Johannesburg, 2006

For the degree of Master of Science in Medicine in Genetic Counselling
the Witwatersrand, Johannesburg, in partial fulfilment of the requirements
A research report submitted to the Faculty of Health Sciences, University of

Andre van der Westhuizen

INHERITED COLORECTAL CANCER
TEST AND MANAGE FAMILIES AT RISK FOR
Counselling Program To Identify,
THE DEVELOPMENT OF A GENETIC
DECLARATION

I, Anthe van der Wüsthenzen, hereby declare that this research report is my own work. It is being submitted for the degree of Master of Science in Medicine at the University of the Western Cape, Cape Town. It has not been submitted elsewhere before for any degree or examination at this or any other University.

[Signature]

24th day of October 2008

[Signature]
Medical career. Support and continued interest through all my university studies and my韦斯特赫兹和海伦·玛格丽特·范·德·韦斯特赫兹（Elly）for their love.

I also dedicate this work to my parents, Frank Johannes van der Speck,
2007 Conference Centre, Manchester, United Kingdom from 22-24 May.
Meeting on Psychological Aspects of Genetic Testing at Manchester Genetic Group and Dutch Cancer Society with the 10th International Colorectal Cancer in South Africa, Joint Meeting of the UK Cancer Screening Program to Identify Individuals at Risk for Inherited


Poster Presentation:

South Africa from 1-3 March 2007 Society of Human Genetics - at Golden Gate, Orange Free State, colorectal cancer, 10th Biennial Congress of the South African screening program to identify individuals at risk for inherited


Oral Presentation:

PRESENTATIONS ARISING FROM THIS STUDY
Personal and family history of colorectal cancer was followed up for their cancer patients through a dedicated questionnaire. The study was a pilot project aimed at identifying families at risk for inherited colorectal cancer.

Abstract
(69%) patients were seen and 28/29 (97%) were correctly classified from data obtained from risk (moderate or high risk) and 15 families (41%) were at average risk. Twenty-nine (29) Forty-eight (48) completed questionnaires were received. 33 families (69%) were at increased category assigned in the questionnaire to test the reliability of the research tool. The initial risk assessment after the consultation was compared to the initial risk recorded. The final risk assessment after the consultation was decided during the consultation but were not formally information with relatives were assessed during the consultation, but were not formally available. In the final group, the research questionnaire for the relatives was offered. The research questionnaire for the relatives was written in patient's relatives were offered and a management plan according to their risk. The third step of the program was to ensure a follow-up consultation with a genetic counselor. The second step of the program was to classify families into one of 3 risk categories (average, moderate or high risk) for inherited colorectal cancer based on the data obtained in the genetic counseling clinic and some were derived from the literature. Questions were constructed by the writer. Some questions were based on clinical experience in Surgery Department and National Society of Lymphoma, the Research tool and University of Queen's University. The research tool Research participants were recruited from 2 private practice oncology centers in Niagara and all the questionnaires (48) that were handed out to patients were completed. All the patients who were recruited and completed the research tool became research involved. All the patients who were recruited and completed the research tool became research involved. All the patients who were recruited and completed the research tool became research involved. The patients were consent to allow access to their histopathology reports and medical notes. The patients were
The study also highlighted the urgent need for a molecular comprehensive family cancer program was developed and introduced into the Genetic University of the Whirlwind. This study formed the basis from which a new and more increased by more than 80% to the Clinical Section of the Division of Human Genes.

Informed risks according to best practice. Consultations for inherited colorectal cancer in advising participants and their families about the multidisciplinary management of their unmet need, but extensive personal and family history of cancer. The program was also helpful colorectal cancer. The research tool provided a reliable and acceptable way of calculating whether colorectal cancer was helpful in the identification of patients and families at increased risk. The Genetic counseling program developed through the use of a self-administered questionnaire that they would inform their relatives of their inherited risks. Consultations were that most of the participants were positive about the service and that most of the results and wanted to bank DNA for future research. The overwhelming after the Genetic were at moderate risk for colorectal cancer. All high-risk patients were interested in Genetic colorectal cancer (GNPC/ Lynch syndrome and 18 families (64%) were at high risk for colorectal cancer (GNPC/Lynch syndrome and 18 families (23%) fulfilled the Amsterdam II clinical criteria for the diagnosis of hereditary non-polyps
National Health Laboratory Service for their support

- forms for specialized testing of patients or cancer surveillance
- letters to patients for their increased risk families members and for sending our cancer
- General Consultants at the Division of Human Genetics for helping us and our associate
e - the cancer genetic testing on the patients recruited in this project
- Prof. Lutzice van Katsenburg for his enthusiasm for cancer genetic research and for doing
- me for the genetic counseling appointments

establishment of cancer genetic services and for their prompt response in attracting to meet

- patients and their families for participating in the research, for being positive about the
- questionnaires to those patients and for helping to recruit high-risk patients and families
- for questions and appointments in private practice and in state hospitals for handing out the
- questionnaires to patients and their positive response to the project

Start at Mary Potter Cancer Centre, Pretoria for her motivation in handing out the
- establishment cancer genetic services and for being my supervisor
- Prof. Amanda Krug for her motivation and support for the project, for her enthusiasm in
- Christiaan Coloured Cancer Research Trust - for generous funding for the project

I would like to thank the following individuals and organizations for their support in making

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HPCC

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Genuinely counselling programs were also made. The final outcome of the project was the cancer. General observations regarding patients' and families' perceptions regarding the counseling and to establish a multidisciplinary service for families of increased risk or information.

Create awareness of the availability of cancer genetics services and the need for molecular Human Genetics, University of the Witwatersrand and National Health Laboratory Service. More specifically, the possibility of the reevaluation, increase cancer genetics referrals to the Division of subsequent, counsel, test and manage patients according to their risk. Secondary aims were to questionnaires linked to an information sheet and consent form to risk stratify families and colorectal cancer. This was achieved through the use of a patient-based, self-administered questionnaire. This study was a pilot project aimed at developing a genuine counselling program for inherited cancer.

Inherited cancer.

Genuinely clinical practice and this provides appropriate referrals of patients at increased risk for melanoma and costs based on these spent with patients. It is frequently accomplished in non-ophthalmic this is time consuming, laborious intensive and expensive due to start initiatives and family history of great importance for assessing risk in inherited cancer programs, but comprehensive inherited cancer program is urgently needed in South Africa. A detailed justice equal amounts of money should be spent on modernising systems of care. But will also save lives. This becomes a matter of ethics because of the principle of distributive justice billions annually in developing new drugs for cancer, but only a fraction is benefitted from the new molecular developments in the field of cancer genetics. Society 2004). If would be na"
development is initiated. Thus, two mutated copies need to be present before function is lost.

Some mutations in the same gene on the other chromosome needs to occur before cancer begins to pass on to the next generation. The percentage of cancer cases because a second in an autosomal dominant way and follow basic Mendelian principles with a 50% chance of inheriting. The germ-line mutations in immunosuppressor and DNA mismatch-repair genes are inherited.

The accumulation of both inherited mutations and somatic mutations before cancer develops.

The individual to cancer development. Cancer is a multi-step process which inevitably involves somatic mutations. Somatic mutations are inherited through the germ-line and these then predispose some mutations. Somatic mutations lead to sporadic cancer and 90-95% of cancers are mostly inherited in the cells of the specific organ where the cancer arises and are known as through the regulation of these three classes of genes. Mutations in the three classes of genes immunosuppressor genes and DNA repair genes. Normal issue homoeostasis is maintained. Black, 2002). Cancer genes are currently classified into these broad classes: proto-oncogenes, and tumour suppressor genes. The selection of a clone of cells with deregulated growth (tumors and mutations promote the selection of a clone of cells with deregulated growth (tumors and these are generally disease that arises from the progressive accumulation of mutations. These

1.2 Inherited cancer

1.2 Literature Review

Levels of care.

Genetic testing without proper counselling will be prevented if the program is instilled at all levels. Based on the principles learned. Incorrect or miss-diagnosed, inappropriate referrals and development of a comprehensive genetic counselling program for all the inherited cancers.
are acquired in the lifetime of the individual. Germline mutations (the first mutation is dominantly inherited) in sporadic cancer both the mutations pertain to cancer and why they are often seen in multiple family members and in successive generations. Why inherited cancers occur at a younger age than the average for the mutations in tumour suppressor or mismatch repair genes. The new diagram shown in Figure Most inherited cancers and all inherited colorectal cancer syndromes are due to inherited mutations is enough to activate the cells to grow and they therefore behave as recessive genes at the cellular level. In proto-oncogenes one
specializes in cancer genetics in the more than 300 cancer genetics programs (Klaeseneyer, et al., 2006). There are more than 450 genetic counseling professionals in the United States who

Australia, Canada, and the United States of America (Klaeseneyer, Londoner, Klemm, et al.,

expansively and has become a recognized subspecialty of clinical genetics in Europe.

The field of clinical cancer genetics dealing specifically with inherited cancers has now grown.

I.2.2 Magnitude of the Problem

and sometimes suggestive syndromic features on clinical examination.

Integration of information from the family tree, the histopathology reports, cancer registries

2005). The mean approach to achieve this is to get as much information as possible by

surveillance guidelines need to be implemented in this group as well (reviewed in Flynn, et al.

carry a mutation. These families are then known to be moderate risk and are at

distinguish these families from families who have a reasonable strong genetic risk, but do not

mutation in a defined gene that will confer a high lifetime risk for colorectal cancer and to

cancers. This is important to identify those families that are likely to carry a germline

significantly increases the risk to relatives and the challenge is to classify families into risk

and most of these genes still need to be elucidated. A family history of the disease

combination of more common multiple low-penetrance genes accounts for the shortfall seen

Known single genes only account for 1-2% of cases (reviewed in Flynn, Hurst, Heli, 2005). A

Genetic susceptibility accounts for 5-10% of colorectal cancer, but germline mutations in the
compared less than 10% of the total number of referrals for the past 5 years and from 2000 to 2003.

Cancer genetics consultation for inherited cancer: Referrals to our unit for cancer genetics consultation has increased significantly. We currently see only a very small fraction of the patients and families that need a consultation. There is currently a low level of referrals for cancer genetics consultation to our genetic counseling service.


Cancer genetics consultation for inherited cancer: 1% of all patients with cancer genetics consultations in 1999-2000, whereas the largest centre in the European survey, in the West Midlands in the United Kingdom, inherited germline mutations are larger (approximately 8 million people) than the population served by the University of Cambridge, South Africa, served by our unit.

The population of Cambridge, South Africa, served by our unit, is different. The demographics of the population served by our unit are different. The demographics of the population served by our unit are different. The demographics of the population served by our unit are different. The demographics of the population served by our unit are different.

The centre (Hopwood, van Asperen, Dorothy, et al. 2003).

Data risk assessment strategies, programs, and genetic counseling protocols were comparable in all inherited cancer depending on the needs of the specific population. Collection of pedigree information and DNA testing for breast and colorectal cancer predisposition genes and many other genetic diseases have access to psychological support. All the centres have access to laboratory centres. All the centres have access to laboratory centres. All the centres have access to laboratory centres. All the centres have access to laboratory centres.

A survey conducted in seven European countries in 2003 showed that the number of cancer
Interpretations (Marie, Spiegel, & Singh, 2004). The variability of the risk assessment criteria used among institutions and individual clinicians has been a major limitation of cancer family risk assessment. Accurate reporting of the family history helps to risk stratify patients and thus in turn determine surveillance and prevention programs. The principle is that all levels of care (primary, secondary, and tertiary) that would be extended to all colorectal cancer could be identified through the use of a patient-based questionnaire. This research project was meant to set up a risk assessment strategy for inherited colorectal cancer only. A decision was made that this study would aim to set up a risk assessment strategy for inherited colorectal cancer. The above studies show there is a definite need to expand clinical cancer genetic laboratory services. The Division of Human Genetics, University of the Western and National Health 2005 only 3 patients were referred for inherited colorectal cancer (pathway submitted data from 2005 only 3 patients were referred for inherited colorectal cancer (pathway submitted data from).
Referrals:

Increased confusion and anxiety levels in the general public can lead to inappropriate self-referral. Current reality of direct-to-consumer advertising of breast screening on the Internet also ensures that all individuals and/or families at risk are identified and referred appropriately. The counseling (Hiney, Withill, Capelle, et al., 1996) of clear guidelines need to be followed to adequately train in Bethesda to identify and refer appropriate candidates for cancer gene testing. Information is important before accurate risk stratification is done. Many physicians lack information on hereditary cancer, but obtaining this by comprehensive, thorough interviews and a detailed family history will at least increase general awareness of the importance of adequate surveillance which will lead to early detection as well as emotional trauma. Overestimation of risk may also lead to unnecessary procedures, treatment, and cancer. Severe stress can be caused if the patient has a false belief in a positive family cancer history. In the literature, there have been several cases in the literature that have resulted in misdiagnosis based on a positive family history. Consequently, patient's and family's cancer risk will result in subsequent inadequate management of the family as well as emotional trauma (Hiney, et al., 2004). In an underestimation of cancer risk and this will lead to missed opportunities for cancer information obtained from the family history. A false negative family cancer history will result in the predictive individuals who may be candidates for gene testing rely almost exclusively on consultation of a thorough family history. (Lynch, de la Chapelle, 2003). Algorithms for the most important step leading to the diagnosis of a hereditary cancer syndrome is the...
Reported family history of colon cancer to a computerized linked population database, which
of colon cancer were checked in a research study in which (Kerber, et al., 1997) a sensitivity
of 0.77% (95% C.I. 0.49-0.68%) was obtained. In this study, the investigators compared self-
no data available on this topic in the South African medical literature. When family histories
breast cancer risk assessments for first-degree relatives (Kerber et al. 2004). There are currently
concerns have also found that patient reported histories are accurate and reliable for colon and
An evidence-based analysis of the accuracy of a family cancer history in overseas cancer

Stange et al. 2006)

= 0.94 for cancers in first-degree and = 0.91 in second-degree relatives (Kerber, et al., 1997).
histories in second degree relatives were only slightly poorer than in first degree relatives (6).
performed with a computerized tool in first and second degree relatives it was found that the
assessment in a study that evaluated the risk-related relativity of family cancer histories
as cancer histories in second degree relatives are also important to make a final risk
The information provided on first degree relatives is however not adequate for risk calculation.

(Tresse et al. 1996). The specificity of the questionnaire was 97% in both centers and the overall accuracy 95%.
Until in Basel, Switzerland, the sensitivity of the questionnaire was 83% (Tresse) and 74% (Basel).
Cancer data collection tool of printed questionnaire. A family cancer history questionnaire on first
inadequate family cancer history information. This may make the form of a computer based
Family history data collection tools are used in many countries to overcome the problem of
risk assessment (56 families). They did not find a statistically significant change in female
risk assessment. Change in female risk assessment was almost always accompanied by a change in
risk assessment and that in 25% of families change was the family’s advantage or disadvantage
that in only 13% of families (12 participants) the history required changes that led to a new
generation to create a patient’s family pedigree. They updated the family history
was found that 59% of cancer cases in the province of Ontario use a family history
and ovarian cancer in Toronto, Canada (Wheeler, et al. 2007). In this study it
was proposed that evaluation the accuracy of self-administered family cancer history
at the congress of genetic counselors in the United States of America in October 2006 a

risk assessment tool for collecting a family history of cancer was validated and the
administrative, computerized tool for collecting a family history information (Agoston, et al. 2006) A self-
computerized tool to collect family history information (Agoston, et al. 2006). A self-
Some cancer genetics clinics in the United States, Europe, Canada and Australia use a

family histories is therefore a reasonable good indicator of actual history.
more accurate reporting of family cancer history. When patients tell clinicians about their
sibships better than males and that a college education was not consistently associated with a
sensitivity were observed among younger subjects, females reported family cancer history
(99% CI: 1.45-0.66), indicative moderate good agreement. This study found that higher
measure of overall agreement between the reported family history and the database. was 0.55
was created by linking gynecological records with the state cancer registry. The kappa score a
are currently exploring the new version of the family history guesstimation has improved.

of risk assessment (with background and counselling) and made it more user-friendly and
previous family history questions were based on the variables that were predictors of a change
2-0-20 minute per counselling session. The investigators have developed a new version of their
that the family history guesstimation is ineffective and that it can also save approximately
different family members (e.g., degree relatives or grandparent's siblings). This study concluded
most commonly addressed during counselling was a change in cancer diagnoses, particularly in
did not significantly affect genetic testing eligibility. It was also found that information that was
allowed for completion of the information obtained by the family history guesstimation and
their setting. Little help with the guesstimation during a genetic counselling session; however
assessment was deemed acceptable to continue the use of the family history guesstimation in
change in risk assessment prior to and post genetic counselling. This level of change in risk
eliciting elasticity prior to and after genetic counselling, but found a statistically significant
relatives. There is an ethical obligation to warn ("duty to warn") a patient's family members if the patient has received genetic counseling and/or testing and is a carrier. If the patient is deceased, then the relatives are at increased risk of the disease. If the patient has received genetic counseling and testing, there is also an obligation to inform the affected member of the family to notify his or her document should be signed to inform the affected individual of the need for further testing and counseling.

The syndrome, the genetic basis, and the importance of genetic counseling and testing about the syndrome should always be a face-to-face interview and should be given to each individual family member differently as their needs may differ. Counseling should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent are given chemotherapy in an oncology practice (Kamwendo et al., 2006), informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic. Especially where patients are given chemotherapy in an oncology practice (Kamwendo et al., 2006) and informed consent should also take place in a quiet environment away from the stress of a busy clinic.
effectively be done in the context of a multidisciplinary team. Inherited colorectal cancer syndrome could be managed and cared for in a multidisciplinary setting with the involvement of a multidisciplinary team. A multidisciplinary service will correctly assess, manage, and screen individuals and families who are at high risk of colorectal cancer. The team needs to include a medical geneticist, a genetic counselor, and a surgeon. In the context of colorectal cancer, the multidisciplinary team aims for the correct management and care of high-risk individuals. Expertise in the field of medical genetics and genetic counseling is essential. The role of the genetic counselor and the genetic counselor in the multidisciplinary team should be seen as a separate and essential part of the holistic management of patients. It is clear from the above that cancer genetics services should be available to all. Preclinical genetic counseling and genetic testing should be performed in consultation with the patient. The new guidelines imposed by the OTH (Office of the Health Insurance Commissioner) require the physician to notify relatives of risk (OHT, 2004). There have already been laws in the United States of America because of the potential liabilities resulting from the physician’s failure to notify relatives of risk (Quinn, 2004). This may also create a conflict between the physician’s obligations to respect the privacy of genetic information and the disclosure of hereditary disease risks (OHT, 2004).
Support of follow-up.

Implications of positive and negative results and patients and families do not get psychological support.

Limitations of genetic testing are also not discussed; patients do not understand the discrimination as well as uncertainties surrounding the quality of genetic testing. The cost-effective due to over servicing and is dangerous due to ethical issues raised to the consumer access of information and testing via the Internet. Direct Genetic testing is not especially with the current line of privatization of genetic testing in South Africa and direct.

Awareness should also be created that genetic testing cannot be offered to just anyone.

The implications for future generations should also be addressed in the counseling session.

Testing and counseling of many family members at risk of inheriting the cancer syndrome
diagnosis, risks and the risks to other family members. This may then also lead to cascade screening within individuals and other families to support, inform and educate them regarding their personal and genetic counseling needs to be in place to address these issues. There should be the psychological implications of an inherited cancer syndrome diagnosis in a family are also.

Genetic Risk

Including discrimination and confidentiality often seen to be related to genetic testing and counseling. This is also also to address ethical and other sensitive issues.

Clinically, the role of the medical geneticist is also to discuss ethical and other sensitive issues.

Clinically challenging. Many of the rare inherited syndromes can only be identified in individuals or families to identify an inherited cancer syndrome. Many of the reports of individuals and families to identify an inherited cancer syndrome. Many of the clinical geneticists must perform a clinical examination and interpret histopathology.
burden of colorectal cancer is inherited in a Mendelian fashion (Lyshchik and de la Chapelle, 2000). Approximately 5-10% of the total colorectal cancer patients (Lyshchik and de la Chapelle, 2000) approximately 20% of all colorectal cancer patients who have a familial risk (those who have two or more first- or second-degree relatives, have a family history of colorectal cancer is high in the western world and has been estimated to be between 2% and 6% (Johnson, Lanceriser, Fuller, et al., 1995) (Schwartz, Wener, Kattan, et al., 1997). Patients with a family history of colorectal cancer is high in the western world and has been estimated to be in Western countries (Bagli and Capehart, 2004). Colorectal cancer is the second leading cause of death from cancer in the United States and presents a major burden in the United States, Australia, and Europe. The individual lifetime risk for colorectal cancer among individuals and families who are truly at increased risk and who need genetic counseling and testing.

Emphasizes the need for an inherited cancer program at all levels of care to identify those barriers to the current strategies to prevent cancer (Haddad, Larkin, Dimond, et al., 2000). This fear of discrimination and concerns about psychological and psychological issues may prevent done for various personal reasons and health care professionals are not always aware of this. Many individuals may also decide after counseling that they do not want genetic testing to be
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<td>Female</td>
<td>17.5/100 000</td>
<td>0/0</td>
<td>1/4/100 000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>14/3/100 000</th>
<th>14/3/100 000</th>
<th>14/3/100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-African</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
</tr>
<tr>
<td>African</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
</tr>
<tr>
<td>White</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
</tr>
<tr>
<td>Mixed Ancestry</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
</tr>
</tbody>
</table>

Table 1. Population data for colorectal cancer in South Africa.

Table 1.1. Population data for colorectal cancer in South Africa.

<table>
<thead>
<tr>
<th></th>
<th>23/4100 000</th>
<th>30/4100 000</th>
<th>3/2/100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>14.1/100 000</td>
<td>6/1/100 000</td>
<td>1/4/100 000</td>
</tr>
<tr>
<td>Female</td>
<td>17.5/100 000</td>
<td>0/0</td>
<td>1/4/100 000</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>14/3/100 000</th>
<th>14/3/100 000</th>
<th>14/3/100 000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-African</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
</tr>
<tr>
<td>African</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
</tr>
<tr>
<td>White</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
</tr>
<tr>
<td>Mixed Ancestry</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
<td>12/1/100 000</td>
</tr>
</tbody>
</table>

The above figures (section 1.2.5.1) suggest that there may be a large group of patients with

1.2.5.2 Colorectal cancer in South Africa

(Coerl, 2001).

The family pedigree is clearly autosomal dominant, this risk increases to as high as 1 in 2

If 1 in 6, this is high it compared to the population risk of 1 in 20 (in the western population). If

2003). The lifetime risk of colorectal cancer in those with two first degree relatives affected is
Inherited syndromes (Baggioni and Cencini, 2004) 

Many of these well-characterized autosomal dominant increased colorectal cancer risk traits inherited in a Mendelian fashion have been cloned. 

The genes for many of the colorectal cancer syndromes and for conditions associated with an increased risk of colorectal cancer (Table 1.2, 3) are the basis of inherited colorectal cancer management.

Families with an inherited colorectal cancer syndrome are essential components of long-term surveillance and counseling. The number of affected first-degree relatives should also be managed with surveillance and preventive measures.

Appropriate management and genetic counseling are essential for the families of affected individuals. These numbers do not reveal the many family members who have not had these evaluations, nor the affected individuals, nor the affected pathophysiological and genetic lesions.

A total of 124 colorectal cancers were reported in South Africa in 1999 and the figure is
Table 1. Inherited colorectal cancer syndromes with known genes.

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Gene</th>
<th>Inheritance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lynch syndrome (HNPCC)</td>
<td>MLH1, MSH2, MSH6, PMS2</td>
<td>AD (5p21-22)</td>
</tr>
<tr>
<td>Gardner syndrome</td>
<td>APC (5q21-22)</td>
<td>AD</td>
</tr>
<tr>
<td>FAP</td>
<td>APC (5q21-22)</td>
<td>AD</td>
</tr>
<tr>
<td>Hereditary mixed polyposis</td>
<td>CRH (18q11.2)</td>
<td>AD</td>
</tr>
<tr>
<td>Cowden syndrome</td>
<td>PTEN (10q22.3)</td>
<td>AD</td>
</tr>
<tr>
<td>Bardenheir-Riley-Reye syndrome</td>
<td>PTEN (10q22.3)</td>
<td>AD</td>
</tr>
<tr>
<td>Gardner syndrome</td>
<td>MUTYH (16p13.3)</td>
<td>AD</td>
</tr>
<tr>
<td>Familial adenomatous polyposis</td>
<td>APC (5q21-22)</td>
<td>AD</td>
</tr>
<tr>
<td>Juvenile polyposis</td>
<td>BMPR1A (10q22.3)</td>
<td>AD</td>
</tr>
<tr>
<td>Peutz-Jeghers syndrome</td>
<td>STK11 (19p13.3)</td>
<td>AD</td>
</tr>
<tr>
<td>MADH4/SMAD4 (18q21.1)</td>
<td>MADH4/SMAD4/HNF6</td>
<td>AD</td>
</tr>
<tr>
<td>Familial adenomatous polyposis (FAP)</td>
<td>MYH (1p34.3)</td>
<td>AD</td>
</tr>
<tr>
<td>Autosomal recessive (AR)</td>
<td>MYH (1p34.3)</td>
<td>AR</td>
</tr>
<tr>
<td>Autosomal dominant (AD)</td>
<td>APC (5q21-22)</td>
<td>AD</td>
</tr>
</tbody>
</table>

*AD = autosomal dominant, AR = autosomal recessive*
The American criteria (Table 12.3.1) are used to make a provisional clinical diagnosis of HNPC.

Table 12.3.1: Clinical diagnosis of Lynch syndrome/HNPC

1. Founda relative is seen, for example in the family (reviewed in Falm et al. 2005).
2. Prevalence is of the order of 1/3000 (reviewed in Falm et al. 2005). In some populations a
   relative prevalence of the order of 1/3000 (reviewed in Falm et al. 2005) is observed.
   HPNCC only occurs for approximately 1% of colorectal cancers and
   colorectal polyps (such as hamartomatous polyps) are associated with HPNCC.
   Most families have mutations in APC gene (90-95% of the cases), and they are equally distributed (reviewed in Falm et al. 2005). A very small number
   of families (< 5%) have mutations in ATM (2q22.3) which have mutations in ATM gene (2q22.3) and they are equally distributed (reviewed in Falm et al. 2005).

The WRN genes that account for most (90%) of the cases are WRN (2q21) and WRN.

Involvement in the DNA mismatch repair system, to know the mismatch repair (MMR) genes.

HPNCC is due to an autosomal dominant inheritance of mutation in one of the genes

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HPNCC is due to an autosomal dominant inheritance of mutation in one of the genes

The WRN genes that account for most (90%) of the cases are WRN (2q21) and WRN.
are known as the Amsterdam II criteria (Table 1.4) (van, et al., 1997). These criteria have now been revised to include all the HNPCC-associated extracolonic cancers and who is most likely to have a positive genetic test in the high-risk patient group. The initial decision who needs genetic counseling or genetic testing, but are helpful in deciding clinically.
and it makes sequencing of all the mismatch repair genes involved in HNPC unnecessary.

something less. Subsequent IHC can direct germ line testing and is more cost-effective under these in high risk families that do not fulfill the Amsterdam criteria, as MSI is a sensitive

Resection of urothelial lesion is therefore the first step before germ-line genetic testing should be

exclusion. HNPC if a urothelial shows normal IHC (revealed in Film, el. 2005),

progression on IHC staining. IHC is not as sensitive as MSI and MSI is still indicated to

in the absence of extraneous factors by increasing germ line testing only to the samples from which the

expression is always associated with MSI (revealed in Film, el. 2005) and helps

to test numerous for the loss of abnormality of MMR protein expression in urothelial. Loss

initial screening test for HNPC (revealed in Film, el. 2005). IHC testing makes it possible

lack of MSI however confirms a high negative predictive value and it is therefore an excellent

adolescent/geriatric cancers show MSI and has a poor positive predictive value for HNPC.

mutations in exons are best observed at d- and mononucleotide repeats, Up to 20% of

the same individual (revealed in Film, el. 2005). The MSI is due to insertion/deletion

is defined as the presence of extra alleles at a microsatellite when compared to normal DNA of

mismatch repair gene proteins (MMR) in a urothelial malignancies, and microsatellite instability and it

microsatellite instability (MSI) testing and immunohistochemical staining (IHC). Loss of the

considered for specialized urothelial genetic testing and pathologic testing. This includes

individuals in the high risk category in the patients at risk for HNPC who need to be

(Rodrigues-Bigas, Bolin, Hamilton, el. 1997) which were used in the definition of

As mentioned, there are further criteria, known as the Bethesda criteria (Table 1.5)
In Table 1.5 (for colorectal hereditary lesions (Colon, Polyp, Tumor, et al.), 2004) screening with antibodies directed against these proteins (i.e., inclusion criteria) or immunohistochemistry (absence of mismatch repair gene products on histopathological involvement colorectal cancer and genetic testing, 2001). They were recently revised again. The Bethesda criteria have been modified by the American Gastroenterology Association.

<table>
<thead>
<tr>
<th>(8) Absence of mismatch repair proteins on immunohistochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Colon polyp adenoma &gt; 40 years</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Signet cell type colorectal carcinoma &gt; 50 years</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Right sided colorectal cancer with unambiguously pattern on histology &gt; 50 years</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Oesophageal or endometrial cancer &gt; 50 years</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>&gt;40 years</td>
</tr>
</tbody>
</table>

HNPPC exclusion colorectal cancer and/or colorectal adenoma (adenoma > 40 years and adenoma > 40 years).

- Individuals with colorectal cancer and a first-degree relative with colorectal cancer and/or colorectal cancer
- Individuals with two HNPPC cancers (including synchronous, metachronous colorectal)
- American Indian positive
- American Indian positive

| Table 1.5 Revised Bethesda Criteria (Table 1.5) |

Belgians criteria positive high risk patients/relatives (Table 1.5) approach and genetic testing of American criteria positive patients/relatives (Table 1.4) and now directed in the following section (1.2.3.4.2) demonstrate the gene colorectal lesion is directed by the results of other special pathological tests. The
managed.

1.2 illustrates how patients and families at risk for inherited colorectal cancer should be
follow-up surveillance colonoscopies in affected individuals. The flow diagram below (Fig
One should imagine and read all affected individuals and should help in coordinating
The risks and costs of colonoscopy should be explained to patients and family members.
unstable microsatellites in their tumour tissue in the absence of a MLH1 germline mutation.
HNPCG, as well as in individuals who have MMR-protein loss on IHC or a high number of
HNPCG genes in Lynch syndrome.
members. Annual colonoscopies is advocated for MMR-gene carriers in Lynch syndrome.
should perform surveillance colonoscopies on affected individuals and increased risk family
MMR-protocols and should have experience in this field. Suggest to start gastrointestinal
Histopathological are involved in immunohistochemical staining (IHC) to identify absence of
Histopathology is done in an experienced molecular laboratory, preferably linked to the Clinical Genetics Section.
(immuno)histochemistry (ISH) and mismatch repair (MMR) gene testing should be done in
the family work-up, genetic counseling and coordinate genetic testing Genetic testing and reach a multidisciplinary approach. A clinical geneticist/Genetic counselor should do
The genetic work-up and management of Lynch Syndrome (HNPCG) is a step-wise process

12.3.13 Genetic work-up and management of Lynch Syndrome/HNPCG

Banking

Guideline could not be used in this research report to select patients who needed to have DNA
cancer histopathology samples in South Africa at present and therefore this recently revised
Bauerfeind, C.R. & du Preez, J. (2009), Immunohistochemistry is not routinely done on colorectal
Figure 1.2 Genetic work-up and management of Lynch syndrome/HNPCC

<table>
<thead>
<tr>
<th>Family History</th>
<th>MSI-H</th>
<th>MMR-Deficiency</th>
<th>MLH1, MSH2, MSH6, PMS2</th>
<th>MSH1, MSH3, MSH5, PMS1</th>
<th>MLH1, MSH2, MSH3, PMS1, PMS2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Family History</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Family History</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 1.1** Revised guidelines for genetic counseling for Lynch syndrome/HNPCC

- MSI-H: Microsatellite instability
- MMR-Deficiency: DNA mismatch repair gene defects
- MLH1, MSH2, MSH6, PMS2: Key genes for MSI
- MSH1, MSH3, MSH5, PMS1: Other genes for MSI
- MLH1, MSH2, MSH3, PMS1, PMS2: All key genes for MSI

- HNPCC: Hereditary Non-Polyposis Colorectal Cancer

- Testing options: Genetic testing, IHC, MSI, other panels

- Management: Counseling, surveillance, genetic counseling

- Genetic testing for high-risk individuals

- Surveillance: Colonoscopy, other tests

- IHC: Immunohistochemistry

- MSI: Microsatellite instability

- HNPCC: Hereditary Non-Polyposis Colorectal Cancer

- Lynch syndrome: Hereditary Non-Polyposis Colorectal Cancer

- MMR-Deficiency: Key to Lynch syndrome/HNPCC
There are a considerable number of colorectal cancer patients, which is different from AFAP. AFAP is responsible for hereditary nonpolyposis colorectal cancer (HNPCC), which is a well-known genetic disorder. The APC gene, located on chromosome 5q21-22, has also been described and is associated with AFAP. The APC gene has been described in the Ashkenazi Jewish population, where mutations in this gene have been observed in a higher percentage of colorectal cancer cases (usually over the age of 40 years). The reason is more often an inherited form of AFAP (APC), less than 100 colorectal adenomas have been described, followed by a family history of AFAP (APC), and more than 9 adenomas and no family history are due to mutations in the APC gene on chromosome 5q21-22.

The prevalence in the European population is estimated to be 1:10,000, while in the Ashkenazi Jewish population, it is estimated to be 1:1,000. Colonoscopy examination of the colon after the age of 12 years, clinical examination of familial adenomatous polyposis (FAP) is made if there are multiple polyps present on colonoscopy (100-200 polyps, reviewed in Cole and Steinheide, 2000).
of all colorectal cancer cases by a clinical examination is therefore important.

due to mutations in the APC gene (Bagnall and Cunliffe, 2004). Cancer clinical assessment

described tumors Whose multicentric nature includes tumors of the skin, dental anomalies, and

and obstruction, multiple epithelial cysts, and tumors of the skin, dental anomalies, and

tumors used for FAP. These endoscopic manifestations, the colonic tumors of the cecum, mesentery,
syndromes and thereby making sure that the correct diagnosis is made. Cancer syndrome is a

reports to identify the histologic and hematological associations associated with each of the polyposis

clinical features associated with the hereditary polyposis syndromes and revealing histopathology

important to distinguish other polyposis syndromes from FAP by examining patients for

example in patients for familial polyposis or familial adenomatous polyposis. It is also

individuals and they need to be monitored, screened, and examined for these indications. For affected

diagnosis. These endoscopic manifestations may also have serious consequences for affected

clinical features outside the gastrointestinal tract that are helpful in making the correct

and some of the rare hematotransfusional polyposis syndromes are multisystem diseases with many

Clinical examination of individuals with multiple colorectal polyps is important because FAP

colorectal cancer syndromes are excluded.

These patients' families can be grouped under the term Wellenbrand FAP, if any inherited

adenomas associated with a significant increase risk of colorectal cancer (Finn, et al. 2005).
The surveillance guidelines for early detection of colorectal abnormalities and cancer in patients
with either age of 10-12 years in children at 50% risk for the condition or in gene carriers.
(Lynch, et al., 2003) (Figure 1.2: section 1.2.3.1.3). Surveillance in FAP needs to start at age
is also indicated if there is strong clinical evidence of HNPCC without genetic confirmation.
For example, HNPCC families should start at an early age (21 years). Annual full colonoscopy
excluding over 15 years (Larson, et al., 2000). Surveillance for cancer in
2004). The benefit of regular colonoscopy has been shown through a controlled clinical trial.
An example of this is annual colonoscopy advised for gene carriers in HNPCC (Lynch, et al.
are important published surveillance recommendations for cancer in these syndromes.
1.2.5.4 Colorectal cancer surveillance
<table>
<thead>
<tr>
<th>Condition</th>
<th>Action</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV+ cancer in the management of cervical cancer in women who have had a hysterectomy</td>
<td>Colescopy with biopsy</td>
<td>Clear to be monitored</td>
</tr>
<tr>
<td>HPV- cancer in the management of cervical cancer in women who have had a hysterectomy</td>
<td>Colescopy</td>
<td>Clear to be monitored</td>
</tr>
<tr>
<td>Non-malignant condition</td>
<td>Colescopy</td>
<td>Clear to be monitored</td>
</tr>
<tr>
<td>Malignant condition</td>
<td>Colescopy</td>
<td>Increase risk</td>
</tr>
<tr>
<td>Invasive cancer</td>
<td>Colescopy</td>
<td>Increase risk</td>
</tr>
<tr>
<td>High risk</td>
<td>Colescopy</td>
<td>Increase risk</td>
</tr>
<tr>
<td>Moderate risk</td>
<td>Colescopy</td>
<td>Increase risk</td>
</tr>
<tr>
<td>Low risk</td>
<td>Colescopy</td>
<td>Increase risk</td>
</tr>
</tbody>
</table>

Table 1.6: American Cancer Society guidelines on surveillance for the early detection of cervical cancer.

Cervical adenomas and cancer in women and men at risk.
Bowel-specific criteria (Table I.5) for Lynch syndrome:

1.3 and 1.4 or the criteria need to decide who needs further genetic testing. For example, the inherited cancer syndrome (Table I.3), for example the Amsterdam criteria for Lynch syndrome (Table I.4.

Sensitive services and are not the criteria that are used to make a clinical diagnosis of an W present (at all 2004). These criteria are used to assess who need to be referred to cancer counselling. Higher-moderate and average risk (Table I.7 and I.8). (Handel, S.)

Different risk levels for colorectal cancer to decide who needs a genetic assessment and genetic risk assessment criteria were developed for categorize individuals and families into these:

1.6.6 Inherited colorectal cancer risk assessment for genetic counselling

Suggests:

Diagnosed and managed according to their inherited risks with appropriate surveillance

In all areas and all levels of care, patients and families need to be clinically assessed where there is no ready available molecular diagnostic service for inherited colorectal cancer syndrome and who do not have affordable easy access to genetic testing in South Africa be withheld from individuals/families who have strong clinical evidence of an inherited gen

I.5.5 Importance of surveillance
Table 1.6. Not only cancer screening initiatives, but also treatment strategies may be affected (Whitney, Pfeiffer, Rux, et al. 2005) and the surveillance recommendations are similar to in this study regarding the management of individuals who are at high inherited cancer risk. Increased cancer surveillance and genetic testing, guidelines are available and were followed in individuals and their families who benefited from referral to a cancer genetics professional. Histories highly suggestive of one of the hereditary cancer susceptibility syndromes. These individuals in the high-risk category therefore have clinical characteristics and/or family

<table>
<thead>
<tr>
<th>Poppos</th>
<th>12.5% of degree relatives within 10 years.</th>
<th>10 years of age.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>and was younger than 50 years at diagnosis.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>One first degree relative had colorectal cancer (multigenic)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Same time (syndromic) or at different times</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 or more HNPC associated cancers at the same generation with no age restriction.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>renal pelvic cancer (all cancers can occur in one small bowel, bladder, liver, pancreas, uterus and include colorectal, endometrial, stomach, ovary.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>With any of the HNPC associated cancers and</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Three or more 12.5% degree relatives affected</td>
<td></td>
</tr>
</tbody>
</table>

Table 1.7 Risk assessment criteria for the high risk group (Whitney, et al. 2005)
of an increased cancer risk as listed in the tables above. Increased cancer surveillance in this average risk is where clinical and pathological characteristics and histories are not suggestive.

Table 1.8 Risk assessment criteria for the moderate risk group (Hampel et al, 2004)

<table>
<thead>
<tr>
<th>Moderate cancer risk criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Degree relatives with colorectal cancer at any age</td>
</tr>
<tr>
<td>Developed colorectal cancer at age &gt; 50 years and one 2nd degree relative</td>
</tr>
<tr>
<td>Two 2nd degree relatives with colorectal cancer</td>
</tr>
<tr>
<td>One 2nd degree relative with colorectal cancer</td>
</tr>
</tbody>
</table>

1.2 5.6.3 Average Risk

Individuals in the moderate risk category have a history which cannot be classified into the high risk category but which still conveys an increased risk for cancer, requiring increased surveillance. Depending on the history (Table 1.9) (Hampel et al, 2004) a cancer gene syndrome is also considered in the moderate risk group.
reduce colorectal cancer risk in the population and showed that there may be a benefit of certain medications, for example, non-steroidal anti-inflammatory drugs (NSAIDS), to have colorectal surgery (Hillner, Lysholm, et al. 2004). Research studies have evaluated the also been shown that mutation carriers were significantly more likely than those defined to patients with hereditary non-polyposis colorectal cancer (HNPCC; Hamada et al. 2004). It has colorectal endoscopy and adherence to recommendations for colorectal cancer screening in It has been shown that genetic testing and counseling significantly influence the use of can be followed and that surgical intervention is unnecessary. reassured that they are not at increased risk and that less stringent screening recommendations relative to the inherited syndrome. Individuals or family members that are negative can be reassured that they are not at increased risk and that less stringent screening recommendations can be followed for the affected family. Colorectal endoscopy and counseling for the general population that was found in the affected family for colorectal cancer. Family members that are at risk can then be offered preventive genetic counseling and testing for the specific mutation that was found in the affected family. General testing is important because the diagnosis of an inherited colorectal cancer syndrome

I.2.5.2 General Testing of Inherited Colorectal Cancer

Years in men and women exceeding 30 American Cancer Society guidelines (www.cancer.org)
is currently only available on a research basis at the Genetics Department of the University of Cape Town. A diagnostic gene testing (microsatellite instability testing and mismatch repair gene evaluation) is currently available on a research basis at the University of Stellenbosch. Western Cape.

Potentially familial (personal communication, R. Ramesar, Medical Genetics, University of Cape Town) genetic testing and immunohistochemistry with subsequent gene testing for the mismatch repair genes of the HNPCC are available for other population groups. The service is expanding and will be available for the family of mixed ancestry of the Cape Province, South Africa (Ramesar, Middleton, R. Ramesar, Medical Genetics, University of Cape Town, personal communication). Ramesar, Medical Genetics, University of Cape Town, (personal communication), personal communication, Ramesar, Medical Genetics, University of Cape Town, (personal communication) is currently available on a research basis at the University of Stellenbosch, Western Cape.

An inherited colorectal cancer genetic testing for familial adenomatous polyposis (FAP) is currently available on an individual basis and not available in Johannesburg, Cape Town. A diagnostic gene testing service in the management of the inherited colorectal cancer syndromes is currently not available for a molecular approach.

(Small, Ray, Daube, et al., 1999). There is therefore an urgent need for a molecular
Specialized centers and the appropriate confidentiality procedures and multidisciplinary and medical terms no more established, formal assessment and testing are only available in special support at population level, the cost-effectiveness in economic, psychological social influence for early surveillance, prevention, treatment, education, counseling and screening are not yet in place at population level (these should include facilities and general population is not yet established, the complete range of services needed for general developed world includes the acceptability of formal assessment and nutrition test in the criteria that are not met for population screening of colorectal cancer susceptibility in the management of prevention centers (Coffin, 2001).

Abnormal polyps in men and women polyps is understood and there is emerging consensus on the fact in the latter or precancerous stages of disease, the natural course from premalignant cancer is sigmoidoscopically able to identify the large population there is a considerable burden of colorectal cancer, and only some of the criteria for population screening at this stage can be met efficiently for population screening in the context of reducing the general susceptibility for screening programs at population level (Wilson, 1968; Coffin, 2001). Criteria have been a 1996 World Health Organization (WHO) report is still used today for the evaluation of these needs to be user-friendly, reliably, cost-effective and sensitive. It can also only be

12.5 Population screening for inherited colorectal cancer
Gynecologic counseling services in a primary care setting may not be included in comprehensive care. An effective integrated screening program and creating awareness of the availability of cancer screening for genitourinary cancers is crucial. Nevertheless, the high risk group of women with a family history and those with suspected genetic anomalies are not always covered by screening programs. The limited sensitivity of current screening strategies renders the identification of women at greater risk challenging. The rarity of mutations in the APC and HNPCC-associated mismatch repair genes, and the limited penetrance of current screening strategies, renders general population screening potentially misleading and not cost-effective. High risk patients need to be identified, counseled, and examined before molecular genetic testing is offered. Developing population screening potentially misclassifies and may not identify high risk patients. It is critical to ensure that colorectal cancer is screened for in a general population. The use of non-invasive population-based screening in the general population is recommended as a screening measure in the general population.

At this time, the use of germline mutation testing to identify families at increased susceptibility to colorectal cancer is not even available in most of the specialized centers in South Africa. A diagnostic genetic test for colorectal cancer is not even available in the developing world and in South Africa these criteria are further away from being accomplished.
Genetic testing is underutilized. Through this program, it is hoped that inappropriate genetic testing is underutilized. Those who are well informed and who made a choice if they want to be informed about the potential for inherited colorectal cancer. Genetic assessment and counseling offers the potential to reduce cancer surveillance on individuals only if increased risk and genetic testing in all patients and families who were found initially to be at increased risk and therefore makes a formal pedigree study essential and directs and standardizes management assessment of a research tool for identifying high-risk families. This step-wise program for the identification and management of these patients and families and the risk for inherited colorectal cancer by the development of a step-wise genetic counseling program for families at risk for inherited colorectal cancer. The study's primary motivation was to prevent mismanagement of patients and families at risk for inherited cancer syndromes.

Follow-up and the delivery of adequate professional services for individuals and confirmation inappropriate referrals and genetic testing without proper counseling and or mis-diagnoses because of incomplete family information and misdiagnosed South Africa today. There is also a lack of awareness of genetic counseling services. Wrong information and attitudes, risk education, management, and follow-up are serious issues in inherited cancer. By professionals without adequate genetic counseling, formal policy and the threats of direct to consumer access of genetic testing and the rejection of genetic tests for the Malignant sense for study.
accordine to their risk.

(3) Facilitating research participation and families, from a genetic point of view.

(2) Classifying families into one of these risk categories for inherited colorectal
identification of increased risk families.

1) Drawing on a personal and family history questionnaire as a tool for the initial

This was achieved by:

The development of a step-wise Genetic Counseling program for inherited colorectal
cancer.

1.4.1. Primary aims

1.4.2. Aims

Risk for inherited cancer.

Improve the detection, counseling, testing, and management of patients and families at
comprehensive programs for all the inherited cancers can be instituted at all levels of care to
colorectal cancer. It is hoped that in future, the program could be expanded to cover a
more comprehensive program. The final outcome of the project was to develop a Genetic Counseling program for inherited

that do not want genetic testing to be undertaken for various personal reasons.

Testing will in future be preformed on moderate and average risk individuals and on individuals
Relatives

- Assess patients' feelings regarding the sharing of cancer risk information with their
  relatives
- Their response to genetic counseling and genetic testing
- Assess patients' and families' attitudes towards the genetic counseling program and
  its impact

In Jamaica

- Create awareness of the need for cancer genetic molecular diagnostic services
  related to the basic management of inherited cancer risk
- Lead in the study of the mutability and importance of genetic counseling and genetic
  testing for colorectal cancer
- Establish a multidisciplinary service for the management of families at increased risk
  of the Wisconsin and National Health Laboratory Service
- Increase cancer genetics referrals to the Division of Human Genetics at the University
  of Wisconsin
- Assess the reliability of the self-administered personal and family history questionnaires

The secondary aims were to:
South African guideline is available for comparison.

Individuals/joining families at risk for inherited colorectal cancer. The similar standardized program or
developed step-wise format containing program to identify, risk and manage prospective observational study that assessed the effectiveness and benefits of using a newly

The study, undertaken over a 28 month period, from May 2005 to August 2007, was a

2.2 Study design

and this chapter.

collected data are then discussed. A statement on ethics approval for the research project will

The methods of how the quantitative calculations and observations were made from the
data collection and the management of participants and families according to their genotype risk

and family history questionnaire) for patients affected with colorectal cancer, the procedure for
describing the distribution of the consensus form, information sheet and research tool (personal

for family members at increased risk of colorectal cancer. A discussion will follow

family history questionnaire); standard letter for average risk participants and cascade letter

information sheet for patients, consent form for minors (>18 years), research tool (personal and

the completion and selection of study participants, the construction of the consent form and

This section will discuss the study design and period under which the study was undertaken.

2.1 Introduction

2. Study design, subjects and methods
private practices where they are successfully managed and medically needed for.

Participants recruited—Patients were recruited from specialists, clinics, and specialists and approached through patient groups.

The questionnaire and signed consent become study participants. No-one who was returned the questionnaire became study participants. All the patients that completed the questionnaire were approached and handed questionnaires by specialists and colorectal cancer was approached and handed questionnaires to all colorectal patients seen at various clinics across Newfoundland province, South Africa, among others.

Study sample—A consecutive group of forty-eight newly diagnosed and follow-up.

2.3 Participant selection

Patients were happy to share their risk information with their relatives.

The program led to the establishment of a multidisciplinary surveillance and follow-up.

Patients and families accepted the program.

Awareness was created of the availability of cancer genetic services.

Patient numbers increased after initialisation of the program.

Information for risk stratification of families.

And consensus form used in the first step of the program was reliable in collecting.

The patient-based self-administered data collection tool linked to an information sheet.

Observations that were made to evaluate the effectiveness and benefits of the program were to
Both the private oncology practices that were used are linked with
\textit{Hillpark Hospital} in Johannesburg. Patients were recruited for such an
involvement in an agreement to discuss inherited risks for colorectal cancer at a
\textit{Medical Oncology} practice in Pretoria, and a special interest in colorectal care at
\textit{Medical Oncology} practice in Johannesburg. Little Company of Mary Hospital,
\textit{Gastroenterology Clinic} and \textit{General Surgery Ward, Donald Gordon Medical Centre},
were used included Johannesburg General Hospital \textit{Medical Oncology Clinic}.

\textit{Practitioners/wards chosen for patient recruitment - the clinics and practices listed}

Program can be instilled in the population level,

measured increased colorectal cancer risk factors before a large scale family cancer
evaluation of a research tool with follow-up counseling was successful in identifying and
where the colorectal patient load was expected to be high. It is a pilot project to
affected with colorectal cancer at least 2 years and a new colorectal practice at a
centre South African population. It was therefore only aimed at a larger population already
not know the acceptability of familial assessment and genetic testing in the general
(Ahwazian, et al. 2003) and the role that genetic counseling professionals currently do
because of the absence of a defined management protocol at a population level.
developed could not be instilled at population level. A considered a screening tool

gastroenterologists and surgeons. The self-administered questionnaire that the writer,
in management and treatment of patients with colorectal cancer include oncologists,
in the research project.

An Information Sheet and Consent Form was constructed. The first paragraph included a

2.4.1 Information Sheet and Consent Form for Patients (Appendix 2A)

A) Overview Risk Participants and Consent Letter

2.4.2 Construction of Information Sheet, Consent Form, Research Tool, Standard Letter for Participants, Gene
testing and Management

an assessing personal and family history information of self-referring patients at risk

Human Genetics at Johannesburg Hospital. Patients who consulted the Division of

the surgery until at Johannesburg Hospital. Patients that participated in the research is linked to

where most of the newly diagnosed colorectal cancer patients are primarily managed.

only other clinics/wards that were approached at Johannesburg Hospital because this is

Dr Constand Schober, the Breastcancerology clinic and General Surgery ward were the

and the Acting Head of Medical Oncology at Pretoria Academic Hospital at the time,

obtained from the Head of Medical Oncology at Johannesburg Hospital, Prof Paul Rutti

Medical Oncology at the University of the Witwatersrand and the University of
participant had any problems with interpretation of the questionnaire.

The investigator's contact numbers were included if there were any questions or if the signature of a witness in case of verbal consent was included for the purpose of consent. A final paragraph with a space for the participants' signatures, a date and place and a date for the final paragraph should take place should the participant be found to be at increased risk for inherited colorectal cancer.

A further paragraph should the procedure that would take place should the participant be found to be at increased risk for inherited colorectal cancer.

The investigator also asked the participants' permission to access their medical records. A fax number was given if the participants wanted to fax the questionnaire to the investigation. A fax number and how the case could complete and return the questionnaire to the investigation.

The third paragraph stated how much of the participants' time is needed to complete the study.

A fourth paragraph was constructed that stated that all the information would be treated confidentially and that the participants' treatment would not be affected in any way.

A fifth paragraph was constructed that stated how they could withdraw from the study.

The information was shared how much of the research project is informed participants that there were no risks involved and that the participants could withdraw from the study at any time.
The West Midlands Family Cancer Registry, United Kingdom (reviewed in Col),

of a computer-based data collection tool (which is a 2009) or a printed questionnaire, and

histories recorded by clinicians in busy oncology and specialist clinics. The form also lists the

States, Europe, Canada and Australia to overcome the problem of in-depth family cancer

Family history data collection tools are used in some cancer genetic clinics in the United

2.4.4. Research tool: personal and family history questionnaire (Appendix C)

Form.

acquaintance from the entire to participate in the study was included at the end of the essay.

my benefit their family members was also constructed. A sentence asking for a verbal

constructed. A final paragraph stating that the study would not benefit from directly, but that it

whether there would be an examination of them and their health records were used was

whether than there would be some questions that their parents need to fill in our questionnaire.

and simple explanation of the purpose of the research project to the patient. A paragraph

An assent form for minors (< 18 years) was constructed and included a general introduction

2.4.3. Assent Form (Appendix 2e)

Research project. The same information discussed in section 2.4.1 was included.

explained in section 2.2. This was constructed for parents of minors who participated in the

A information sheet and consent form for parents was constructed on the same principles

2.4.2. Information sheet and consent form for parents (Appendix 2d)
accuracy of family cancer history reporting in the South African medical literature. Genetic counselling clinics. There is currently no evidence-based guidelines available on the use the first part of the questionnaire, and was based on the woman's clinical experience in the family history questionnaire on second degree relatives was conducted in the same format. Therefore another developed for the purpose of accurate risk stratification. The second part of risk assessment. The family history cancer history questionnaire used in this research project was based on the questionnaire used in the study of Mussio et al. (1998).

Family History

The first part of the family history questionnaire constitutes for this research project was attained through the Clinical Cancer Research Unit in Basel, Switzerland (Mussio et al. 1998).

A family cancer history questionnaire on first degree relatives was validated in two European centres which may have increased the accuracy of the information.

In their specialist clinics, which may have increased the accuracy of the information.

discuss family cancer histories with their relatives at home in their own time before returning to South Africa. The printed questionnaire also gave participants the opportunity to print the questionnaire at a data collection tool. It was thought to be more acceptable in the South African context. The latter developed a patient-based self-administered computer-based questionnaire on tertiary health care settings' most preferred practice and it was validated and the test-retest reliability was found to be high (Ahearn et al. 2006).
would not be shown to anyone, except to the researcher and his supervisor.

The page was included stating that the section of the questionnaire was confidential and that it was based on the writer’s experience in the genetic counseling clinic. A statement at the top of the page begins with the sentence “This information is invaluable in assessing inherited risk and the likelihood of cancer in the family.”

The section on the participant was also included here. The type of cancer the participant had, the section of the questionnaire with the family history section can be removed from the first page of

The histopathology samples are done for the purpose of confidentiality. This will be used in future when genetic counseling is done for the purpose of confidentiality. For the participant’s study code was constructed. This will be used in future when genetic counseling is done for the purpose of confidentiality. The questionnaire is a space for a pattern code was left on the first page to link it to the rest of the questionnaire. Family name (maiden name) could help in linking families who have

A personal information sheet on the second page of the questionnaire was constructed and included a

participant’s first and middle names, family name/ surname (maiden name in case of females) and married name were included. The participant’s street and postal address, contact and sex number, e-mail address and contact numbers of other close relatives were included. A
The professionals that work in the Genetic Counseling Clinic at the National Health

are able to advise them about measures to screen and possibly prevent cancer. Colorectal cancer is one of

explaining the significant familial influence with a familial syndrome stating that doctors would be

might need to be involved if the genes involved. In general, a paragraph

The letter was sent to family members of the proband. This letter consisted of a basic

A cascade letter for family members at increased risk of colorectal cancer was constructed.

(Appendix 5)

2.4.6 Cascade Letter for Family Members at Increased Risk of Colorectal Cancer

information.

Consulting Clinic were included should the study participants require any further

participants. Consultation numbers and test numbers of the investigator and the Genetic

people who have a personal history of colorectal cancer was included for the selected study.

this may alter their risk classification. A paragraph stating the management guidelines for

Clinical trials and any changes arise in phase II their family history Information regulations for

Society). The letter also stated that families should notify the Genetic Counseling

average colorectal cancer risk were shared in this letter (Wray Cancer Genetics.

Information they provided in the questionnaire. The information population guidelines for

members were at the average population risk for colorectal cancer according to the

category. Thus, letters thanked them for their participation and stated that their family

A standard letter was constructed and sent to all participants who fell into the average risk

(Appendix 4)
involved were informed about the procedure to discuss the questions.

The questions were also distributed to surgical-in-patients at John Hunter Hospital by
after the patients' appointments or by their staff members after their specialist appointments
were followed-up for colorectal cancer. The distribution was done by the receiving specialists
(research tool) were distributed specifically to all patients who were newly diagnosed with or

The information sheets, consent forms and personal and family history questionnaires

2.5.1 Distribution of Information Sheet, Consent Form and Research Tool

2.5 Data Collection

cancer risks and in hand out the cascade letters to them.

session. If interested, the patients/responsibles/responsible to inform their relatives about their colorectal
wanted to contact the staff at the Genetic Counseling Clinic to arrange a Genetic Counseling

The cascade letter gave the family members the opportunity to decide for themselves if they

Hand paragraph of the cascade letter.

put the family member under no obligation to undergo a Genetic test was also included in the
secretary at the Clinic. A sentence stating that a consultation with Genetic professionals would

Laboratory Service in John Hunter Hospital were included as well as the contact number of the
kept in a separate confidential file until collection at the specialist practice. Faxed or posted
Confidentiality was maintained throughout the program. The completed questionnaires were

aspects of their cancer.

the information sheet if help was needed or if patients had questions or wished to discuss
clinical division (a research nurse) was available to help. Completed numbers were provided on
If there were any problems with interpretation or understanding English, a translator from our

questionnaires to the Division of Human Genetics in Johannesburg.

at the specialties practice for collection or study participants could also fax or post the
questionnaires at the clinic/practice or in the ward. The completed questionnaires could be left
questionnaires home to discuss cancer histories with their relatives or complete the
personal and family history questionnaire in their own time (Appendix 2). Participants could take
a signed consent form if they were willing to participate (Appendix 1) and then complete a
Study. Those patients who agreed to participate were asked to read an information sheet and
approached to discuss the project and were asked to participate in forming patients in the

Doctors, their receptions and nurses of cancer and gastroenterology services were

2.5.2.1 Step 1

and managed patients and their families affected with colorectal cancer (Appendix 1).
A three-step approach was followed to identify, enrol in the study, risk stratify, counsel, rest
In an opportunity to be seen.

General risk counseling and surveillance

need were to identify patients/families who would benefit from a clinical genetic consultation.

or families that needed genetic testing as the criteria are not sensitive enough. The criteria listed in Table 1 and Table 12. The criteria used were not aimed at identifying individuals in the family and personal history.

Participants were classified by the study investigators.

Letters were sent only and kept in a locked filing room with controlled access. Access to

questionnaires were addressed to the patient only and were directly handed to the patient by a

questionnaires were addressed to the patient only and were directly handed to the patient by a
Third parties.

Colorectal cancer, genetic testing and the sharing of genetic information with relatives and
risks. The wider addressed the psychosocial aspects and ethical issues related to inherited
understanding the genetic basis of colorectal cancer, the inheritance patterns and the familial
regarding the inherited risks. Visual materials were used to guide them through the process of
specific genetic counselling techniques were used to address patients', relatives' and concerns.

Family members could be enlisted into a cancer surveillance program or offered genetic testing.

Malignant and the family history information needed to be confirmed before patients and
diagnostic surgery and chemotherapy. This information was important because the cancer
medical and histopathological reports regarding the microscopic appearance of tumors, the

A detailed three-generation family tree was constructed and information was gained from

Each appointment was given an approximate time frame of one and a half hours to complete.

They were examined and counselled.

When interviewed, a formal pedigree study was done, histopathology reports were assessed and
found to be at moderate or high risk. Patients who agreed to the clinical appointment were

Patients/relatives were phoned for an appointment at a place convenient to them if they were

2523 step-3
perceived benefit. The responses were recorded in a handwritten way and were not
participants' perspective. The program was well accepted and it was to the participants' 
indication if the cancer program and subsequent genetic testing were needed from the 
their responses and their reasons in their lives. This was done to give the writer some 
whether they would pursue genetic testing were also sought. The writer noted 
resulting in their thoughts that they or their family members at risk would benefit from 
consenting and genetic testing were assessed. Participants were asked how they felt about genetic 
families, although as part of the genetic counseling program and their responses to genetic 
asked about their reasons for sharing the risk information with their families. Participants and 
family and they were asked to inform their family members of these risks. They were also 
During this interview, participants were informed about the inherited risks to their extended
considered, increasing the chance that a familial mutation may be present in that family.
(FAP), a diagnosis of Lynch syndrome needs to be
in HNPCC) or familial adenomatous polyposis (FAP) more often in cancer or colorectal polyps. The 
mutations were associated with colorectal cancer or colorectal polyps. The "Lynch syndrome" nomenclature
induces mismatch repair gene mutations in specific mismatch repair genes (MSH2 and 
HNPCC to diagnose a variant of this syndrome called Muir-Torre syndrome, which usually
for benign or malignant sessile or polypoid lesions. The writer also examined the skin
adenomatous polyposis (FAP). If this condition was present, the writer also examined the skin
abnormalities, developmental abnormalities, and polypoid skin manifestations of these
based on clinical examination, specific signs of the disease in mental
The writer examined the affected study participants for clinical signs of the cancer familial

2
Investigations for colorectal cancer screening and screening for associated cancers included a detailed management program with information about the frequency of special risk factors. The genetic assessment included genetic counseling and ethical issues, discussions, and the participants were sent detailed information letter about the genetic counseling and the results of the testing.

The Human Genetics Department of the University of Pretoria offered a service to those patients. The information in this study was provided to each patient. The testing will be performed at the John and Germaine Genetic Testing Laboratory. The testing will be performed on all the high-risk patients that were part of the study. When DNA was extracted and prepared for testing, the genetic testing was performed.

The revised Bethesda criteria (Table 1.2) were used in our study to decide who needed to be in a generalized fashion.

Therefore, only make a statement on this perceived impression of the participants and families, for better revision as this fell beyond the purpose of this research project. The writer could qualitatively assessed, specifically recorded word for word in the participants’ lives, or added into the study.
Report evaluation and clinical examination of affected program.

- Increased risk of recurrence (moderate and high risk)
- Increased risk of cancer surveillance was sent (Appendix 4)
- Average risk of recurrence and families - a standard letter with population guidelines for

Participants were managed according to their risk as summarized below:

2.6 Management of Participants and Families

Participants were managed according to the appropriate clinician's guidelines, management of individuals and families would also involve their primary care physicians.

Surgery was indicated; therefore the need for a multidisciplinary approach long-term follow-up with clinical excretions and/or special investigations, medical treatment or referral to the radiation oncologist (Appendix 4). Risk reduction may include regular

Risk reduction guidelines of the National Institute of Cancer of the United States of America this study. The management of these individuals and families was based on the most recent

The establishment of a multidisciplinary service for the management of participants and their family members was

Also included in this letter, copies of these letters were sent to their doctors.
their insurance and the age of onset of their cancer.

Participants in the moderate and high-risk groups gave the correct information regarding information in patient’s medical files and histopathology reports to assess how many moderate and high-risk groups. This was to see if the questionnaire was informative the risk classification based on family history data in the questionnaires in the

The risk classification obtained after the genetic counseling session was compared to

2. Quantitative calculations and observations from collected data

Information (Appendix 5)

e. Sending cascade letters to participants for their family members with risk

Guidelines to patients and their referring doctors and specialists

Organ surveillance and sending follow-up information letters with surveillance

Directing management of participating families according to their risk with

Humoral immune if they wanted to pursue the role of genetic testing

Directing genetic testing if they were found to be at high risk and then banking

c. Often genetic testing if they were found to be at high risk and then banking

1. The indications for and availability of genetic testing

Immunological, familial pedigree study and clinical examination, information

Obtained from the familial pedigree study and clinical examination, information

Reassessing participating families into risk categories according to the data
Appendix 8.

Consent Form in 2005, the ethics clearance number is R.14/49, protocol number M/050272.

Ethics approval for the research project was received from the Human Ethics Research

2.8 Ethical Considerations

Sharing cancer risk information with their families was calculated.

- The number of patients in the moderate and high risk groups who were positive about
  moderate and high risk groups.

- The number of patients who were positive about these results were calculated in the
  multidisciplinary service were done during the genetic counseling sessions and the
  testing. Further management of the their families' inherited risks and the need for a
  clearance of the patient's alleles towards genetic counseling.

- Observations regarding the patient's attitudes towards genetic counseling services.

- Similar time span in previous years (approximately 2 years, from 2003-2005),
  the program in 2005 until completion in 2007 were compared to figures seen over a
  period of 10 years at the University of the Westerweld an Unilex, Pediatric & Health
  Sciences Service Section of the Division of Human Genetics at the National Hospital Laboratory Service.

- The increase in patient numbers seen for inherited colorectal cancer at the Clinic.

- For genetic work-up in the high risk group was calculated.

- The number of patients who were interested in genetic testing and banking their DNA
  of patients that participated in the study was calculated.

- The number of patients seen for genetic counseling as a percentage of the total number
had medical aid and were from various sections of society (34%). Seven of the participants were from other provinces in South Africa and one participant (2%) was not from the participants' province (90%). Table 3.2: Most of the participants came from Gauteng Province (43%) and 17 speaking indigenous languages (22%). 6% were Ashkenazi Jewish females and of the group of participants, 4% were Ashkenazi Jews. Forty-two (88%) of the total number of 48 participants were white (22 males and 20 females). 42% of the participants in the study (Table 3.2) were included.

On the basis of the questionnaire, thirty-three (33%) families were assessed to be at increased risk (moderate or high risk) and 15 families (31%) were assessed to be at average risk for an inherited colorectal cancer syndrome (Table 3.1). Just more than two-thirds of the families included in the study were therefore found to be in a high risk category.

Four such (46) completed questionnaires were received in a 25 month period from the time questionnaires were mailed and completed from September 2005 until August 2007 (28 months).

RESULTS
<table>
<thead>
<tr>
<th>Percentage (%)</th>
<th>Number</th>
<th>Average risk (moderate/high risk)</th>
<th>Total Complied questionnaires</th>
</tr>
</thead>
<tbody>
<tr>
<td>31%</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>69%</td>
<td>33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100%</td>
<td>48</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 3.1: Completed questionnaires and risk stratification

To population group is summarized in Table 3.3.

- Human Ceramics. The patient participation according to self-reporting she as well as according to records, nursing clinics and wards as well as from telephone surveys to the Division of Mental Health. The patients/families that participated in the study were recruited from various levels and had an age of the mean 47.5 years (SD ± 13). None of the participants was under the age of 18 (Table 3.2).

- Group was 61 years (SD = 15) and the mean 47 for the increased risk group was 49 years. For the average risk group fell into the increased risk category was 27-78 years. The mean age for the average risk participants that fell in the average risk category was 52-73 years and the age range of those were pensioners (14.5%) and 7 were housewives (1.5%) (Table 3.2). The age range of...
<table>
<thead>
<tr>
<th>Age Range</th>
<th>Average Age (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-18 years</td>
<td>Increased risk</td>
</tr>
<tr>
<td>49 years (SD: 13)</td>
<td></td>
</tr>
<tr>
<td>61 years (SD: 5)</td>
<td></td>
</tr>
<tr>
<td>21-24 years</td>
<td>Increased risk</td>
</tr>
<tr>
<td>62 years (SD: 5)</td>
<td></td>
</tr>
<tr>
<td>25-27 years</td>
<td>Increased risk</td>
</tr>
<tr>
<td>64 years (SD: 5)</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Occupation</th>
<th>Number of Participants %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Housewife</td>
<td>7 (14.5%)</td>
</tr>
<tr>
<td>Pensioner</td>
<td>7 (14.5%)</td>
</tr>
<tr>
<td>Employed/employed</td>
<td>24 (48%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Characteristics</th>
<th>Number of Participants %</th>
</tr>
</thead>
<tbody>
<tr>
<td>National</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other Province</th>
<th>Number of Participants %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pretoria Central</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Pretoria North</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Pretoria East</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Gauteng</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Free State Province</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Northern Province</td>
<td>3 (6%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Address</th>
<th>Number of Participants %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Johannesburg North</td>
<td>10 (20%)</td>
</tr>
<tr>
<td>Johannesburg South</td>
<td>4 (8%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gender</th>
<th>Number of Participants %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>60 (12%)</td>
</tr>
<tr>
<td>Male</td>
<td>69 (14%)</td>
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<table>
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<tr>
<th>Education</th>
<th>Number of Participants %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-6 years</td>
<td>42 (84%)</td>
</tr>
<tr>
<td>7-10 years</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>11-13 years</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>14-17 years</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>18+ years</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Religion</th>
<th>Number of Participants %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catholic</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Hindu</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Islamic</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Other</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Number of Participants %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>20 (42%)</td>
</tr>
<tr>
<td>White</td>
<td>28 (58%)</td>
</tr>
</tbody>
</table>

Table 3.2 Demographic data
Table 3.3 Patient participation according to recruitment site

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Number of Patients</th>
<th>Recruitment Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>2%</td>
<td>1</td>
<td>Johnsmending Hospital Cleft Surgery Clinic</td>
</tr>
<tr>
<td>4%</td>
<td>2</td>
<td>Johnsmending Hospital General Surgery Ward</td>
</tr>
<tr>
<td>4%</td>
<td>2</td>
<td>Johnsmending Hospital General Oncology Ward</td>
</tr>
<tr>
<td>6%</td>
<td>3</td>
<td>Telephone enquiries</td>
</tr>
<tr>
<td>8%</td>
<td>4</td>
<td>Hospital Surgery Practice</td>
</tr>
<tr>
<td>11%</td>
<td>5</td>
<td>Oncology Johnsmending Donald Gordon Medical Centre</td>
</tr>
<tr>
<td>65%</td>
<td>31</td>
<td>Mary Potter Oncology Centre</td>
</tr>
</tbody>
</table>

Note: Table 3.4 outlines the completion of the study by the end of August 2007.
<table>
<thead>
<tr>
<th>Percentage</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>60%</td>
<td>26</td>
</tr>
<tr>
<td>69%</td>
<td>33</td>
</tr>
<tr>
<td>100%</td>
<td>48</td>
</tr>
</tbody>
</table>

Table 3.4 Final number of clinically assessed cases

- Apply to their first degree family members.
- Cancer Institute of America (www.cancer.org) for colorectal cancer (after the age of 50 years)
- Risk for colorectal cancer and other familial population screening guidelines of the National
- Risks within surveillance guidelines. These letters specified that they are at greater population
- Study participants at average risk were sent standard letters informing them of their genetic
- Average risk affected probands were not officially assessed and counseled. The 16 affected

For the genetic counseling appointment because of novel problems:

- One proband lived in another province in South Africa and could not arrange to come
- One proband did not leave any personal contact details or an address
- One proband missed away before the genetic counseling appointment date

Worse:

- One proband was undergoing chemotherapy in 2007 and cancelled the appointment

These probands/families could not be seen for the following reasons:

- Affected study participants/probands or increased risk families (12%) were therefore not
was only done on probands from families that were found to be at increased risk (moderate or high risk). A tentative diagnosis of moderate risk for these families could not be verified.

(Table 3.5)

Their cancers were associated with medical and histologically clear evidence that their cancer was of one of the four cancer groups that were included in the study. (Table 3.4)

The one family (see Family pedigree 1 - Figure 3.1) that was incorrectly classified changed risk category assigned from the raw data obtained in the completed questionnaire (Table 3.5) and was found that 28% of 28 families (28/229) were correctly classified into their initial.

A formal pedigree study and clinical assessment were done on 29 affected probands (Table 3.3). Accuracy of questionnaire data used in risk stratification of increased risk families.
certain (Table I.5) were positive and that genetic studies are indicated.

(Table 3:6) High risk indices that the Amsterdam criteria (Table 1:4) or the Bethesda
and 26 families (26/28) or 93% were at high risk for an inherited colorectal cancer syndrome
found clinical assessment and pedigree study. 2 families (2/28) or 7% were at moderate risk
of the 28 families that remained in an increased risk category (moderate/high risk) after the

3.4.1 Final Risk Assessment

3.4 Increased risk families - Final risk assessment, clinical diagnosis and genetic testing

<table>
<thead>
<tr>
<th>Percentage</th>
<th>100%</th>
<th>29</th>
<th>Personal data correct</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>97%</td>
<td>29</td>
<td>26</td>
</tr>
<tr>
<td>100%</td>
<td>100%</td>
<td>29</td>
<td>29</td>
</tr>
</tbody>
</table>

Table 3.5: Accuracy of questionnaire data in increased risk families assessed.
The table below summarizes the findings of a study on the prevalence of certain genetic markers in families with a history of breast cancer. The table provides data on the percentage of families with specific genetic markers, as well as the number of families meeting certain criteria.

<table>
<thead>
<tr>
<th>Percentage</th>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>93%</td>
<td>26</td>
<td>DNA banking on proband</td>
</tr>
<tr>
<td>0%</td>
<td>0</td>
<td>Related to FAP/HNPCCC</td>
</tr>
<tr>
<td>0%</td>
<td>0</td>
<td>Mullerian manifestations</td>
</tr>
<tr>
<td>0%</td>
<td>0</td>
<td>CDH1/p16 synrome</td>
</tr>
<tr>
<td>7%</td>
<td>2</td>
<td>HLA DQ beta 1 antigen</td>
</tr>
<tr>
<td>4%</td>
<td>1</td>
<td>High-risk FAP positive</td>
</tr>
<tr>
<td>64%</td>
<td>18</td>
<td>High-risk Bethesda criteria</td>
</tr>
<tr>
<td>25%</td>
<td>7</td>
<td>High-risk Amsterdam criteria positive</td>
</tr>
<tr>
<td>93%</td>
<td>26</td>
<td>High-risk Amsterdam criteria positive</td>
</tr>
<tr>
<td>100%</td>
<td>28</td>
<td>Risk classification/diagnosis assessment</td>
</tr>
</tbody>
</table>

Table 3.6: Final risk assessment, provisional clinical diagnoses and DNA banking
indicated (Table 1.2). Further research is required to determine the precise role of HPC in the genetics of familial adenomatous polyposis (FAP). The

research report the Netherlands Laboratory did not find a mutation on sequencing of the

University of Stellenbosch has not yet completed the research at the time of writing up the

was also performed at an overseas laboratory in the Netherlands for diagnostic purposes. The

performed in South Africa as part of a research project of the University of Stellenbosch (and

research for the AGC genotype mutation on chromosome 5 in this family member is being

adenomatous polyposis (FAP) (Table 1.6). The

in 1 family (4%) the affected proband had different clinical criteria for a diagnosis of familial

3.4.1 Familial adenomatous polyposis

should these tumour characteristics of HNPC be present

which greater than equal (Figure 1.2). Germ-line genetic testing may then be indicated in patients

HNPC. Immunohistochemistry (IHC) should follow in all positive MSI results to decide

microsatellite instability (MSI) testing to determine if they have unusual characteristics of

revised Bethesda criteria (Table 1.5). The affected probands in these 18 families should have

Erbilstein (18) (64%) families (Table 1.6) were at high risk for HNPC according to the

3.4.2 Bethesda criteria positive

In collaboration with a research laboratory

microsatellite gene mutations. This is an ongoing service to these families and is being done

In all 7 of these families are undergoing germ-line (blood lymphocyte) genetic testing for

"Table 1.2"
syndrome that was considered in the particular family (Table 3.6). There were any external features of one of the hamartomas or polyposis syndromes (Table 3.6). None of the affected study participants clinically assessed in the increased risk families had

3.4.7 Clinical Features

...
Amsterdam criteria positive family (Figure 3.4),

risk family (Figure 3.2), one Bethesda criteria positive family (Figure 3.3) and one
following four pages are included to illustrate an average risk family (Figure 3.1), a moderate

For clarification of the risk classification of Table 3.2, family pedigrees (anonymously) on the

3.5 Family pedigree examples illustrating risk classification

members of their risk and inviting family members for genetic counseling

among the relatives at risk. The cascade letters are information sheets informing family

Cascades letters (Appendix 5) were sent to probands of all high risk families to distribute

3.4.8 Family notification of risk
Figure 3.1. Family pedigree - L. Average risk

None of the other relatives that died had cancer

HNPC-associated cancer

Diagnosis of prostate cancer was confirmed in brother (prostate cancer is not a
reported as kidney cancer in questionnaire) risk decreased to average risk when
II-1- Brother who was diagnosed at 60 years (died of prostate cancer) that was
II-4- Affected proband (arrow) colorectal cancer at age 60 years

3.5.1. Family pedigree - L (average risk)
Increased surveillance is indicated in first degree relatives from the age of 40 years.

None of the other relatives that died had cancer.

died of colorectal cancer

- I-4 - Affected grandfather of proband - colorectal cancer diagnosed at age 50 years

- III-1 - Affected proband (arrow) - colorectal cancer at age 61 years

\[\text{\textit{3.6 Family Pedigree-2 (Moderate Risk)}}\]
None of the other relatives that died had cancer.

- I-1: Paternal grandfather of proband - died of cancer; but diagnosis was uncertain and of stomach cancer
- I-4: Maternal grandmother of proband - stomach cancer diagnosed at age 65 years - dead
- II-4: Mother of proband - breast cancer diagnosed at age 54 years - died of breast cancer years
- III-1: Paternal first cousin of proband (3d, degree relative) - colorectal cancer at 39
- II-3: Father of proband - colorectal cancer diagnosed at age 46 years - died of disease
- III-5: Affected proband (arrow) - colorectal cancer diagnosed at age 55 years
mother and her side of the family is not at increased risk for colorectal cancer above the
and adenoma > 40 years). Genetic lesion is therefore indicated (M5 lesion). The proband's
cancer and/or an HNPCC extracolonic cancer and/or colorectal adenoma (cancer > 50 years
L.5 criteria no ? Individuals with colorectal cancer and a first degree relative with colorectal
The paternal side of the proband's family in Fig. 3 is positive for the Bethesda criteria (Table
Figure 3.4 Family pedigree - High Risk - Amsterdam criteria positive

I-1. Parental first-degree relative of proband - colorectal cancer diagnosed at age 35 years - dead

I-1. Parental first-degree relative of proband - colorectal cancer diagnosed at age 39 years - dead

II-1. Male first cousin of proband - colorectal cancer diagnosed at age 29 years

II-2. Parenteral uncle of proband - colorectal cancer diagnosed at age 46 years

II-4. Father of proband - colorectal cancer diagnosed at age 40 years - dead of colon cancer

III-3. Affected proband (arrow) - colorectal cancer diagnosed at age 39 years

Positive for the Amsterdam criteria and genetic testing is indicated (misnomer report gene testing).

None of the other relatives had died of cancer. The parental side of the proband's family is of colon cancer.

I-1. Parental first-degree relative of proband - colorectal cancer diagnosed at age 35 years - dead

I-1. Parental first-degree relative of proband - colorectal cancer diagnosed at age 39 years - dead

II-1. Male first cousin of proband - colorectal cancer diagnosed at age 29 years

II-2. Parenteral uncle of proband - colorectal cancer diagnosed at age 46 years

II-4. Father of proband - colorectal cancer diagnosed at age 40 years - dead of colon cancer

III-3. Affected proband (arrow) - colorectal cancer diagnosed at age 39 years

III-4. Family pedigree - Amsterdam criteria positive
Information sheets, the personal and family history questionnaire, the options for genetic testing.

General observations were made about the participants' attitudes and how they perceived the

| % 91% | 28 | Cases seen in 25 months after institution of study |
| 6% | 3 | Cases seen in 25 months before institution of study |
| 100% | 32 | Colorectal cancer cases seen in 25 months - Total |

Table 3.7 Increase in patient numbers

individual/families (91% of cases) in the follow-up, 25 months (June 2005-June 2007). Individuals/families (6% of cases) seen in the previous 25 months from May 2003 to May 2007. A four-fold increase in the number of patients counselled for inherited colorectal cancer was observed in the division of Human Genetics (Table 3.7) as a result of follow-up on the research patient questionnaire. The number of cases seen for inherited colorectal cancer over a similar time span (25 months) increased from 3 individuals/families (6% of cases) (data from research patient questionnaire.)

The number of cases seen for inherited colorectal cancer over a similar time span (25 months) increased from 3 individuals/families (6% of cases) (data from research patient questionnaire.)

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important and they wanted to benefit from the information generated in the field of cancer.

Overall, patients generally wanted genetic testing because they thought that it was
patients already affected with colorectal cancer pursued genetic counselling and genetic
inherited risks to mostly first degree family members were therefore the main reason why
from genetic information and genetic testing.

cancer. The patients also felt that other family members (siblings and parents) would benefit
would assist future generations in testing for inherited colorectal cancer and in preventing
colorectal cancer to future generations and thought that genetic testing and DNA
lesions was to reduce their children's risks. They were mostly concerned about the risks of
patients with children wanted to take part in the cancer program and wanted to pursue genetic

In the genetic counselling interview specifically about the inherited risk to affected
Questions in the genetic counselling interview specifically about the inherited risk to affected

3.8 Patients' Reasons for Participation

The information with their relatives.

Genetic testing were also positive about the genetic counselling service and agreed to share
appointments. The two participants who were at moderate risk and were not offered further
with their relatives. None of the patients had genetic counselling prior to their genetic
about the multidisciplinary service, the genetic testing and the sharing of their information
receiving genetic counselling after completion of the questionnaires and that they were positive
whether had the impression after counselling the participants that they were positive about
and the management issues that were discussed during the genetic counselling interview.
Family members inquired if they were informed of their genetic risks. Information is confidential and it would have been inappropriate to independently contact (probands) informing their first-degree relatives about their increased cancer risks. This genetic information from their relatives is uncertain whether all the members were addressed and none of the patients wanted to withdraw confidentiality within families were addressed and none of the patients wanted to withdraw. All the patients seem agreed that they would inform their relatives of their risks and the management of these risks. It was the patients' impression that they generally had positive attitudes regarding sharing the information with their extended families. Issues regarding publicity or concerns about the surveillace and management protocols. It was the patients' impression that the genetic counseling provided by the physicians and psychologists was not always clear. All patients seemed requested that the sharing of information with these third parties. All the patients were concerned about discrimination from medical aids or insurance. In general, patients were not concerned about discrimination from medical aids or insurance.

3.9 Concerns about confidentiality, discrimination, and sharing of genetic information

Service for cancer genetics is inadequate and wondered why it was not already an essential benefit. One patient was upset when he realized that South Africa’s molecular diagnostic
be involved in any further research regarding colorectal cancer after his father died of this disease.

Consulting session and this member also sent the writer a letter requesting that he wanted to

Only one family member has been in contact with the writer for a separate individualized
that the family history questionnaire is an effective tool and that it can also save approximately
questionnaire and did not significantly alter genetic testing eligibility. This study concluded
therefore allowed for completion of the information obtained by the family history
eligibility for genetic testing. Updating the questionnaire during a genetic counseling session
led to a new risk assessment and that in only 3% of families changes affected the family’s
questionnaires were updated by asking targeted questions during a genetic counseling session.
Canada was also evaluated (McGee et al., 2007). In this study the family history
consolidating tool in a familial cancer setting a familial breast and ovarian clinic in Toronto.

The accuracy of a self-administered family cancer history questionnaire as a genetic
in previous study and the self-report reliability was found to be high (Asherson et al., 2006).
A self-administered, computerized tool for collecting a family history of cancer was validated.
Reliability and lack of interest from health care professionals, especially in the gate system
questionnaires to all the patients affected with colorectal cancer because of poor organization.

For the problem to work effectively and there may be difficulties in distinguishing the
cancer. The questionnaires need to be distributed by an interested and pro-active site member
acceptable way of collecting an unverifiable, but extensive personal and family history of
The self-administered questionnaire used in this cancer study provides a simple, reliable and

4. Discussion
rectal cancer, which is an HNPCC-associated cancer. It was not possible to assess if
believed cancer was verified and was found to be prostate cancer rather than
increased from medium to average risk in this family because the history of one of the
colonctal cancer. Only one patient was incorrectly classified and the risk classification
correctly identified 97% of the increased risk families (medium and high risk) for inherited
Data used from the self-administered questionnaire to risk status. Families were reliable and

needs and address psychological and ethical issues related to genetic testing.

issues makes it particularly impossible for specialists to work on every individual’s
counseling moves. The large patient numbers that are seen daily, especially in medical
relation to inherited cancer, especially in clinical practice where the cost can double with a
extensive family history data, calculating genetic risks and addressing psychological issues
clinical care also essential for each individual consultation. In busy clinics and large
clinical consultation is too time consuming in any busy oncology, specialists of general practice
and does a full three generation family history on each patient during a normal non-genetic
cancer. The risk assessment and screening criteria for inherited cancer are not easy to interpret.
not bring in the patient numbers that should have been seen at the Genetic clinic for colorectal
cancer in the past referred from other specialists and self-referred from affected patients/families did

preparing for the Genetic assessment and counseling session.

collective information from individuals affected with colorectal cancer that is also useful in
assessment and genetic counseling. It is an easy, entry point and fast assessment method for
families when decisions need to be made about who needs to be referred for a Genetic
The data from the completed questionnaire can therefore effectively be used in risk study.
could benefit from being informed of their genetic risk. (2007) also demonstrated that patients affected with colorectal cancer understood that relatives
genetic profiles were positive and specialists as shown previously by Espin et al. (2000). Kohn et al. demonstrated positive attitudes regarding the sharing of their genetic information with their
Medeirosky, Pyle et al. (2001) (Kohn, Medeirosky, Calliari, et al. 2007). The participants also
increased certainty about their own risk and thinking that relatives could benefit from being
more screening tests were needed, obtaining information about the risk for offspring.
Genetic work-up. The primary motivations for genetic testing included wanting to know if
high risk families were interested in genetic testing and in banking their DNA for future
the specific management guidelines for their risk. All the affected study participants from the
the risks of cancer in family members and the psychosocial issues associated with this risk or
patients had received any prior genetic counseling about the inheritance of colorectal cancer
and surveillance for themselves and their family members, specific inherited risk. None of the
management of their inherited risks. Patients needed more information regarding management
collecting personal and family history data and the multidisciplinary approach relied on the
they were positive about the clinical genetic service, the information sheet and need to
It was the writer’s impression after counseling the moderate and high risk participants that
risk (medium and high risk) patients were assessed clinically and had a formal pedigree study.
patients who were classified as average risk were truly at average risk because only increased
comprehensive South African studies.

Gene testing. These numbers need to be extrapolated from international studies or more
affected colorectal cancer patients/families in South Africa are eligible for reimbursement
may appear falsely high. It is also not possible to use these figures to extrapolate how many
cancer population in South Africa that needs clinical genetic assessment and counseling, as it
is not possible to extract from these numbers the potential size of the affected colorectal

Section 4.2.1

The young age or significant family history decided to take part in the study (see limitations)
also possible that only individuals who were concerned about their genetic risks because of
handheld questionnaires to patients whom they thought were at sufficiently increased risk. It is
because of selection bias. Selection bias may have existed if some specialists only referred or
colorectal cancer in the general population (approximately 1 in 900) (Lynch et al., 2003) possibly
numbers were much higher in the high risk group than would be expected for inherited
clinical assessment and familial pedigree study.
found to be at high risk (26 patients/3.9%) compared to moderate risk (2 patients/7.9%) after the
(31%). There is also an unexpectedly high number of the increased risk category that were
increased risk category (moderate and high risk) (66.9%) compared to the average risk category
a higher number of patients than expected (27.0%) (Lynch et al., 2003) were found to be in the
4.2 Pedigree numbers and risk stratification
especially the genetic risks to their children. Most participants thought that genetic testing and

Patients participated because of concerns around inherited risks to first degree relatives.

4.2 Patients' Reasons for Participation

cases evaluated (69%) were found to be at increased risk.
estimated that the limitations were not taken into account as more than 20% of colorectal cancer
of up to 700 families per year in South Africa, that need genetic counseling would have been
associated cancers (i.e. included, if the numbers from the research report were used, a figure
seen in patients with families with other associated extracolonic cancers (HNPC).
colorectal cancer cases are reported in South Africa, all patients younger than 50 years are
Cancer Registry (Mphahlele et al, 2004). This number is conservative and may be higher if all
in South Africa it only the reported cases are taken into account from the South African
will need genetic testing and screening. This amounts to approximately 200 families per year,
colorectal cancer patients in South Africa will need genetic counseling and approximately 5%
We can therefore estimate from these figures that approximately 20% of the yearly burden of

represent very high-risk inherited predispositions (Lawlet et al, 2003).

Some families in which tumors develop at a young age (less than 50 years) and this
have a role in up to 30% of cases, but only a small proportion (up to 5%) arise in families with
in name (Lawlet et al, 2003). In the United Kingdom it is estimated that genetic factors may
(colorectal cancer) and that 5-10% of the total annual burden of colorectal cancer is Mendelian
colorectal cancer have increased risk (two or more first degree relatives or both) with
Colorectal cancers in the United States of America show that up to 20% of patients with
discrimination before a comprehensive large scale inherited cancer program can be initiated.

be in place regarding sharing of cancer genetic information with third parties and were under no obligation to do so. As this area is still new in South Africa, guidelines need to be clear. © 2012 Intechopen

The study participants were informed that they would not be shared with any third parties (insurance companies and medical aids) unless they were however informed that their genetic risk information would remain confidential and

(Germain, 1998). Study participants in the current research project

/3 Concerns about confidentiality, discrimination and sharing of genetic information

Nwadike et al. (2007), and thinking that relatives could benefit from being informed of genetic risk (Thompson, 1999), the participants in the current study were participants corresponded to previous studies in the literature which showed that the primary

willingness to participate in research studies in the field of cancer genetics. The reasons for

preventing cancer. Participants also generally wanted genetic testing because they wanted to

banking DNA would assist future generations in making informed choices for inherited colorectal cancer and in
Inherited risk did not have any implications in being managed by a team of professionals also
physicians about their genetic risks (Nelson et al. 2001). The legal implications of an
accordance with the literature, showing that most individuals would inform their attendants
of their genotype information with their general practitioners and specialists. This is in
management protocols. The participants demonstrated positive attitudes regarding the sharing
some cases to their general practitioners to inform them about the surveillance and
All the patients seen revealed that the wider send letters to their surgeons, oncologists and in

(NIH) also provides protection against genetic discrimination (www.genome.gov/10002077)
Information from the National Human Genome Research Institute
legislation to provide protection to its constituents (National Conference of State Legislatures
Act (ADA) provide some protection on a Federal level and a number of states have enacted
insurance reform and accountable care (HIPA) and the Americans with Disabilities
this survey for not pursuing genetic testing (Kamensky et al. 2006). In the USA, the Health
potential for insurance employment discrimination were two reasons given by respondents in
and cancer genetic testing. Insufficient coverage of testing by insurance companies and
insurance discrimination and lack of insurance coverage for clinical cancer genetics services
employment discrimination. However, misperceptions still exist in the USA regarding
some form of insurance discrimination and how none of the participants experienced
the United States showed that only 5 out of 156 patients (3%) perceived, whether real or not,
experience with the cancer genetic counseling process in various cancer genetics programs in
America, Canada and Australia (www.ornl.gov/Publications/120113). A survey of patient’s
These ethical guidelines are already in place in most European countries, the United States of
Sharing general information with family members (transmitted, eal. 2006).

Less (2.2%) of respondents in this survey experienced difficulties or challenges with

the telephone (69.3%). Less frequent means of communication included email (16.3%) and by

members. Means of communication with family members were in person (86.9%) and by

(98.7%) showed information from their cancer risk assessment or genetic testing with family

the literature showed that an overwhelming majority of patients (153 of 156 surveyed)

experiences with the cancer genetic counseling process in various cancer genetics programs in

which of the relatives should be informed (Kohn et al. 2007). A survey of patients

on screening can be completed between the genetic counselor and the patient/relative.

should be encouraged in a discussion on familial implications before genetic testing is done and

risk, but their family may not be willing or able to inform all of their family members. Patients

NCCCG. Generally, understanding the relatives could benefit from being informed of their genetic

family members. A previous study showed that patients undergoing genetic testing for

information is confidential and it would have been inappropriate to independently contact

(probands) informed their first-degree relatives about their increased cancer risks. Thus

information from their relatives. It is however uncertain whether all the reviewed patients

and it was the wider's impression that none of the patients wanted to withhold genetic

with their extended families. Issues regarding confidentiality with families were addressed

management of these risks and they had positive attitudes regarding sharing the information

All the patients seen confirmed that they would inform their relatives of their risks and the

demonstrates their positive attitudes towards a multidisciplinary service and sharing of genetic
The information provided in the letters was not understood by any of the patients. To help patients understand the information better, the patients were also given the opportunity to phone in the consultation sessions. As most of the information was not given to them by their healthcare providers, issues and effects of treatment and diet were also discussed during the follow-up.

For patients' needs and follow-up:

Appropriate for them:

Family members: Family members come for genetic counselling when the family is involved in any further research regarding colorectal cancer after the other member was diagnosed with this disease. The genetic counselling clinic will provide a separate and individualized consultation session and letters for any family member. However, only one family member has been in contact with the clinic.

The genetic counselling clinic should help need genetic counselling. Some patients asked that the consultation letters to patients to hand out to their family members who may be at increased risk for cancer. The writer received in this letter that family members could contact the genetic counselling letter to patients to hand out to their family members who may be at increased risk for cancer.
the genetic counseling session. Confirming human papilloma virus with the pathology laboratory

professionals an opportunity to trace relevant and important pathological information prior to

an initial risk assessment prior to the genetic counseling session. It also assists the health

during the genetic counseling session. It allows for consultation of a family pedigree and for

If family history information is complete prior to the genetic appointment, time is saved.

assessments.

needed. Patients also understand that accurate information is important for the risk

proper to know prior to genetic counseling exactly where details of their family history are

primarily clear level when a cancer genetic referral was received (Cole et al, 2000). Patients

relates to clearly relevant cancer history information and this method has saved time at

family history data form in the patient's own time at home, reduces discussion with

Cancer Genetics, Clinical Genetics Unit, Birmingham Women's Hospital) to completion of a

has been shown at a clinic in genetic counseling in the united kingdom (West Midlands) Family

data collection sheet home to verify cancer histories, especially in second degree relatives. It

advantage over a computer based program in that it gives patients the opportunity to take the

The personal personal and family history questionnaire with information sheet demonstrates an

and consent form

4. Advantage of the use of a printed self-administered questionnaire. Information sheet

held.

of this research report. However, this was a relatively short time period to fully assess the

shared after genetic counseling or for a follow-up appointment up to the time of submission
and histopathology reports. Patients, families, and healthcare workers all need increased knowledge and education.

Promoting some changes to use the questionnaires:

- The option of completing and assessing information on the questionnaires may help in assessing the patients' health in the questions. The questionnaires have been developed after the end of the research project (Appendix-7 Information Sheet for doctors).

Inherited cancer pedigrees that were developed after the end of the research project are shown in a separate information sheet. The information sheets are designed specifically for the clinicians and their health care workers.

Information is needed to remove medical practitioners' authority and this is now intended to take an active role in family counseling. The self-administered questionnaire and information sheet should also be seen at the

...
Inadequate education to increase this awareness. Patients should be informed that genetic counseling services are available and everyone should have access to these services.

Education is needed to increase this awareness. Patients should be informed that genetic counseling services are available and everyone should have access to these services.

Awareness of how patients and families who are at risk of all inherited cancer syndromes other than breast/ovarian cancer syndrome. As a result of this study, awareness of the availability and need for clinical genetic services for inherited colorectal cancer increased in the specialties practices used for the patient recruitment.

Increased in cancer gene service awareness.

Feed back to patients is important and should always be provided. Patients can have a formal risk assessment or otherwise risk assessments and families may be performed. It is important that the questionnaires are given to all patients with colorectal cancer so that all questionnaires to hand out questionnaires to the patients.

Responsibility of the specialists or their health care workers and/or secretaries in the screening could not be identified if they were not handed the questionnaires. If remained the
affected individuals. One or two separate appointments with a genetics professional, possibly
specialists, might be where the primary focus is identification and management of the cancer risk.

It is difficult to deal with during normal medical appointments and during busy oncology and
risk of occurrence in their children and to address the psychological issues. All these points are
the clinical surveillance and management programs. The general basis of their cancer and the
more associated numerical data about the risk of cancer in their family members, to explain
draw a detailed three-generation family tree to inform patients about their risks of developing
positive about involving cancer genetics services in their practices. It is time consuming to
inherited cancer. Genes that are inherited and pro-active doctors and medical personnel are needed. who are
involved. The role of clinical cancer genetics in the overall management of patients at risk for
regarding the role of clinical cancer genetics in the overall management of patients at risk for
information regarding the familial risks. Health professionals therefore need more education
members affected with cancer and in those whose children, patients needed detailed
minds of all the patients seen, especially in patients that were young, who had other family
individuals at risk for an inherited malignancy. The question of cancer inheritance was on the
South Africa with its limited resources, do not yet see it as an essential part of the care of
The field of cancer genetics is relatively young and many medical personnel, especially in

Patients are already involved in the process.

Cancer risk and easier and determined have awareness can be increased if professionals and
services. The appropriate advice given to identified patients is not to be informed that the
risk cancer syndromes are under-diagnosed, incorrectly managed and not referred to genetic
advisors. Therefore and information sessions. It will also prevent a situation where high
in a large scale inherited cancer risk-assessment program is established through the self-
information sharing regarding inherited risks of cancer (Seyfer, 1999). This can be prevented
Inherited cancer syndromes, such as the breast/ovarian cancer syndrome, colorectal cancer, and others, are some of the other common
conditions. Not only are inherited colorectal cancers but also for some of the other common
conditions, urgent need to establish a cancer genetic diagnostic service in

4.8 Need for Inherited Molecular Diagnostic Services

Clinical cancer genetic services increase the patient numbers; more patients will be empowered to personally contact
the physician. Increased patient awareness of how inherited cancer should be managed. This will
increase in the public domain. Easy access of cancer information via the Internet exists and
Cancer genetics will also become more important as awareness of the inherited cancers

(For doctors).

Sheets have been drawn up as a result of this research project (Appendix 7: Information Sheet)

professionals why involvement of cancer genetic services is important. These information
sheets have been necessary that information sheets are available that inform health care
providers. Establishment of a functional multidisciplinary service that involves all the necessary
specialists is important in the management of inherited cancer as demonstrated in this study.

Doctors need to become aware that they cannot deal with all these issues themselves and that
direct genetic investigations

in a different environment are therefore necessary and essential to address these issues and to
Interested and proactive staff members therefore played an essential role in recruiting patients.

Patient management handled out the questionnaires. A primary link with a moderator indicated that some selection bias was removed if staff members not directly involved in numbers are closer to the numbers that are expected in the average population (section 4.2). The average risk patients were 45% of the total number of patients from this practice. These patients increased in risk patients were found to be 55% of the total from this practice and 99.9% (94 of 95) of the patients recruited for this study came from this practice and 1/15 families had in one of the oncology practices. Patients were not selected by their specialists to participate in determining who of the end received the questionnaires.

The practices/specialties used for patient recruitment. In many instances what criteria were used to questionnaires were therefore not handed out to all patients with colorectal cancer at most of the specialists wanted to keep their autonomy in deciding who they wanted to refer. The specialists wanted to keep their autonomy in deciding who they wanted to refer. Therefore, it appears as if there are specialists who do not refer patients or referred patients or handed questionnaires. It seems that some of the specialists only referred patients or handed questionnaires. Selection bias almost certainly existed in this study as the wider had to depend on the
not associated in any way.

Patients were positive about the service. Patients who did not complete the questionnaires were
research. This may be a reason why the whole family received genetic counseling and wanted to participate in the
their risk was modified to receive genetic counseling were already more interested in
members who completed the self-administered genetic counseling were already more interested in
had a positive response to the program and the genetic counseling service. Patients and family
Selection bias may also have existed in observations regarding the numbers of patients who
was not possible to remove this bias.
choice if they wanted to take part in the program after they read the information sheet and if
complete the self-administered genetic counseling, even after it was handed to them. Patients had a
risks because of their family history. Some individuals were concerned about their genetic
selection bias, as it is possible that only individuals who were concerned about their genetic
Patients who took part in the research all the recruitment sheets may have contributed to the
knowledge of their strong colorectal cancer family histories.
questionnaires were also selected either by their referring specialists or by their own
Patients who completed or who were referred to our department and subsequently sent
the program.
other practices were increased risk. Patients were selected by specialists for participation in
as this practice as the numbers were much higher of average risk patients compared to the
would appear as if questionnaires were not often handed to patients in the same hospitals and

association was poor in the state sector, as only five patients participated in the study. If

patient populations from private practices contrasts most with the population group. The

were patients with European ancestry (42 patients) participated in the study because the

were English speaking.

study were fully multilingual and the two Indian and two colorectal patients that participated

field in the questionnaire needed a translator. The two Indian patients that participated in the

in questionnaires were able to understand and speak English and none of the patients who

and minority population seen at a tertiary/ specialist level was used. All the patients who filled

The study is not representative of the South African patient population, a well-educated urban

4.9.2 Limited population representation

assessed during the clinical genetic assessment in all the medium and high risk families.

in the questionnaire used to identify a history of colorectal polyps was used by some patients and was

affected with polyps are usually not referred to oncologists (mainly oncologists) but rather to gastroenterologists

patients/families where there was only a history of pre-malignant colorectal polyps. Patients

were all HNPC-associated cancers. The questionnaire was also not able to identify

cancer: upper gastrointestinal cancer, cancer of the bladder, head or neck, renal, or renal/retinal cancer.

questionnaire was used if they presented with any other cancer. For example, endometrial

colorectal cancers already existed in the population. Patients/families would have been missed

when colorectal cancer and was only used at tertiary/ specialist level where a diagnosis of
To assess the accuracy of patient self-reported data by Mussiso et. al. (1998), the accuracy of a history questionnaire in their population was assessed and compared between the two datasets. Mussiso et al. (1998) have validated the Massachusetts General Hospital Cancer Registry data in the South African context for only European American and self-reported data. The validity of the data was assessed by comparing the family history questionnaire responses in the same patient population.

4.9. Validity of Family History Questionnaire

Society with the rural, suburban and urban communities, the study can also highlight the problems expected in our multilingual and varied population. The study can also highlight the problems expected in our multilingual and varied population. The study can help to identify areas in which knowledge of family medical history may be effective, acceptable and applicable across different population groups. The study can also help to identify areas in which knowledge of family medical history may be effective, acceptable and applicable across different population groups. The study can also help to identify areas in which knowledge of family medical history may be effective, acceptable and applicable across different population groups.

Acknowledgements

The study was not aimed at validating the family history questionnaire by comparing patient data. The study was therefore not a direct representation of the patient. When establishing a large-scale program, the questionnaire is available in two or three common African languages as well as in English and when starting a comprehensive initiative cancer program, it will also be preferable to make the questionnaire available in at least three hospitals and this will be a major point to be addressed.

A function of the clinic's relationship with the medical personnel is to ensure that medical personnel always work together. The number of black questionnaires would remain in the ward or clinic month after month. It may be a function of the clinic's relationship with the medical personnel.

choices because questionnaires were left at a certain place in the ward or clinic and the same
Patients for the research project also included the numbers under histopathology reports. The time span (approximately 7 years) set up for recruitment controlled in this study and to sign consent before we could have access to their medical files.

Problems because of the confidential nature of their personal and cancer information. Patients and did not contact any patients that were previously seen for colorectal cancer at these at the specialist clinics were recruited. We did not retrospectively look at any patient records of the clinicians' clinics. Only patients that were newly seen or followed-up for colorectal cancer some of the clinicians. Only patients that were newly seen or followed-up for colorectal cancer numbers are small because of the prospective nature of the study and the poor cooperation of

4.9. Limited patient numbers

unresolved.

accuracy of patient self-reported data in the South African context. Therefore, family history remains largely untested. The accuracy of self-reported family histories in our population, the generation of traditional family views of cancer and how it is perceived in the African culture may be

risk participant groups.

from the study participants during the clinical genetic assessment in the moderate and high

comparing information in the completed questionnaires with information gained personally

made by the writer in this research project to verify personal and family history data. By asking targeted questions during a general counseling session. However, an attempt was made by McGrath et al. (2007) and in their study the family history questionnaires were updated by the cancer setting at a familial breast and ovarian clinic in Toronto, Canada was evaluated by self-administered family cancer history questionnaires as a genetic counseling tool in a familial
This study is unique in that it helped to create awareness of the importance of genetic counseling and testing in inherited cancer management at the practices/schools used for the project. Information sheet and a doctor information sheet (Appendix 7).

achieved by drafting up a new personal and family history information questionnaire, a new and the University of the Western Cape, Division of Health Sciences, National Health Laboratory Service in the Clinical Section of the Division of Human Genetics, National Health Laboratory Service in the Western Cape, Division of Health Sciences, National Health Laboratory Service in the Clinical Section of the Division of Human Genetics, National Health Laboratory Service.

The unique observations from this study have been used in the planning and setting up of a genetic risk information and the multidisciplinary management of their inherited cancer risks.

Attributes and feelings of patients regarding genetic testing: Genetic counseling, screening of patient and family history information in risk estimation, but also adequately assessed the other unique feature of the study was that not only addressed the effectiveness of using a multidisciplinary team approach in the management of colorectal cancer.

Colorectal cancer were formally instilled in Johannesburg with a view to creating a colorectal cancer surveillance and follow-up genetic counseling services for inherited and similarly, as a cancer that is developed in South Africa. No similar study exists in the South African medical literature. This study is unique in that it is the first time that a step-wise program using a self.

4.10 Limitations of the study
The new Family Cancer Program was introduced into the Clinic Section of the Division of Human Genetics, National Health Laboratory Service and the University of Toronto (Appendix G). This study formed a platform from which further planning was done to develop a comprehensive family program for all the inherited cancer syndromes (Appendix G).

The new Family Cancer Program delivered diagnostic services for all the inherited cancer syndromes. It is hoped that this need will be addressed and for all family members. It also highlights the urgent need for cancer molecular diagnostic services for screening and for subspecialist cascade testing for the work-up and confirmation of their diagnoses. This study focused on high-risk and high-susceptibility individuals, in many patients in genetic counseling service for inherited colorectal cancer in London, Scripture, LK (Cole, et al. 2000) and the Familial Breast and Ovarian (Chinese Family History Cancer Questionnaire) developed in the UK and Canada, the West Midlands Family Cancer Questionnaire used in this research project, built on previous Family and Ethnic History Questionnaires developed by the new patient information sheet and a doctor information sheet, the new and concise personal WHERETEST? The new Family Cancer Program was developed in the Clinic Section of the Division of Human Genetics, National Health Laboratory Service and the University of Toronto.

Appendix F, The study formed a platform from which further planning was done to develop a comprehensive family program for all the inherited cancer syndromes (Appendix G). This study formed a platform from which further planning was done to develop a comprehensive family program for all the inherited cancer syndromes (Appendix G).

4.11 Future Directions

That diagnostic services will be instilled.

For all the other inherited cancer syndromes, it is hoped that this need will be addressed and for all family members. It also highlights the urgent need for cancer molecular diagnostic services for screening and for subspecialist cascade testing for the work-up and confirmation of their diagnoses. This study focused on high-risk and high-susceptibility individuals, in many patients in genetic counseling service for inherited colorectal cancer in London, Scripture, LK (Cole, et al. 2000) and the Familial Breast and Ovarian (Chinese Family History Cancer Questionnaire) developed in the UK and Canada, the West Midlands Family Cancer Questionnaire used in this research project, built on previous Family and Ethnic History Questionnaires developed by the new patient information sheet and a doctor information sheet, the new and concise personal WHERETEST? The new Family Cancer Program was developed in the Clinic Section of the Division of Human Genetics, National Health Laboratory Service and the University of Toronto.

Appendix F, The study formed a platform from which further planning was done to develop a comprehensive family program for all the inherited cancer syndromes (Appendix G).
levels of care for the successful implementation of a comprehensive program in South Africa.

In Australia, where patients and families present with a prevalent condition, the problem of patients and families affected with cancer is also a significant concern. The new step-wise family cancer program is also aimed at contributing to a more effective management of cancer genetics as an essential component of care. It will also help in the establishment of clinical cancer genetics as an essential component of care of patients with genetic disorders. This will be beneficial for the management, counseling, and genetic testing of patients and families affected by any of the inherited cancer syndromes. It will also be beneficial for the management, counseling, and genetic testing of patients with genetic disorders.

In Africa, the problem of patients and families affected with cancer is also a significant concern. The new step-wise family cancer program is also aimed at contributing to a more effective management of cancer genetics as an essential component of care. It will also help in the establishment of clinical cancer genetics as an essential component of care. It will also be beneficial for the management, counseling, and genetic testing of patients and families affected by any of the inherited cancer syndromes. It will also be beneficial for the management, counseling, and genetic testing of patients with genetic disorders.
The success of such a program relies on the co-operation of clinicians making diagnoses and

...
can therefore be done based on experience gained through this study.

Future research, patient recruitment, and data collection for all the inherited cancer syndromes
different population groups. This can be done once an inherited cancer registry is established.
phenotypic differences are present in the malignant behavior of the inherited tumors in the
inherited cancer syndrome. Positive genetic test results can also be followed up to observe if
In future research, patients and families from different population groups with a confirmed

In South Africa,

hoped that there will be an increase in patient numbers from all the different population groups
have not been increased in patient numbers as expected and it is
interest in these mutations for HNPCC also occurs in the local African population.
coordinated by the NCI, Weite, Chin, Kogilnaza-Bigas, et al. 1999). If we would like to be
$HMLH2$ and $MLH1$ and $MSH2$ germ line mutations have been identified in African Americans with
more African patients need to be recruited for future research on this topic because novel

context.

$HMLH1$ and $MLH1$ and $MSH2$ germ line mutations have been identified in African Americans with

Gene mutations for inherited colorectal cancer that may be present in the South African
be completed as a first attempt at the subsequent identification of population differences in
University of the Witwatersrand, once the confirmatory genetic testing is completed. This will
database at the Clinical Division of Human Genetics, National Health Laboratory Service and
The molecular data from this research report will be entered into an inherited cancer registry
Summary and Conclusions
Geneva Research in South Africa

Geneva Cancer in this Registry will be an invaluable data source for future inherited cancer.

Presented in this report (and from future molecular data obtained during this Research Project) will not

stem from the clinical and molecular data obtained during this Research Project (but will be

inherited cancer syndromes, including colorectal cancer. An inherited cancer Registry will be

University of the Western Cape in July 2007 and is used as a data collection tool for all the

General Section of the Division of Human Genetics, National Health Laboratory Service and

General Section used in this Research Project. The new program was introduced into our Clinic.

This Program was developed to reduce some of the limitations (section 4.2) identified with the

and Family History Questionnaire and a new Patient Information Sheet. This new Family Cancer

cancer was developed with a doctor information sheet a new and more generalized personal

cancers, forming the basis from which a new Family Cancer Program expanded to all Family

Inherited Cancer

Work-up. This highlights the high-risk patients. High-risk colorectal cancer patients were all referred in the clinical and molecular services. For

Inherited cancers, High-risk colorectal cancer patients were all referred in the clinical and molecular and Research service and about the multidisciplinary management of their and their families.

All the participated consents appeared to be positive about the clinical genetic counseling

Significant Family Histories will be more proactive.

Complete the questionnaires and will be expected that younger patients and those with more

essential in the success of the study. However, there is always the potential for patients not to

Skill cooperation and motivation in hand out the questionnaires to patients at the clinics were
and of research related to inherited cancer in South Africa.

expansion of cancer genetic counselling services, cancer molecular diagnostic testing services
professionals as well as self-requests are then expected to increase. This will lead to the
education is done at all levels of care. Referrals from doctors and other health care
information sheets for doctors and medical personnel are widely distributed and more
especially be seen once the new family cancer program is instituted on a large scale.
more aware of the availability of cancer genetic counselling and testing services. This will
Clinicians, medical administrative personnel, nursing staff and patients will eventually become
STEP 3: Risk evaluation and recommended cancer surveillance consultation depending on

 syndrome

Specify non-multifocal/exophytic multifocal/mixed lesions associated with I or any cancer
1 cancer defined as 10 years earlier than usual for the specific I type of cancer

I cancer with the same syndrome and the same risk

High risk

- Any PDG or SDR with <10 years

- 2 PDG with colorectal carcinoma > 50 years

- 1 PDG with colorectal carcinoma > 50 years or 2 PDG with colorectal carcinoma at any age

Moderate risk

- I PDG with colorectal carcinoma > 50 years

- I PDG with colorectal carcinoma > 50 years or 2 PDG with colorectal carcinoma at any age

Low risk

The index case is > 50 years

- I PDG with colorectal carcinoma > 50 years or 2 PDG with colorectal carcinoma

- 1 PDG or SDR with 2 or more HNPCC associated cancers

- 2 PDG or SDR with 2 or more HNPCC associated cancers

- 2 or more PDG members belonging to HNPCC kindreds can be accepted in lieu of these subtypes.

- HNPCC associated cancers include colorectal, endometrial, stomach, kidney, small bowel, pancreatic, and ovarian, respectively.

- Any of the following

- recessive inherited non-polyposis colon cancer (HNPCC)

COLON:

c-6

With more or less than the Amsterdam II criteria (updated as of 2004), from cancer family consultation of mutation carriers. The criteria are more stringent and sensitive than the Amsterdam II criteria (updated as of 2004), more index cases and family consultation of mutation carriers are recommended to serve as a guide to escalate surveillance. Less restrictive criteria than the Amsterdam II criteria are used because the Amsterdam II criteria are based on large familial colorectal cancer studies. Less restrictive criteria than the Amsterdam II criteria are used because the Amsterdam II criteria are based on large familial colorectal cancer studies.

STEP 2 - Classify families into three risk groups according to validated criteria

- First degree relative, SDR - second degree relative

APPENDIX I
26) Assent Form (for minors > 18 years old)

2b) Information Sheet and Consent Form for Parents (in case of minors > 18 years old)

2a) Information Sheet and Consent Form for Patients

In this study:

On the following pages are included the Information Sheet, consent form and assent form used

Appendix 2
cancer

because we need specific information regarding the histology (microscopic appearance) of your
...number, and discuss the information with you. You can also phone me (numbers are provided below) if you need me to arrange collection of data or if you have any questions. I hope you will feel free to...

...and will be done in collaboration with your doctor.

...that the management team focus on evidence-based practices and thereby develop guidelines for treatment of ulcerative colitis. Generally, a colostomy may be considered when nutritional support is required and medical management with medications and/or surgery is unlikely to be effective.

...to develop guidelines for treatment of ulcerative colitis. Generally, a colostomy may be considered when nutritional support is required and medical management with medications and/or surgery is unlikely to be effective. We are also developing a consensus panel to make referrals to our Gastroenterology Clinic more effective for initiating colorectal cancer (cancer of the large bowel). We are developing a screening program for individuals who have colorectal cancer or are at risk for...

...in the University of the Witwatersrand and University of the Witwatersrand and National Health Laboratory Service (NWLS). We would like you to take part in a study to establish a method to identify individuals and/or families at risk for...

Dear Patient

Consent Form and Information Sheet

DH Social 49-2014 DH AB Lave 48-2019 DH T Wessels 49-2013

Professor DR Vkeleton 49-2018 Professor A Raun 49-2012 Professor A Raun 49-2012

Fax: 27-11 468-2268 Telephone: 27-11 468-2492024920249202492024

Box 1033, Johannesburg, 2000 2000 Division of Human Genetics

University of the Witwatersrand, School of Pathology

Laboratory Service

National Health
If you need interpretation of the questionnaire or need more information regarding the study, or if you need specific help to understand your role in the study, please contact me on the following numbers: 011 489-9902/082 603 1128/011 489-9244, I can arrange with someone at the Department of Psychology for this purpose. If you wish to discuss some aspects of your cancer, please do not hesitate to contact me on the following numbers: 011 468-9902/082 603 1128/011 489-9244, I can arrange with someone at the Department of Psychology for this purpose.

Signature (in case of verbal consent):

Date:

Name:

Signature:

Date:

This is a consent form. Please sign and date here to show that you have understood what has been written (or said to you by an interpreter) and that you willingly agree to answer questions and that you give us permission to use your medical records.

Available in dealing with these risks.

done in order that you and your family understand fully the potential risks involved and options
consulting a genetic professional will be arranged at a time convenient to you. This will be
increased risk for inherited colorectal cancer, you will be connected genetically and benefit
If after completing this questionnaire and after assessment by me, we feel that you may be at
If you or a family member/relative have a history of cancer, please indicate it clearly on the form. This information will be used to provide targeted genetic counseling and follow-up services. If you have any questions or concerns, please do not hesitate to contact us at 1-888-GENETICS (436-8387), Monday to Friday, 8:30 AM to 5:00 PM (ET).
questionnaire. Should there be any difficulties in understanding English, you can arrange with someone at your specific clinic to help you with the interpretation of the study. If you wish to discuss some aspects of your child's cancer, please do not hesitate to contact me on the following numbers: 111-469-9037/082 605 1128/011-489-9224. 1 If you need interpretation of the questionnaire or need more information regarding the study, please sign the attached form: in Appendix B.

Date

Signature of witness (in case of verbal consent)

Name:

Date

Signature

Please answer questions and let us know if you give us permission to use your child’s medical records. This will be done in order that your and your family understand fully the potential risks involved and options available in dealing with these risks.

May be considered risk for inherited colorectal cancer: you will be counseled.

If you feel certain that it will not affect the treatment by the specialists in any way, you are also free to withdraw your child from the study at any time. Please answer some questions, you can be certain that it will not affect the treatment by the specialists.