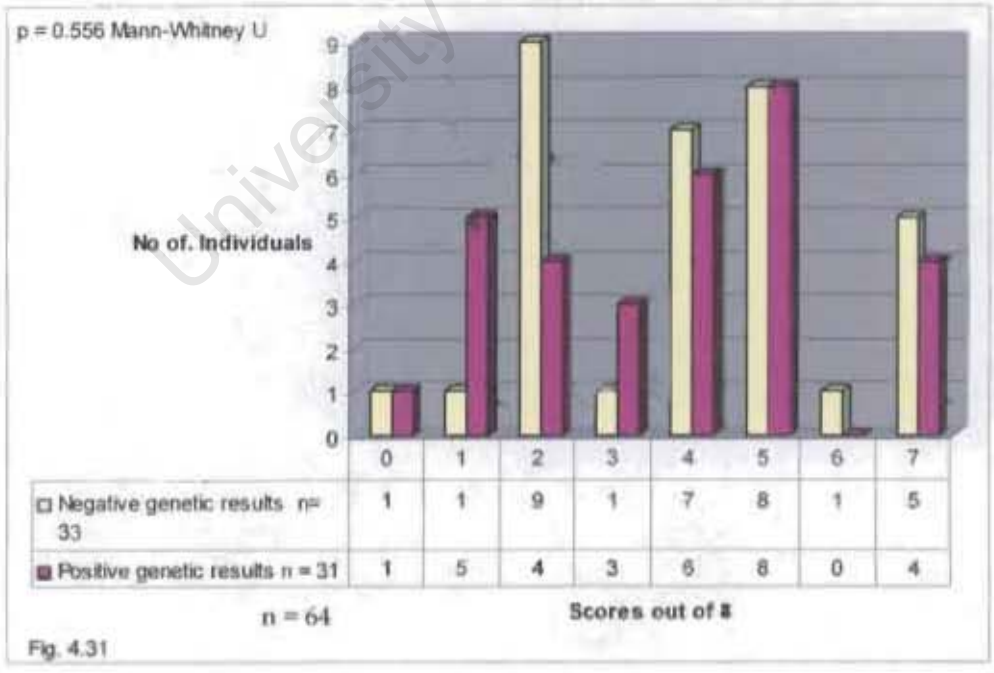


Figure 4.31: The distribution of respondents' scores, out of eight, to the HNPCC knowledge questions compared to their genetic mutation results

Of the 33 respondents who had negative genetic results 9(27%) scored 2 out of 8 and a further 19(59%) scored 4 to 7 out of 8. 20(65%) of the 31 respondents with mutation-positive results scored 4 to 7, while 13(38%) scored 0 to 3 out of 8 (Figure 4.31).

4.2.3 Psychological and functional health status

4.2.3.1 Coping Style

Coping style scale n = 60.

The median monitors score = 6.5, q1-q3 3 - 9.

The median blunters score = 2, q1-q3 1 -3.

Median sum score was 4.5, q1-q3 2 -7. Individuals scoring ≥ 4.5 were considered to be monitors and <4.5 blunters.

Four individuals did not complete this section. 30(50%) were monitors and blunters respectively.

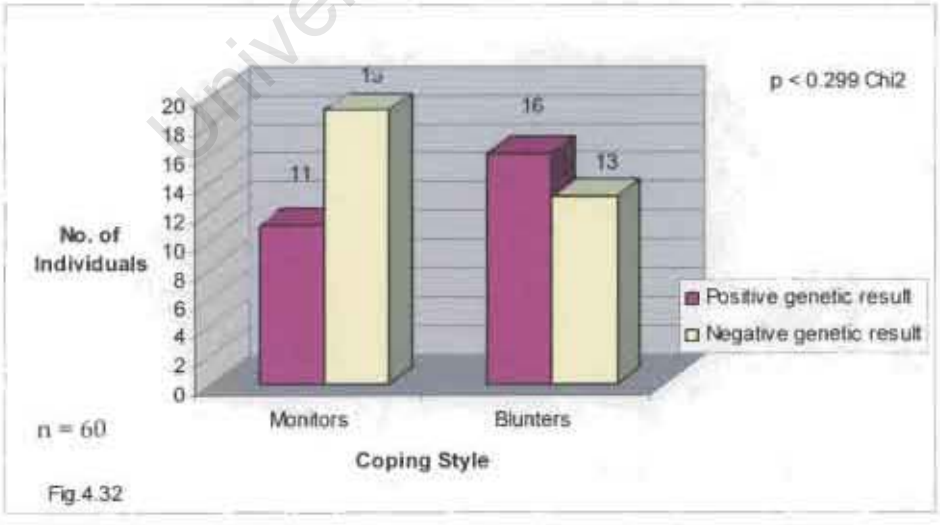


Fig.4.32

Figure 4.32: The respondents' allocated coping styles compared to their genetic mutation results

Of the four individuals who did not answer the coping style questions three had positive genetic results, resulting in 28(47%) mutation-positive and 33(55%) mutation-negative respondents to the coping style questions

Of the 30 monitors 11(36%) had positive genetic results and 19(63%) were negative, while 16(53%) of the 30 blunters had positive genetic results and 14 (46%) had negative results (Figure 4.32).

4.2.3.2 Stress

While 32(50%) respondents reported not having had a stressful life event in the last year, 22(34%) claimed they had and 10(16%) did not answer the question. Although 22(35%) respondents claimed they had a stressful life event, 30(47%) individuals listed at least one stressful event in the next question. Of these, 24 individuals listed a single stressful event, five listed two events and one person listed four events. One respondent claimed they had had a stressful life event but did not document what that event was.

Although five of seven respondents claimed they did not have a stressful life event in the last year, one individual claimed one event and two, two events. Two respondents did not answer the life stress question but allocated three events between them.

A total of 31 respondents seem to have had a stressful life event in the year prior to this study. 38 events were logged for 31 individuals who reported stressful events (Table 4.5).

Table 4.5: Listed stressful events in the last year

Stressful event in the last year	Number of events
Parents diagnosed with cancer	2
Parents died of cancer	2
Siblings diagnosed with cancer	6
Siblings died of cancer	2
Death of a family member or friend from a cause other than cancer	11
Own diagnosis of benign bowel disease	3
Work related stress	8
Other	4
Total	**38**

Of the 38 stressful events, 15(39%) events were related to deaths (four were cancer related) and 12 were related to cancers.

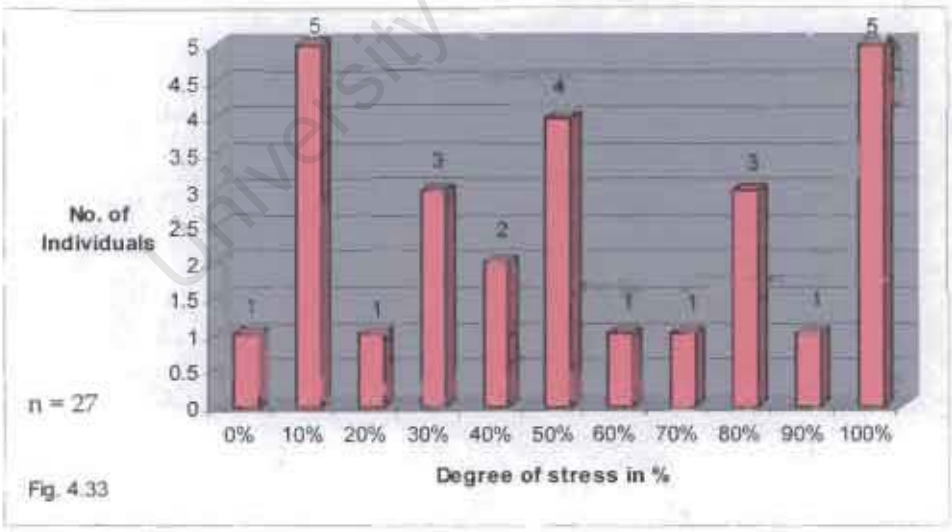


Figure 4.33: The degree of stress caused by the reported stressful event

The degree of stress created by the stressors was measured using the Likert scale.

27 respondents completed this question. The range was 0 to 100% with the median at 50% and q1-q2 20- 80 (Figure 4.33).

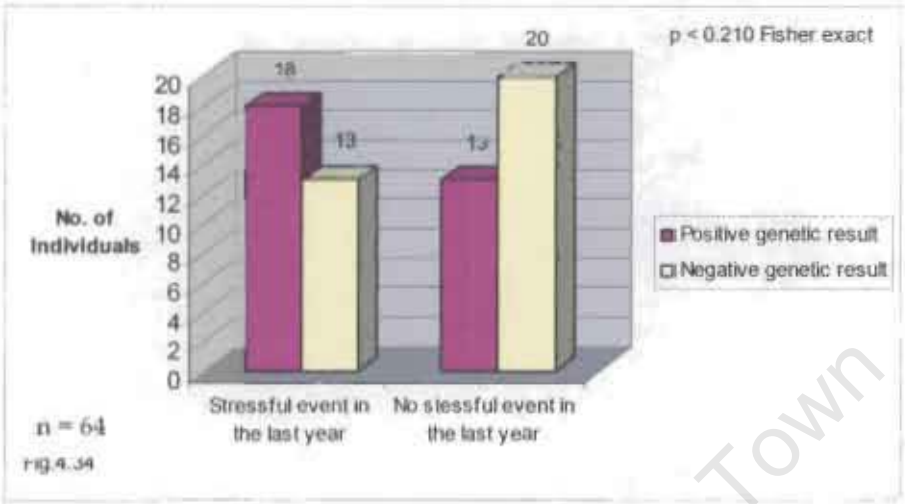


Figure 4.34: Stressful events and genetic mutation results

A total of 31(48%) respondents reported having stress, or a stressful event in the last year. 33(52%) recorded no stress and in addition did not document a stressful event in the last year (Figure 4.34).

4.2.3.3 Impact of Events

Items were scored by frequency of their occurrence (n = 64).

The avoidance subscale median = 9.5, q1-q2 3 -15.

The intrusion subscale median = 4, q1-q3 0 - 9.5.

Total score (sum of total intrusion and avoidance scale scores) median = 15, q1-q3 4 -23.

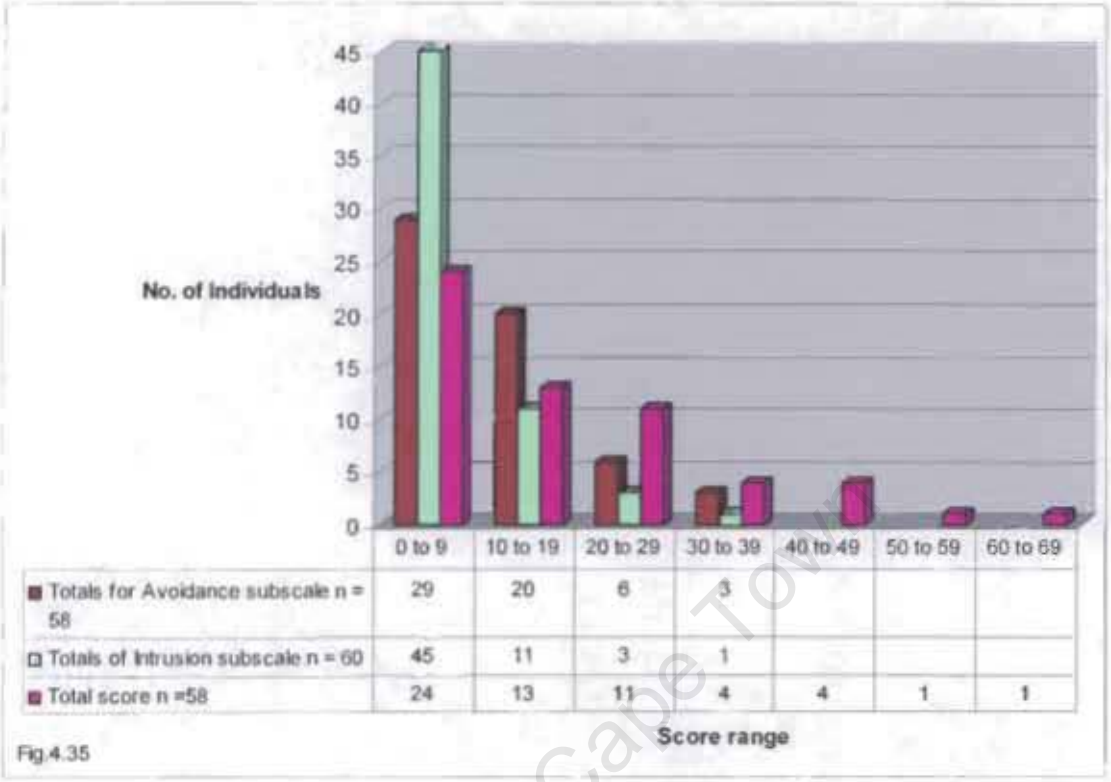


Figure 4.35: The impact of events scale consists of three scores (avoidance, intrusion and total)

Of the 58 respondents, 6(10%) had a total score of ≥ 40, indicating a significant stress response (Figure 4.35). Four of the six were mutation-negative and two were positive.

4.2.3.4 Depression Scale

n= 61. Median = 4, q1-q3 1 – 8.

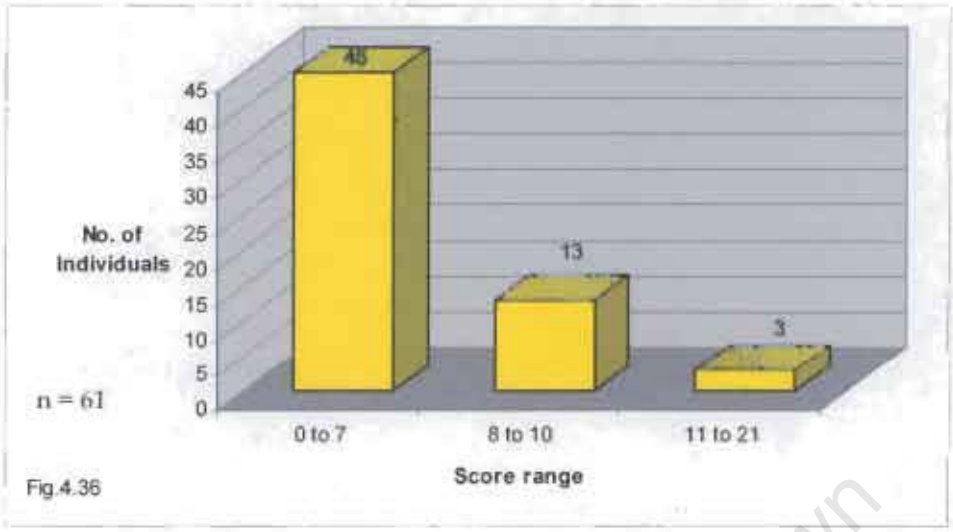


Figure 4.36: The depression score range of the respondents

Of the 61 respondents 3(5%) had a depression score of 11 and above (probable presence of depression) while 13(21%) had scores above 8 (suggestive of depression) (Figure 4.36).

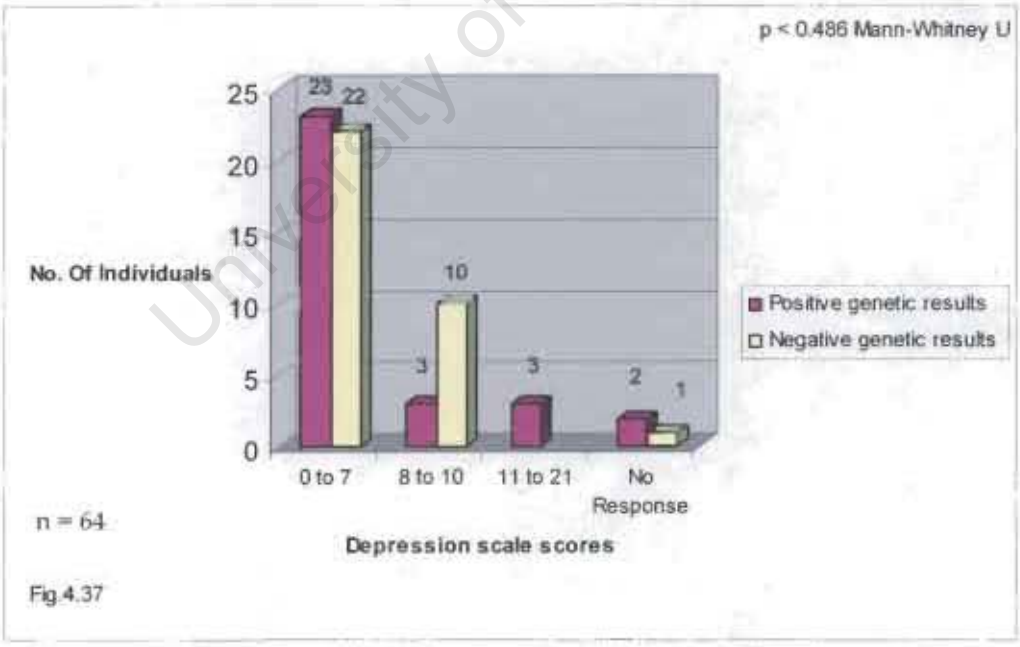


Figure 4.37: Respondents' depression scores compared to their genetic mutation results

Of the 64 respondents 10(16%) who showed probable signs of depression were mutation-negative (Graph 4.39), 11 were female and five were male.

The three subjects with clinical depression were mutation-positive (two were female and one was male).

4.2.3.5 Anxiety Scale

Five individuals either responded to only one or none of the scales' statements, n= 59 and the median 11, q1-q3 27-47.

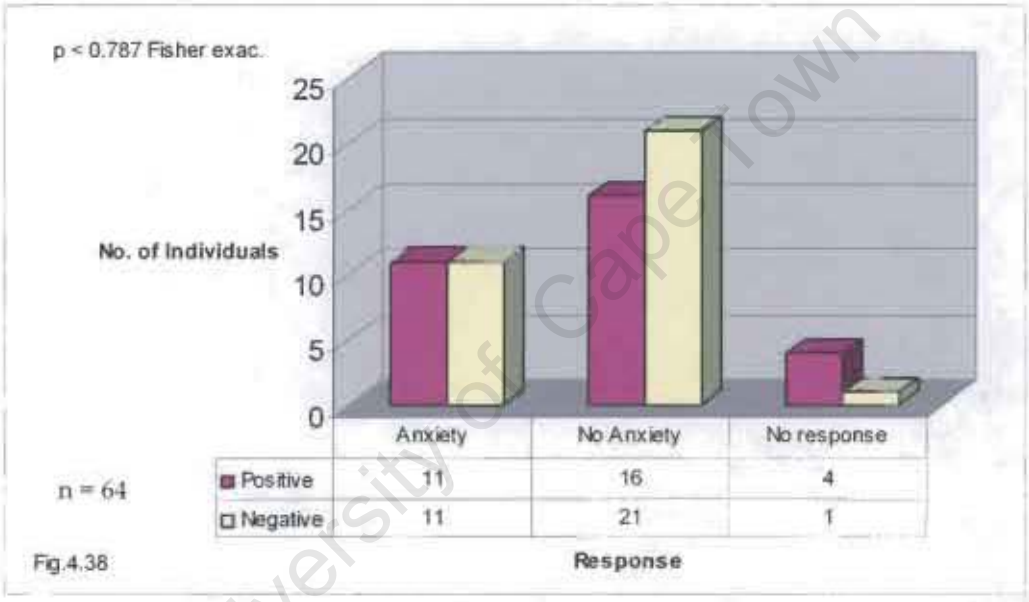


Figure 4.38: Anxiety scale results compared to genetic mutation results

Of the 59 respondents, 22(37%) had a pro-rated anxiety score above 42 of whom 11 subjects were mutation-positive and 11 subjects were mutation-negative (Figure 4.38).

4.2.3.6 Comparisons with coping style

- 14 blunters and 14 monitors experienced stressful events.
- Four blunters and two monitors had an impact of colon cancer event stress response.

- Four blunters and 11 monitors had potential depression.
- 11 blunters and 11 monitors had anxiety.

4.2.4 How genetic testing impacts on medical decisions

4.2.4.1 Awareness of risk and medical decisions made

Of the 64 respondents, 18(28%) had surgery, two were genetic mutation-negative but had surgery for breast cancer.

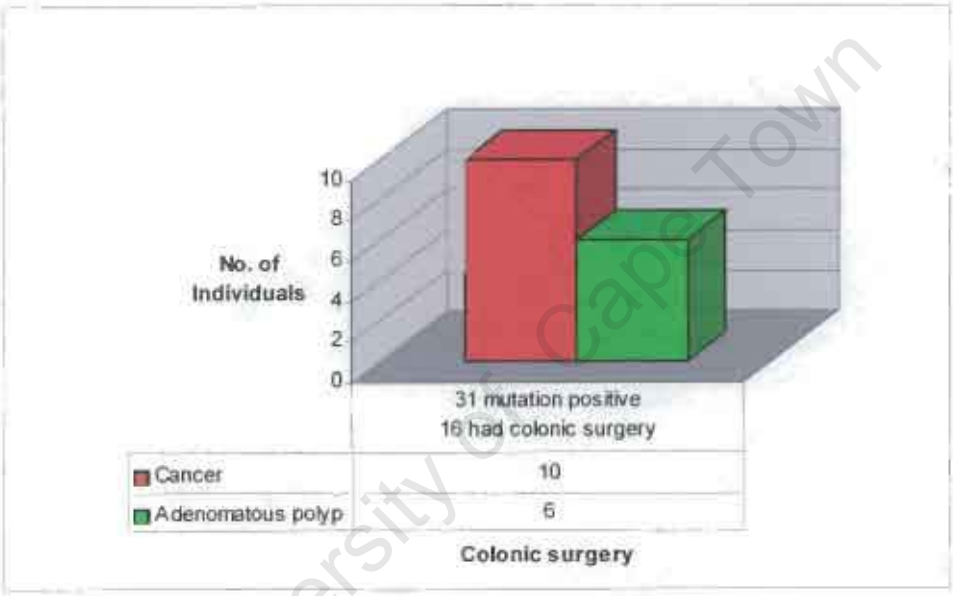


Figure 4.39: The reasons for colonic surgery

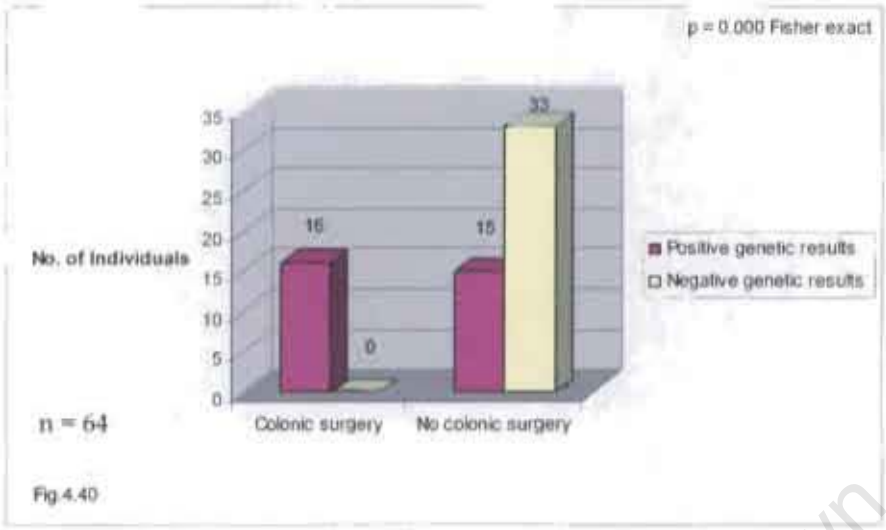


Figure 4.40: The genetic mutation results of those who had colonic surgery

Of the 64 respondents, 16(25%) had colonic surgery and were mutation-positive (Figure 4.40).

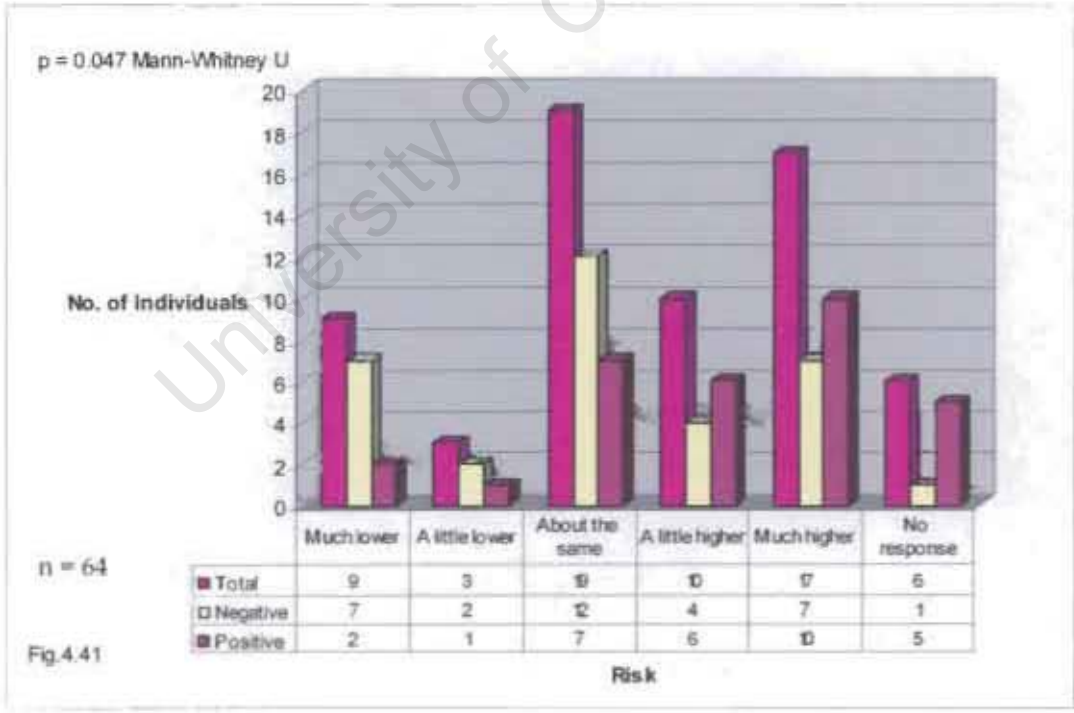


Figure 4.41: Respondents' genetic mutation results and opinions of their risk for

colon cancer compared to people their own age

Of the 6(9%) respondents who did not answer this question, five were mutation-positive and four had colonic surgery for colon cancer.

Of the 64 respondents, 19(30%) felt their risks were the same and 12(19%), a little or much lower than people their own age. Of these respondents, ten were mutation-positive and four had colonic surgery

Of the 64 respondents, 27(42%) felt their risks were a little or much higher than people their own age and 11 of these individuals were genetic mutation-negative, 16 were mutation-positive with half having had colonic surgery (Figure 4.41).

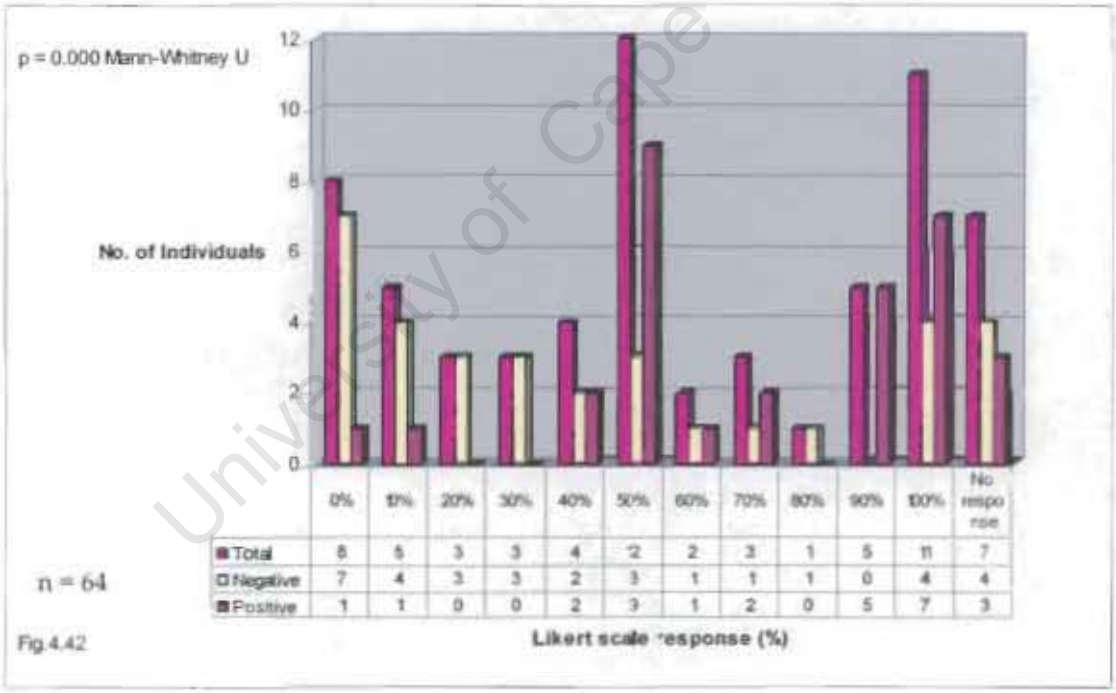


Figure 4.42: Opinions of risk for developing colon cancer and genetic mutation results

Of the 64 respondents, 7(11%) did not give their opinion, three of these non-respondents were mutation-positive and one had colonic surgery.

n = 57, Median 50%, q1–q3 20% - 90%.

Using a Likert scale, 23(36%) of the 64 respondents felt their chances of developing colon cancer were less than 50% and four of these respondents were genetic mutation-positive and three had colonic surgery.

Of the 64 respondents, 34(53%) felt they had a 50% and greater chance of developing colon cancer and ten of them were mutation-negative (Figure 4.42).

4.2.4.2 Health related decisions

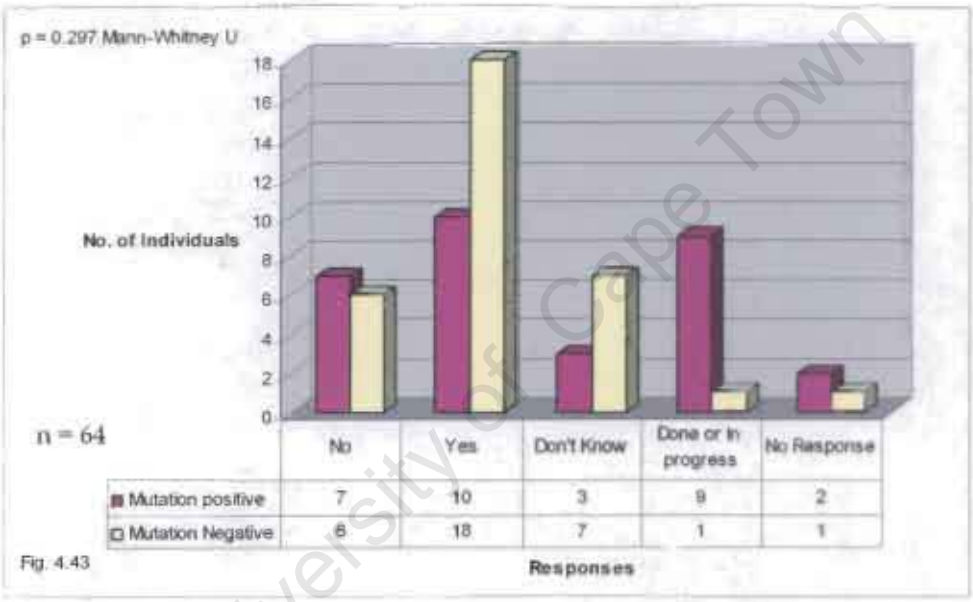


Figure 4.43: Opinions on preventative colectomy compared to respondents' genetic mutation results

Of the 64 respondents, 28(44%) reported that they would choose to have a preventative colectomy if they were genetic mutation-positive (Figure 4.43).

4.2.4.3 Surveillance decisions

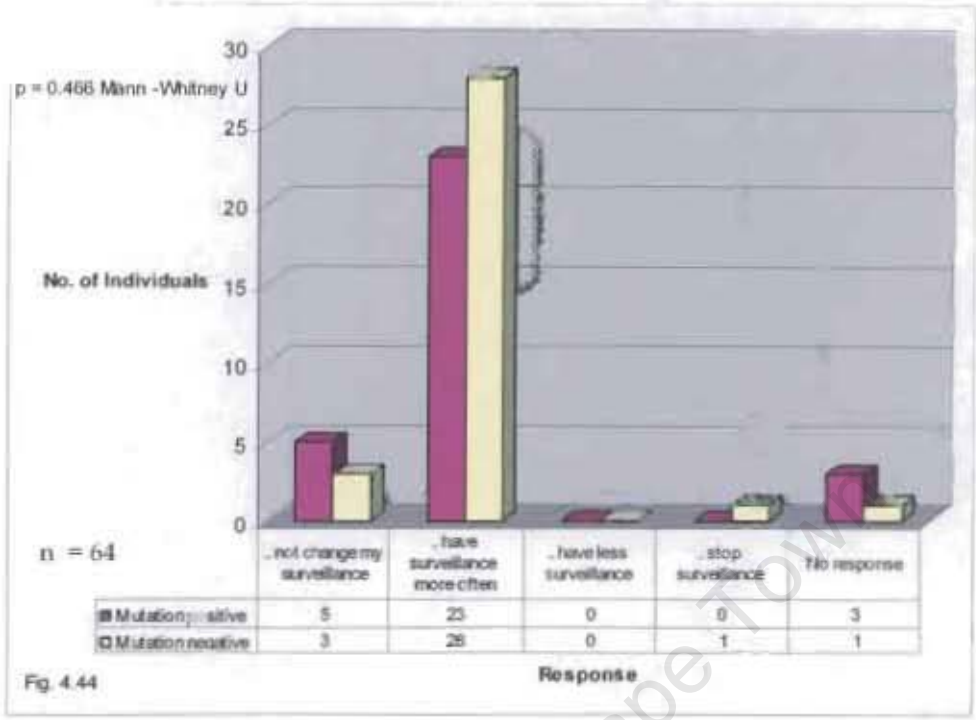


Figure 4.44: Respondents' surveillance choices if they had been mutation-positive compared to their genetic mutation results

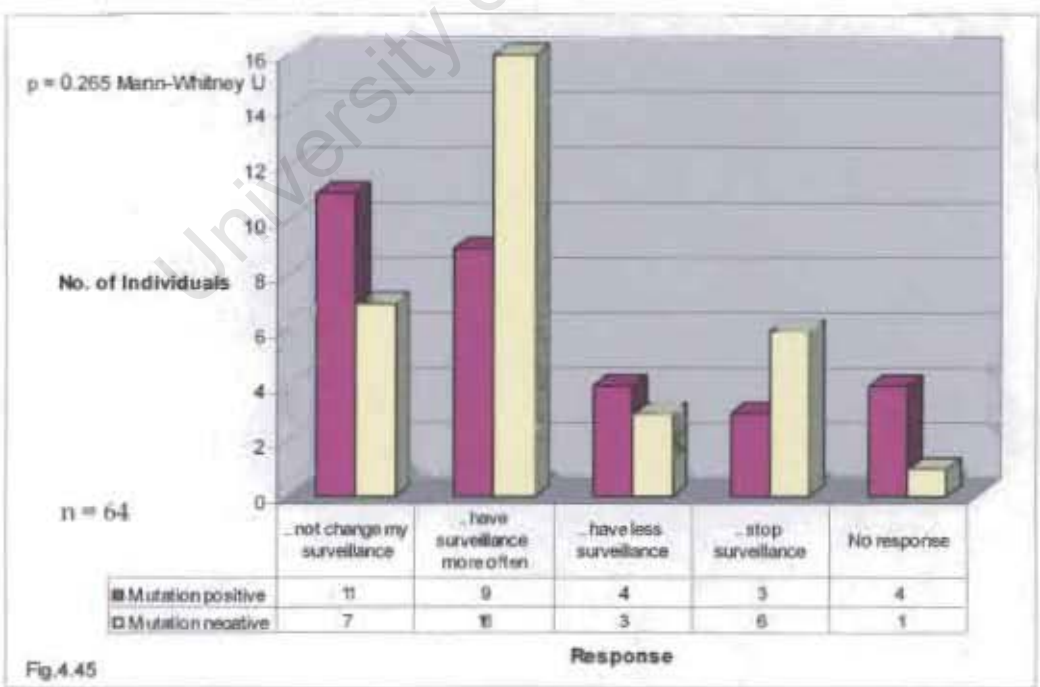


Figure 4.45: Respondents' surveillance choices if they had been mutation-negative compared to their genetic mutation results

Of the 64 respondents, 25(39%) would have more surveillance, and 16 of these respondents were mutation-negative.

Of the 64 respondents, 17(27%) would not change surveillance and 11 of these respondents were mutation-positive.

Nine mutation-positive and 16 mutation-negative respondents would choose more frequent surveillance (Graph 4.47).

4.2.4.4 Effects of genetic results on beliefs about effectiveness of surveillance methods

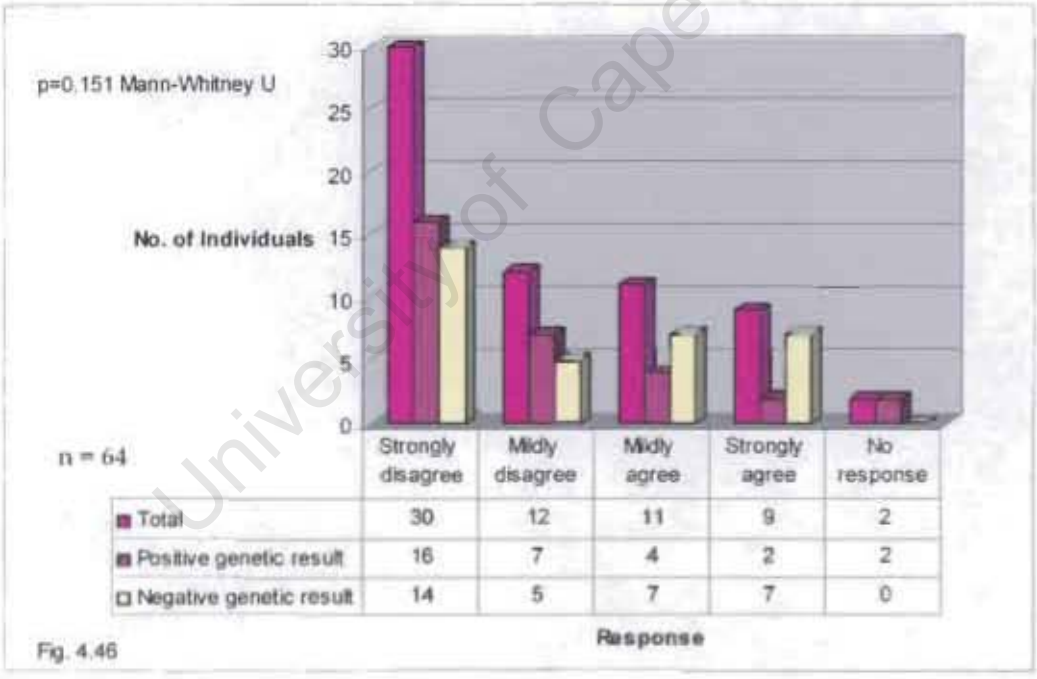


Figure 4.46: Respondents' opinions of the severity (chance of survival) of colon cancer and their genetic mutation results

Of the 64 respondents, 42(66%) felt that people with colon cancer had a good chance of survival. More than half of these respondents were mutation-positive

and 12 of them had colonic surgery. Of the 64 respondents, 20(31%) felt that the chances of survival were slim and 14 of them were mutation-negative (Figure 4.46).

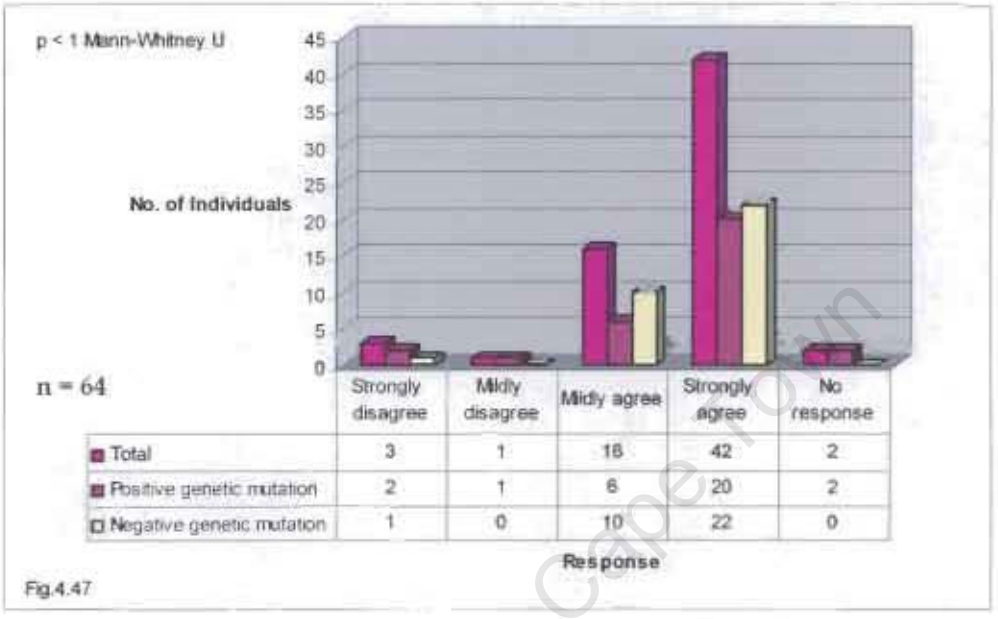


Figure 4.47: Respondents opinions of the curability of colon cancer if found early and their genetic mutation results

Of the 64 respondents, 58(90%) felt that colon cancer could be cured (Figure 4.47).

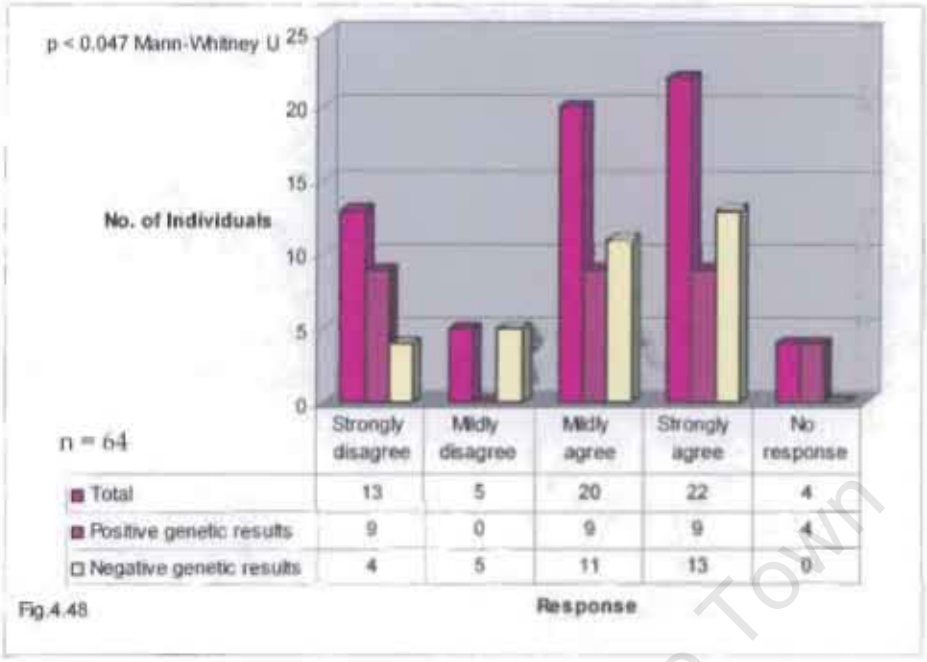


Figure 4.48: Responses by respondents to the 'worry' associated with colonoscopic surveillance detecting a colon cancer and their genetic mutation results

Of the 64 respondents, 42(66%) were concerned that surveillance might detect a colon cancer and 24 of these subjects were mutation-negative (19 female and five males). Of the 64 respondents, 18(28%) were not concerned that surveillance might detect colon cancer and nine of these subjects were mutation-positive (Figure 4.48).

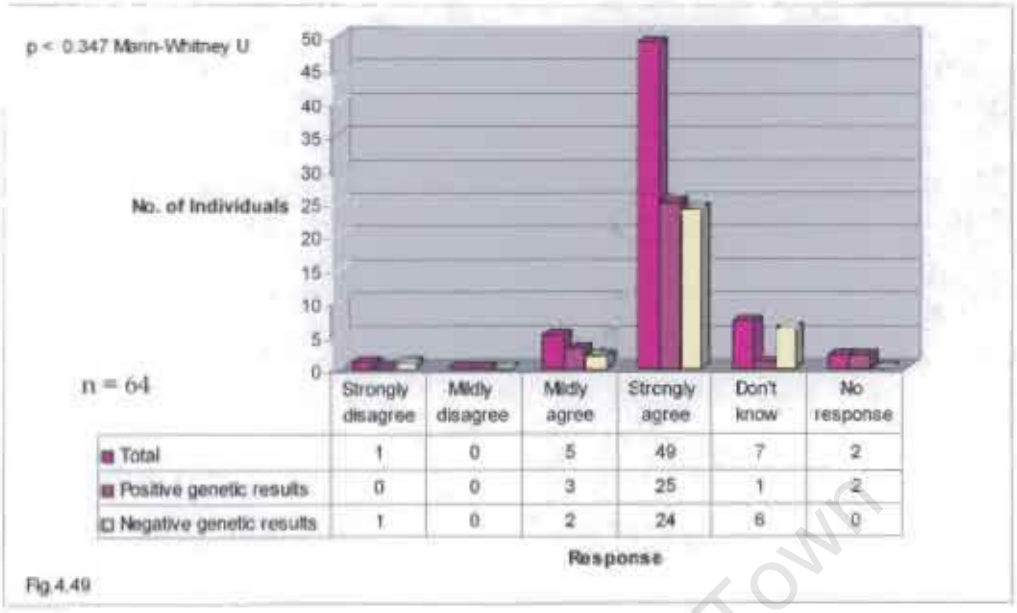


Figure 4.49: Opinions on the effectiveness of colonoscopy at detecting colon cancer and genetic mutation results

Of the 64 respondents, 54(84%) felt that colonoscopy was effective at detecting colon cancer while seven respondents were unsure of the efficacy of colonoscopy (six of these subjects were mutation-negative) (Figure 4. 49).

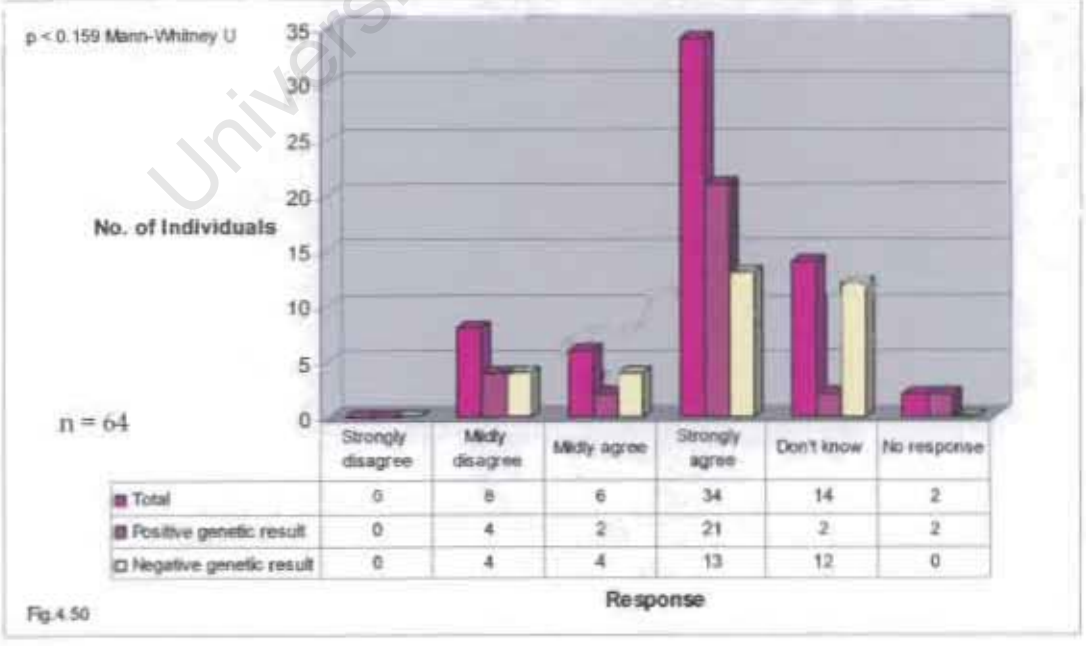


Figure 4.50: Opinions of the 'salience' (find it easy to do) of having a colonoscopy and genetic mutation results

Of the 64 respondents 40(63%) felt that colonoscopy was not a difficult procedure for them to endure. Of the 64 respondents, 14(22%) did not know and 12 of these subjects were mutation-negative (Figure 4.50).

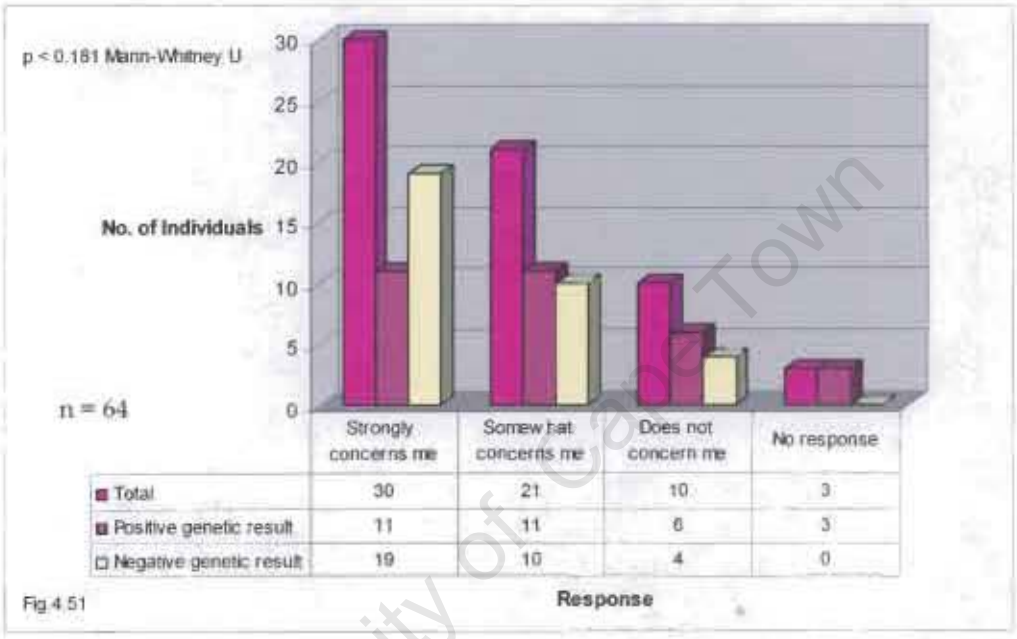


Figure 4.51: Opinions of the respondents 'worry' about being at-risk for extracolonic cancers and genetic mutation results

Of the 64 respondents, 51(80%) were concerned about extracolonic cancers (Figure 4.51).

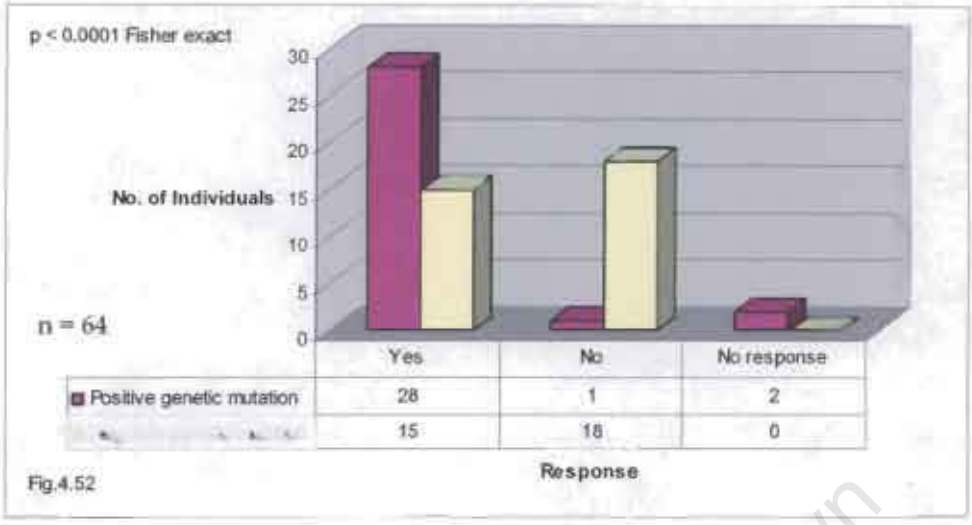


Figure 4.52: Recollection of having had a colonoscopy and genetic mutation results

Of the 64 respondents, 43(67%) had previously had a colonoscopy and 15 of these subjects were mutation-negative (Figure 4.52).

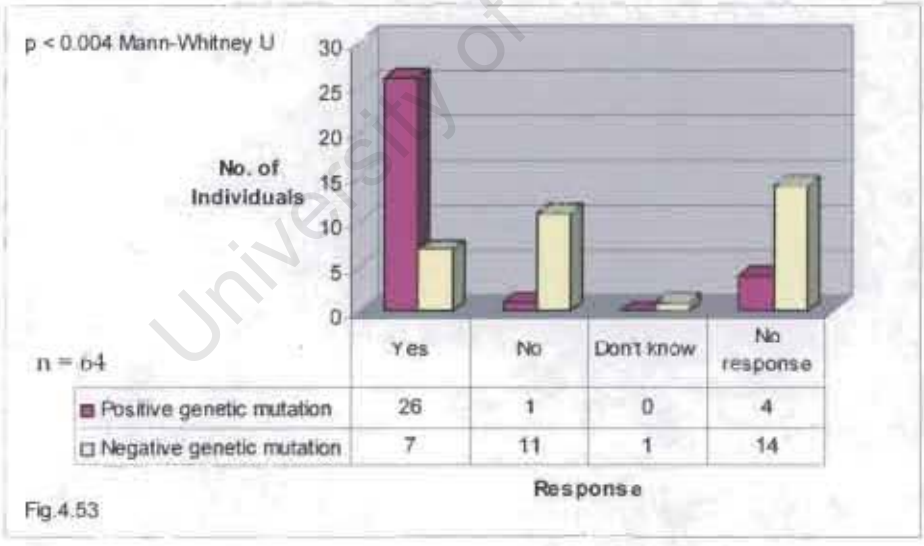


Figure 4.53: Recollection of having had a colonoscopy in the last two years and genetic mutation result

Of the 64 respondents, 33(52%) said they had a colonoscopy in the last two years

and 26 of these subjects were genetic mutation-positive and seven were negative.

Of the 64 respondents, 12(19%) had not had a colonoscopy in the last two years but only one was mutation-positive (Figure 4.53). This individual had colonic surgery.

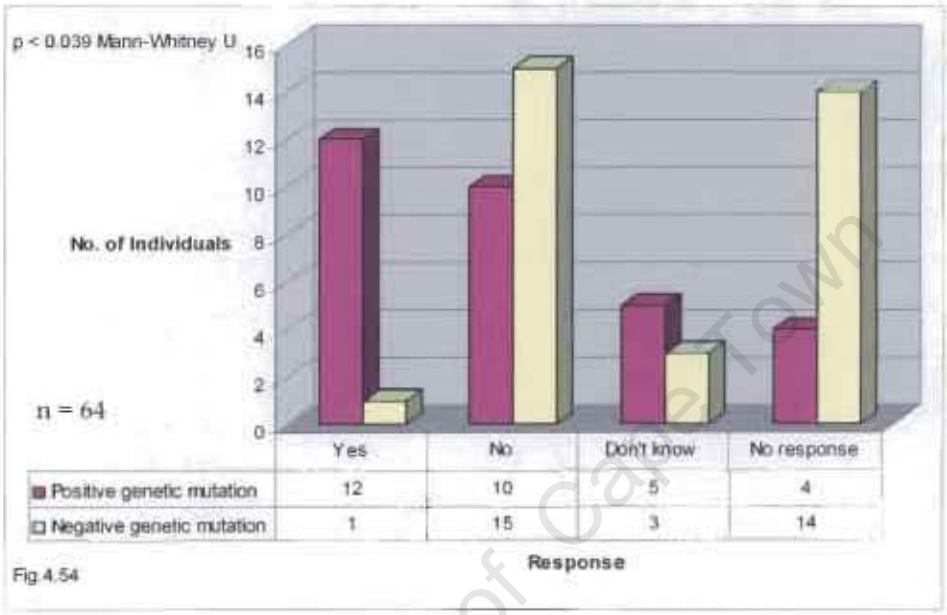


Figure 4.54: Recollection of having an adenomatous polyp removed at colonoscopy and genetic mutation results

Of the 64 respondents, 13(20%) had an adenomatous polyp removed at colonoscopy, 12 of whom were mutation-positive and nine of these subjects went on to have colonic surgery (Figure 4.54).

4.2.5 Significant associations

Figure.	Association variables		Statistical Test	p <
Figure 4.4	Area distribution of respondents	Area distribution of non – respondents	Fisher exact	0.007
Figure 4.40	Colonic surgery	Genetic results	Fisher exact	0.0001
Figure 4.41	Opinions of personal risk for bowel cancer compared to people their own age	Genetic results	Mann - Whitney U	0.047
Figure 4.52	Had a colonoscopy	Genetic results	Fisher exact	0.0001
Figure 4.53	Had a colonoscopy in the last 2 years	Genetic results	Mann - Whitney U	0.004
Figure 4.54	Adenomatous polyp removed at colonoscopy	Genetic results	Mann - Whitney U	0.039
Figure 4.55	Number of Children	Coping style	Mann - Whitney U	0.012
Figure 4.56	Had a colonoscopy	Coping style	Fisher exact	0.025
Figure 4.57	Chance of survival with a colon cancer - Severity	Knowledge of colon cancer	Mann - Whitney U	0.009

Figure 4.58	Colonoscopy is an easy thing for me to do -salience	Perceived benefits and limitations	Mann - Whitney U	0.047
Figure 4.59	Had a colonoscopy	Affected 1st degree relatives	Fisher exact	0.013
Figure 4.60	Knowledge scores	When found early colon cancer can be cured - curability	Mann - Whitney U	0.0001
Figure 4.61	Chance of survival with a colon cancer - Severity	When found early colon cancer can be cured - curability	Mann - Whitney U	0.0001
Figure 4.62	Choice of screening if mutation-negative	Chance of survival with a colon cancer - Severity	Mann - Whitney U	0.013
Figure 4.63	Colonoscopy is an easy thing for me to do - salience	Chance of survival with a colon cancer - Severity	Mann - Whitney U	0.026
Figure 4.64	Number of relatives affected	Colonic surgery	Mann - Whitney U	0.041
Figure 4.65	Opinions of preventative colectomy	Colonic surgery	Mann - Whitney U	0.0001
Figure 4.66	Potential depression	Anxiety	Fisher exact	0.011
Figure 4.67	Colonoscopy is an easy thing for me to do -salience	Anxiety	Mann - Whitney U	0.019

Figure 4.68	Worry' that bowel cancer screening will show a bowel cancer	Potential depression	Mann - Whitney U	0.017
Figure 4.69	Worry that bowel cancer screening will show a bowel cancer	Impact of events (stress) scores	Mann - Whitney U	0.020
Figure 4.70	Opinions of personal risk for bowel cancer compared to people their own age	Stressful life events	Mann - Whitney U	0.042
Figure 4.71	School Education	Post - school education	Fisher exact	0.009
Figure 4.72	Number of Children	Post - school education	Mann - Whitney U	0.034
Figure 4.73	Worry that bowel cancer screening will show a bowel cancer	Gender	Fisher exact	0.009
Figure 4.40	Colonic surgery	Genetic results	Fisher exact	0.0001
Figure 4.41	Opinions of personal risk for bowel cancer compared to people their own age	Genetic results	Mann - Whitney U	0.047

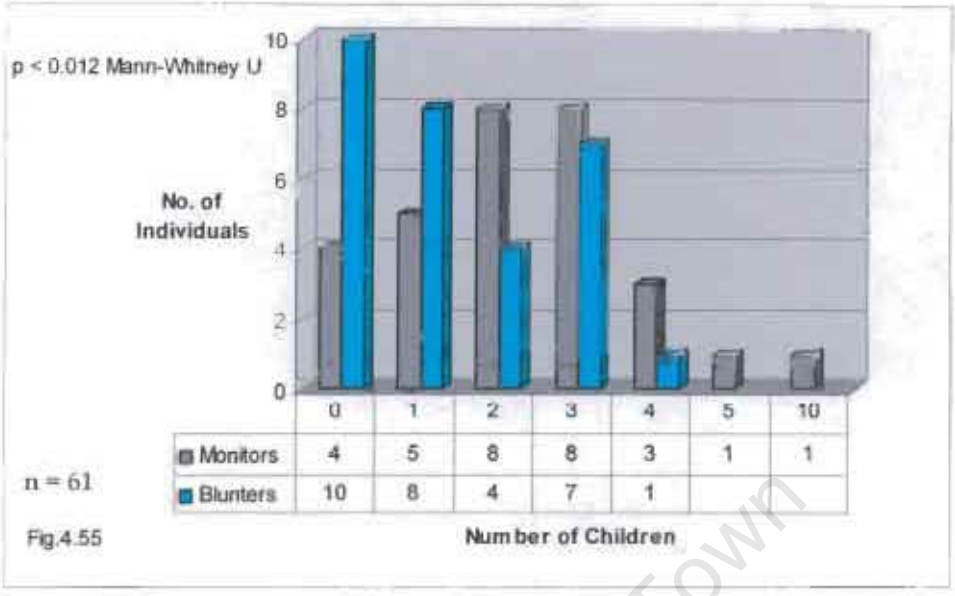


Figure 4.55: Respondents coping styles compared to the number of children they had

The respondents with a blunting coping style had families of 0 to 3 children, while monitors had a range of 0 to 10 children (Figure 4.55)

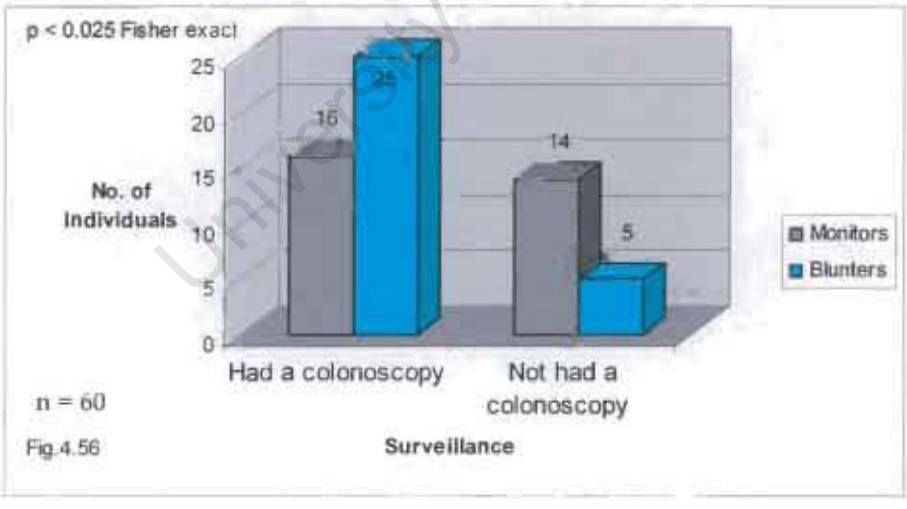
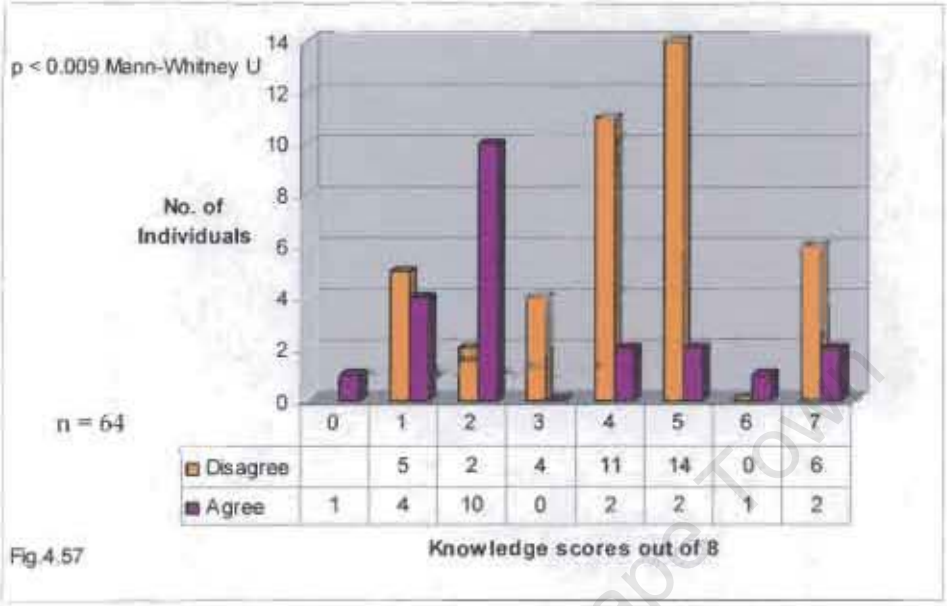


Figure 4.56: Coping style and recollection of having had a colonoscopy

Of the 60 respondents, 41(68%) had colonoscopies and more than half (25) of these subjects had a blunting coping style.

Of the 60 respondents, 19(32%) had not had a colonoscopy and 14 of these subjects had a monitoring coping style (Figure 4.56).



	0	1	2	3	4	5	6	7
Disagree		5	2	4	11	14	0	6
Agree	1	4	10	0	2	2	1	2

Figure 4.57: Association between colon cancer knowledge scores and opinions of survival chances with colon cancer

Of the 64 respondents, 38(59%) had higher colon cancer knowledge scores (4 to 7) and 31 of them felt that there was a good chance of survival with bowel cancer.

Of the 64 respondents, 23(36%) had lower knowledge scores (0 to 3) and 11 of these subjects also felt positively toward survival with colon cancer (Figure 4.57).

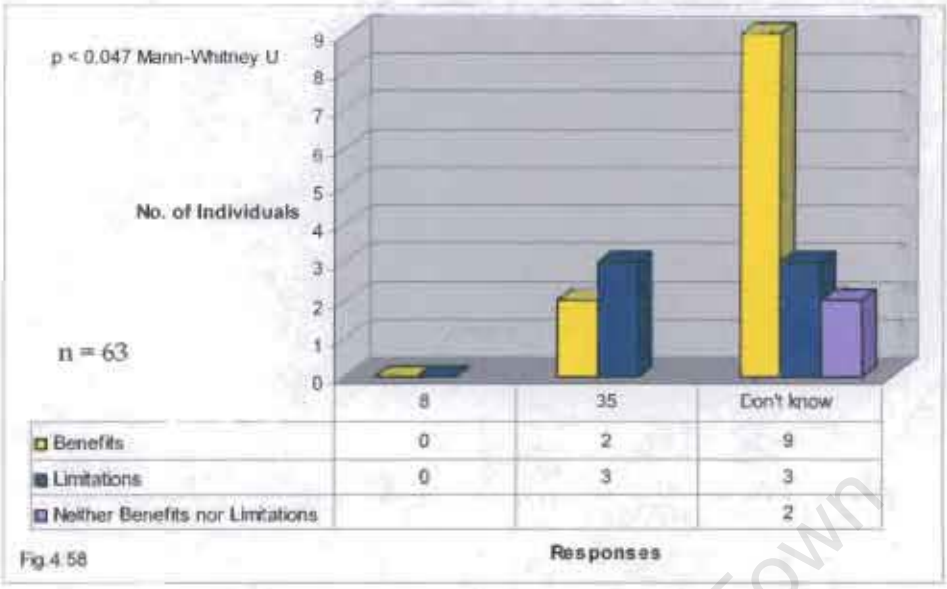


Figure 4.58: Association between colonoscopy salience and those who experience benefits or limitations with the predictive genetic testing process

Of the 63 respondents, 52(83%) felt they had benefited from predictive genetic testing of whom 35 agreed that a colonoscopy would be a procedure they would endure (Figure 4.58). Of the 63 respondents, 5(8%) had felt harm (limitations) from predictive genetic testing but felt they could endure a colonoscopy.

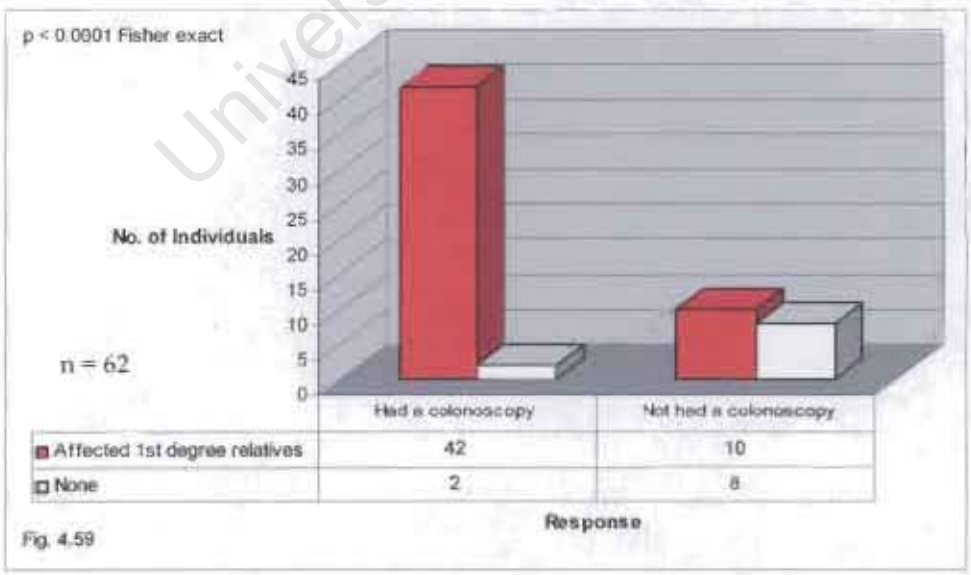


Figure 4.59: Association with having had a colonoscopy and affected first-degree relatives

Of the 62 respondents, 52(84%) had a first-degree relative affected with colon cancer, 42 of them had a colonoscopy. Of the 62 respondents, 10(16%) respondents did not have an affected first-degree relative and eight of them had not had a colonoscopy (Figure 4.59).

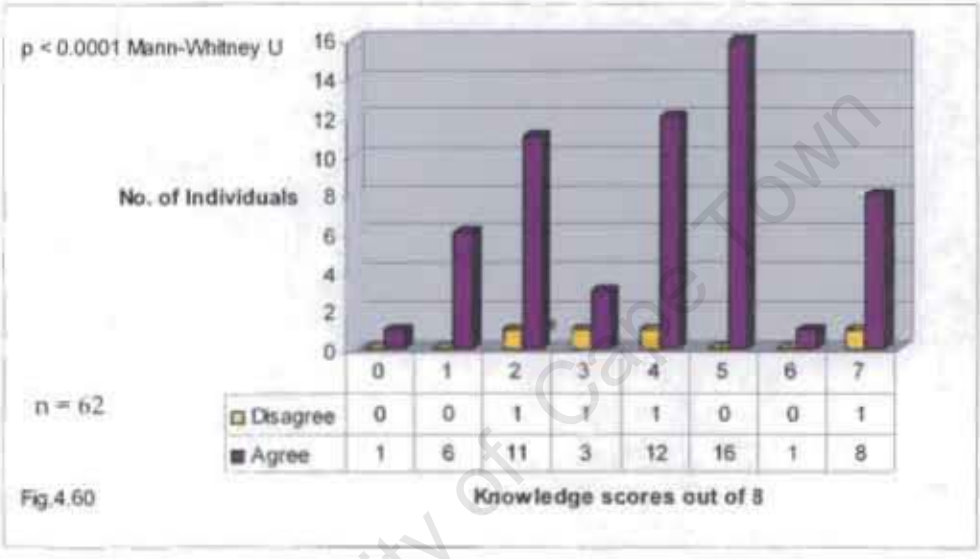
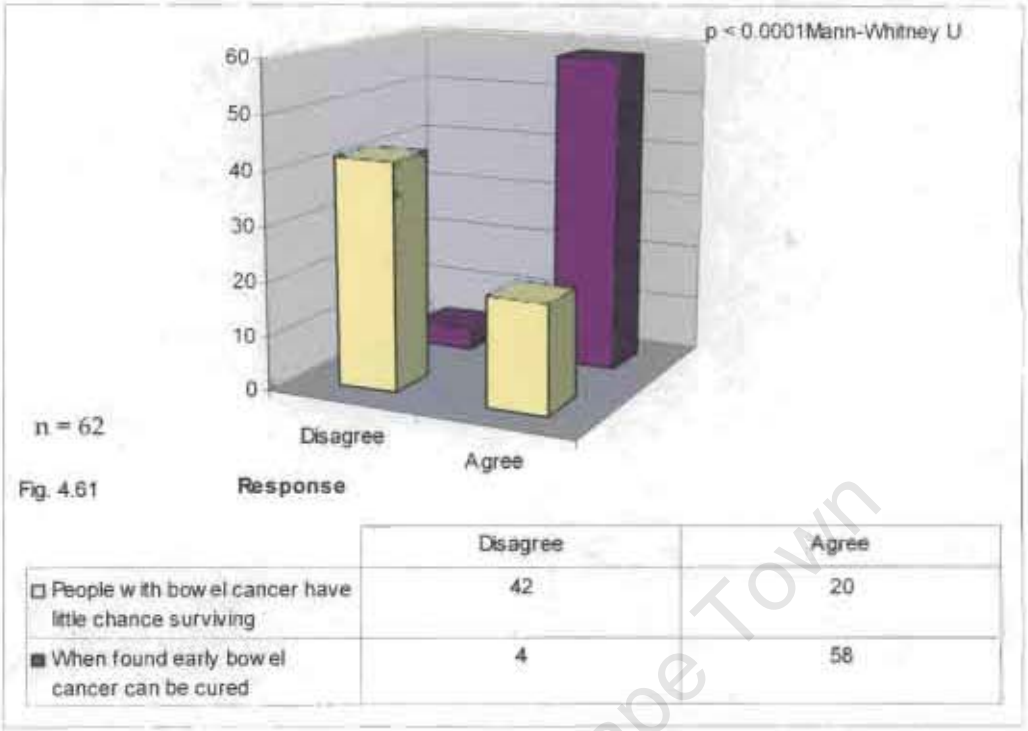


Figure 4.60: Association with opinions of early detection and curability of colon cancer and colon cancer knowledge scores

Of the 63 respondents, 39(63%) had high colon cancer knowledge scores (4 to 7) and 37 of these subjects felt that colon cancer could be cured if found early. Of the 63 respondents, 24(38%) had low knowledge scores (0 to 3) and 23 of these subjects also agreed about the curability of colon cancer (Figure 4.60).



	Disagree	Agree
People with bowel cancer have little chance surviving	42	20
When found early bowel cancer can be cured	4	58

Figure 4.61: Association between opinions of 'severity' and 'curability' of colon cancer

Of 62 respondents, 58(94%) felt cancer could be cured if found early and 42(68%) felt that people with colon cancer would survive (Figure 4.61).

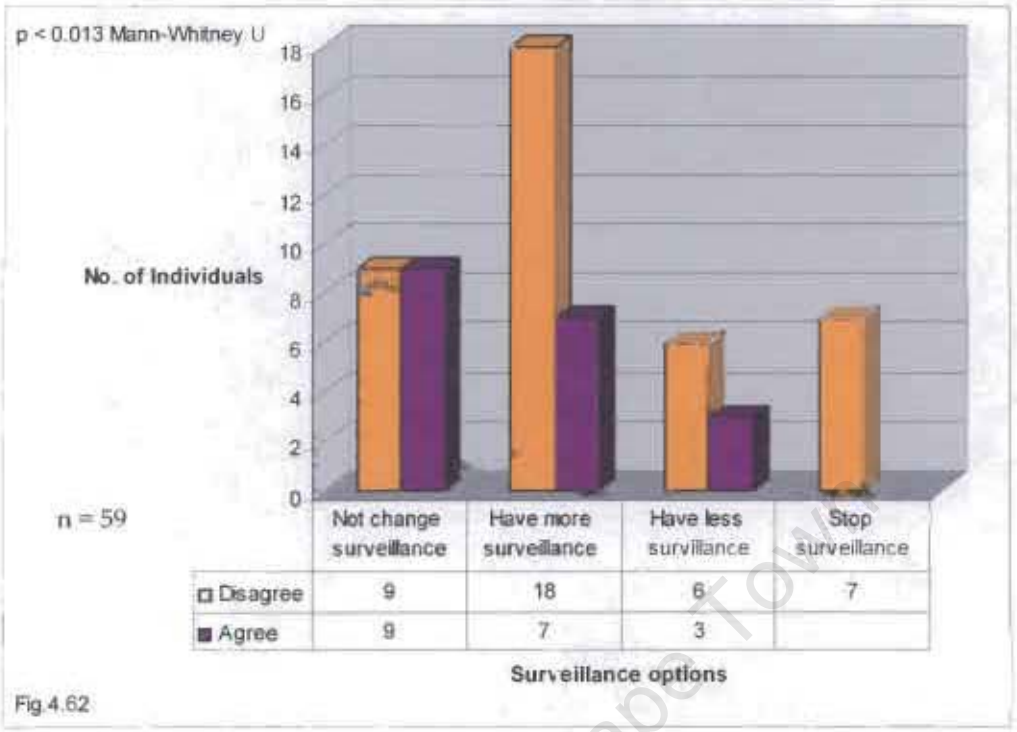
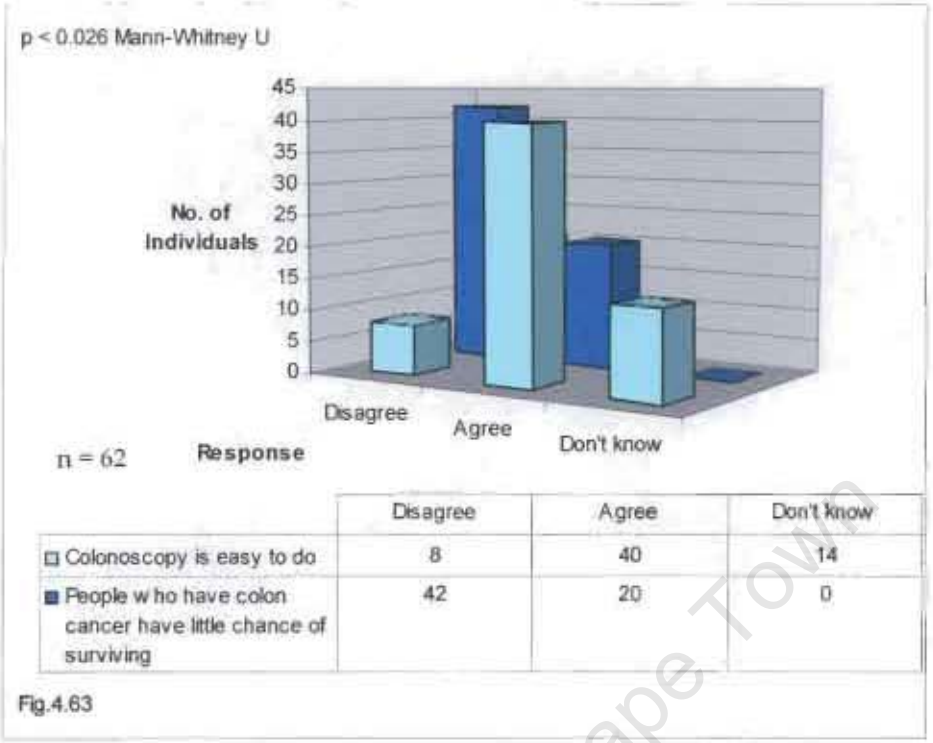


Figure 4.62: Association of surveillance opinions if mutation-negative and severity of colon cancer

Of the 59 respondents, 40(68%) felt that people who have colon cancer had a good chance of survival and 27 of them felt they would either not change or have more surveillance if their mutation result was negative. Of the 59 respondents, 19(32%) felt colon cancer gave little hope and 16 of them also wanted to continue with surveillance if their mutation result was negative (Figure 4.62).



	Disagree	Agree	Don't know
Colonoscopy is easy to do	8	40	14
People who have colon cancer have little chance of surviving	42	20	0

Fig.4.63

Figure 4.63: Association of opinions of salience and severity of colon cancer

Of the 62 respondents, 42(68%) felt that people with colon cancer had a good chance of survival and 40(65%) considered a colonoscopy easy to do (Figure 4.63).

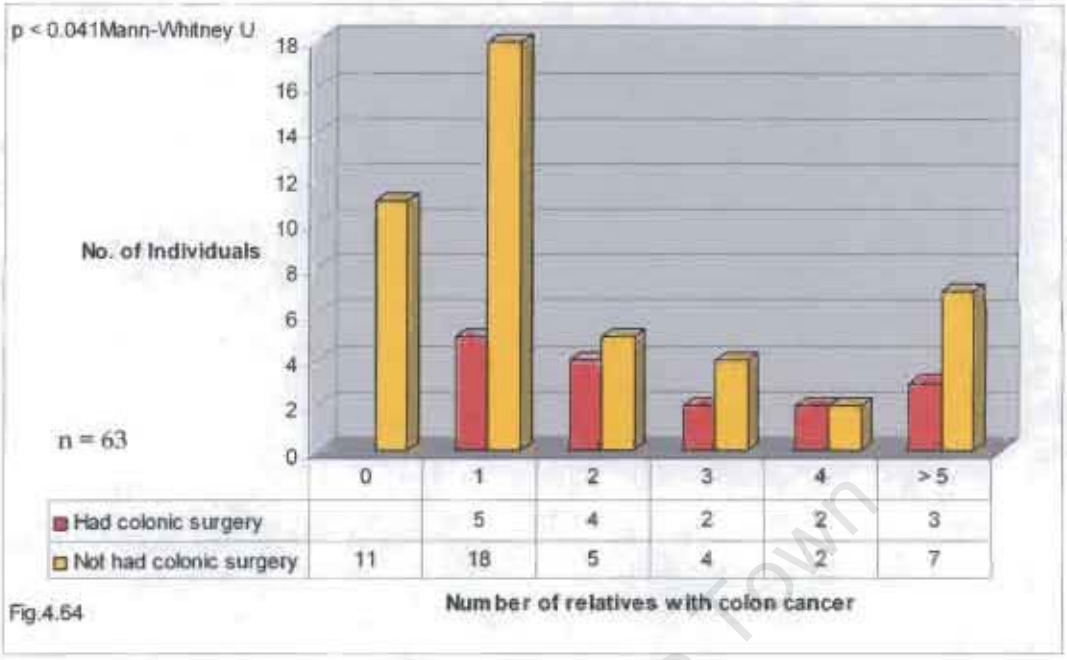


Figure 4.64: Association with having had colonic surgery and relatives affected with colon cancer

Those that had colonic surgery all had relatives with a colon cancer. 11 respondents who had not had colonic surgery also did not have relatives with colon cancer (Figure 4.64).

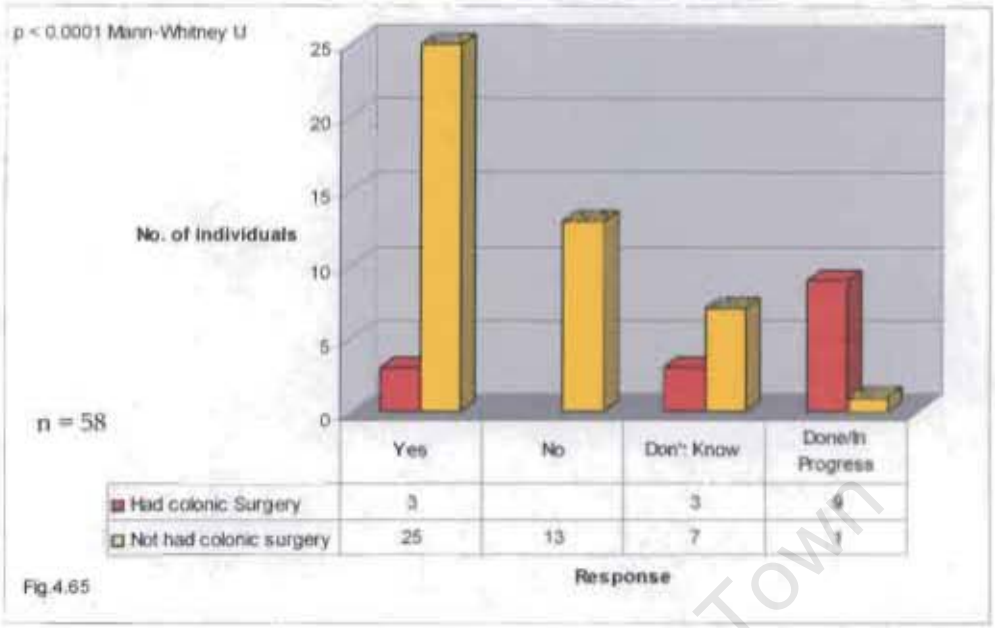


Figure 4.65: Association between colonic surgery (or not) and opinions toward preventative colectomy

The data base information of individuals who had colonic surgery corresponded to those respondents who reported having had colonic surgery. No-one who had colonic surgery said no to a preventative colectomy (Figure 4.65). Most, 25(43%), of those subjects who had not had colonic surgery said they would consider it and seven had a positive genetic mutation and 18 a negative mutation result.

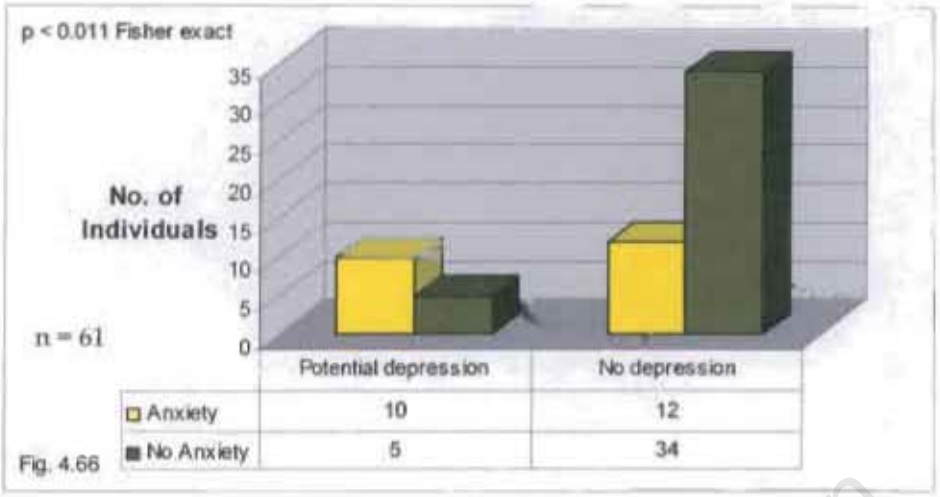


Figure 4.66: Association with respondents with potential depression and anxiety

Of the 61 respondents, 15(24%) had a potential depression and 10 subjects also had anxiety. Of the 61 respondents, 46(75%) had no depression, and 34 of these subjects also had no anxiety (Figure 4.66).

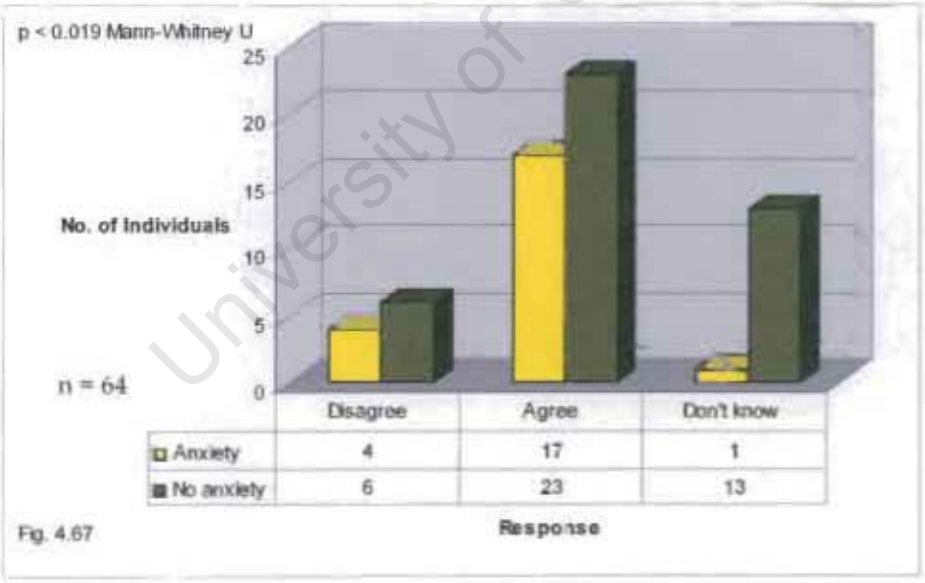


Figure 4.67: Association with the opinion of salience of having a colonoscopy and anxiety

Of the 64 respondents, 40(63%), agreed that they could have a colonoscopy and

23 of these subjects had no anxiety while, 10(16%) respondents felt a colonoscopy would be difficult to do and six of these subjects also had no anxiety.

Of the 64 respondents, 14 (22%) were not sure and 13 of these subjects also had no anxiety (Figure 4.67).

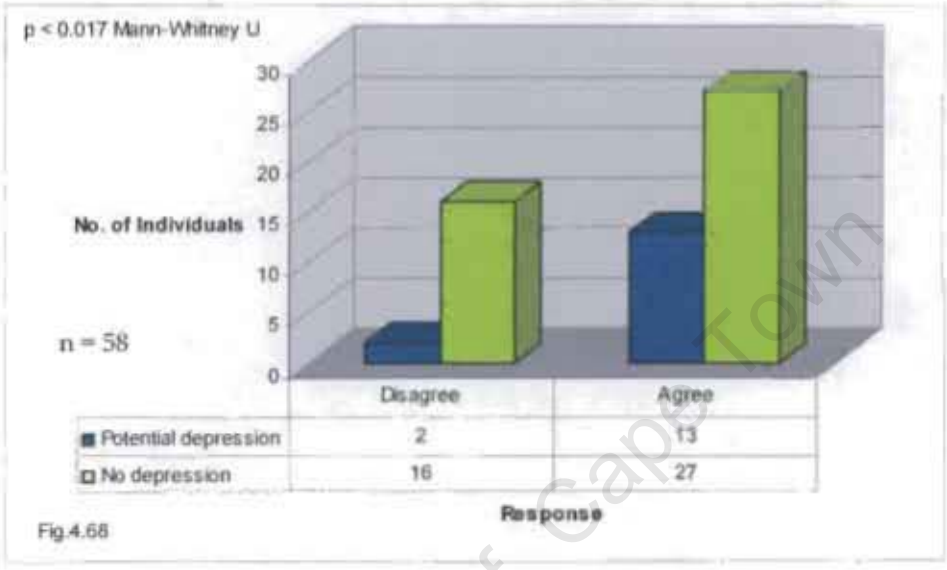


Figure 4.68: Association with the respondents worry about surveillance detecting a colon cancer and depression

Of the 61 respondents, 15(26%) had a potential depression and 13 of these subjects agreed that they were concerned that surveillance may detect a colon cancer, while 43(70%) respondents were not depressed and 27 of them were worried about finding a colon cancer at surveillance (Figure 4.68).

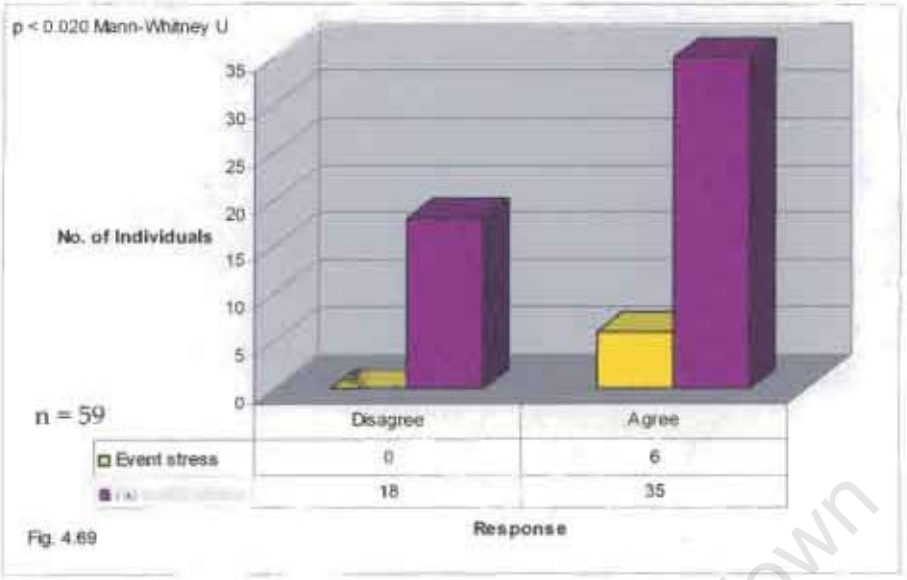


Figure 4.69: Association of stress scores (IES) and worry of colonoscopy surveillance detecting a bowel cancer

Of the 59 respondents, 41(69%) agreed that they were worried about a colon cancer being found at surveillance colonoscopy and 35 of these subjects reported no event stress, while six respondents who had experienced colon cancer as an event stress, were worried (Figure 4.69).

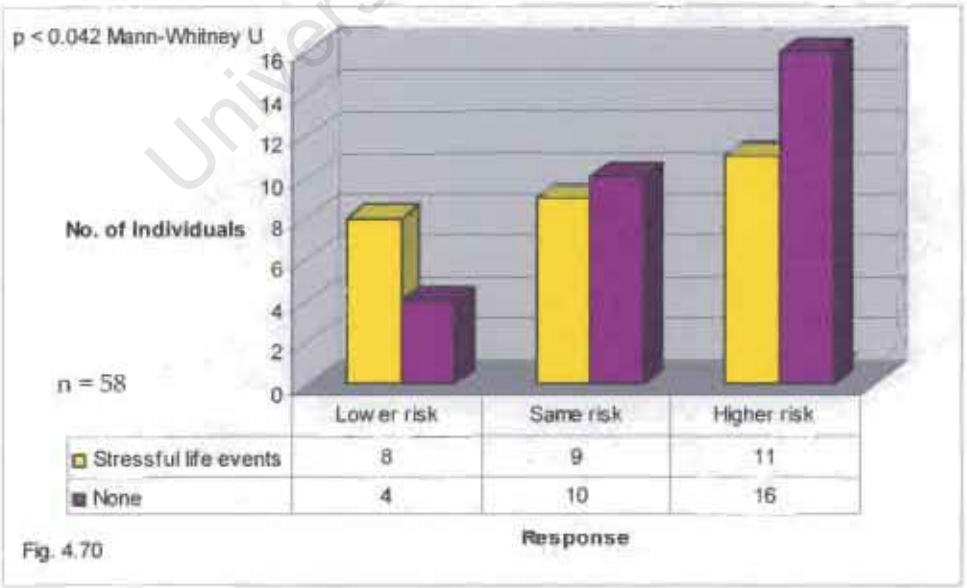


Figure 4.70: Opinion of personal risk for colon cancer and experience of stressful life events

Of the 58 respondents, 12(21%) felt they had lower colon cancer risk than their peers and eight of these subjects experienced stressful events while 46(79%) subjects felt they had the same or higher risk than their peers and 26 of them experienced no stressful events (Figure 4.70).

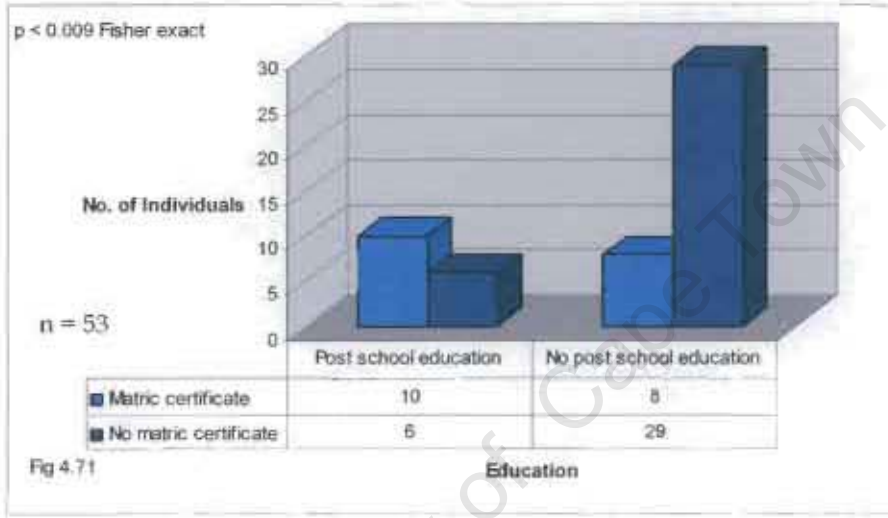


Figure 4.71: Association with school and post-school education

Of the 53 respondents, 35(66%) had no matric certificate and 29 of these subjects had no post-school qualifications, while 18(31%) had a matric certificate and ten of these subjects had a post-school education (Figure 4.71).

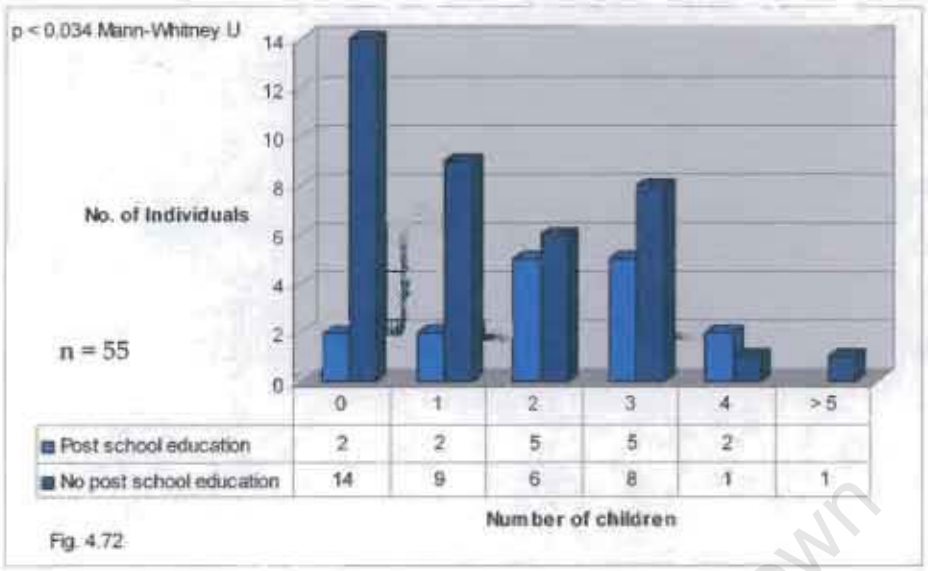


Figure 4.72: Association of post-school education and number of children.

Of the 55 respondents, 39(71%) had no post-school education and 37 of these subjects had 0 to 3 children, while 16(29%) had a post-school education and 14 of them had children aged 0 to 3 (Figure 4.72).

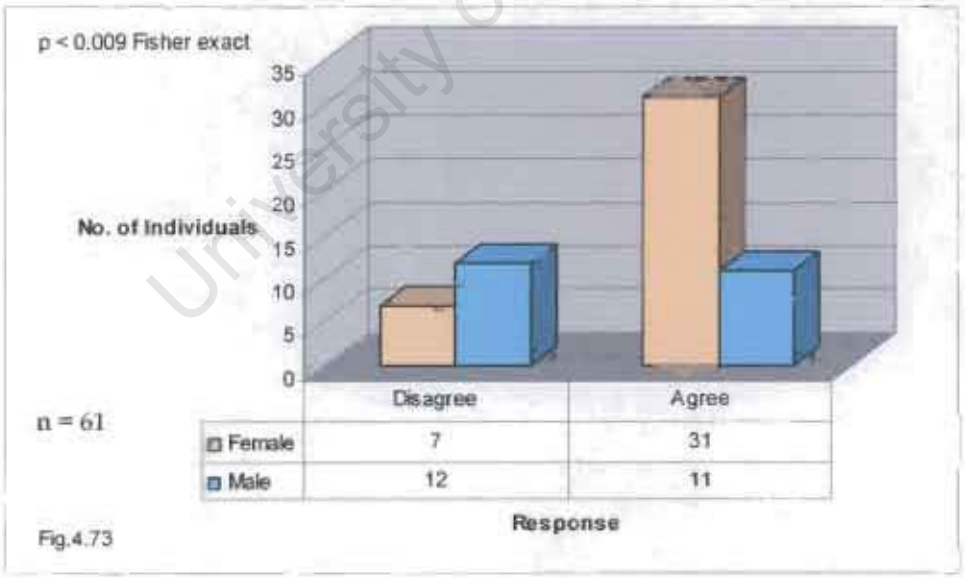


Figure 4.73: Gender and opinion on worry that cancer surveillance would detect a colon cancer

Of the 61 respondents, 42(69%) agreed that they were worried about a colonoscopy finding a colon cancer, 31 of these subjects were female while 19 (31%) subjects were not worried, 12 of them were males (Figure 4.73).

4.2.6 Substantiation of reliability

In order to prove that scores could be produced repeatedly and consistently within the instrument, questions about faecal occult blood testing, which were asked in two different objective sections (impacts on medical decisions and knowledge and attitude) of the instrument, involving five questions (Questions 22, 26d, 26e, 34 and 35), were isolated.

The statistician was consulted as faecal occult blood information had not been part of the background knowledge of this research sample. He felt associations could be made between these variables, which could show reliability of the instrument.

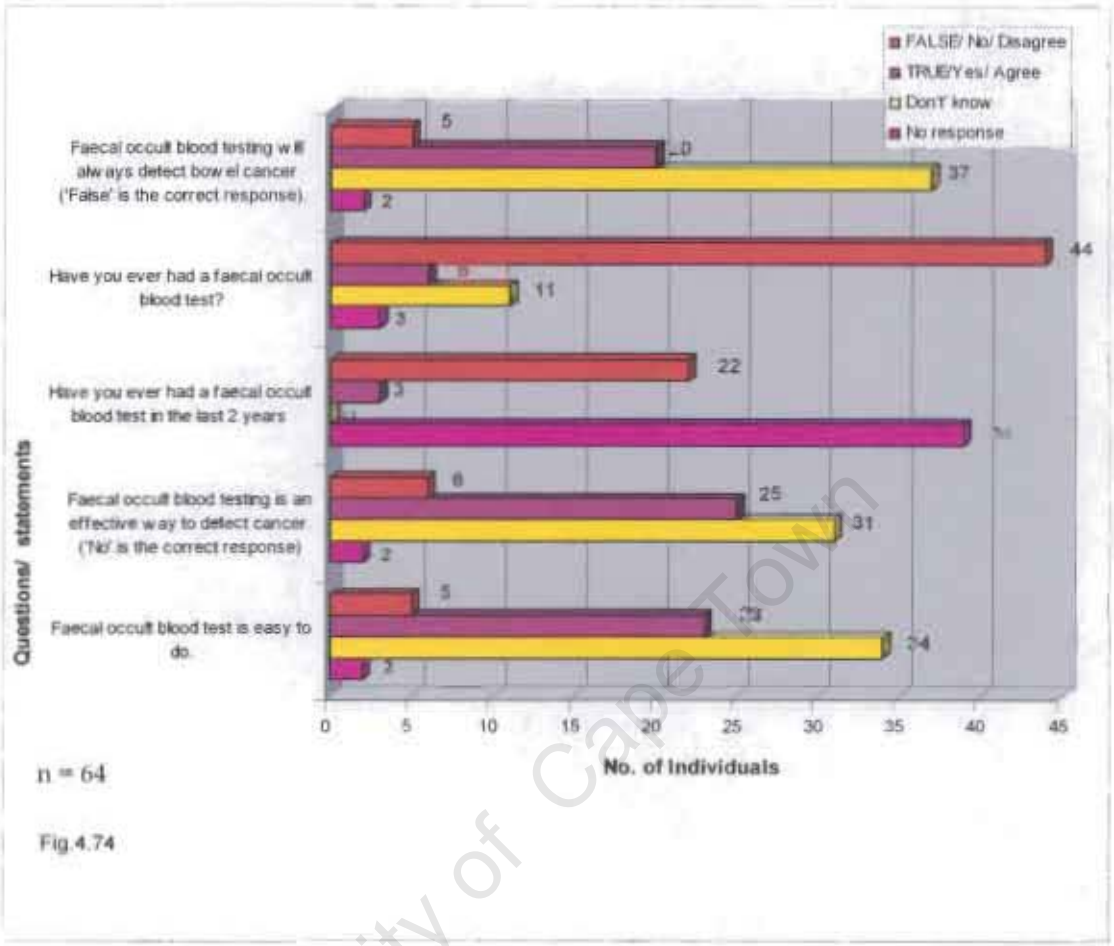


Figure 4.74: Responses to five questions on faecal occult blood testing

Of the 64 respondents, 37(58%) were unsure if faecal occult blood was a reliable way to detect colon cancer, 20(31%) thought it was and 5(9%) thought it was not.

Of the 64 respondents, 44(69%) had never had a faecal occult blood test and 31 (48%) did not know if a faecal occult blood test was an effective way to detect cancer, or (34 (53%)) if it was an easy thing to do (Figure 4.74).

4.3 Conclusion

The analysed data within the four objectives leads into a discussion of the meaning and value of the results. The credibility of these results can also be assessed by comparing them to published research. The significance of some of

these associations has resulted in the recommendations described in Chapter 5.

5 CHAPTER 5 - DISCUSSION

5.1 Introduction

The aim of this study was to evaluate the benefits and limitations, as perceived by family members, of the current management of inherited colorectal cancer in South Africa. A unique cohort of individuals from four different families, who all share a single *h*MLH1 mutation as a result of a C to T transversion at nucleotide 1528 in exon 13 on chromosome 3p, was chosen. All subjects received their predictive genetic test results and information sessions from the same person, using the predictive genetic testing protocol (documented in Appendix 1) over a six-year period from 1997 to 2002.

5.2 Research associations

5.2.1 Response

The research sample had all been through a predictive genetic testing program with information sessions about colon cancer including pre- and post-test counselling. Those who are mutation-positive were enrolled in a surveillance program while those who are mutation-negative become part of the normal population risk for colon cancer and are released from follow-up. Nearly half of the targeted sample chose not to return a completed questionnaire. Those who did not return the questionnaire were significantly more likely to live in a rural environment in the Northern Cape. They were of similar age, gender and mutation status compared to those who had returned the questionnaires. The other possible reason for their non-response was:

1. The altered data collection strategy required that questionnaires be collected a month later (on the annual colonoscopy surveillance trip). The

arrangements were of an ad hoc nature thus creating this possible methodology flaw.

2. Most non-respondents were mutation-negative and did not need a surveillance colonoscopy, thus it could have been potentially difficult for them to return the questionnaires to the research assistant.
3. They may have had difficulty completing the questionnaire from an educational level.
4. They may have just forgotten to complete the questionnaire or felt that they did not want to participate.

The final sample size was 119 individuals with a response rate of 54 %, resulting in a power of 36%. The response rate in this study was similar to other studies with similar design who had response rates of 24% to 77 %(54;63;65;66;97). The response rate in studies where telephonic or personal interviews were performed reported higher response rates of 63% to 96 %(47;55;56;58;69;81).

5.2.2 Sociodemographics

The majority of respondents had limited economic resources. Few had achieved higher education. Most studies about predictive genetic testing examined older individuals with higher education and economic resources (47;58;64;78;98;99).

5.2.3 Knowledge and attitudes

5.2.3.1 Knowledge

The majority of this cohort had experienced cancer in a first-degree relative. The average knowledge score amongst them was 42%. The knowledge score recorded by Lerman et al(58) was higher at 55% and Meiser et al(82) at 57% in studies of cohorts with higher education. The data presented here showed no association between knowledge score, education level or exposure to cancer.

Meiser et al(82) did find an association with education but not with cancer exposure.

The information retained by the respondents showed that they had a good knowledge of colonoscopic surveillance but moderate to low levels of recall about colon cancer and its inheritance. A significant association was found between knowledge scores and the understanding of the severity of colon cancer ($p < 0.009$).

5.2.3.2 Benefits and Limitations

Most respondents thought that predictive genetic testing was beneficial or did no harm. Five individuals felt that predictive genetic testing was harmful because of the effect they felt it had on their family. Four of them also distrusted modern medicine and three found it difficult to handle emotionally, as they believed that cancer was inevitable.

The benefits with the highest ratings were that of being certain about, and understanding how to reduce risk. Helping research, planning for the future and learning about their children's risk were also rated highly and just under half of the respondents used the testing process to make decisions about having children. In similar studies, learning about children's risk(55;58;61), planning for the future(55;61) and participating in research(60) were stated as the most important beneficial reasons for wanting genetic tests.

Concerns about coping emotionally with predictive genetic testing information were the most important perceived limitations amongst the majority of respondents. This was not found in a study by Balmana et al(20). Other important concerns cited in the current study were that predictive genetic testing may have an effect on families, also found by Meiser et al (61), and that they believed cancer was inevitable. The honesty and sensitivity of this response should send a strong message to future managers of these families that they

require the necessary support. Other studies however have shown that the accuracy of the test was the most highly rated limitation(20;58) and that concern about losing insurance seemed to be unimportant (20;55;58). The South African cohort seemed to have trust and confidence in the test results and in modern medicine.

5.2.4 Psychological and functional health status

5.2.4.1 Stress

Stressful events, related to deaths and cancers, in those respondents with positive genetic mutations, were more common in the year prior to the study than in those with negative results.

In this study, the minority of subjects expressed stress about being at-risk for colon cancer. Of the six individuals who were stressed by their risk of colon cancer, four had a negative genetic mutation result.

5.2.4.2 Coping style

Although there was no difference in the coping styles related to mutation status, blunters had more colonoscopies performed compared to monitors ($p < 0.025$). An increased frequency of colonoscopy attendance was expected of the monitors based on the findings of Steptoe and Sullivan(77), who found that monitors were more likely to undergo pap smears than blunters. It was expected that monitors would also have higher knowledge scores, as found by Steptoe and Sullivan(77), but this cohort had similar numbers of monitors and blunters with high knowledge scores. Blunters in this cohort had an increased frequency of colonoscopy attendance and this may be a reflection of the slightly higher number of mutation-positive individuals who were blunters. There is a greater proportion of mutation positive individuals in the blunter group (16 vs 13 blunters, and 11 vs 19 monitors mutation positive vs negative (Fig. 4.32)). This

difference was not statistically different (p=0.3). However, each mutation positive individual is likely to have many colonoscopies, while a mutation negative may never have any. This multiplier effect is probably the cause of the statistically significant result of more colonoscopies in the blunter group, rather than it being a reflection of the coping style.

In addition, blunters were found to have had smaller families ($p < 0.012$). This may be significant when considering the discussion of inheritance of colon cancer.

Coping styles in this cohort were not related to demographics, anxiety and depression. This finding is similar to others(61;75) but differs from Phipps and Zinn(76) who found that monitors were more anxious than blunters and that there were significant interactions between coping styles, anxiety and depression scores.

5.2.4.3 Anxiety

Just over a third (37%) (German general population with anxiety = 7% and non-patients with a health complaint = 33 %(100)) of the respondents appeared to experience anxiety, and equal numbers of these subjects had positive and negative genetic mutation results. Esplen et al(60) found 22% of their sample (who are at intermediate and high-risk for familial colon cancer) had anxiety. Again, a significant association was found between the salience (it would be easy to have) of having a colonoscopy and those respondents with low anxiety levels.

5.2.4.4 Depression

Scores suggestive of potential depression were found in 13(21%) of respondents and 10 of them were mutation-negative while all three (5%), that had scores showing the probable presence of depression, were mutation-positive (German general population with depression = 5% and non-patients with a health complaint = 13%(100)). Esplen et al(60) found 15% of her sample to be

depressed. A significant association was found with anxiety ($p < 0.011$) which was also shown by Esplen et al(60).

Most respondents, not only those who had depressive symptoms ($p < 0.017$) or event stress ($p < 0.020$), were concerned about a colon cancer being found during colonoscopy.

In their search for predictive factors for psychological distress, Murakami et al(68) found that a history of major or minor depression was a significant predictor, but genetic test results were not. According to Lerman et al(55) depression was the strongest predictor of an anticipated negative impact of genetic testing. Bleiker et al(99) reiterate that the best predictor of distress was an existing pre-test emotional state.

There was no difference in the levels of depression in mutation-positive and negative subjects in this cohort. Lerman et al(101) found that depression rates in subjects undergoing breast cancer genetic testing (pre- and post-testing), were reduced in non-carriers (mutation-negative) while it remained the same in the carriers (mutation-positive). Overall the mutation-positive subjects had a higher depression rate than the mutation-negative subjects.

No more than a third of the South African cohort had a form of psychological distress. The distress was not due to genetic results (supported by Bleiker et al(99)), coping-style or sociodemographic factors.

5.2.5 Genetic testing and medical decisions

5.2.5.1 Risk

Individuals with positive mutation results thought that they were at higher risk than those who were mutation-negative ($p < 0.047$). However, it was disappointing to find that a third of individuals who had been counselled and had information sessions over many years, still had not grasped their

appropriate risk for the development of colon cancer. Ten individuals, who had a positive genetic mutation result, thought that they were at a lower risk of developing colon cancer than the general population. Four of these subjects had already had surgery for a colonic neoplasm. Eleven individuals, who had negative genetic mutation results, thought that their risk of developing colon cancer was higher than the general population. These findings were confirmed by a Likert scale assessment of the chance of developing colon cancer. It was disappointing that Lloyd et al(102) found 66% of women who had attended genetic counselling, could not recall their lifetime risk for breast cancer accurately. Atkan-Collan et al(53) found that one month after receiving their results, individuals with a negative genetic mutation result understood their post-test risk more often than those with a positive genetic mutation result. They found this difference in understanding to be even greater after a year.

A significant association was found between awareness of risk and experiencing stressful life events ($p < 0.042$). Those who felt they were at higher risk and experienced stressful life events had a positive genetic mutation result and those who were at the same or lower risk and had not experienced stressful life events had negative results.

5.2.5.2 Colectomy

Preventative colectomy for HNPCC positive genetic mutation individuals with normal colons has not been routinely offered because the potential complications of surgery are far higher than those of colonoscopy. Nearly half of this cohort felt that it was a reasonable option. It appears that this option for management should be more openly discussed with high-risk individuals. The individuals who had not had colonic surgery felt strongly that preventative colectomy was an option ($p < 0.0001$).

5.2.5.3 Surveillance

Possible reasons for these answers may be fear of cancer. Imagining what it could be like to have the opposite genetic mutation result may have been too difficult or they may have felt that they were not doing enough when it came to surveillance. It may have been a reflection of hypervigilance which Hadley et al(81) showed amongst young mutation-positive individuals or, that there was a reluctance to cease surveillance even after a low-risk result(36;52;80). They may have thought it was what they were expected to say or that they did not understand the question.

This may explain the South African cohorts' enthusiasm to increase their surveillance even amongst mutation-negative individuals who had a colonoscopy in the last two years.

5.2.5.4 Severity and Cure

This cohort felt strongly that colon cancer could be cured and that survival was possible ($p < 0.0001$). There was a significant association found between cure, survival and colon cancer knowledge scores ($p < 0.009$).

5.2.5.5 Worry

The following statements: - "I am worried that surveillance may find bowel cancer" and "being at-risk for cancers other than colon cancer... "stirred the perceived worry in the cohort. It is understandable that mutation-positive individuals would carry the burden of this worry but it seems that mutation-negative individuals do as well. Eighteen subjects had found a way to dispel this burden and half of them had a positive genetic mutation result. The six subjects who reported having event stress were all incorporated in the group who were concerned about a colonoscopy finding a cancer ($p < 0.020$). Females were more worried about this than males ($p < 0.009$). Those with a potential depression ($p < 0.007$) were also concerned that cancer would be detected on colonoscopy.

It is of interest that mutation-negative respondents were more worried about the chance of a colonoscopy finding a colon cancer ($p < 0.047$) than mutation-positive individuals.

The strong thread of awareness of colonoscopy surveillance was continued with strong agreement about the effectiveness of the colonoscopy procedure in finding a colon cancer as well as the salience (easy to do) of the procedure itself. A significant association was found between this sentiment and those who had benefited from predictive genetic testing ($p < 0.047$). They also felt that individuals with colon cancer would survive ($p < 0.026$). Even those respondents with anxiety felt they could endure this procedure ($p < 0.019$).

The majority of respondents had a colonoscopy (even some mutation-negatives). A significant association was noted between those that had a colonoscopy and those that had affected first-degree relatives ($p < 0.0001$) (Figure 4.59) as well as being mutation-positive ($p < 0.0001$) (Figure 4.52). Those that had a colonoscopy in the last two years ($p< 0.004$) (Figure 4.53) and had an adenomatous polyp removed ($p < 0.039$) (Figure 4.54) were also mostly mutation-positive respondents.

Lerman et al(47) found that persons with lower socioeconomic status or alternatively, lack of formal education had low levels of utilisation of colorectal cancer surveillance. This was not the case in this South African cohort. This has been a challenge for health care professionals to convey complex risk and surveillance information in an easily accessible manner to people of different socioeconomic and cultural backgrounds. It also highlights the vulnerability of these populations and according to Hadley(36) and Johnson et al(79) the most common reason given for an individuals' decision to screen (or not to screen) was that the doctor did (or did not) recommend it.

Johnson et al(79) also found that factors which increase adherence to surveillance

were that the physician had recommended the procedure, knowledge of others with colon cancer, previous preventative health behaviour and a perception of a benefit of surveillance.

This cohort had an overwhelming confidence in the colonoscopy surveillance program with 49/64 (77%) respondents being sure of the effectiveness of colonoscopy to detect a colon cancer. With regards to the salience of colonoscopy, 40/64 (63%) respondents stated it would be easy for them to do.

Continuity of care may be the reason for the positive attitude toward surveillance and treatment, as the colonoscopy surveillance team is well known to the subjects. If a polyp or lesion was found, the same team is involved in their surgical management and follow-up.

5.3 Reliability

The following two examples show the reliability of the instrument:

1. Faecal occult blood testing had not been part of the information package given to this cohort as part of the predictive testing programme. It was felt that the high frequency of the 'don't know' responses, reflecting that the majority of respondents had never had the test, would be a sign of the honesty with which this questionnaire was answered. The results substantiate the reliability of the instrument by proving that the majority of these research subjects constantly were not sure of faecal occult blood testing.

2. The confidence shown by the cohort of the role of colonoscopy in the detection of colon cancer, was consistent throughout the questionnaire (e.g. test of colon cancer knowledge, surveillance decisions, effectiveness of surveillance methods, 'salience' of the colonoscopy procedure and participation in surveillance). This evidence suggests that the instrument

was reliable.

3. Two questions asked for an opinion on the risk of developing colon cancer. The responses of the subjects to the two questions were very similar. A significant association was found between risk and genetic mutation results. This was a reflection of true risk thus showing honesty in the subjects' responses.

4. The validated Miller's Behavioural Style Scale was used by Petersson (75) in her thesis about group rehabilitation of cancer patients. In her search for monitor and blunting coping styles she suggested utilising a sum score, created by subtracting the total blunting score from the total monitoring score. She claimed her sum median to be four. This median was also achieved with this sample.

5.4 Limitations

5.4.1 Sample size

This is a small study with a power of 36%. To achieve an 80% power with a 95% confidence interval would require 194 respondents. Assuming a 50% response rate, the sample size would need to be 388 individuals. This is not possible when using subjects with a single mutation.

5.4.2 Methodology

- No research has been done in South Africa on 'predictors' for accepting or rejecting predictive genetic testing for HNPCC. International studies have been done in this field, and in retrospect, this may have been a limitation of the methodology, the research subjects were asked to express opinions of what they may do or think if their genetic mutation result were different.

- A different method of data collection may have resulted in a higher response rate and sample size. i.e. telephonic or personal interview.
- The altered data collection strategy required that questionnaires be collected a month later (on the annual colonoscopy surveillance trip). The arrangements were of an ad hoc nature thus creating this possible methodology flaw.
- Multiple logistic regression analysis could have been used to examine the relationship between the dependant variable (genetic results) and independent variables. Bivariate analysis was used to analyse the associations between categorical variables. Multiple logistic regression could not be used due to the low statistical power and sample size as well too few significant associations.

5.4.3 Bias

5.4.3.1 Instrument

The length of the instrument, and time it took to fill it in, may have created a bias towards not completing some of the latter questions. Many of the research subjects solved the problem on their own by requesting to take the questionnaire home and completing it in their own time and comfort zone. This eliminated the problem of reactivity to the location and a strange environment.

Those that took the questionnaire home had a month to complete it. This administration variation might have created a bias. It may also have reduced the participation rate by not enabling queries to be readily answered by the research assistant.

5.4.3.2 Non-respondents

The non-respondents were mostly from the rural areas of the Northern Cape and were mostly mutation-negative. Even though the colonoscopy

surveillance team visited the area a month later, it may still have been difficult to return the completed questionnaire.

5.4.3.3 Response set bias

One (Question 28) of the questions shows what appears to be a response set bias. The responses to two questions seem to connect the researcher to the colonoscopy surveillance team and the responses are uncharacteristically inflated.

5.5 Summary

The sociodemographics showed middle to lower socioeconomic group of single and two parent families with mostly dependant children. They were also low scholastic achievers who predominantly reside where they were born.

Frequent exposure to cancer, knowledge of genetic risk, and a predictive genetic test were recalled by most of this group. Their retained knowledge of the consequences of HNPCC inheritance and subsequent effects was moderate to low except with regards to the question about colonoscopic surveillance. This showed a high level of insight into how to prevent colon cancer. The majority of this group also had a positive attitude toward predictive genetic testing.

At the time of the study most of the cohort was not experiencing stress about being at-risk for colon cancer, but there were those who had experienced stressful events. Most of the subjects with positive genetic mutation results had experienced a stressful event in the last year and these were mainly caused by death or cancer. At the time of the study most of the respondents were coping psychologically and did not have anxiety or depression.

The subjects were confident that the medical team would find, cure and enable survival after colon cancer was diagnosed. Even though the accuracy of the surveillance worried them, they seemed positive about undergoing the

procedure and were eager to decrease its intervals.

These health decisions are made based on an understanding of risk, and those individuals, who had misunderstood their risk, even after a predictive genetic test result had been disclosed, could have misdirected their health decisions.

5.6 Recommendations

This research shows that even though the same information is given to individuals, the retention and understanding varies considerably. The essence of the message conveyed in a predictive genetic information and result session is that of reduced (mutation-negative) or increased (mutation-positive) risk. Vital future health decisions are made with this information. In finding that there were individuals with both negative and positive genetic mutation results who had; i) misunderstood their risk, ii) low colon cancer knowledge scores, iii) experienced harm from predictive genetic testing iv) found that the impact of being at-risk for colon cancer had caused stress and; v) experienced depression and anxiety, it was important to recommend that not only individuals with positive genetic mutation results, but also those with negative results, require ongoing counselling.

The admission of concerns regarding not coping emotionally with genetic results strengthens this recommendation. The significant association with the worry about colonic and extracolonic cancers being detected, especially by mutation-negative individuals, also stresses the need for ongoing counselling.

Those mutation-positive individuals who had not already had surgery supported the concept of a preventative colectomy. Mutation-negative respondents also felt that it was an option. More research would need to be done to explore this clinical treatment option for HNPCC.

In the literature, a history of depression was found to be a barrier to genetic

testing and could delay preventative medical care(20;47;68). It is a recommendation that depression should possibly be screened for in an individual prior to embarking on a predictive genetic testing program. This information would be a guide for the counsellor.

Assessing depression status could also be a guide in assisting those individuals who know their high-risk genetic mutation results but do not utilise preventative health care.

Differences in coping styles of individuals were reported to effect assimilation of information as well as the engagement in preventative health behaviours(77). Assessment of an individuals' coping style, prior to entering a predictive genetic testing program, may be a useful guide for the counsellor. The method, style and volume of the information delivered to those with different coping styles, may require variation. More research is required to establish these variations.

5.7 Conclusion

This research has taken a broad but pointed look at individuals from four families, all of whom who have had predictive genetic results for a unique HNPCC mutation. What they have understood and experienced about this process, how they are coping and what decisions they have made, or will have to make, has been documented and analysed.

The respondents were forthcoming about their perceptions of current management. With the increasing role that genetics is playing in clinical medicine, there is an equally important role for nurses to fulfil in creating the support structures that these families need. This can only be achieved by education and funding for these key positions in the management of heritable diseases.

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7 APPENDICES

7.1 Appendix 1: Protocol for surveillance of high-risk HNPCC patients

- Initial colonoscopy is performed at age 16.
- Pre-predictive test counseling is offered at age 18.
- Those who wish to know their predictive genetic result have bloods taken after signing consent.
- Prior to releasing the test result they are counseled again.
- Results are released by the Professor of Human Genetics (Frof. Raj Ramesar).
- Those who choose not to have mutation analysis are offered surveillance colonoscopy on alternate years till age 30 and then annually to age 50.
- Those who test positive are offered colonoscopy on alternate years till age 30 and a total colectomy and ileorectal anastamosis will be the surgery of choice if a significant lesion is found.
- All women must have annual gynecological checkups.

7.2 Appendix 2: Original Australian Questionnaire

Registration number MF(noendo)

Date issued

Genetic Testing Questionnaire 1

We would like to ask you to complete the following questionnaire. All the information will be treated as *strictly confidential* and your identity will never be revealed in any reports. The completed questionnaires will be kept separately from any information that could identify you and will be kept securely under lock and key. There is no need for you to write your name on this questionnaire.

There are no right or wrong answers, and we ask you simply to tick those answers that most apply to you. *Some of the questions may not be relevant to you. However, it is important for the study that, if at all possible, you answer all the questions.*

Participation in this study is entirely voluntary; you are not obliged to participate and if you do participate you can withdraw at any time. Whatever your decision, it will not affect your medical treatment or your relationship with medical staff.

Before completing the questionnaire, may we request that you read and *sign the enclosed Consent Form.*

When you have completed the questionnaire, please return the questionnaire in the enclosed reply paid envelope and post it within the next seven days, if possible.

Would you like to receive a free summary report of the findings?

- ☐ Yes
- ☐ No

Thank you very much for your help in this study.

The first section of the questionnaire asks some general background questions which will be helpful to us in analysing the data. It will not be used for identification.

1. What is your current employment status? (Please tick the box that best describes your main job)
   - ☐[1] Full-time employed
   - ☐[2] Part-time employed
   - ☐[3] Unemployed
   - ☐[4] Self-employed
   - ☐[5] Homemaker
   - ☐[6] Full-time student
   - ☐[7] Part-time student
   - ☐[8] Permanently unable to work
   - ☐[9] Retired
   - ☐[10] Other_____

2. What is the *highest* qualification you have obtained since leaving school?
   - ☐[1] No post-school
   - ☐[2] Trade / apprenticeship
   - ☐[3] Certificate from college / TAFE
   - ☐[4] Diploma (beyond Year 12)
   - ☐[5] Bachelors degree
   - ☐[6] Postgraduate diploma / degree
   - ☐[7] Other _____

3. Do you speak a language other than English *at home*?
   - ☐[1] No, only English
   - ☐[2] Yes, Italian
   - ☐[3] Yes, Greek
   - ☐[4] Yes, Chinese
   - ☐[5] Yes, Arabic
   - ☐ Other _____

4. What is your country of birth?
   - ☐[1] Australia
   - ☐[2] United Kingdom
   - ☐[3] Greece
   - ☐[4] Vietnam
   - ☐[5] Lebanon
   - ☐ Other _____

5. What is your present marital status?
   - ☐[1] Never married
   - ☐[2] Widowed
   - ☐[3] Divorced
   - ☐[4] Separated but not divorced
   - ☐[5] Married or de facto

8. What is your age?

   Age: _____ years

7. Do you have children?
   - ☐[1] No. Please go to question 8.
   - ☐[2] Yes

   1st Child: Age: _____ Boy? ☐[1] Girl? ☐[2]

   2nd Child: Age: _____ Boy? ☐[1] Girl? ☐[2]

   3rd Child: Age: _____ Boy? ☐[1] Girl? ☐[2]

   4th Child: Age: _____ Boy? ☐[1] Girl? ☐[2]

   If you have more than four children, could you please supply further information on the last page of this questionnaire.

Now we would like to ask you some specific questions about genetic testing for HNPCC, a condition which predisposes to bowel cancer. The answers you give are *completely confidential* and will not be shown to the genetic counsellor or doctor in the genetic clinic. It is possible that the clinic staff may ask you some of these questions again during your consultation.

8. Whose idea was it to come to have a genetic test for HNPCC?
   - ☐[1] My own idea
   - ☐[2] Other family member
   - ☐[3] General practitioner
   - ☐[4] Specialist
   - ☐[5] Family bowel clinic
   - ☐[6] Other _____

9. HNPCC gene tests (blood tests which assess your likelihood of developing bowel cancer) may be discussed with you by the genetic counsellor or clinic doctor. Are you interested in having an HNPCC gene test?
   - ☐[1] Yes, definitely
   - ☐[2] Yes, probably
   - ☐[3] Probably not. Please go to Question 15.
   - ☐[4] Definitely not. Please go to question 15.
   - ☐[5] Don't know

10. Many people have considered reasons for having or not having an HNPCC gene test. We would like to know how much *each* of the following factors influenced your decision about whether or not to have a gene test.

Please continue on next page

A factor which influenced my decision about whether or not to have a gene test is...

a. ...to learn about my children's risk

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much
- ❑4 Not applicable

b. ...to help me understand what steps to take to reduce my risk of developing cancer

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

c. ...to plan for the future

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

d. ...to help research

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

e. ...to be certain about my risk

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

f. ...to make decisions about having children

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much
- ❑4 Not applicable

g. ...that I am worried about losing insurance

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

A factor which influenced my decision about whether or not to have a gene test is...

h. ...that I am concerned about the effect of gene testing on the family

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

i. ...that I believe that cancer is inevitable

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

j. ...that I would find it difficult to handle the knowledge emotionally

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

k. ...that the test result might be inaccurate

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

l. ...that I distrust modern medicine

- ❑1 Not at all
- ❑2 Somewhat
- ❑3 Very much

The following questions are to see how much you already know about genes for HNPCC, a condition which predisposes to bowel cancer. Please indicate whether you think each item is True or False or if you Don't Know.

11. Bowel cancer is always inherited.

- ❑1 True
- ❑2 False
- ❑3 Don't know

12. Everyone who has a gene for HNPCC will get bowel cancer.

- ❑1 True
- ❑2 False
- ❑3 Don't know

13. A person who does not have an altered HNPCC gene can still develop bowel cancer.

- ❑1 True
- ❑2 False
- ❑3 Don't know

14. There is more than one gene that can cause bowel cancer.

Please continue on next page

- ❑1 True
- ❑2 False
- ❑3 Don't know

15. The gene for HNPCC cancer can also increase the risk for other cancers.

- ❑1 True
- ❑2 False
- ❑3 Don't know

16. Colonoscopy (the inside of the bowel is viewed with a special tube) is very likely to detect bowel cancer if it is present.

- ❑1 True
- ❑2 False
- ❑3 Don't know

17. Faecal occult blood testing (a test which tests for blood in stool) will always detect bowel cancer.

- ❑1 True
- ❑2 False
- ❑3 Don't know

18. In a family where a gene for HNPCC has been found, those *without* the gene have the same risk for getting bowel cancer as the general population.

- ❑1 True
- ❑2 False
- ❑3 Don't know

19. If a person looks like, or has the personality of, a relative who has or has had bowel cancer, they are likely to have inherited the gene from that person.

- ❑1 True
- ❑2 False
- ❑3 Don't know

---

20. The following statements ask your opinions about being at risk for bowel cancer. In your opinion, compared to other people of your own age, what are your chances of getting bowel cancer?

- ❑1 Much lower
- ❑2 A little lower
- ❑3 About the same
- ❑4 A little higher
- ❑5 Much higher

b. Please rate your chances of getting bowel 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, that is prior to gene testing. In your opinion, what number from 0 to 100 reflects your chances of getting bowel cancer?

0 ——— 100

This section asks about your experience of having cancer screening tests. Please tick the box that comes closest to your situation.

21.

a. Have you ever had a colonoscopy (the inside of the bowel is viewed with a special tube)?

- ❑1 No. Please go to Question 22a.
- ❑2 Yes
- ❑3 Don't know. Please go to Question 22a.

b. If you have answered yes, have you had a colonoscopy *in the past two years*?

- ❑1 No
- ❑2 Yes
- ❑3 Don't know

c. Have you ever had an adenomatous polyp removed during a colonoscopy (a polyp is a small, usually benign growth)?

- ❑1 No
- ❑2 Yes
- ❑3 Don't know

22.a. Have you ever had a faecal occult blood testing (a test which tests for presence of blood in stool)?

22b. If you have answered yes, have you had a faecal occult blood test *in the past two years*?

- ❑1 No
- ❑2 Yes

Please continue on next page

25. It would be helpful to know what options you would consider should you decide to have a gene testand the test result indicate that you carry the gene for HNPCC. Below is a list of options, *some of which may not be relevant to you*. These options do not represent proven methods for preventing cancer but may be discussed with you by the genetic counsellor or clinic doctor who will explain what they involve. *Please note* your preferences as indicated here in no way limit the choices or options when the gene test result is available to you. Please tick the box which represents your preferred option.

If my blood test showed that I carry the gene for HNPCC, I would consider...

...a preventative colectomy (an operation to remove the bowel)

- ☐1 No
- ☐2 Yes
- ☐3 Don't know
- ☐4 Done / in progress

---

26. It would be helpful to know how the gene test result would affect your plans for having screening for bowel cancer. If your blood test showed that you do carry the gene for HNPCC, would you change your plans for bowel cancer screening? Please tick the box which is closest to your views.

If my blood test showed that I do carry the gene for HNPCC I would...

28a.
- ☐1 ...not change my screening
- ☐2 ...have more screening often
- ☐3 ...have less screening

If your blood test showed that you do NOT carry the gene for HNPCC, would you change your plans for bowel cancer screening?

- ☐1 No. Please go to Question 25.
- ☐2 Yes
- ☐3 Don't know. Please go to Question 25.

If my blood test showed that I do NOT carry the gene for HNPCC I would...

28b.
- ☐1 ...not change my screening
- ☐2 ...have more screening
- ☐3 ...have less screening

This section asks about your opinions about bowel cancer and having bowel cancer screening tests. We would like to know how much you agree with *each* of the following statements. Please answer all questions even if you have never had bowel cancer screening. Please tick the statement which comes closest to your opinion.

29. I think people diagnosed with bowel cancer have little chance of surviving the disease.

- ☐1 Strongly disagree
- ☐2 Mildly disagree
- ☐3 Mildly agree
- ☐4 Strongly agree

30. When found early, bowel cancer can be cured.

- ☐1 Strongly disagree
- ☐2 Mildly disagree
- ☐3 Mildly agree
- ☐4 Strongly agree

31. I am worried that bowel cancer screening will show that I have bowel cancer.

- ☐1 Strongly disagree
- ☐2 Mildly disagree
- ☐3 Mildly agree
- ☐4 Strongly agree

32. Colonoscopy (the inside of the bowel is viewed with a special tube) is an effective way to find bowel cancer early.

- ☐1 Strongly disagree
- ☐2 Mildly disagree
- ☐3 Mildly agree
- ☐4 Strongly agree
- ☐5 Don't know

33. Having a colonoscopy would be an easy thing for me to do.

- ☐1 Strongly disagree
- ☐2 Mildly disagree
- ☐3 Mildly agree
- ☐4 Strongly agree
- ☐5 Don't know

34. Faecal occult blood testing (a test which tests for blood in stool) is an effective way to find bowel cancer early.

- ☐1 Strongly disagree
- ☐2 Mildly disagree
- ☐3 Mildly agree
- ☐4 Strongly agree
- ☐5 Don't know

---

35. Faecal occult blood testing would be an easy thing for me to do.

Please continue on next page

- ☐1 Strongly disagree
- ☐2 Mildly disagree
- ☐3 Mildly agree
- ☐4 Strongly agree
- ☐5 Don't know

---

41. In some families the gene for HNPCC also increases the risk for cancer in other parts of the body. We would be interested to know how concerned you are about being at risk for cancers other than bowel cancer.

Being at risk for cancers other than bowel cancer...
- ☐1 ...strongly concerns me
- ☐2 ...somewhat concerns me
- ☐3 ...does not concern me

Please explain (optional)

_____
_____
_____
_____
_____

Different people cope with stress in different ways. In the following, four imaginary scenarios are described and we would like to know how you think you would react in each of these situations. Please read each question carefully and tick alongside *all* the statements that would describe what you would do.

42. Vividly imagine that you are afraid of the dentist and have to get some dental work done. Which of the following would you do? Please tick *all* of the statements that might apply to you.

- ☐ I would ask the dentist exactly what he was going to do.
- ☐ I would take an anti-anxiety drug or have a drink before going.
- ☐ I would try to think about pleasant memories.
- ☐ I would want the dentist tell me when I would feel pain.
- ☐ I would try to sleep.
- ☐ I would watch all the dentist's movements and listen for the sound of his drill.
- ☐ I would watch the flow of water from my mouth to see if it contained blood.
- ☐ I would want to do mental puzzles in my mind.

43. Vividly imagine that you are being held hostage by a group of armed terrorists in a public building. Which of the following would you do? Please tick *all* the statements that might apply to you.

- ☐ I would sit by myself and have as many daydreams and fantasies as I could.
- ☐ I would stay alert and try to keep myself from falling asleep.
- ☐ I would exchange life stories with the other hostages.
- ☐ If there was a radio present, I would stay near it and listen to the news items about what the police were doing.
- ☐ I would watch every movement of my captors and keep an eye on their weapons.
- ☐ I would try to sleep as much as possible.
- ☐ I would think about how nice it's going to be when I get home.
- ☐ I would make sure I knew where every possible exit was.

44. Vividly imagine that, due to a large drop in sales, it is rumoured that several people in your department at work will be dismissed. Your supervisor has handed in an evaluation of your work for the past year. Please tick *all* the statements that might apply to you.

- ☐ I would talk to my fellow workers to see whether they knew anything about what the supervisor's evaluation of me said.
- ☐ I would review the list of duties for my present job and try to work out if I had fulfilled all of them.
- ☐ I would go to the movies to take my mind off things.
- ☐ I would try to remember any arguments or disagreements I might have had with the supervisor that would have lowered his opinion of
- ☐ I would tell my spouse that I'd rather not discuss my chances of being dismissed.
- ☐ I would try to think which employees in my department the supervisor might have thought had done the worst job.
- ☐ I would continue doing my work as if nothing special was happening.

45. Vividly image that you are on an aeroplane, thirty minutes from your destination, when the plane unexpectedly goes into a deep dive and then suddenly levels off. After a short time, the pilot announces that nothing is wrong, although the rest of the ride may be rough. You, however, are not convinced that all is well. Please tick *all* statements that might apply to you.

- ☐ I would carefully read the information provided about safety procedures in the plane and make sure I know where the emergency exists were.
- ☐ I would make small talk with the passenger beside me.
- ☐ I would watch the end of the movie, even if I had seen it before.

Please continue on next page

- ☐ I would call for the flight attendant and ask exactly what the problem was.
- ☐ I would order a drink or tranquilliser from the stewardess.
- ☐ I would listen carefully to the engines for the unusual noises and would watch the crew to see their behaviour was out of the ordinary.
- ☐ I would talk to the passenger beside me about what might be wrong.
- ☐ I would settle down and read a book or magazine or write a letter.

Office use only:
Score M _____
Score B _____

46.a. Have you experienced serious, stressful life event/s over the past year?

☐[1] No. Please go to Question 47.
☐[2] Yes

b) What were the life events? Please circle the number to the left of the life event/s.

(1) Parent's diagnosis with bowel cancer
(2) Parent's death from bowel cancer

This questionnaire is designed to help us know how you feel. Please read each item below, and tick the box which comes closest to how you have been feeling in the PAST WEEK. There are no right or wrong answers. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought out response.

47. I still enjoy the things I used to enjoy.

(3) Sibling's diagnosis with bowel cancer
(4) Sibling's death from bowel cancer
(5) Death of relative or friend from causes other than bowel cancer
(6) My own diagnosis of benign bowel disease
(7) Moving household
(8) Separation or divorce from my partner
(9) Work-related stress
(10) Other (please specify)

c.)How stressful were these event(s) on you over the past year? Please make a mark on one of the vertical lines to indicate how stressful.

Not stressful Very stressful

- ☐ Definitely as much
- ☐ Not quite so much
- ☐ Only a little
- ☐ Hardly at all

48. I can laugh and see the funny side of things.

- ☐ As much as I always could
- ☐ Not quite so much now
- ☐ Definitely not so much now
- ☐ Not at all

49. I feel cheerful.

- ☐ Not at all
- ☐ Not often
- ☐ Sometimes
- ☐ Most of the time

50. I feel as if I am slowed down

- ☐ Sometimes
- ☐ Not at all
- ☐ Very often
- ☐ Nearly all the time

51. I have lost interest in my appearance.

- ☐ Definitely
- ☐ I don't take as much care as I should
- ☐ I may not take quite as much care
- ☐ I take just as much care as ever

53. I can enjoy a good book or radio or TV program

- ☐ Often
- ☐ Sometimes
- ☐ Not often
- ☐ Very seldom

A number of statements which people have used to describe themselves are given below. Read each statement and then tick a box to indicate how you feel RIGHT NOW AT THIS MOMENT.

	Not at all	Somewhat	Moderately	Very much
54. I feel calm	☐	☐	☐	☐
55. I feel tense	☐	☐	☐	☐

Please continue on next page

56. I am upset	☐	☐	☐	☐
57. I feel relaxed	☐	☐	☐	☐
58. I feel content.....	☐	☐	☐	☐
59. I am worried	☐	☐	☐	☐

Below is a list of comments made by people about being at risk for bowel cancer. Please tick a box to indicate how frequently these comments were true for you during *the last seven days*.

	Not at all	Rarely	Sometimes	Often
60. I thought about it when I didn't mean to	☐	☐	☐	☐
61. I avoided letting myself get upset when I thought about or was reminded of it	☐	☐	☐	☐
62. I tried to remove it from my memory	☐	☐	☐	☐
63. I had trouble falling asleep or staying asleep because of pictures or thoughts about it that came into my mind	☐	☐	☐	☐
64. I had waves of strong feelings about it	☐	☐	☐	☐

Please continue on next page

		Not at all	Rarely	Sometimes	Often
65.	I had dreams about it	❑	❑	❑	❑
66.	I stayed away from reminders of it	❑	❑	❑	❑
67.	I felt as if it wasn't real	❑	❑	❑	❑
68.	I tried not to talk about it	❑	❑	❑	❑
69.	Pictures popped up into my mind	❑	❑	❑	❑
70.	Other things kept making me think about it	❑	❑	❑	❑
71.	I was aware that I still had a lot of feelings about it, but I didn't deal with them	❑	❑	❑	❑
72.	I tried not to think about it	❑	❑	❑	❑
73.	Any reminder brought back feelings about it	❑	❑	❑	❑
74.	My feelings were sort of numb	❑	❑	❑	❑

Office use only:
Subtotal I _____
Subtotal A _____

---

75. Are there any other issues that we have not addressed in this questionnaire?

_____

_____

_____

_____

_____

_____

May we request that you post this questionnaire and the enclosed Consent Form at your earliest convenience, using the prepaid return envelope addressed to the Murdoch Institute.

YOU HAVE MADE IT!!
THANKS AGAIN.

7.3 Appendix 3: Permission to use the Australian Questionnaire

Subject: Re: Contact
Date: Mon, 02 Apr 2001 16:42:50 +1000
From: "Bettina Meiser "<B.Meiser@unsw.EDU.AU>
To: <ursula@curie.uct.ac.za> "Algar U Ursula Sr"

Dear Ursula,

Thank you very much for contacting me with regard to previous studies on knowledge, attitudes and beliefs of families towards genetic testing for HNPCC.

For the past three years I have been involved in a study assessing the impact of genetic testing for HNPCC. Baseline data collection for this study will be completed in December this year, and 12-month follow up in December 2002. The study is being administered at the Victorian Clinical Genetics Services, Melbourne, and data is being collected through six familial cancer clinics, in Sydney, Perth, Brisbane and Melbourne.

As part of this study, we also assessed knowledge and attitudes towards genetic testing for HNPCC. To assess perceived importance of benefits and limitations of genetic testing for HNPCC, we modified a previously used scale on attitudes towards BRCA1 testing. The publication details are:

Lerman C, Narod S, Schulman K, et al. BRCA1 testing in families with hereditary breast-ovarian cancer. JAMA 1996;275(24):1885-1892.

To assess knowledge about HNPCC genetics, we modified the scale assessing breast cancer genetics knowledge used in the above study.

Over the past few years several studies of attitudes, knowledge of genetic testing for HNPCC have been published. I undertook a literature search recently and found the following articles:

Codori AM, Petersen GM, Miglioretti DL, et al. Attitudes towards colon cancer gene testing: Factors predicting test uptake. Cancer Epidemiol Biomarkers Prev 1999;8:345-353.

Croyle R, Lerman C. Interest in genetic testing for colon cancer susceptibility: Cognitive and emotional correlates. Prev Med 1993;22(2):284-292.

Glanz K, Grive J, Marchand LL, Gotay C. Underreporting of a family history of colon cancer: Correlates and implications. Cancer Epidemiol Biomarkers Prev 1999;8:635-639.

Lerman C, Marshall J, Audrain J, Gomez-Caminero A. Genetic testing for colon cancer susceptibility: Anticipated reactions of patients and challenges to providers. Int J Cancer 1996;69:58-61.

Lerman C, Hughes C, Trock BJ, et al. Genetic testing in families with hereditary nonpolyposis colon cancer. JAMA 1999;281(17):1618-1622.

Petersen GM, Larkin E, Codori AM, et al. Attitudes toward colon cancer gene testing: Survey of relatives of colon cancer patients. Cancer Epidemiology, Biomerkers and Prevention 1999;8:337-344.

Smith KR, Croyle RT. Attitudes toward genetic testing for colon cancer risk.
Am J Pub Health 1995;85(10):1435-1438.

Vernon SW, Perz CA, Gritz ER, et al. Correlates of psychological distress in colorectal cancer patients undergoing genetic testing for hereditary colon cancer.
Health Psychol 1997;16(1):73-86.

You might consider matching some of your outcome measures with one of the scales published in these articles.

I hope this information is helpful to you. Please do not hesitate to contact me again, should you require further information.

Best wishes,
Bettina Meiser

Bettina Meiser, PhD
Head of Psychosocial Research, Department of Medical Oncology,
Prince of Wales Hospital, Randwick, NSW 2031, Sydney
Thursday & Friday: Tel 0061-2-9382-2638, Fax 0061-2-9382-2588

NHMRC Post-Doctoral Fellow, Department of Psychological Medicine
Block 4, Level 5, Royal North Shore Hospital, St Leonards, NSW 2065

Date: Mon, 09 Apr 2001 17:19:41 +1000
To: "Algar, U, Ursula, Sr" <ursula@curie.uct.ac.za>
From: Bettina Meiser <B.Meiser@unsw.EDU.AU>
Subject: Re: Help again

Dear Ursula,

I checked with the other members of our team about shring the measures we
used. Everyone felt happy with this provided you acknowledge our group in
any publications that may emerge from your research work.

Please find attached (i) a short research plan, (ii) the baseline questionnaire for women (with questionaires about ovarian and endometrial
cancer), (iii) the baseline questionnaire for men (without questions about
ovarian and endometrial cancer), (iv) the one-year follow up questionnaire
for women, and (v) that for men.

I hope this is helpful information. Please let me know if you have difficulty opening the files, and I will save them in a different format.
Please do not hesitate to contact me again should you require further details.

Best wishes,
Bettina Meiser

Subject:
Re: Re connecting Date: Sun, 23 Feb 2003 16:42:03 +1100
From: Bettina Meiser <b.meiser@unsw.edu.au>
To: ursula@curie.uct.ac.za

Dear Ursula,

Good to hear from you.

It's a shame you weren't able to work on your HNPCC study over the past, year, but I am sure as you say, that you will be able to continue again.

As for our study, it turns out that we won't be able to complete 12 month follow up data collection until May 2003. Therefore, there are no results to report as yet. I anticipate that we will be submitting a manuscript in about July/August next year.

Good luck with your study!

Best wishes,
Bettina

Bettina Meiser, PhD
Head of Psychosocial Research, Department of Medical Oncology,
Prince of Wales Hospital, Randwick, NSW 2031, Sydney
Tel 0061-2-9382-2638, Fax 0061-2-9382-2588
http://www.psycho-oncology.net/Webpage20021.html

You could make a reference to our group (there is no official name as yet for this group) by saying that the group is undertaking an Australian multicentre study on the psychological impact of genetic testing and that the Chief Investigators are: Dr Jane Halliday, Dr Bettina Meiser, Dr Clara Gaff, and Associate Professor James St John. You could make reference to our e-mail correspondence, confirming that we are happy to share our questionnaire with you.

7.4 Appendix 4 : South African English version of the Questionnaire

Registration number

Date issued

Genetic Testing Questionnaire

Thank you for your interest in our research project.

We would like to ask you to complete the following questionnaire. All the information will be treated as strictly confidential and your identity will never be revealed in any reports. The completed questionnaires will be kept separate from any information that could identify you and will be kept securely under lock and key. There is no need for you to write your name on this questionnaire.

There are no right or wrong answers, and we ask you simply to tick those answers that most apply to you. Some of the questions may not be relevant to you. However, it is important for the study that, if at all possible, you answer all the questions.

Participation in this study is entirely voluntary; you are not obliged to participate and if you do participate you can withdraw at any time. Whatever your decision, it will not affect your medical treatment or your relationship with medical staff.

Before completing the questionnaire, we request that you read and sign the enclosed Consent Form. _____ is available to answer any questions you may have about the questionnaire. Once you have completed the questionnaire, please return it to _____

Thank you very much for your help in this study.

Consent Form

I, ..., hereby consent to participate in this survey.

I declare that all information given is an honest reflection of my thoughts and feelings at the time of the survey.

I am aware that all the information I have given will remain confidential.

I understand that my participation in the survey is voluntary and of my own free will and that I may withdraw my participation at any stage.

Signature: _____

Date: _____

The first section of the questionnaire asks some general background questions, which will be helpful to us in analysing the data. It will not be used for identification purposes.

1. What is your current employment status?
(Please tick the box that best describes your main job)

☐1 Full-time employed
☐2 Part-time employed
☐3 Unemployed
☐4 Self-employed
☐5 Housewife
☐6 Full-time student
☐7 Part-time student
☐8 Permanently unable to work
☐9 Retired
☐10 Other_____

2. What standard did you reach at school?

☐1 Standard 10 (Matric)
☐2 Standard 9
☐3 Standard 8
☐4 Standard 7
☐5 Standard 6
☐6 Standard 5
☐7 Other _____

3. What is the highest qualification you have obtained since leaving school?

☐1 No post-school
☐2 Trade / apprenticeship
☐3 Certificate from college
☐4 Diploma (beyond Std 10)
☐5 Bachelors degree
☐6 Postgraduate diploma / degree
☐7 Other _____

4. What is your present marital status?

☐1 Never married
☐2 Widowed
☐3 Divorced
☐4 Separated but not divorced

□5 Married or married in common law

5. What is the town of your birth?

_____

6. What is your date of birth?

_____

7. Do you have a strong faith?

□1 Yes
□2 No

8. Do you have a medical aid?

□1 Yes
□2 No

9. Are you male or female?

□1 Male
□2 Female

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

□1 No.
□2 Yes

10a) 1st Child: Age: _____
Boy? □1
Girl? □2

10b) 2nd Child: Age: _____
Boy? □1
Girl? □2

10c) 3rd Child: Age: _____
Boy? □1
Girl? □2

10d) 4th Child: Age: _____
Boy? □1
Girl? □2

If you have more than four children, could you please supply further information on the last page of this questionnaire.

11. Some questions about your family.

11a) How many brothers do you have?

_____

11b) How many sisters do you have?

_____

11c) How many of your brothers have had cancer?

_____

11d) How many of your sisters have had cancer?

_____

11e) How many of your brothers are still alive?

_____

11f) How many of your sisters are still alive?

_____

11g) Did one of your parents have cancer?

□1 Yes
□2 No

11h) How old were you when you realised you were at risk for bowel cancer?

_____

12. Whose idea was it to come to have a genetic test for hereditary bowel cancer?

□1 My own idea
□2 Other family member
□3 General practitioner
□4 Specialist
□5 Family bowel clinic
□6 Other _____

13. Have you had a genetic blood test result for hereditary bowel cancer?

□1 Yes
□2 No
□3 Not sure

14. Who do you visit if you feel sick?

□1 General practitioner
□2 The clinic sister/doctor
□3 No one
□4 Other _____

15. Many people have considered reasons for having or not having a Hereditary Bowel Cancer gene test. We would like to know how much each of the following factors influenced your decision about having a gene test.

A factor which influenced my decision to have a gene test is...

15a. ...to learn about my children's risk

□1 Not at all
□2 Somewhat
□3 Very much
□4 Not applicable

15b. ...to help me understand what steps to take to reduce my risk of developing cancer

□1 Not at all
□2 Somewhat
□3 Very much

15c. ...to plan for the future

□1 Not at all
□2 Somewhat
□3 Very much

15d. ...to help research

□1 Not at all
□2 Somewhat
□3 Very much

15e. ...to be certain about my risk

□1 Not at all
□2 Somewhat
□3 Very much

15f. ...to make decisions about having children

□1 Not at all
□2 Somewhat
□3 Very much
□4 Not applicable

A factor which influenced my decision to have a gene test is...

15g. ...that I was worried about losing insurance

□1 Not at all
□2 Somewhat
□3 Very much
□4 Not applicable

15h. ...that I was concerned about the effect of gene testing would have on the family

□1 Not at all
□2 Somewhat
□3 Very much

15I. ...that I believed that cancer was inevitable

□1 Not at all
□2 Somewhat
□3 Very much

15j. ...that I would have found it difficult to handle the knowledge emotionally

□1 Not at all
□2 Somewhat

□3 Very much

15k. ...that the test result might be been inaccurate

□1 Not at all
□2 Somewhat
□3 Very much

15L. ...that I distrusted modern medicine

□1 Not at all
□2 Somewhat
□3 Very much

The following questions are to see how much you already know about genes for Hereditary Bowel Cancer (a condition which predisposes to bowel cancer). Please indicate whether you think each item is True or False or if you Don't Know.

16. Bowel cancer is always inherited.

□1 True
□2 False
□3 Don't know

17. Everyone who has a gene for Hereditary Bowel Cancer will get bowel cancer.

□1 True
□2 False
□3 Don't know

18. A person who does not have an altered Hereditary Bowel Cancer gene can still develop bowel cancer.

□1 True
□2 False
□3 Don't know

19. There is more than one gene that can cause bowel cancer.

□1 True
□2 False
□3 Don't know

20. The gene for Hereditary Bowel Cancer can also increase the risk for other cancers.

□1 True
□2 False
□3 Don't know

21. Colonoscopy (the inside of the bowel is viewed with a special tube) is very likely to detect bowel cancer if it is present.

□1 True
□2 False
□3 Don't know

22. Faecal occult blood testing (a test which tests for blood in stool) will always detect bowel cancer.

□1 True
□2 False
□3 Don't know

23. In a family where a gene for Hereditary Bowel Cancer has been found, those without the gene have the same risk for getting bowel cancer as the general population.

□1 True
□2 False
□3 Don't know

24. If a person looks like, or has the personality of, a relative who has or has had bowel cancer, they are likely to have inherited the gene from that person.

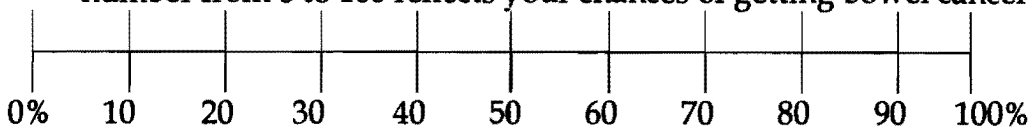
□1 True
□2 False
□3 Don't know

25a. The following statements ask your opinion about being at risk for bowel cancer. In your opinion, compared to other people of your own age, what are your chances of getting bowel cancer?

□1 Much lower
□2 A little lower
□3 About the same
□4 A little higher

□5 Much higher

25b Please rate your chances of getting bowel 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?



This section asks about your experience of having cancer-screening tests. Please tick the box that comes closest to your situation.

26a. Have you ever had a colonoscopy (the inside of the bowel is viewed with a special tube)?

□1 No. Please go to Question 26d.
□2 Yes
□3 Don't know. Please go to Question 26d.

26b. If you have answered yes, have you had a colonoscopy *in the past two years*?

□1 No
□2 Yes
□3 Don't know

26c. If you have answered yes, have you ever had an adenomatous polyp removed during a colonoscopy (a polyp is a small, usually benign growth)?

□1 No
□2 Yes
□3 Don't know

26d. Have you ever had a faecal occult blood test (a test which tests for presence of blood in stool)?

□1 No. Please go to Question 27.
□2 Yes
□3 Don't know. Please go to Question 27.

26e. If you have answered yes, have you had a faecal occult blood test *in the past two years*?

□1 No
□2 Yes

27. It would be helpful to know what options you would consider if your gene test result indicated that you carry the gene for hereditary bowel cancer.

Below is a list of options, *some of which may not be relevant to you.* These options do not represent proven methods for preventing cancer but may be discussed with you by the genetic counsellor or clinic doctor who will explain what they involve. Please tick the box which represents your preferred option.

If my blood test showed that I carry the gene for hereditary bowel cancer, I would consider...

...a preventative colectomy (an operation to remove the bowel)

☐1 No
☐2 Yes
☐3 Don't know
☐4 Done / in progress

28. It would be helpful to know how the gene test result would affect your plans for having screening for bowel cancer. If your blood test showed that you do carry the gene for hereditary bowel cancer, would you change your plans for bowel cancer screening? Please tick the box which is closest to your views.

28a. ☐1 ...not change my screening
☐2 ...have screening more often
☐3 ...have less screening
☐4 ...stop screening

If your blood test showed that you do NOT carry the gene for hereditary bowel cancer, would you change your plans for bowel cancer screening?

If my blood test showed that I do NOT carry the gene for hereditary bowel cancer I would...

28b. ☐1 ...not change my screening
☐2 ...have more screening
☐3 ...have less screening
☐4 ...stop screening

This section asks about your opinions about bowel cancer and having bowel cancer screening tests. We would like to know how much you agree with

each of the following statements. Please answer all questions even if you have never had bowel cancer screening. Please tick the statement which comes closest to your opinion.

29. I think people diagnosed with bowel cancer have little chance of surviving the disease.

□1 Strongly disagree
□2 Mildly disagree
□3 Mildly agree
□4 Strongly agree

30. When found early, bowel cancer can be cured.

□1 Strongly disagree
□2 Mildly disagree
□3 Mildly agree
□4 Strongly agree

31. I am worried that bowel cancer screening will show that I have bowel cancer.

□1 Strongly disagree
□2 Mildly disagree
□3 Mildly agree
□4 Strongly agree

32. Colonoscopy (the inside of the bowel is viewed with a special tube) is an effective way to find bowel cancer early.

□1 Strongly disagree
□2 Mildly disagree
□3 Mildly agree
□4 Strongly agree
□5 Don't know

33. Having a colonoscopy would be an easy thing for me to do.

□1 Strongly disagree
□2 Mildly disagree
□3 Mildly agree
□4 Strongly agree
□5 Don't know

34. **Faecal occult blood testing (a test which tests for blood in stool) is an effective way to find bowel cancer early.**

☐1 Strongly disagree
☐2 Mildly disagree
☐3 Mildly agree
☐4 Strongly agree
☐5 Don't know

35. Faecal occult blood testing would be an easy thing for me to do.

☐1 Strongly disagree
☐2 Mildly disagree
☐3 Mildly agree
☐4 Strongly agree
☐5 Don't know

36. In some families the gene for hereditary bowel cancer also increases the risk for cancer in other parts of the body. We would be interested to know how concerned you are about being at risk for cancers other than bowel cancer.

Being at risk for cancers other than bowel cancer...

☐1 ...strongly concerns me
☐2 ...somewhat concerns me
☐3 ...does not concern me

Please explain (optional)

_____
_____
_____

Different people cope with stress in different ways. In the following, four imaginary scenarios are described and we would like to know how you think you would react in each of these situations. Please read each question carefully and tick alongside all the statements that would describe what you would do.

37. Vividly imagine that you are afraid of the dentist and have to get some dental work done. Which of the following would you do? Please tick **all** of the statements that might apply to you.

37a)☐ I would ask the dentist exactly what he was going to do.

37b)□ I would take an anti-anxiety drug or have a drink before going.

37c)□ I would try to think about pleasant memories.

37d)□ I would want the dentist tell me when I would feel pain.

37e)□ I would try to sleep

37f)□ I would watch all the dentist's movements and listen for the sound of his drill.

37g)□ I would watch the flow of water from my mouth to see if it contained blood.

37h)□ I would want to do mental puzzles in my mind.

38. Vividly imagine that you are being held hostage by a group of armed terrorists in a public building. Which of the following would you do? Please tick **all** the statements that might apply to you.

38a)□ I would sit by myself and have as many daydreams and fantasies as I could.

38b)□ I would stay alert and try to keep myself from falling asleep.

38c)□ I would exchange life stories with the other hostages.

38d)□ If there was a radio present, I would stay near it and listen to the news items about what the police were doing

38e)□ I would try to sleep as much as possible.

38f)□ I would think about how nice it's going to be when I get home.

38g)□ I would make sure I knew where every possible exit was.

39. Vividly imagine that, due to a large drop in sales, it is rumoured that several people in your department at work will be dismissed. Your supervisor has handed in an evaluation of your work for the past year. Please tick **all** the statements that might apply to you.

39a)□ I would talk to my fellow workers to see whether they knew anything about what the supervisor's evaluation of me said.

39b)□ I would review the list of duties for my present job and try to work out if I had fulfilled all of them.

39c)□ I would try to remember any arguments or disagreements I might have had with the supervisor that would have lowered his opinion of me.

39d)□ I would push all thought of being dismissed out of my mind.

39e)□ I would tell my spouse that I'd rather not discuss my chances of being dismissed.

39f)□ I would try to think which employees in my department the supervisor might have thought had done the worst job.

39g)□ I would continue doing my work as if nothing special was happening.

40. Vividly image that you are on an aeroplane, thirty minutes from your destination, when the plane unexpectedly goes into a deep dive and then suddenly levels off. After a short time, the pilot announces that nothing is wrong, although the rest of the ride may be rough. You, however, are not convinced that all is well. Please tick ***all*** statements that might apply to you.

40a)□ I would carefully read the information provided about safety procedures in the plane and make sure I know where the emergency exists were.

40b)□ I would make small talk with the passenger beside me.

40c)□ I would watch the end of the movie, even if I had seen it before.

40d)□ I would call for the flight attendant and ask exactly what the problem was.

40e)□ I would order a drink or tranquilliser from the stewardess.

40f)□ I would listen carefully to the engines for the unusual noises and would watch the crew to see their behaviour was out of the ordinary.

40g)□ I would talk to the passenger beside me about what might be wrong.

40h)□ I would settle down and read a book or magazine or write a letter.

41a. Have you experienced serious, stressful life event/s over the past year?

□[1] No. Please go to Question 42.

□[2] Yes

41b. What were the life events? Please circle the number to the left of the life event/s.

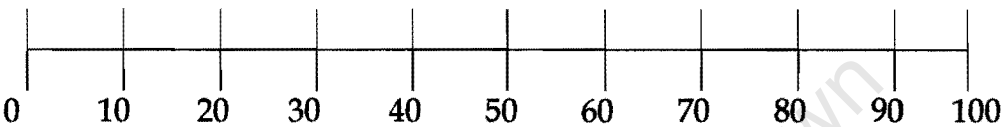
(1) Parent's diagnosis with bowel cancer

(2) Parent's death from bowel cancer

(3) Sibling's diagnosis with bowel cancer
(4) Sibling's death from bowel cancer
(5) Death of relative or friend from causes other than bowel cancer
(6) My own diagnosis of benign bowel disease
(7) Moving household
(8) Separation or divorce from my partner
(9) Work-related stress
(10) Other (please specify)

_____

41c. How stressful were these event(s) on you over the past year? Please make a mark on one of the vertical lines to indicate how stressful.



Not stressful stressful Very

This questionnaire is designed to help us know how you feel. Please read each item below, and tick the box which comes closest to how you have been feeling in the PAST WEEK. There are no right or wrong answers. Don't take too long over your replies; your immediate reaction to each item will probably be more accurate than a long thought out response.

42. I still enjoy the things I used to enjoy.

☐ Definitely as much
☐ Not quite so much
☐ Only a little
☐ Hardly at all

43. I can laugh and see the funny side of things.

☐ As much as I always could
☐ Not quite so much now
☐ Definitely not so much now
☐ Not at all

44. I feel cheerful.

☐ Not at all
☐ Not often
☐ Sometimes
☐ Most of the time

45. I feel as if I am slowed down

- ☐ Nearly all the time
- ☐ Very often
- ☐ Sometimes
- ☐ Not at all

46. I have lost interest in my appearance.

- ☐ Definitely
- ☐ I don't take as much care as I should
- ☐ I may not take quite as much care
- ☐ I take just as much care as ever

47. I look forward with enjoyment to things.

- ☐ As much as I ever did
- ☐ Rather less than I used to
- ☐ Definitely less than I used to
- ☐ Hardly at all

48. I can enjoy a good book or radio or TV program

- ☐ Often
- ☐ Sometimes
- ☐ Not often
- ☐ Very seldom

A number of statements which people have used to describe themselves are given below. Read each statement and then tick a box to indicate how you feel RIGHT NOW AT THIS MOMENT.

		Not at all	Somewhat	Moderately	Very much
49.	I feel calm	☐1	☐2	☐3	☐4
50.	I feel tense	☐1	☐2	☐3	☐4
51.	I am upset	☐1	☐2	☐3	☐4
52.	I feel relaxed	☐1	☐2	☐3	☐4
53.	I feel content	☐1	☐2	☐3	☐4
54.	I am worried	☐1	☐2	☐3	☐4

Below is a list of comments made by people about being at risk for bowel cancer. Please tick a box to indicate how frequently these comments were true for you during *the last seven days.*

		Not at all	Rarely	Sometimes	Often
55.	I thought about it when I didn't mean to	□1	□2	□3	□4
56.	I avoided letting myself get upset when I thought about or was reminded of it	□1	□2	□3	□4
57.	I tried to remove it from my memory	□1	□2	□3	□4
58.	I had trouble falling asleep or staying asleep because of pictures or thoughts about it that came into my mind	□1	□2	□3	□4
59.	I had waves of strong feelings about it	□1	□2	□3	□4

		Not at all	Rarely	Sometimes	Often
60.	I had dreams about it	□1	□2	□3	□
61.	I stayed away from reminders of it	□1	□2	□3	□4
62.	I felt as if it wasn't real	□1	□2	□3	□4
63.	I tried not to talk about it	□1	□2	□3	□4
64.	Pictures popped up into my mind	□1	□2	□3	□4
65.	Other things kept making me think about it □4		□1	□2 □3	
66.	I was aware that I still had a lot of feelings □4 about it, but I didn't deal with them		□1	□2 □3	
67.	I tried not to think about it	□1	□2	□3	□4
68.	Any reminder brought back feelings about it	□1	□2	□3	□4
69.	My feelings were sort of numb	□1	□2	□3	□4

70. Are there any other issues that we have not addressed in this questionnaire?

10cont.

10f) 5th Child: Age: _____
Boy? □1
Girl? □2

10g) 6th Child: Age: _____
Boy? □1
Girl? □2

10h) 7th Child: Age: _____
Boy? □1
Girl? □2

10I) 8th Child: Age: _____
Boy? □1
Girl? □2

10j) 9th Child: Age: _____
Boy? □1
Girl? □2

10k) 10th Child: Age: _____
Boy? □1
Girl? □2

YOU HAVE MADE IT!!
THANKS AGAIN.

7.5 Appendix 5: Afrikaans translation of questionnaire prior to piloting

Registrasienommer

Datum uitgereik

Genetiese Toetsingvraelys
Dankie vir u belangstelling in ons navorsingsprojek.
Ons wil u graag vra om die volgende vraelys te voltooi. Al die inligting sal streng vertroulik hanteer word en u identiteit sal nooit in enige verslag openbaar word nie. Al die voltooide vraelyste sal apart gehou word van enige inligting wat u sou kon identifiseer en sal weggesluit word. U hoef nie u naam op hierdie vraelys te skryf nie.
Daar is geen regte of verkeerde antwoorde nie - ons vra dat u slegs die antwoord merk wat die meeste van toepassing is op u. Van die vrae mag dalk nie op u van toepassing wees nie, maar dit is belangrik vir die opname dat u so ver as moontlik al die vrae beantwoord.
U deelname aan hierdie projek is vrywillig; u is nie verplig om deel te neem nie en as u wel deelneem, kan u op enige stadium onttrek. U mediese behandeling en verhouding met die mediese personeel sal geensins deur u besluit geaffekteer word nie.
Voordat u die vraelys voltooi, sal u asseblief eers die aangehegte toestemmingsvorm lees en teken. _____ is beskikbaar om enige vrae wat u aangaande die vraelys mag hê, te beantwoord. Sodra u die vraelys volledig voltooi het, sal u dit asseblief terugbesorg aan _____ .

Baie dankie vir u deelname aan hierdie projek.

Bylaag 4

Toestemmingsvorm

Ek, ..., gee hiermee my toestemming om deel te neem aan hierdie opname.
Ek verklaar dat al die inligting wat ek verskaf het, 'n eerlike weergawe van my gedagtes en gevoelens ten tyde van die opname is.
Ek is bewus van die feit dat al die inligting wat ek verskaf het, streng vertroulik sal bly.
Ek begryp dat ek heeltemal vrywillig aan hierdie opname deelneem en dat my deelname op enige stadium onttrek kan word.

Handtekening: _____

Datum: _____

Die eerste gedeelte van hierdie vraelys is algemene vrae oor u agtergrond wat vir ons sal help wanneer ons die inligting verwerk. Dit sal nie gebruik word vir enige identifkasie doeleindes nie.

1. Wat is u werkstatus op die huidige oomblik?
(Merk asseblief die boksie wat die mees toepaslik is.)

☐1 Voltydse werk
☐2 Deeltydse werk
☐3 Werkloos
☐4 Eie besigheid
☐5 Huisvrou
☐6 Voltydse student
☐7 Deeltydse student
☐8 Permanent ongeskik om te werk
☐9 Afgetree
☐10 Ander_____

Wat is die hoogste vlak wat u op skool behaal het?

☐1 Standerd 10 (Matriek)
☐2 Standerd 9
☐3 Standerd 8
☐4 Standerd 7
☐5 Standerd 6
☐6 Standerd 5
☐7 Ander_____

Wat is die hoogste kwalifikasie wat u sedert skool behaal het?

☐1 Geen naskoolse kwalifikasies
☐2 Ambagswerk
☐3 Sertifikaat van 'n kollege
☐4 Diploma (na Std. 10)
☐5 Baccalaureusgraad
☐6 Nagraadse diploma of graad
☐7 Ander _____

Wat is u huidige huwelikstatus?

☐1 Nooit getroud
☐2 Weduwee/wewenaar
☐3 Geskei
☐4 Uitmekaar, maar nie geskei nie
☐5 Getroud (insluitend gemeenregtelike huwelik)

In watter stad/dorp is u gebore?

_____

Wat is u geboortedatum?

_____

Het u 'n sterk geloof?

□1 Ja
□2 Nee

Behoort u aan 'n mediese fonds?

□1 Ja
□2 Nee

Wat is u geslag?

□1 Manlik
□2 Vroulik

Het u enige kinders?

□1 Ja
□2 Nee

1ste kind: Ouderdom: _____
Seun? □1
Dogter? □2

2de kind: Ouderdom: _____
Seun? □1
Dogter? □2

3de kind: Ouderdom: _____
Seun? □1
Dogter? □2

4de kind: Ouderdom: _____
Seun? □1
Dogter? □2

Indien u meer as vier kinders het, sal u asseblief verdere inligting op die laaste bladsy van die vraelys verskaf.

Vrae oor u gesin.

Hoeveel broers het u?

_____

Hoeveel susters het u?

_____

Hoeveel van u broers[1] en susters[2] het al kanker gehad?

□[1]_____ □[2]_____

Hoeveel van u broers[1] en susters[2] lewe nog?

□[1]_____ □[2]_____

Het een van u ouers kanker gehad?

□[1] Ja
□[2] Nee

Hoe oud was u toe u besef het u is 'n risikogeval?

_____

Wie het u aangeraai om vir 'n genetiese toets vir oorerflike kolonkanker te gaan?

□[1] My eie idee
□[2] 'n Lid van my gesin
□[3] Algemene praktisyn
□[4] Spesialis
□[5] Familie dermkliniek sister?
□[6] Ander _____

Het u al 'n genetiese bloedtoets resultaat vir oorerflike kolonkanker gehad?

□[1] Ja
□[2] Nee
□[3] Weet Nie

Wie gaan u sien wanneer u siek voel?

□[1] Algemene praktisyn
□[2] Klinieksuster/dokter
□[3] Niemand
□[4] Ander_____

Mense het verskeie redes hoekom hulle die Oorerflike Kolonkanker genetiese toets wil ondergaan of nie. Ons wil graag weet hoeveel *elk* van die volgende faktore u besluit om vir 'n genetiese toets te gaan, beinvloed het.

'n Faktor wat my besluit om vir 'n genetiese toets te gaan, beinvloed het, is...

a. om te weet wat my kinders se risiko is

□1 Glad nie
□2 Effens
□3 Baie
□4 Nie van toepassing

b. ...om te kan vasstel hoe ek my risiko vir die ontwikkeling van kanker, kan verminder

□1 Glad nie
□2 Effens
□3 Baie

c. ...om vir die toekoms te beplan

□1 Glad nie
□2 Effens
□3 Baie

d. ...om navorsing te bevorder

□1 Glad nie
□2 Effens
□3 Baie

e. ...om seker te wees van my eie risiko

□1 Glad nie
□2 Effens
□3 Baie

f. ...om 'n besluit te kan neem oor gesinsbeplanning (om kinders te hê of nie)

□1 Glad nie
□2 Effens
□3 Baie
□4 Nie van toepassing

'n Faktor wat my besluit om vir 'n genetiese toets te gaan, beinvloed het, is...

g. ...omdat ek bekommerd is dat ek my versekering mag verloor/nie kan kry nie

□1 Glad nie
□2 Effens
□3 Baie
□4 Nie van toepassing

h. ...ek is bekommerd oor die uitwerking van genetiese toetsing op my gesin

□1 Glad nie
□2 Effens
□3 Baie

I. ...ek glo dat kanker onvermydelik is

□1 Glad nie
□2 Effens
□3 Baie

j. ...ek sal dit te moeilik vind om die resultaat emosioneel te kan verwerk

□1 Glad nie
□2 Effens
□3 Baie

k. ...die toetsresultaat mag miskien foutief wees

□1 Glad nie
□2 Effens
□3 Baie

l. ...ek het 'n wantroue in moderne medisyne

□1 Glad nie
□2 Effens
□3 Baie

Die volgende vrae is net om uit te vind hoeveel u al weet van gene wat Oorerflike Kolonkanker veroorsaak ('n toestand wat dermkanker voorafgaan). Dui asseblief aan watter antwoord volgens u Waar of Vals is, of Weet Nie.

15. Dermkanker is altyd oorerflik

□1 Waar
□2 Vals
□3 Weet nie

16. Almal wat 'n geen vir Oorerflike Kolonkanker het, sal dermkanker kry

□1 Waar
□2 Vals
□3 Weet nie

17. Iemand wat nie 'n veranderde Oorerflike Kolonkankergeen het nie, kan nog steeds dermkanker kry

□1 Waar
□2 Vals
□3 Weet nie

18. Daar is meer as een geen wat dermkanker kan veroorsaak

□1 Waar
□2 Vals
□3 Weet nie

19. Die geen vir Oorerflike Kolonkanker kan ook die risiko vir ander kankers verhoog

□1 Waar
□2 Vals
□3 Weet nie

20. 'n Kolonoskopie (die binnekant van die derm word met 'n spesiale buis besigtig) is heel moontlik in staat om dermkanker op te spoor indien dit teenwoordig is

□1 Waar
□2 Vals
□3 Weet nie

21. 'n Okkultebloed-stoelgangtoets ('n toets wat onsigbare bloed in die stoelgang aandui) sal altyd dermkanker opspoor

□1 Waar
□2 Vals
□3 Weet nie

22. In 'n familie waar 'n geen vir Oorerflike Kolonkanker gevind is, sal die' sonder die geen dieselfde risiko hê om dermkanker te kry as die algemene bevolking

□1 Waar
□2 Vals
□3 Weet nie

23. Indien iemand lyk soos, of dieselde persoonlikheid het as, 'n familielid wat dermkanker het of gehad het, het hy/sy heel moontlik die geen van daardie persoon geërf

□1 Waar
□2 Vals
□3 Weet nie

24a. Die volgende stellings wil u mening omtrent u vatbaarheid vir dermkanker bepaal. Volgens u mening, in vergelyking met ander mense van u eie ouderdom, wat is u kanse om dermkanker te ontwikkel?

□1 Baie kleiner
□2 Effens kleiner
□3 Min of meer dieselfde
□4 'n Bietjie groter
□5 Baie groter

24b 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?

0_____100

Hierdie afdeling handel oor die ondervinding wat u al met kankersiftingstoetse gehad het. Merk asseblief die boksie wat volgens u omstandighede die naaste aan reg is.

25a. Het u al ooit 'n kolonoskopie gehad (die binnekant van die derm word met 'n spesiale buis ondersoek)?

☐1 Nee. Gaan asseblief voort met Vraag 26a
☐2 Ja
☐3 Weet nie. Gaan asseblief voort met Vraag 26

25b. Indien u ja geantwoord het, het u in die laaste twee jaar een gehad?

☐1 Nee
☐2 Ja
☐3 Weet nie

25c. Was 'n poliep al ooit tydens een van u kolonoskopieë vewyder ('n poliep is 'n klein, gewoonlik nie-kwaardaardige vergroeisel)

☐1 Nee
☐2 Ja
☐3 Weet nie

26a. Het u al ooit 'n okkultebloed - stoelgangtoets gehad ('n toets vir onsigbare bloed in die stoelgang)?

☐1 Nee. Gaan asseblief voort met Vraag 27
☐2 Ja
☐3 Weet nie. Gaan asseblief voort met Vraag 27

26b. Indien Ja, het u bogenoemde toets in die afgelope twee jaar gehad.

☐1 Nee
☐2 Ja

27. Dit sal van hulp wees om te weet watter opsies u sou oorweeg indien u geentoets aandui dat u die geen vir Oorerflike Kolonkanker besit. Hieronder is 'n lys van opsies - van hulle mag glad nie op u van toepassing wees nie. Hierdie opsies verteenwoordig nie bevestigde metodes vir die voorkoming van kanker nie, maar kan met u deur die genetiese berader of kliniekdokter bespreek word, oor wat dit behels . Merk asseblief die boksie wat u keuse aandui.

Indien my bloedtoets aantoon dat ek die geen vir Oorerflike Kolonkanker besit, sal ek die volgende oorweeg ...

...'n voorkomende kolektomie ('n operasie om die dikderm te verwyder)

□1 Nee
□2 Ja
□3 Weet nie
□4 Klaar gedoen/ sal gedoen word

28. Dit sal van hulp wees om te weet hoe u geentoets - resultaat u planne vir toekomstige skandering vir dermkanker sou beinvloed. Indien u bloedtoets toon dat u wel die geen vir Oorerflike Dermkanker gedra het , sou u u planne om dermkankerskandeering te ondergaan verander? Merk asseblief die boks wat die naaste is aan u siening.

28a. □1 Ek sou nie my skanderingsessies verander nie
□2 Ek sou meer gereelde skanderingsessies ondergaan
□3 Ek sou my skanderingsessies verminder
□4 Ek sou my skanderingsessies stop

Indien u bloedtoets toon dat u NIE die geen vir Oorerflike Dermkanker dra nie, sou u u planne om dermkankerskandering te ondergaan, verander?

28b. □1 Ek sou nie my skanderingsessies verander nie
□2 Ek sou meer gereelde skanderingsessies ondergaan
□3 Ek sou my skanderingsessies verminder
□4 Ek sou my skanderingsessies stop

Hierdie gedeelte handel oor u siening omtrent dermkanker en dermkanker - skanderings. Ons wil graag weet tot watter mate u saamstem met elk van die volgende stellings. Antwoord asseblief al die vrae selfs al het u nog nooit dermkankerskandering ondergaan nie. Merk asseblief die stelling wat die naaste is aan u seining is.

29. Ek dink mense wat met dermkanker gediagnoseer word, het min kans om die siekte te oorleef

□1 Verskil sterk
□2 Verskil effens
□3 Effens saamstem
□4 Sterk saamstem

30. Dermkanker kan genees word indien vroetydig opgespoor

□1 Verskil sterk
□2 Verskil effens
□3 Effens saamstem
□4 Sterk saamstem

31. Ek is bekommerd dat dermkankerskandering sal aantoon dat ek dermkanker het

□1 Verskil sterk
□2 Verskil effens
□3 Effens saamstem
□4 Sterk saamstem

32. Kolonoskopie (die binnekant van die derm word met 'n spesiaale buis besigtig) is 'n effektiewe manier om dermkanker vroegtydig op te spoor

□1 Verskil sterk
□2 Verskil effens
□3 Effens saamstem
□4 Sterk saamstem
□5 Weet nie

33. Dit sal vir my maklik wees om 'n kolonoskopie te ondergaan

□1 Verskil sterk
□2 Verskil effens
□3 Effens saamstem
□4 Sterk saamstem
□5 Weet nie

34. 'n Okkultebloed-stoelgangtoets ('n toets wat onsigbare bloed in die stoelgang aandui) is 'n effektiewe manier om dermkanker vroegtydig op te spoor

□1 Verskil sterk
□2 Verskil effens
□3 Effens saamstem
□4 Sterk saamstem
□5 Weet nie

35. Dit sal vir my maklik wees om vir 'n okkultebloed - stoegangtoets te gaan

□1 Verskil sterk
□2 Verskil effens
□3 Effens saamstem
□4 Sterk saamstem
□5 Weet nie

36. In sommige families verhoog die besit van die geen vir Oorerflike Dermkanker ook die risiko om kanker in ander dele van die liggaam te kry. Ons wil graag weet hoe besorg u is omtrent u vatbaarheid vir ander kankers as dermaknker.

Om vatbaar te wees vir kanker buiten dermkanker.....

□1 ... bekommer my erg
□2 ... bekommer my effens
□3 ... bekommer my glad nie

Verduidelik asseblief (opsioneel)

_____
_____
_____
_____
_____

Verkillende mense hanteer stres op verskillende maniere. Hieronder volg vier opgemaakte situasies en ons wil graag weet hoe u dink u in elk van die volgende situasies sal reageer. Lees asseblief elke vraag aandagtig deur en merk al die stellings wat beskryf wat u sou doen.

37. U is bang vir die tandarts en dat daar aan u tande gewerk moet word. Watter van die volgende sal u doen? Merk asseblief AL die stellings wat op u van toepassing mag wees.

□ Ek sou die tandarts vra wat hy presies gaan doen
□ Ek sou 'n kalmeermiddel neem of 'n drankie drink voor ek gaan
□ Ek sou probeer dink aan aangename herinneringe
□ Ek sou wil hê dat die tandarts vir my moet sê wanneer ek pyn gaan voel
□ Ek sou probeer slaap
□ Ek sou al die tandarts se bewegings dophou en luister na die geluid van die boor

□ Ek sou die waterstroom vanuit my mond dophou om te sien of daar bloed in is

□ Ek sou breinspeletjies in my gedagtes wil speel

38. U word as gyselaar gehou deur 'n groep gewapende terroriste in 'n publieke gebou. Watter van die volgende sal u doen? Merk asseblief AL die stellings wat op u van toepassing mag wees.

□ Ek sou alleen gaan sit en soveel dagdroom en fantaseer as wat ek kan
□ Ek sou op my hoede wees en probeer verhoed om nie aan die slaap te raak nie
□ Ek sou my lewensverhaal met die ander gyselaars deel
□ Indien daar 'n radio was, sou ek naby probeer bly om na die nuus te luister oor wat die polisie gaan doen
□ Ek sou probeer om soveel as moontlik te slaap
□ Ek sou daaraan dink hoe lekker dit gaan wees om by die huis te kom
□ Ek sou seker maak dat ek weet waar elke moontlike uitgang is

39. As gevolg van 'n groot daling in verkope, is daar 'n gerug dat verskeie mense in u werksdepartement afgedank gaan word. U hoof het 'n evaluasie van u werk van die afgelope jaar ingehandig. Merk asseblief AL die stellings wat op u van toepassing mag wees.

□ Ek sou met my medekollegas praat om uit te vind of hulle enige iets van my evaluasie af weet
□ Ek sou my lys van pligte vir my huidige beroep nagaan en probeer uitwerk of ek aan almal voldoen het
□ Ek sou enige argumente of verskille wat ek met my hoof gehad het, wat moontlik sy opinie van my mag benadeel het, probeer onthou
□ Ek sou enige gedagtes van afdanking uit my kop verban
□ Ek sou aan my lewensmaat sê dat ek my kanse van afdanking liewer nie wil bespreek nie
□ Ek sou probeer dink wie van die werknemers in my departement deur die hoof gesien word as die' wat die swakste werk verrig
□ Ek sou aangaan met my werk asof niks besonders gebeur het nie

40. U is op 'n vliegtuig, dertig minute vanaf u bestemming wanneer die vliegtuig onverwags duik en dan weer stabiliseer. n Kort rukkie daarna kondig die loods aan dat niks verkeerd is nie, alhoewel die res van die rit onstuimig mag wees. U is egter nie oortuigdaarvan dat alles in orde is nie. Merk asseblief AL die stellings wat op u van toepassing mag wees.

□ Ek sou die inligting omtrent veiligheidsprosedures wat in die vliegtuig verskaf word, deeglik deurgaan en seker maak dat ek weet waar al die nooduitgange is

□ Ek sou oor onbenullighede met my medepassasier gesels

□ Ek sou die fliek tot aan die einde kyk, selfs al het ek dit voorheen gesien
□ Ek sou die lugwaardin roep en vra wat presies die probleem was
□ Ek sou 'n drankie of kalmeermiddel bestel
□ Ek sou aandagtig na die enjin luister vir enige ongewone geluide en sou die bemanning dophou vir enige ongewone gedrag
□ Ek sou met my medepassasier gesels oor wat moontlik verkeerd kon wees
□ Ek sou rustig raak en 'n boek of tydskif lees of 'n brief skryf

41a. · Het u enige ernstige, stresvolle lewensgebeure die laaste jaar ondervind?

□[1] Nee. Gaan asseblief voort met Vraag 42.
□[2] Ja

41b. Wat was hierdie lewensgebeure? Omsirkel asseblief die nommer wat op u van toepassing is.

(1) Ouer met kanker gediagnoseer
(2) Ouer oorlede aan dermkanker
(3) Broer of suster met dermkanker gediagnoseer
(4) Broer of suster aan dermkanker oorlede
(5) Dood van 'n familielid of vriend aan oorsake buiten dermkanker
(6) Ekself is gediagnoseer met 'n nie-kwaadaardige dermkwaal
(7) Verhuising
(8) Egskeiding of skeiding van my lewensmaat
(9) Werksverwante stres
(10) Ander (spesifiseer asseblief)

_____

41c. Hoe stresvol was hierdie gebeure vir u? Merk asseblief die horisontale lyn om aan te dui hoeveel stres u gehad het.

_____

Nie stresvol Baie stresvol

Hierdie vraelys is ontwerp om ons te help bepaal hoe u voel. Lees asseblief elke item hieronder en merk die een wat die naaste is aan hoe u die afgelope week gevoel het. Daar is geen regte of verkeerde antwoorde nie. Moenie te lank oor u antwoord dink nie; u onmiddelike reaksie op elke item sal heel moontlik meer akkuraat wees as 'n goed deurdagte antwoord.

42. Ek geniet nog steeds die dinge wat ek voorheen geniet het.

□ Beslis soveel
□ Nie heeltemal soveel nie
□ Net 'n bietjie
□ Omtrent geensins

43. Ek kan lag en die snaakse kant van dinge insien.
□ Net soveel as voorheen
□ Nie meer heeltemal soveel nie
□ Beslis nie meer so veel nie
□ Glad nie

44. Ek voel opgewek.

□ Glad nie
□ Nie dikwels nie
□ Partykeer
□ Meeste van die tyd

45. Ek voel asof ek traag geword het.

□ Amper die heeltyd
□ Dikwels
□ Partykeer
□ Nooit

46. Ek het belangstelling in my voorkoms verloor.

□ Defnitief
□ Ek versorg my nie soveel as wat ek moet nie.
□ Ek mag my dalk nie genoeg versorg nie.
□ Ek versorg my net soveel soos altyd.

47. Ek sien met ogewondenheid uit na dinge.

□ Soveel soos voorheen
□ Redelik minder as voorheen
□ Defnitief minder as voorheen
□ Amper niks

48. Ek kan 'n goeie boek, radio-of TV-program geniet.

□ Dikwels
□ Partykeer
□ Nie gereeld nie
□ Baie selde

'n Verskeidenheid van stellings waarmee mense hulleself beskryf, word hieronder gegee.. Lees elke stelling en merk dan 'n boks om aan te dui hoe u PRESIES OP HIERDIE OOMBLIK voel.

		Glad nie	Effens	Redelik	Baie
49.	Ek voel kalm	☐	☐	☐	☐
50.	Ek voel gespanne	☐	☐	☐	☐
51.	Ek is onsteld	☐	☐	☐	☐
52.	Ek voel ontspanne	☐	☐	☐	☐
53.	Ek voel tevrede	☐	☐	☐	☐
54.	Ek is bekommerd	☐	☐	☐	☐

Hieronder is 'n lys van uitsprake wat deur mense gelewer is omtrent hulle vatbaarheid vir dermkanker. Merk asseblief 'n boks om te toon hoe gereeld hierdie uitsprake op u van toepassing was gedurende die laaste sewe dae.

		Glad nie	**Selde**	**Partykeer**	**Dikwels**
55.	Ek het daaraan gedink sonder dat ek wou	☐	☐	☐	☐
56.	Ek het myself daarvan weerhou om ontsteld te raak wanneer ek daaraan gedink het of daaraan herinner is	☐	☐	☐	☐
57.	Ek het dit uit my gedagtes probeer ban	☐	☐	☐	☐
58.	Ek het moeilik aan die slaap geraak of aan die slaap gebly a.g.v. beelde en gedagtes daaroor wat in my kop gekom het	☐	☐	☐	☐
59.	Ek het met tye sterk gevoelens daaroor gehad	☐	☐	☐	☐

		Glad nie	**Selde**	**Partykeer**	**Dikwels**
60.	Ek het daaroor gedroom	☐	☐	☐	☐
61.	Ek het probeer om nie daaraan herinner te word nie.	☐	☐	☐	☐

62. Ek het gevoel asof dit nie 'n werklikheid was nie	☐	☐	☐	☐
63. Ek het probeer om nie daaroor te praat nie	☐	☐	☐	☐
64. Beelde het in my gedagtes bly verskyn	☐	☐	☐	☐
65. Ander dinge het gemaak dat ek gedurig daaraan dink	☐	☐	☐	☐
66. Ek was bewus daarvan dat ek nog baie opgekropte gevoelens daaroor het, maar ek het nie aandag daaraan gegee nie	☐	☐	☐	☐
67. Ek het probeer om nie daaraan te dink nie	☐	☐	☐	☐
68. Enige herinnering daaraan het gevoelens daaromtrent teruggebring	☐	☐	☐	☐
69. My gevoelens was soort van afgestomp	☐	☐	☐	☐

70. Is daar enige ander sake wat ons nie in hierdie vraelys aangespreek het nie?

_____

_____

_____

10. cont. 5de kind: Ouderdom: _____
Seun? ☐1
Dogter? ☐2

6de kind: Ouderdom: _____
Seun? ☐1
Dogter? ☐2

7de kind: Ouderdom: _____
Seun? □1
Dogter? □2

8de kind: Ouderdom: _____
Seun? □1
Dogter? □2

9de kind: Ouderdom: _____
Seun? □1
Dogter? □2

10de kind: Ouderdom: _____
Seun? □1
Dogter? □2

_KNAP GEDAAN!!

WEEREENS BAIE DANKIE.

7.6 Appendix 6: Final Afrikaans questionnaire after piloting

Registrasienommer

Datum uitgereik

Genetiese Toetsingvraelys

Dankie vir u belangstelling in ons navorsingsprojek.

Ons wil u graag vra om die volgende vraelys te voltooi. Al die inligting sal streng vertroulik hanteer word en u identiteit sal nooit in enige verslag openbaar word nie. Al die voltooide vraelyste sal apart gehou word van enige inligting wat u sou kon identifiseer en sal weggesluit word. U hoef nie u naam op hierdie vraelys te skryf nie.

Daar is geen regte of verkeerde antwoorde nie - ons vra dat u slegs die antwoord merk wat die meeste van toepassing is op u. Van die vrae mag dalk nie op u van toepassing wees nie, maar dit is belangrik vir die opname dat u so ver as moontlik al die vrae beantwoord.

U deelname aan hierdie projek is vrywillig; u is nie verplig om deel te neem nie en as u wel deelneem, kan u op enige stadium onttrek. U mediese behandeling en verhouding met die mediese personeel sal geensins deur u besluit geaffekteer word nie.

Voordat u die vraelys voltooi, sal u asseblief eers die aangehegte toestemmingsvorm lees en teken. _____ is beskikbaar om enige vrae wat u aangaande die vraelys mag hê, te beantwoord. Sodra u die vraelys volledig voltooi het, sal u dit asseblief terugbesorg aan _____.

Baie dankie vir u deelname aan hierdie projek.

Toestemmingsvorm

Ek, ..., gee hiermee my toestemming om deel te neem aan hierdie opname.

Ek verklaar dat al die inligting wat ek verskaf het, 'n eerlike weergawe van my gedagtes en gevoelens ten tyde van die opname is.

Ek is bewus van die feit dat al die inligting wat ek verskaf het, streng vertroulik sal bly.

Ek begryp dat ek heeltemal vrywillig aan hierdie opname deelneem en dat my deelname op enige stadium onttrek kan word.

Handtekening: _____

Datum: _____

Die eerste gedeelte van hierdie vraelys is algemene vrae oor u agtergrond wat vir ons sal help wanneer ons die inligting verwerk. Dit sal nie gebruik word vir enige identifkasie doeleindes nie.

(Merk asseblief die blokkie wat die mees toepaslik is.)

Wat is u werkstatus op die huidige oomblik?

☐1 Voltydse werk

☐2 Deeltydse werk

☐3 Werkloos

☐4 Eie besigheid

☐5 Huisvrou

☐6 Voltydse student

☐7 Deeltydse student

☐8 Permanent ongeskik om te werk

☐9 Afgetree

☐10 Ander_____

Wat is die hoogste vlak wat u op skool behaal het?

☐1 Standerd 10 (Matriek)

☐2 Standerd 9

☐3 Standerd 8

☐4 Standerd 7

☐5 Standerd 6

☐6 Standerd 5

☐7 Ander_____

Wat is die hoogste kwalifikasie wat u sedert skool behaal het?

☐1 Geen naskoolse kwalifikasies

☐2 Ambagswerk

☐3 Sertifikaat van 'n kollege

☐4 Diploma (na Std. 10)

☐5 Baccalaureusgraad

☐6 Nagraadse diploma of graad

☐7 Ander _____

Wat is u huidige huwelikstatus?

□1 Nooit getroud
□2 Weduwee/wewenaar
□3 Geskei
□4 Uitmekaar, maar nie geskei nie
□5 Getroud (insluitend gemeenregtelike huwelik)

In watter stad/dorp is u gebore?

_____

Wat is u geboortedatum?

_____

Het u 'n sterk geloof?

□1 Ja
□2 Nee

Behoort u aan 'n mediese fonds?

□1 Ja
□2 Nee

Wat is u geslag?

□1 Manlik
□2 Vroulik

Het u enige kinders van u eie (bloedverwande)?

□1 Ja
□2 Nee

10a.) 1ste kind: Ouderdom: _____

Seun? □1

Dogter? □2

10b.) 2de kind: Ouderdom: _____

Seun? □1

Dogter? □2

10c.) 3de kind: Ouderdom: _____

Seun? □1

Dogter? □2

10d.) 4de kind: Ouderdom: _____

Seun? □1

Dogter? □2

Indien u meer as vier kinders het, sal u asseblief verdere inligting op die laaste bladsy van die vraelys verskaf.

Vrae oor u familie.

11a) Hoeveel bloedverwande broers het u?

_____

11b) Hoeveel bloedverande susters het u?

_____

11c) Hoeveel van u bloedverwande broers het al kanker gehad?

_____

11d) Hoeveel van u bloedverwande en susters het al kanker gehad?

_____

11e) Hoeveel van u bloedverwande broers lewe nog?

_____

11f) Hoeveel van u bloedverwande susters lewe nog?

_____

11g) Het enige en van u bloedverwande ouers al kanker gehad?

□1 Ja

□2 Nee

11h) Hoe oud was u toe u besef het dat u 'n risiko geval vir kanker is?

_____

Wie het u aangeraai om vir 'n genetiese toets vir oorerflike dermkanker te gaan?

☐1 My eie idee

☐2 'n Lid van my familie

☐3 Algemene praktisyn

☐4 Spesialis

☐5 Familie dermkanker sister?

☐6 Ander _____

Het u al 'n genetiese bloedtoets resultaat vir oorerflike dermkanker gehad?

☐1 Ja

☐2 Nee

☐3 Weet Nie

Vir wie gaan u sien wanneer u siek voel?

☐1 Algemene praktisyn

☐2 Klinieksuster/dokter

☐3 Niemand

☐4 Ander_____

Mense het verskeie redes hoekom hulle die oorerflike dermkanker genetiese toets wil ondergaan of nie. Ons wil graag weet hoeveel *elk* van die volgendefaktore u besluit om vir 'n genetiese toets te gaan, beinvloed het.

'n Faktor wat my besluit beinvloed het om vir 'n genetiese toets te gaan, is...

15a.) ...om te weet wat my bloedverwande kinders se risiko is

□1 Glad nie

□2 Effens

□3 Baie

□4 Nie van toepassing

15b.) ...om te kan vasstel hoe ek my risiko vir die ontwikkeling van kanker, kan verminder

□1 Glad nie

□2 Effens

□3 Baie

15c.) ...om vir die toekoms te beplan

□1 Glad nie

□2 Effens

□3 Baie

15d.) ...om navorsing te bevorder

□1 Glad nie

□2 Effens

□3 Baie

15e.) ...om seker te wees van my eie risiko

□1 Glad nie

□2 Effens

□3 Baie

15f.) .om 'n besluit te kan neem oor gesinsbeplanning (om kinders te hê of nie)

□1 Glad nie

□2 Effens

□3 Baie

□4 Nie van toepassing

'n Faktor wat my besluit kon beinvloed het om nie vir 'n genetiese toets te gaan, is...

15g.) ...omdat ek bekommerd was dat ek my versekering mag verloor/nie kon kry nie

□1 Glad nie

□2 Effens

□3 Baie

□4 Nie van toepassing

15h.) ...ek was bekommerd oor die uitwerking van genetiese toetsing op my familie

□1 Glad nie

□2 Effens

□3 Baie

15i.) ...ek het geglo dat kanker onvermydelik was

□1 Glad nie

□2 Effens

□3 Baie

15j.) ...ek sou dit te moeilik vind om die resultaat emosioneel te kon verwerk

□1 Glad nie
□2 Effens
□3 Baie

15k.) ...die toetsresultaat sou miskien foutief gewees het

□1 Glad nie
□2 Effens
□3 Baie

15L.) ...ek het 'n wantroue in moderne medisyne gehad

□1 Glad nie
□2 Effens
□3 Baie

Die volgende vrae is net om uit te vind hoeveel u alreeds weet van gene wat oorerflike dermkanker veroorsaak ('n toestand wat dermkanker voorafgaan). Dui asseblief u antwoord aan, volgens 'Waar', 'Vals', of 'Weet Nie'.

Dermkanker is altyd oorerflik

□1 Waar
□2 Vals
□3 Weet nie

Almal wat 'n geen vir oorerflike dermkanker het, sal dermkanker kry

□1 Waar

□2 Vals

□3 Weet nie

Iemand wat nie 'n veranderde oorerflike dermkankergeen het nie, kan nog steeds dermkanker kry

□1 Waar

□2 Vals

□3 Weet nie

Daar is meer as een geen wat dermkanker kan veroorsaak

□1 Waar

□2 Vals

□3 Weet nie

Die geen verantwoordelik vir oorerflike dermkanker kan ook die risiko vir ander kankers verhoog

□1 Waar

□2 Vals

□3 Weet nie

'n Kolonoskopie (die binnekant van die derm word met 'n spesiale buis besigtig) is heel moontlik in staat om dermkanker op te spoor indien dit teenwoordig is

□1 Waar

□2 Vals

□3 Weet nie

'n Okkultebloed-stoelgangtoets ('n toets wat onsigbare bloed in die stoelgang

aandui) sal altyd dermkanker opspoor

□1 Waar

□2 Vals

□3 Weet nie

In 'n familie waar 'n geen vir oorerflike dermkanker gevind is, sal die persone sonder die geen dieselfde risiko hê om dermkanker te kry as die algemene bevolking

□1 Waar

□2 Vals

□3 Weet nie

Indien iemand lyk soos, of dieselde persoonlikheid het as, 'n familielid wat dermkanker het of gehad het, het hy/sy heel moontlik die geen van daardie persoon geërf

□1 Waar

□2 Vals

□3 Weet nie

Die volgende stellings wil u mening omtrent u vatbaarheid (risiko) vir dermkanker bepaal.

25a) Volgens u mening, in vergelyking met ander mense van u eie ouderdom, wat is u kanse om dermkanker te ontwikkel?

□1 Baie kleiner

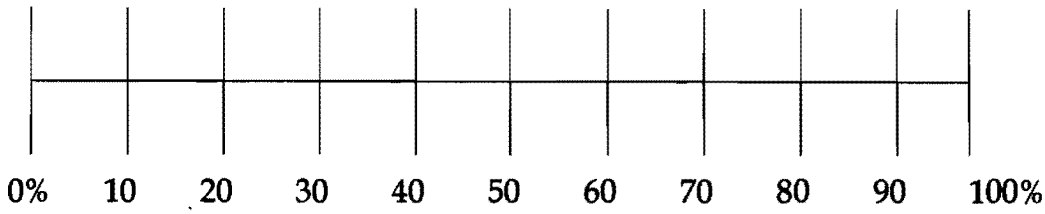
□2 Effens kleiner

□3 Min of meer dieselfde

□4 'n Bietjie groter

□5 Baie groter

25b) Dui asseblief u kans aan om dermkanker te kry, op 'n skaal van 0 tot 100, waar 0 = 'n 0% of geen kans is, en 100 = 'n 100% kans is, bedoelende dat jy dit beslis sal kry. Merk, met 'n kruis, asseblief een van die lyne om jou kans op dermkanker aan te dui.



Hierdie afdeling handel oor die ondervinding wat u al met kankersiftingstoetse gehad het (Toetse vir die vroetydige opsporing van kanker). Merk asseblief die blokkie wat volgens u omstandighede die naaste aan reg is.

26a. Het u al ooit 'n kolonoskopie gehad (die binnekant van die derm word met 'n spesiale buis ondersoek)?

□1 Nee. Gaan asseblief voort met Vraag 26d

□2 Ja

□3 Weet nie. Gaan asseblief voort met Vraag 26d

26b. Indien u ja geantwoord het, het u in die laaste twee jaar 'n kolonoskopie gehad?

□1 Nee

□2 Ja

□3 Weet nie

26c. Indien u ja geantwoord het , was 'n poliep al ooit tydens een van u kolonoskopieë vewyder ('n poliep is 'n klein, gewoonlik nie-kwaardaardige vergroeisel)

□1 Nee

□2 Ja

□3 Weet nie

26d. Het u al ooit 'n okkultebloed-stoelgangtoets gehad ('n toets vir onsigbare bloed in die stoelgang)?

□1 Nee. Gaan asseblief voort met Vraag 27

□2 Ja

□3 Weet nie. Gaan asseblief voort met Vraag 27

26e. Indien Ja, het u die okkultebloed-stoelgangtoets in die afgelope twee jaar gehad.

□1 Nee

□2 Ja

Dit sal van hulp wees om te weet watter opsies u sou oorweeg het, indien u geentoets aandui dat u die geen vir oorerflike dermkanker besit.

Hieronder is 'n lys van opsies - van hulle mag glad nie op u van toepassing wees nie. Hierdie opsies verteenwoordig nie bevestigde metodes vir die voorkoming van kanker nie, maar kan met u deur die genetiese berader of kliniekdokter bespreek word, oor wat dit behels. Merk asseblief die blokkie wat u keuse sou aandui.

Indien my bloedtoets sou aantoon dat ek die geen vir oorerflike dermkanker besit, sou ek die volgende oorweeg ...

...'n voorkomende kolektomie ('n operasie om die dikderm te verwyder)

□1 Nee

□2 Ja

□3 Weet nie

□4 Klaar gedoen/ sal gedoen word

Dit sal van hulp wees om te weet hoe u geentoets-resultaat u planne vir toekomstige opsporing vir dermkanker sou beinvloed. Indien u bloedtoets toon dat u wel die geen vir oorerflike dermkanker gedra het , sou u u planne om

vir toetse vir die vroetydige opsporing van dermkanker te ondergaan verander het? Merk asseblief die blokkie wat die naaste is aan u siening.

28a. □1 Ek sou nie my dermkanker - opsporingtoetse verander nie

□2 Ek sou meer gereelde dermkanker - opsporingtoetse ondergaan

□3 Ek sou my dermkanker - opsporingtoetse verminder

□4 Ek sou my dermkanker - opsporingtoetse stop

Indien u bloedtoets toon dat u NIE die geen vir oorerflike dermkanker dra nie, sou u u planne om dermkankeropsporing toetse te ondergaan, verander?

28b. □1 Ek sou nie my dermkanker - opsporingtoetse verander nie

□2 Ek sou meer gereelde dermkanker - opsporingtoetse ondergaan

□3 Ek sou my dermkanker - opsporingtoetse verminder

□4 Ek sou my dermkanker - opsporingtoetse stop

Hierdie gedeelte handel oor u siening omtrent dermkanker en dermkanker - opsporing toetse. Ons wil graag weet tot watter mate u saamstem met elk van die volgende stellings. Antwoord asseblief al die vrae selfs al het u nog nooit dermkankeropsporing toetse ondergaan nie. Merk asseblief die stelling wat die naaste is aan u seining is.

Ek dink mense wat met dermkanker gediagnoseer word, het min kans om die siekte te oorleef

□1 Verskil sterk

□2 Verskil effens

□3 Effens saamstem

□4 Sterk saamstem

Dermkanker kan genees word indien vroetydig opgespoor

□1 Verskil sterk

□2 Verskil effens

□3 Effens saamstem

□4 Sterk saamstem

Ek is bekommerd dat dermkanker - opsporing toetse sal aantoon dat ek dermkanker het

□1 Verskil sterk

□2 Verskil effens

□3 Effens saamstem

□4 Sterk saamstem

Kolonoskopie (die binnekant van die derm word met 'n spesiaale buis besigtig) is 'n effektiewe manier om dermkanker vroegtydig op te spoor

□1 Verskil sterk

□2 Verskil effens

□3 Effens saamstem

□4 Sterk saamstem

□5 Weet nie

Dit sal vir my maklik wees om 'n kolonoskopie te ondergaan

□1 Verskil sterk

□2 Verskil effens

□3 Effens saamstem

□4 Sterk saamstem

□5 Weet nie

'n Okkultebloed-stoelgangtoets ('n toets wat onsigbare bloed in die stoelgang aandui) is 'n effektiewe manier om dermkanker vroegtydig op te spoor

□1 Verskil sterk

□2 Verskil effens

□3 Effens saamstem

□4 Sterk saamstem

□5 Weet nie

Dit sal vir my maklik wees om vir 'n okkultebloed - stoegangtoets te gaan

□1 Verskil sterk

□2 Verskil effens

□3 Effens saamstem

□4 Sterk saamstem

□5 Weet nie

In sommige families verhoog die teenwoordigheid van die geen vir oorerflike dermkanker ook die risiko om kanker in ander dele van die liggaam te kry. Ons wil graag weet hoe bekommerd u is omtrent die risiko vir ander kankers as dermkanker.

Om vatbaar te wees vir kanker buiten dermkanker.....

□1 ... bekommer my erg

□2 ... bekommer my effens

□3 ... bekommer my glad nie

Verduidelik asseblief (opsioneel)

_____

_____

_____

_____

Verskillende mense hanteer stres op verskillende maniere. Hieronder volg vier denkbeeldige situasies en ons wil graag weet hoe u dink u in elk van die volgende situasies sal reageer. Lees asseblief elke vraag aandagtig deur en merk al die stellings wat beskryf wat u sou doen.

Daar moet aan u tande gewerk moet word en u is bang vir die tandarts. Watter van die volgende sal u doen? Merk asseblief AL die stellings wat op u van toepassing mag wees.

37a) ☐ Ek sou die tandarts vra wat hy presies gaan doen

37b) ☐ Ek sou 'n kalmeermiddel neem of 'n drankie drink voor ek gaan

37c) ☐ Ek sou probeer aan aangename herinneringe dink

37d) ☐ Ek sou wil hê dat die tandarts vir my moet waarsku wanneer ek pyn gaan voel

37e) ☐ Ek sou probeer slaap

37f) ☐ Ek sou al die tandarts se bewegings dophou en luister na die geluid van die boor

37g) ☐ Ek sou die waterstroom vanuit my mond dophou om te sien of daar bloed in is

37h) ☐ Ek sou breinspeletjies in my gedagtes wil speel

U word as gyselaar deur 'n groep gewapende terroriste in 'n publieke gebou aangehou. Watter van die volgende sal u doen? Merk asseblief AL die stellings wat op u van toepassing mag wees.

38a) ☐ Ek sou alleen gaan sit en soveel dagdroom en fantaseer as wat ek kan

38b) ☐ Ek sou op my hoede wees en probeer verhoed om nie aan die slaap te raak nie

38c) ☐ Ek sou my lewensverhaal met die ander gyselaars deel

38d) ☐ Indien daar 'n radio was, sou ek naby probeer bly om na die nuus te luister oor wat die polisie gaan doen

38e) ☐ Ek sou probeer om soveel as moontlik te slaap

38f) ☐ Ek sou daaraan dink hoe lekker dit gaan wees om by die huis te kom

38g) ☐ Ek sou seker maak dat ek weet waar elke moontlike uitgang is

As gevolg van 'n groot daling in verkope, is daar 'n gerug dat verskeie mense in u werksdepartement afgedank gaan word. U hoof het 'n evaluasie van u werk van die afgelope jaar ingehandig. Merk asseblief AL die stellings wat op u van toepassing mag wees.

39a)□ Ek sou met my medekollegas praat om uit te vind of hulle enige iets van my evaluasie af weet

39b)□ Ek sou my pligtelys van my huidige beroep nagaan en probeer uitwerk of ek aan almal voldoen het

39c)□ Ek sou enige argumente of verskille wat ek met my hoof gehad het, wat moontlik sy opinie van my mag benadeel het, probeer onthou

39d)□ Ek sou enige gedagtes van afdanking uit my kop verban

39e)□ Ek sou aan my lewensmaat sê dat ek my kanse vir afdanking liewer nie wil bespreek nie

39f)□ Ek sou probeer dink wie van die werknemers in my departement deur die hoof gesien word, as die werker wat die swakste werk verrig

39g)□ Ek sou aangaan met my werk asof niks besonders gebeur het nie

40. U is op 'n vliegtuig, dertig minute vanaf u bestemming wanneer die vliegtuig onverwags duik en dan weer stabiliseer. n Kort rukkie daarna kondig die loods aan dat niks verkeerd is nie, alhoewel die res van die rit onstuimig mag wees. U is egter nie oortuig daarvan dat alles in orde is nie. Merk asseblief AL die stellings wat op u van toepassing mag wees.

40a)□ Ek sou die inligting omtrent veiligheidsprosedures wat in die vliegtuig verskaf word, deeglik deurgaan en seker maak dat ek weet waar al die nooduitgange is

40b)□ Ek sou oor onbenullighede met my medepassasier gesels

40c)□ Ek sou die fliek tot aan die einde kyk, selfs al het ek dit voorheen gesien

40d)□ Ek sou die lugwaardin roep en vra wat presies die probleem was

40e)□ Ek sou 'n drankie of kalmeermiddel bestel

40f)□ Ek sou aandagtig na die enjin luister vir enige ongewone geluide ensou die bemanning dophou vir enige ongewone gedrag

40g)□ Ek sou met my medepassasier gesels oor wat moontlik verkeerd kon wees

40h)□ Ek sou rustig raak en 'n boek of tydskif lees of 'n brief skryf

41a. Het u enige ernstige stresvolle lewensgebeure die laaste jaar ondervind?

□[1] Nee. Gaan asseblief voort met Vraag 42.

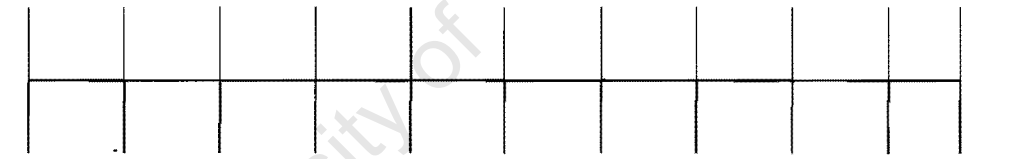
□[2] Ja

41b. Wat was hierdie lewensgebeure? Omsirkel asseblief die nommer wat op u van toepassing is.

(1) Ouer met kanker gediagnoseer
(2) Ouer oorlede aan dermkanker
(3) Broer of suster met dermkanker gediagnoseer
(4) Broer of suster aan dermkanker oorlede
(5) Dood van 'n familielid of vriend aan oorsake buiten dermkanker
(6) Ekself is gediagnoseer met 'n nie-kwaadaardige dermkwaal
(7) Verhuising
(8) Egskeiding of skeiding van my lewensmaat
(9) Werksverwante stres
(10) Ander (spesifiseer asseblief)

_____

41c. Hoe stresvol was hierdie gebeure vir u die afgelope jaar? Merk asseblief die vertikale lyn om aan te dui hoeveel stres u gehad het.



Nie stresvol Baie stresvol

Hierdie vraelys is ontwerp om ons te help bepaal hoe u voel. Lees asseblief elke item hieronder en merk die een wat die naaste is aan hoe u die afgelope week gevoel het. Daar is geen regte of verkeerde antwoorde nie. Moenie te lank oor u antwoord dink nie; u onmiddelike reaksie op elke item sal heel moontlik meer akkuraat wees as 'n goed deurdagte antwoord.

42. Ek geniet nog steeds die dinge wat ek voorheen geniet het.

□1 Beslis soveel

□2 Nie heeltemal soveel nie

□3 Net 'n bietjie

□4 Omtrent geensins

43. Ek kan lag en die snaakse kant van dinge insien.

□1 Net soveel soos voorheen

□2 Nie meer heeltemal soveel nie

□3 Beslis nie meer so veel nie

□4 Glad nie

44. Ek voel opgewek.

□1 Glad nie

□2 Nie dikwels nie

□3 Partykeer

□4 Meeste van die tyd

45. Ek voel asof ek traag geword het.

□1 Amper die heeltyd

□2 Dikwels

□3 Partykeer

□4 Nooit

46. Ek het belangstelling in my voorkoms verloor.

□1 Defnitief

□2 Ek versorg my nie soveel soos wat ek moet nie

□3 Ek mag my dalk nie genoeg versorg nie

□4 Ek versorg my net soveel soos altyd

47. Ek sien met opgewondenheid uit na dinge.

□1 Soveel soos voorheen
□2 Redelik minder as voorheen
□3 Defnitief minder as voorheen
□4 Amper niks

48. Ek kan 'n goeie boek, radio-of TV-program geniet.

□1 Dikwels
□2 Partykeer
□3 Nie gereeld nie
□4 Baie selde

'n Verskeidenheid van stellings waarmee mense hulleself beskryf, word hieronder gegee. Lees elke stelling en merk dan 'n blokkie om aan te dui hoe u PRESIES OP HIERDIE OOMBLIK voel.

		Glad nie	Effens	Redelik	Baie
49.	Ek voel kalm	□1	□2	□3	□4
50.	Ek voel gespanne	□1	□2	□3	□4
51.	Ek is onsteld	□1	□2	□3	□4
52.	Ek voel ontspanne	□1	□2	□3	□4
53.	Ek voel tevrede	□1	□2	□3	□4
54.	Ek is bekommerd	□1	□2	□3	□4

Hieronder is 'n lys van uitsprake wat deur mense gelewer is omtrent hulle risiko vir dermkanker. Merk asseblief 'n blokkie om aan te toon hoe gereeld hierdie uitsprake op u van toepassing was gedurende die laaste sewe dae.

Glad nie **Selde** **Partykeer** **Dikwels**

55.	Ek het daaraan gedink sonder dat ek wou	□[1]	□[2]	□[3]	□[4]
56.	Ek het myself daarvan weerhou om ontsteld te raak wanneer ek daaraan gedink het of daaraan herinner is	□[1]	□[2]	□[3]	□[4]
57.	Ek het dit uit my gedagtes probeer hou	□[1]	□[2]	□[3]	□[4]
58.	Ek het moeilik aan die slaap geraak of aan die slaap gebly a.g.v. beelde en gedagtes daaroor wat in my kop gekom het	□[1]	□[2]	□[3]	□[4]
59.	Ek het met tye sterk gevoelens daaroor gehad	□[1]	□[2]	□[3]	□[4]

		Glad nie	**Selde**	**Partykeer**	**Dikwels**
60.	Ek het daaroor gedroom	□[1]	□[2]	□[3]	□[4]
61.	Ek het probeer om nie daaraan herinner te word nie.	□[1]	□[2]	□[3]	□[4]
62.	Ek het gevoel asof dit nie 'n werklikheid was nie	□[1]	□[2]	□[3]	□[4]
63.	Ek het probeer om nie daaroor te praat nie	□[1]	□[2]	□[3]	□[4]
64.	Beelde het in my gedagtes bly verskyn	□[1]	□[2]	□[3]	□[4]
65.	Ander dinge het gemaak dat ek gedurig daaraan dink	□[1]	□[2]	□[3]	□[4]
66.	Ek was bewus daarvan dat ek nog baie opgekropte gevoelens daaroor het, maar ek het nie aandag daaraan gegee nie	□[1]	□[2]	□[3]	□[4]
67.	Ek het probeer om nie daaraan te dink nie	□[1]	□[2]	□[3]	□[4]
68.	Enige herinnering daaraan het gevoelens daaromtrent teruggebring	□[1]	□[2]	□[3]	□[4]
69.	My gevoelens was soort van verdoof	□[1]	□[2]	□[3]	□[4]

70. Is daar enige ander sake wat ons nie in hierdie vraelys aangespreek het nie?

_____

_

_____
_

_____
_

_____
_

_____
_

_____
_

10. cont.

10e)	5de kind:	Ouderdom:	____
		Seun?	□[1]
		Dogter?	□[2]
10f)	6de kind:	Ouderdom:	____
		Seun?	□[1]
		Dogter?	□[2]
10g)	7de kind:	Ouderdom:	____
		Seun?	□[1]
		Dogter?	□[2]
10h)	8de kind:	Ouderdom:	____
		Seun?	□[1]
		Dogter?	□[2]
10i)	9de kind:	Ouderdom:	____
		Seun?	□[1]
		Dogter?	□[2]
10j)	10de kind:	Ouderdom:	____
		Seun?	□[1]
		Dogter?	□[2]

KNAP GEDAAN!!
WEEREENS BAIE DANKIE.

7.7 Appendix 7: Extract from Research proposal for research criteria(1)

'Investigation of the genetic basis of colorectal cancers in the Western and Northern Cape provinces of South Africa' (1)

'5. RESEARCH PROTOCOL:

5.1 Patient and family recruitment, and access to archival material

Currently, there are three regions in which a significant degree of cancers have been confirmed to be due to a common *hMLH1* gene mutation; these areas are (refer to Figure 1 for geographic location):

(a) the Hondeklipbaai, Springbok, Port Nolloth triangle (incorporating Nababiep, O'Kiep, Steinkopf, Kommagas and Kleinzee), individuals have also been identified from villages such as Garies and Upington in the northern Cape
(b) the Wupperthal/Clanwilliam corridor (in the north of the Western Cape province), and
(c) the greater Cape Flats region (from Cape Town, to Bellville/Ravensmead, Eersterivier and extending to Maccasar near Somerset West).

5.1.1 Blood relatives (of 'satellite sporadic individuals' who have already been identified with the disease-predisposing mutation), will be contacted and informed of the disorder and their familial risk for the disease and be forwarded an information brochure describing the disorder, with details of our research (Appendix 1a/b for current brochure in English and Afrikaans, respectively); they will be given the option of participating in the research. Participants will be questioned regarding their ancestral origins, their medical history, particularly regarding signs, symptoms and treatment for the range of malignancies associated with HNPCC (i.e. Lynch syndrome II) in themselves and other blood relatives (Lynch et al., 1993). A standard questionnaire regarding dietary habits and gastrointestinal function will be administered for correlation with mutation status and penetrance of disease.

5.1.2 'New', sporadic individuals, under 50 years of age, affected with colorectal or one one of the spectrum of HNPCC tumors, originating from the Western and Northern Cape, who present at one of the collaborating centres/departments will be recruited for molecular genetic investigations. The recruitment protocol will involve informed consent to collect and use resected tissue, as well as 2 X 10 ml peripheral blood samples (Appendix 1c for consent/lab DNA forms). In the absence of fresh resected tissue, archived tumour material will be obtained from the collaborating Departments of Pathology. With any evidence of a positive family history of the disorder (or as a follow-up on detection of a disease-causing mutation in the subject), other

members of the subject's family will be contacted and recruited as described above.

5.1.3 Archived material: **The participating Departments of Pathology/Oncology will provide information on material that has been archived over the past 10 years, mainly from individuals who presented primarily with colorectal cancer (or the Lynch II spectrum, and under the age of 50 years). Appropriate material from deceased subjects will be obtained as 10 X 25μm sections of paraffin embedded tumour tissue from Pathology archives. At the same time, information requested under epidemiology below (see section 5.3) will be supplied with each sampling.**

5.2 Molecular Genetic Investigations

5.2.1 Extent of founder mutation in mixed ancestry population: **For consenting patient and familial referrals, and for individuals who meet the selection criteria (Lynch I/II spectrum of cancers, <50 years of age), 10 ml blood samples (drawn separately into two tubes) will be obtained by venepuncture, and processed to DNA using standard methods in the laboratory. Archived pathology specimens from patients who have undergone surgery for colorectal cancer, and who were under 50 years of age at that time, will also be processed to DNA, using standard methods for de-paraffinization of tissue and isolation of DNA. The DNA from each individual/sample will be investigated for the *hMLH1* mutation identified in the 10 families previously. The methodology will involve using a set of primers designed to amplify the mutated exon within the *hMLH1* gene through the polymerase chain reaction. Restriction digestion using the enzyme *Mva*1, provides a reliable means for preliminary testing of large numbers of samples (Ramesar et al., 1999). DNA sequencing will be carried out for confirmation.**

5.2.2 Microsatellite instability. **Microsatellite instability together with pathology and histology is very likely to provide prognostic indication for the subject, while providing a pointer to candidate disease-causing genes (Shibata et al., 1993; Jass, 1998, and see candidate genes under *5.2.3*). Investigation of this phenomenon will be carried out with tumour and non-tumour tissue of subjects, obtained either from Surgery or Pathology.**

5.2.3 Association with candidate genes. *In the event of material being available from 3 or more affected individuals, with a history of colorectal cancer (or cancers typical of the Lynch II syndromic spectrum, and which do not exhibit the major hMLH1 mutation described), a screen of highly polymorphic microsatellite markers (Genome Data Base; http//gdbwww.gdb.org) will be carried out to indicate the most likely of the*

candidate genes hMLH1, hMSH2, hPMS1, hPMS2, hMSH6 (Fishel et al., 1993; Leach et al., 1993; Bronner et al., 1994; Nicolaides et al., 1994; Papadopoulos et al., 1994; Miyaki et al., 1997)

Samples triaged out of the initial mutation screen, and material which suggests association with a candidate gene, will be processed through a comprehensive mutation screen of the candidate genes, which together account for approximately 90% of HNPCC. Although single stranded polymorphism analysis (Spritz et al., 1992) has been the method of choice for mutation analysis in the applicant's laboratory for several years, denaturing gradient gel electrophoresis and protein truncation testing (Jass, 1998) have been attempted and will be used as a suite of methodologies to enhance the detectability of DNA changes.

5.2.4 Genealogical Investigation and extension of families. **In relatives of affected individuals know to be mutation positive with disease: Individuals found to be negative for the mutation will be informed of their results, and discharged from further investigation. Individuals shown to be mutation positive will be referred for gastroenterological followup screening, and questioned for further information on at-risk relatives, as far back inter-generationally as is possible. This will require substantial effort and will be facilitated by a genetics nurse with adequate training. This endeavour in genealogical tracing will help identify possible links with other families along the West coast. Older living relatives will be targeted for anecdotal information and personal medical histories.**

In 'sporadic' individuals identified from pathology specimens and from screening 'sporadic' colorectal cancer patients under the age of 45 years (source: Groote Schuur Hospital, Tygerberg Hospital, Kimberly Hospital; private surgeons and pathology laboratories). Living, mutation-positive individuals will be contacted immediately, for a full familial medical history, endeavouring to establish genealogical ties with other families under investigation. Recruitment of family members (also of deceased individuals identified through pathology specimens), with informed consent, will aid the genealogical expansion of the kindred.

5.2.5 Age/Origin of the disease-associated mutation/s. **Studies in Finland have shown that the majority (approximately 70%) of colorectal cancers (associated with HNPCC) are due to only two mutations in the hMLH1 gene (Moisio et al., 1996; Nystrom-Lahti et al., 1996). Our investigations to date show the widespread occurrence of a single mutation underlying HNPCC in individuals of mixed ancestry deriving from the Northern Cape.**

The material from mutation positive subjects in our preliminary studies, shares a minimum haplotype of three microsatellite markers flanking and internal to the *hMLH1* gene. This together with a set of 10 markers flanking these markers

will be used to estimate age and possible migratory direction of the founder phenomenon. The age of the mutation will likely be important in providing a reasonable estimate of its dispersal, and its possible role in disease burden; furthermore, this will also enable a prediction of the migration into geographical regions which have not yet been investigated for the disease and mutation.

5.2.6 Search for genetic modifier loci. Although there is clear recognition of the likelihood of environmental factors which influence the initiation process, progression and spread of disease in a predisposed individual there are likely to be genetic elements which modify the effect of the primary predisposing mutation. The temporal and spatial existence of a common widely spread disease-associated mutation is extremely valuable for assessing purported biological modifier mechanisms. In this regard, approximately 400 markers spread across the human genome will be tested (at intervals of 5-10 cM) with approximately **50** subjects who are uniformly mutation carriers and who vary with regard to phenotype. The two oldest non-manifesting survivors (>70 yrs of age), and material from the youngest affected individual (deceased at 15 yrs of age) will form a focal component of the screening panel. Fifty non mutation-carrying siblings of the 'primary panel' will form the control group for a comprehensive screen. It is envisaged that this investigation will be facilitated by access to an automated genotyping facility, (which is being acquired by the applicant's[RSR] laboratory).

Certain areas of the human genome will be covered with a finer screen, e.g. the major histocompatability locus on the short arm of chromosome 6 will be interrogated for HLA subtypes, which might indicate whether this genomic entity has any influence on development and progression of disease.

5.3 Epidemiology of colorectal cancers, incorporating a database/registry for mutation and disease correlation

There is a lack of systematic statistics on cancers, particularly in the Northern Cape province. Even in the Western Cape province there is a dirth of cohesive information to extract reasonable demographic data. As referred to earlier, there is anecdotal and unpublished information suggesting a higher incidence of cancers in individuals of mixed ancestry along the west coast of South Africa (unpublished data gathered from referrals to Tygerberg Hospital: Albrecht, Smit and Mouton, unpublished). This requires further investigation, and will be a valuable adjunct to the genetic projects proposed earlier. The current aspect of the study is intended to begin with obtaining information in a stepwise manner which will ultimately provide basic data on the spatial and temporal variations in cancer patterns in the regions, particularly with regard to colorectal and associated (Lynch II; Lynch et al., 1993) cancers

The project will involve use of active and passive data collection methods to obtain information from clinics, laboratories and the referral hospitals that have been mentioned. All patients admitted, and with diagnosis of colorectal and

associated Lynch II cancers, will be documented, and the database will be constructed in close association with the superintendents of these hospitals, and relevant specialists. At the same time, the pathology archives of the referral hospitals of Groote Schuur, Tygerberg, and Kimberly (which serve the catchment population under consideration), will be asked for specimens from patients with colorectal cancer and who were 45 years and under at the time of surgery. Contact has already been established with the private pathology laboratories which are likely to complement sampling of this catchment western seaboard population. An added selector to be invoked in the database screening will be area of residence. General practitioners, and physicians along the West Cape Coast will also be approached during the course of this study in order to provide them with information on the disorder, and to suggest referrals from patients meeting the above-mentioned criteria of having colorectal cancer and being 45 years of age or younger (at the time of diagnosis or surgery).

The design of the data forms will be overseen by the Director of the NCR, Dr Freddy Sitas, (who will provide registry information as is available on the Western Cape and other relevant subregions) and will ensure uniform and consistent information collection, which will be admitted to the National cancer registry.

- Information that will be obtained will include: (a) hospital, (b) hospital reference number, (c) surname and name of individual, (d) gender, (e) date of birth/age, (f) ethnic group, (g) usual address and contact information, (h) date of consultation/treatment, (i) diagnosis/disease, (j) site of disease, (k) extent/stage of disease/histological type of disease, (l) date of last consultation and dates of various treatments, (m) details of treatment/ resection, (m) tissue available from, (n) further details, including family history.

The National Cancer Registry (NCR) currently serves the population of South Africa in terms of archiving and analysing information on cancers from around the country. The northern Cape province has, unfortunately been under-resourced and has minimal data in the NCR. The data acquired though our investigations will be fed into the NCR, via Dr Sitas. At the same time, however, our collaboration with Dr Sitas is based on the NCR providing access to reports of cancers submitted to the NCR through private pathologists. This will allow for verification and data qualification, and also provide a means of acquiring data which is not otherwise easily obtainable.

Some duplication of feedback from the different specialities and NCR to us is inevitable; however careful auditing of information at data entry onto the computerised system (currently functional in the applicant's laboratory on a

Microsoft Access platform) will avoid any interference with emerging statistics.'

7.8 Appendix 8: Step by step changes to the questionnaire

Permission to use this instrument is contained in Appendix 2.

The original Australian Questionnaire (Appendix 2) was converted from the original Rich text format with columns (as it was received electronically) to a straight- forward word doc.

This instrument (Appendix 2) was modified to the South African situation in English (Appendix 4) and then translated into Afrikaans (Appendix 5).

The original Australian information sheet was not altered in its content but the last paragraph, which was an instruction about posting the questionnaires, was altered to suit my research plan for a data collector to be available to answer questions and collect the questionnaires at completion (Appendix 6).

An English consent form was created for this study and translated into Afrikaans (Appendix 5 and 6). These (Information sheet and Consent form) were incorporated into the English and Afrikaans questionnaire packages.

The abbreviation 'HNPCC' was changed throughout the questionnaire to 'Hereditary colon cancer' to make translation manageable.

Numbering required to be altered throughout the document as additional demographic questions were added to the original questionnaire.

Sociodemographics

The demographic section changed from Questions 1 to 7 to 1 to 14 incorporating questions to suit the South African situation.

Question 1 was not changed.

Original Question 2: What is the *highest* qualification you have obtained since leaving school?

□1 No post-school

□2 Trade / apprenticeship

□3 Certificate from college / TAFE

□4 Diploma (beyond Year 12)

□5 Bachelors degree

□6 Postgraduate diploma / degree

□7 Other _____

Altered Question 2: What standard did you reach at school?

□1 Standard 10 (Matric)

□2 Standard 9

□3 Standard 8

□4 Standard 7

□5 Standard 6

□6 Standard 5

□7 Other _____

Original Question 3: Do you speak a language other than English *at home*?

□1 No, only English

□2 Yes, Italian

□3 Yes, Greek

□4 Yes, Chinese

□5 Yes, Arabic

□6 Other _____

Altered Question 3: What is the highest qualification you have obtained since leaving school?

□1 No post-school

□2 Trade / apprenticeship

☐3 Certificate from college

☐4 Diploma (beyond Std 10)

☐5 Bachelors degree

☐6 Postgraduate diploma / degree

☐7 Other _____

Original Question 4: What is your country of birth?

☐1 Australia

☐2 United Kingdom

☐3 Greece

☐4 Vietnam

☐5 Lebanon

☐6 Other _____

Altered Question 4: What is the town of your birth?

_____

Original Question 5: What is your present marital status?

☐1 Never married

☐2 Widowed

☐3 Divorced

☐4 Separated but not divorced

☐5 Married or de facto

Altered Question 5: What is your present marital status?

☐1 Never married

☐2 Widowed

☐3 Divorced

□4 Separated but not divorced

□5 Married or married in common law

Original Question 6.What is your age?

Age: _____ years

Altered Question 6: What is your date of birth?

_____

These were additional questions added to the South African Questionnaire. The reason for adding them was that they might add to socio-economic status thus possibly showing a pattern for stress.(70)

Question 7: Do you have a strong faith?

□1 Yes

□2 No

Question 8: Do you have a medical aid?

□1 Yes

□2 No

Question 9: Are you male or female?

□1 Male

□2 Female

Question 7 in the original questionnaire is. Do you have children?

This question was used unchanged as question 10

Question 11 was an added 6 point question about family and family members who have had cancer. The literature review showed that experience with disease was a factor associated with reduced levels of stress (70). In the Petersen article on attitudes to colon cancer testing {Petersen, Larkin, et al. 1999 ID: 4971 she uses a similar set of questions to depict family history and experiences with

colon cancer in the family

Question 12,13,14 were in the original questionnaire as Questions 8,9,10. They asked questions about testing for HNPCC. The Australian sample had not yet had predictive genetic testing, but this sample group have all received their predictive results. The questions were altered to suit their situation. Instead of asking if they wanted to participate in a predictive testing programme. The altered questions were a test to see if they knew they had had predictive genetic results for HNPCC.

After translation a new Question was added

Question 13 Have you ever had a predictive genetic result for HNPCC?

The thought was that Q12 asks 'who referred you to having a test?' and Q14 asks 'who you go to for clinical help?' It seemed incomplete not to ask if a result had been given.

Genetic risk status' is measured by Question 10 in the original questionnaire now Question 15 in the altered questionnaire. It is a modified '12 item' scale from a previously validated measurement of perceptions of benefits, limitations and risks of genetic testing in breast cancer {Lerman, 1996 4953 /id;Lerman, 1995 4981 /id}. The scale has been adapted and piloted in Australia (See Appendix 2) to assess the intention to request genetic testing and the acceptance of preventative surveillance strategies should a predictive result be gene positive for HNPCC.

The Australians altered the statements to suit their cohort. The Lerman BRCA1 study has these 12 items:

Benefits of testing –

- a) To learn about my children's risk
- b)To know if I need to increase screening
- c)To plan for the future

- d)To make surgery decisions
- e)To be reassured
- f)To make childbearing decisions
- Limitations and risks of testing -
- g)Worried about loosing insurance
- h)Concerns about effect on family
- i)Don't believe I can prevent getting cancer
- j)Couldn't handle it emotionally
- k)Test results might not be accurate
- l)Don't trust modern medicine

- In the Australian questionnaire d) and e) were left out and replaces by;

  To help Research

  To be certain about my risk

  The wording to i) was altered slightly to

  that I believed that cancer was inevitable

Contrary to the Australian cohort, my sample population had all already received their predictive results. The leading statement to Q15 would require these individuals to attempt to remember what might have made them decide to have themselves tested as well as what might have given them cause to hesitate. The leading statement was thus altered.

Original Question 10 stated

'A factor which influenced my decision about whether or not to have a gene test is...'

Revised Question 15

A factor which influenced my decision about whether to have a gene test is...

The reason for leaving out 'or not' in this leading sentence seemed more direct to a sample population who had already made this decision and could now comment on why they had made the decision at the time.

Knowledge

A Revised Version of a scale, used to measure the knowledge about inherited breast cancer and BRCA1 testing, has been integrated into the questionnaire. The scale used in the BRCA1 study included items from an instrument used by the National Centre for Human Genome Research Cancer Studies Consortium (58).

'Knowledge about colon cancer' is measured with Questions 16 - 24 (Original questions 11 - 19). The similarities of predictive testing for breast and colon cancer have been alluded to in the background.

Risk perceptions

Two measures provide for an assessment of the perception of the individual's risk of developing colorectal cancer (64).

Question 25 (Original Question 20) asks about perceptions of risk for developing colon cancer. The medical measurement of risk utilizes family history and colonoscopy screening yielding adenomatous polyps (42-44;87). In a study measuring 'Attitudes toward colon cancer gene testing' (66)it was found that risk perception was linked to affected relatives, cancer worry and a younger age. These 2 measures will give a baseline of risk perception to which screening and health behaviours can be compared. (Objective 2 i.e. cancer risks)

In the preventive health model (78) Page 144. a broad set of factors which influence an individual's decision to take preventative action and this set of questions combined to Q 26 and Q 28 also form part of the representation section of the Preventative Health Model.

Attitudes

Questions assessing the beliefs about the effectiveness of the surveillance methods are included. In addition, individuals will be asked their reasons and motivations for accepting or rejecting surveillance (56).

Question 26 and 27 (Original questions 21 and 22) consists of 3 baseline questions about colonoscopic screening to compare attitudes/beliefs about other health-related behaviours (Objective 2 - how to prevent development of cancer)

In question 26 - 'adenomatous' is removed as having a polyp found on colonoscopy is enough. 'Adenomatous' just adds to the difficulty in understanding.

Question 27 (Original Question 25) . The original wording was 'It would be helpful to know what options you would consider **should you decide to have a gene test and the test result indicate** that you carry the gene for **HNPCC.** Below is a list of options, some of which may not be relevant to you. These options do not represent proven methods for preventing cancer but may be discussed with you by the genetic counsellor or clinic doctor who will explain what they involve. **Please note your preferences as indicated here in no way limit the choices or options when the gene test result is available to you.** Please tick the box which represents your preferred option.'

Altered Question 27

'It would be helpful to know what options you would consider **if your gene test result indicated** that you carry the gene for **Hereditary colon cancer.** Below is a list of options, some of which may not be relevant to you. These options do not represent proven methods for preventing cancer but may be discussed with you by the genetic counsellor or clinic doctor who will explain what they involve. Please tick the box which represents your preferred option.'

The changes were made to read in the past tense as the research population have all had their predictive genetic results. Thus the '**Please note your preferences as indicated here in no way limit the choices or options when**

the gene test result is available to you' section was also removed as it was not applicable.

Question 28 also follows from question 27 in that it also asks the individual to contemplate what they may have done differently if they had received a different result, as well as what they would possibly change about what they had done.

In the translation to Afrikaans an extra 4th choice was added to the selection. The 4th option of 'stopping surveillance' was added. This is what is advised when an individual is mutation negative. They know they may request a procedure if they are worried but it is not offered as a regular surveillance/ screening as in those that are mutation positive.

Questions 28 - 36 (Original questions 25 – 35) These questions assess the beliefs about effectiveness of surveillance methods and the reasons and motivations for accepting/rejecting screening. An explanatory framework called the preventative health model with concepts believed to be important in self initiated preventative health behaviour were drawn from the Health belief model, the theory of reasoned action and social learning theory (78).These 4 factors make up a preventative health model which comprises 3 sets of variables:

1. Background factors - sociodemographic info
2. Representation factors – perceptions with the respect to the 'threat' and procedures available to cope with the potential threat
3. Social influence factors – relationships of individuals with health care professionals and social norms re. prevention
4. Program factors – individual, group, or mass communications

A shortened version of this model was used in the Australian questionnaire and relates to the representation factors. A 4 point Likert- type response was used in (78) to describe the variables.

(Objective 4 – how genetic testing impacts on medical decision making)

Question 36 has an optional open- ended question about attitude toward risk of cancer development (Objective 2)

Psychological and functional health status

Miller's behaviour style scale has been included as it enables measurement of coping in threatening situations and possible responses to these situations (56;74). Life event questions are used to assess the possibility of confounding effects on psychological outcomes measures. They have been piloted and tested for a related study in the Australia study.

Question 37 – 40 Miller's behaviour style scale is a measure of coping style in threatening situations and possible responses to these situations (74). (Objective 3 psychological health status)(Phipps and Zinn: 4997) The coping styles are divided into those who seek information (monitors) and those that avoid information (blunters). In Questions 37 – 40. The words 'Imaginary scenarios' in the introduction to the scale is self explanatory, thus the words 'imagine vividly' were left out as it did not change the meaning and would be easier to translate.

Question 41. 3 Components (a, band c) asking if the respondents had had a) a stressful life event in the last year b) if 'yes' in a) what was the event. They have a choice of 10 specifics and c) a Likert scale asking how stressful the event was for them on a scale of 0 (not stressful) to 100 (very stressful)

Impact on Medical Decisions

Questions 42 – 48. These questions make up a depression scale from the hospital anxiety and depression scale (HADS) (103). This is a rating scale that has been designed specifically for patients with physical illness. It has 14 items divided into 2 subscales, 7 for anxiety and 7 for depression with somatic items excluded. Only the depression scale has been used.

Questions 49 - 54 is the Spielberger State -Trait Anxiety Inventory (STAI- State Short version) that is included as a measure for situational

anxiety. Objective 3 psychological health status. (56;86).

Questions 55 -70. is an 'intrusion and avoidance' subscale of the Impact of Events Scale (IES) (61;61;83). In this study the 'stressor' is the concern of being at risk for colon cancer. The IES has 2 subscales. 1 x is an 'intrusion subscale which refers to ideas, images and feelings or bad dreams that intrude into every day thoughts' (Ref Esplen, MJ Journal of psychometric research pg. 429) and the other avoidance refers to ' consciously recognised avoidance of certain ideas, feelings or situations.' The intrusion scale has 7 items (score range 0 - 35) higher score indicating more reported intrusion and 8 items for the avoidance scale (0 - 40) with the higher score indicating a more reported avoidance'

Items are scored by frequency of their occurrence.

Question 70. This is an open-ended question allowing the participant to air any views not covered in the questionnaire that they may feel strongly about.

The abbreviation 'HNPCC' throughout the original questionnaire was then changed to hereditary colon cancer. In the context of the questionnaire all the individuals had received predictive results for HNPCC and understood it to be a hereditary form of colon cancer. It would then make translation into Afrikaans easier as well as easier to understand.

7.8.1 After Piloting:

- The numbering in had to be altered to suit data capture.

The numbering in question10 had to be altered to suit data capture. This was noted after the pilot. Each child had to be captured as a separate entity e.g. 10a for '1st child' and 10b for '2nd child' etc.

Question 11 required renumbering as it was found to be too difficult to add to the data so each potential answer was given a separate allocation thus changing 11 a - 11f to 11 a - 11 h

In question 11 and 15h the piloted Afrikaans translation ' Vrae oor u gesin' was used as a description for the set of questions. This was changed to ' Vrae oor jou familie' as the meaning of 'gesin', in Afrikaans, implied a more nuclear family whereas 'familie' was more in line with the meaning of ' your wider family' which is what the question is about.

- Translated words or phrases required altering to make the meaning more descriptive e.g.

The tense of statements was altered to the past tense as it was felt that it would make the subjects realise that they were being asked to remember why they agreed to enter the predictive genetic testing programme.

Words were added to make statements more clear and in some cases more polite.

Instructions were clarrified

In questions 11a to 11g and question15a the word 'bloedverwande' (translated directly means 'blood relative') was added to each question as it was realised that in the South African context using only the words 'brothers' and 'sisters' could have had a different meaning to our population, hence 'bloedverwande' was added to make the meaning clearer.

In question 15 the words 'Oorerflike Kolonkanker' (Inherited Colon Cancer) in the intro were changed to 'oorerflike dermkanker'. It was felt that the term 'derm' was more explicit and simple to understand than 'kolon'.

In question 15 the wording in the Afrikaans translated leading statements were slightly re-arranged to flow more easily from ' 'n Faktor wat my besluit om vir 'n genetiese toets te gaan, beinvloed het, is ...' to n Faktor wat my besluit beinvloed het om vir 'n genetiese toets te gaan, is ...'. This change was made after the pilot test.

For questions 15g to 15l the tense in these statements and the leading statements was changed after the pilot was done. The present tense was used in the piloted

Afrikaans questionnaire as a direct translation from the original Australian questionnaire. After changing the leading statement to suit the research subjects, who had all had predictive results, it was felt that the change of tense, to the past tense, would make the subjects realise that they were being asked to remember why they agreed to enter the predictive genetic testing programme. It was felt that it would not change the meaning of the set of questions but would make the subjects feel that the questions were specifically suited to them.

Number15 was used twice in the piloted questionnaire. All questions from 15 onwards were renumbered.

In question 20 the word 'verantwoordelik' was added to the statement. It was felt that it made the meaning of the Afrikaans statement more clear.

In question 23 the 'persone' was added to the statement to make the sentence more simple to understand and more polite instead of 'die'.

The Likert scale line in question 25 b was marked with percentages to choose from. The instructions were then altered to explain what to do.

Question 26 uses the word 'kankersiftingstoetse' as the Afrikaans translation for 'cancer -screening tests'. This was not well understood in the pilot. An explanation of 'toetse vir die vroetydige opsporing van kanker' was added.

The work 'boksie' was used in the pilot questionnaire but changed to 'blokkie' as the word seemed more correct.

Question 26c. 'It was felt that clarification needed to be given about having answered 'yes' or 'no' in 26a so 'Indien u ja ge-antwoord' was added to this question.

Question 27. The work 'boksie' was used in the pilot questionnaire but changed to 'blokkie' as the word seemed more correct.

Question 27. The leading statement was changed to the past tense after the pilot to make the statement more pertinent to the research subjects. The word 'sal' was replaced with 'sou'.

In the pilot Question 28 and 31 the word 'skandering' was used to translate the word 'screening 'but it was replaced with 'opsporing'. This was at the request of one of the pilot subjects who asked 'what skandering was?' In the responses 'skanderingsessies 'was replaced with dernkanker-opsporingtoetese'

Question 36. The word 'besit' was replaced with 'teenwoordigheid'. The word 'teenwoordigheid' created a 'presence of the gene' rather than 'besit' which had 'ownership' qualities to it. . A spelling mistake was corrected in the word 'dermkanker'.

Question 37 - 41. The leading statement for the next 4 questions explains that 'four imaginary scenarios are described'. In the pilot the words 'opgemaakde situasies' was used but it was decided after the pilot that 'denkbeeldige situasies' was more in line with the original meaning.

Question 37. Initially in the pilot a direct translation of the words was used. English - 'Vividly imagine that you are afraid of the dentist and have to get some dental work done'. Afrikaans -'U is bang vir die tandarts en dat daar aan u tande gewerk moet word'. After the pilot the wording was re-arranged so that the Afrikaans sounded better. Post pilot Afrikaans - 'Daar moet aan u tande gewerk moet word en u is bang vir die tandarts'.

The Likert scale line in question 41c was marked with percentages to choose from. The instructions were then altered to explain what to do. Question 41 asked about stressful life events in the last year. This was left out of Question 41c in the pilot. It was re - added after the pilot.

In the leading statement to questions 55 - 69 the word 'vatbaarheid' was used in the pilot as a translation for 'at risk' but changed to 'risiko'. It was felt that this word was used before in the questionnaire and understood.

In the pilot question 57 the word 'ban' was used as a translation for 'remove'. It was replaced with 'hou'. It was decided that 'Ban' was not suitable in this instance.

In question 69 the word 'afgestomp' was used as a translation for the word 'numb' but, after the pilot, 'verdoof' was used, as it was a better match.

7.9 Appendix 9: Answers to data set questions

Hi.....Below are the responses

The excel file entitled 'Ques data 1' is compiled of the numbers from the questionaire 'Appendix 3 no 3'. The yellow colums are the ones I have questions about.

1. Column B = date on the front page. Is this format OK? YES

2. Colums E Ques. 3 = What should I enter if a question is not answered? Do not enter, leave as blank

3. Colum M Ques. 10 a = There are 2 answers per question. An age and a tick box. Does one record the age in writing? Eg. twenty two to differentiate from '2' from the tick box. Is this format of recording this OK? Enter Age as a value (number)

4. Column w Ques 11a. Answer is a number of people. Doe I use Number 2 or two here? Number

5. Column AD Ques. 11h. The individual had completely misunderstood the question and given an inappropriate answer. What do I enter? Enter Age as a value (number)

6. Column BD Ques 25b. Asking to mark a line with a percentage score. Do I just enter the number e.g. 50 ?

7. Column BI Ques 26e. This question had an option to skip. What should I enter? You have to enter 1 or 2

8. Column BU - This is an area where they can explain their choice in Ques. 36. Where do I write this? Type in their response

9. Column BV quest 37a. Quest 37 a - h is a section in which they could choose more than one. I put a star to represent the answer chosen. Is this OK Do not use a star enter a 1

10. Column Ques 41b. One individual chose more than one answer. I thought should allocate the colums to accomadate this Yes eg 41b (1), 41b (2) etc and use a star as in ques 37. Do not use a star enter a 1

Thank you so much

Ursula Algar

7.10 Appendix 10: Itinerary for a preparatory West Coast Colonoscopic surveillance trip

Sunday 29 July 2003
Collect car at the airport
Monday 28 July 2003

Depart: Cape Town
See patients in: Clanwilliam 12h00 - 16h00
Drive to Wuppertal - Booked @ soetbekkie 027 492 3410

Tuesday 29 July 2003
See patients in: Wuppertal 09h00 - 12h00
Drive to Vredendal/ Lutzville.
See patients in: Lutzville 14.30 - 16h00
Booked Marina Visagie - Komkans farm 027 642 4015
Wednesday 30 July 2003
Drive to Okiep.
See patients in: Okiep 12h00 -16h00
Booked @ Okiep Hotel 027 441 000
Thursday 31 July 2003
See patients in: Okiep, Springbok 08h00 - 12h00
See patients in: Steinkopf 14h00 - 16h00
Booked @ Okiep Hotel 027 441 000
Friday 1 August 2003
See patients in: Kommagas, Hondeklipbaai, Kleinsee
Saturday 2 August 2003
See patients in: Kleinsee, Port Nolloth

Sunday 3 August 2003

Monday 4 August 2003
Arrival of Prof. Raj Ramesar (Department of Human genetics)
See patients in: Kleinsee, Port Nolloth, Okiep
Booked accommodation @ Okiep Hotel 027 441 000
Tuesday 5 August 2003
See patients in: Okiep, Kammieskroon, Nourivier
Booked accommodation @ Okiep Hotel 027 441 000
Wednesday 6 August 2003
See patients in: Springbok/ Okiep
Arrive back in Cape Town
Thursday 7 August 2003
Drop car at Newlands depot by 8 am

Summary

DATE	PLACE	IND. SEEN	PREP GIVEN	QUEST. GIVEN
28 JULY 03	CLANWILLIAM	6	6	8
29 JULY 03	WUPPERTAL	12	8	30
29 JULY 03	LUTZVILLE	7	5	0
30 JULY 03	GARIES	2	0	1
30 JULY 03	KHARKHAMS	1	0	0
31 JULY 03	OKIEP	6	7	7
1 AUGUST 03	KOMMAGAS	17	16	19
1 AUGUST 03	HONDEKLIPBAAI	3	2	4
2 AUGUST	PORT NOLLOTH	3	11	13
4 AUGUST	KLEINSEE	2	1	1
4 AUGUST	STEINKOPF	7	4	0
5 AUGUST	KAMMIEKROON	7	2	0
5 AUGUST	NOURIVIER	12	5	0

7.11 Appendix 11: Ethics Clearance cerificate

UNIVERSITY OF CAPE TOWN

Research Ethics Committee
Faculty of Health Sciences
OMB E46 Room 26, GSH
Queries : Xolile Fula
Tel : (021) 406-6492 Fax: 406-6411
E-mail : Xfula@curie.uct.ac.za

12 March 2003

REC REF: 334/2001

Ms U Algar
Gastrointestinal Clinic

Dear Ms Ulgar

THE KNOWLEDGE AND ATTITUDES OF FAMILY MEMBERS WHO HAVE RECEIVED PREDICTIVE GENETIC TESTING FOR HEREDITARY NON POLYPOSIS COLON CANCER IN SOUTH AFRICA

Thank you for your letter to the Research Ethics Committee dated 07 March 2003

*It is a pleasure to inform you that the revised proposal and English and Afrikaans questionnaire has been **approved** with reference to the above-mentioned study.*

Please quote the Reference number in all correspondence.

Yours sincerely

A/PROF. CR SWANEPOEL
CHAIRPERSON