Psychological Aspects of Genetic Testing for Cancer

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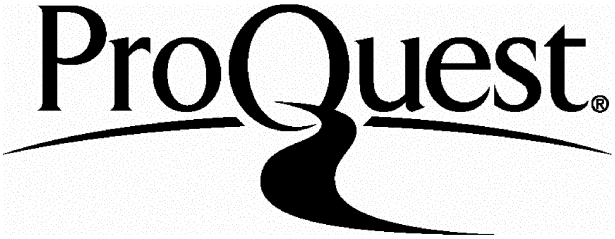

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Abstract

The aim of this thesis is to explore psychological aspects of genetic testing for cancer, testing theoretical models to determine predictors of intention to have a genetic test. The main study disease is colon cancer, which is a good model for studying psychological aspects of genetic testing.

This thesis will address two main themes. The first will explore the associates of intent to have a genetic test for colon cancer in people with a family history, but who are currently asymptomatic. The second theme will explore the generalisability of these results to other groups.

In the first study, correlates of intention to have genetic testing were explored within asymptomatic patients at high risk of colon cancer. Specific comparisons assessed the effect of gender on intent to undergo genetic testing and on anticipated emotional outcomes. A year later the stability of the theoretical models used was assessed.

The second theme was explored firstly by comparing views of genetic testing held by people at high risk of colon cancer with views held by their partners. In the next study participants with a personal history of cancer were included to explore differences between them and unaffected participants.

In the sixth study the enquiry extended to encompass a general population sample, focusing on the influence of objective risk. Finally, comparisons were made between the original sample and women attending a Regional Genetics Service for counselling about breast cancer risk.

The studies found high levels of intent to have a genetic test and supported the Theory of Reasoned Action, with the addition of Health Belief Model components. Comparison studies revealed strong similarities between correlates of intent to have genetic testing in people at risk of colon cancer compared with other groups. This supports a general theory of correlates of intention to have any predictive genetic test.

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Chapter 1

Genetics and Genetic Testing

1.1 History of Genetics

The role of family history in the development of ill health and disease has been recognised for thousands of years. Many cultures prohibit the union of closely related individuals to reduce the chance of children being born with a disorder. Inbreeding is now known to increase the chances that a child inherits two recessive traits, and can reduce the genetic health of a population. As early as 200AD haemophilia was recognised as a familial disease (Jones 1996), however the existence and nature of other genetic disorders is still being uncovered.

The understanding of the means and pattern of inheritance has been much debated and argued over. Aristotle believed that reproduction occurred simply by the mixing of purified bloods, this belief persisted in various forms into the last century. Another popular notion was that individuals were actually pre-formed within the ovum of the mother, there even before the mother was born - leading to a 'Russian doll' like series dating from Eve. The sperm merely triggered the expansion of the outermost miniature person (Bowler 1989). Lamark's theory (1809) also was commonly accepted, that characteristics developed in one generation (e.g. strong muscles) are passed on to the next.

Gregor Mendel made the discovery of the true nature of inheritance in the 1860's, and his observations and theory form the basis of modern genetics. Mendel proposed that units of information are passed down from one generation to another, and that it is these units of information that form the basis of inheritance of characteristics. The unit of information is separate from the organism that carries it, and does not change even when new characteristics are acquired, such as strong muscles.

Mendel also explained why some features are seen to appear, disappear and then reappear in generations of organisms. Using pea plants as a study organism, he observed that characteristics such as pea colour are not simply a blend of the colours of the parent plants, but rather the offspring all took on one parent's colour. Mendel explained this phenomenon as being due to the pollen and egg from the parent plants each carrying one

copy of the unit of information. These units were of two sorts, the first was a dominant type, which if present would be manifest. In Mendel's study this was a yellow pea colour. There was however another type - a recessive type - in Mendel's study a green pea colour. When one or both of the units of information coded for a yellow pea colour, this colour was observed, only when both the units coded for the green pea colour, was this colour observed. This description of inheritance is still used to explain the inheritance of many characteristics.

Despite Mendel's publication in 1860, his work was not widely known until its rediscovery in 1900 by Correns, de Vries & von Tschermak. At the time of Mendel's publication the major discussion was about evolution, so his work published in an obscure German journal was overlooked. In addition, there is some doubt as to whether Mendel was aiming to understand mechanisms of inheritance, or was working on hybridisation. If the later was the case, he too might have been ignorant of the importance of his findings.

1.2 Modern Applications of Genetics

Since the emergence of the science of genetics in 1900 the understanding of the pattern and nature of inheritance has developed at a great rate, aided by modern technology. It is now possible to document DNA composition, DNA strands can be artificially produced, DNA can be inserted into cells to change the nature of the cell and its products (gene therapy & genetic engineering), and individual's genes can be examined to determine whether a harmful mutation is present. The applications of this new biotechnology are widespread, and include the identification of criminals from genetic fingerprints, the production of genetically engineered plants and animals to increase a food production, and many medical applications.

1.3 Medical Genetics

The use of genetic knowledge in medicine has revolutionised many aspects of the practice of medicine. Drugs can now be designed to specifically combat aspects of a bacteria or virus by understanding its genetic composition and reproduction (e.g. the development of anti-AIDS medication). Transplants can be performed which ensure that the organs complement the recipient, and it may be possible to breed animals with human genes to provide a ready supply of replacement organs. Genetic engineering has

made it possible to make yeast organisms which can manufacture human insulin protein and clotting proteins, reducing the risk of side-effects from the use of animal proteins and transmission of disease from human donors. Gene therapy is being developed to insert missing genes into cells - for example in cystic fibrosis, gene therapy may soon be the treatment of choice. This would produce a lasting change in respiratory cells, enabling them to produce their own proteins, rather than relying on drugs and physiotherapy (Jaffe, Bush, Greddes & Alton 1999). Finally, diagnosis of diseases can now be made on the basis of genetic composition rather than simply clinical observation, sometimes decades before the development of the actual disease. These advances in genetic understanding are revolutionising the practice of medicine, however the effect of these changes on patients and patient care are as yet unclear.

Genetics is now able to determine who is likely to suffer from which disease, who might respond well to different treatments, and to ultimately change the fate of people with a genetic predisposition to diseases. The influence of genetics means that people will be able to know whether they will develop a disease and they will be able to choose to have children pre-screened for all major genetic disorders. Appropriate preventative treatment regimes could be started before a disease develops; and the understanding of the genetic basis of various diseases could lead to new treatments and cures for many problems.

1.3.1 Ethical Issues

Genetic knowledge may come at a price. Already insurance companies are concerned about the potential impact on their business - if clients know they will develop a disease, they may increase their insurance cover. This concern could lead to higher premiums for people with a family history of genetic disorders, or even the exclusion of people from holding policies. Discrimination against 'genetically disadvantaged' individuals may also occur in the work place, with employers unwilling to employ or train staff who may develop a disease and prematurely end their working life. Some occupations might screen for people who might later in their life develop a disorder that might jeopardise safety.

Genetic knowledge may have an effect on a person's social position; it may become difficult to find a partner without one having a clean bill of health. It may also be difficult to have children - in China pre-natal testing can already be enforced, with

pregnancies terminated if a disorder is found. The effect of knowledge about future illness might have a damaging effect on a person's psychological well being, leading to anxiety and depression, or may lead to a reckless approach to life. For these reasons it is important to study the effect of these medical advances on the people they are intended to help, to determine what value this knowledge has in today's society.

1.3.2 Inheritance of Genes

In order to fully understand the choices facing individuals who want to know about their genetic composition, it is important to understand the basic mechanisms of genetic inheritance, their role in disease development, and the options available to treat such disorders. In sexual reproduction, each parent randomly gives the offspring a copy of one of its two chromosomes. If on one of these chromosomes there is a mutated gene (so that it does not code correctly for its intended use) this may be passed on to the child with varying consequences.

1.3.3. Recessive Disorders

Serious diseases caused by recessive genes such as cystic fibrosis are often expressed in childhood or adolescence. The recessive gene is perpetuated through the generations via healthy carriers, whose reproductive potential is not affected by the presence of a recessive trait. The disease is only expressed when both parents are carriers of the recessive gene and both pass the recessive trait to the child. For the carrier of a single recessive gene there is no effect on their health, in fact in some disorders, people who are carriers are at a small advantage, e.g. in sickle cell anaemia, carriers have some resistance to malaria. As carriers are not disadvantaged, the mutated version of the gene survives in the population, despite the significant disadvantage that may be attached to carrying two copies of the recessive gene. One in four children of two carriers will develop the disease. As people who are carriers of a recessive trait show no signs of ill health, their carrier status is usually only detected upon the birth of an affected child.

1.3.4 Dominant Disorders

Dominant disorders are ones in which only one copy of the mutated gene is sufficient to produce the disease. The disease is passed directly from an affected parent to an affected child, however often these diseases do not become apparent until adulthood, after any children have been born. Dominant diseases do not affect the person's chance of

reproducing in the way that someone with a recessive disorder is less likely to reproduce due to shortened life expectancy.

1.3.4.1 Huntington's disease

A major clinical model of a dominant disease is Huntington's disease (HD), which causes extensive neurological damage - leading to dementia, paralysis and ultimately death. Although the disease may develop at any time between 2- 80 years of age, the usual age of onset is in the forth or fifth decade, after most people have had their children. Because of the late age of onset, and despite the serious nature of the disease, the gene has remained prevalent because it does not affect reproductive health. There is currently no way to prevent the onset or treat the disease, therefore carriers are destined to develop this condition, unless they die of another cause first. Despite the unalterable nature of the disease, there has been great interest in the discovery of the gene for HD, and the prospect of genetic testing. Many people wish to have a test in order to plan their families, although for many others there are more psychologically driven motives for wanting testing. A test has been available since 1987 although this was a linkage analysis which was about 95% accurate, mutation analysis became available in 1995 - offering a nearly 100% accuracy.

With both recessive and dominant disorders, the potential of the person to reproduce depends on the severity and fatality of the disease, the effect of the disease on fertility, and the social stigma associated with the disease, making it more difficult to find a mate.

1.3.4.2 Sex-linked disorders

Sex-linked disorders (for example haemophilia) are ones that are caused by mutations not on the 22 somatic chromosomes, but on either of the sex chromosomes. Usually a mutation will be on the X-chromosome. In women there are two X-chromosomes so a mutation acts like a recessive gene (the second chromosome compensates for the mutation in the other one). A sex-linked disease is usually only expressed in a woman in the rare event that her mother was a carrier of the gene, and her father was a sufferer of the disease. Men, however only have one X and one Y chromosome so a mutation on the X-chromosome will be expressed as a disease.

1.3.5 Genetics of Cancer Predisposition

The hereditary nature of various type of cancer has been observed for many years (Broca 1866). In some ways all cancers are 'genetic' in that they are caused when the monitoring and repair systems are defective, and a cell grows and divides unchecked, leading to a tumour. In some individuals these systems are not as efficient due to an inherited defect, which leads to a higher incidence of cancer in these individuals. The pattern of this inheritance has only recently been understood.

Mendel's observations of dominant and recessive traits in peas produced very clear patterns of inheritance, as do some known genetic disorders such as Huntington's Disease and Cystic Fibrosis, where the genetic characteristics of a person match the observed characteristics. Cancer does not follow such a simple pattern of inheritance. There are a number of reasons why this might be so. Firstly the particular characteristic may be controlled by many genes (a polygenetic trait), this means that recessive mutations on different genes controlling that characteristic would not have an effect on the person, only recessive mutations on both copies of one of the genes.

Another reason for the lack of consistency is the role of the environment in affecting the expression of genes. The environment may affect gene expression in a number of ways. In lung cancer, for example, although genes are thought to play a role, the over-riding cause is the inhalation of pollutants such as tobacco smoke and asbestos. In other diseases the environment may have a more subtle effect.

The final model is one that is thought to be the main way in which some breast and colon cancers are inherited. This is a proposal by Knudson (1971) which incorporates elements of both concepts. In this model a person inherits one mutated allele from the parent who is carrying a trait which makes them susceptible to cancer, the other allele from the healthy parent is healthy. Over time the cell is exposed to carcinogens that may cause a change in the healthy allele, this mechanism is known as loss of heterozygosity. The change in the other gene only has to occur in one of millions of cells in order to precipitate cancer. This mutation does not always occur, which explains why cancer does not always develop. It is not yet clear what effect environmental modifications, such as changing diet or reducing exposure to carcinogens will have on the health of an

individual predisposed to cancer. Loss of hetrozygosity is thought to be one part of the reason why cancers develop, however tumourigenisis involves a complex chain of events, so other environmental factors must act at other points in the chain to allow a tumour to develop.

1.3.5.1 Breast Cancer

Breast cancer is one of the three major cancers (lung, breast and colon) which account for 43% of all cancers in the UK, and a similar proportion of deaths. Breast cancer itself had an incidence of 33240 in 1995, and accounted for 14% of all cancers. It accounted for a smaller proportion of all deaths (9%), with 13760 deaths from breast cancer in 1996 in the UK. Approximately 1 in 12 women will develop breast cancer by the age of 70. Of these cancers, approximately 10% are thought to be primarily attributable to an inherited tendency (CRC website 2000).

Inherited breast cancer is thought to be a result of a problem in the tumour suppressor system, which is thought to suppress the proliferation of cells (Hodgson & Maher 1993). Two genes are currently used in clinical practice to detect an increased risk of breast cancer – BRCA1 and BRCA2, and a third one - BRCA3 has been localised to chromosome 8 (Seitz, Rohde, Bender, et al 1997). These genes are thought to lead to cancer by the process outlined above of loss of heterozygosity. As other changes are necessary in order for cancer to develop, possessing a faulty copy of BRCA1; BRCA2 or BRCA3 does not mean that cancer will inevitably develop, but it may increase the risk of breast cancer developing from 8% to 85% (Burke, Daly, Garber et al 1997a). This incomplete penetrance means that it may be possible to avert the development of cancer by early interventions to ensure that the other copy of the gene remains healthy. The mechanism by which it mutates is not yet fully understood. In addition, early screening and treatment may reduce the seriousness of the cancer, and improve the prognosis. The development of cancer is typically earlier than in the general population, with onset in the forth or fifth decade, rather than after the sixth decade of life, as seen in the general population.

Susceptibility to breast and ovarian cancer may be inherited from either parent, although in men the gene rarely has an effect. The risk of some cancers increases slightly for some men, and men carrying certain mutations of the BRCA2 gene may develop breast

cancer, a condition that is extremely rare in men. Only women with mutations at certain points on the BRCA1 gene are at an increased risk of ovarian cancer, and occasionally this is the only cancer seen in such families. The genes involved are very long, and the mutations responsible for the increased risk may be found at any point along the genes. This great variation in mutation locus means it is essential to test a family member with cancer first, before non-symptomatic family members can be offered the test. This variation also results in varying clinical features and risks, such as risk of other cancers and age of onset, for this reason it is essential to look also at the pattern of cancers within the family to give an indication of the effect of that mutation.

The possibility of early detection and treatment, the option of masectomy (removal of both breasts) or oophrectomy (removal of the ovaries), and the possibility of preventative therapies such as tamoxifen, makes this disorder very amenable to genetic testing. The outlook for people found to be carrying the gene is much more optimistic than for people carrying the HD gene, and there is a good clinical basis for careful monitoring and early intervention in those people found to carry the gene.

1.3.5.2 Colon Cancer

Colon cancer is another major cancer, with 31,320 new cases in 1995, and leading to 17, 620 deaths from colon cancer in 1996 in the UK (CRC website 2000). Colon cancer affects both men and women, and it has a similar level of incidence in the general population as breast cancer, but it accounts for considerably more deaths. The poor survival rate for colon cancer is due in part to late detection, the symptoms are often hidden until late in the disease course, when they do arise people are often embarrassed to attend their GP. The symptoms of colon cancer can be ambiguous and may be missed by doctors, prolonging the time to diagnosis. There is currently no national screening programme for colon cancer in the UK, so unlike breast cancer, the presentation is often later, and may be at an inoperable stage. Finally the advent of the use of tamoxifen in 1987 is considered to have made a large impact on the rates of breast cancer (Peto, Boreham, Clarke, et al 2000), however in colon cancer there have been fewer breakthroughs in treatment, and surgery is often the first line defence.

Up to 10% of colon cancer cases are thought to be due in part to an inherited predisposition to cancer. Three main categories have been proposed, the first is a

syndrome known as Familial Adenomatous Polyposis (FAP). This is a syndrome with almost a 100% penetrance, people who have inherited a mutated gene from a parent are almost certain to develop colon cancer, if it is not prevented. There is one gene responsible for this condition (the APC gene on chromosome 5), which has clear clinical symptoms, in the form of numerous polyps (pre-cancerous lesions) in the lower colon from adolescence onwards, although cancers are not usually diagnosed until the third decade of life (Giardiello 1997).

Traditionally screening has been offered, with prophylactic colectomies recommended in some cases. Although the clear symptoms make a positive clinical diagnosis fairly accurate, genetic testing can be used to confirm the clinical diagnosis, particularly to reassure those who are currently asymptomatic. In addition genetic testing is now used to screen children and young people prior to their first colonoscopy, to determine whether such an invasive procedure is justified. The demand for testing is high, only 24/218 people at high risk of FAP over 10 years of age did not have a genetic test to detect FAP (Evans, Maher, Macleod et al 1997). Testing for FAP pre-implantation has been carried out by some clinicians, in an attempt to ensure that children born to carriers do not carry the APC mutation that leads to FAP (Ao, Wells, Handyside et al 1998).

1.3.5.3 Non Polyposis Colon Cancer

The next major category of disorders encompasses people who have a strong family history of colon cancer, however the clinical presentation is more ambiguous. The main diagnostic category is termed Hereditary Non-Polyposis Colorectal Cancer (HNPCC). This is more common than FAP and is thought to account for 5-10% of all colorectal cancers (Mecklin 1987; Kee & Collins 1991). This syndrome was first identified by Warthin (1913) whose seamstress told him that most of her family had died from colon cancer, and correctly predicted that she too would die this way.

HNPCC is thought to be a result of a mutation in the DNA mismatch repair system, so that any mutations occurring through environmental mutation are not detected and corrected, so cancers are more likely to develop. A number of genes (including hMSH2, hMLH1, hPMS1 and hPMS2) are thought to influence the development of this type of cancer. An inherited mutation may occur in any one of them, although most are thought

to occur in hMSH2 or hMLH1 (Peltomaki et al 1993, Lindbolm, Tannerguard, Werelius et al 1993).

HNPCC presents clinically as a few polyps arising periodically in middle to later adult life. The reduced numbers of polyps mean that the development of a cancer is less inevitable, however, still up to 80% of people with this gene mutation are thought to develop cancer. Criteria have been set up for the research study of this disorder, these are termed the Amsterdam criteria (Vasen, Mecklin, Khan & Lynch 1991), and a person's family history must fulfil certain criteria to meet this classification. They are:-

- Three or more blood relatives must be affected by colon cancer, one of whom is a first degree relative (FDR) of the other two
- At least two generations are affected
- At least one individual should be less than 50 years of age at the time of diagnosis
- Clinical symptoms are not indicative of FAP.

A person with this degree of family history (i.e. indicative of the presence of a deleterious gene would have a pre-genetic testing risk of dying from colon cancer of approximately 1 in 3. This assumes the equal and random (50:50) distribution of this gene to offspring, an 80% penetrance of the gene in gene carriers and includes the poor prognosis associated with colon cancer. With regular screening this risk would be substantially reduced (Houlston, Murday, Harocopos, Williams & Slack 1990).

These criteria have been criticised as they do not include the extracolonic cancers that are also associated with this type of colon cancer (principally endometrial cancer, but also gastric, pancreatic, ovarian, and upper urinary tract cancers (Aarino, Mecklin, Aaltonen et al 1995). There is also a reduced probability of three cases in smaller families and an increased chance of false positives in large families (Percesepe, Anti, Roncucci et al 1995). A third problem with the criteria is that germline mutations have to occur for the first time at some point, so a new mutation in a family may cause a very early cancer to develop. A new mutation may be passed on to subsequent generations, however, it will not be classified as HNPCC until at least three people in two generations are affected. For these reasons these criteria, although useful for genetic research, have proved somewhat less useful in clinical practice due to the potential under-estimation of cases.

In this thesis, the less stringent Amsterdam criteria are used, in which a person may be considered to be at high risk if three or more of their relatives have colon cancer AND/OR a related extra-colonic cancer (principally endometrial cancer), and all other criteria are met. In addition people will be included in this group if they meet all the criteria except the youngest affected family member was over 45. These people are still thought to be at a 1 in 3 risk, however the cancer will develop later.

A large number of people do not fall into either of these categories, but are still thought to be at a higher than population risk of developing colon cancer. One category which has been suggested is that of familial colorectal cancer, which is defined as being the presence of colon cancer in two or more relatives with a later age of onset (Lynch 1990). Even individuals with only one affected relative over 45 are still thought to be at a somewhat higher risk of colon cancer (Houlston et al 1990). This study will concentrate on people who either fall into the second category of HNPCC, or who have a less strong family history and fall into the lower risk category. A 'low' risk group will include all the participants with just one affected FDR who was over 45 (1 in 17 risk of dying). A moderate risk group will include the remaining participants (risk of 1 in 6 to 1 in 12 of dying from colon cancer) (Houlston, et al 1990).

A person who is found to be at high risk of colon cancer can be offered regular colonoscopic surveillance, which, although unpleasant, can detect cancers early enough to be treated, and so prolong life-expectancy (Vasen, Nagengast & Meera Khan 1995). This is currently offered to many individuals who are at high risk, however this is an inefficient use of resources, as half of these individuals will not develop colon cancer, additionally colonoscopy is associated with a low risk of a perforated bowel (Solomon & McLeod 1994). Genetic testing would enable those not affected to cease participation in intensive screening protocols, whereas those testing positive would have regular screening, and may be eligible for prophylactic chemotherapy trials or prophylactic colectomy (Lynch 1999). Genetic testing may also reassure those found not to be gene mutation carriers; and assist individuals in reproductive decision making.

1.4. Genetic Testing

There are a number of different types of genetic testing according to the nature of the disease, and in addition in the advances in technology. The earliest form of genetic testing available was familial linkage analysis. This technique is based on the observation that genes which are close together are often passed on through the generations together, the closer the genes are, the more likely they are to be passed on together. Once the general area in which the gene responsible for the disorder has been identified, analysis on the DNA of family members with the disease can look at markers close to the responsible gene. If markers have been found which are always found on affected individuals, currently healthy individuals can be screened to see whether they too carry these markers. If they do then they will probably also carry the affected gene. This technique does not yield a definitive result, as the markers may have become separated in the process of reproduction, so that a person may inherit a marker which is on one side of the gene, but not the one on the other side. It is not possible to know from this analysis whether the affected gene went with the first or second marker. This type of analysis is typically 90-98% reliable.

Further developments have made it possible to increasingly look at the actual gene itself, in a mutation analysis. For some disorders - such as HD, the same mutation is responsible for all cases of Huntington's making it possible to simply look at that point to determine whether any individual is likely to develop Huntington's. Other disorders may be caused primarily by a few mutations; cystic fibrosis is one such disorder, with 80% of cases in Northern Europeans being caused by one type of mutation. This means that it is possible to screen a population for the most common mutations, although rarer mutations may be missed, this is a cost-effective way of providing widespread screening.

The final category of disorders includes most cancers, where the mutation may be found at any point along the gene, although most cluster in one area. In order to identify a mutation, the entire gene responsible must be examined; this is a lengthy process as each gene is very long. For this reason, this type of analysis is always carried out first on an affected individual, before being extended to their family members. If genetic testing was conducted first on the genes of an asymptomatic individual, not finding a genetic mutation may be because there is no defective gene in the family, or because that person

has not inherited the gene, or because the mutation is on another gene not examined. These mutation analyses are more accurate than the linkage analyses, and as long as the mutation identified is the one responsible for the cancer, will be 100% accurate. There is a small possibility, however, that there may be more than one gene causing the cancers.

1.5 Timing of Genetic Testing

The time at which a genetic test is offered depends on the type of disorder that is being screened for, and the reason why the person wants the test. The times at which a person may undergo a genetic test fall broadly into four categories: - preconception, prenatal, childhood and adult screening.

1.5.1 Preconception & Population Testing

For recessive disorders, the main aim of testing is to give potential parents the option of not having children affected by a particular disorder. Some programmes have been set up which aim to do this, either on an individual or population basis.

The use of genetic testing before reproduction has been widely employed in the Jewish community and in communities where marriages are often arranged in part by the community. Results of testing before marriage can prevent the marriage, and therefore the birth of children of two carriers of the same recessive gene. This type of testing has been shown to be successful in reducing the numbers of children born with thalassaemia in Iran (Ghanei et al 1997), where marriages were strongly discouraged between carriers. As abortion is illegal, this was considered the best option. This method has also been employed in Montreal, where targeted screening of Ashkenazi-Jews and people of Mediterranean origin for Tay-Sachs and β-thalassemia diseases respectively, has reduced the incidence of these diseases by over 90% in the last 20 years (Mitchell, Capua, Clow & Scriver 1996). In this study testing had been carried out at high school at age 16 and the students followed-up into adulthood. Those who were found to be carriers were informed of this, and when they wanted to start a family, they requested testing for their partner (if they had not been tested). At this stage they were offered counselling and prenatal testing. Population screening before reproduction has the advantage of detecting the gene in a family before it has been expressed, and gives people the option to choose their partner according to their genotype.

If both partners are carriers and want unaffected children, but they do not wish to terminate a pregnancy, donor eggs or sperm from non-carriers could be used, to ensure the child is healthy, or the couple may consider adoption. Many couples do not discover that they are both carrying recessive genes until they have had one affected child, or despite knowing that they are carriers still wish to have their own biological children. Testing prior to pregnancy means that decisions can be made with more thought and less time pressure than during a pregnancy.

1.5.2 Preimplantation & Prenatal Testing

If carriers wish to avoid having an affected child, the main option is pre-natal testing and termination of an affected child. It is also possible to opt for in-vitro fertilisation, in which the embryo is examined prior to implantation, and only healthy embryos implanted. This is an expensive option, but may be more acceptable as it does not involve abortion. Testing can prove to be stressful- and may affect the woman's feelings towards her baby. Prenatal testing has been the main option available to couples with a known risk of having a child with a recessive disorder who wish to have their own child.

Testing in a known carrier can occur early in a pregnancy using chorionic villus sampling, or later using amniocentesis. Both procedures carry some risk of miscarriage (Roper, Konje, De-Chazal et al 1999), and may give an inaccurate result, if the mother's blood infects the sample. Testing of pregnant women for recessive disorders on a population basis is being piloted, however this procedure takes longer, as first the parents must be screened, then if both are carriers, the foetus can be. This may cause more stress than testing known carriers, as prior to testing the women had no idea that her child might be affected. Pre-natal testing is also an option if the child might be at risk of Huntington's disease; the foetus can be aborted if they are found to be carrying the affected gene. If a parent knows that they are carrying the gene, then this is an accurate procedure, however elimination testing may be carried out if the parent does not want to know if they have the gene. The DNA of the grandparents can be used, and if the child has inherited either of the affected grandparent's copies of the gene, then it can be aborted, 50% of foetuses aborted in these conditions would not have developed HD.

Another option that is currently being explored, is the use of pre-implantation testing. This involves in-vitro fertilisation of embryos, these embryos are each then allowed to develop to 8 cells, one of which is then removed for analysis (Verlinsky & Kuliev 1994). Those embryos that are found to have two copies of a deleterious recessive gene or one copy of a deleterious dominant gene can be destroyed, and only healthy embryos implanted. This may be more acceptable than an abortion to many people and means that in the case of HD, the parents need not know whether any of the embryos were carrying the Huntington's gene, and hence their genetic status also remains unknown. This is an expensive option with a low success rate, however may be particularly useful if in-vitro fertilisation is recommended for another reason.

1.5.3 Infant & Childhood Screening

Once a child has been born it is often not obvious that the child has inherited a genetic disorder. Without testing, the disease may not be identified until clinical symptoms appear. Even after the first symptoms appear, the disorder may not be noticed until these symptoms become more severe. For some disorders such as Tay Sachs disease, nothing can be done to change the prognosis. In other disorders - such as cystic fibrosis, identification at birth, and early preventative interventions can reduce the impact of the disease, and the damage caused to the lungs - leading to an increased life expectancy and quality of life (Dankert-Roelse & Meerman 1995). The same is true for other disorders, such as haemeopathologies (e.g. haemophilia, β-Thalassemia), where there are treatments available which could save the child's life (e.g. factor VIII), or could prolong and improve the quality of life.

Childhood screening for adult onset disorders is usually not recommended, as the child is often not able to fully understand the implications of testing, and the effect that this knowledge will have on their future, for example in choosing careers, reproductive decision making and for insurance. They may also not be mature enough to understand or cope with the knowledge that the result will give. Screening may however be indicated for adult-onset conditions that may be affected by actions taken in childhood or adolescence. Genetic testing for FAP may be offered to children or teenagers, with appropriate explanation, before they are due to undergo colonoscopy. In this way carriers can be identified, so that healthy children do not need to undergo this uncomfortable and potentially hazardous procedure.

1.5.4.Adult Screening

For many disorders there is no need to undergo testing in childhood, indeed for some disorders there is no health benefit in knowing whether someone is going to develop a disorder at all. Even when there is no health benefit, many people from families that have a history of a genetic disease want to know whether they will develop it. Some people wish to use this information to help them choose a career, decide whether to get married or to plan a family, other people seek psychological benefits such as simply wanting to know to decrease uncertainty. Before a definitive diagnostic test is carried out, it is important to establish with the person what they hope to gain from testing, as it may be that they expect testing to answer all their questions, when it might just raise more. For some genetic diseases, such as cancers caused by a genetic predisposition, genetic testing might be the first step, followed up by lifestyle modifications, regular screening, and maybe even prophylactic surgery.

1.6. Scope of Thesis

The era of genetic testing is already here, with testing for the development of childhood onset disorders (such as cystic fibrosis), tests for adult onset disorders (such as Huntington's disease) and for predispositions to diseases (such as for cancer). It is important to study and determine the effect that new genetic technology has on individuals, families and society. It is fundamental to ensure that this new knowledge is used to improve individual's well-being, and that the ethical issues surrounding genetic testing such as insurance discrimination are addressed from both an individual and societal perspective.

Colon cancer provides a good study disease. Compared with HD, colon cancer is not always fatal, especially when treated early, additionally the responsible genes do not have as great a penetrance as for HD - for which everyone with the genetic disorder develops the disease. These aspects mean that colon cancer is more amenable to prevention and treatment, therefore there is a clear case for early detection via genetic testing. Colon cancer is also similar to many other disorders that are thought to be genetically linked, but are not as strongly associated with the gene as HD.

The study of colon cancer provides a good model for adult onset disorders which are caused by one faulty copy of a gene (dominantly inherited), compared with childhood onset disorders, which are often sex-linked, or recessive. In adult onset disorders a genetic test will reveal whether the person themselves is likely to develop a disorder - not just whether their children will. Finally the action of the gene leads to the development of cancer in men as well as in women, so the results are more generalisable to the general population, whereas in studying breast cancer, men are usually just carriers of the gene, with no effect on their own health. Although the effect of the gene is slightly different in women, with endometrial cancer being found in addition to, or instead of colon cancer, both genders are at high risk of cancer.

This thesis will address two main themes. The first theme will encompass an exploration of the associates of intent to have a genetic test for colon cancer in people with a known family history, but are currently asymptomatic. The second theme will then explore the generalisability of these results to other population groups, and whether the same factors also are important in considering intent to have a genetic test for breast cancer.

The exploration of associates of intent to have a genetic test for colon cancer will take the form of a quantitative investigation of high-risk people's views of genetic testing (Chapter 4). The main theoretical frameworks adopted are the theory of planned behaviour and the health belief model. These models have been chosen for their applicability to the issue of genetic testing which will be discussed in Chapter 3. The models will be compared to test their sufficiency in explaining intent to have a genetic test for colon cancer. In addition other psychological and demographic factors will be considered, which may explain variance in addition to that explained by these two frequently used models of behaviour.

The next study (Chapter 5) utilises the same database of responses from asymptomatic individuals, but explores issues of gender difference. Gender difference has rarely been explicitly explored in relation to intent to have a genetic test, and in some circumstances it has not been possible to untangle the effects of gender from the differing effects of the genes in males and females. The advantage of making such a comparison in this sample is the similar action of the genes of interest in both men and women. This study will

examine whether men and women differ in their intent, in the extent to which they hold other related views, and in the predictors of intent to have a genetic test.

The theory of planned behaviour has been widely utilised to explore a number of different behaviours. The novel nature of having a genetic test raises issues about the stability of intentions and the structure of beliefs which may be less apparent when considering more established behaviours. This issue will be explicitly explored in more detail in a follow-up study to determine the stability of the derived model over time (Chapter 6).

The second main theme is the generalisability of the results to different populations. As direct comparisons are required, a consistent, quantifiable approach is important, therefore a questionnaire methodology is adopted, asking different people similar questions and comparing their answers.

The first comparison (Chapter 7) explores the differences between the responses from a subset of the original sample and their partners. This will provide important information for clinical applications, determining the likely impact of a genetic test on the wider family. In addition it will permit an exploration of the nature of the relationship between an individual's wishes and that of a significant other. This will be particularly explored in relation to subjective norms (from the theory of planned behaviour), which will be compared with actual norms.

The second comparison considered consists of people who also have a family history of colon cancer, but have already developed colon cancer themselves (Chapter 8). These people are at a higher risk of developing colon cancer, but are also presumed to be gene carriers. It is thought that the effect of a genetic test for these people will not be as great as they are already aware of their likely gene status. This perception, however, has been inadequately explored in the literature to date.

The third group to be compared is a general practice sample (Chapter 9). A number of studies have already explored the views of people with no family history of colon cancer, however these people are unlikely to be offered genetic tests in the foreseeable future. A comparison with this group will firstly indicate whether similar factors are

important in determining intent in this group as compared with a high-risk group. Without such a comparison it is difficult to know whether there is any value in contacting a general practice group to explore issues of intent. In addition the comparison will indicate the current interest in genetic testing in the wider population. This will indicate the possible demand on genetics services were a test ever developed that could be used on a general practice sample.

The final group to be compared will be women who are at risk of developing breast cancer (Chapter 10). The associates of their intentions will be compared with the associations of the intent of women at risk of colon cancer. With the function of genes still being uncovered, and many more cancers being attributable to some genetic influence, a model which can be applied to any new late onset genetic disease is desirable, as this will reduce the time required for research into the test implications prior to the clinical introduction. The comparison will determine how similar the associates of intent are in the groups of women at risk of different cancers.

Chapter 2

Psychological Aspects of Genetic Testing

2.1 Psychological Issues involved in Genetic Testing

Studies of the psychological aspects of genetic testing have involved three main areas - the interest/intention, uptake and impact of genetic testing. Interest in genetic testing has been studied for many years, even before tests were actually available. This dimension is usually measured by a simple question about whether a person would want to have a genetic test, or by asking about whether they would want family members to undergo testing. Intention to have a genetic test has been explored more recently now that genetic testing is more widely available for these diseases. Other research in this area has involved looking at people's reasons for wanting or not wanting testing, risk perception, anticipated emotional reactions and correlates of intent.

Despite the high level of interest generally reported for genetic testing, the uptake has been surprisingly low, especially for HD where most research has been carried out into testing for adult onset disorders. The discrepancy between interest and uptake is one that has not adequately been explained.

The final area of research concerns the impact of genetic testing. Most research has focused on the psychological effect of testing on the person undergoing testing - such as anxiety and depression. Other studies have looked at the effect on a spouse. There is a lack of research into the effect of testing positive or negative on behavioural outcomes, or the social implications of testing.

This review will initially examine psychosocial aspects of testing for Huntingdon's Disease and recessive disorders, as this is where much of the early work has concentrated. The focus will then transfer to the two diseases examined in this thesis, hereditary breast/ovarian cancer and hereditary colon cancer.

Within this review a number of questions will be addressed in relation to these diseases. One area that will be examined is the perception of risk of developing a disease in people with a family history of a genetic disorder. This will be examined as perceived susceptibility to cancer (colon or breast/ovarian) in the studies included in this thesis. The next main areas reviewed are reported attitudes towards genetic testing and the motivation for undergoing genetic testing. This has been the major area concentrated on by most previous studies of genetic testing. Some studies have also sought to determine how attitudes and motivations are associated with intention and uptake of testing. The next area examined is emotional reactions which people anticipate experiencing if they receive a favourable or less favourable result. Some studies have examined these in the context of intent and uptake of genetic testing. A major focus of many studies has been the level of intent and uptake of genetic testing. In addition to the reported levels of intent and uptake, most studies have also used regression techniques to identify the correlates of intention and uptake.

The studies reported in this review have been identified through systematic literature searches. The initial searches used three databases- MedLine, Embase and PsychLit. These three databases were searched using the search terms 'test*' and 'screen*' to identify papers relating to testing and screening. To restrict the search to genetic testing the search terms 'gene*' and 'DNA' were used to identify those papers reporting on genetic testing. The searches were then further restricted to the diseases of interest using the terms 'recessive'; 'Huntington*'; 'breast'; 'bowel' and 'colo*'. The use of the wildcard character (*) identified papers which used slightly different terms. These databases were re-examined every six months to update the review following the initial searches in 1997. The reference section of papers identified in this way was used to identify any other relevant papers that had not been identified in the initial searches.

2.2 Attitudes, Uptake & Interest in Genetic Testing for Recessive Traits

People with serious recessive diseases often died in early adulthood, or due to social circumstances did not have children. This is now changing as modern medicine and

society's view of disabilities changes. People with recessive traits are living longer and they too are having children, therefore passing on the gene. These people too may request genetic testing for their partners. Despite the changes in modern medicine, many people still perceive preventing the birth of a child with a genetic disorder as the best solution.

As discussed in the last chapter, there are a number of different times at which it may be appropriate to use genetic testing to detect recessive disorders. The first opportunity is before marriage or even before marriage is even considered. Screening at this stage has been used in schools, and on a population level. Targeted screening has also been employed, as many recessive traits are strongly linked with ethnicity. For example, Tay Sachs screening may be targeted at a Jewish population (Lowden, Zucker, Wilensky & Skomorowski 1974), whereas screening for sickle cell anaemia is targeted at people of African descent. Screening refers to a widespread testing programme, where as genetic testing for recessive disorders is used when there is a known or suspected mutation in a family (Mitchell, Scriver, Clow & Kaplan 1993).

Screening for recessive disorders has been extensively studied, and particularly screening for cystic fibrosis, Tay Sachs, B thalassemia and sickle cell anaemia. Most people believe that the option to be tested should be widely offered (Mennie, Compton, Gifillan et al 1993a, Magnay, Wilson, el Hait et al 1992). Reasons given by the 15% of women not having a test for cystic fibrosis were primarily opposition to abortion either in general or specifically (54% of those refusing gave this reason) (Mennie, Gilfillan, Compton et al 1993b).

Motivation to undergo genetic testing for cystic fibrosis was found to be associated with high perceived seriousness, higher perceived personal risk, higher knowledge and lower perceived barriers (Leonard, Bartholomew, Swank & Parcel 1995). Three of these concepts (perceived seriousness, perceived risk and perceived barriers) are components of the health belief model (HBM) discussed in Chapter 3. The main remaining component is perceived benefits of testing. In another examination of the health belief model (Becker, Kaback, Rosenstock & Ruth 1975), intent to have a test for carrier status of Tay Sachs was associated with higher motivation to have children,

higher perceived susceptibility of being a carrier and lower perceived severity of being a carrier. The apparent contradiction in the effect of seriousness/ severity may be due to a difference in assessment – Leonard et al (1995) assessed seriousness of having cystic fibrosis, whereas Becker et al (1975) measured perceived severity of being a carrier for Tay Sachs. In recessive disorders there is a significant difference in the seriousness of carrier status compared with homozygous affected status. As the test shows the likelihood of carrier status, the seriousness of carrier status is the more appropriate variable to assess.

People undergoing screening for these recessive diseases report an increase in anxiety when being tested (Schneiderman, Lowden & Rae-Grant 1977). This increase is found particularly in pregnant women if a stepwise approach to testing is used[1]. Anxiety is greatest in the time between receiving a carrier status result for the woman and a non-carrier status result for her partner (Mennie et al 1993a; Hartley, Scotcher, Harris et al 1997; Bekker, Denniss, Modell et al 1993).

Some studies have found that anxiety over receiving a carrier test result quickly dissipated (Mennie et al 1993a; Bekker et al 1993), however other studies have found more long term effects (Brandt et al 1996). The main long-term effect of testing has been that carriers perceive their own health to be significantly poorer than those who were not carriers, this was found for both cystic fibrosis (Axworthy, Brock, Bobrow & Marteau 1996) and Tay Sachs (Marteau, van Duijin & Ellis et al 1992). Although this result has not been universally reported (Bekker et al 1994), it is concerning, as neither disease is known to have any effect on heterozygotic carriers of the gene. Those people found to be carriers are experiencing long term problems in their perception of their health as a result of receiving a test result when there is no physical reason why this should be.

Ethical issues other than the possible adverse psychological impact have also been raised. As recessive traits are often ethnically specific, testing may lead to indirect discrimination if employers and insurers do not understand the results correctly. It is

important to consider the cultural situation before testing, as stigmatisation may occur, so that those who are known to be carriers are regarded as a reproductive underclass, so can only find partners who are also carriers (Stamatoyannopoulos 1974). This may be less likely in major cities where people's medical family history can be more easily hidden than within a close rural community. A simple solution to the problem has been found by the Orthodox Jewish community in New York, where marriages are arranged by matchmakers, who consider the family's health, wealth and background, before recommending marriages. In this community, adolescents are offered anonymous testing, the results of which are stored on a computer. If a match is considered, the records can be checked, and only if both people are carriers is the match rejected. As matches are decided on a number of other factors, the carriers need never know the true reason for stopping the marriage (Jones 1996).

There are many ethical issues that surround testing for carriers of recessive genes. These include whether it is acceptable to decide issues of marriage on the basis of genetic make-up, whether prospective partners have the right to know if a person is carrying a recessive gene, and whether abortion of a foetus with two recessive genes is morally acceptable. In spite of these issues, screening and testing on a voluntary basis for recessive disorders has been is widely taken up, with few negative effects, and a drop in the numbers of affected children born (Mitchell et al 1996).

Testing for Dominantly Inherited Disorders

2.3 Huntington's Disease

2.3.1 Perception of Risk of Huntington's Disease

In HD the risk to a child of an affected individual of inheriting the gene, and hence developing the disease is 50%. After testing the risk of developing the disease is 100% if the person tests positive, and assuming they do not die of other causes first. If the

[1] A stepwise procedure tests the woman first, and her partner is only tested if this test shows a carrier status; for a couple test both are tested simultaneously, so the risk for the pregnancy is known when the woman's risk status is disclosed.

person tests negative there is a negligible risk. These risk rates are somewhat less accurate for linkage analysis - the risk usually increases to 95-98%, or decreases to below 10%, although some results may be inconclusive.

The issue of risk has been viewed as a crucial part of genetic counselling, to ensure a person can make informed judgements, however risk is a difficult concept for people to grasp, and often people's risk perception is inaccurate due to misinformation or denial. In one study, 81 participants requesting genetic testing for HD were asked for their perception of their risk of carrying the gene (Decruyenaere, Evers-Kiebooms, Boogaerts et al 1995). These individuals had already undergone some genetic counselling and had been told of their 50% risk status. Of these participants, 35.8% overestimated their risk of being a carrier; 39.5% gave an accurate assessment; 7.4% underestimated their risk; and 17.3% did not answer the question. As risk perception was assessed at only one time point, it is impossible to determine the effect that the genetic counselling had on this perception, although it clearly hasn't convinced a substantial number of people that they only have a 50% risk. Other studies have also found results in this direction (Meissen, Mastromauro, Kiely et al 1991; Tibben, Frets, van de Kamp et al 1993a), although to a lesser extent. Decruyenaere et al (1995) suggest that this pessimistic outlook is an attempt by the at risk person to prepare for the worst, and that believing one is a carrier may motivate them to take the test as they believe they have nothing to lose.

2.3.2. Attitudes and Motivations for Genetic Testing for Huntington's Disease

Many studies have attempted to evaluate reasons for undergoing genetic testing, all emerging with common themes (Table 2.1). In assessing the studies conducted so far, it is important to recognise that for most studies participants were able to indicate more than one reason for undergoing testing. Often this was in a fixed choice paradigm, however some studies gave participants an opportunity to give their own responses. Many studies just asked for reasons for undergoing testing, a few also asked reasons for not wanting testing. The early studies were conducted prior to, or around the time that genetic testing was first being developed, so these results may differ, as the prospect of testing was remote.

Table 2.1 Reasons given for and against genetic testing for Huntington's Disease

Paper	Country	Participants (numbers, risk, age, gender)	Reason for testing	Reason against testing	Comments
Mastromauro, Myers & Berkman (1987)	USA	131 people at 50% risk; mean age 32 yrs, 43% male.	End uncertainty(40%) Learn children's risk (30%) Financial Plans (21%) Family Planning (10%)	Rather live in hope (53%)	Reasons given only for own intent
Meissen and Berchek (1987)	USA	56 people at 50% risk; mean age - 37 yrs' 37% male.	Plan for future (58%) Eliminate doubts & worry (42%) To know (33%) Family Planning* (100%)	Emotional reaction (43%) Not want to know (36%) Afraid of bad result (29%)	Reasons given for own intent; Can endorse multiple reasons (* - under 35)
Evers-Kiebooms, Swerts, Cassiman, and van den Berghe (1989)	Belgium	104 High risk (82% at 50% risk) mean age - 32yrs; 49% male	To be certain (72%) Plan for future (63%) Informing children (69%)* Family Planning (66%)* Financial Reasons (44%)	Difficult to live with result (61%) Prefer uncertainty (48%) Will not know disease course (43%) No treatment (41%) Effect on relationships (38%)	Multiple reasons (* for those who have children/ are under 40)
Evers-Kiebooms et al (1989)	Belgium	55 Partners mean age - 36 yrs; 55% male.	To be certain (69%) Plan for future (66%) Informing children (80%)* Family Planning (49%)* Financial Reasons (38%)	Difficult to live with result (55%) Will not know disease course (40%) No treatment (40%) Prefer uncertainty (39%)	Multiple reasons (* for those who have children/ are under 40)
Evers-Kiebooms Cassiman, and van den Berghe(1987)	Belgium	28 High Risk individuals; 77% under 39yrs, ~50%male	Have certainty (29%) Family Planning (21%)		open format question - multiple reasons; 42% did not answer
		12 Partners; Slightly older than 39yrs	Have certainty (33%) Family Planning(33%)		open format question 32% did not answer
Tyler, Morris, Lazarou et al (1992)	Wales	38 participants: Gender and age distribution not given	Inform children (mean=9.4) Family Planning (8.5) Desire to inform partner (7.6) Relieve uncertainty (7.6) Preparation for future (7.5)	Adverse effect on self or others (48%)	Motivation for testing Items calculated for those for whom issue is relevant. (Score for motivation 1-10).

Tibben et al (1993a)	Netherlands	70 High risk; mean age - 31.9 yrs, 36% male	Family Planning (60%) Relieve uncertainty (43%) Obtain certainty (38%) Planning for future (3%)	Fear of adverse effects (30%)	open format question - multiple reasons
	Netherlands	55 Partners; Age not given	Family Planning (55%) Relieve uncertainty (2%) Obtain certainty (16%) Planning for future (76%)	Fear of adverse effects (24%)	open format question - multiple reasons
Decruyenaere et al (1995)	Belgium	81 test applicants, mean age 34.2yrs, 46% male	Reduce uncertainty (55.6%) Family Planning(20%) Inform children (20%)		Most important reason only
Babul, Adam, Kremer et al (1993)	Canada	Whole study 250 participants; mean age 34.5 yrs, 39% male, response rate 71%		Emotional reaction (20%). Happy with life as is (20%) Might not happen for years (13.3%) No cure (11.1%)	Ranked 3/13 reasons – only reports responses of 24 not having test.
Kreuz (1996)	Germany	300, (93% at 50% risk); median age 31 yrs, 42% male.	Desire for certainty (75%) Family Planning (61%) Plan future (54%)	Emotional reaction (79%) Social problems (28%) Insurance problems (27%)	Direct test Multiple reasons possible
			Desire for certainty (45%) Family Planning (55%) Plan future (50%)	Emotional reaction (24%) Social problems (30%) Insurance problems (34%) No cure (38%) Inevitability of suffering (44%)	Indirect – linkage

In these studies, the common themes emerging are the desire for certainty and the desire to know about genetic risk to assist in making decisions about childbearing, either for oneself or to inform one's children. In addition, for some people, testing is seen as assisting in making plans for the future, specifically in relation to financial planning. The most salient reasons given for not wanting a test were fear of adverse emotional reactions, the lack of treatment options, and a wish to not know. The issue of coping with uncertainty appears to polarise the sample, with some giving the 'desire to reduce uncertainty' or 'to know' as the primary reason for having a test, and others giving the 'desire to not know' as their main motivation for refusing testing.

The relative importance of each factor varies markedly between studies. One reason for this is the variability in the ways that motivation has been measured. Some studies have asked participants to give the most important reason whereas others have asked how important a number of different reasons are. By forcing participants to chose one factor one can see the relative importance of different factors, however by allowing them to endorse a number of factors, one can see more clearly the range of implications people consider. Variations in the mean age of participants entering the study also may affect the importance of each factor. Younger individuals may be more concerned about childbearing decisions, whereas older individuals may just want to end uncertainty, as the onset of the disease is potentially imminent. Most studies have relatively equal numbers of male and female participants, however few explicitly state that separate analyses were carried out to examine the effect of gender on reasons for wanting genetic testing. More detailed analyses, controlling for age and gender may overcome these problems.

2.3.3 Anticipated Response Towards Genetic Testing for Huntington's Disease

A number of studies have asked test participants how they think that they will react to genetic test results (Table 2.2). These studies enquire about how the person thinks they would cope with a good or bad result, and/ or whether they would change their behaviour or future plans.

Table 2.2 Anticipated responses to genetic test results for Huntington's Disease

Paper	Country	Participants (numbers, risk level, age, gender)	Anticipated Response - Positive result	Anticipated response - negative result	Comments
Mastromauro et al (1987)	USA	131 people at 50% risk; mean age 32 yrs, 43% male.	Depressed; anxious; sad Suicidal thoughts (29%) Experience relief (20%) Guilt (20%) Diminished self worth (20%)		Multiple responses possible.
Meissen and Berchek (1987)	USA	56 people at 50% risk; mean age - 37 yrs' 37% male.	Prepare for the future (27%) No anticipated reaction (20%) Enjoy life more (16%) Have no more children (15%) Emotional problems (11%)	Do nothing (75%) Have children (20%) Be less anxious (16%)	Multiple responses possible.
Tibben et al (1993a)	Netherlands	70 High risk; mean age - 31.9 yrs, 36% male	Plan own life (70%) Plan family's life (75%) Impact on partner (65%) Impact on children (51%) Poor quality of life (9%) Depression (4%).	Decrease own problems (59%) Decrease partner's problems (70%) Decrease children's problems (63%) Plan for the future (60%) Improve mood (46%) Increase quality of life (33%)	Multiple responses possible.
		55 Partners; Age not given	Plan own life (49%) Plan family's life (59%) Impact on their children (61%).	Decrease own problems (51%) Decrease partner's problems (71%) Decrease children's problems (76%) Plan for the future (42%) Improve mood (40%) Increase quality of life (20%)	Multiple responses possible.
Kessler, Field, Worth, and Mosbarger 1987	USA	63 High risk; mean age - 39.3 yrs; 39% male	Have no more children (70.9%)* Have fewer children (12.9%)* Consider suicide(11.1%)		Multiple responses possible. *- in those under 40

Most studies have found that people anticipate that receiving a test result will empower them to be in control of their personal future and their family's lives. Although people do acknowledge that a positive result may lead to emotional distress and even suicide, these are the minority of the responses, and most people see testing as having a positive impact on their lives.

The numbers indicating that they would consider suicide were relatively high, however most said they would be most likely to do so when symptoms appeared, or when the symptoms became disabling. As the incidence of suicide in people with HD is high (Farrer 1986), and as these people indicated that they would not attempt it until the onset of symptoms, the introduction of testing is unlikely to significantly increase the suicide rate.

2.3.4 Intention, Uptake and Correlates of Intention and Uptake of Genetic Testing for Huntington's Disease

In studies of interest for HD, there have been problems with the sampling of patient groups. Most studies have recruited at risk participants from, or with the help of, interest groups such as Combat. These interest groups may be especially concerned and informed about their risk and current research, this may bias the findings. Other studies targeted people who are relatives of patients on a HD register, this sample is likely to be less biased. In addition to difficulties of access to participants, there are problems of non-response, as people opposed to genetic testing may be less likely to respond. The populations studied by these studies have varied. Usually the sample includes only those at 50% risk (for whom the question is most relevant) but occasionally other blood relatives at lower risk have been included. One study included spouses (Barette & Marsden 1979), without clearly differentiating between their responses and those of people at direct risk. Whilst it is valid to compare views of high risk individuals and their spouses, this study did not report the rates of interest separately, which may have biased this study due to the different implications of testing for spouses. Despite these sampling differences many studies have now been conducted into interest in, or intent to undergo testing, most of which have found comparable levels of interest(Table 2.3).

The options for testing have changed with technological advances. The earliest studies examined a theoretical interest 'if there were a gene', later ones looked at intent for the linkage test which was about 97% accurate, and the most recent studies have examined intent to have the mutation analysis which is 100% accurate for most people.

Table 2.3 Intent and uptake of genetic testing for Huntington's disease

Paper	Country	Sample (source, response rate)	Intent to have test
Before gene marker discovered			
Teltscher & Polgar 1981	Australia	Random selection 50 participants (68% response rate)	84%
Barette & Marsden 1979	UK	153 from interest group (relatives and partners) (36% response rate)	80%
Stern & Eldridge 1975	US	1065 people from interest group (Response rate 41%)	77%
Tyler & Harper (1983)	Wales	random sample 91 respondents (91% response rate)	56%
After gene marker discovered			
Meissen & Berchek (1987)	USA	56 participants from interest group (87.5% response rate)	65% (84% supported testing
Evers-Kiebooms et al (1987)	Belgium	49 from interest group	57% (60% partners)
Evers-Kiebooms et al (1989)	Belgium	104 high risk, 58 partners from interest group (46% response rate)	66% (74% partners)
Mastromauro et al (1987)	USA	131 high risk - interest group/ clinic (42% response rate)	66% (22% undecided)
Kessler et al (1987)	USA	63 High risk, interest group/ media	79% (14% undecided)
Mutation analysis			
Kreuz et al (1996)	Germany	Comparison of interest - recruited via interest groups/ clinic	46% - linkage 51% mutation
Babul et al (1993)	Canada	Re-offered to those offered/ given linkage test. Initially recruited via interest group and media.(71% response rate)	Increased risk by linkage - 82% Decreased by linkage - 64%. Refused linkage - 46%
Uptake of test			**Uptake**
Crauford, Dodge, Kerzin-Stoorrar & Harris (1989)	UK	Invited for testing by clinic Volunteers for testing from clinic Requested referral for test	7.3% 35% 59.6%
Bloch, Fahy et al (1989)	Canada	750 unselected sample	12.6%
Tyler et al (1992)	Wales	238 referrals - 86 offered test	46.5% of those offered test
Holloway, Mennie, Crosbie et al (1994)	Scotland	80 patients considering testing	21% withdrew 18% unable to have test 61% received result
Decruyenaere et al (1995)	Belgium	157 candidates in predictive test programme	32% withdrew 5% symptomatic 8% uninformative 41% received result 13% waiting

The average level of interest was around 70% but with great variation between studies (range: 46% to 84%). Interestingly the more remote the possibility of testing was, the higher the level of interest, indicating that whilst the principle of undergoing predictive testing is attractive, the reality of testing is more challenging.

When examining the interest in having a more accurate test for those people who have already been offered linkage analysis there are differences based on their previous response. Babul et al (1993) suggest that for the group who previously refused testing, the original barriers are still in place for many participants - such as the lack of a cure or preventative treatment. Those participants who had previously received a reduced risk test result may feel that they have much to lose if their risk status increased from about 5% to 100%, but less to gain if they were told that it was decreased to 0%, which might explain their reluctance. These participants were recruited from patients who had previously expressed an interest in genetic testing, and had been enrolled in the Canadian Collaborative study, so even those previously deciding against testing are likely to be more supportive of the testing programme than the entire population of those at risk.

The initial interest in genetic testing has not been translated into a high level of uptake. Despite initial predictions of a 70% or higher level of interest in HD testing, over a decade has passed, and many people have not undergone testing. Even since the offer of a 100% reliable test, most at risk individuals choose not to know. Reports of the uptake of testing can be divided into those which sample an entire population of at risk individuals, and those which report on the numbers of participants initially interested in testing, but who subsequently withdraw. Those studies that have drawn from unselected samples have found much lower levels of uptake than other studies.

Attempts have been made to determine why the uptake of testing is low. Quaid & Morris (1993) sent 123 questionnaires to individuals who had been invited to attend for testing a year earlier, but had not responded, 66(54%) returned the questionnaire. The individuals sampled were quite knowledgeable, and most (95.5%) thought that the test should be available. About 60% said that they would have the test if the procedure were simpler, or it was 100% accurate, 95.5% would have the test if treatment were

available. Babul et al (1993) found that 46% of those who had previously refused linkage analysis say they would use a 100% accurate test - however these individuals were all already enrolled in the research aspect of an original study, but had decided not to undergo clinical testing. Despite their apparent interest in having testing if the test was easier or more accurate, those who gave a reason for not undergoing testing predominantly said their reason was that they did not want to deal with the emotional and psychological consequences of an increased risk result (9/19 (47%)).

The role of perceived emotional difficulties in coping with the result as a barrier to testing has been studied by Codori, Hanson & Brant (1994). In a study of the reasons given for not completing the test programme by those who had initially expressed an interest, 32 responded (19 by questionnaire, 13 by telephone interview). There were in total three groups - 66 individuals who had undergone testing, 12 who had decided not to, and 20 who were undecided. Those who had decided definitely not to undergo testing expressed the most concern about potential emotional reactions (75% endorsed this item, compared with 30% of the undecided, and 38% on a pre-testing evaluation of those who underwent testing). Thus anticipated emotional response is a significant factor in deciding whether to have a test.

A study of the difference between tested and untested individuals (Evers-Kiebooms & Decruyenare 1998) found that those who did not want a test were more likely to have one or more children than those who wanted the test (80%:50%). Tested individuals adopted active, problem solving reactions with optimistic thoughts and social-support seeking behaviour. Untested individuals were more varied in their responses. Some untested people seemed to be able to examine their decision not to have the test, and were happy to live in uncertainty, the others avoided mention of the disease and the test.

In a qualitative analysis of the differences between requesters (n=22) and non-requesters (n =32) (Binedell, Soldan & Harper 1998), non-requesters emerged as holding different views in a number of areas. Non-requesters were more suspicious of the motives of the interviewer and the genetics service, fearing that acknowledging HD may lead to insurance problems and disclosure to children not currently aware of their

risk. Non-requesters were concerned that they would be pressurised into taking a genetic test. Non-requesters were also less knowledgeable about genetic testing. This which may be due in part to the lower levels of communication about HD reported in these families. Non-requesters rated their likelihood of developing the disease as lower than requesters, however they acknowledged that this may be wishful thinking. Individuals who wanted the test thought that the uncertainty of their current at risk status was more stressful than non-requesters did, with non-requesters more likely to want to 'wait and see'.

Uptake of testing for HD has been much lower than the levels of interest and intent reported earlier. The main reasons given for not wanting a test are concerns about test accuracy, anticipated emotional difficulties and the lack of a cure for HD. The low levels of uptake may indicate that people are self-selecting whether to have the test, based on their own anticipated reactions (Codori & Brant 1994). This selection bias may mean that the impact for these people is less than it would be for people who anticipate more problems. The people who have the test may be more psychologically robust, and considering the low uptake rate, this must be considered when assessing the psychological impact of testing.

2.3.5 Impact of Genetic Testing for Huntington's Disease

Many of the studies of people undergoing genetic testing are limited by the small numbers in each geographical area who take the test, these groups are then further divided into three - those receiving negative results, those receiving positive results, and those for whom the test was inconclusive. There is often an uneven distribution of results, as only those without symptoms have a predictive test, so those patients who are older are more likely to receive a negative result, as those who would have received positive results will have started to show signs of illness. Additionally some studies exclude those for whom the test was inconclusive, who may nevertheless have been affected psychologically by the experience of testing.

Most studies have found that there are short and longer term effects of receiving a positive test for HD (Meissen, Myers, Mastromauro et al 1988). These are usually not

very severe, and for people found to be at low risk there are psychological benefits (Brant et al 1989; Tibben, Stevens, de Wert et al 1997; Decruyenaere, Evers-Kiebooms, Boogaerts et al 1996). Some research has indicated that receiving any result - positive or negative brings more psychological improvements, than receiving no result. Patients do report adverse life events, but these appear to be hastened by the test result, rather than caused by it (Wiggins et al 1992).

Survivor guilt has been reported by those who are found to be at low risk, and those at high risk experience an 'emotional burden'(Tibben, der Vilis, Skaraastad et al 1992; Codori & Brant 1994). Testing has also brought benefits such as forming life priorities and, for those at low risk - less symptom searching (Codori & Brant 1994). There was no reported evidence of insurance discrimination, but there were some people who experienced work difficulties (Tibben, Frets, van den Kamp et al 1993c). It would appear that the long term effects of genetic testing for HD are limited, and of more importance in determining outcome are pre-test measures of psychological adjustment (Decruyenaere et al 1996; Tibben, Duivenvoorden, der Vilis et al 1993b).

In the only comparative study to date, DudokdeWit, Tibben, Duivenvoorden et al (1997) studied participants at risk of four potentially fatal late onset disorders - HD, cerebral haemorrhage, breast and ovarian cancer and polyposis coli (FAP). A comparison of psychological distress revealed that those found to carry the gene for HD reported more intrusion on the Impact of Events Scale, than any other group (people carrying the gene for FAP reported less than other groups). Those carrying the gene for HD or cerebral haemorrhage reported more avoidance than those did with a gene for one of the cancer syndromes. This is evidence for the variable impact of the test result, dependent on the type of disease being tested for. The pre-testing differences between two diseases (colon cancer and breast/ovarian cancer) will be explored in this study.

2.4 Breast and Ovarian Cancer

2.4.1 Perception of Risk of Breast / Ovarian Cancer

The risk of developing breast cancer for a woman whose parent carries a genetic mutation is approximately 40%. This is because the chance of any child inheriting a given gene is 50%; carrying a gene which predisposes to breast cancer gives an approximate lifetime risk of 80%- giving a pre-testing risk of 40%. After testing this risk would either rise to 80% if the daughter had inherited the mutation, or drop to 8% if she had not. When people attend for initial consultations they often do not know whether they are likely to carry such a gene, thus a calculation of the likelihood that an inherited gene is responsible for a family's cancer history must also be made. This approaches 100% in a family with a strong family history and young first age of onset, however it decreases rapidly with decreasing numbers of affected relatives and the increasing age of onset in affected relatives. Any information given to a woman is likely to be more complex than that given to a person at risk of HD.

Lynch, Watson, Conway & Lynch (1993) found that among the older women in their study (over 45 years), most thought they were at a lower risk of developing breast cancer than was calculated considering their age and family history. Among women under 45, 16 out of 17 thought that their risk was 50% or greater, three thought that it was 100%. After linkage genetic testing all linkage-negative women reported a reduced risk assessment, although some still thought their risk was substantially greater than the population risk. For ovarian cancer most women had little idea of their risk prior to counselling, but after counselling and test disclosure, all linkage positive women had a reasonably accurate view of their personal risk. Linkage negative women also reported a more accurate perceived risk level than they had previously.

Lerman, Seay, Balshem & Audrain (1995) found that in their study of female first degree relatives of breast cancer patients, 21% thought they were at much higher risk of developing breast cancer than the average woman, 57% thought they were at a higher risk, and only 21% thought their risk was the same or less than the 'average' woman. Over half believed they were moderately likely to have inherited BRCA1, and 15% thought they were very likely to have. These results were despite the fact that 90%

had only one first-degree relative affected with breast cancer, many cases occurring in older women. Most participants had risk estimates calculated at less than 15%.

In a study of 155 women with a family history of breast cancer, only 11% were able to identify the correct population risk. Over half were unable to assess own lifetime risk within 50% of clinician's estimate, they were equally likely to under or over estimate it (Evans, Burnell, Hopwood & Howell 1993). Another study found that for women at high risk, perceptions of their own risk were inaccurate, and more reported a higher perceived risk than their actual calculated risk was. This higher perceived risk was also associated with higher levels of screening behaviour with over a third of women under 30 having received at least one mammogram (Lerman, Kash & Stefanek 1994).

Attenders at genetics clinics were assessed before and after receiving genetic counselling (Watson, Lloyd, Davidson, et al 1999). All 282 women had a family history of breast cancer. Prior to counselling the participants had a poor knowledge of their numerical lifetime risk, with their perceived risk having no correlation with their assessed risk. When perceived risk was assessed using quantifiers (e.g. higher, lower than the average woman etc.) there was an association between this and their objective risk. Genetic counselling improved women's accuracy, however just over 27% continued to over-estimate their risk.

In a comparative study of women who all had a family history of cancer, but were from different groups (White, African/American, Ashkenazi Jewish and lesbian/bisexual), there were large discrepancies between actual and perceived risk. All sub-groups overestimated their risks, with African Americans on average overestimating their risk by the greatest proportion, and lesbians/ bisexuals overestimating it by the least (Durfy, Bowen, McTiernan, et al 1999).

Most women in these studies have an unrealistically pessimistic view of their risk of developing breast/ovarian cancer, believing that they have a risk far higher than that calculated clinically. Evidence for unrealistic pessimism with regard to cancer risk has been documented before specifically for cancer risk (Wilcox & Stefanick 1999), and may in part be due to peoples' misunderstanding of risk assessments.

2.4.2 Attitudes and Motivations for Genetic Testing for Breast / Ovarian Cancer Susceptibility

The issues facing people at a high-risk of breast cancer are likely to be different from those which people at high risk of HD consider to be important. A lesser emphasis is likely to be placed on the importance of the finding in childbearing decisions, as treatment is available, so not having affected children may be less important. A highly motivating factor may be the desire to make more informed decisions about screening and preventative options. Screening is recommended for women at risk from an earlier age than that recommended for the general population (Burke, Daly et al 1997a). Screening itself is not without risks - the X-rays used in mammography (despite using minimal exposure levels) may have a damaging effect - cumulative over many more years than in the national screening programme (Jatoi 1999). Preventative options include mastectomy (Hartman, Schaid, Woods et al 1999) and oophrectomy (removal of the ovaries)(Struewing, Watson, Easton et al 1995a) - which carry surgical risks, and may have a negative effect on the woman's self-esteem. Tamoxifen may have a preventative effect, although it can have unwanted side effects and its efficacy in women at high risk is still not clear (Powels, Eeles, Ashley et al 1998).

The reasons for wanting to undergo genetic testing to determine risk of breast / ovarian cancer have been explored in a number of papers; nine using quantitative methods are summarised below (Table 2.4). These papers have adopted various methods, concerning recruitment of participants, format of questions, and proportions of high-risk individuals. The implications of these methods will be discussed below.

Table 2.4 Reasons given for and against genetic testing for breast cancer.

Paper	Country	Participants (numbers, risk level, age)	Reason for testing	Reason against testing	Comments
Lynch et al 1993	USA	4 men, 28 women	Early detection (71% women under 45). Learn children's risk(100% men; 75% women 45+) Decide re prophylactic mastectomy (53%) Decide re prophylactic oophrectomy(71%)		% responding yes
Lerman, Daly et al 1994	USA	121 female FDRs of ovarian cancer patients. 87% only one affected FDR. 70% under 50yrs.	Learn children's risk (76%) Increase use of screening(71%) Be reassured (70%) Take better care of self (52%) Childbearing decisions (48%).		Likert response categories (% stating factor very important). Multiple responses.
Lerman et al 1995	USA	105 female FDRs of breast cancer patients. 90% only one FDR. 50%+ under 40yrs old	Learn children's risk (90%) Take better care of self (88%) Increasing screening (85%) Planning for the future (62%) Childbearing decisions (42%)	Test accuracy (25%) Insurance concerns (15%) Emotional reactions (15%) Reactions of partners and family (8%)	Likert response categories (% agreeing or strongly agreeing). Multiple responses.
Struewing, Lerman, Kase et al 1995b	USA	91 women (19 families). All from high risk families, 11 had cancer. 64.8% under 50.	Learn of children's risk (~84%) Increase screening (~84%) Take better care (~ 75%) Plan for the future (~65%) Just want to know (~70%) Family planning (~40%)	Insurance concerns (13%)	Multiple responses possible. Numbers not exact, derived from graph.
		49 men from same families as above. 67.3% under 50.	Learn of children's risk (~90%) Plan for the future (~50%) Just want to know (~45%) Family planning (~35%)		Multiple responses possible. Numbers not exact, derived from graph.
Lerman, Narod & Schulman et al 1996	USA	129 women; 66 men from 13 high risk families on high risk registry	Learn of children's risk (78%) Decide about screening (70%) Plan for the future (67%) Make surgery decisions (63%) Be reassured (61%) Family planning (41%)	May lose insurance (16%) Effect on family (15%) Don't believe can prevent cancer (9%) Not handle emotionally (7%) Test result not accurate (7%) Don't trust modern medicine (4%)	Benefits and risks of testing - multiple responses possible. % responding very important.

Hughes, Gomez-Caminero, Benkendorf et al 1997	USA	310 white women. Majority had just 1 affected relative. 74% 50yrs or under.	Prevent cancer (79%) Increase screening (~77%) Reduce uncertainty (~65%) Reassurance (~58%) Decide about surgery (~45%) Learn children's risk (~50%) Childbearing decisions (~10%)	Effect on family (13%) Emotional reactions (~4%) Affect insurance (~19%) Concern about confidentiality (~13%) Distrust modern medicine (~3%)	Multiple responses possible. Most numbers not exact, derived from graph.
		97 African American women. Majority had just 1 affected relative. 75% were 50 or under.	Prevent cancer (90%) Increase screening (~88%) Reduce uncertainty (~80%) Reassurance (~75%) Decide about surgery(~65%) Learn children's risk (~54%) Childbearing decisions (~22%)	Effect on family (23%) Emotional reactions (~18%) Affect insurance (~13%) Concern about confidentiality (~7%) Distrust modern medicine (~12%)	Multiple responses possible. Most numbers not exact, derived from graph.
Meiser Butow, Barratt et al 2000	Australia	461 women. 66% had 3 or more affected relatives. 82% under 50 yrs.	Reducing risk cancer (87%) Learn of children's risk (77%)* Certain about own risk (> 75%) Help research (~ 60%) Plan for the future (58%) Childbearing decisions (14%)	Effects on family members (16%) Concern cancer not prevented (10%) Insurance concerns (15%)	Multiple responses. % viewing factor as very important. *in women who had children - higher if daughters not sons.
Phillips, Warner, Meschino et al 2000	Canada	134 Ashkenazi Jewish women, 59% more than one affected FDR, 41% no affected FDRs. Median age-59 yrs	Benefit family members (96%) Contribute to research (96%) Curiosity (92%) Relief if not carrier (74%) Just need to know (71%) More screening (28% - 52%)	Insurance discrimination (28%) Concern about confidentiality (24%) Concern about test accuracy (30%) Impact on family members(26%) Guilt if positive (12%)	Multiple responses possible. Screening, confidentiality and insurance issues raised by younger women.
Metcalfe, Liede, Hoodfar et al 2000	Canada	79 female carriers of BRCA genes. Mean age 50.4 years	Learn personal risk (49.4) (34.2% as 1st reason) Learn children's risk (48.1) (16.5% as 1st reason) Learn family's risk (46.8) (11.4% as 1st reason) For screening advice (25.3) (3.8% as 1st reason) To support research(27.8)(8.9% as 1st reason) Doctor's recommendation(6.3)(2.5% as 1st reason) Family recommendation(11.4)(3.8% as 1st reason)		Three reasons given retrospectively (mean 17.3 months before study)

The proportion of people in each study citing areas as important again varies by method. Those in which free responses are required generate lower percentages agreeing with each category, than those giving prompted reasons do. Despite these methodological inconsistencies new themes emerged about the perception of reasons for and against testing. In the study including both men and women, (Struewing et al 1995b) a clear gender division was demonstrated on matters concerning desire for certainty and for knowledge to plan for the future, with women citing these reasons as more important than men did. In addition women regarded their own health and screening as a major reason for testing, whereas men, who are unlikely to develop breast cancer, did not report any personal health benefits.

The experiences of men in families at risk of breast cancer are likely to be very different from those of women in such families. Although some men do develop breast cancer, this is very rare. Men do have concerns that may often be overshadowed by those of their female relatives. A qualitative study of men from breast cancer families (McAllister, Evans, Ormiston & Daly 1998) found that men were aware that breast cancer in their families may be inherited, some were themselves concerned about developing breast or another cancer, and they were also concerned about their daughter's risk. Men however tended to adopt an avoidance strategy, which may explain why they are reluctant to undergo genetic testing, and why their daughters are also less likely to be tested. Men reported that they are often not included in family conversations, which take place among the female family members. The reasons suggested for this are male avoidance of these conversations, embarrassment in both men and women, and the stereotype that women are more interested in such discussions.

The issue of ethnicity has also been raised in relation to reasons for testing. A comparison of reasons given by Caucasian and African American women (Hughes et al 1997) showed that reasons for testing were similar for both groups, although more African American women endorsed most items as important. African American women expressed significantly more positive attitudes towards genetic testing (at $p<0.01$ level) than did Caucasian women. Although this study highlights the importance of including ethnicity in studies, many studies have not recruited enough

people from ethnic minorities for meaningful comparisons. People who had a lower level of education or who had not experienced any genetic testing before (e.g during pregnancy) also expressed much higher pros scores than other people. People who were not married or who had low income levels indicated that they saw more disadvantages to testing than other groups, particularly those with no health insurance reported a high level of disadvantages or costs of testing.

A qualitative study (Bernhardt, Geller, Strauss et al 1997) found women in focus groups identified benefits of testing including gaining information leading to risk reduction, relief from uncertainty, more responsible parenting and assisting in research. There are no data about the proportion of women regarding each benefit as important. Risks of testing were cited as the discomfort and cost of the test itself, the anxiety and a false sense of security a negative result might bring. Insurance discrimination was rarely mentioned, in comparison to quantitative studies that often prompt for responses to categories. This indicates this may not be a salient reason for not having genetic testing.

Tessaro, Borstelmann, Regan et al (1997) also used focus groups, with women who had had breast cancer, and women who were in a high risk group. The major advantage perceived by the women was the increased information that a genetic test would bring. This, it was felt, would decrease uncertainty and assist with decisions concerning screening and treatment options. The women voiced concerns that family members might engage in less healthy behaviours if the threat of cancer was taken away, also they were concerned about the stress which might be associated with cancer. For many women, the lack of proven options to prevent cancer was seen as frustrating, and meant that many women thought they would rather not know if they could not stop the cancer.

For breast cancer, clearly one of the most important factors is the desire to take action so that the risk may be minimised through screening and healthy lifestyle - the participants expect that the news will motivate a lifestyle change which they otherwise might not make. In most studies the desire to know the risk to their children was as important, if not more important than for screening decisions, and for the men in Struewing's study (1995b), this is the main motivating factor. This desire to know

children's risk is however not translated into a desire for the knowledge to affect their childbearing plans. This may be because breast and ovarian cancer is preventable and treatable, there is optimism that a cure may be found for their children. The age of onset and the severity of breast cancer may also mean that this is not as important as it is for people at risk of HD. People at risk of HD usually develop symptoms in their late thirties and their forties, these people are therefore not usually included in the studies of HD, so more respondents are younger in these samples, and childbearing is more salient. For breast/ ovarian cancer it may not be clear so early in life whether the person has inherited the mutated gene, so many people surveyed are older, and have passed their childbearing years, but could still be gene carriers.

Another key motivation is again the desire to know. This is expressed either as a desire to reduce uncertainty, or as a wish to plan for the future, or to gain reassurance. There was a gender division over the need for certainty, but it is not possible to know whether this reflects different dispositions towards uncertainty between genders, or the different risk factors for men. In the assessment of disorders such as colon cancer, it should be possible to separate these factors.

2.4.3 Anticipated Response Towards Genetic Testing for Breast / Ovarian Cancer Susceptibility

The effect of a positive (high risk) or negative (low risk) test result for people with a family history of breast or ovarian cancer, is likely to be different from the effect of a positive result given to a person at risk of HD. The options for prevention via chemoprevention (such as Tamoxifen), prophylactic surgery and early detection of pre-malignant lesions or cancer, mean that a positive result will provide important information for treatment, and might delay or eliminate the onset of cancer. This hope for the future means that anticipated reactions towards a positive or negative result may be less than those reported by people at risk of HD.

Anticipated responses to receiving both positive and negative genetic test results have been explored in both men and women who may carry genetic mutations which predispose to breast/ ovarian cancer (Table 2.5).

Table 2.5 Anticipated responses to genetic test results for breast cancer

Paper	Country	Participants (numbers, risk level, age)	Anticipated Response - Positive result	Anticipated response - negative result	Comments
Lerman et al 1994	USA	121 female FDRs of ovarian cancer patients. 87% only one affected FDR. 70% under 50yrs.	Become depressed (80%) Become anxious (77%) Feel more in control (68%) Impair quality of life (32%) Consider suicide (1% n=1)	Feel less anxious (83%) Improve quality of life (83%) Feel more in control (82%) Feel less depressed (68%). Still worry (42%) Feel guilty (25%)	
Lerman et al 1995	USA	105 female FDRs of breast cancer patients. 90% only one FDR, age- over half under 40.	Become anxious (83%) Become depressed (80%) Feel more in control (80%) Poorer quality of life (46%) Affect marriage (16%) Consider suicide (2% n= 2)	Feel less anxious (76%) Better quality of life (76%) Feel less depressed (64%) Still worry (72%) Feel guilty (32%) Improve marriage (52%)	Multiple responses on Likert scale
Struewing et al 1995b	USA	91 women (19 families). All from high risk families, 11 had cancer. 64.8% under 50.	Feel anxious (72.5%) Feel depressed (46.2%) Negative mood (45.6%) Feel more in control (73.3%) Feel better about decisions (72.9%) More frequent screening (84.4%) Want an oophrectomy (73.5%) Have fewer children (~36%)	Decrease in anxiety (79.3%) Decrease in depression (57.1%) Positive mood (70.1%) Improve marriage (51%) More frequent screening (69%) Want an oophrectomy (21%). Want more children(53%)	Comparative study of men and women from the same high risk families
		49 men from same families as above. 67.3% under 50.	Feel anxious (32.7%) Feel depressed (16.7%) Negative mood (20.4%) Less children (~36%)	Decrease in anxiety (47.5%) Decrease in depression (42.9%) Positive mood (36.6%) Improve marriage (18.5%) Want more children(26%)	

Durfy et al 1999	USA	307 white Americans; 46% had two affected FDRs Mean age 42.7	Increase breast self exam (96%) More clinical examinations(86%) More mammographies (73%) Consider prophylactic surgery (11%) Change childbearing decisions(12%)		Comparative study of four risk groups. All participants were asked every question, proportion reporting probably or definitely intending to carry out action is reported
		87 lesbian/ bisexual women, 41% had two affected FDRs. Mean age 40	Increase breast self exam(93%) More clinical examinations(86%) More mammographies (80%) Consider prophylactic surgery (11%) Change childbearing decisions(15%)		
		31 African Americans 32% had two affected FDRs. Mean age 42.9	Increase breast self exam (100%) More clinical examinations(100%) More mammographies (94%) Consider prophylactic surgery(6%) Change childbearing decisions(13%)		
		113 Ashkenazi Jews, 44% had two affected FDRs. Mean age 46.8	Increase breast self exam (98%) More clinical examinations (86%) More mammographies (70%) Consider prophylactic surgery(18%) Change childbearing decisions(13%)		

Most people anticipate that receiving a positive test result will lead to some negative emotional responses (anxiety, depression), but also empowerment (feeling more in control, seeking more screening). Some respondents anticipated that they may change their childbearing decisions, but few in comparison to the studies of HD. Most people anticipated that a negative test would improve their psychological well-being, but some people thought they would still worry about developing cancer, and may feel guilty.

Women tended to anticipate more reactions than men did, which is likely to reflect the greater relevance of the result to them (Struewing et al 1995b). In addition to the greater influence of both positive and negative test results on mood, women also anticipate that the result will have a greater influence on their childbearing decisions, even though they have a similar risk of parenting affected daughters. It is possible that the differences between men and women are not just due to their differential risks of developing breast/ ovarian cancer, but also due to different emotional awareness or patterns of responding between the genders. To investigate this possibility, a disease such as colon cancer is a more appropriate study disease as it affects both men and women, so remaining differences will be due to gender effects alone.

There were differences in anticipated emotional consequences for women whose relatives had breast cancer compared with those who had ovarian cancer when using the same method (Lerman et al 1995 c.f. Lerman et al 1994). Women with a history of breast cancer assessed a positive test to have more negative impact, and a negative test to have less positive emotional benefits than the women at risk of ovarian cancer.

Despite the reduced severity of breast and ovarian cancer and the possibility of prevention and cure, the anticipated reactions are similar to those anticipated towards a positive result on a test for HD. These studies, however, do not report the anticipated severity of reaction to the test result, only the number of people reporting that they would experience those reactions to some extent. The anticipation that one will experience an emotion does not predict how severe the emotional reaction will be. People at risk of HD may anticipate a more severe depression than those at risk of breast/ovarian cancer, even though the proportion who expect to experience depression are the same.

2.4.4 Intention, Uptake and Correlates of Intention and Uptake of Genetic Testing for Breast / Ovarian Cancer Susceptibility

The expressed level of intent to have a test for hereditary breast and ovarian cancer is even higher than for HD testing, and, although there have been fewer studies, initial indications are that uptake of genetic tests are higher, although not as high as intention to have a test. Studies of intention and uptake are outlined in the table below with reported significant univariate correlates and factors found to be significantly associated with intent / uptake in regression analyses (indicated by *) (Table 2.6).

Table 2.6 Intent and uptake of genetic testing for breast / ovarian cancer.

Paper	Country	Sample (source, response rate)	Intent to have test	Univariate correlates of high intent
Lerman et al 1994	USA	121 women FDRs of ovarian cancer patients- 87% had only one affected FDR Telephone interview	75% yes definitely 20% yes probably 2% definitely not	More education Younger age Higher perceived risk of cancer More cancer worry Mood disturbance Perceived more likely to carry mutated gene*
Lerman et al 1995	USA	105 women FDRs of breast cancer patients 90% had only one affected FDR	91% intend to have test 5% undecided 4% intend not to have test	
Struewing et al 1995b	USA	91 women at high breast cancer risk	86% yes definitely 14% yes probably	Perceived more likely to carry mutated gene Female
		49 men from families at high breast cancer risk	65% yes definitely 21% yes probably 4% undecided 10% not want test	
Durfy et al 1999	USA	White Americans; 46% two affected FDRs	89.9% probably/ definitely yes	Higher perceived risk of breast cancer*
		Lesbian/ bisexual, 41% two affected FDRs	88.1% probably/ definitely yes	Higher cancer worry* Low perceived stigma of positive result*
		African American, 32% two affected FDRs	87.1% probably/ definitely yes	High perceived access to testing*
		Ashkenazi Jews, 44% two affected FDRs	82.9% probably/ definitely yes	
Meiser, Butow, Barratt et al 2000a	Australia	461 women from family cancer & outreach clinics (89% response rate)	92% probably or definitely intend to have test	Perceive as likely to carry mutated gene*

Geller, Doksum, Bernhardt, & Metz 1999	USA	70% of original sample declined counselling.	83% (33) of those counselled intended to ask FDR to have test, 50% tested.	Higher if just recruited for testing protocol via clinic than via cancer registry
Cappelli, Surh, Humphreys et al 1999	Canada	Affected women and women from general population	60% wanted genetic test 72% in those who had breast cancer - 49% had counselling	Had breast cancer High benefits Few perceived costs High concern for relatives
Tambor, Rimer & Strigo 1997.	USA	General population telephone survey, 473 women aged over 50	69% interested in having test 11% unsure 20% not want test	Being white Under 60 Believe family benefits if have mammogram Mammogram gave control over health
Uptake of testing				**Correlates of uptake**
Valdimarsdottir, Bovbjerg, Brown, et al 1999		105 women attended for counselling	55% gave blood sample with the intent of learning result	Being older Objective risk* Perceived risk* Moderate cancer distress
Wagner, Moslinger, Langbauer et al 2000	Austria	138 family members from 35 families	93 (67%) requested the test results	
Lynch et al 1993	USA	One extended family	71% women; 15% men wanted results	
Lerman Narod et al 1996	USA	192 from 13 families on registry (69% response rate)	60% received test results, 40% declined	Being female, Higher education Had health insurance
Lerman, Schwartz, Lin et al 1997	USA	149 high risk men and women from 11 families. (76% response rate)	66% of women received results 44% men	Being female* Higher objective risk (including affected individuals)* Being younger* Moderate/high cancer - specific distress*
Lerman, Hughes, Benkendorf, et al 1999.	USA	228 Caucasian women 70 African American women all had family history of breast cancer	52% of Caucasian women gave a blood sample, 29% of African American women did.	White rather than African American Being married High income level High objective risk Self-referred rather than referred via FDR Being older (African Americans)
Meijers-Heijboor, Verhoog, Brekelmans et al 2000	Netherlands	682 unaffected people from 53 families at high risk of carrying a mutation	48% (198) women requested a test 22% (59) men requested testing	Being female Amongst women:- Being younger Having children At high risk

In addition to the quantitative assessment of intention to have a genetic test, one study has observed the changes in intention during the course of the exploration of genetic testing in focus groups using a psycho-educational approach (Bernhardt et al 1997). Overall levels of interest were observed to be high, however this decreased, particularly in high SES women as more was disclosed about the limitations of the test. Interest declined particularly when they were told that testing would not generate definitive prevention or curative options and that it is only appropriate for women with a strong family history.

Initial indications show that intent to have a genetic test for breast cancer is higher than for HD. This may be because of the possibilities for prevention and cure for people at risk of breast/ ovarian cancer. Psychological correlates of intention to have a test include higher perceived risk, higher perceived likelihood of being a carrier and higher cancer worry. In addition high perceived benefits and low perceived costs have also been found to correlate highly with intent in (Cappelli et al 1999). The lack of a clear picture of the psychological correlates of intent was a motivation for this thesis, and the associated work examining interest in genetic testing for breast cancer.

Three of the six studies reporting on the association between intent and objective risk found that there was no relationship, whereas the others found that people who were more at risk had higher levels of intention. The demographic correlates of intent have not been conclusive, with some studies finding higher levels of intention in people with more education, and others finding no effect or lower intention. The influence of age is also contentious, with studies finding different effects of age on intention. Where there is an effect often younger women are more interested, however the opposite result was found in one study (Valdimarsdottir et al 1999). Ethnic group has also been identified as being associated with intention in American studies, with white women being more likely to intend to have a test than women from other ethnic groups are.

It is still early to determine clear uptake levels for testing for breast and ovarian cancer in the at risk population, although initial reports put the figure higher than for HD, but lower than reports of intention. In the Netherlands, about 15% of people at risk of HD have undergone testing, whereas more than twice that proportion (33%) have

undergone testing from families at risk of breast and ovarian cancer (DudokdeWit et al 1997).

The main reason for the higher intent in breast cancer testing could be the possibility of treatment and prevention, especially if the individual undergoes regular screening. Another reason may be self-selection in referrals to genetics services. HD is a discrete illness, and relatives are likely to be informed of the genetic nature of the disorder when a family member becomes ill. They may also receive follow-up support from the neurological services, including genetic advice, even after the person has died. Hereditary breast/ ovarian cancer is, however more difficult to distinguish from sporadic cancer, as the clinical presentation is similar, so might be regarded as sporadic unless the family history is known. Family members might only become aware of their risk if they seek out this information, this group may then be more motivated to act on the information which they have sought.

The higher levels of intent have ramifications for support services, not just because the numbers undergoing testing increase, but additionally a greater proportion may have difficulties adjusting to a bad result. The small numbers undergoing testing for HD may reflect self-selection, only those who believe they are able to cope with a bad result request testing (Codori et al 1994). In comparison those requesting testing for breast and ovarian cancer may be more heterogeneous, and may experience more diverse reactions to a bad test result (Lerman et al 1994).

Variables associated with uptake are similar to those reported as correlates of intention. The main findings have been of increased uptake in women who are at high objective risk of developing breast/ ovarian cancer. Younger women again have been more likely to have a test, particularly if they have children, are white and well educated. There needs to be more studies of why these groups are particularly interested, and whether other groups are well-informed about the testing options available, as education may reduce these apparent inequalities in desire for testing (Lerman et al 1999).

Although most studies have emerged with similar results, within studies a number of differences have been found between groups of people. Some of these differences are

now explored. The main difference, although rarely studied is the difference between men and women in their attitudes, intent and uptake.

In the only study of intent (Struewing et al 1995b) to include men as well as women, there were clear gender differences, with women holding higher intentions to have a test than male relatives. In studies of uptake, again there was a much higher level of test acceptance in women compared with men (Lynch et al 1993; Lerman et al 1997; Meijers-Heijboor et al 2000). This may be explained in part by the lack of expression of a mutated gene in most men, so they may see genetic testing as irrelevant for them. This difference may also be due to gender differences, however as discussed earlier this can not be assessed in the case of breast/ovarian cancer due to the differential effect of the gene in men, which is likely to have a large impact on intent and uptake.

Although there may be less immediate clinical gains, male relatives should be made aware that they may also be at risk of certain cancers, and that their daughters could inherit a gene from them. Without testing potential male carriers, the risk to their daughters could be hidden, so they do not receive appropriate information and screening. Gender factors may not just be a factor in the generation being tested, women who only have sons are less likely to identify genetic testing as advantageous because they will learn of their children's risk (Meiser, Butow, Barratt et al 2000a). Families should be informed of the need to inform men that their daughters may be affected, as well as the moderately increased personal risk that a male BRCA1 or BRCA2 carrier is exposed to. The differential interest of men and women in genetic screening needs to be explored in a disease model such as colon cancer, where the risks are similar, or additionally in a disease which is only expressed in males, such as prostate or testicular cancer.

Other studies have concentrated on differences within populations of women at high risk. The main difference explored has been that of ethnic difference. In studies of intention, most studies have either not reported on ethnic differences, or have contained too few ethnic minorities for meaningful comparisons. One study that did explore the issue of ethnicity found that white women were more likely to intend to undergo a genetic test than black women were (Tambor et al 1999). Another study of

ethnic groups found that although white women were more likely to want a test than African Americans, and both groups were more likely to want a test than Ashkenazi Jews, these differences were not significant (Durfy et al 1999). When these women were asked, however whether they would still want the test if they had to pay for it themselves, the levels of intent fell for all women, but particularly for African Americans. The financial implications of not just the test, but also for insurance may have more of an impact on this group's intentions. The African American group did not contain as many women in the lowest income bracket as some groups, however there was also a smaller proportion of women in the highest income bracket - it may be these middle income women who fear they have the most to lose from genetic testing. Few studies have evaluated uptake of genetic testing for breast cancer, one which has found that white women are more likely to undergo genetic testing (in a research setting) than African American women (Lerman, Hughes, Benkendorf et al 1999). This indicates that even when the cost of the genetic test is not a factor, African American women are still less inclined to have a genetic test for breast cancer.

A further difference that has emerged both within and between studies, is the influence of different recruitment sources and methods. One approach to recruiting participants has been through the relatives of people who are being treated for cancer. This method has a number of advantages and disadvantages. The advantages of this approach are that the researchers have definite evidence of the individual's family history, without having to seek out old patient notes to verify the reported history. In conjunction with an oncology unit, the recruitment of participants is fairly straightforward, and large numbers can be recruited in this way for each new study. The difficulty with this approach is that participants recruited in this way typically report higher levels of cancer related distress, however this may be due to the current illness of their relative. The average levels of cancer distress experienced by at risk people between episodes of family illness may be much lower than at this stressful time. Families at high risk are likely to go through a cycle of illness as each successive generation is affected, however in between these episodes, people at high risk of cancer may not focus so much on this disease.

Studies (Lerman et al 1994; Lerman et al 1995) recruiting in this way also recruit relatively low numbers of people who are very likely to be gene carriers, many only have one affected FDR, and often FDRs are post menopausal, and so their cancer is likely to be sporadic. The other problem with this approach is that the participants are referred by affected relatives, who may selectively give researchers names of people who they think will be more willing to take part, and more in favour of genetic testing. In a related theme, those people who take part may feel more in debt to the researchers as they are perceived as being associated with their relative's care, they may feel more obliged to give researchers the answers which they are wanting to hear.

Another approach to recruiting involves recruiting via the media (e.g. Durfy et al 1999) and public notices. This approach is likely to contact people who have not previously been in contact with the genetics services, and who are not as likely to currently have affected relatives. The views of these people are less likely to be affected by prior medical opinions. The women who respond to such publicity are probably more motivated, and may be more interested in genetic testing than those who see the publicity but do not respond. There is validity in the between group comparisons as they were recruited in a similar way, however caution must be exercised in generalising these findings to the wider population.

The other main route of recruiting participants has been via established clinics and family registries (Meiser, Butow, Barratt et al 2000). People recruited in this way are either new patients or have been in contact with health services for a period of time before the study begins. For the new patients attending clinics similar biases as noted above may apply. New patients may be attending because they are interested in having a genetic test or because a relative has recently been found to be affected by cancer. There is, however, likely to be a wider range of intent compared with those recruited via the media. Existing patients may have originally attended for a reason other than to have a genetic test, often for access to screening programmes. For some of these patients genetic testing may be seen as a welcome addition, removing the need for additional screening, for others it may be a threat to their continued clinical screening regime.

These differences in recruitment are likely to account for some of the differences in the observed attitudes and levels of intent and uptake across studies. Most studies recruit via one source, but this makes it difficult to make direct comparisons. One study has compared intent by recruitment source (Geller, Doksum, Bernhardt et al 1999), and found that women attending clinics as new patients who had at least one affected relative held higher intent to have a genetic test than FDRs contacted via cancer patients.

2.4.5 Impact of Genetic Testing for Breast / Ovarian Cancer Susceptibility

Testing for breast and ovarian cancer has only recently become available, so it is still not clear how people will react to this information. Most studies have examined the impact of a test result, taking the pre-test 'baseline' measure when an individual is attending for genetic counselling. This may be a time when the candidates for testing are anxious about many issues concerning the test and the possible impact. In a Dutch study, this pre-result time has been examined (Lodder, Frets, Trijsburg et al 1999) in 85 asymptomatic women and their partners who were waiting for test results. Levels of anxiety and depression were found to be similar to those reported in the general population. The majority of people did not exhibit high levels of general or cancer related distress, however cancer related distress was high in 25% of women and 10% of their partners. Increases in distress were reported by women who anticipated more problems if they tested positive, thought that they might have a mastectomy, suppressed their emotions, were under 40, and were more aware of the consequences of hereditary breast and ovarian cancer. There was no effect of the amount of time a person has been aware of their risk status. This overall low level of distress is encouraging for the likely wider use of genetic testing, and may reflect the use of strategies by women having testing to minimise the impact.

Immediately following receiving a test result, over a third of people who tested positive appeared (to the genetic counsellor/ medic) to be sad or crying (36%), but slightly more than a quarter did not seem to be surprised by the result (27%); a fifth showed no visible reaction (19%). In response to a negative test result most people showed signs

of relief and happiness (80%), some were surprised (8%), but few reported feelings of survival guilt (4%) (Lynch et al 1997).

In the immediate short term (1-2 weeks) after receiving a test result, carriers reported higher levels of test-related distress than non-carriers. Levels of general distress declined after testing from the pre-test level but this was still higher in those who received a positive test result than those receiving negative results. The highest level of test related distress was reported by women who had not had any prophylactic surgery (Croyle, Smith, Botkin et al 1997).

Often undergoing a genetic test is an event that is undertaken by many individuals within the same family. The result of one family member may therefore impact on other family members. In a study of 87 men and 125 women (Smith, West, Croyle & Botkin 1999), there was a higher degree of test related distress upon learning of carrier status in women who were found to be carriers, than that reported by cancer patients 10 weeks after being diagnosed. The only women for whom this was not true were women whose siblings had received mixed results; those whose siblings had not yet been tested, or who had all tested negative or positive reported high levels of distress. Amongst the men who were found to be carriers the only group which reported high levels of distress were those whose siblings had not been tested. In both men and women who were found not to be carriers, levels of distress were lower, except for people whose siblings were all carriers.

There were small sample sizes in some sub-groups (5-37 individuals), so these findings may need to be replicated in a larger sample size. All the individuals are members of one extended family with more than 750 living adult members. This means that there is likely to be less variance in responding within the family than if unrelated individuals were contacted. This is because many of the individuals knew each other and shared common environmental situations and had other shared genetic factors that may have affected emotional responses. This study demonstrated that there is an effect on a family member when another family member receives a test result. However as all participants are from the same family this supposed interaction will have biased the likelihood of detecting an effect, as one individual's positive result may have had a

personal impact on more than one person in the study (i.e. not just siblings but also cousins). This study needs to be replicated in unrelated people who do not know each other, or an approach should be employed which is more sensitive and adaptive to the vast complexity of the issue (e.g. through qualitative research).

In a telephone interview 3 to 6 weeks after receipt of test results (Lynch et al 1993), most women receiving a positive test result reported some psychological distress - including persistent worry, depression, confusion and sleep disturbance. All these people had, however, felt able to continue with their normal activities and had not needed medical advice or medication. These results however, are consistent with those reported by women at risk of carrying a gene who do not know their genetic status (Lerman, Daly, Sands et al 1993). Half of non-carriers still said that they worried about whether they carried the gene. When asked if they would undergo the procedure again, given the opportunity, all said that they would.

One month and six months after receiving a test result, the impact of the test is still apparent (Lerman, Hughes, Lemon et al 1998). There were no significant differences between the groups at baseline (before receiving test results), however at the one month follow-up more carriers and decliners were depressed (14% and 19% respectively) than were non-carriers (8% depressed). The proportion of people who were depressed after testing was related to their baseline levels of stress. People who declined the test and had a high level of baseline stress had higher levels of depression one month later (26% to 47%). People who had a high level of baseline stress but tested negative had lower levels of depression (41% to 11%), there was no significant change in people who were carriers (20% to 23%). People who had a low level of baseline stress showed no difference in depression by result group. This pattern was replicated at the six-month follow-up. This study indicates that sometimes not knowing is worse than actually knowing the result of a test, as once the test result is known, the person can begin to develop coping strategies to deal with the future. This also indicates that although a person indicating a high level of baseline stress may be considered to be at risk of poor adaptation to a positive test result, not having a test result may be more detrimental.

With HD the important outcomes are the psychological implications. In breast / ovarian cancer, whilst these are still important, there are also screening and other clinical outcomes to be studied, to determine whether testing has a clinical impact on risk of actually developing cancer. In a study of Canadian women (Metcalfe et al 2000) a mean of 17.4 months after learning they were carriers, 58% of women reported that their screening practices had changed, although baseline levels were not reported on. Although many women had considered prophylactic mastectomy (58%), only 23% of those who had not had a prophylactic mastectomy prior to the test result disclosure underwent the procedure subsequently.

In an assessment a year after learning of genetic risk (Lerman, Hughes, Croyle et al 2000), few carriers had had mastectomies (3%). Although the rates of adherence to mammography screening were higher in carriers (68%) than non carriers (44%), a large number of carriers were not attending for recommended screening. The main reason for the significant difference between carriers and non carriers was that non carriers were likely to reduce their screening after testing, rather than carriers increasing their screening. Of the carriers eligible for oophrectomies 5% underwent the procedure, of the remainder only 21% reported using CA125 screening, and 15% had transvaginal ultrasound, both are recommended for carriers. The psychological impact of testing may be minimal, but in this study the impact on health behaviour was also minimal. For full benefit to be gained from genetic testing, not only must it address psychological needs, but also reduce cancer risk. There is a strong need to provide a clear follow-up regime for test participants to adhere to, with support services to encourage screening utilisation, to maximise the benefit of genetic testing. This will involve investigation of why screening adherence is so poor, and the development of interventions to increase screening tailored specifically to those with a known genetic risk of cancer.

The initial reports have demonstrated that despite the greater proportion of people undergoing breast/ ovarian cancer genetic testing (compared with HD), the likely increased heterogeneity of the population does not appear to lead to more people experiencing adverse effects. This is important as it was not clear if the low levels of emotional distress in people found to be carriers of HD could have been due to self-

selection into the programme of only those who were particularly emotionally resilient. The results do indicate that pre-testing psychological well-being is associated with post-testing levels, so some people may need more support than others if they were more anxious or depressed prior to undergoing testing.

2.5 Colon Cancer

There has been less research into interest in pre-symptomatic genetic testing for colon cancer, particularly in high-risk populations. Research using participants with a family history has primarily recruited people from genetic counselling clinics or existing research groups. Other populations studied include current cancer patients (Vernon, Gritz, Petersen et al 1999) or lower risk individuals who have a relative who currently has cancer (Lerman, Marshall, Audrain & Gomez-Caminero 1996; Petersen, Larkin, Codori et al 1999: Glanz, Grove, Lerman et al 1999). A number of studies have also involved recruiting participants from the general population. These assessments are likely to be free of previous medical input, however testing on a population basis is a distant proposition. The relative merits of these different recruitment methods have already been discussed.

In the discussion of colon cancer most studies reported (unless otherwise stated) have examined HNPCC type colon cancer or people at lower risk. This distinction was made because testing for FAP is on a different basis, because as discussed in Chapter 1 in FAP the gene penetrance is almost 100% and clinical symptoms develop early. Other forms of colon cancer are more comparable to the prognosis of gene carriers for BRCA1 or BRCA2.

2.5.1 Perception of Risk of Colon Cancer

In a study of families with at least one FDR who has had colon cancer (Petersen et al 1999), most people believed that they had a higher (41.8%) or much higher (36.1%) chance of getting colon cancer compared with other people. This means that 22% believed their risk was either the same or lower than other people of their age, gender

and race. These proportions were higher in the sample contacted by telephone (initial non-responders N=156) than in the participants who responded to the initial mail survey (N=1, 217). When asked how likely they thought they were to get colon cancer 16.4% thought that they were unlikely to get it, and a further 10% had no opinion on the matter. Again those in the telephone survey (follow-up of non-responders) were less likely to think that they would develop colon cancer. These people are at a higher risk of developing colon cancer than the general population, so this optimism in some people may mean that they do not seek screening.

In another study, recruiting participants through FDRs and community groups, 56% of participants believed that their lifetime risk of developing colon cancer was greater than 50% (Kinney, Choi, DeVellis et al 2000). This is despite the highest risk in children of known carriers (before testing) being 50% for FAP, and 40% for HNPCC. In the same sample almost 32% of participants believed that their chances of carrying a gene which predisposes to colon cancer was over 50%. Unless both parents are gene carriers, there is only a 50% chance of inheriting a mutated gene from an affected parent. These figures highlight the gap in understanding between individuals at risk of colon cancer and the reality of their actual risk.

2.5.2 Attitudes and Motivations for Genetic Testing for Colon Cancer Susceptibility

As with breast/ ovarian cancer and HD, a number of studies have explored the reasons given for wanting to undergo genetic testing for colon cancer. Most of these have again used Likert scales with multiple response categories, reporting those people who agree or strongly agree with the reasons cited. An outline of these studies and their findings is given in Table 2.7.

Table 2.7 Reasons for and against genetic testing for colon cancer

Paper	Country	Participants (numbers, risk level, age)	Reason for testing/ Attitude towards testing	High distress	Low distress	Reason against testing	High distress	Low distress	Comments
Gritz, Vernon, Peterson et al 1999	USA	296 cancer patients 48% under 50, 56% male	Relief Learn child's risk Just want to know Concern for family Relatives reduce risk Relatives family planning	4.5 4.8 4.3 4.9 4.8 4.7	4.1* 4.7 3.9** 4.7 4.7 4.3**	Get too upset Not accurate Family's reactions Don't want to know Relatives worry more Affect relationships	1.6 1.9 1.8 1.6 1.9 1.5	1.2** 1.5* 1.5* 1.3* 1.6 1.2*	Mean response on Likert scale (1-5). Compared two clusters - those reporting high distress, and low distress. High distress rated advantages and disadvantages more highly.
Lynch, Watson, Shaw, et al 1999	USA	199 participants -7 families with gene mutations. Mean age 44yrs, 48% male.	For children or family (66%) Future health management (51%) Curiosity (24%) To know (10%) Decide about surgery (4%)						Respondents could give more than one answer
Lerman et al 1996	USA	45 FDRs of affected patients. Mean age 48yrs, 44% male	Screening decisions (89%) Learn children's risk (85%) Reassurance (84%) Marital decisions (33%) Childbearing decisions (50%)			Insurance concerns (60%) Concerns about accuracy (46%) Emotional reactions (~33%) Concerns about family reaction (32%)			Respondents could give more than one important reason.
Aktan-Collan, Mecklin, Jarvinen et al 2000b	Finland	299 test acceptors, 13 decliners from high risk families. Mean age 43 yrs, 45% male.	Reduce uncertainty (97%) Clarify risk for children(69%) Plan for the future(62%) Prevent disease (30%) Childbearing decisions (16%) Marital decisions (9%) Employment decisions (13%) Doctor recommendation (47%)			Test acceptors No reason (78%) Emotional reactions (12%) Decliners (n =13) No reason (n =7) Too old & no children (n=3) Not trust result (n=2) Current pregnancy (n=1)			Reasons were given retrospectively so likely to be biased by outcomes. Few decliners contacted.

In these studies, as in the studies of breast/ ovarian cancer, the main reasons for wanting a genetic test are to reduce uncertainty, to clarify their children's risk, and to decide upon possible screening options. Childbearing plans, although important to some respondents are not as important to the majority of those sampled. This is likely to be for the same reasons as those discussed in relation to breast cancer. Many people could see few reasons for refusing a test. The concerns expressed were with regard to insurance implications, test accuracy, family reactions and emotional responses to testing.

2.5.3 Anticipated Response towards Genetic Testing for Colon Cancer Susceptibility

In a general population sample recruited by telephone (Smith & Croyle 1995), people's main concern if they tested positive would be to reduce the risks of developing cancer (21.7%), to change their diet (13.6%) and find out about cures (10.6%). Many people would be concerned about their families and their children's health (12.1%). A significant proportion (24.8%) of participants expressed concerns about the worry or anxiety that they might feel, the uncertainty about it developing, and the prognosis. Very few expressed concerns about insurance in the face of a positive result, and no one considered the potential effect on their future employment prospects.

Among people with a family member currently affected by cancer (Lerman et al 1996), over half believed that they would become very depressed if they were found to carry a genetic mutation, and almost 60% thought that they would become very anxious. Most thought that a positive test would motivate them to increase screening (~98%), reduce their dietary fat (~90%), and take medication (~80%), and despite the anticipated negative effect on their psychological health, they would be prepared to make lifestyle changes. If they received a negative test result, most (over 75%) thought that it would improve their quality of life, that they would feel less anxious (over 50%) and less depressed (over 40%). Despite these gains, a large proportion (over 55%) thought that they would still worry, and 25% thought they would feel guilty. A negative test may reduce health behaviours, 40% thought that they would not reduce their fat intake if they tested negative, whereas most people would if they had the gene. Many who tested

negative thought that they would reduce their use of screening (40%), however it is not clear whether they were receiving any increased surveillance due to a family history, or whether this was an intended reduction from the USA general population screening guidelines. The former would be a desirable change in health behaviour, as intensive screening is not recommended for people at low risk due to the potential dangers associated with it, whereas the latter would be a less desirable change in health behaviours.

In colorectal cancer patients (Gritz et al 1999), participants who reported higher levels of distress were more worried about carrying a predisposing gene for HNPCC, and fewer thought that they would cope with problems regarding their test results. This indicates the importance of screening people prior to testing, and following them up, to ensure that people at risk of not coping with the results receive adequate support.

In a comparison of four adult onset disorders (HD, cerebral haemorrhage, breast and ovarian cancer and FAP), participants at risk of FAP reported less intrusive thoughts about their risk, and also less avoidant thoughts than the other groups did (DudokedeWit et al 1997). This is attributed to the possibility of treatment for FAP, and that many of the FAP individuals were asymptomatic beyond an age at which clinical indicators of FAP emerge, so they may be less concerned that they carry a mutation. People at risk of HNPCC are likely to be more concerned than these individuals, but still express a lower level of concern than those people anticipating a test for HD did.

The anticipated reactions were similar to those anticipated in response to breast/ ovarian cancer. If a test was positive, most people felt that this would motivate them to take preventative actions including having more screening, reducing fat intake and taking medication to prevent cancer. They did however anticipate some psychological disturbance, with increased levels of worry, depression and anxiety. In response to a negative test result most people believed that they would feel less anxious and depressed, however they may also reduce their adherence to health behaviours (e.g. low fat diet), which may leave them at risk of sporadic cancers.

2.5.4. Intent, Uptake and Correlates of Intention and Uptake of Genetic Testing for Colon Cancer Susceptibility

The research currently published indicates that interest in pre-symptomatic genetic testing for colorectal cancer is high. Uptake of testing for HNPCC mutations is difficult to gauge at the present time, as the techniques for testing are still being refined, and few studies have published reports on large populations (Table 2.8).

Table 2.8 Intent and uptake of genetic testing for colon cancer.

Paper	Country	Sample (source, response rate)	Intent to have test	Correlates of high intent
Lerman et al 1996	USA	45 FDRs cancer patients (72% response rate)	51% yes definitely 31% yes probably 7% uncertain 11% not want test	Being female African Americans Catholics Less education Unmarried
Kinney et al 2000	USA	95 FDRs cancer patients (90% response rate, but 42 self-referred)	84% would accept test	Self referred participants under 40 Believe few colon cancers genetic
Petersen et al 1999	USA	1373 at risk individuals (56.6% response rate)	77.4% very likely 15% somewhat likely	Being female* High cancer worry*
Glanz et al 1999	USA	40 Caucasian, 336 Japanese,50 Hawaiian FDRs of affected individuals. 160 families (77% response rate)	Yes definitely Caucasian - 35%; Hawaiian - 35%; Japanese - 24%	High cancer worry* High perceived risk* Older age* Caucasian/ Hawaiian * Family support*
Vernon et al 1999	USA	510 patients with colon cancer eligible for testing, 455 had blood drawn, 342 eligible for survey, 269 (79%) participated	90% of those giving blood intended to receive result, early drop out of 11% pre blood sample means actual intent 81%	Tests help relatives prevent cancer* Worried carry gene* Report more pros testing*
General Population studies of intent				
Smith & Croyle 1995	USA	383 randomly selected sample (344 no family history), response rate 81%	47% very interested 37% somewhat interested 16% not interested	Higher income* High perceived risk*
Croyle & Lerman 1993	USA	401 random sample. Response rate 76%	47% very interested 35% somewhat 16% not interested	High perceived risk* High cancer worry
Croyle, Dutson et al 1995	USA	271 female undergraduates	Mean interest in testing 77.4 (scale 0-100)	Having family history High cancer concern* High perceived risk Test reduces uncertainty*
Graham, Logan et al 1998	Canada	504 random sample, response rate 24%	40% very interested 41% somewhat interested (19% and 48% respectively when told 1% carry gene)	Having life insurance Nervousness Cancer worry* Belief genetic Affected relatives* High perceived risk*

Uptake of testing				Correlates of uptake
Codori, Petersen, Miglioretti et al 1999	USA	505 FDRs invited to participate in study (1.5% undelivered) - 118 kindreds (13 with known mutations)	46% interested (3% later withdrew) 52% not interested	Perceived ability to cope with result * High risk perception* High rate cancer thoughts* Previous clinical screening*
Aktan-Collan Mecklin, Jarvinen et al 2000b	Finland	446 members 36 families with known mutation (response rate 90%)	75% accept test (1 refuses result)	Having partner Being employed* More educated (Non-participants more likely to be male, live alone and refuse screening)
Lerman, Hughes, Trock et al 1999	USA	208 high risk family members	43% received result 57% declined	Interview participation More educated* Being married Not depressed* Prior study participation*

*significant in regression analyses

There has been little consensus about which factors are associated with intent to have a genetic test. The most consistent findings are an effect of gender, with an increased interest in females (Lerman et al 1996; Petersen et al 1999), however other studies have found no effect of gender (Glanz et al 1999). The relationship of other demographic variables with intent is inconclusive, and does not follow the same pattern as that found in examining breast and ovarian cancer. This might indicate that there is no single demographic profile of people interested in genetic testing, but rather it appeals to a wide range of individuals from differing backgrounds.

When examining psychological correlates of intent, high perceived risk of cancer was universally associated with higher intent to have a genetic test. Another consistent finding is a high level of cancer worry or cancer concern is associated with increased interest in having a genetic test (Vernon et al 1999; Glanz et al 1999; Petersen et al 1999). In two of these studies though the participants either had colon cancer themselves, or were contacted through a relative who had colon cancer at the time of the study. The levels of cancer worry may have been particularly high because a person in the family was currently affected. In participants who were not aware that a family member currently had cancer – cancer worry was lower (Glanz et al 1999).

With the exception of a few studies (Glanz et al 1999; Codori et al 1999; Lerman et al 1999), no attempt has been made to account for the relationships between participants. There is likely to be a higher level of similarity between family members than between individuals drawn randomly from a population. This similarity may be due to shared environment, and the effect of discussing the topic with other family members. Without accounting for these relationships the estimates of standard errors may be inaccurate.

Demographic correlates of uptake are more consistent. Higher uptake is associated with more education, being married, younger, female and having participated in previous screening. Those who choose to have the test perceive themselves to be at higher risk, worry more about cancer and believe that they will cope better with a positive test result. The studies of uptake however may have been more subject to the influences of intrafamily effects, owing to the small numbers of families actually contacted.

2.5.5 Impact of Genetic Testing for Colon Cancer Susceptibility

Few studies have followed sufficient numbers of people through the process of undergoing genetic testing for HNPCC to be able to draw clear conclusions about the impact of genetic testing on the individual.

In a qualitative study of anticipated and actual responses to genetic testing for FAP (Michie, McDonald & Marteau 1996) (which gives more definite test results than testing for HNPCC) people who received a low-risk result were very reluctant to give up screening because of fear that they may still be at risk. With any testing for predisposition to cancer there is a risk that a person receiving a low risk result will develop cancer. This may be due to the person developing a sporadic cancer, as there is still the risk that they may develop it due to environmental circumstances. The other possibility is that they may have inherited two genes predisposing to hereditary colon cancer, either from the same parent who is affected, or the other parent. There is one gene known to cause FAP (APC gene), however many genes predispose to HNPCC

cancers. If an 'at risk' person is screened for a known mutation at a specific gene site found in an affected family member, either for FAP or HNPCC, there may be another gene which predisposes which is not tested for. The risk of this happening is very low, but cannot currently be eliminated. There was also an opinion expressed that bowel screening gave more certain and reassuring feedback, that 'seeing was believing' in a way that DNA testing could not reassure.

Many people also expressed confusion about the meaning of the risk results, with uncertainty about what the meaning of the risk values were, and about the implication of these risk results. People also expressed concern that the medical profession did not seem to understand or believe the results that had been given either. Medical personnel appeared to the participants to give conflicting accounts of the implications of the test result, saying that the person was at low risk but implying that they might still be at risk.

In anecdotal evidence (Lynch et al 1999), some people appear to see being a carrier as a part of being one of the family, and feel a sense of solidarity when they are informed that they too are a carrier for the gene. There was also some evidence of survivor guilt, regretting that they have escaped whilst other relatives are affected. Among carriers there was a high desire to undergo prophylactic colectomy, despite scepticism of the value of this option in the medical community.

In an addendum to a larger study, 11 patients were monitored in the two weeks following receipt of a mutation positive test result (Gritz et al 1999). These participants were from a study of colorectal patients, so a positive result is expected, and other results are all inconclusive. Between the baseline time when the sample was taken, and two weeks after the test result was given, the mean anxiety and depression levels had fallen in both people exhibiting high and low baseline distress. There are insufficient numbers to determine whether this is a significant result, but this finding is in the same direction as those found for HD and for breast/ovarian cancer.

In a larger study of individuals who had received test results (Aktan-Collan et al 2000b), after one month there was no difference in satisfaction with having a genetic

test by mutation status. By one year, those who had not inherited the mutation were slightly more satisfied with their decision, although both groups reported a slightly lower level of satisfaction than they had at one month. At both times, those who were given a mutation-negative result were less confident about the results than those who were told that they had the mutation. When asked about when they most needed support (Aktan-Collan, Mecklin, de la Chapelle et al 2000a), both carriers and non carriers identified the test disclosure time as when they needed most support (46%). Other times of high need for psychological support were in making the decision (16%), waiting for the result (19%) and soon after test disclosure (14%).

The results of these studies of impact indicate that the impact of having a genetic test is for most people within acceptable limits, and it decreases over time. The findings from the last cohort (Aktan-Collan et al 2000b) raise some concern that the psychological benefits of receiving a genetic test result decline in their salience over time, however people may continue to worry as many anticipate that they will. The relinquishing of regular screening may also have adverse effects on some individuals as evidenced in the qualitative study, this may be even more pronounced in people at risk of HNPCC, for whom a clear colonoscopy at one time is no guarantee of continued good health. For those with a history of FAP who are beyond their twenties, a clear colonoscopy is a good clinical sign that they are not at risk, so they may already be aware that they are at lower risk, this is not the case in HNPCC.

2.6 Summary of previous findings

The study of dominantly inherited disorders has shown that most people initially express great interest in learning of their true risk of developing diseases to which they are prone, and in some cases diseases for which they have no specific family history. The actual number undergoing genetic testing is substantially smaller, although this is less so in the cancers where prevention and treatment is possible.

Despite extensive measurement of demographic variables, few have emerged as consistently being associated with intent to have a genetic test. Gender has been found to often be associated with higher intent, with women having greater intention to have

a test, although this association has not always been found. Gender has been found to be a factor in studies of breast/ ovarian cancer, but in this condition there is an effect of gender on gene expression. Many studies have found that people who are younger, white, and well educated are more likely to want a test, however some studies have produced contradictory findings. The associations between intent, uptake and psychological variables have been more consistent, with people who want the test perceiving themselves as more susceptible, being more worried about cancer and perceiving more benefits and less barriers to undergoing a genetic test.

Reasons given for wanting to undergo a genetic test are relatively consistent between illnesses, however the emphasis placed on each varies. The main reasons given for undergoing any test are to reduce uncertainty, learn about children's risk, and plan for the future. In HD an additional motivating factor is family planning - although this is cited by people at risk of other disorders, as HD cannot be cured or prevented many perceive family planning or pre-natal interventions as the best way of reducing the chance of having affected children. In breast/ ovarian cancer and colon cancer, an additional motivating factor is the desire to plan screening and preventative options, including lifestyle changes that may be perceived as being more healthy. Reasons for not wanting testing typically include not wanting to know, concern about insurance and possible emotional consequences of learning of their actual risk levels.

In studies of actual impact of genetic testing, even for the more severe disorders, serious emotional reactions are rare. Most studies have found that people adapt well to their results, and regardless of the actual outcome usually fare better than those who chose not to have a test do.

In response to a positive result people typically experience shock, disbelief and anxiety, which tends to dissipate somewhat over time, to an acceptance and adaptation to the news (Wiggins Whyte, Huggins et al 1992). A person may however become 'stuck' at one of the stages, and never come to terms with the result. The person may experience regret that they decided to have the test, as it may have somehow changed their fate. They may also become unduly anxious, looking for the slightest symptom of the impending disease.

The psychological benefits of receiving a negative genetic test are reassurance and reduced worry. There are sometimes disadvantages too, some people experience 'survivor guilt', that they have been spared the family illness, while others have been cursed (Codori & Brant 1994). Families themselves may even reject someone who tests negative, as they no longer share something that has been part of the family identity (Lynch et al 1999). In addition people may regret previous decisions, made when they thought they might develop the disease, or they may regard the test as inaccurate, and believe that they are still at risk (Aktan-Collan et al 2000).

2.7 Criticisms of previous research

There are a number of issues that are important to consider in assessing these findings described in this Chapter. As the methods used in studying interest in genetic testing for breast cancer are similar to those used to study interest in genetic testing for colon cancer, the criticisms of these methods also are similar. These criticisms, their implications and how the points will be addressed in this series of studies will be discussed in this section. In addition a table outlining how these criticisms relate to individual papers can be found in Appendix C.

2.7.1 Level of objective risk

The first criticism is that many of the studies reviewed do not use very high risk participants (e.g. Lerman, et al 1995 - 90% had only one affected first degree relative (FDR) affected by breast cancer; Glanz et al 1999 - only 9% had more than one affected FDR). Participants who only have one first degree relative who had breast cancer over the age of 40 have at most a 1 in 8 risk of developing breast cancer (Eccles, Evans, Mackay 2000). There is also a low chance that their relative's cancer is caused by a high penetrance genetic mutation. A similar situation is true for those people at risk of colon cancer.

This population is unlikely to be offered a genetic test in the near future, and may differ significantly from the population of people who will be offered a genetic test (people

with two or three affected relatives who were young when they developed cancer). People who only have one FDR (who in many studies is still receiving treatment), are unlikely to have considered their risk for as much time as people are in families with multiple affected members and a long history of cancer. Secondly they may be less likely to regard themselves as being at genetic risk of cancer, and indeed many are not at high genetic risk of cancer. These two factors may explain in part the finding that actual objective risk is a significant correlate of the uptake of genetic testing in a number of studies (e.g. Valdimarsdottir, Bovbjerg, Brown et al 1999; Lerman, Schwartz, Lin et al 1997).

Some studies even recruit people from the general population who have no family history of cancer (e.g. Croyle & Lerman 1993; Croyle, Dutson et al 1995; Graham et al 1998). These studies do give important information about the baseline level of intent to have a genetic test, and, as Graham et al (1998) identifies, show the need to educate people about the inappropriateness of high levels of intent in those with no family history. Their use to explore correlates of intent to have a genetic test should not however contribute to the discussion about intent in people at high risk, as none of these studies present evidence that the process is similar in general population samples and high risk samples.

Not using a population which is at high risk means that the results are less immediately transferable to a population which is likely to have a genetic test than they would be if the study were conducted in a high risk population. In the series of studies reported in this thesis, many of the participants are at moderate to high risk of colon and breast cancer. Most of the participants have a number of affected relatives and/ or relatives affected at a young age. Where people are at lower risk this is either controlled for (e.g. in Chapter 4), or explicitly studied (e.g. in a comparison of people with a family history compared with a no cancer history general practitioner sample - Chapter 9). By examining the differences between people at high risk and people with no family history it will be possible to establish whether intent is correlated with the same factors in high risk individuals as it is in people with a lower risk. This will provide retrospective validation or demonstrate the lack of validity of examining a general population sample with the aim of understanding a high risk sample.

2.7.2 Inter-relationship between study participants

The use of a high risk population generates other problems. It would be very difficult to recruit large numbers of people at high risk from an unselected population. Most breast and colon cancers are sporadic, this means that very few high risk people would be contacted via all but the largest population surveys or even via currently affected individuals. Because of this problem most studies of high risk individuals have recruited participants from cancer registries, identifying families thought to have a genetic mutation. In doing this, most studies have recruited parts of, or whole families to the research programmes (e.g. Petersen et al 1999; Struewing et al 1995b). The ratio of participants per families varies from study to study (e.g. from 1.1 participant per family (Metcalfe, Lide et al 2000), to an average of 50 per family (Lerman et al 1999)).

Although recruiting whole families means that familial interactions can be explored, this has rarely been the aim of the studies reviewed here. Often the families have been recruited as a whole to collect genetic samples, and for possible testing, rather than to investigate psychological factors.

The presence of multiple family members in one study raises statistical problems that are not adequately addressed in the majority of research in this area. Most statistical tests rely on the independence of observations - i.e. there is no a-priori reason to expect that the response of one individual will be related to the response of any one other person. This can not be assumed when recruiting whole families. Family members are likely to have discussed their family history with each other, and may have come to common views about genetic testing. Even if testing has not been discussed, other genetic or family environment factors such as personality, value for health and attitude towards screening are likely to be more similar in family members than between strangers.

If the observations are not independent the main consequence is that the standard errors and significance tests will be incorrect. The precision and statistical significance of the observed relationships will be over estimated. In this thesis, the ratio of participants to

families is low (1.3 participants per family, with the majority of families represented by just one participant), so clustering effects are less likely to be a problem than in some previous studies (Lerman, Narod, Schulman et al 1996). In this study 195 men and women from 13 families participated (a ratio of approximately 15 people per family). In addition, in this thesis, in the analysis of correlates of intent a cluster analysis has been used to provide adjusted significance tests.

2.7.3 Source of recruitment

Different studies have adopted various recruitment methods, each of which has a different influence on the results. One route of recruitment of unaffected people has been via relatives who are currently affected by cancer. As discussed previously this usually means that most of them are at relatively low risk of cancer, and less likely to be offered genetic testing in the near future as most people with cancer have sporadic cancers. In addition this group of people are likely to have a heightened concern about their risk of cancer due to the current illness of their relative. In a recent study (Meiser, Butow, Schnieden et al 2000), having experienced a 'breast cancer event' within the past year was associated with higher cancer related anxiety. The association between concern and intent in this group may be in part an artefact of this higher than usual level of concern in some people, whereas in other studies there is less variation in intent. This level of concern is likely to be more acute than that experienced by a person who is at high risk but has no currently affected relatives and people who have known for some time that they are at high risk are likely to have become habituated to their risk.

Another problem with recruiting via patients is that it is difficult to assess participation rates. For example in a study of FDRs of breast cancer patients (Lerman et al 1995), 66% of index patients approached gave permission to contact their relatives, then 78% of these relatives participated. There may have been many reasons why index patients refused permission to contact relatives, but one likely reason is that they and/ or their relatives object to genetic testing. If this were true, and they had a similar number of relatives to those who gave permission, this would bring the participation rate down to 51.5%, and the proportion intending to have a genetic test down from 91% to 47%. It is

also possible that even among those index patients who did give relatives' names they omitted details of people they thought might disagree with the study or genetic testing, this would further reduce the true participation rate.

Another population group which has been targeted (and which will be used in this thesis) is recruited via cancer registries. This method of recruitment ensures that sufficient high risk families are recruited to the study as there are a large number of people to choose from, and their family histories are known. The participants are less likely to be affected by the current illness of a family member, so the results may be more representative of the larger population of people at risk.

As the studies select known people from the database, it is easy to assess participation rates, and thus determine how generalisable the results may be to the wider registry. People on such a registry may, however, differ from those not registered if registration is voluntary (as it is in the population used in this study). People less interested in clinical screening or less concerned about their cancer risk may choose not to register, and therefore cannot be contacted. This population may not therefore be representative of the wider population at risk.

Usually people on high risk registries are offered screening for the at risk cancer, which means that they may perceive their risk to have decreased slightly due to the screening, so for them genetic testing may be less important than it is for someone not receiving screening. Some people may also be concerned that they will lose the reassurance of screening if they are found not to carry a genetic mutation. These factors may influence intent to have a genetic test, so will be assessed in this study.

A further difference in recruitment methods differentiate those who were recruited via one of the above methods and those who self-referred themselves to the study. Where both methods have been used, people who self-referred themselves to a study of genetic testing were more likely to intend to have a genetic test than those on existing registers (Geller, Doksum, Bernhardt & Metz 1999). This is in part because it is not known how many people saw the advert and did not respond. It is not possible to determine a non-response rate in a self- referred sample.

2.7.4 Reporting of findings from affected and unaffected individuals

Most studies have concentrated on unaffected (asymptomatic) individuals who have no personal history of the cancer of interest. A number of studies have recruited affected individuals as well (Lerman, Hughes, Trock et al 1999; Struewing et al 1995; Metcalfe, Lide et al 2000; Wagner, Moslinger et al 2000; Lerman, Hughes et al 1998; Cappelli, Surh, Humphreys et al 1999). With the exception of one study (Cappelli, Surh, Humphreys et al 1999), the findings have been reported without differentiating the effect in people who have had cancer from those who have not. Having a genetic test if one has already had cancer would be a confirmatory test, and the implications of such a result are likely to be different from those if the test is predictive (in a person with no personal history).

Cancer status is often controlled for, however studies do not investigate the possibility that having had cancer may not only explain variation in intent, but may also influence how some of the other variables interact with intent. In order to explore this interaction terms would need to be entered into the regression equations, or intent in people who had already had cancer would need to be explored in a separate analysis. In the sample recruited for this study there are few people who have had cancer, so it will not be possible to carry out such regression analyses (this will only be done for intent to have a predictive test). The differences between those with and without cancer will be explored and reported to identify how views of testing vary between those at high risk and those at lower risk.

2.7.5 Treatment of intent as a dependent variable

Intent has been the main dependent variable of interest in many of the studies. In most studies this has been measured on a five point scale, however this is usually very skewed, with most people saying that they probably or definitely intend to have a genetic test. In the majority of studies the responses have been dichotomised to yes definitely compared with all other responses (Lerman, Marshall et al 1996; Petersen et al 1999; Glanz et al 1999; Lerman, Daly et al 1994; Struewing et al 1995b; Meiser,

Butow, Barratt Butow et al 2000). The responses have then been compared using logistic regressions. The small numbers of people giving responses other than yes definitely or yes probably have meant that there have been insufficient numbers to meaningfully combine the two positive responses and compare them with the negative or more neutral responses. This is a problem of insufficient power, which may have been overcome by recruiting more respondents.

One problem with dichotomising the sample at this point is that the prediction is then who is likely to definitely intend to have a genetic test, compared with predominantly those who say they probably would intend to have a genetic test. It is unclear whether this is going to be a useful distinction, as those who say that they probably intend to have a genetic test may simply be more cautious in their endorsement. 'Probably' is still a relatively positive quantifier - meaning that it is likely that they will have a test. Dichotomising also eliminates the possibility of revealing whether there is a linear pattern in the prediction of intent by various factors. For example is perceived risk linearly associated with intent - does high risk equate to high intent, moderate risk to moderate intent and lower risk to lower intent or is there a threshold effect with only a certain level of risk necessary to produce positive intent to have a test? By dichotomising the sample these researchers have lost some of the original sensitivity and are answering a less interesting question (are people who say 'yes definitely' different from those who say 'yes probably').

In this study intent will be examined with the assumption that it represents an underlying linear variable, using both linear regression techniques and ordinal regressions. The sample is larger than most of the studies reported here so this will also increase the numbers of people who endorse responses other than 'yes definitely' or 'yes probably'.

2.8 Areas Identified as Needing Research

The studies on genetic testing to date provide generally consistent results with some variations. In this thesis previous findings should be replicated, and certain areas will be examined in more detail than in previous studies.

One area that has not been explored in great detail is the transferability of models of health behaviour to the issue of genetic testing. Most of those studies that have employed a model have used the health belief model to varying degrees. Few studies have used this model in its entirety, and where it has been used it has often been used in conjunction with other factors, so the model itself has not been tested. Another model used was the transtheoretical model of change (Vernon et al 1999), for which support was found. The 'attitudes' component of the theory of reasoned action has also been used (Glanz et al 1999), but the whole model was not used and the sufficiency of the model was not tested; rather it was combined with other variables, so the influence of these constructs on behaviour is not clear. The use of models has been widely established in other areas of health psychology, although some problems emerge when these are applied to genetic testing. This will be discussed in greater detail in the next Chapter.

Previous studies of why people intend to have a genetic test have, with a few exceptions, used survey methods. There have been flaws in some of this work, as many researchers have collapsed intention into dichotomous variables, and so have lost some of the original sensitivity. In this study the linear nature of intent will be explored using both linear and ordinal regressions which preserve the original data.

Gender has been explored in a number of studies, but a consensus has yet to be reached on whether there are any gender differences. One problem has been that for breast / ovarian cancer, the effects of carrying a predisposing gene vary between genders, this may explain why women are more interested in testing than men. The differences in intent though could be due to differences between men and women in their evaluation of and anticipated reactions to knowing their genetic composition in general rather than because they are specifically considering their risk of breast/ ovarian cancer. The

findings in studies of intent to have a genetic test for colon cancer are more equivocal. Although women have been found to be more interested in some studies this has not been found in all reports. Differences between men and women will be examined in terms of their evaluation of and anticipated reactions to genetic testing for colon cancer.

Another area which has received little attention since the early studies of HD is the effect of genetic testing on the partners of people at high risk, and whether they actually want their partners to undergo a genetic test. This will be examined by recruiting both people at high risk of developing colon cancer and their partners to the study to compare their views of genetic testing.

Few studies have recruited both affected and unaffected individuals, and those which have, have used this factor as an additional predictor variable, rather than exploring the differences. There are likely to be a number of differences as testing in people who have had cancer is seen as confirmatory, whereas it is predictive if a person has no clinical signs of cancer. Struewing et al (1995b) found that although not significant, women who had had breast or ovarian cancer held higher intent than the men and women in the study who had not had cancer. In another study (Cappelli et al 1999), women who had breast cancer were compared with a general population control group. In this study those women who had breast cancer held higher levels of intent than women from the general population. This study does not inform the debate about whether affected women are more likely to want a test than unaffected women at high risk are, and whether there is likely to be a difference between the women on other aspects related to genetic testing. In this thesis this issue will be addressed, to determine whether genetic testing has a different meaning for those people who have already had cancer, compared with those at increased risk, but currently unaffected.

The issue of risk is one that has not been adequately explored in relation to genetic testing for colon cancer. Many studies use participants who are at only a low or moderate risk of developing colon cancer, and there have been insufficient comparisons across risk categories to determine the influence of objective risk on intention. The use of high risk samples who meet the Amsterdam Criteria, people at a

slightly lower, but still at risk and a general practice sample will permit a greater investigation of the influence of objective risk on psychological aspects of genetic testing for colon cancer.

One more area that deserves greater research is the comparability of outcomes for different disease models. With the completion of the Human Genome Project and the development of better technical skill to identify predisposing genes, it is possible that in the near future genetic testing will be available for a greater diversity of diseases. The time required to pursue an in depth evaluation of all possible genetic disorders and the possible psychological consequences will not be available. It will be necessary to determine the likely effect that testing for any given disease will have, with consideration to the penetrance of the gene, the severity of the illness and any additional disease specific factors. Determining similarities and differences across disease models will permit the development of a model of intent, which should be applicable to other diseases.

Chapter 3

Theoretical Basis of Thesis

3.1 Theoretical approaches to investigating genetic testing

As the previous review of the literature has shown, there are certain common themes that have emerged from research in the last few decades. Many studies have reported a high initial interest, followed by a subsequent low uptake in testing. This has been particularly apparent in HD where initial surveys indicated an interest level of about 70%, but uptake levels have been closer to 10%. In the example of breast cancer, initial interest has been even higher, with up to 95% of women probably or definitely interested in having a test, with uptake ranging between 30% and 70%.

The main reasons given for requesting testing are to reduce uncertainty, to assist in family planning, and in the case of cancer, a desire to make an informed decision about screening and prophylactic surgery. The reasons given for intending to have a test may reveal important clues about who is likely to intend to have a genetic test and how the results may affect them. A woman requesting testing to determine whether she has inherited a genetic predisposition to cancer may state that she wishes to know so that she will not feel so uncertain. Testing may reveal that she does indeed carry a mutation but it will not tell her that she definitely will develop cancer or when she will. In this way the investigation of motivating reasons may predict likely reactions to news, and highlight the need to discuss fully with the person the potential impact of the results.

Those studies that have followed people after they have undergone testing have found that for most people there are few long-term negative effects of receiving a genetic test result. Among those who have tested positive for a gene, after an initial period of psychological distress, most people are either as well adjusted, or more well adjusted after receiving a test result. In those who have tested negative there are usually few ill effects, however some report feelings of guilt that they have survived when others in their family have been found to carry the gene. Those who are least well adjusted are those who have opted out of testing or who have been unable to have testing.

Despite the numbers of studies undertaken in this area, there have been few studies which have adopted a theoretical approach to the issue of genetic testing based on the application of established psychological theories. Shiloh (1996) identified the need for theoretical frameworks in this field of research. The use of established psychological models to explain the factors that influence intention to have a genetic test means that this complex health behaviour could be explained in terms of concepts widely used in health psychology. The uniqueness of this behaviour may however prove a problem to some models. This may necessitate the development of new theories, which may in turn be applicable to other health behaviours.

There are a number of models of behaviour that have been widely applied in the context of health behaviours to explain why a particular individual chooses to act in a certain way (Conner & Norman 1995). These models include the health belief model (HBM), the theory of planned behaviour (and reasoned action), the transtheoretical model of change, the self-regulatory model of illness and the health action process approach.

Before discussing the merits of different models it is important to consider the nature of this 'health behaviour'. For some behaviours (e.g. smoking, exercise or sexual activity) - there is a clear health benefit to be gained from participating in or abstaining from certain activities. Genetic testing currently does not usually have accepted positive or negative values attached to it. Medical advice given concerning whether to undergo testing or not varies depending on the type of disease to be tested for and the culture the person lives in.

In FAP, testing may be suggested for children prior to their first colonoscopy (to determine the need for colonoscopic screening), although genetic testing is not essential for clinical screening to commence. For HD the decision whether to undergo testing is currently one of personal preference, as there is no clinical benefit in knowing, except for family planning. In the cases of breast and ovarian cancer and HNPCC, genetic testing may mean that additional information is available on which to base decisions concerning screening regimes and possibly prophylactic surgery. The screening recommendations remain the same whether a person has been found to carry the gene, or has not undergone testing but is at high risk of carrying a gene. The main

clinical and economic benefit of genetic testing is the identification of non-carriers, so that surveillance can be reduced or stopped in this group.

In Britain genetic testing (particularly for adult onset disorders), is viewed as entirely a choice of the individual, with neither a right or wrong choice. Genetic counselling has espoused the concept of non-directiveness, giving information rather than recommendations (Bartels, LeRoy, McCarthy & Caplan 1997). For recessive disorders such as Tay Sachs Disease or Thalassemia, some cultures have encouraged testing, to identify carriers, and reduce the incidence of marriages, conception or birth of affected infants (Ghanei, Adibi, Movahedi, et al 1997). China's Maternal and Infant Health Care Law 1994 gives doctors the right to terminate a foetus found to carry a genetic mutation even against the parent's wishes. This situation is clearly not advocated in this country (BMA 1998 p25).

Choosing to know about one's genetic status, particularly for adult onset disorders, therefore cannot currently be viewed as healthy or unhealthy. Each decision must be viewed in the context of whether it is better for that individual to know or not know, rather than whether knowing or not knowing per se is to be encouraged. In these circumstances, a move towards shared decision making may be appropriate, in which both health professional and patient take an active role in finding the optimum decision for that person (Elwyn, Gray & Clarke 2000). Recommendations may change if a preventative treatment was proven to be effective in gene carriers, and it was important that only gene carriers received the treatment. Until this time theories which include a value judgement concerning whether treatment is right or wrong are inappropriate frameworks within which to study this decision making process.

The choice of model was decided by considering the attributes of the target behaviour (having a genetic test), and the likely predictors of intention to perform this behaviour. Protection motivation theory (Rogers 1983) was considered as a possible framework, however this model assumes that one behaviour is maladaptive, and may be influenced by perceived severity and vulnerability, and that one behaviour is adaptive, and is influenced by response efficacy and self-efficacy. It is difficult to match this model to genetic testing, as there is currently no 'adaptive' or 'maladaptive' behaviour, as discussed above. It would have been possible to use some of these concepts, however

the basis of the model could not have been tested with the current lack of recommendations from the medical profession. It may be argued that the labels 'adaptive' and 'maladaptive' are simply terms without values attached, however this may not always be clear to other health professionals who may regard these as inappropriate terms to use with respect to genetic testing. This model was therefore rejected.

Other models include the study of the maintenance of a health behaviour, which is also inappropriate to examine in genetic testing which is a discrete, one off event, which cannot be either maintained or rejected once it has been experienced. The health action process approach (Schwarzer 1992) was also considered. Again some components (risk perception and outcome expectancies) may be particularly pertinent in considering genetic testing. The role of self-efficacy in actually undergoing testing may not be as important as the model theorises, as it simply involves giving a blood sample. The action phase may be very short (giving a blood sample at a local hospital) and the behaviour once performed cannot be maintained as it is a one-off behaviour. This model also was excluded from this thesis. Two models were finally selected - the health belief model and the theory of planned behaviour.

Although these models have been widely applied to identify factors which might be used to encourage the adoption of 'healthy' behaviours, they do not assume a priori the 'correct' health behaviour. They also do not assume any prior experience of the behaviour or any need to maintain the behaviour. These models have therefore been adopted and applied to the issue of genetic testing in this thesis. Although both models are designed to predict the uptake of the behaviour, because genetic testing was only offered to a minority of the sample during the time frame of the thesis, intent to undergo genetic testing will be taken as an indication of likely uptake of genetic testing. Intention to act in a certain way can predict who will actually act in a certain way, however as has been seen in the case of HD, intention to undergo genetic testing may be a poor predictor of actually undergoing testing. This discrepancy between intent and uptake has also been observed in other situations and has been termed the 'intention-behaviour gap'. This discrepancy between intent and uptake has also been observed in many other situations (Sutton 1998). The relationship between intent and

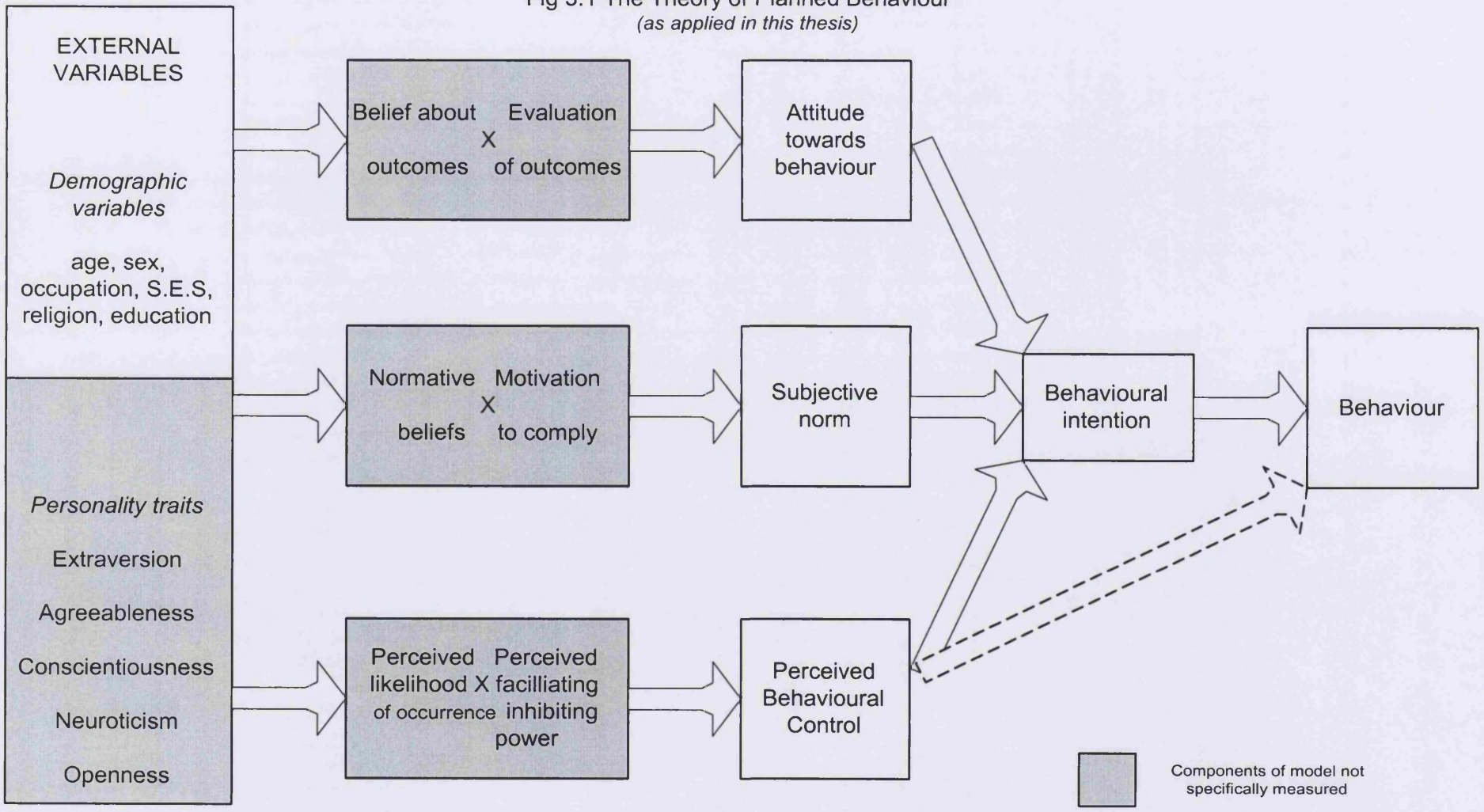
uptake is not within the scope of this thesis, but can be evaluated in more detail in the continuing follow-up of the participants of this thesis.

3.2 Theory of Planned Behaviour

The theory of planned behaviour (TPB) was proposed by Ajzen (1985) and includes perceived behavioural control as an extension to the theory of reasoned action (TRA) proposed by Fishbein and Ajzen (1975). The TPB contains three main components - attitudes, subjective norm and perceived behavioural control (see Fig 3.1). Attitudes are personal evaluations of performing the target behaviour, subjective norms are the person's belief about whether significant others think he or she should undertake the specific action, and perceived behavioural control assesses whether the person believes that the action will be easy or difficult to perform. The determinants of these concepts were not measured in this thesis, however these are also laid out in the model. These three components are held to predict intent to undergo a genetic test, intention in turn predicts uptake of a genetic test. Perceived behavioural control is also hypothesised to have a direct effect on behaviour over and above the effect of intention.

According to the principle of correspondence (Fishbeing and Ajzen 1975) (renamed the principle of compatibility by Ajzen 1988), for the maximum predictive effect, all measures of the TPB should be measured at the same level of specificity as the evaluated intention or behaviour. In the prediction of intent to have a genetic test for colon cancer, attitudes towards having a genetic test for colon cancer should be measured, rather than attitudes towards genetic testing in general, or at a more general level - attitudes towards medical tests. It is also important to specify who will be performing the behaviour. Usually a certain timeframe would be stated as well, except in this thesis the test was hypothetical at the time of the survey. Positive attitudes towards undertaking a specific behaviour are hypothesised to be predictive of high levels of intention and uptake of the behaviour.

Fig 3.1 The Theory of Planned Behaviour
(as applied in this thesis)



Subjective norms are people's beliefs about the social pressures on them to undertake a specific behaviour. Clearly for some people, other people's attitudes might be very important - particularly when the outcome of a parent's test will have an effect on their children's risk. Partners might wish to know or not know whether their spouse is likely to die young so they can plan for the future. Subjective norms only measure what the person perceives that others would want them to do in such a situation. For some behaviours the social norm may be well established, and it is likely that a person will translate this into a subjective belief about the norms. Other behaviours may not have a well-established norm, so it may be more difficult for a person to imagine what others would want them to do. In this case if they do not know, they may seek the opinion of others, in which case the norm is no longer subjective, or they may extrapolate from their own intention, which will lead to a better correlation with intention, however it may not reflect the views of others.

These two concepts (attitudes and subjective norms) are the determinants of intention in the TRA (Ajzen & Fishbein 1980). This theory was found to be useful in explaining intention and behaviour in the case of volitional behaviours, but those behaviours that are non-volitional are poorly predicted. Behaviours requiring skills, resources or opportunities not freely available are thought to be poorly predicted by the TRA. The TPB, with the additional explanatory power of perceived behavioural control is hypothesised to be a better predictor of non-volitional behaviours (Sutton 1997).

Perceived behavioural control is a measure of the control that a person believes that they have over the behaviour in question, and whether the behaviour would be easy or difficult to perform. This concept was originally introduced as a proxy for actual control (Ajzen 1988), as it was theorised that a person will tend to perform desirable behaviours that they have control over, and not perform behaviours that they have little control over. In this situation, actual control would be a desirable measure to have, but due to difficulties obtaining this, perception of control was thought to have the same effect as long as it correlates with actual control (Ajzen 1988). Perceived behavioural control may also be seen as a similar concept to self-efficacy (Bandura 1977). Self-efficacy is a measure of a person's perception of their ability to successfully perform a given behaviour – if a person believes that they can take action to change a situation, they become more inclined to do so and feel more committed to the action. Self-

efficacy is based on experience, and a sense of competence obtained through the completion of other related actions, it is not blind optimism.

The actual control over a behaviour may not always be apparent to a respondent in a study so although PBC is in theory aligned with actual control, there may not always be a strong correlation between the two, and PBC may be more of a subjective measure. Self-efficacy would suggest that a person would base their evaluation of control on not only their own perceived personal sense of control in general but also the information which they have available to them about the task. This may predict their intent to perform a behaviour, however when faced with the reality of the situation they may be unable to actually undertake the behaviour. This focuses on the person's perception of their control as being the important factor in motivation, rather than their actual control. This is directly applicable to the case of genetic testing where the perception of control may differ from actual control. The perception of control may be important in predicting who intends to have a test, although in reality actual control is often removed from the person, because crucial blood relatives are either dead or not willing to give blood, or a mutation cannot be traced. The actual behaviour of undergoing a genetic test is a blood test, so there should be few reasons why most people would not be able to perform this one off behaviour.

In recent years researchers have examined the possibility of adding more concepts to the TPB to add to its ability to explain intention (Conner & Armitage 1998). One such concept is anticipated affect. This concept has been found to explain variance in addition to that explained by the TPB variables (Parker, Manstead & Stradling 1995; Richard, van der Pligt & de Vries 1996). Anticipated regret is a measure of how the person anticipates that they will feel if they chose to engage in or abstain from certain behaviours. This concept is an appropriate one to explore in the context of genetic testing, as genetic testing is an emotive issue, which might have very different anticipated emotional consequences depending on the outcome of a test result. In addition it is a behaviour which once done cannot be undone, or redone with a different outcome. For this reason a person might carefully consider how they might feel in various situations in order to help them decide whether to undergo a test. Some have suggested (Parker Stradling & Manstead et al 1996) that changing anticipated affect may have a greater impact on changing behaviour than changing attitudes. The findings

of Lerman et al (1999) that education focused on emotional consequences increased intent in African American women are consistent with this idea. There is as yet no consensus as to whether anticipated affects are certain sorts of behavioural beliefs, which predict attitudes, or whether they independently predict intention/ behaviour.

3.2.1. Previous Research and Current Thesis

The theories of reasoned action and planned behaviour have been widely used in social as well as health psychology. A number of reviews have been carried out to examine the degree of relationship between the determinants of intention, intention and behaviour. Across 87 studies of the TRA the correlation of intent with attitudes and subjective norms was 0.66 (Sheppard, Hartwick & Warshaw 1988). In a review of the performance of the TPB an even higher level of correlation with intent was found (0.71)(Ajzen 1991) however this was only in a small number of studies. The relationship between intention and behaviour has also been examined and has been found to be lower than the degree of relationship between intent and determinants of intent. Randall and Wolff (1994) found an overall correlation with intent of 0.45; Sheppard et al (1988) found a mean correlation of 0.53. There is however considerable variation between behaviours with correlations between intent and behaviour ranging from 0.35 in screening studies to 0.56 in studies of addictive behaviours (Godin & Kok 1996). For more in depth reviews of the theory of planned behaviour see Abraham & Sheeran (1997) and Conner & Sparks (1995). Despite the widespread application of the TPB in health psychology, surprisingly few studies have employed it to examine intention and behaviour to have a genetic test.

The TRA was used in one published study (Glanz et al 1999). In this article however the theory was not operationalised in accordance with published recommendations. The individual contribution of the component 'attitudes' was not reported, and subjective norms were not explicitly used, but rather were replaced with a measure of social support. The model tested was divided into predisposing factors (cancer worry, risk perception, well being) and enabling factors (decision preferences, social support, rapport with physician, source of medical care, health insurance cover). It is not possible to draw any conclusions about the usefulness of the theory from this study because the contribution of the theory of reasoned action to the model was not

independently identified. It is also not clear from this study how the theory was operationalised. This study was therefore an inadequate test of the TRA.

Searches of PsychLit using 'theory of reasoned action' and 'theory of planned behavio* r' as key words, failed to identify any which also used the terms 'genetic', 'gene' or 'DNA'. A parallel study to this thesis used the TPB to investigate predictive genetic testing for breast/ovarian cancer (Bish, Sutton, Hodgson et al 1998). This study found that the TPB predicted a substantial amount of the variance in intention (67%), this was significantly improved with the addition of anticipated emotional reaction (comparative data reported in Chapter 8).

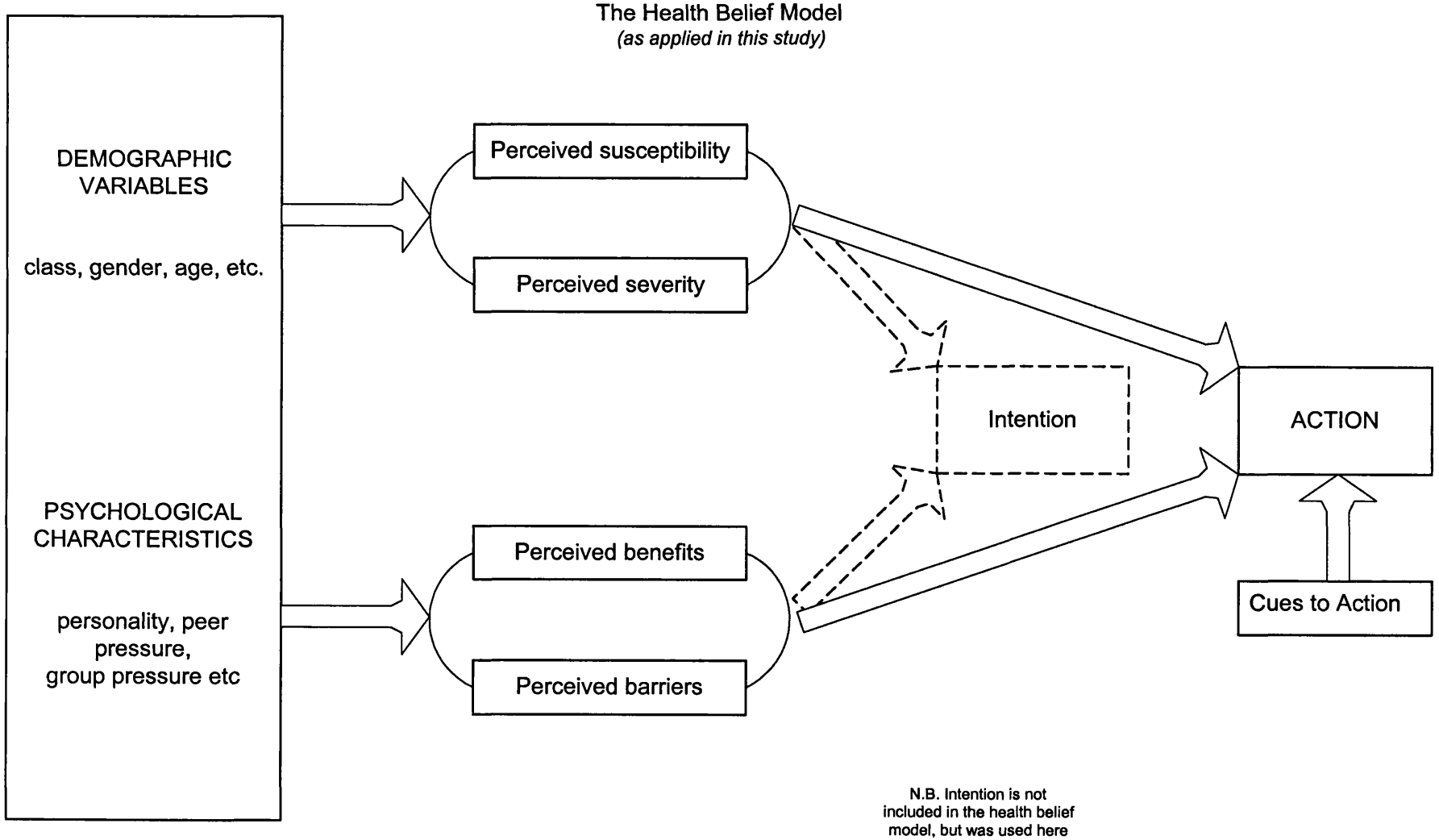
The TPB has been applied to compliance with screening for colon cancer in people at high risk of colon cancer (DeVellis, Blalock & Sander 1990). Here support was found for the utility of the theory in explaining intention to complete a faecal occult blood test, and for the value of perceived behavioural control in explaining behaviour above that explained by intention.

In this thesis positive attitudes towards having a genetic test, norms that reflect that important others would want the person to have a genetic test and high perceived control over having a test are hypothesised to be associated with a strong intention to have a genetic test for colon cancer. Additional correlates of high intent to have a test should be high anticipated negative affect if the person does not have the test, low anticipated negative affect if the test is positive, and high anticipated positive affect if the test is negative.

3.3 Health Belief Model

The HBM (as defined by Becker Haefner, Kasl et al 1977) has six components. Only the four main components of this model were used in this thesis - these are perceived benefits, perceived barriers, perceived susceptibility and perceived severity (see Fig 3.2). The HBM does not include the concept of intention to act, but rather predicts action without this intermediate variable. A number of researchers have used intention

The Health Belief Model
(as applied in this study)



N.B. Intention is not included in the health belief model, but was used here as a proxy for action

in addition to the HBM constructs as this is thought to partially or wholly mediate the effect of health beliefs in explaining behaviour (Sheeran & Abraham 1995). In this thesis however, intention was included as a proxy for action, as at the first time point no individual had the opportunity to act. The act of having a genetic test is a pre-meditated one therefore it is reasonable to assume that at some point the person must form an intention. Cues to action were not measured, as these are hypothesised to directly affect the performing of the act rather than necessarily affecting intention.

3.3.1 Perceived Benefits and Perceived Barriers to Genetic Testing

The perceived benefits of taking an action are the anticipated rewards of taking a specific action in comparison to not taking that action or taking an alternative action. These benefits may be both medical benefits and psychosocial benefits of engaging in a health-promoting behaviour. Benefits have also been conceptualised as the perceived efficacy of the action in preventing an undesirable event, however as genetic testing cannot in itself prevent anything happening, this aspect of this construct was not used. The important aspect of this and other components of the HBM is that it is the perception of likely benefits which is important in predicting intention, not necessarily the actual consequences of the behaviour.

Perceived barriers are costs which may stop a person undertaking an activity, these may be barriers to undergoing an activity such as insufficient time; transport difficulties; anticipated undesirable consequences such as insurance problems and negative emotional consequences. In the case of genetic testing for colon cancer, particularly among people who already attend for screening, the short term difficulties of attending for counselling and a blood test are unlikely to be barriers, as colonoscopies are more invasive, however long term consequences may affect uptake. Anticipated affect, measured in conjunction with the TPB may be a particular type of benefit and barrier, although this will not be explored in this thesis, this may add to the explanatory value of this measure.

3.3.2 Perceived Severity and Susceptibility Towards Genetic Testing

Perceived severity is often the least predictive component of the HBM (Sheeran & Abraham 1996). With an illness such as cancer, a ceiling effect is often observed, as most people rate cancer as either moderately or very severe, so there is little

discrimination between participants on this measure. It has been argued that severity needs to reach a certain threshold before it influences behaviours, but once this has been reached, decisions are influenced more by susceptibility than severity (Weinstein 1988). Perceived severity was included in the thesis, despite the possibility that it would not correlate strongly with intention to have a genetic test, as this enables the complete model to be tested.

Some operationalisations of the model have included combining the benefits and barriers components and the severity and susceptibility components to form two predictive variables. There have been problems reaching a consensus on this issue. Weinstein (1988) argues that benefits and barriers may serve different functions rather than being points on a continuum. Benefits may be more hypothetical and based on probability, whereas barriers are often more concrete and certain. Benefits and barriers are themselves multidimensional constructs, comprising practical and psychological implications, as well as efficacy considerations in the measurement of benefits. A composite measure may not accurately capture the different dimensions of these concepts. There are also problems with identifying the best way of combining the measures. Perceived benefits are often subtracted from perceived barriers, however the arguments are more complex for susceptibility and severity. Some have argued that the measures should be added, others that they should be multiplied, and others that susceptibility should be added to the product of susceptibility and severity. In this thesis the components will be used individually.

3.3.3. Previous Research Utilising Aspects of the HBM

The heath belief model has been widely used in various forms to study a wide variety of health behaviours (for a review see Sheeran & Abraham 1995). Two main reviews have been conducted to explore its utility in explaining behaviour. In the first (Janz & Becker 1984) percentages were calculated to reflect the number of times each component of the HBM was significant in the direction predicted. Using this method the significance ratios demonstrated good support for the HBM, with components showing a significant effect in between 65% (severity) and 89% (barriers) of studies. In prospective studies barriers were found to be the most reliable predictors of behaviour, followed by susceptibility, benefits and severity. This approach was criticised by

Sheeran & Abraham (1995) because results do not indicate sizes of any associations, and do not adequately control for differing numbers of participants in different studies.

Using a different approach, Harrison, Mullen & Green (1992) conducted a meta analytical review of the 16 out of 234 papers that met their inclusion criteria. The fact that many studies do not meet these criteria is a reflection of the heterogeneous approaches to measuring the constructs and the lack of continuity in using all components. Harrison et al (1992) converted the results for each construct into a common effect size and then computed a weighted average for each aspect of the model. In this analysis again severity was the least effective component in explaining behaviour ($r = 0.08$), followed by benefits ($r=0.13$), susceptibility ($r=0.15$) with barriers again the most effective component ($r=-0.21$). This analysis did not however examine the combined predictive value of the four components, which may be greater than the individual effects. In addition there was heterogeneity in effect sizes across studies, suggesting that despite the strict inclusion criteria there were design or measurement differences which may have influenced the results of the different studies.

A number of researchers have used the HBM to study genetic testing. Some have used the whole model, whereas others have used only some components or one component of the model. One study (Leonard et al 1995) used all four of the main components of the HBM (benefits, barriers, susceptibility and severity) as well as cues to action, to explore the uptake of genetic testing for cystic fibrosis. Participants were given one of two educational booklets, one with usual information and one with an additional role model example based on the HBM. There was no difference in uptake between those who had read the different booklets, however, people who had the test perceived fewer barriers, and greater motivation (benefits). Perceived risk and perceived severity did not have a direct effect on uptake of the test, but greater susceptibility and greater perceived severity were positively associated with greater motivation for testing and greater knowledge, both of which were positively associated with uptake of the test.

The HBM was used to examine intent to have a genetic test for breast cancer in 329 students (Welkenhuysen, Evers-Kiebooms, Decruyenaere et al 2001). The research measured breast cancer awareness, attitudes, perceived susceptibility, perceived seriousness, perceived benefits, perceived barriers and demographic variables. The

intent measure was dichotomised, comparing those who intended to have a genetic test with those who did not intend to have a genetic test. A logistic regression was used to assess the contribution of the variables. The variables retained in the model predicting *low intent* were low perceived benefits, negative attitudes, having a family history of breast cancer and having more children. The last two findings (that people are less likely to intend to have a genetic test if they have a family history of breast cancer and if they have more children) are contrary to those reported in the rest of the literature (Chapter 2).

The analysis used a stepwise approach to entering variables. In this study the only HBM variable that independently predicted intent was perceived benefits. The study was unable to assess the total contribution of the whole model as the four variables were not all entered together. The study also found that high susceptibility was associated with more negative intentions to have a genetic test. This is contrary to the predicted direction, and that found in most previous research. One reason suggested by the authors for the poor performance of the HBM is that it pays insufficient attention to emotional mechanisms. This will be addressed in this thesis by the inclusion of anticipated affect.

In a general population study of intent to have a genetic test for cancer susceptibility (no specified cancer), higher perceived susceptibility, more perceived benefits and fewer perceived barriers were all significantly associated with intent to have a genetic test (Bosompra et al 2000). In addition to these factors, dispositional pessimism also contributed to the explanation of intent to have a test. The complete model accounted for 34% of the variance in intention. More distal predictors of intent, mediated by the above factors, were age, socio-economic status, family history of cancer and an awareness of the existence of genetic tests.

Another paper explored the application of three components of the HBM (health motivation, susceptibility and severity) to genetic testing for Tay-Sachs (Becker et al 1975). In this situation people who underwent a genetic test reported greater perceived susceptibility of being a carrier than those who did not, they also perceived that being a carrier would be less severe than those who did not have testing did. Health motivation was measured by two questions, the first (desire to have (additional) children)

predicted uptake well, the second (own current health values) did not. The focus was on the health of future children, not personal health, so this may account for the discrepancy. Low severity was associated with greater uptake, which is contrary to the usual hypothesis, that higher severity or a threshold level of severity is required. This apparent contradiction may be because the question examines perceived severity of being a carrier, when a person sees this as less severe they may be more likely to have the test as they see that they have little to lose.

Studies of benefits and barriers to testing have used a variety of methods, either a free response category (participants generate benefits and barriers), set choice categories, (participants rate each benefit or barrier), or nomination of principal benefits and barriers. Other studies have examined the related concepts of pros and cons, within the framework of the transtheoretical model. These will also be discussed.

Barriers to genetic testing for colon cancer were explored in a general population sample together with perceived risk (Smith & Croyle 1995), however the relationship between barriers and intent to have a genetic test was not explored. Barriers elicited surrounded issues of worry, family and economic implications. Other concerns were involved with prevention, however these were more positive actions that participants would want to take on receiving a risk result. In this study high perceived risk did predict higher levels of intention.

Motivation for testing, or benefits of testing have generally centred around issues of children's risk, making screening decisions, reassurance, life style changes and planning for the future (Lerman et al 1994, 1996). Reasons for not wanting a test (barriers) were again insurance concerns, emotional and family reactions, but also concerns about test accuracy and whether cancer could be prevented (Lerman et al 1996). Again the relationships between these factors and intent to have a genetic test were not explored, but in one paper (Lerman et al 1994) high perceived susceptibility was found to be associated with high intent.

In women, some of whom had had breast cancer and others had not, intention to have a genetic test was found to be significantly related to perceived benefits and barriers (Cappelli et al 1999). Those who intended to have a test perceived significantly more

benefits and fewer costs than those who did not intend to have a genetic test. In a logistic regression, having had breast cancer and perceiving few costs emerged as the best predictors of high intent to have a genetic test. Perceived risk was not found to be different between those who intended to have a genetic test and those who did not. Some of these women (those who had had cancer) were given the opportunity to discuss actually having a genetic test. People who attended for this were those who perceived fewer costs to having a genetic test. This study showed that perceived costs or barriers to testing were the best predictors of intent, followed by perceived benefits; perceived susceptibility did not differentiate. This study did not measure perceived severity of breast cancer as this was deemed to be of lesser importance.

In a subsequent paper (Cappelli, Surh, Walker et al 2001), intent was assessed in a general population sample and a sample of women who had at least one FDR diagnosed with breast cancer. Again those who intended to have a test perceived more benefits and fewer costs of testing, but there was no difference in perceived susceptibility. In a logistic regression only low perceived costs emerged as independently predicting intent to be tested, and there was a trend ($p=0.06$) towards higher intent among the women with a family history compared with those without.

In an analysis of the pros and cons of genetic testing (Hughes et al 1997), benefits of genetic testing were seen again as assisting in preventing cancer and aiding screening decisions, as well as providing reassurance and knowledge of children's risk. These benefits were rated as higher by African American women, those with less education and less exposure to information about genetic testing. Barriers or costs were again seen as composed of the effect on the family, emotional reactions, insurance implications, and by predominantly African American women, that cancer is not preventable, and they mistrust modern medicine. Single respondents on lower incomes rated cons as more important. The relationship between these pros and cons and intent or uptake was not assessed, so it is not possible to determine their predictive power or impact on the actual decision to have a genetic test.

A few studies have sought to determine the predictive value of pros and cons within the framework of the transtheoretical model. In one of these (Vernon et al 1999), pros and cons were both found to be correlated with intention. When these were entered

with other variables in a multivariate analysis the cons of testing were no longer significantly associated with intention. Instead intention was predicted by belief that testing would help family members, worry about carrying a mutated gene and the pros of learning the test result. The pros and cons scores were standardised, and a composite decisional balance score was computed by subtracting the cons scores from the pros scores. This was also significantly associated with intention, those who reported more pros than cons were more likely to intend to have a genetic test. This supported the transtheoretical framework that was used in this study.

Another study which employed the transtheoretical model (Jacobsen, Valdimarsdottir, Brown & Offit 1997), found that within first degree relatives of people with breast cancer, mean pros scores were significantly higher and cons scores significantly lower among women who wanted a test as soon as possible (preparation), compared with contemplators and precontemplators. Women who wanted a test as soon as possible saw more pros than cons, the other groups saw more cons than pros. The entire sample was however quite small (74 people) and the smallest group of women (precontemplators) contained only 14 participants. Older age and greater perceived risk was also associated with intention to undergo a genetic test.

Perceived susceptibility and the related concept of perceived risk has perhaps been the most widely studied component of the HBM in respect to genetic testing. Perceived risk or susceptibility to hereditary breast/ovarian or colon cancer has been generally found to be higher than actual risk, and is more predictive of intent than actual susceptibility (Stuewing et al 1995b, Glanz et al 1999). Despite the high level of perceived susceptibility a substantial number of people cannot accurately report their own personal risk, even after individual genetic counselling and risk calculation (Watson et al 1999).

A further paper has been cited as examining genetic testing (Hoogewerf, Hislop, Morrison et al 1990), however on examination this was found to report on Faecal Occult Blood screening which is not genetic testing. This study did not explore perceived susceptibility to colon cancer, however it did examine the person's perceived severity of high blood pressure, ulcers and heart disease, to relate these to test usage. Although the test requires that a person undergoes a special diet and does not take

aspirin for a short time before the test, the relevance of the detailed analysis of perceived severity of other illnesses was not explored in this paper.

In studies utilising the HBM, most have found support for the role of perceived benefits, perceived barriers and perceived susceptibility in predicting the decision to have a genetic test. There has been no consensus about which of these factors are most important, however, according to the transtheoretical model, the importance of the related concepts of pros and cons is influenced by the stage a person is at in deciding whether to have a genetic test or not. The evidence does not indicate that any one of these concepts is the most important. Perceived severity has almost universally been excluded from the studies in this area to date. This concept may be found to be unrelated to genetic testing, particularly for cancer, which most people would regard as a severe disease, however without including this concept, the complete model cannot be tested.

3.3.4 Current Thesis

In this thesis, four of the concepts of the HBM will be measured – perceived benefits, perceived barriers, perceived susceptibility and perceived severity. Perceived benefits and perceived susceptibility are predicted to be positively associated with intention to have a test, and perceived barriers negatively with intention. If perceived severity is significantly associated with intention then it will be positively associated so that a person who perceives it as more severe will be more likely to intend to have a genetic test to detect a genetic mutation. As previous studies have been inconclusive it is not possible to determine which of these four concepts will emerge as the most important in the final regression analysis.

3.4 Comparison of Models

3.4.1 Previous comparison studies of theory of planned behaviour and health belief model

Despite the extensive use of both models in the field of health psychology few studies have been explicitly compared the two models, although there are a number that have combined the two models. One of the earliest comparisons of the HBM and TRA (Oliver & Berger 1979) demonstrated that the TRA explained 50% of the variance in

intent to have a flu vaccination, compared with the 30-35% explained by the HBM. A study exploring different health behaviours (Mullen, Hersey & Iverson 1987) found that the theories explained different relative proportions depending on the behaviour examined. After accounting for demographics and baseline behaviour, the TRA and the HBM explained approximately equal amounts of variance in measurement of the number of cigarettes smoked (14.7%) and fried food consumption (13.8% and 13.6% respectively). The TRA outperformed the HBM on one behaviour (attempts to quit smoking) explaining 24.7% and 7.9% of the variance respectively. On two behaviours the HBM explained more variance than the TRA – exercise (17.9%/ 9.5%) and sweet food consumption (11.5% / 9.6%).

In a study of medication compliance in women with urinary tract infections (UTIs) (Ried & Christensen 1988), the HBM alone only explained 10% of the variance in compliance, whilst the TRA explained 23% of the variance. When the two theories were combined the resultant model explained 29% of the variance in medication compliance.

In an assessment of the comparative power of the TPB and the HBM (Conner & Norman 1994) to explain screening intentions and behaviours, the HBM and the TPB explained 55% and 52% of the variance in intention respectively. The HBM however contained a larger number of variables (7 compared to 5), thus the R^2 for this model would be expected to be higher. When the two models were combined the proportion of variance explained increased (61%) but non-significantly. The significant predictors in this combined model were benefits, barriers, health value, behavioural beliefs and attitudes. Neither model explained much of the variance in behaviour, and when combined only 5% of the variance was explained.

An exploration of the TRA and HBM (Vanlandingham, Suprasert, Grandjean & Sittitrai 1995) found that components of both models were associated with prior condom use when visiting prostitutes in Northern Thailand. In direct comparisons of the models the TRA was found to be the superior theory, it also classified a higher proportion of the cases correctly. The effect of peers (subjective norm) was found to be the largest influence in this model on behaviour, as measured retrospectively.

The two models have also been combined in studies to produce emergent models that contain components of both. In exploring adherence to different malaria prophylactics (mefloquine c.f. chloroquine and proguanil) on return from foreign travel (Abraham, Clift & Grabowski 1999) a combined model was used. Intention, PBC, attitude, injunctive norms, perceived side effects, perceived susceptibility and perceived severity explained between 39.5% and 50.2% of behaviour, with adherence in the affected region explaining an additional 10.1% of variance for the latter regime (chloroquine and proguanil). In the explanation of intention the combined model performed very well, explaining 65% and 77.1% of the variance in intention for the two drug regimes. The main correlates of intent were perceived behavioural control, perceived side effects, perceived susceptibility and perceived severity. Whilst not providing a direct comparison, this study has provided evidence for the additive value of the HBM to the TPB.

The previous studies have therefore produced somewhat inconclusive results, with the TPB/TRA usually performing marginally better in most studies than the HBM. In studies that have combined the two models, the combined model explains more variance in intention, indicating that there may be components of each model which explain unique variance.

3.4.2 Differences and Commonalities in the Models

The theory of planned behaviour and the health belief model have both been used extensively in the health psychology literature. It is clear from using combined models that there is both shared and unique variance between the models. Both models investigate the person's own evaluations of genetic testing. In the HBM this is operationalised as the perceived benefits and barriers towards them undergoing genetic testing, and in the TPB attitudes are explored - i.e. their overall evaluation of the behaviour.

The influence of attitude, or the balance of benefits and barriers, may be important factors for a person in deciding whether to undergo testing. Genetic screening remains an emotive issue, particularly in connection with prenatal testing, although many people do not fully understand the issues involved. Those who are aware of a particular disease in their family may be better informed, however, without a clear explanation

they may still not grasp the implications of testing, or may hold misinterpretations of the information that they have received. Without fully understanding the issues involved it might be difficult to form a strong opinion about testing based on fact. This raises the possibility that decision making may be based less on concrete factors such as benefits and barriers, but more on general measures of attitudes, and emotional evaluations such as anticipated affect. There are clearly differences between the benefits and barriers in the HBM and attitudes in the TPB, however it is at this point that the two theories are most closely related, and it is expected that shared variance would occur when these three variables are all in the model.

At this point the models diverge. The TPB focuses on the person's perception of what other people would want them to do (subjective norm), and whether they believe that they can actually carry out the behaviour (perceived behavioural control). Perceived behavioural control is hypothesised to influence not only the intention to undergo testing, but also whether the person actually undergoes testing. These variables are not adequately measured in the health belief model. The desire to please others may be construed as a particular benefit or barrier to undergoing an activity, but is not explicitly included in the model. Perceived behavioural control is not measured in the health belief model, and may be particularly important in the decision to have a genetic test that is not under volitional control. Perceived behavioural control could be a specific example of a barrier to testing, but again is not explicitly tested in the HBM for which there is no standardised format beyond the main variables. These two parts of the theory of planned behaviour would therefore be expected to continue to explain unique variance when the HBM is entered into a model.

The HBM introduces two concepts that are not included in the TPB – perceived susceptibility to the disease and the perceived seriousness of the disease. Perceived susceptibility might also play a role in the decision to undergo testing, as a person who does not perceive themselves to be susceptible to a rare disease in theory should be unlikely to request testing for it. This has been supported in research reported so far, as intention is correlated with perceived susceptibility, however even when informed that their risk of hereditary colon cancer was very low, many people in the general population persist in their desire to have a genetic test (Graham et al 1998). The role of perceived severity of the disease, especially with regard to cancer, as discussed

previously may not be particularly useful, as there is often little variation in this predictor variable. Although not explicitly explored within the TPB, these factors may contribute to the formation of a person's attitudes, although it is most likely that perceived severity and perceived susceptibility will emerge as distinct factors explaining unique variance in intent to have a genetic test.

There are therefore commonalties between the two models, and distinct differences, so a comparison of these two models is appropriate to explore the actual influences on intentions to have a genetic test. These models cannot be regarded as all-inclusive. Clearly a general model which aims to describe the uptake of all health behaviours (as these models do), cannot be expected to cover factors unique to certain behaviours. In order to identify other important correlates of intention other measures will also be taken to explore what additional effect these might have on the variance explained by each model.

3.5 Uncertainty Orientation

One theme that has occurred repeatedly in the research concerning genetic testing is individuals need for certainty and the desire to resolve unwanted uncertainty in relation to their genetic status. Resolution of uncertainty could be seen as a benefit of undergoing a genetic test, however this is only one benefit, and it might not have a large influence on the overall measurement of benefits. Rather than the resolution of uncertainty being just a benefit, it may actually reveal an underlying personality factor, which may discriminate between those who want to know, and those who don't want to know. Some people may see few clear advantages or disadvantages, and in the case of a general population sample they may perceive a very low susceptibility, however despite the lack of other clear benefits, they may 'just want to know'. Other individuals in the same situation may want to act more 'like an ostrich', and not want to know, even if they perceive themselves as susceptible and they can see other benefits.

A related concept that has been explored in the health psychology literature is monitoring and blunting (Miller 1987). 'Monitors' are characterised as people who scan for and amplify threatening cues – looking for any negative aspects of information or experience, whereas 'blunters' distract themselves from any such experiences. This

concept has been applied to genetic testing in people who had colon cancer (Vernon et al 1999), but no difference was found between those who wanted to receive their result and those who did not on either the monitoring or the blunting scale. These people had already given a blood sample, so their decision not to receive the result may have been based on other factors. Although this concept is clearly applicable to both the uptake and impact of genetic testing, the current thesis took a slightly different approach.

The concept examined in this thesis is the extent of desire of an individual to resolve uncertainty. This has also been variously described as 'intolerance of ambiguity' (Budner 1962); 'tolerance of ambiguity' (Furnham 1994); 'need-cognition' (Rydell & Rosen 1966); 'need for cognitive closure' (Webster & Kruglanski 1994); and 'intolerance of uncertainty' (Freeston, Rheaume, Letarte et al 1994). This concept has been measured using different scales, which seem to reflect a multi-dimensional concept, however this may be an artefact of the scales developed. The aspect of ambiguity tolerance explored in this thesis is the desire to reduce or eliminate uncertainty in order to resolve emotional or cognitive conflicts associated with knowing or not knowing, specifically in relation to medical situations.

Previous work (Furnham 1994) has examined the factors measured in four measures of ambiguity tolerance, and has found that they measure diverse concepts. From the four scales, 21 factors were derived including measures of conservatism, philosophy, and adventurousness. Even within scales, many factors emerge (e.g. Budner 1962 – 4 factors; Rydell & Rosen 1966 – 6 factors), and the internal reliability is often low (e.g. Budner 1962 - α= 0.49). Some of the scales examined also contained items which it was felt may be difficult for some respondents to identify with or respond to. Examples of such items are:- 'it is always better to have a definite course of action than to be vacillating' (O'Connor 1952); 'if I were a doctor, I would prefer the uncertainties of a psychiatrist to the clear and definite work of someone like a surgeon or X-ray specialist' (Rydell & Rosen 1966); 'Mysticism is too abstract and undefined for me to take it seriously' (Norton 1972). These questions may have caused confusion in people who were responding to a questionnaire on genetic testing, as they lack face validity and real-world applicability. In a different approach to the measurement of 'uncertainty orientation', (Sorrentino, Roney & Hanna 1992), people were presented with sentences to complete in a projective measure of this construct, for example 'Two persons are in

a laboratory working on a piece of apparatus.....'. This approach would have been difficult to implement in a postal questionnaire, and again may be more difficult for a general population sample than an academic one.

Despite the lack of a good questionnaire that is specifically related to medical uncertainty (which might be a field in which fewer people are willing to tolerate uncertainty), this concept has been explored in relation to genetic testing (Croyle, et al 1995). This study examined intent to have a genetic test for breast cancer in a general population sample of students. The study included two sub-scales of the Need For Closure Scale (Kruglanski, Webster & Klem 1993) – Preference for predictability and Discomfort with ambiguity (17 items). The first measure examined people's preferences for predictable situations for example when going for dinner and socialising. The second examined people's reactions when other people appear to be inconsistent in what they do or say.

In this study one group of participants was given standard information about breast cancer, genetic testing, and possible early detection options, the other group received this, and information highlighting the residual risk of sporadic cancer for a woman who receives a low risk genetic test result. The results showed a high level of interest as found in other studies. When the control and experimental groups were compared, in the control group those who had a high need for certainty reported much higher interest levels, but those in the experimental group reported a much lower interest. Those who reported a low need for certainty reported interest levels lower than those with a high need for certainty in the control group, but higher than those with a high need for certainty in the experimental group. This highlights again the differences between monitoring and blunting, as people who have a low need for control are not avoiding information about their risk, the average level of interest in this group is still over 70 (on a scale 0-100), whereas blunters would avoid seeking such information. It is likely that monitoring and blunting and dislike of uncertainty are obliquely related constructs.

In this thesis a measure of dislike of medical uncertainty was used, this was more specific to medical tests than other scales. The specificity was important as uncertainty reduction in medical situations may be different to the desire to reduce uncertainty for example in more social situations (e.g. Kruglanski et al 1993). The scale used

questions such as 'I would rather live with uncertainty than find out I was going to develop a disease' and 'I would rather have a medical test and be certain about my future health, even if the result is bad news'. This was hypothesised to be positively related to intent to have a genetic test, with people who dislike medical uncertainty being more likely to intend to have a genetic test.

3.6 Other constructs

Other variables measured in this thesis included cancer worry, anticipated reassurance from genetic testing compared with other screening, anxiety and depression.

Cancer worry has been widely hypothesised to be related to intent and uptake of genetic testing for colon cancer. This concept has been measured in a number of ways. One approach has been to use a modified version of the Impact of Events scale (Horowitz, Wilner & Alvarez, 1979) to measure the degree to which a person has intrusive thoughts about the target disease. Another way is to determine the extent to which the thought content is distressing, interferes with daily life and is difficult to control (Kent, Howie, Fletcher et al 2000). One measure which has been increasingly applied not only to cancer in the setting of genetic testing, but more widely, is the cancer worry scale.

Most studies have found that high cancer worry is associated with a higher intent to have a genetic test (Croyle & Lerman 1993; Graham et al 1998; Durfy et al 1999; Petersen et al 1999, Glanz et al 1999; Vernon et al 1999). This has not been universally found (Meiser, Butow, Barratt et al 2000), and it has been suggested (Valdimarsdottir et al 1999) that rather than a linear relationship, there may be a bell-curve relationship between cancer worry and intent. Many studies have contacted people who are currently affected by cancer (e.g. Vernon et al 1999), or people who currently have affected family members (Glanz et al 1999), this may lead to higher reported levels of cancer worry, as cancer is more salient to these individuals.

Little has been published about the final aspect that will be examined as a potential correlate of genetic testing – anticipated reassurance. As most of the participants in the studies in this thesis currently receive clinical screening by colonoscopy or faecal

occult blood test, the relative value of these compared with genetic testing may be an important factor in determining interest. Following a clear genetic test, most people will be discharged from the screening service, as they are no longer considered at high risk. The relative anticipated reassurance obtained from current screening as compared with genetic testing may indicate that those who believe that genetic testing is more reliable are more likely to intend to have genetic testing that those who value clinical screening more highly.

There has been a reported reluctance among people who are found not to be at high risk of FAP to relinquish screening following their genetic test result (Michie et al 1996). This has been suggested to be because either the perceived threat of FAP has been unaltered, or colon cancer screening has become a strongly valued and reinforced activity. An alternative explanation may be that that people are aware that there will remain a residual risk of bowel cancer due to environmental factors. These participants have already invested time in an unpleasant activity. If they were then to cease the screening, but later develop a sporadic cancer this could be psychologically disturbing as well as clinically threatening. They will have gained nothing for their early investment. This anticipated comparative reassurance will be explored using two questions, comparing anticipated reassurance from a clear genetic test with both a clear colonoscopy and a clear FOB test.

3.7 Summary of Theoretical Orientation

The thesis will therefore investigate two main models - the TPB and the HBM. Additional concepts will be introduced following these two models to determine whether these general models provide sufficient explanatory value, or whether there is benefit to be gained from adding more disease specific variables (Chapter 4). The emergent correlates of intent may either be ones that could be applied to a wide range of disease models (e.g. uncertainty, cancer worry), or ones that are specific to this disease model (e.g. comparative reassurance). These correlates will also be explored separately in men and women, utilising the more even distribution of risk in men and women in this sample to discover whether genetic testing will have a differential impact on the different genders (Chapter 5). Once the correlates of intent have been established, the stability of these variables, and the causal relationships within the

theory of reasoned action will be explored in a follow-up study conducted a year after the initial study (Chapter 6).

These models will be explored in different subject groups, to determine whether these models can be applied in a more global way, and in different diseases. The fourth study (Chapter 7) will examine how these factors vary between people who are at risk and their partners, to examine the role of actual norms as well as perceived subjective norms. In the following study people who have already had cancer will be compared with those who have not, to explore the impact of personal history in addition to family history on intent to have genetic testing.

As genetic technology advances, more disorders may be tested for, and more diverse subject groups will be involved. This has already happened in the movement from a well-defined group of people who had a family awareness of their risk of HD (a discrete disease), to the application to cancers which are both genetic and sporadic, and where family awareness may be lower. As testing techniques improve, people who would not have considered themselves at risk of a genetic disorder will need to form opinions about genetic testing. By asking a sample drawn from a general practitioner's list in the sixth study, the views of genetic testing in the wider population can be explored.

Many more diseases are also being identified as having a genetic component that can be tested for. The decision is increasingly going to be not just testing to determine future risk of incurable diseases, but testing to provide indications of screening strategies and lifestyle changes. Colon and breast cancers provide better models for genes which predispose rather than cause disease, than HD does. In the final study, therefore correlates of intent to have genetic tests for these two diseases will be compared, to establish whether there is a common model which can be used as a basis for exploring more genetic disorders.

This thesis will therefore explore psychosocial issues surrounding genetic testing for colon and breast cancer, in different groups of people, to determine the appropriateness of established health models and other variables in explaining intention to have a genetic test.

Chapter 4

Psychosocial Aspects of Genetic Testing For Colon Cancer in Asymptomatic Individuals with a Family History

4.1 Introduction

The first study examines the correlates of intention to have a predictive genetic test for colon cancer in people who have not had colon cancer themselves, but whose first degree relatives have.

Intent to have genetic tests has been explored for a number of years with respect to a range of diseases including Huntington's disease, breast cancer and colon cancer (for full review see Chapter 2). This research has identified a number of different factors that may be related to intent to have a genetic test for colon cancer in diverse populations. Most studies have identified demographic factors that discriminate between those who want testing and those who do not (e.g. age, gender, ethnicity). These studies are not always consistent (e.g. Lerman et al (1996) and Petersen et al (1999) found women were more likely to want a test, but Glanz et al (1999) found no effect), and are occasionally contradictory (Kinney et al (2000) found younger women more interested whereas Glanz et al (1999) found older women more interested).

In addition to demographic factors, some studies have also found that perceived risk (Glanz et al 1999) and cancer worry (Petersen et al 1999 & Glanz et al 1999) are also associated with increased intent to have a genetic test for colon cancer. These studies have revealed some interesting initial information about the likely profile of a person intending to have a genetic test, however on the whole there is paucity in the application of existing socio-cognitive theory used in examining the predictors of intent. These studies have also predominantly contacted fairly low-risk individuals - many participants have only one affected first degree relative, whose cancer may be sporadic. In addition the people contacted are often either self-referred to the project (Kinney et al 2000) or are contacted whilst their relative is undergoing treatment for colon cancer. These people may have a higher level of cancer worry than the majority of people who

are at risk of cancer whose relatives may have had cancer some or many years previously.

This study will address these issues, in addition to the factors already shown to be associated with intent to have a genetic test (age, gender, risk perception, cancer worry). Two theoretical frameworks will be employed. The health belief model (see Chapter 3) has been used in some studies of genetic testing for cancer (e.g. Bosompra et al 2000, Smith & Croyle 1995, Cappelli et al 1999), but most studies do not evaluate the power of the four main components (barriers, benefits, susceptibility and severity) in predicting intent or uptake of genetic testing. The theory of planned behaviour, although widely used in other areas of health psychology, has been infrequently applied to the issue of genetic testing. In this study these two main socio-cognitive models will be compared to determine which best explains the variation in intent, and whether the other model explains additional variation.

Additional factors will also be included in this study (anticipated affect, cancer worry, attitude towards medical uncertainty, comparative reassurance of genetic testing and clinical screening, anxiety, depression). These factors are all included because previous research (e.g. cancer worry) has identified that it may be influential in determining intent or there is a theoretical reason for including it in the study (e.g. attitude towards medical uncertainty – see Chapter 3).

The sample has been carefully chosen to include people at various levels of risk of colon cancer, to determine whether clinical risk is a factor in influencing intent. This may either be via increasing perceived susceptibility, or as an independent effect. The sample includes people who have a strong chance of having a genetic test in the near future, but also a sample of people with only one first degree relative with a late cancer onset. This latter group is more comparable to the samples used in previous studies.

These analyses only include people who have not had colon cancer so a genetic test would predict whether they are likely to develop cancer in the future. Affected individuals were not included as for them genetic testing may have different implications, as it is seen as confirming the person's status as a gene carrier. The

affected person is likely to already be aware that they are likely to be a gene carrier. For people who have not had cancer the outcome of the test is less predictable. Comparisons between affected and unaffected people with a family history of colon cancer will be made in a later chapter (Chapter 8).

This was originally planned as the first stage in a longitudinal study, however few patients have been offered a test so it is not yet possible to explore the relationship between intention and behaviour or the correlates of intention. All the data reported in this thesis are collected prior to any offer of a genetic test.

4.2. Aims

The aim of this study is to determine the relative contribution socio-cognitive models, other psychological variables and demographic correlates have in explaining variance in intention. In addition anticipated actions following screening were also examined to explore what may be the likely effect of a test result not only on emotions (anticipated affect), but also on behaviour.

4.3. Hypotheses

- The theory of reasoned action (attitudes and subjective norms) will explain a significant amount of the variance in intention to undergo a genetic test for colon cancer.
- The theory of planned behaviour (theory of reasoned action plus perceived behavioural control) will account for additional variance.
- Anticipated affect will explain variance in intention in addition to that explained by the theory of planned behaviour. High anticipated negative affect if the person does not undergo genetic testing will be positively correlated with intention to have a test. High anticipated negative effect if the test is positive will be negatively correlated with intent to undergo testing.
- Within the health belief model, high perceived benefits, susceptibility and severity will be positively correlated with intention, and high perceived barriers will be negatively correlated with intention. Overall the theory of planned behaviour will explain more of the variance in intention than the health belief

model, however perceived severity and perceived susceptibility will explain variance in addition to that explained by the theory of planned behaviour as these concepts are not captured by this theory.

- Other variables - i.e. high cancer worry, high perceived likelihood of carrying a deleterious gene, higher anticipated reassurance from a genetic test and high dislike of medical uncertainty will all be positively correlated with intent to undergo testing, and will contribute variance in addition to that explained by the theory of planned behaviour.
- Previous studies of genetic testing have been inconclusive in their analysis of demographic correlates of intention. No hypotheses are made about the effect of demographic variables on intent to have a genetic test. Gender differences have been observed in relation to genetic testing for breast cancer, with women being more likely to intend to have a test. It is unclear whether this is due to the different risks for each gender, or differences in the attitudes of men and women to genetic testing. Gender will be explored in more detail in a later chapter (Chapter 5).

4.4. Method

4.4.1 Procedure

Patients were contacted who were registered with St Mark's Family Cancer Clinic as being at risk of developing colon cancer. All participants have at least one first degree relative affected by colon cancer, but not FAP type. The clinic is funded as an Imperial Cancer Research Fund research clinic in North London. Most patients live in London and the Home Counties, however a few participants live further away but have historical or family links with the clinic. Patients are offered regular screening options, dependent on their estimated risk of developing colon cancer. Individuals with more than one affected relative, or an affected relative under 45 are offered colonoscopies every 1 to 5 years, individuals with only one affected relative over 45 receive yearly Faecal Occult Blood (FOB) testing kits. Some of these individuals may have given blood for research purposes to investigate the genetic basis of colon cancer, but none of the participants had been offered a clinical genetic test.

The data for this study was collected between September 1998 and March 1999. Ethical approval was sought and obtained from UCL/UCH Medical Ethics Committee and Harrow Research Ethics Committee (Appendix D).

Questionnaires (see Appendix A) were sent to all the participants with a covering letter and a freepost envelope for the return of the questionnaire. Reminder letters and questionnaires were sent after 3 months. In total 743 questionnaires were sent out, 17 were returned by the Royal Mail – recipient unknown, and 5 had died, this left a total of 721 to account for. 516 questionnaires were returned (71%) in total by the end of the data collection period. The proportions returning questionnaires from the two high risk groups (71%) were similar to those returning them from the lower risk group (72.2%). The only data available on non-attenders was their gender. The original list contained 480 women (66.6%), and 241 men (33.4%), and 22 unidentified. This reflects the clinic population, with men being less likely to register and receive screening than women. The sample that responded had very similar proportions of men and women as the population sampled (69% female, 31 % male). There is no response bias for this questionnaire in terms of gender, however these findings indicate that gender selection had occurred prior to registration with the clinic. The sample therefore is representative of the clinic population in terms of gender, but does not represent the general population on this variable.

4.4.2 Materials

The colon cancer study was informed in the questionnaire design by a parallel project examining intent to have a genetic test for women with breast cancer. It was planned that the two studies should be as compatible as possible to facilitate this comparison. The questionnaire was developed using identical wording and response categories where there were planned comparisons.

An elicitation study was also conducted, to determine whether there were any additional factors that were of concern to individuals at high risk of colon cancer, which had not emerged in the development of the questionnaire for women at risk of breast cancer. This study recruited 21 individuals attending for colonoscopy who were registered on a database at St Marks Hospital North London. These individuals were then excluded from all further data collection. Participants answered 12 open-ended statements about

perceived benefits, barriers, advantages, disadvantages, normative beliefs and anticipated affect. These data were collated and categorised. Few novel topics arose more than once. From this study 'Motivation to adopt a healthier lifestyle' was added as a benefit. This and related topics arising from this study were also explored in a section examining the anticipated effect a test result would have on subject's behaviour.

The responses to these questions were used to design the main questionnaire (Appendix A), using standard measures where available, and designed in parallel with the breast/ ovarian cancer study to facilitate comparisons. This was given to a general population sample to determine comprehension prior to the main study. Subsequent questionnaires are based on this questionnaire, including the follow-up control study, the partner's questionnaires, and the general population questionnaire that was informed by this study.

4.4.2.1. Intent

Intention to undergo testing was the main outcome variable of this study. This has proved a difficult variable to measure due the high interest in undergoing genetic testing, leading to little variability (Croyle & Lerman 1993; Smith & Croyle 1995). Both a five point and a nine point scale were used to measure intention, however both variables were very skewed, with most people responding that they definitely intended to have a genetic test. The measures were highly correlated with each other ($r=0.78$, $p<0.0001$). The measures were too skewed to be satisfactorily transformed - the transformed variables were still very skewed, and the results of the analysis were not altered by the transformation. It was decided to use the five point scale as a categorical scale in an ordinal analysis, and to compare this with using this variable (despite its limited variability and skewness) in a linear analysis. The five point scale was chosen in preference to the nine point scale as this is most closely related to measures used by other researchers in the field. The question used was 'Would you have a genetic test, if you were offered it? (*yes, definitely, yes probably, unsure, no, probably not, no, definitely not*).

4.4.2.2 The Theory of Planned Behaviour

The three components of the theory of planned behaviour were measured using a standardised format. The subscales all had acceptable scale reliability co-efficients, so summary scores were used.

General attitude scores were rated on three, five-point semantic differentials – wise-foolish, desirable-undesirable, good-bad. It was decided not to use a more indirect method of assessment, as in a previous study on interest in testing for genetic susceptibility to breast cancer (Bish et al 1998), this added little to the explanation of variance in intention, and some aspects of this are covered by the assessment of benefits and barriers (see Health Belief Model). The three attitude items were averaged to give a scale of 1 to 5 *(1-negative attitudes, 5 positive attitudes)* (Cronbach's $\alpha = .89$).

Subjective norms were measured using five statements for which participants had to state the degree to which they agreed or disagreed with them *(strongly disagree/disagree/unsure/agree/strongly agree)*. The first item was a general subjective norm measure, the next three items determined the normative beliefs of others specified as 'partner, family and friends'; the final item asked whether they thought other relatives would have the test (behavioural norm). These five items were all highly correlated ($0.5<r<0.87$, $p<0.001$, $n=318$). A principal components factor analysis was carried out to determine the factor structure of these five items to determine whether they were measuring the same concept. This extracted only one factor with an eigenvalue of 3.7 and a shared variance across the five measures of 74%. Exploratory analyses showed that using all five measures instead of one summary score did not affect the relationship with intention, except to decrease the power of the analysis. The five measures were therefore averaged to give a theoretical range of 1-5 *(1 – perception that norms were strongly against testing, 5- perception that norms were strongly for testing)*. Using the five measures as one scale means that there is greater reliability and power as opposed to using the measures independently. For people who reported no partner, the scores were averaged over the four questions that were applicable. Internal consistency of Subjective Norms (5 items) scale was good -Cronbach's $\alpha = .92$.

Perceived Behavioural Control was measured using three items. A fourth item was dropped after it was decided that the wording confused the issue of behavioural control with intent. The three items were 'Whether or not I have the genetic test is entirely up to

me' *(strongly disagree/disagree/unsure/agree/strongly agree)*; 'In general how difficult do you think it would be for you to have the genetic test' *(extremely difficult/fairly difficult/not very difficult/not at all difficult)*; and 'How much control do you feel that you have over whether or not you have a genetic test?' *(no control/some control/a lot of control/ complete control)*. Two of these items were on a four point scale and the third on a five point scale, this is reproduced from the breast cancer study, and these scales used for reasons of consistency and to facilitate comparisons. The items were averaged as before, yielding a scale from 1-4.3 *(1- no perceived behavioural control, 4.3- high perceived behavioural control)*. The different scales mean that the four point scales have a marginally greater influence on the final score than the five point scale. A factor analysis extracted only one factor. The internal consistency for this scale was not as high ($\alpha = 0.62$), indicating that this construct may not have been so reliably measured as the others have.

4.4.2.3 Anticipated Affect

Questions were asked about anticipated affect in response to various outcome scenarios with respect to genetic testing. The three scenarios used were anticipated affect in response to not having the test, anticipated affect in response to receiving a high risk result, and anticipated affect in response to receiving a risk result indicating that they are at low (general population) risk of colon cancer. All responses were measured on four point scales to indicate the degree to which people thought they would experience the various reactions *(not at all/ a bit/ fairly/ extremely)*. The Cronbach's αs for the first two scenarios were high (0.84 and 0.73), so these were used as 6 and 8 item scales respectively, with the resulting scales averaged to give ranges of 1 to 4. On the first scenario (with 6 possible reactions), a low score (1) indicated that participants anticipated low levels of negative feelings if they decided not to have a genetic test. On the second scenario (with 8 possible reactions), a low score (1) indicated that participants anticipated low levels of negative feelings if the test showed that they were at high risk. The inter-item correlations for the final scenario were poor, and a factor analysis revealed two factors emerging. The first consisted of five negative feelings (guilty, depressed, worried, regretful, angry), this measure (Anticipated Affect negative feelings) demonstrated good internal reliability ($\alpha = 0.77$). A low score indicated low anticipated level of negative feelings. The second factor included four positive or surprised feelings (relieved, surprised, hard to believe, happy), this measure (Anticipated

Affect positive/surprised feelings) yielded a lower alpha value (α = 0.61). On this measure a low score indicated a low anticipated level of positive/ surprised feelings.

4.4.2.4 The Health Belief Model

Four components of the Health Belief Model were measured - Perceived Benefits, Perceived Barriers, Perceived Severity and Perceived Susceptibility. Perceived Benefits and Perceived Barriers were assessed by measuring how much participants agreed with statements of perceived barriers and benefits derived from the responses of 21 high risk participants during a qualitative elicitation pilot study and from the elicitation phase of the breast cancer study. There were six possible perceived benefits (α = 0.73), and three perceived barriers (α = 0.61). All responses were measured on a five point scale *(strongly disagree/disagree/unsure/agree/strongly agree)* and averaged to give a range of 1-5 for each scale.

Perceived susceptibility was measured by asking:- how likely the person thought they were to carry a mutated gene *(extremely unlikely/fairly unlikely/unsure/fairly likely/extremely likely)*; whether they thought that they would develop colon cancer at some point in the future *(strongly disagree/disagree/unsure/agree/strongly agree)*; their perceived personal risk of developing colon cancer *(1 in 75 or less/ 1 in 50/ 1 in 25/ 1 in 12/ 1 in 4 or greater)*; and the difference between their perceived personal risk and their perceived general population risk (this was based on quintiles of perceived difference, with approximately 20% of the respondents in each category *(1- lower risk than population, 2- same risk as population, 3- slightly more at risk than the population, 4- somewhat more at risk than the population and 5- considerably more at risk than the population)*). These components of perceived susceptibility were averaged to give a theoretical range of 1 -5 *(1- low perceived susceptibility, 5- high perceived susceptibility)* (Cronbach's α = 0.72).

Perceived severity was measured by asking participants how serious, how curable, and how much they thought colon cancer would affect their lives. Responses were on five point scales *(strongly disagree/disagree/unsure/agree/strongly agree),* which were averaged to give a theoretical range of 1-5 (Cronbach's α = 0.55). This scale reliability was low, and indicates that either this concept was poorly measured, or the questions measure a more heterogeneous concept than 'severity'. Removing items from the scale

would not have produced a more acceptable level of reliability. This will limit the conclusions that can be drawn about this measure.

4.4.2.5 Cancer Worry

Cancer Worry was measured using the Cancer Worry Scale (Lerman, Kash, Stefanek et al 1994, Lerman, Trock, Rimer et al 1991). Although this scale was developed in a US sample, it has also been used in a British sample in which its internal validity and factor structure were confirmed (Hopwood & Howell 2001) Six items were used to assess cancer worry - frequency of colon cancer worries (2 questions), impact of worries on mood (2 questions), impact on daily functioning, level of colon cancer concern (Cronbach's $\alpha = .81$). This scale was adapted for the studies in this thesis by replacing the word cancer with the more specific 'bowel cancer'. The reason for making the scale more specific was that people might also be concerned about other types of cancer such as breast or lung cancer. The degree of worry about these other cancers is likely to vary within the sample by gender and smoking status. By making the target cancer more specific, the between subjects error for this variable is reduced. The term 'bowel' cancer was used in preference to the term 'colon' cancer, as this is the term used in the clinic and preferred by participants in the elicitation study.

4.4.2.6 Anticipated Reassurance

In having a genetic test or clinical screening for colon cancer, a person may derive a sense of reassurance when the test is negative. As a person is unlikely to be offered continuing screening if they are found not to carry a genetic mutation, those who anticipate that genetic testing will provide more reassurance than traditional clinical screening should be more interested in undergoing a genetic test. Participants who prefer the reassurance of a clinical test should be less interested. This was measured using two items, the first asking whether a clear genetic test would be more reassuring than a clear Faecal Occult Blood (FOB) test*(strongly disagree/disagree/unsure/agree/strongly agree)*, and the second if a clear genetic test would be more reassuring than a clear colonoscopy*(strongly disagree/disagree/unsure/agree/strongly agree)*. These were not combined as they may have prompted different responses from different groups of respondents.

4.4.2.7 Attitude towards medical uncertainty

Desire to reduce uncertainty is a commonly cited reason for wanting a genetic test. A literature search had not revealed any other measures of this concept in patients. Existing measures of tolerance of uncertainty or ambiguity either did not tap the concept in a clear way (e.g. Budner 1962) or did not have the required specificity (e.g. Freeston et al 1994). In accordance with the principle of compatibility advocated by Ajzen (1988) variables are most predictive when they are specific to the behaviour. Reaction to uncertainty in medical situations may differ from that experienced in non-medical situations. For this reason a scale was developed to measure this concept, which was based on Freeston et al's interpretation of the concept of uncertainty. Eight items that had good face validity were used to measure this concept. The eight items used were:-

'I would rather have a medical test, and be certain about my future health, even if the result is bad news.'

'I would like to know now if I am likely to be ill, so I can get used to the news'

'If I didn't have a medical test, I would always be wondering whether I was going to develop the disease'

'The relief I would get from a good result makes it worth the risk that the result is bad'

'I think it is tempting fate to ask questions about future illness'

'I would rather live with uncertainty, than find out I was going to develop a disease'

'Knowing the result of a medical test would mean I felt more in control'

'It is better to know that I will develop a disease, even if I can't prevent it'

The items were rated on a five-point semantic differential scale (*strongly disagree - strongly agree*). The individual items were all highly inter-correlated with each other and demonstrated good internal reliability (Cronbach's α =0.84) so a summary scale was used.

4.4.2.8 Anticipated actions upon receiving test result

Participants were asked to rate how likely they thought they were to undertake certain actions if they received either a positive or negative result. The actions concerned included health behaviours, screening intentions, family planning and planning for the future. Participants were asked to indicate on five point scales *(no, definitely not/ no,*

probably not/ unsure/yes probably/yes definitely) whether they thought that they would engage in the various behaviours firstly if a genetic test showed them to be at high risk and secondly if a test showed them to be at low risk. All items were used individually rather than using a composite score so that specific intended actions could be examined.

4.4.2.9 Demographic Variables

Demographic variables included age, gender, marital status, number of children, ethnicity, religion, affluence (employment status, housing tenure, car ownership) and educational status. These variables were included because they have all been variously associated with intent or uptake of testing in previous research (Chapter 2).

4.4.2.10 Health Variables

Health variables included subjective health and personal history of cancer (both colon and other cancers). Risk categories were available on all families and were used to determine objective risk categories.

4.4.2.11 Other measures

Other measures were anxiety and depression measured using the Hospital Anxiety and Depression Scale (Zigmond & Snaith 1983). This scale was developed for people who are physically ill, and excludes items such as experiencing headaches and weight loss, which may be caused by an illness rather than by depression or anxiety. Severely psychopathological items are not included as this improves the acceptability and makes the scale more sensitive to milder disorders. This scale has been used with in-patients, out patients and general population controls (Herrmann 1997), and with candidates for genetic testing (Lodder et al 1999). The range of this scale was 0-21, with 8 or above indicating possible and 11 and above indicating probable incidence of anxiety or depression. This scale was included firstly to determine whether the presence of anxiety or depression affects intention to undergo genetic testing. It was also included to assess any effects of genetic testing in the longitudinal arm of the study that is still in progress. Both subscales demonstrated good internal validity (anxiety Cronbach's $\alpha = 0.86$; depression Cronbach's $\alpha = 0.81$).

4.4.3 Participants

4.4.3.1 Selection Procedures

The individuals were receiving regular opportunities to participate in a screening programme and had not been offered genetic testing prior to the study. All participants had at least one FDR who had been affected by colon cancer. There were three original groups of individuals contacted.

The first group (selection group 1) was obtained using an existing list of individuals who themselves had had colorectal cancer, or who had a family member who had. All of these individuals had an affected relative who had previously given blood for research purposes, although it had been made clear that no result would be given. Genetic testing was most likely to be offered to these individuals as the required genetic material was available. These individuals had a risk of between 1 in 3 and 1 in 12 of dying from colon cancer (without screening intervention). All eligible individuals on this list were contacted (n=215), this meant that family members were all contacted, thus some participants were related to other participants.

A second group (selection group 2) was contacted who are also at high risk of dying from colon cancer (1 in 3 to 1 in 12), but have no family member alive or willing to give blood who has had colon cancer. Individuals in this group are unable to have a genetic test in the near future. The original pool of these individuals was substantially larger than the first group (1500 individuals), therefore 195 individuals were selected from the database. The selection was carried out using random numbers, however as the other groups contained family groups, if one individual in a family was selected, their relatives were all also selected until 195 individuals were selected. This group did not differ from the first group in initial analyses, and the participants were not aware of the different classification, or that they were not likely to be offered a genetic test in the near future. This was originally intended to be a control group in the longitudinal study.

A third, low risk group (selection group 3) was obtained from the population of individuals who receive Faecal Occult Blood (FOB) testing kits, and have one family

member who has had colorectal cancer over the age of 45 (risk of dying from colon cancer is 1 in 17). All eligible individuals on the FOB testing programme were contacted (n=333).

The only exclusion criteria were:- anyone who had not responded to the clinic's attempts to contact them for more than five years, individuals under 18, anyone known to the clinic as suffering from a mental illness, and anyone who was known not to understand English. There was no one actually selected who would have been excluded on the last two criteria. It was not possible to contact individuals known to the clinic to be at high risk but who were not actually registered with the clinic (e.g. siblings and children).

4.4.3.2 Subsequent classifications

The methodology above was used to select a group of people for the longitudinal study who were most likely to undergo genetic testing. This selection however led to groups with overlapping risk categories. As no testing occurred, and participants were unaware of the sampling procedure used, these categorisations were not used for most of the analyses in this study. Firstly the sample was divided into those who had already had colon cancer and those who had not had colon cancer. In this first study only the responses of those who had not had cancer were examined, as this investigated correlates of predictive testing. In a subsequent study (Chapter 8) the differences between those who have and have not had cancer are explored. For the purposes of this study asymptomatic participants were classified according to clinical risk as described below.

- **High risk group** - all respondents who met the Amsterdam criteria for HNPCC (see Chapter 1). The clinic adopt the less stringent criteria in categorising patients, which includes those who have a family history of extracolonic cancers such as endometrial cancer. In addition a group of participants were included in this group (under the advice of the clinic staff) who meet all the Amsterdam criteria except the youngest affected relative was over 50. These people were also considered to be at a 1 in 3 or greater risk of dying from colon cancer, however they are unlikely to

develop cancer until later in life (after 50). Participants for whom complete data available - 123.

- **Moderate risk group** - a range of individuals whose family history indicated that their risk of dying from colon cancer was between 1 in 6 and 1 in 12. Participants in this group included those who either had less than three affected blood relatives, or their affected relatives were not FDRs of each other or only one generation was affected. The age of the youngest affected relative was not assessed except where there was only one affected relative. If a person only had one affected FDR the affected relative had to have been affected under 45 years of age to be included in this moderate risk group. Participants for whom complete data available - 59.

- **Lower risk group** - all those who were receiving FOB testing kits who were at 'low' risk group. All these participants had just one affected FDR who was over 45 (1 in 17 risk of dying from colon cancer). Participants for whom complete data available - 175.

4.4.3.3 Sample Characteristics

The sample was a relatively old sample (Mean age =47.49 years; s.d. = 11.51, range 22-78). Most of the sample was married (79%); employed or retired (86.2%); owned their own home (88.8%) and had at least one car (93.4%). The majority (64.9%) of the participants reported more than two years education after the age of 16 (school leaving age). The population reported predominantly Christian religious beliefs - 62% were Protestant; 13.3% Catholic; 6.2% Jewish; 2.3% reported other religious beliefs and 15.5% said they had no religious beliefs, or were atheists or agnostics. The sample was predominantly white (98.2%), reflecting the clinic population from which they were drawn. Due to the lack of variation in this variable, the effects of ethnicity were not explored in this study as there are insufficient numbers of people from ethnic minorities for any analyses.

4.4.4 Statistical Analyses

The results were all entered using Excel 97. SPSS version 9 was used for most analyses, STATA was used for ordinal and linear analyses in the first study. ANOVAS and Chi-squared analyses were used for the initial analysis to determine differences between

intent groups. Correlates of intent were then assessed using regression analyses (linear and ordinal). Intended actions following receipt of a genetic test were compared using t-tests (intended actions if positive result : intended actions if negative result).

4.4.4.1 Missing values

There were a number of missing values, primarily on measures of perceived susceptibility (7.3% missing), where people did not answer, despite being told to guess if they did not know. This indicates the low level of knowledge about their numerical risk of developing colon cancer. This is supported by other literature, which also has found that people are often unable to put a numerical figure on their risk of developing a disease (Hallowell, Green, Statham, Murton & Richards 1997). Other questions that had a large number of missing values were measures of attitude (7.5% missing) and anticipated affect (5.5% missing). On these measures, despite instructions, respondents often only ticked one box in the battery of questions, rather than responding to each item.

The presence of missing values was problematical for subsequent hierarchical analyses as a drop in sample size at each stage leads to a drop in power, and therefore affects the significant contribution of subsequent stages more than the first stage. For this reason participants with missing values on any of the variables in the regression equation were dropped from the analysis. This meant that the sample size was reduced from a potential n= 469 to n=357. This will lead to a subsequent drop in power over the whole analysis, however it means that the loss of power is consistent over all the steps of the analysis.

To investigate the possibility that people who do not complete questions are different from those who do, a series of one-way ANOVAs (analysis by analysis deletion of cases) were run comparing people who had missed some questions with those who had not. These showed that there was no difference between the groups in any of their responses to the questions used in the regression analyses.

4.4.4.2. Family relationships

Genetic testing involves families rather than individuals, and most people registered with St Marks have at least one relative also registered there. In the selection of

participants, people were included from family groups, however this means that the participants are not truly independent of other participants, and some people are likely to hold similar views by virtue of their family relationships. The appropriate unit of analysis in this case is the family, so that analyses are calculated after the error due to family relatedness is accounted for. This was achieved by using the statistical package STATA for the regression analysis, and using family as a clustering variable. There were 272 family groups, so calculations of significance are based on this figure. This may produce a more conservative estimate of significance, but was considered a worthwhile exercise to counter biases due to inter-relatedness of participants.

4.4.4.3. Characteristics of the dependent variable.

The main dependent variable is intent. This was initially measured with two questions, the first was on a nine point scale, and the second on a five point scale. The nine point scale was included because of concern when examining previous studies that a five point scale would not be sufficiently sensitive. Both measures of intention were highly skewed (Skewness –1.07, se 0.129), with the majority of people responding that they intended to have a genetic test for colon cancer. On the five-point scale 55.7% of people said that they definitely intended to have a genetic test, 29.4% said that they probably would have a genetic test, 13.7% were unsure, and only 1.1% (4 people) said they would probably or definitely not have a genetic test. The distribution was not normal, therefore linear analyses with the assumption of normality may give inaccurate results. Even after transforming the intent measure there was still a large degree of skewness, and there was no difference in the results of the regression analyses. It was therefore decided to leave the data in an untransformed state (as this was necessary for the ordinal regression).

The main way this problem has been approached in other papers in the area has been to dichotomise responses into 'yes definitely' compared with all other responses. This approach means that some of the richness of the data is lost, as examination reveals that on the whole there is a linear relationship between intent and other variables. This means that some variables would be significantly associated with intent when the original multi-categorical intent measure is used, but when only the dichotomous measure is used, some of the variation is lost, and so the association is no longer significant.

To illustrate this point, in the case of age, in this sample, when a dichotomous classification is used, there is no significant difference in age between people who respond 'yes definitely' to the measure of intent, and people who give other responses (Table 4.1)

Table 4.1 Age by dichotomous intention variable.

	N	Mean Age	Std. Deviation	F(1, 354)	Significance of F
Yes definitely	199	46.41	10.96		
Other response	157	45.56	11.42	0.504	0.48

Using the three main categories of responses, as opposed to dichotomising the responses, reveals a different pattern of responding (Table 4.2)

Table 4.2 Age by three categories of intention response.

	N	Mean Age	Std. Deviation	F(2, 353)	Significance of F
Yes definitely	199	46.41	10.96		
Yes probably	104	47.15	11.64		
Unsure & no	53	42.43	10.40	3.44	0.033

Here, although there is no significant difference between people responding 'yes definitely' or 'yes probably', the mean ages in both these groups are significantly higher than among people responding that they were unsure about whether to be tested.

The numbers of people responding probably or definitely not intending to have a genetic test were very small (n=3, n=1 respectively). These were therefore classified together with 'unsure'. Although this does lead to some loss of sensitivity, the numbers in these response categories were so small that alone it would not be possible to draw statistical conclusions from the data. The classification of these three groups together will not actually matter for the intended ordinal analysis. The analyses conducted regard intent as a grouping variable – with three groups – unsure and not intending to have a genetic test; probably intending to have a genetic test and definitely intending to have a genetic test.

Ordinal regression analysis enables the modelling of the dependence of a polytomous ordinal response on a set of predictor variables. The analysis does not assume that the response variable (intent) is measured on an equal-interval scale, but rather that it is measured on a number of arbitrary response categories that reflect an underlying continuous variable. This applies to this study, as it is not possible to say that a person

responding that they would probably have a genetic test holds an underlying intent to have a genetic test that is half-way between someone responding yes definitely and someone responding that they were unsure or that they did not intend to have a test. The dependent variable (intent) must be ordered, so it is possible to say that someone responding that they are unsure holds a lower intent to have the test than someone responding that they definitely would have the test.

The analysis was carried out in STATA using the OLOGIT procedure. The resulting coefficients are unstandardised. They were therefore standardised by dividing the regression coefficient for each predictor variable by the calculated standard deviation of the predicted dependent variable, then multiplying this by the standard deviation of the predictor variable. This standardises each coefficient and is equivalent to the Beta coefficient in a linear regression. STATA does not calculate the significance of the change in R^2 after each block, therefore the TESTPARM function was used, to calculate the significance of removing the block from the analysis, which is an equivalent value. The ordinal regression does not use an ANOVA to test the model, but a Wald chi^2 test, as intention is treated as an ordinal variable. A pseudo R^2 is calculated, which is analogous to an R^2 obtained in a linear regression, but does not as accurately reflect the variance explained

This ordinal approach will be compared with using a linear approach to the analysis (linear regression), to determine whether there is any difference in the outcomes using different statistical techniques.

4.5. Results

4.5.1. Demographic influences on intentions to have a genetic test.

Analyses were conducted using the three levels of intention as a grouping variable (Table 4.3). The three levels were used to determine any demographic differences across the three groups. Any variables differing by group would be used in the subsequent hierarchical ordinal regression to determine whether they account for the effect on intention of the social cognitive and other psychological variables.

Table 4.3. Comparisons between intention groups on demographic variables

Variable	Unsure & other N= 53	Yes probably N=104	Yes definitely N=199	Significance Levels
	Frequency (%)			χ^2 , p
Gender				
Male	11(20.8)	37(35.2)	62(31.2)	
Female	42(79.2)	68(64.8)	137(68.8)	3.49 ns
General Health				
Poor	1(1.9)	3(2.9)	6(3)	
Fair	5(9.6)	13(12.4)	26(13.1)	
Good	32(61.5)	59(56.2)	108(54.5)	
Excellent	14(26.9)	30(28.6)	58(29.3)	1.03 ns
Marital Status				
Married/ cohabiting	42(79.2)	77(74)	167(83.9)	
Not married	11(20.8)	27(26)	32(16.1)	4.27 ns
Religion				
Protestant	26(49.1)	66(64.1)	123(62.1)	
Catholic	5(9.4)	14(13.6)	29(14.6)	
Jewish	5(9.4)	5(4.9)	13(6.6)	
Other	4(7.5)	2(1.9)	4(2)	
None	13(24.5)	16(15.5)	29(14.6)	10.89 ns
Deprivation				
Working / retired	45(84.9)	87(82.9)	179(89.9)	
Not working	8(15.1)	18(17.1)	20(10.1)	3.35 ns
Own home	47(88.7)	94(89.5)	182(91.5)	
Renting home	6(11.3)	11(10.5)	17(8.5)	0.53 ns
1 or more cars	52(98.1)	98(93.3)	190(95.5)	
No car	1(1.9)	7(6.7)	9(4.5)	1.83 ns
2+ yrs education after 16	39(73.6)	68(64.8)	134(67.3)	
Less 2yrs education after 16	14(26.4)	37(35.2)	65(32.7)	1.26 ns
Risk group				
Low risk	32(60.4)	49(46.7)	94(47.2)	
Moderate Risk	3(5.7)	25(23.8)	31(15.6)	
High Risk	18(34)	31(29.5)	74(37.2)	10.08 p<0.05
	Mean (sd)			F(df), p
Age	42.43 (10.4)	47.15(11.64)	46.4 (11)	3.44 (2,353) p<0.05
Children	1.4(1.12)	1.53(1.14)	1.8(1.24)	3.51(2,354) p<0.05

*People who are unsure about having a genetic test are younger than the other two groups
*People who are unsure about having a genetic test have a lower average number of children.
*People who are at low risk are more likely to be unsure about having a genetic test.

There were few demographic differences between people in the different response categories of intent. Older people and people with more children were more likely to intend to have a genetic test than younger people and those with fewer children. People in the higher risk groups are more likely to intend to have a genetic test. Age, number of children and risk level will be entered into the regression equation, to determine whether

they can explain some of the effect of the psychological determinants of intention. There was no significant effect of gender on intention in this sample.

4.5.2. Psychological correlates of intention to have a genetic test.

A multivariate analysis of variance was conducted, entering age, number of children and risk group as co-variates (Table 4.4). The three levels of intention were entered as one factor, and the remaining variables were entered as dependent variables. Although most of the variables were skewed, there was a similar pattern in all three groups. The ANOVA is a very robust statistical procedure, particularly with regard to deviations from the normality assumption (Howell 1997 p321). The use of a multivariate ANOVA controlling for covariates means that it is not possible to conduct post hoc tests as there is no longer a true standard deviation, and the means are now reported as marginal means which account for the influence of the covariates. An indication of the likely differences between the groups was found by conducting a separate analysis removing the covariates, and using a Games Howel post hoc test (this test can be used even with heterogeneous variances - discussed below)

Table 4.4. Comparisons between intention groups for psychological variables controlling for age, risk level and number of children.

Variable	1.Unsure & other N= 51		2.Yes probably N=104		3.Yes definitely N=198		F (5,347)	Location of difference
	Mean (Marginal Means)	SD	Mean (Marginal Means)	SD	Mean (Marginal Means)	SD		
Attitude	3.14(3.15)	0.97	4.08(4.08)	0.63	4.73(4.72)	0.54	58.15***	(1:2); (1:3); (2:3)
Subjective Norm	2.92(2.93)	0.62	3.51(3.52)	0.54	4.12(4.11)	0.59	40.95***	(1:2); (1:3); (2:3)
Perceived Behavioural Control	3.11(3.14)	0.59	3.08(3.07)	0.63	3.24(3.24)	0.76	2.27*	not possible to localise
Anticipated Negative Affect if decided not to have test	1.96(1.97)	0.38	2.33(2.35)	0.56	2.62(2.61)	0.69	13.94***	(1:2); (1:3); (2:3)
Anticipated Negative Affect if positive result	2.52(2.51)	0.60	2.20(2.21)	0.50	2.02(2.02)	0.50	9.92***	(1:2); (1:3); (2:3)
Anticipated Negative Affect if negative result	1.09(1.09)	0.19	1.08(1.08)	0.16	1.06(1.07)	0.23	1.63	
Anticipated Positive Affect if negative result	2.57(2.58)	0.60	2.63(2.64)	0.60	2.78(2.78)	0.54	2.66*	not possible to localise
Perceived Benefits	3.34(3.37)	0.49	3.54(3.53)	0.50	3.81(3.81)	0.58	9.59***	(1:3); (2:3)
Perceived Barriers	3.25(3.24)	0.64	2.72(2.73)	0.65	2.31(2.31)	0.63	20.19***	(1:2); (1:3); (2:3)
Perceived Susceptibility	3.01(3.01)	0.87	3.16(3.18)	0.76	3.35(3.35)	0.74	8.48***	(1:3)
Perceived Severity	3.58(3.56)	0.70	3.68(3.69)	0.67	3.63(3.63)	0.76	0.9	
Uncertainty	3.11(3.12)	0.70	3.70(3.7)	0.55	4.21(4.21)	0.64	29.71***	(1:2); (1:3); (2:3)
Worry	9.29(9.2)	1.94	9.44(9.5)	2.4	9.71(9.7)	2.65	1.83	
Anticipated Reassurance GT compared with FOB	2.78(2.78)	0.92	2.58(2.57)	0.78	2.19(2.19)	1.03	4.53***	(1:3); (2:3)
Anticipated Reassurance GT compared with colonoscopy	3.27(3.3)	0.80	3.10(3.08)	0.84	2.83(2.83)	1.07	3.06**	(1:3); (2:3)
Anxiety	6.69(6.51)	4.21	6.76(6.83)	4.21	5.94(5.96)	3.74	2.18	
Depression	2.57(2.6)	3.05	3.45(3.43)	3.00	2.86(2.82)	2.78	1.64	

***p<0.001
**p<0.01
*p<0.05

The analysis shows that there are a number of factors that associated with intent to have a genetic test. Most of these have a linear relationship with intent to have a genetic test. The overall F test was highly significant (Pillais F Trace =9.15(34,664), P<0.001). Levene's test of the equality of error variances indicated that there were a number of variables in which the variances were not equal across all groups. To adjust for the heterogeneity of variance the Welch Procedure (Welch 1951 - see Howell 1997) was used, this adjusts the degrees of freedom and F-value to account for the heterogeneous

distribution of variance, and is more suitable than the solution suggested by Box (1954) when there are unequal sample sizes. This procedure does not, however account for the large number of analyses included in the original multivariate procedure or the covariates, so the degree of significance should still be interpreted with some caution. The Welch procedure showed a different level of significance on only one of these variables[1]. Perceived behavioural control was no longer significant, whereas it had been marginally significant, it was also not significant without the covariates. Due to the marginal nature of this finding, it is not possible to conclude whether the finding from the MANCOVA is a true finding or not, as the Welch procedure does not account for covariates.

Overall the level of positive attitudes was high – even the mean value of the unsure group was above the midpoint of the scale (mean =3.14, s.d. 0.97), scale range 1-5. In the high intent group the mean attitude score was 4.73, indicating a very high level of positive attitudes. Subjective normative beliefs were not so strongly positive as attitudes towards testing, and here the mean value of the unsure group was below the mid-point. In line with the theory of reasoned action, both subjective norm and attitude towards having a genetic test are positively and highly significantly correlated with intent to have a genetic test.

Perceived behavioural control was only marginally significantly related to intention, and the relationship was not linear. People who said that they would probably have the test demonstrated a lower level of perceived behavioural control than people in the other two groups did. The average score for this measure (3.18)(scale range 1-4.3, midpoint 2.15), was above the mid point for all levels of intention indicating that most people in all intention groups perceived the action to be within their control.

Responses to the anticipated affect measures were in the direction predicted. People who intended to have a test reported more anticipated negative affect if they did not

[1] Values from Welch procedure on variables with heterogeneous variance across intention groups:-
Attitudes (F"=91.46, $p<0.001$); Perceived Behavioural Control (F"= 2.1, ns);
Anticipated negative affect if decided not to have test (F"= 42.41, $p<0.001$);
Anticipated negative affect if positive result (F"= 16.93, $p<0.001$);
Anticipated negative affect if negative result (F"=0.63, ns); Cancer Worry (F"= 0.94, ns);
Anticipated Reassurance GT compared with FOB (F"= 11.32, $p<0.001$);
Anticipated Reassurance GT compared with colonoscopy (F" = 6.17, $p<0.01$).

have a genetic test; more anticipated positive affect if they tested negative; and lower anticipated negative emotions if they received a positive (high risk) test result. People who were unsure about having a test anticipated more negative affect if they tested positive (2.52) than if they did not have the test (1.96) (range of scale 1-4). The groups who probably or definitely intended to have a test anticipated more negative affect if they did not have the test (mean 2.33, & 2.62 respectively), than if they tested positive (mean 2.20, 2.02 respectively). Most people anticipated low levels of negative affect, and high levels of positive affect if they were found not to be gene carriers, although again these are linearly related to intention, indicating that people who definitely intend to have a genetic test anticipate more emotional benefits to finding that they were at low risk than other groups.

The components of the health belief model also discriminated clearly between the three intention groups. High intent to have a test was associated with high perceived benefits of testing, low perceived barriers, and high perceived susceptibility. This is in line with the health belief model. The greatest effect was the difference in perceived barriers between the three groups, with the low intent group perceiving more barriers than the high intent group. There was no difference in perceived severity of colon cancer between the three groups. Although in all three groups perceived severity was moderately high (mean 3.64, s.d. 0.73; scale range 1-5), it was not at a ceiling level. These individuals do receive regular screening, so they maybe do not anticipate great problems if they did develop cancer, as they believe it would be caught early.

There was a significant relationship between people's dislike of medical uncertainty and their intention to have a genetic test. People who would rather know in advance about likely illnesses are much more likely to intend to have a genetic test, than those who would rather not know. This finding was true for all the items of the scale, which measured different aspects of dislike of uncertainty.

There was no difference in levels of cancer worry across the intention groups, and overall levels of cancer worry were low (overall mean 9.6, s.d.2.5) (scale range 6-30). This finding is contrary to that reported by a number of other researchers (Vernon et al 1999; Glanz et al 1999; Petersen et al 1999) who found that cancer worry was associated

with intent to have a test. The low levels of cancer worry across the population may indicate that the participants are reassured by their screening and therefore do not think about colon cancer very much.

People who intend to have a genetic test are significantly more likely to think that a genetic test will reassure them more than a faecal occult blood test or a colonoscopy will. Most respondents believe that a genetic test will reassure them more than a faecal occult blood test will (overall mean = 2.39 s.d.= 0.98 scale range 1-5, midpoint 3 (1 - genetic test more reassuring, 5 - FOB more reassuring)). People who definitely intend to have a genetic test reported that it would reassure them more than a colonoscopy (mean = 2.83 s.d. = 1.07, range as above), however those who probably intended to have the test or are unsure, tended towards seeing genetic testing as less reassuring (mean(sd) = 3.1(0.84) and 3.27 (0.8) respectively). There were no differences between the intent groups on measures of anxiety or depression.

4.5.3. Correlates of intention to have a genetic test

4.5.3.1. Hierarchical ordinal regression analysis

A hierarchical ordinal regression analysis controlling for family clusters was conducted to determine the relative contribution of the correlates of intent in explaining the variance in intent. A forced entry block-wise procedure was used, and all components of models were entered to test the sufficiency of the whole model in explaining intention.

The first ordinal regression examined the contribution to explaining intention of the components of the theory of reasoned action (attitudes and subjective norm) at the first step. This was followed by perceived behavioural control, to test the explanatory power of the theory of planned behaviour. The additional explanatory power of anticipated affect was explored in the third step. The fourth step tested whether components of the health belief model accounted for additional variance in intention. The fifth step added attitudes towards medical uncertainty to the equation, which was found in the initial analysis to be highly related to intention. The sixth step included the remaining psychological variables – reported cancer worry, and anticipated reassurance, and the final step included age, number of children and risk category, which were the only demographic correlates of intention (Table 4.5).

Table 4.5 Ordinal Regression testing the sufficiency of the theory of reasoned action and planned behaviour.

Number of observations =357; Number of clusters = 272

Step	Variable	Standardised coefficient	Final Sig^n
1	Attitude	0.297	<0.001
	Subjective Norm	0.245	<0.001
2	Perceived Behavioural Control	0.022	0.961
3	Anticipated Negative Affect if decided not to have test	0.056	0.331
	Anticipated Negative Affect if positive result	-0.029	0.573
	Anticipated Negative Affect if negative result	-0.022	0.612
	Anticipated Positive Affect if negative result	0.058	0.264
4	Perceived Benefits	0.117	0.02
	Perceived Barriers	-0.210	<0.001
	Perceived Susceptibility	0.038	0.479
	Perceived Severity	-0.052	0.198
5	Uncertainty	0.252	<0.001
6	Cancer Worry	-0.100	0.076
	Anticipated Reassurance GT compared with FOB	0.008	0.886
	Anticipated Reassurance GT compared with colonoscopy	0.040	0.407
7	age	0.002	0.73
	Nº children	0.066	0.159
	Risk group	-0.066	0.172

Table 4.6 Ordinal Regression testing the sufficiency of the theory of reasoned action and planned behaviour.

Step	Wald chi^2 (df)	Prob > chi^2	Pseudo R^2	Change in Pseudo R^2	Significance of additional blocks (χ^2,p)
1	117.55 (2)	0.0001	0.3542		
2	117.20 (3)	0.0001	0.3549	0.0007	0.43; p=0.52
3	126.98 (7)	0.0001	0.3677	0.0128	10.32;p<0.05
4	163.66 (11)	0.0001	0.4022	0.0345	23.54; p<0.0001
5	152.90 (12)	0.0001	0.4365	0.0343	22.59; p< 0.0001
6	158.93 (15)	0.0001	0.4446	0.0081	5.03;p=0.17
7	165.81 (18)	0.0001	0.4547	0.0101	5.54; p=0.14

Both attitudes towards having a genetic test and subjective normative beliefs were positively related to intent to have a genetic test, and remained highly significant predictors in the final model. The theory of reasoned action alone explained an estimated 35% of the variance in intention to have a genetic test, however this did not improve with the addition of the theory of planned behaviour. Although none of the

anticipated affect variables were significantly related to intention in the final equation, the block as a whole did significantly add to the explanation of variance in intent (Pseudo $R^2 = 0.3677$; significance of the addition of this block ($\chi^2 = 10.32$;$p<0.05$)).

The health belief model variables added to the explained variance in intention, explaining an additional 3.5% variance in intention (Pseudo R2 = 0.40, significance of adding step 4 $p<0.0001$). Perceived benefits and perceived barriers remained significant in the final model ($p<0.05$ and $p<0.001$ respectively). High perceived benefits and low perceived barriers were associated with higher intention to have a genetic test. Perceived susceptibility and severity did not contribute to the explanation of intention.

Attitude toward medical uncertainty explained an additional 3.4% of the variance in intention, and was significantly related to intention in the final equation. At this stage the model explained 44% of the variance in intention, with this block adding significantly to the model ($p<0.0001$). The final two blocks (Cancer Worry & comparative reassurance, and age, number of children & risk group) did not explain a significant amount of additional variance in intention, and none of the individual variables were significantly related to intention in the final equation.

The final model explained 45% of the variance in intent, and was highly significant ($p<0.00001$, Wald chi^2 (18)= 165.8). The strongest predictor of intention was attitude (standardised coefficient = 0.3), followed by subjective norm and attitude towards uncertainty (Standardised coefficients = 0.254 and 0.253 respectively). The other two correlates of intention were perceived barriers (standardised coefficient = -0.21), and perceived benefits (standardised coefficient = 0.12). The theory of reasoned action components were therefore the strongest predictors of intention, followed by attitude towards uncertainty. Components of the health belief model did explain significant additional variance in intent, indicating that these have additional predictive power, particularly in terms of perceived barriers to acting. When the individual components of the barriers term were explored, it was concern that the test would make them worry more about cancer that was most significantly correlated with intent ($r=0.43$, $p<0.001$), followed by concern about family reactions ($r=0.34$, $p<0.001$) and concern about insurance (0.29, $p<0.001$).

4.5.3.2. Ordinal regression entering health belief model variables first

To test the relative predictive power of the health belief model and the theory of planned behaviour with the addition of anticipated affect, a second ordinal regression was conducted, entering the health belief model at the first step, followed by the other variables (Table 4.7). The health belief model alone explained 21.2% of the variance in intention, but with the addition of the theory of reasoned action, this was increased to 39.3%. The subsequent blocks with the theory of planned behaviour and anticipated affect did not contribute significantly to the explanation of variance in intent. The theory of reasoned action was therefore the best model to explain intention accounting for 35% of the variance in intention. This was not improved by adding perceived behavioural control (theory of planned behaviour), but anticipated affect did explain additional variance. Although the health belief model did not perform as well as the theory of planned behaviour, it did alone explain 21% of the variance in intention, with three of the components (perceived benefits, perceived barriers and perceived susceptibility) significantly related to intention at this stage. In both this and a linear regression, low perceived barriers was the most significant health belief model predictor of high intent, followed by high perceived benefits; both of these were highly significant ($p<0.001$). High perceived susceptibility was still a significant predictor at this stage, but the effect was not as strong as perceived benefits and barriers. Perceived benefits, barriers, and attitude towards medical uncertainty did add to the explanatory power of the theory of reasoned action in the final equation, indicating that the theory of reasoned action was not sufficient to explain intention alone.

Table 4.7 Ordinal regression entering health belief model variables first

Step		Wald chi^2 (df)	Prob > chi^2	Pseudo R^2	Significance of additional blocks (χ^2,p)
1	Health belief model	133.00 (4)	0.0000	0.2116	
2	Theory of reasoned action	155.22 (6)	0.0000	0.3929	71.35; p<0.0001
3	Perceived behavioural control	156.42 (7)	0.0000	0.3936	0.50; p= 0.48
4	Anticipated Affect	155.36 (11)	0.0000	0.4043	7.26; p=0.123

4.5.3.3. Comparison of statistical methodology

The decision to use an ordinal regression was data driven. This is a relatively recent development, and with important implications for psychology, particularly in fields using Likert type scales, which may not have equal intervals. The analysis was therefore repeated using a linear regression analysis to ascertain whether the different methods yield different results.

Although the original response variable had five points, only 3 [2] individuals used the 'no, probably not' category and 1 person used the 'no definitely not category'. An initial exploration of the data indicated that there was little difference in the variance explained by a linear regression analysis using three (Final $R^2 = 0.619$; $F = 36.10$, $p<0.001$) rather than five (Final $R^2 = 0.596$; $F = 36.19$, $p<0.001$) response categories. It was decided to use the three response categories, so that the results would be directly comparable with those obtained from the ordinal regression.

The analysis was a hierarchical linear regression analysis, controlling for family clusters. The statistical package used was STATA, using the REGRESS command, and clustering for family groups[3] (Table 4.8).

[2] 6 people responded 'no, probably not', however three of these participants had missing data for one or more variables, so therefore were excluded from the regression analysis.

[3] With the clustering option, robust standard errors are used, therefore the F test is no longer used, rather the Wald test is used based on the robustly estimated variance matrix. R2 is still a good indicator of the fit of the model, but should not be used to obtain F statistics. Adjusted R2 is not generated with this option. See STATA manual Vol 3(P-St) pages 165-166.

Table 4.8. Linear Regression of intention onto psychological and significant demographic correlates.
Number of observations =357; Number of clusters = 272

		Regression of intent onto psychological variables					
		Ordinal Regression			Linear Regression		
Step		Final standardised coefficient	Pseudo R^2	R^2 change (sig^n)	Final Beta	R^2	R^2 change (sig^n)
1	Attitude	0.297***			0.334***		
	Subjective Norm	0.245***	0.354		0.188***	0.511	
2	Perceived Behavioural Control	0.022	0.355	0.0007ns	-0.04	0.511	0.0002 ns
3	Anticipated Negative Affect if decided not to have test	0.056			0.031		
	Anticipated Negative Affect if positive result	-0.029			-0.021		
	Anticipated Negative Affect if negative result	-0.022			0.009		
	Anticipated Positive Affect if negative result	0.058	0.368	0.0128*	0.061	0.522	0.0109 p = 0.06
4	Perceived Benefits	0.117*			0.085*		
	Perceived Barriers	-0.210***			-0.188***		
	Perceived Susceptibility	0.038			-0.020		
	Perceived Severity	-0.052	0.402	0.0345***	-0.050	0.556	0.0339***
5	Uncertainty	0.252***	0.437	0.0343***	0.222***	0.589	0.0325***
6	Cancer Worry	-0.100			-0.065		
	Anticipated Reassurance GT compared with FOB	0.008			0.032		
	Anticipated Reassurance GT compared with colonoscopy	0.040	0.445	0.0081ns	-0.046	0.593	0.0039 ns
7	age	0.002			0.005		
	N° children	0.066			0.052		
	Risk group	-0.066	0.455	0.0101ns	-0.086*	0.603	0.0099*

***p<0.001
**p<0.01
*p<0.05

The two methods produce broadly similar results in terms of significant correlates of intention to undergo genetic testing. Within both, attitudes and subjective norms emerge as significant predictors, however in the linear regression attitude towards uncertainty is a more powerful predictor than subjective normative beliefs. Perceived barriers again are significantly correlated with intention, however perceived benefits are less significant when using a linear regression approach. Only in the linear regression equation is risk group (high, moderate or low) significantly correlated with intention, (people at high risk more likely to intend to have a genetic test). This effect is, however,

only marginally significant, and in the ordinal regression there is a similar but non-significant effect detected. The comparison of these methods has revealed that for these data the results are comparable, and indicate that the intention categories behave as if they constitute an approximately equal interval scale.

4.5.4. Intended actions following genetic testing

Participants were asked about any intended life changes that they would make if they tested positive or negative on a genetic test for colon cancer.

4.5.4.1. Screening

People were asked if they would want more regular screening if they were found to carry the gene. 447/ 464 (96.3%) said that they probably (21.6%) or definitely (74.8%) would want more regular screening if they were found to be at high risk. Few people however said that they would stop having screening if they were found to be at low risk 5.6% said they probably would and 1.3% said they definitely would. This may pose difficulties, with people being reluctant to forgo the reassurance of regular screening based on a genetic test.

4.5.4.2. Healthy Lifestyle

Most people (86.6%) felt that they would probably or definitely be more careful to avoid unhealthy foods if they were found to carry a gene that predisposed them to colon cancer, however only 18.5% felt that they would not worry so much about eating unhealthy foods if they were found not to have the gene. Genetic testing may lead people to make positive dietary changes if the result is positive, but encouragingly people do not see a clear result as enabling them to eat unhealthily. Any result seems to prompt more positive life changes. When asked whether they would adopt a healthier lifestyle, 85.2% believed they would if the test was positive, but 61.3% still believed they would if the test showed them not to be at risk. There was a significant difference between the anticipated response to a positive and a negative test on a paired sample t-test ($t(452) = 14.967$, $p<0.001$) on this item, showing that people are more likely to anticipate adopting a healthier lifestyle if they are shown to be at high risk. The belief that one will adopt a healthier lifestyle if the test is negative may reflect a (possibly

optimistic) belief that this result will encourage them to maintain their health, or it may just reflect a general desire to 'be healthier' regardless of the circumstances.

4.5.4.3 Future plans

Over two thirds (69.9%) of people thought they would plan more financially for the future if they received a high risk test result, whereas only 47.3% thought that they would if they received a low risk result. This difference was significant ($t(445) = 12.564$, $p<0.001$). Most people also thought that they would also make other plans more if they received a high risk result (69.8% probably or definitely would); whereas only 40% thought they would if the result showed they were not at high risk. Again there was a significant difference between the responses in the different scenarios ($t(452) = 10.74$, $p<0.001$). People also saw a high risk result as greater motivation to seek life fulfilment; 50.1% probably or definitely would do all the things they wanted to if they were found to carry the genetic fault, whereas only 34.5% would if they did not have the genetic fault. Again this difference was significant on a paired t-test ($t(451) = 9.47$, $p<0.001$). This desire for life fulfilment does not extend to seeking a more fulfilling job under either circumstance with few people indicating that they would want to change occupation if they received a positive or a negative result (10.3% and 6.2% respectively). This difference, although small was again significant ($t(430) = 5.79$, $p<0.001$).

In the special case of future childbearing plans, only those people who answered the question who were 45 or under were included in the analyses. Many respondents did not think that they would restrict their childbearing decisions if they were found to carry a genetic fault (40.9% responded probably or definitely not), many people were uncertain (32.3%), some people thought that they probably would (8.1%), but a larger proportion (18.7%) thought that they definitely would. This indicates a possible polarisation of views, with some people definitely intending to use the results in childbearing decisions, but the majority not using the results in this way. If they received a negative test result only a small number anticipated having more children (13%).

4.6 Discussion

This chapter has provided ample evidence for the applicability of social cognition models to the issue of genetic testing for colon cancer. Both the theory of reasoned action and the health belief model have been supported, and although there is considerable overlap between the constructs, there is also evidence for some independent explanatory value in both models. Evidence has also been found for other psychological constructs and their role in the decision making, also the influence that the stage of life may have on this behaviour. The findings in relation to all the measures used in this study will be discussed. The statistical techniques used will also be discussed and the implications of the different methods.

There was a high level of intention to undergo genetic testing for colon cancer (55.7% definitely intending to have a test and a further 29.4% probably intending to have a test), consistent with that found in previous studies. The response rate was high (72%), however it is possible that some of the non-responders held lower levels of intent as has been found in other studies (Petersen et al 1999). Initial analyses established that there was a strong linear relationship between intention and most of the variables measured within both models and the additional constructs explored. These initial analyses were to determine the association between individual variables and the dependent variable of intention, prior to determining the importance of these individual variables in a regression analysis.

4.6.1. Demographic Factors

Although the main focus of this project has been the psychological variables, demographic factors were also explored to determine whether these have any influence over the decision to have a test. Factors with significant associations with intention were entered into the regression analysis. Family history was significantly associated with the intention to have a genetic test, with people at higher risk intending to have the test more than people do at lower risk. Family history is correlated with perceived susceptibility, and this is likely to explain much of this finding, as those who are more at risk may perceive themselves as more susceptible than those who have a less strong family history.

The other two demographic variables that were associated with intending to have a

genetic test were older age and having a larger number of children. It may be that with increasing age the advantages and disadvantages of testing become less important, having a test becomes a matter of personal choice whether to know. Being older has been found to be associated with higher intent in another study of colon cancer (Glanz et al 1999), but in breast/ ovarian cancer, being younger is more predictive of high intent (Lerman et al 1994; Lerman et al 1997; Tambor et al 1997; Meijers-Heijboor et al 2000).

Time of life was also an influence for other participants who were more likely to have a genetic test if they had children. This means that either people who don't have children are delaying knowing until they do (or are just not interested), or people who do have children are more motivated to have the test. It is not possible in a cross-sectional study to determine which of these possibilities is correct, however it does indicate that knowing for another generation is likely to be an important factor in deciding to have a genetic test. This concern about family indicates that a systemic approach to the issue of intent may be required, looking not only at individuals' attitudes and cognitions, but the potential impact of the decision on other people and other factors (Kessler & Bloch 1989). It is also not known whether it is actually of benefit for children to learn of their parent's risk, without first choosing to know themselves. A systemic approach would examine the impact of these decisions on other family members, who themselves may or may not want to know.

Gender was not found to be associated with intent to have a genetic test, this is contrary to the findings of Lerman et al (1996) and Petersen et al (1999) but concurs with the findings of Glanz et al (1999). One possible reason for the lack of influence of gender on intent in this study is a sampling bias. The sample was drawn from entire sub-populations, or randomly from the original database. The original target sample, and the responding sample, all matched the proportions found in the original database (66% women, 33% men), however this sample is biased, as both men and women are affected by colon cancer, so the clinic should see both men and women equally. The reasons why men are less likely than their female relatives to be registered is open to speculation, but this same reason may also have reduced the chance of observing any gender difference in intent to have a genetic test. Those men who chose not to attend the clinic and seek colonoscopic screening may also not intend to have a genetic test for the same reasons.

Issues of gender and further comparisons by gender will be discussed in more detail in Chapter 6.

4.6.2 Psychological variables

Most psychological variables were related to intent to have a genetic test for colon cancer. These will be discussed in the order in which they were entered into the initial regression analyses.

Amongst the psychological variables, those comprising the theory of reasoned action (TRA) were entered first, followed by perceived behavioural control to test the theory of planned behaviour. The attitudes component of the TRA was very highly associated with intention, and accounted for the majority of the variance explained in the regression analyses. The attitudes component was the best single correlate of intention in the study. People who hold more positive attitudes are more likely to intend to have a genetic test.

Subjective normative beliefs were also highly positively associated with intent to have a genetic test in all the analyses, although attitudes explained more variance in the regression analyses than normative belief measures. The finding that family support is associated with higher intent has also been found by Glanz et al (1999).

Support has been found in this study for the power of the theory of reasoned action in explaining variance in intention. The multiple correlation of intention with attitudes and subjective norms is lower than some studies have found, and below the average level found from reviews of multiple studies (e.g. Sheppard et al 1988). The amount of variance obtained (51%) however indicates that the theory can be used to explain over half the variance in intention to have a genetic test for colon cancer. This does not mean that these factors 'cause' changes in intention. To demonstrate causality a longitudinal study is required. In the next study the findings of a one-year follow-up will be discussed in which the causal relationships within the theory of reasoned action will be explored.

The addition of perceived behavioural control to these variables to form the theory of planned behaviour explained no additional variance. There was a small but significant difference in perceived behavioural control across intention groups, however this was

not linear - people holding high levels of intent reported the greatest control; people holding moderate levels of intention reported the least control. The 'U-shaped' nature of this relationship may indicate that people who are more cautious in their desire to have a genetic test hold this view because they are not sure whether they can or not. People holding more positive or more negative intentions to have a genetic test perceive more control. In this sample therefore perceived behavioural control may support attitudes and subjective norm, but not have such a large independent effect. The effect of perceived control may not always be in favour of acting, but may, as in this case, be a perception of power over the decision leading to a more extreme level of intention, whether positive or negative.

Anticipated affect was measured to determine whether this added to the explanatory power of the theory of planned behaviour/ reasoned action in relation to intention to have a genetic test for susceptibility to colon cancer. In analyses of variance there were differences in the directions anticipated, with those intending to have a genetic test anticipating more negative affect if they did not have the test, less negative affect if it was positive and more positive affect if they were found not to be gene carriers. Overall the levels of anticipated affect, both positive and negative were moderate in all the scenarios, indicating that not most individuals do not anticipate strong emotional reactions to genetic testing.

In the final regression analyses none of the measured anticipated affects in relation to different possible scenarios were significant correlates of intention. In the ordinal regression however, when the block containing the anticipated affect variables was entered after the theory of planned behaviour, it added significantly to the amount of variance explained in intention to have a test. In the linear regression a trend in this direction was observed. This indicates that there is a difference in anticipated affect with different intentions, but the individual measures of anticipated affect are not as strongly predictive as the components of the theory of reasoned action (attitudes and subjective norm) in explaining the variance in intent.

The other major model examined in this study was the health belief model. Four aspects of this model were tested - perceived benefits, perceived barriers, perceived susceptibility and perceived severity. All of these, with the exception of perceived severity, varied linearly with intention, which was associated with higher perceived

benefits, lower perceived barriers and higher perceived susceptibility. The lack of a linear relationship between intent and perceived severity may be due to a threshold effect, with all individuals perceiving colon cancer as severe enough to want to reduce the risk, so there is no additional influence of increased perceived severity on intent. The measure of severity used had low internal validity, so this may have been poorly measured, or a more heterogeneous variable may have been measured than was intended. Thus is may be that a more narrowly defined measure of severity could have varied with intent in a linear way.

In the examination of the correlates of intention the health belief model was found to add significantly to the amount of variance in intention explained, after the theory of planned behaviour and anticipated affect were entered. In the final model perceived benefits and perceived barriers were still significantly associated with intention, with the strongest association being between perceived barriers and intention. To examine which theory alone explains the most variance in intention, a regression analysis was re-run, adding the health belief model first, followed by the other blocks. This analysis revealed that the initial variance in intention explained by the health belief model is less than that explained by the theory of planned behaviour. These analyses have demonstrated that although the theory of planned behaviour explains more variance than the health belief model, the health belief model does add significant explanatory power to the developing model.

It is important to note that the two components that were found to add to the model are perceived benefits and perceived barriers. Of the four components of the health belief model measured, these are the factors that, in theory have the most in common with the theory of planned behaviour so may be expected to add the least to the model. The lack of correlation between perceived severity and intention has already been discussed.

Perceived susceptibility did vary by intent, however it did not add to the model to explain intent, after the variance explained by other models had been accounted for. The lack of evidence for the role of perceived susceptibility in 'predicting' intent is surprising as many other studies have found an association between perceived risk or susceptibility and intent to have a genetic test (Glanz et al 1999, Graham et al 1998, Struewing et al 1995b, Durfy et al 1999). The lack of association in the regression analyses may be due to the relatively homogeneous sample in this study. Although there

were variations in clinical risk, most people would have been at relatively high risk of developing colon cancer compared with the general population. This may mean that perceived susceptibility in a high risk population has less importance than it might have in a comprehensive sample from the general population. There was no evidence to suggest that the theory of planned behaviour would be improved by adding a measure of perceived susceptibility, despite the original model not including this concept.

Attitude towards medical uncertainty was found to be a very strong correlate of intention to have a genetic test, with a similar degree of association with intent as subjective norms. When added after the theoretical models, attitude towards uncertainty explained additional variance in intention. Greater dislike of medical uncertainty was associated with higher intention to have a genetic test for colon cancer. This finding lends support to the hypothesis that people intend to have a genetic test to reduce feelings of uncertainty.

Contrary to most studies, there was no significant difference between people on the measure of cancer worry by intent response. Most other researchers have found that cancer worry and cancer concern have been significant correlates of intent to have a genetic test, with worry increasing with intent (Vernon et al 1999; Glanz et al 1999; Petersen et al 1999). One other study has also found no relationship between intention and cancer worry (Meiser et al 2000). It has been suggested that a curvilinear relationship may fit the data better, with people who are low and high in cancer worry being less likely to intend to have a test than those with moderate levels of cancer worry (Valdimarsdottir et al 1999). There was no evidence to suggest that this was the explanation either (the means suggest a non-significant positive linear relationship between cancer worry and intent).

This anomaly may be due to the differences between this cohort and others that have been looked at in the past. This group has lived with the prospect that they may develop cancer at some point for a number of years, and are already enrolled in a programme that will minimise the chances of them developing cancer. Many other research programmes have contacted people through a relative who is currently affected, so the concept of cancer is very salient in their minds, this may have influenced their responses. The mean response in this group is between not worrying about cancer at all or rarely worrying

about it. This indicates that the overall level of worry in this group is very low, and is likely to be lower than that found in other studies.

It would be interesting to explore this topic further to determine whether there is a relationship between proximity to the illness of a relative and cancer worry, this was not measured in this study. The only index that was available in this study was the order in which families had been entered into the programme, but there was no relationship between this and cancer worry.

One issue that is particularly pertinent to this cohort is the relative reassurance of traditional screening compared with the anticipated reassurance of genetic testing. This was assessed using two questions to determine whether a clear genetic test result would be more reassuring than a clear faecal occult blood testing, or colonoscopy result. The mean response was that genetic testing would be moderately more reassuring than traditional screening methods. There was however, a linear relationship so that people with lower levels of intent held less positive views of genetic testing, and in both the lowest intent group, and the 'yes probably' group colonoscopies were rated as marginally more reassuring than a genetic test. This effect was not significant when entered into either a linear or ordinal regression analysis after the other theoretical constructs had been entered.

The receipt of a 'clear' low risk genetic test would mean that the recipient was no longer considered to be at greater than population risk, and therefore would only receive the screening appropriate to that risk level. Within the UK there is currently no national screening programme for colon cancer so screening would be withdrawn. In practice this would be assessed by clinical judgement in addition to the genetic test result, such that a person in whom polyps have previously been detected would receive follow-up assessments appropriate to that clinical condition even if the genetic test was negative. The comparative reassurance of genetic testing is therefore important, as a person who is more reassured by a colonoscopy may be reluctant to relinquish that screening, even when the evidence indicates that they are at low risk.

A reluctance to relinquish screening was found in this study when people were asked about their intended actions following receipt of a genetic test result. As expected, most people would want to continue or increase their rates of screening if the test proved to

be positive, however few people said that they would want to stop having screening if a result was negative.

This response to the prospect of the loss of colonoscopy screening has been documented elsewhere (Michie et al 1996), and may have an impact on the uptake rates of testing for colorectal cancer in those already receiving clinical screening. Future operationalisations of the theory of planned behaviour should compare individual's attitudes to these competing behaviours - genetic testing versus unconditional continuation of colonoscopy screening to determine the relative strength of the competing behaviours (Norman & Conner 1995).

One aspect of the reluctance to relinquish screening may be the lack of understanding of genetic testing, and its implications. People may not have fully understood that genetic testing is an alternative to colonoscopy screening, indicating definite risk levels, and mitigating all genetically linked family history. This cautious approach may be in part justified as although they may not share the same genes as an affected individual, the environment is often shared. This may indicate an increased risk factor, as the genes indicating risk of colon cancer are not 100% penetrant so even in gene carriers, environmental influences affect the development of cancer. In addition a person found not to carry a predisposing gene still has a risk of colon cancer equivalent to that in the general population (approximately 1 in 20). This risk may indeed be a justification for not wishing to relinquish screening.

The implications of genetic testing extend beyond the influence on screening behaviour to include the impact on other aspects of lifestyle, and future plans. For most people the receipt of a genetic test would lead to the adoption of a healthier lifestyle, only moderated in degree not direction of effect between different test outcomes. This is an encouraging finding, as colon cancer is not the only health risk that these participants are exposed to, so low risk test results will not lead to a decrease in healthy behaviours if their anticipated reactions are accurate predictions. This may not translate into a large actual positive effect of test result on behaviour, as intentions often do not translate into behaviours, however the direction of effect indicates that most people would not reduce their adherence to healthy behaviours.

In addition to the health benefits that may come with genetic testing, increased knowledge about the future also permits more detailed forward planning. In this sample few saw childbearing plans or job plans as being affected by genetic test results in either direction. More general future planning was anticipated in the event of a positive genetic test, indicating that this scenario is one in which people feel a need to gain control. The development of plans, not only for coping with future illness, but also with leading a fulfilling life in the present, would be adaptive ways of actively coping with the threat, to maximise the benefit of foreknowledge.

One area that raises concern is the finding that many people would want to make more financial plans for the future in the event of a positive result, compared with a negative (low risk) result. This is an area which has been widely discussed in recent years, with permission having been given for insurance companies to request the outcomes of existing genetic test results for Huntington's Disease before setting levels of premiums for some insurance. The finding that many people would want to selectively make financial arrangements based on the results of a genetic test lends support to the insurer's argument that they may be disadvantaged if they are not privy to risk information that the potential insurance candidate has access to. Insurance may depart further from the original mutuality basis, beyond the current risk behaviour analysis and actuarial calculations utilised today, to a system based not on environmental risks but biological ones. This probability indicates the potential impact that genetic testing for adult diseases will have not only on the individual and their immediate family, but also for the community and society.

In conclusion the analyses have supported most of the hypotheses predicting the direction of association of psychological variables with intent. The exceptions to this are the lack of association with intent of aspects of anticipated affect, perceived severity and cancer worry. Support was found for the independent effects of both the theory of reasoned action and the health belief model in predicting intention.

Other factors were identified which should also be considered when assessing intention to have a genetic test, these were emotional factors such as anticipated affect, personality or trait factors, such as attitudes towards uncertainty, and external influences - familial and societal factors.

4.6.3. Statistical Procedures and Methodological Factors

The use of ordinal regression, and the treatment of intent as an ordinal variable, permitted a different exploration of the associates of intent from that used when intent is treated as an equal interval scale. The use of logistic regression however was not considered valid, as there is a clear linear relationship by intent for most variables. The dichotomisation between 'yes probably' and 'yes definitely' leads to a loss of information from the range of responses and assumes people endorsing 'yes probably' are more similar to those endorsing the more negative responses than to those definite about their decision. There was no evidence to suggest that the measures of intent did not represent an underlying continuous variable, and the similarity of the results from the linear regression indicated that this method may also be appropriate in this situation. In the subsequent analyses linear regressions were utilised, as the populations included in these report more diverse attitudinal beliefs reflecting the continuous nature of this variable.

The use of only one measure of intent may have adversely affected the reliability and validity of the study. This is, however, a complex issue that will be explored in detail. Only measuring intent with one item at one point in the questionnaire means that the study relies upon the correct interpretation of the question by participants, accurate reporting of the answer and that the question is valid (it measures what it sets out to measure). There was no evidence from the pilot studies or the completion of the questionnaire that the first two points were problematic for this particular item. Only having one item means that it is not possible to determine the reliability of this measure, however it did correlate very highly with the other measure of intent (section 4.4.2.1) indicating that there is consistency in responding to the two measures of intent. The issue is therefore in the validity of the question.

Using only one measure necessarily means that intent is narrowly defined within this study. The appropriateness of this approach depends on whether intent is a complex concept which is difficult to accurately identify (like, for example, intelligence), or a simple, specific concept which can be easily captured and assessed. If intent is a complex concept which is difficult to identify then many items should be used to ensure that all perspectives of intent to have a genetic test are encompassed in the question. In an intelligence test such as the WAIS, for example there are three main variables- verbal

intelligence, performance intelligence and overall intelligence, with eleven subscales to measure specific aspects of these variables and 260 items. Intent is clearly not as complex a concept as intelligence, and indeed may be adequately captured with a simple question, does a person report that they would have a genetic test if it were offered to them.

It could be argued that some people may only have a genetic test if it was offered to them (passive intent) rather than actively seeking testing (active intent). As the original protocol was that the test was only going to be available through the clinic offering it, it was the more inclusive passive intent which was of interest (it may be reasonably assumed that a person who would actively seek a test would also accept a test if offered).

Using many items to measure one simple concept may have resulted in bloated specifics (Cattell 1973), in which the items had very high internal consistency, but were simply paraphrases of one another. While this may be justified if the concept is one that is difficult to accurately identify, and difficult for participants to report their views on, intent is probably not such a concept. Repeated asking the same question in a different format may be counterproductive, leading participants to grow dissatisfied with answering the questions, and may lead them to doubt their own answers.

The same, or similar questions to measure intent could have been placed at more points throughout the questionnaire, to ensure that the participants answers are consistent. This could be beneficial if a person's intent is stable and not likely to change, however as will be discussed in the next chapter, this may not be the case, and intent may be influenced by previous answers. Differences in responding throughout the questionnaire could be evidence for the instability of intent. Similarities in responding could be evidence for the unidimensional nature of intent or the stability of intent. Both situations would confuse rather than clarify this issue.

The use of one measure of intent may have led to a narrow definition of intent, and a misinterpretation of the question would have adverse consequences to the data analysis. Despite these issues the appropriate use of statistics has addressed the lack of variability in the measure, there would have been other problems if a larger number of items were

used and the use of just one item means that this study is more comparable to other studies in the field.

4.7 Conclusion and Next Study

This study has demonstrated the applicability of social cognition models to the study of genetic testing. Intent to have a genetic test can be predicted from other measures, including those suggested in the theory of reasoned action and the health belief model. In the next chapter the model will be examined separately in men and women. This comparison between genders will determine whether factors associated with being male or female may have an influence on psychological aspects of genetic testing for colon cancer.

Chapter 5
Gender and Genetic Testing

5.1 Introduction

Little is known about the differences in attitudes between men and women with respect to genetic testing. As discussed in Chapter 2, men are less likely to intend to have a genetic test to indicate presence of a mutation predisposing to breast cancer (Struewing et al 1995b). Men in this study also gave different reasons for wanting genetic testing, and anticipated different emotional reactions. Due to the differing influence of breast cancer-causing genetic mutations in men and women, it is not possible to separate any differences caused by varying levels of gene penetrance from differences in the reactions of men and women to the prospect of genetic testing in general. For this reason it is important to study these factors in relation to a disease such as hereditary colon cancer, where both men and women are affected in similar ways.

Studies of intent to have a genetic test for colon cancer have so far found mixed effects of gender. Some studies found that women were more interested in testing than men (Lerman et al 1996; Petersen et al 1999) and others found no difference (Glanz et al 1999). The first of these studies (Lerman et al 1996) there were very few participants (n=45), with 8/20 men definitely interested and 15/25 women definitely interested. The small numbers men that it is unlikely that this sample was representative of people at risk, and Chi-squared tests do not reveal any differences (although the authors still report the gender effect). The small numbers preclude any further investigation of gender effects. The other two studies contained larger numbers of participants (1373 (Petersen et al 1999) and 426 (Glanz et al 1999)), the first of these found a highly significant ($P<0.001$) gender effect and the second found no effect of gender on intent (in fact, if anything slightly more men wanted testing than women). The samples were drawn from similar populations, predominantly having only one FDR (although 25% of those contacted by Glanz et al (1999) and known to have affected relatives denied this). The main difference between the studies is that over 90% of those recruited by Glanz et al (1999) were not white, whereas over 90% of those recruited by Petersen et al (1999) were white. Although neither study found an effect of ethnicity, there may have been insufficient power to detect white/ other ethnic minority differences which may have

explained the inconsistency. Another possible explanation is that if there are any gender differences they are difficult to detect.

In all of these studies of intent to have a genetic test for colon cancer gender was treated as one of a range of possible influences, without fully exploring the differences between the sexes. Although this is important for predicting intent and uptake in clinics, there are also important questions to be asked about the differences between men and women. These studies have not investigated the differing reasons for wanting (or not wanting) testing and possible different anticipated responses of men and women to the prospect of genetic testing. By exploring the determinants of intent it should be easier to establish whether there are gender differences in the evaluation of predictive genetic testing which are just difficult to measure in terms of intent alone. Alternatively the process may actually be very similar in men and women, with the differences found by Petersen et al (1999) due to other factors not measured in the current thesis or reported by them.

It has been demonstrated in Chapter 4 that amongst this sample there was no significant difference in intent between men and women. This chapter, however, will explore whether there are any differences between men and women on other associated variables. It will be possible to determine whether the gender differences found by Struewing et al (1995b) are also found in these participants who face a more equal risk of developing cancer as a result of any mutated gene found. These differences will be explored in detail and then the correlates of intention in men will be compared with those in women.

5.2 Aims

The aim of this study is to explore whether there are any differences between men and women on variables associated with genetic testing other than intention. The study will then compare the correlates of intention in men and women.

5.3 Hypotheses

- This study is exploratory and theoretically there should be no significant difference between men and women in the main correlates of intent to have a genetic test (theory of planned behaviour, health belief model, and attitude towards uncertainty). If these had differed significantly then they would have an influence on intention in the first study and, assuming that the decision to have a test is similar in both

genders (see third hypothesis) there would be a significant difference between the genders on the measure of intent. Although this analysis will not prove that there are no differences between men and women in terms of correlates of intent it would indicate that differences are at least difficult to detect. The alternative hypothesis which could be made is that the influence of the theory of reasoned action varies by gender, but the reason that there are no differences in intent is that other factors counteract this difference.

- Women will anticipate more emotional reactions to genetic testing than men will (based on Struewing et al 1995b).
- As there is no significant difference between men and women in intent to have a genetic test, and assuming that men and women engage in similar decision making processes with respect to the decision to have a genetic test, the correlates of intention will be similar in both men and women.

5.4 Method

5.4.1 Procedure & Materials

This study uses the same data as collected in study 1. The procedure for the collection of this data and the materials used are outlined in section 4.4 of Chapter 4. This study utilised the same measures, but in addition the anticipated affect measures were considered individually, to determine whether there were variations in specific anticipated emotions, as found in a study on male and female candidates for genetic testing for breast cancer (Struewing et al 1995b).

5.4.2 Participants

Participants were all registered with St Marks Family Cancer Clinic as having a family history of colon cancer, but none of those included in this analysis had a personal history of colon cancer. There were 109 men (mean age 44.3 years, s.d. = 11.8, range 22-78 years) and 247 women (mean age 46.79 years, s.d. = 10.78, range = 23-76). There was no significant age difference between the men and women ($F(1, 354) = 3.77$). Although the proportion of men and women in this sample do not reflect that found in the general population, they do reflect the proportions found in the population from which the sample was drawn (St Marks Family Cancer Clinic database).

5.4.3 Statistical analyses

Differences between genders was explored using multivariate ANOVAS carried out in SPSS version 9. The use of multivariate ANOVAS means that the number of comparisons is controlled for in the analysis, thus reducing the risk of a type 1 error that would otherwise be more likely when conducting a large number of analyses. The differences in anticipated emotional affect were explored using t-tests. The correlates of intention in men and women were determined using separate linear regression analyses, using the same procedure as discussed in Chapter 4.

5.5 Results

The first analysis is a multivariate analysis of variance, comparing responses given by men and women.

Table 5.1 Comparison between genders for psychological variables.

Variable	Male N=109		Female N=246		F (1,355)
	Mean	SD	Mean	SD	
Attitude	4.44	0.78	4.25	0.88	3.77
Subjective Norm	3.87	0.70	3.72	0.73	3.35
Perceived Behavioural Control	3.25	0.70	3.14	0.70	1.71
Anticipated Negative Affect if decided not to have test	2.41	0.68	2.45	0.65	0.3
Anticipated Negative Affect if positive result	2.0	0.48	2.21	0.55	12.91***
Anticipated Negative Affect if negative result	1.04	0.12	1.09	0.23	4.85*
Anticipated Positive Affect if negative result	2.61	0.61	2.75	0.55	5.12*
Perceived Benefits	3.61	0.55	3.68	0.58	1.15
Perceived Barriers	2.5	0.79	2.6	0.69	1.60
Perceived Susceptibility	3.28	0.75	3.24	0.79	.17
Perceived Severity	3.65	0.72	3.64	0.73	.02
Uncertainty	3.97	0.71	3.87	0.75	1.52
Worry	9.09	1.99	9.78	2.65	5.98*
Anticipated Reassurance GT compared with FOB	2.42	1.02	2.38	0.96	.11
Anticipated Reassurance GT compared with colonoscopy	2.91	0.99	3.00	0.98	.70
Anxiety	5.65	3.81	6.59	4.00	4.24*
Depression	2.78	2.42	3.1	3.09	.91

***p<0.001
**p<0.01
*p<0.05

The overall analysis of variance showed that there were some differences between the groups by gender (Pillai's Trace F= 1.95 (17, 336), p<0.05). There were no significant differences between genders in terms of theory of planned behaviour and health belief model constructs, although there was a trend towards men holding more favourable attitudes, and perceiving more supportive norms (p=0.053 and 0.068 respectively).

There were differences in measures of emotional responses. Women reported worrying more about developing colon cancer ($F= 5.98$, $p<0.05$), anticipated more negative consequences of a positive test ($F= 12.91$, $p<0.001$), anticipated more negative consequences of a negative test ($F= 4.85$, $p<0.05$), anticipated more positive consequences of a negative test ($F= 5.12$, $p<0.05$), and reported higher levels of overall anxiety ($F= 4.24$, $p<0.05$).

5.5.1 Anticipated emotional reaction to genetic testing – microanalysis of anticipated responses

The data collected on some aspects of anticipated affect in relation to various outcomes were explored in more detail in the sample, dividing the sample by gender. Anticipated affect in response to four different possible outcomes were explored using t-tests to determine gender differences. As there were multiple analyses within this section which were not statistically controlled for, a more stringent level of significance ($p<=0.01$) was adopted. This decreases the chance of a type 1 error, however this does mean that there is an increased chance of a type 2 error. Where results lie between $p<0.05$ and $p<0.01$, these are indicated in parentheses (Table 5.3). Levene's Test for equality of variances was computed for each variable, and where there were heterogeneous samples ($p<0.05$), a t-test for unequal variances was used.

Table 5.2 Anticipated affect if decided not to have a genetic test

Responses on scale 1-4 (not at all, a bit, fairly, extremely)

Response	Male N=110		Female N= 247		Differences between Genders
	Mean	SD	Mean	SD	t(df)
Guilty	2.16	1.10	2.18	1.07	-0.15 (355) ns
Relieved	1.29	0.6	1.53	0.77	-3.24 (268) p<0.001
Depressed	1.52	0.83	1.53	0.76	-0.18 (355) ns
Worried	2.01	0.85	2.27	0.91	-2.59 (222) p<0.01
Regretful	2.37	1.01	2.39	0.97	-0.18 (355) ns
Forever Wondering	2.67	1.05	2.83	0.96	-1.34 (193) ns

There were two significant differences between the genders in this analysis. Women anticipated feeling more relieved if they did not have the test than men did, but also anticipated feeling more worried. The most common anticipated reaction is that they will be forever wondering (54.6% of men and 62.8% of women said they would

experience this reaction). Other common anticipated reactions were regret (41.8% and 42.5%), worry (23.7%, 37.6%) and guilt (39.1%, 37.3%).

Table 5.3 Anticipated affect if a genetic test showed a high risk (positive) result

Responses on scale 1-4 (not at all, a bit, fairly, extremely)

Response	Male N=110		Female N= 247		Differences between Genders
	Mean	SD	Mean	SD	t(df)
Guilty	1.15	0.47	1.17	0.49	-0.52 (355) ns
Relieved	1.74	1.06	1.64	0.92	0.87(186) ns
Depressed	2.11	0.84	2.51	0.94	-4.02 (232) p<0.001
Worried	2.55	0.76	2.89	0.85	-3.57 (355) p<0.001
Surprised	1.9	0.82	1.80	0.88	1.0 (355) ns
Regretful	1.83	0.91	2.05	1.08	-2.04 (246) (p<0.05)
Hard to believe	1.64	0.86	1.79	0.91	-1.49 (355) ns
Angry	1.51	0.83	2.15	1.04	-6.17 (257) p<0.001

There were a number of differences in the ways that men and women anticipated that they would react to a high risk genetic test result. Women anticipated feeling more depressed, more worried and more angry than men did. There was also a tendency towards women anticipating more regret if the test was positive. 50% of men and 64.7% of women anticipated feeling fairly or extremely worried if they tested positive, and 28.2% of men and 44.1% of women anticipated feeling fairly or extremely depressed.

Table 5.4 Anticipated affect if a genetic test showed a low risk (negative) result

Responses on scale 1-4 (not at all, a bit, fairly, extremely)

Response	Male N=110		Female N= 247		Differences between Genders
	Mean	SD	Mean	SD	t(df)
Guilty	1.04	0.23	1.05	0.27	-0.42 (355) ns
Relieved	3.25	0.79	3.46	0.80	-2.26 (355) (p<0.05)
Depressed	1.01	0.1	1.05	0.25	-2.15 (349) (p<0.05)
Worried	1.09	0.29	1.23	0.47	-3.33 (322) p<0.001
Surprised	2.15	0.9	2.21	0.86	-0.61 (355) ns
Regretful	1.04	0.23	1.05	0.31	-0.49 (355) ns
Hard to believe	1.70	0.8	1.84	0.86	-1.43 (355) ns
Angry	1.01	0.1	1.08	0.4	-2.51 (301) (p<0.05)
Happy	3.33	0.79	3.53	0.82	-2.23 (355) (p<0.05)

As anticipated, most people believed that they would experience few negative emotions in response to a low risk result, and anticipated predominantly surprised and positive feelings; this was true for both men and women. Although there were some trends, the only significant difference was anticipated worry following a low risk result, with more

women than men believing that they would feel worried following a low risk result. Few people anticipated feeling even a little guilt after a low risk result (2.7% men, 4% women thought they might feel a little or fairly guilty), so 'survivor guilt' is clearly not anticipated in this sample. The only 'negative' emotion which people believed they might experience was worry, with 10% of men and 20.6% of women believing that they might experience some degree of worry. Most people thought that they would be fairly or extremely happy (87.3% men, 89.4% women), and fairly or extremely relieved (83.6% men, 89.4% women). Most people did not think that they would be surprised or find a low risk result hard to believe. More people felt that they would find a low risk result more surprising (21.6% overall fairly or extremely surprised at high risk result, 30.8% low risk); but a high risk result harder to believe (20.5% c.f. 16.8%).

5.5.2 Differences in correlates of intention in men and women

The final analysis was a multiple linear regression, entering variables in blocks as discussed in Chapter 4. This analysis was used to explore whether there were any differences in the correlates of intention to have a genetic test.

Table 5.5 Linear regression of intention onto psychological and demographic correlates - separate analyses for men and women

		Regression of intent onto psychological variables							
		Men				Women			
Step		Final Beta	R^2	Adjusted R^2	R^2 change (sig^n)	Final Beta	R^2	Adjusted R^2	R^2 change (sig^n)
1	Attitude	0.379***				0.334***			
	Subjective Norm	0.227**	0.601	0.593		0.174**	0.487	0.482	
2	Perceived Behavioural Control	-0.161*	0.606	0.595	0.005ns	0.019	0.489	0.482	0.002ns
3	Anticipated Negative Affect if decided not to have test	-0.061				0.071			
	Anticipated Negative Affect if positive result	-0.002				-0.01			
	Anticipated Negative Affect if negative result	0.002				-0.023			
	Anticipated Positive Affect if negative result	0.085	0.619	0.593	0.013ns	0.021	0.506	0.491	0.017ns
4	Perceived Benefits	0.151*				0.055			
	Perceived Barriers	0.198*				0.204***			
	Perceived Susceptibility	-0.015				0.063			
	Perceived Severity	-0.129*	0.676	0.639	0.057**	-0.055	0.534	0.513	0.029**
5	Uncertainty	0.24**	0.711	0.675	0.035***	0.208***	0.56	0.538	0.026***
6	Cancer Worry	0.054				-0.077			
	Anticipated Reassurance GT compared with FOB	0.037				-0.108*			
	Anticipated Reassurance GT compared with colonoscopy	-0.085	0.716	0.67	0.005ns	0.079	0.572	0.545	0.012ns
7	age	0.03				-0.009			
	N^o children	-0.004				0.092*			
	Risk group	0.074	0.712	0.665	0.005ns	-0.153***	0.599	0.567	0.027**

***p<0.001
**p<0.01
*p<0.05

The linear regression models which emerged explained more of the variance in intention in males (Adj R^2 = 0.665) than in females (Adj R^2 = 0.567). Both models were highly significant. Examinations of the residuals and Cook's distance indicated that there were no cases that had undue influence on the regression equation. In the final equation, the standardised regression coefficients (β) for attitudes was 0.379 and for women 0.334. At the same step, the beta values for subjective normative beliefs were 0.227 and 0.174 respectively. Both variables were positively related to intention. At the second block perceived behavioural control explained no additional variance in intent in women. In men there was a significant negative standardised regression coefficient when perceived behavioural control was entered into the equation and in the final analysis. This indicates that this is a suppressor variable, and has a higher correlation with the residual than the predicted value of intent. Examination of the univariate correlation co-efficient between perceived behavioural control and intent confirmed that this was a non-significant correlation in men (r=0.013 p=0.89). Anticipated affect did not explain additional variance in either the men or the women when entered at the third step of the analysis and was not significant in the final equation.

Variables composing the health belief model (benefits, barriers, susceptibility and severity) were entered at the next step. In women the only variable to emerge in the final equation with a significant beta value was perceived barriers (β = 0.204), this block explained a significant additional 2.9% of the variance in intent. In men the standardised regression coefficients for perceived benefits (β = 0.151), perceived barriers(β = 0.198) and perceived severity (β = -0.129) were all significant in the final equation; the block explained an additional 5.7% of the variance in intent. An examination of the correlation of perceived severity with intent showed that contrary to that predicted and the correlation in the whole sample, lower perceived severity was associated with higher intent (r=-0.083) in men.

Attitude towards medical uncertainty, entered at the 5th step, remained significant in the final equation for both men and women, explaining an additional 3.5% of the variance in intent in men and 2.6% of the variance in intent in women. This was the last variable to add significantly to the variance in intent for men. In women anticipated re-assurance of genetic testing compared with FOB testing was significant in the final equation (β =-

0.108), but the block as a whole was not. The final block entered for women did explain significant additional variance in intent (2.7%), with number of children and clinical risk group having significant beta values at this stage ($\beta = 0.092$ and $\beta = -0.153$ respectively). Clinical risk, although just positively correlated with intent, here is negatively correlated; again indicating that this is acting as a suppressor variable.

In the final equation to predict intent in men, the order of the standardised regression coefficients (which is an indicator of the likely importance) was:- attitudes, attitude towards medical uncertainty, subjective norms, perceived barriers, perceived behavioural control (suppressor), perceived benefits and perceived severity. In women the order was slightly different:- attitudes, attitude towards medical uncertainty, perceived barriers, subjective norms, clinical risk (suppressor), anticipated reassurance of genetic testing compared to FOB testing and number of children.

The unstandardised regression co-efficients were then compared between men and women. These analyses indicated that there was no significant difference between men and women in the relative strengths of the predictors.

5.6 Discussion

The exploration of gender issues with respect to genetic testing for colon cancer has revealed some important differences between men and women. The first finding was that, there were no significant differences between men and women in the main correlates of intent (as found in Chapter 4) to have a genetic test - attitudes, subjective norms, perceived benefits, perceived barriers and attitude towards uncertainty. Although this cannot be interpreted as indicating that intent was formed in the same way in both men and women, it does show that on these important correlates there is no difference. The issue of the process by which intent may be formed will be explored in more detail below.

Despite the lack of difference on these measures, there were significant differences on other factors. Compared with men, women did anticipate more negative emotional reactions whether the test result was positive or negative. They also anticipated more positive emotions if the test was negative, showing that they were at no more than

population risk of colon cancer. Women also reported that they currently worry more about cancer, and they indicated a higher score on the anxiety sub-scale of the HADS than men did. Taken together these findings indicate that women are currently experiencing, and are anticipating more emotional responses to the prospect of both being at risk of cancer (cancer worry) and receiving a genetic test result. This indicates that the finding that men anticipate different emotional reactions to the prospect of genetic testing for breast cancer (Struewing et al 1995b) may not just be a function of their different risk status with respect to developing breast cancer, but may be due in part to a more fundamental gender difference.

Gender differences with respect to anticipated emotional reactions to genetic testing were explored in more detail. The first question participants were asked was their anticipated reaction if they decided not to have a genetic test. The only differences between men and women was that women anticipated feeling more relieved, but also more worried. The higher levels of anticipated relief in women is an interesting finding, as it may indicate that at one level they may actually be happier then men if they did not actually discover their genetic makeup. The high levels of anticipated worry in women, are likely to be for the same reasons as their higher current cancer worry, these two variables are highly correlated ($r=0.37$, $p<0.001$).

When considering their anticipated reaction if a genetic test was positive (showing that they carried a gene leading to susceptibility to colon cancer), women anticipated feeling more depressed, worried and angry than men did. The higher anticipated depression in women compared to men is similar to that found by Struewing et al (1995b). In that study 46.2% of women and 16.7% of men anticipated depression if they knew they carried a gene mutation, whereas in this study 44.1% of women, and 28.2% of men anticipated feeling fairly or extremely depressed. Men in this study anticipate less depression than the women in this study, but whereas the women in this study anticipate similar levels of depression as those in Struewing's study, men in this study anticipate considerably higher levels of depression than those anticipating testing for breast cancer gene carrier status. In an analogous finding looking at the related concepts of anxiety and worry, women in this study anticipate experiencing more worry and in Struewing's study anticipate more anxiety than the men do, but levels of worry in men in this study are considerably higher than levels of anxiety in men in Struewing's study. These

associations indicate that there are genuine differences between the two genders in terms of their anticipated responses to genetic testing for cancer, but in Struewing's study the difference was in part due to the differential impact of the gene mutation on the men's risk of developing breast cancer. The higher levels of anticipated anger if the test is positive in women again indicate that the decision to have a genetic test may be associated with mixed feelings for women more than men.

In response to a negative (low risk) genetic test result women believe that they will still worry more than men do. The mean overall levels of anticipated worry in both groups are quite low, so worrying after receiving a low risk result is unlikely to prove problematic to either men or women.

These analyses have shown that there are differences between men and women on measures related to genetic testing for colon cancer, and that men and women anticipate different emotional reactions. This difference in anticipation of emotional responses may not translate into actual differences in response, as it may be difficult for people to imagine how they will feel. The differences in anticipated affect between the genders may not be due to actual differences in emotional response that would emerge at testing, but rather one gender may be more accurate in anticipating how they will feel. In addition it has frequently been reported that women are more willing to report their emotional state than men, this may mean that men do anticipate similar reactions to women, but are unwilling to report them. These issues will need to be examined in a longitudinal analysis of the emotional reactions to testing.

Despite all these results, the unresolved issue is whether, although there is no difference in intent between men and women, is there a difference in the correlates of intention?

For both men and women attitudes and attitude towards uncertainty are the most important correlates of intent. Other than these factors, in men, subjective norms, perceived benefits, perceived barriers and perceived severity were associated with intent. Contrary to the established theory, perceived severity of colon cancer was inversely related to intent in men. It may be that men are more willing to consider genetic testing if they perceive colon cancer to be less severe. Perhaps those men who perceive colon cancer to be more severe would rather not have a genetic test because

then they would need to confront the disease. The importance of social-cognition variables in the regression equation predicting intent means that all these factors are likely to be important in making their decision, rather than the more limited list which emerged when the entire population was considered together. In men these variables together explain a large proportion of the variation in intent.

In women a different picture emerges, with only perceived barriers and subjective norms emerging as additional social- cognition factors. Other significant correlates of intent are anticipated reassurance of genetic testing compared to FOB testing and the number of children a woman has. Women are considering factors outside of those usually considered in social cognition models when deciding whether to have a genetic test. Screening and the likely benefits for children are additional factors that explain variation in intent. In women these variables also explain less variation in intent than it was possible to explain in the male population. These findings raise important questions, not only about which other factors may explain women's intent to have genetic testing for colon cancer, but also whether for other behaviours social cognition variables explain a greater proportion of intent and behaviour in men than in women.

When the regression models were compared the moderated regression analyses would appear to indicate that there are no differences that would suggest that men and women consider different factors when forming their intention regarding genetic testing for colon cancer.

5.7 Conclusion and Next Study

The previous studies have established the correlates of intent to have a genetic test for colon cancer, and factors associated with this decision in asymptomatic individuals (Chapter 4) and the different nature of the decision in men and women (this chapter). The next study will examine the stability of these models over time, and examine whether it is possible to determine the causal direction of the theory of reasoned action in the case of genetic testing for colon cancer.

Chapter 6

One Year Follow-up Study

6.1 Introduction

When the participants received the first questionnaire, it was the first information about clinical genetic testing that they had received from St Mark's hospital. This means that the concept would have been novel for a number of participants. Following completion of the questionnaire they may have thought more about testing and they may have changed their views. In addition their responses and the formation of their intention may have influenced their consideration of the issues concerning genetic testing, and so this may have fed back into their attitude formation.

Many studies of social cognition models only observe outcome behaviours or just take all measures at one cross-sectional time point. Few contact the same participants again to see whether views have changed, not just their intent or behaviour. There is, however, an important issue of the stability of intention over time. Without the establishment of the stability of intention and stability of the correlates of intention, it is not possible to separate changes that have occurred due to being offered a genetic test from those which would have occurred anyway due to further consideration of the concept of having a genetic test.

In a longitudinal study it is also possible to determine causal relationships between factors. For example in the first study it was shown that attitude was a good predictor of intent, this means that if a person's attitudes are known, it is possible to 'predict' what their likely intention will be. This is distinct, however, from demonstrating a causal relationship, which must be explored in experimental or longitudinal studies. The usual diagram of the theory of reasoned action / planned behaviour (Fig 3.1) implies that attitudes, subjective norms and perhaps perceived behavioural control are determinants of, or cause intention. Despite this implication, the causal relationships within the theory of reasoned action/ planned behaviour have rarely been explored. Attitudes *may* cause intent, but alternate hypotheses have not been eliminated – it is still possible that intent may cause attitudes, or a third unmeasured variable underlying both intent and attitudes may account for the high predictive power of attitudes.

Few studies have explored the causal relationships implied within the theory of planned behaviour using a test-retest approach. In an exploration of food choice (Armitage and Conner 1999), no causal relationship was found between behavioural beliefs and attitudes or between attitudes, subjective norms and perceived behavioural control and intent. The components of the theory of planned behaviour did however predict intention and behaviour. This was a relatively large study (n=413) conducted over 3 months. This study raises questions about the nature of causality within the theory of planned behaviour and why, despite strong inter-correlations between the components, there appears to be no dynamic relationship between them. Is the lack of a causal relationship because food choice is a relatively stable behaviour with well formed (possibly concrete) attitudes, subjective norms and perceived behavioural control?

To examine the causal relationships with the variables reported in time 1, a subgroup of the original sample were re-contacted a year after completing the first questionnaire.

6.2 Aims

The aim of this study was to establish the stability of intention and correlates of intention over time, and to explore the causal structure of the theory of planned behaviour

6.3. Hypotheses

- Intention will remain stable between time 1 and time 2, as these participants have not been offered or undertaken a genetic test.
- The other constructs will remain stable between time 1 and time 2, as there has been no intervention that may have caused this change, other than the original questionnaire.
- There will be a causal relationship, with attitudes, subjective norms and perceived behavioural control predicting intent at the follow-up session.

6.4. Method

154 questionnaires (Appendix A) were sent to people at moderate or high risk of colon cancer who had responded to the study 1 questionnaire. As stated above this was a subgroup of the original sample, as the remaining participants were either involved in a

different arm of the study (not reported in this thesis), or were at lower risk of colon cancer. Where the person had indicated that they had a partner, a questionnaire was sent for their partner to complete too (the analysis of this information is presented in Chapter 7). A freepost envelope was again included for the return of the questionnaire

6.4.1 Materials

The questionnaires were worded the same as those used at time 1. The key variables measured in this questionnaire were:- intent, attitudes, subjective norms, perceived behavioural control, anticipated affect, perceived benefits, perceived barriers, perceived severity, perceived susceptibility, uncertainty, cancer worry, anticipated reassurance, anxiety and depression. In addition respondents were asked if they thought their responses had changed, and if anything had influenced them. At the end of the questionnaire, respondents were given an opportunity to name three main reasons why they would want a test, and three main reasons why they would not. This questionnaire can be found in Appendix A.

6.4.2. Participants

88 individuals responded, 66 did not respond, this represents a response rate of 57.1%. Non-responders to this follow-up study were compared with responders in terms of gender, age, intent to have a genetic test at time 1 and whether they had a personal history of cancer (the group contacted contained both affected and unaffected individuals). There were no significant differences between the responders and non responders by gender, age or cancer history. There was a trend towards a significant difference in intention ($F=3.58$, $p=0.061$), with responders holding marginally higher levels of intention at time 1 (mean = 4.57; s.d. =0.074) than non-responders (mean = 4.35; s.d. =0.74).

6.4.4 Statistical analyses

Comparisons between responses at time 1 and time 2 were initially made using correlation co-efficients and paired difference t-tests. The direction of causal relationships was established using cross-lagged panel correlations.

6.5. Results

Pearson correlations and paired t-tests were calculated to determine differences between the responses at time 1 and time 2 (Table 6.1).

Table 6.1. Pairwise comparison of time 1 and time 2 responses.

	Time 1		Time 2		Paired difference		Test-retest correlations
Variable	Mean	S.D.	Mean	S.D.	t(df)	Sig^n t (p)	r(p)
Intent	4.57	0.62	4.47	0.71	1.41(86)	0.16	0.505***
Attitude	4.62	0.54	4.34	0.74	3.38(80)	0.001	0.404***
Subjective Norm	3.96	0.75	3.60	.82	-5.10(86)	<0.001	0.643***
Perceived Behavioural Control	3.36	0.71	3.32	0.77	0.52(84)	0.61	0.636***
Anticipated Negative Affect if decided not to have test	2.60	0.77	2.50	0.76	1.37(81)	0.18	0.599***
Anticipated Negative Affect if positive result	1.98	0.42	2.00	0.48	-0.52(84)	0.61	0.582***
Anticipated Negative Affect if negative result	1.08	0.25	1.09	0.24	-0.08(81)	0.94	0.378***
Anticipated Positive Affect if negative result	2.73	0.59	2.73	0.69	0.04(84)	0.97	0.496***
Perceived Benefits	3.82	0.61	3.73	0.67	1.74(83)	0.085	0.707***
Perceived Barriers	2.38	0.61	2.45	0.64	-1.07(84)	0.29	0.532***
Perceived Susceptibility	3.48	0.81	3.51	0.79	-.30(84)	0.76	0.496***
Perceived Severity	3.49	0.73	3.44	0.60	.83(84)	0.41	0.588***
Cancer Worry	9.79	2.53	9.40	2.46	1.81(86)	0.07	0.675***
Anxiety	6.61	3.72	6.16	4.35	1.35(82)	0.18	0.719***
Depression	3.24	3.16	3.07	3.14	.77(83)	0.44	0.802***

* $p<0.05$
** $p<0.01$
*** $p<0.001$

There was a high degree of correlation between the reports on all measures at time 1 and time 2, with correlation coefficients ranging from $r=0.378$, $p<0.001$ (anticipated negative affect if negative result), to $r=0.802$, $p<0.001$ (depression). Variations in the degree of correlation is likely to be partly due to errors in responding at time 1 compared with time 2, some questions are answered consistently accurately and others are not (test-retest error). The other reason is that people's opinions may have changed over the intervening year, this difference is demonstrated in the paired differences findings.

Over the intervening year the individuals sampled have maintained relatively stable views about genetic tests, and most other psychological variables have not changed over time. The exception to this is attitudes towards having a genetic test, and perceived normative beliefs of other people as to whether they should have a genetic test. Both measures showed significant decreases, with people holding less positive attitudes about

genetic testing for colon cancer (t (80) = 3.38, p<0.001), and believing that other people do not think so strongly that they should have a genetic test (t(86) = -5.1, p<0.001) . A decrease in positive regard for genetic testing is also seen in the measure of intention. Intercorrelations between these three variables were calculated (Table 6.2.) and show that at time 2 the degree of correlation between all the variables was higher than at time 1. Significance tests using Fisher's transformed r did not indicate that these differences were significant. The relationship between attitudes and intention was marginally stronger at time 2 compared with time 1 (z=1.33, p=0.09), and the other results were all in the same direction.

Table 6.2. Correlation coefficients

			Time 1			Time 2		
			Intent	Attitudes	Subjective norm	Intent	Attitudes	Subjective norm
Time 1	Intent	Pearson Correlation	1.000					
		Sig. (2-tailed)	.					
		N	88					
	Attitudes	Pearson Correlation	.519***	1.000				
		Sig. (2-tailed)	.000	.				
		N	84	84				
	Subjective Norm	Pearson Correlation	.567***	.486***	1.000			
		Sig. (2-tailed)	.000	.000	.			
		N	88	84	88			
Time 2	Intent	Pearson Correlation	.484***	.290**	.440***	1.000		
		Sig. (2-tailed)	.000	.008	.000	.		
		N	87	83	87	87		
	Attitudes	Pearson Correlation	.358***	.345**	.404***	.656***	1.000	
		Sig. (2-tailed)	.001	.002	.000	.000	.	
		N	84	81	84	83	84	
	Subjective norm	Pearson Correlation	.466***	.274*	.643***	.649***	.542***	1.000
		Sig. (2-tailed)	.000	.012	.000	.000	.000	.
		N	87	83	87	87	83	87

The causal relationships between these variables were explored to determine why they are more highly correlated at time 2, and where any causal effects are occurring which might explain why the variables have become more highly correlated. As the constructs were synchronous (attitudes, subjective norms and intent were all measured at the same time point) and there appears to be at least proportional stationarity (the means of all the variables have moved in the same direction), cross-lagged panel correlation (Kenny 1975) is an appropriate method by which the causal relationships between these factors can be assessed.

In order to determine the causal relationship between attitudes and intention the formula r_{a1i2}-r_{a2i1} was used as a basis, where a = attitudes, i = intent, 1 = time 1 and 2 = time 2.

This was calculated as a z score using a Pearson and Filon test as detailed in Kenny (1975), the z statistic equalled -0.635, which is not significant. The causal relationship between subjective norms and intention was z = –0.027 (again not significant). These analyses indicate that there is no significant causal relationship between firstly attitudes and intent and secondly subjective norms and intent. Due to the difficulty of detecting any significant effect in this type of analysis, Kenny (1975) suggests that the direction of causality should still be considered in the absence of significance. This indicated that intent as measured at time 1 influences attitudes at time 2, and subjective norms at time 2 (because the cross-lagged differential was negative). This is contrary to the direction implied in the theory of planned behaviour, whereby attitudes and subjective norms 'cause' intent.

6.6 Discussion

Overall there have been few differences in intention over time, however some people report less favourable evaluations of genetic testing the second time that they are questioned.

The surprising finding was that it was possible that intent at time 1 may be causing attitudes and subjective norms at time 2. This effect was not significant, but it is contrary to the direction predicted by the theory of reasoned action. These tests frequently are not significant even with this number of participants (Kenny 1975). This may be for a number of reasons:- a) there is no causality between the variables; b) there is a third or other common co-variates; c) there is a positive feedback loop; d) the magnitude of effect is too small to detect or e) the lag between measurements does not correspond to the length of the causal lag between the variables. These factors all mean it is often difficult to detect a significant effect, even when there is an effect there. Due to the low power intrinsic in this type of analysis, it has been suggested that many replications should be included in a longitudinal study, with the difference replicating across different time lags, different groups of subjects and different operationalisations of the same construct (Kenny 1975). Such a study would involve a high demand on the participants, which was not appropriate in this situation. The direction of the effect is however in itself is an interesting finding.

The finding indicates that there is a correlation not only between attitudes and subjective norms at time one and intent at time two, but that there is also an association between intent at time one and attitudes and subjective norms at time 2. Indeed it is this latter association which is stronger. This means that causality appears to be bi-directional within the theory of planned behaviour when applied to this situation. This raises the plausible possibility that there may be a feedback mechanism within the theory of planned behaviour.

The stronger association between intent at time 1 and attitudes and subjective norms at time 2 (compared with the reverse direction) may be because the target behaviour (having a genetic test) is a novel experience, which many people would not have previously considered. The expression of attitudes, subjective norms and intent at the time of the first questionnaire may have been formed more rapidly than is usual for intention formation. Having formed an intention it is possible that some people reassessed their attitudes to align them with their intent, and that they sought more information to support their stated intent. This would be supported by established theories such as selective attention bias and cognitive dissonance. The formation of intent outwith the artificial situation created by this study may occur in a more linear pattern. It would, however, be difficult to study such naturalistic attitude formation, as clearly this would be one situation in which observing the phenomenon affects the outcome (Berkley).

There is always the risk that by observing the formation of attitudes, the process of formation of attitudes will be altered. This may be the reason for the apparent feedback loop in this situation. The initial questionnaire required the participants to state attitudes, subjective norms, perceived behavioural control and intent the first time. The stating of these responses, which may not have been previously articulated, may have then biased the participants' later enquiries about genetic testing. It would be difficult to devise a study which did not have this effect, as it is not possible to directly observe the individual's internal cognitions, so the participant would have to be aware at least of the topic of interest and articulate their feelings.

In addition it is likely that any dynamic adjustment of the four factors (intent, attitudes, subjective norms and perceived behavioural control) would happen at a different rate in

different people. This may be because of differences in exposure to information about genetic testing, different rates of processing information and differences in the rate and degree to which people tend to form stable beliefs. This likely individual variation in the nature of the feedback loop would make it difficult to determine the appropriate time lag in studying this loop, other than in an experimental situation.

Despite these theoretical and practical problems, the nature of intention formation and the nature of any causal relationships within the theory of planned behaviour is clearly an area which deserves much closer investigation.

6.7 Conclusion and Next Study

This study has demonstrated that whilst psychological factors associated with genetic testing remain relatively stable over time, the direction of influence of the components of the theory of reasoned action is less than clear. The evidence from this study points towards the possibility that there may be a feedback loop operating between the key concepts of this theory. This would be more appropriately studied in a more controlled experimental study beyond the remit of this thesis.

Having established the validity of using social cognition models to examine correlates of intent in a high-risk population, even if the direction of causality is not clear, the remainder of the thesis will proceed to examine differences in psychological factors between groups of people. The first comparison will compare people from this database with their spouses, to explore the issue of genetic testing from a different perspective. In addition to exploring the differences between the views of people at high risk and their partners, the chapter will also address theoretical issues concerning the nature of subjective norms, and their role in the theory of reasoned action.

Chapter 7

Comparison of Psychosocial Aspects of Genetic Testing For Colon Cancer in Asymptomatic Individuals and their Partners

7.1 Introduction

Genetic testing is not only seen as an individual issue, but also a family issue (Smith, West, Croyle & Botkin 1999); however, very few researchers have investigated the views of partners when studying attitudes towards genetic testing. The research that has been conducted has primarily examined the differences in views between people at risk of Huntington's Disease and their spouses. In this research the partners generally reported similar reasons for wanting testing as the high-risk individuals (Evers-Kiebooms et al 1989, Evers-Kiebooms et al 1987, Tibben et al 1993a). Slightly more partners wanted the at risk individuals to have a genetic test than the at-risk individual themselves reported wanting (Evers-Kiebooms et al 1989, Evers-Kiebooms et al 1987).

These studies have not compared the responses of an individual with the responses of their own spouse, but rather they report descriptive statistics on a group level, and include in the patient group high risk individuals with no data for their partner. Whilst these descriptive results indicate general trends in responding, there is no direct comparison between a high risk individual and their own partner. Additionally including people in the high risk group who do not have a partner in the other group introduces a possible bias. These people with no participating partners may have different views about genetic testing which are influencing the results for the whole group. This may be either because their partners are less in favour of genetic testing, so do not participate, and influence their partner's subjective beliefs, or they may not have a partner, which previous research has shown to decrease the likelihood of intending to have a genetic test (Lerman, Hughes et al 1998; Lerman, Hughes et al 1999; Aktan-Collan et al 2000b).

The purpose of the next study is to determine how the views of spouses varied from the views of the at-risk partner. This study compares each couple's views directly rather than using the group level approach adopted by previous studies. In addition at-risk participants were only included in the analysis when their partner had also participated. This ensures that there is no risk of an attrition bias accounting for any differences.

In the literature there is also a lack of information about the views of partners in relation to genetic testing for cancer. The burden of caregiving for a person affected by breast or colon cancer may not be as great as that experienced by a spouse of someone affected by Huntington's Disease, and cancer is certainly not as fatal, however there are still important issues to be considered. Firstly the spouse may have different views about whether genetic testing is desirable. Secondly they may believe that they will themselves have an adverse reaction to the result. Thirdly they may have concerns for any children which may not be considered in the same way by the at-risk individual when making their decision. These issues may in turn have an effect on the at-risk individual either before taking the test, or after receiving the result. These issues are explored within the theory of planned behaviour to a limited extent in the question 'Would your spouse want you to have a genetic test'. This question, however, only measures perceived norms, not actual norms. It is possible that when a test is more likely actual norms will exert a greater influence as the forthcoming test may be discussed more openly and others' views may be expressed more.

This raises a theoretical issue - the relationship between subjective norms and actual norms. The formation of norms has been shown to be shaped by the influences of a group (Sherif 1935) or an individual. The relationship between subjective norms and the actual intent of a partner however has not been studied within the context of the theory of planned behaviour and intent to have a genetic test. If subjective norms with respect to genetic testing are formed in the way proposed by Sherif, then the participant will observe the views of their partner and form a perception of their view (subjective norm). This internal representation of their views (subjective normative beliefs) should in turn influence their intention.

7.2 Aims

In this study the degree of relationship between the actual and subjective norms will be explored and compared with the relationship between subjective norms and intention among the participants.

7.3 Hypothesis

This was an exploratory analysis, as few papers have examined the issue of genetic testing from the partner's perspective. Based on the research involving partners of people at risk of Huntington's Disease and the theory of planned behaviour, the following hypotheses were formed:-

- Partners of high risk individuals will hold a stronger intent for their partner to have the genetic test than the high risk person themselves holds.

- Other measures will show that spouses hold similar views to their partners concerning genetic testing

- High-risk individual's subjective normative beliefs with respect to their partner will be highly correlated with their partner's wish for them to have a genetic test.

7.4. Method

7.4.1 Procedure

This study was conducted in conjunction with the follow-up study outlined in Chapter 6. Questionnaires were sent to individuals who had completed a previous questionnaire, and included a questionnaire for their partner, which they could give to them if they were willing for the spouse to be included. The partners could not be contacted directly as this would breach the patient's medical confidentiality.

7.4.2 Materials

For this study the key variables were:- intent, attitudes, perceived behavioural control, anticipated affect, perceived benefits, perceived barriers, perceived severity, perceived susceptibility, uncertainty, cancer worry, anticipated reassurance, anxiety and depression. Questions were re-worded to explore the perception of the partner in respect to the high-risk individual undergoing a genetic test - for example, 'During the

past month how often have you thought about your **partner's** chances of developing bowel cancer'(cancer worry scale). Intent was measured with respect to the high-risk person having a genetic test (i.e. for partners:- 'Would you want your partner to have a genetic test if they were offered it?' *(yes, definitely, yes, probably, unsure, no, probably not, no, definitely not)*)

Subjective normative beliefs were not measured in the questionnaire for the spouses, as this was not relevant for the purposes of this study, but the at risk individuals did complete these questions. Only one item was used to measure perceived behavioural control (How much control do you feel you have over whether or not your partner has the genetic test- 4 point scale), the at-risk individuals' responses on just this item were used for the comparison. Perception of partner's risk was measured using just one item (What would you say are your partner's chances of developing bowel cancer?- 7 point scale), which was compared with the response of at risk individual's to the question 'What would you say are your chances of developing bowel cancer?' (7 point scale). Both parties also stated their perception of the population risk, and the spouses stated their perception of their own risk of developing colon cancer.

Demographic details were also taken, as well as questions about length of marriage, when the partner had learned of the genetic risk and whether they had discussed the cancer risk.

7.4.3 Participants

Of those who returned the questionnaires (see response rates in Chapter 6), 58 people had been sent a questionnaire for their partner to complete at the same time. Partner responses were returned for 41 of these individuals (71%), 17 partners did not respond. This non-response could be because the index patient did not want their partner to complete the questionnaire, or because the partner did not want to complete it. The differences were examined between those couples who returned both, and those for whom only the index patient responded.

The groups did not differ by age, cancer status or intent of the high risk individual to have a genetic test at the first or second survey time. There was a significant effect of

gender. All of the partners of the male index patients (14) returned questionnaires, and 27 of the partners of the female index patients returned questionnaires. The seventeen partners who did not return questionnaires were all partners of female index patients – indicating that there was a tendency for the partners of female patients (the majority of whom would be male) not to return the questionnaire. This was significant at a level of $p<0.01$ ($\chi^2 = 7.65$).

7.4.4 Statistical analyses

Comparisons between high-risk individuals and their spouses were made using correlation co-efficients and paired difference t-tests.

7.5. Results

Firstly the similarities and differences between the views held by high-risk individuals and their partners were explored using paired t-tests (Table 7.1.). This technique explores whether the difference in beliefs about genetic testing between the index patient and their partner is significantly different from zero. The questions asked of the partners related to the index patient's risk of colon cancer and the patient having a genetic test, so the responses were all related to the same hypothesised event.

Table 7.1. Paired t-tests comparing beliefs of index patients with their partners.

	Index patients		Partners			Paired difference
Variable	Mean	S.D.	Mean	S.D.	Inter-group correlation	T(df) sig^n.
Intent	4.54	0.68	4.38	0.85	0.32*	1.06(38)
Attitude	4.45	0.66	4.5	0.74	0.47**	-0.44(38)
Perceived Behavioural Control	3.05	1.1	1.89	0.68	-0.03	5.5(38)***
Anticipated Negative Affect if patient decided not to have test	2.46	0.75	2.09	0.60	0.16	2.6(37)*
Anticipated Negative Affect if positive result	2.14	0.55	2.09	0.53	0.13	0.5(36)
Anticipated Negative Affect if negative result	1.10	0.33	1.05	0.11	0.30	0.95(36)
Anticipated Positive Affect if negative result	2.83	0.68	2.74	0.69	0.17	0.57(36)
Perceived Benefits	3.90	0.72	3.74	0.61	0.14	1.08(37)
Perceived Barriers	2.67	0.75	2.65	0.73	0.18	0.11(38)
Perceived Susceptibility	4.95	1.72	4.11	1.87	0.23	2.29(36)*
Perceived Severity	3.46	0.65	3.45	0.42	0.11	0.72(39)
Cancer Worry	9.75	2.81	9.98	3.25	0.50***	-0.47(39)

***$p<0.001$
** $p<0.01$
*$p<0.05$

The index patients' and their partners' views were closely related on three measures - intent to have test ($r=0.32;p<0.05$) attitudes towards genetic testing ($r=0.47;p<0.01$) and cancer worry ($r=0.50;p<0.001$). Most of the other constructs were positively related between the two groups, but the relationships not significant. Overall intent for the partner to have a test was very high in both groups.

The mean responses of patients and partners differed significantly on just three measures- perceived behavioural control over high risk person having the test ($t= 5.5$ (38), $p<0.001$), anticipated negative affect if the index patient decided not to have a test ($t=2.6(37)$, $p<0.05$), and perceived susceptibility ($t=2.29$ (36), $p<0.05$). Partners felt that they had low control over whether the high risk patient had a test, anticipated lower levels of negative affect if the index patient did not have a genetic test, and they perceived their partner to be less at risk of colon cancer than the index patient themselves did.

The differences in perceived susceptibility were examined in more detail. Further paired t-tests examined a number of relationships between risk perception variables.

There were large variations in the assessment of the population risk. On the fixed choice format responses all options were endorsed, from a population risk of developing colon cancer from 1 in 2 to 1 in 125. At the time the original questionnaire was designed the population risk was estimated as 1 in 25 (1995 figures), it is now estimated at 1 in 20 (1999 figures from CRC website).

The assessment of population risk should act as a baseline measure, and should not vary between participants and their partners. This was found to be true ($t = 1.5(37)$, $p = 0.14$), although partners rated the population risk (on the 7 point scale) (mean 2.98, s.d. 1.37) as lower than the index patients did (mean 3.45, s.d. = 1.548). The analysis of the personal risk assessments showed clear differences though. Index patients rated their own risk as significantly higher (mean =4.95, s.d. =1.72) than partners rated the index patient's risk (mean = 4.11, s.d. =1.87), $t(36) = 2.29$, $p<0.05$. Again there were marked variations in assessment of risk in both groups, ranging from 1 in 125 to 1 in2 (1-7). Partners did however rate the index patient as more at risk of colon cancer (mean =4.05, s.d. =1.87) than they rated their own risk (mean =2.63, s.d. = 1.53), $t = -4.7(37)$, $p<0.001$).

An additional analysis demonstrated the presence of an optimistic bias in the partner's assessment of their own risk. Partners rated their own risk (mean = 2.63, s.d. =1.53) as a significantly lower risk than they estimated the general population risk of developing colon cancer (mean 2.93, s.d. =1.40) ($t(37) = 2.3$, $p<0.05$).

The data from the spouses enabled a consideration of the differences between subjective normative beliefs of the index patient, and the actual beliefs of their partner. The index patients were asked whether their partner wanted them to have a genetic test, this item was compared with their own intent to have a genetic test and their partner's desire for them to have a genetic test (Table 7.2). The index patient's evaluation of their partner's wish for them to have a genetic test, was more highly correlated with their own intent to have a genetic test than with their partner's desire for them to have a genetic test. Significance tests using Fisher's transformed r indicated that the difference between the correlation of patient's intent and subjective norm, and partner's intent and subjective norm approached significance ($z = 1.63$ $p =$

0.0513). Thus it is likely that the patient's view of their partner's beliefs is more closely related to their own intent than their partner's actual intent for them to have a genetic test.

Table 7.2 Correlations of Patient's Subjective Norm by Patient's and Partner's intent.

		Subjective norm	Patient's intent
Patient's intent	Pearson Correlation	0.666	
	Sig. (2-tailed)	0.001	
	N	40	
Partner's intent	Pearson Correlation	0.398	0.315
	Sig. (2-tailed)	0.012	0.05
	N	39	39

This finding may be due to a response bias, due to patients not knowing what their partners would want them to do, or due to the misperception of their partner's wishes and an alignment of these with their own. The second of these options was explored by examining the frequency of responding to the items on the question evaluating the patient's evaluation. In response to the statement 'My partner would want me to have the genetic test' – 11(27.5%) strongly agreed, 15 (37.5%) agreed, 10(25%) were unsure, and 4 (10%) disagreed. If the majority of people did not know what their partners would want, 'unsure' would have been the modal response.

7.6 Discussion

Overall patients and partners reported very similar opinions of genetic testing. The anticipated difference in reported intent for the affected individual to have a genetic test was not observed. Previous research had found higher levels of intent for the affected person to have a test among the partners of affected individuals (Evers-Kiebooms et al 1989, Evers-Kiebooms et al 1987). There was no significant difference in this study, and examination of the means indicated that intent was non-significantly lower in partners than in high-risk patients.

The second hypothesis found moderate support. There were very few significant differences between high-risk individuals and their partners (perceived behavioural control, anticipated negative affect if not tested and perceived susceptibility). Despite this, there were also few variables that were significantly correlated between the two

groups (intent, attitudes and cancer worry). For the majority of the variables therefore, there was no significant difference between the two groups, but additionally no clear relationship between them either. The individual variation in responding appears to be greater than any variation due to the group, or the couple to which the respondent belongs.

The lower perceived control over the test being carried out and the lower anticipated affect if the test is not carried out probably reflect a view that the choice is one which the patient would, and perhaps should make, rather than one which the spouse should have a strong influence over.

The other area in which there was a significant difference was in the responses to the perceived susceptibility questions. Despite giving a similar assessment of the population risk of developing colon cancer, the index patient's estimate of their risk was much higher than their partner's estimate of the patient's risk. Index patients reported assessment of their own risk was much closer to their clinical risk than the risk level estimated by their partners. The partners did however report that they believed that the index patient was at more risk of developing colon cancer than the population or themselves. The partners also showed an optimistic bias in assessing their own risk in relation to the population. In all of these analyses it is the partners who are minimising the risk, not only of their partner, but also of themselves of developing colon cancer. This minimisation may either be due to a lack of knowledge of their partner's true risk, or it may be a denial of their risk.

The 'optimism' in connection with their own risk, may simply be optimism that they won't develop cancer, perhaps from an erroneous view that 'lightning won't strike twice', i.e. for both they and their partner to be at risk of cancer would be unlikely. They may, however have been crudely calculating their own risk based on the knowledge that their partner was at high risk, and there are likely to be others like them who raise the average rate of colon cancer in the population. The presence of people at high risk means that the likely risk for an individual with no family history is slightly lower than the average rate in the population. Whether this cognitive process

is actually engaged in, or whether it is a simple example of optimistic bias is open to question.

The final issue addressed was the to explore the relationship between actual norms and subjective norms. The analysis of this relationship showed that although there was a weak positive relationship between the partner's intent (actual norm) and the index patient's reported subjective norms, there was a much stronger relationship between the patient's subjective norms and their intent to have a genetic test. This means that the index patient's perception of their partner's desire for them to have a genetic test is more closely related to their own intention to have a genetic test than it is to their partner's actual desire for them to have a test. As few patients reported that they were unsure about their partner's wishes, the finding is due to a responding bias, or a misperception of the partners' wishes.

If the difference is due to a misperception of their partner's wishes, then this has important implications for the theory of planned behaviour (/reasoned action). The theory does not explicitly state that subjective norms are anything more than an internal representation of the perception of other's views. Despite this, norms are held to be distinct from attitudes and intent, and the implication is that they are formed as a result of the interpretation of external influences. This study has shown that the much stronger association is between intention and subjective norms than between subjective norms and actual norms.

One explanation is that the subjective norms were formed when the actual norms were different, but subsequently the actual norms (partner's views) have changed and the subjective norms have not been re-evaluated. Alternatively the subjective norms may not have been based on actual norms, but are an extrapolation of their own intent. It could be that people believe that others want them to have the test because that is their own belief. This may be a false consensus effect (Marks & Miller 1987) to help them rationalise their own beliefs in a situation in which the society norms are not yet fully established.

If this were the case then this would cast strong doubt on the role of subjective norms in *causing* intent. This would support the finding in Chapter 6 that subjective norms

do not cause intent, and possibly the reverse is true. This does not detract from the role of subjective norms in being a strong correlate of intention, however it does question whether the concept may simply be a less direct way of measuring intent.

To explore this issue further a longitudinal study would be required, assessing partner's views, patient's normative beliefs and patient's intent at more time points to construct a model of the causal influences on all of the theory of planned behaviour constructs. Considering the nature of genetic testing it would also be appropriate to explore the perception of the views of other important family members, and the causal role of these norms in forming intention.

There is some concordance between the views of patients and the views of their partners - the positive relationship between intention and attitudes in the two groups, and the low rate of discordance between the participants, however the views are not as similar as those found by previous researchers. This may be because previous research has firstly focused primarily on specific reasons for testing but the differences and similarities were not assessed statistically, just descriptively, and comparisons were made on a group level (in terms of percentages) rather than exploring the difference or the correlation between the views of the two people in each couple.

This study has also raised theoretical issues concerning the theory of planned behaviour, which again question the causal relationship between attitudes, subjective norms, perceived behavioural control and intention to have a genetic test. These issues deserve a more extensive enquiry, over a longer study period to explore the initiation, formation and establishment of intention over time.

7.7 Conclusion and Next Study

This study has shown that partners hold broadly similar views to those expressed by people at high risk of colon cancer. Partners perceive their own and their partners' risks to be lower than they actually are. They also perceive that they have less control over whether the high risk person is tested and anticipate less emotional consequences following test result disclosure. The nature of the causation of subjective norms was questioned in this study, and deserves more extensive consideration in future research.

The focus of the thesis will now shift away from exploring simply the issues facing people who are asymptomatic and have a family history of colon cancer. By including spouses in this study, attention has begun to turn away from just those at risk. The following chapters will compare the individuals from the original database with other groups of individuals. The first group with which they will be compared is a group of people who also have a strong family history and are registered with St Mark's Hospital database, but who already have a personal history of colon cancer. For these people a genetic test is no longer predictive, but confirmative, as the medical profession assumes them to be carriers of a genetic mutation which has caused their cancer. The important issue that will be examined is whether the decision for these people is in any way different to that for asymptomatic individuals.

Chapter 8

Comparison of Psychological Aspects of Genetic Testing in those who have had Cancer and those who have not

8.1 Introduction

The decision to take a genetic test by people who have had cancer has generally been regarded as a more straightforward decision than the decision to have a predictive genetic test. The genetic test is seen as confirming what is already suspected, that the person is a carrier for a gene which has predisposed them and their relatives to develop colon cancer. This test is, however, necessary if asymptomatic family members wish to have a genetic test, as it is only through identifying the mutation in affected members that unaffected members can be tested.

Little attention has been paid to the views of people who have had cancer in the literature reviewed in Chapter 2. In Huntington's Disease there are clinical signs of the disease in symptomatic people so there is no need to confirm the diagnosis, if they are from an at risk family. The characteristics of the diseased gene are now established and a genetic test can be offered to anyone, negating the need to have testing for relatives. In addition neurological impairment associated with Huntington's Disease may impair the ability to give informed consent or understand the result and would make it difficult to separate the effects of receiving a test result from those of the disease.

In studying the effects of genetic testing for breast cancer, most studies have only included unaffected people with a moderate family history. Struewing et al (1996b) did include 11 women who had cancer, however the differences between these women and other women in the study were not explored. In another study (Cappelli et al 1999) women who had breast cancer before the age of 50 (n=60) were compared with a general population control group (n=50). In these analyses women who had had breast cancer reported higher rates of intent to have a genetic test but perceived that the influence of genes in breast cancer was important in a smaller number of cases than the control group did. These women also reported more concern about the risk of their children developing breast cancer than the general population group did. This study, however, did not compare the views of people with breast cancer with those of women from an at risk family but without breast cancer. From Cappelli et al's study it is not

possible to conclude whether it is the personal history of breast cancer, or whether it is the perception of familial genetic risk which is important.

In a study of people with colon cancer (Vernon et al 1999) those who intended to have a genetic test were more worried that they might carry a predisposing gene, thought their family would benefit more if they had the genetic test and saw more pros to testing. This study however reports the findings from this sample in isolation, so conclusions cannot be made about how these patients' views may differ from those of their relatives.

This study will seek to establish whether a personal history of cancer has an influence on people's perceptions of genetic testing above and beyond that of being at risk by virtue of family history. The lack of previous literature in this area means that the likely results can only be theorised about at this stage.

The different situation of people who have had cancer is likely to influence their views of genetic testing. The genetic test is not likely to bring unexpected news, as their family history is likely to have been discussed when the cancer was detected, and the probability that they are carriers for a gene may have been covered at this stage. This means that the emotional effect of a positive test result is unlikely to be as great in people who have already had cancer themselves.

The discovery of the presence of a high risk gene is likely to have a smaller effect on their lives than in asymptomatic individuals. At this stage insurance is already likely to be problematic to acquire, they will already be aware of the risk of re-occurrence of the cancer, any lifestyle changes prompted by the knowledge that they carry a gene are likely to have already been prompted by the cancer itself (healthier lifestyle, financial planning etc), and offered screening is likely to already be at a maximum. The main benefit is likely to be increased knowledge for themselves and their families. Thus although people who have had cancer may have the least to gain from knowing whether they carry a mutated gene, they also have the least to lose.

The two groups are also likely to hold different views about their own susceptibility to cancer, and the likely severity of any cancer. People who have had cancer are likely to perceive themselves as more susceptible to cancer. This increased susceptibility will be

in part because of knowledge that prior cancer history indicates that they probably have a gene that will cause future illness. Another reason for this heightened perceived susceptibility is the suspension of the general belief that it couldn't happen to them. The higher perceived susceptibility in this group is likely to also lead to higher levels of cancer worry. Those who have had cancer however, are likely to see it as less serious, as they have all survived, so their perception is likely to differ from that of the whole group of people who develop cancer, some of whom subsequently die. Within the asymptomatic group, as first degree relatives of a person who has had cancer, they will all be aware of the nature of the illness, but as the survival rate for cancer is low, most of them will have experienced the death of a relative from the disease. Thus on average their perceptions of severity are likely to be higher.

The people who have had cancer are likely to hold more favourable attitudes towards genetic testing as for them genetic testing would have fewer disadvantages. Barriers were more strongly associated with attitudes than benefits were in the first study (Appendix B). As barriers are expected to decrease but benefits also decrease, in the absence of previous research, attitudes are expected to reflect the change in barriers more than the change in benefits. People who have had cancer may also believe that their family and significant others would also want them to have a genetic test. For their families it will not be possible to determine whether children or other younger relatives carry a mutated gene until evidence of such a gene has been found in an affected family member. For this reason any asymptomatic family members who want a genetic test themselves are likely to be more in favour of their relative having the test. If family members do not want a genetic test at the moment, they may discourage the affected individual from having a test, however, there would be little for them to gain or lose whether the person has a test or not. As the affected member is not dependent on the results of someone else's test they should perceive that they have more control over having a genetic test than those in the asymptomatic group.

8.2 Aims

The aim of this study was to explore the differences in responding to questions about psychological aspects of genetic testing between those who have had colon cancer and those who have not but are at high risk. As no studies have examined this question in colon cancer risk families this will be an exploratory analysis.

8.3 Hypotheses

- Participants who have had cancer will see fewer benefits but also fewer barriers to testing, anticipate fewer negative emotional effects of receiving a positive test result, anticipate more positive affect if they receive a negative test result, and perceive themselves as more susceptible to colon cancer. Cancer patients will, however, perceive cancer as less severe, because they have already survived one episode.
- Cancer patients are more likely than non-cancer patients to develop cancer in the future, so they should display higher levels of cancer worry.
- People who have had cancer will have more positive attitudes (due to fewer perceived barriers/ disadvantages to testing) towards having a genetic test, they will see few objections from significant others, and they will feel more control over whether they have a genetic test, as the analysis can be done first on their blood sample.
- These differences will lead to increased intention to have a genetic test in people who have had cancer.
- The main predicted demographic and health differences are that those affected by colon cancer will be in poorer health, older and not working. This is due to the nature of the illness that it has a moderately late onset, so the youngest people are unlikely to be cancer patients, and the incapacitation some cancer patients' experience would preclude the possibility of them working.

8.4 Method

8.4.1 Procedure

The procedure was the same as that outlined in Chapter 4. All participants were recruited at the same time via the same method, postal questionnaire and freepost envelope.

8.4.2 Materials

All participants answered the same questions that are outlined in Chapter 4. Two questions (*Have you had bowel cancer?* and *Have you had any other type of cancer?*) and clinical evaluations of risk were used to identify the groups as outlined below.

8.4.3 Participants

These analyses included all respondents with a risk of 1 in 12 or greater of dying from colon cancer (selection groups 1 and 2). Participants were excluded if their familial clinical risk was assessed as being less than one in 12. There were no participants who had had cancer in this risk group and their risk of developing colon cancer in the future is much lower than the risk for the other groups. Secondly those who reported that they personally had had colon cancer were placed in the personal history of cancer group. Finally participants were excluded from the no-cancer group if they reported that they had had another type of cancer, as this may or may not have been due to extra-colonic cancers associated with the same gene as caused colon cancer in other family members. Those people who reported another type of cancer may or may not have been aware that this could indicate the presence of a gene. For this reason these participants were excluded from all analyses in this chapter. Comparisons were therefore made between those in this group who had had colon cancer (n=41), and those who were at moderate to high risk but currently unaffected (n=230).

8.4.4 Statistical analyses

The first analysis explored whether there were any reported health or demographic differences between the two groups using a series of chi-squared analyses, and one-way ANOVAs for those variables that were on a linear continuous scale. Any variables that did differ across the groups were then entered as co-variates in a multivariate analysis of variance to determine whether there were any differences in responses to the psychological variables between the people in the two groups.

8.5 Results

8.5.1. Demographic and health differences between people with and without colon cancer

A series of chi-squared analyses were conducted to determine whether there were any significant demographic or health differences between people who have and have not had cancer (Table 8.1). Analyses of variance were used to examine differences in age and number of children between the two groups.

Table 8.1. Comparison of 'had colon cancer' vs 'have not had cancer'

Variable	Not Had Colon Cancer N=230	Had colon cancer N=41	Significance Levels
	Frequency (%)		χ^2 , p
Gender			
Male	140(29.9)	18(41.9)	
Female	329(70.1)	25(58.1)	2.663 ns
General Health			
Poor/ Fair	31(13.5)	12(29.3)	
Good	134(58.5)	23(56.1)	
Excellent	64(27.9)	6(14.6)	9.09, p<0.05
Marital Status			
Married/ cohabiting	172(75.8)	31(77.5)	
Not married	55(24.2)	9(22.5)	0.56 ns
Religion			
Protestant	139(61.2)	26(65)	
Catholic	31(13.7)	4(10)	
Jewish	14(6.2)	4(10)	
Other	6(2.6)	1(2.5)	
None	37(16.3)	5(12.5)	1.481 ns
Deprivation			
Working / retired	201(87.4)	33(80.5)	
Not working	29(12.6)	8(19.5)	1.407 ns
Own home	204(88.7)	37(90.2)	
Renting home	26(11.3)	4(9.8)	0.085 ns
1 or more cars	212(92.2)	38(92.7)	
No car	18(7.8)	3(7.3)	0.013 ns
2+ yrs education after 16	155(67.4)	21(51.2)	
Less 2yrs education after 16	75(32.6)	20(48.8)	3.997 p<0.05
Risk group			
Moderate Risk	72(31.3)	19(46.3)	
High Risk (HNPCC and older onset dominant pedigree)	61(26.5)	3(7.3)	3.53 ns
		Mean (sd)	F(df), p
Age	46.11(11.64)	50.98(11.21)	5.999(1, 266) p<0.05
Children	1.65(1.26)	1.98(1.25)	2.307(1, 265) ns

*Respondents who had had colon cancer reported poorer general health – the low number of people may affect the reliability of this finding, however the same result was found when the categories 'poor' and 'fair' were collapsed.

*The affected group are on average older than the unaffected group, this is because the likelihood of developing cancer increases with age, some of the young unaffected individuals will develop cancer as they get older. This may explain some of the association between cancer status and education, as older people are less likely to have further education.

The groups differed on three variables. Those people who had had cancer did report poorer overall health (χ^2 = 9.09, p<0.05). Due to small expected frequencies in one of the cells two levels of this variable were collapsed into one category (poor/fair) so that no cells had an expected frequency of less than 5.

Participants who had had cancer were older than those who had not had cancer, with a difference in mean of almost five years (F=5.999 (1,266), p<0.05). These participants

were also less likely to report attending education beyond the age of 16. There is a trend towards a significant relationship between age and education (r= 0.082, p= 0.064). There was no difference in terms of working status.

8.5.2. Psychological differences

Those who had had colon cancer were then compared with those who had not on the psychological variables. A multivariate analysis of co-variance was performed comparing people who had had cancer with other high risk individuals on psychological variables (Table 8.2). Subjective health and age were entered as covariates, education was not entered, as this was correlated with age.

Table 8.2. MANCOVA comparing cancer patients with high risk non cancer patients on psychological variables, controlling for age and subjective health.

Variable	Not Had Colon Cancer N=187		Had colon cancer N=28		F (3.211)	F"(df) - Welch Procedure
	Mean (Marginal Means)	SD	Mean (Marginal Means)	SD		
Intent	4.46(4.47)	0.71	4.68(4.64)	0.61	2.11(ns)	
Attitude	4.47(4.48)	0.68	4.75(4.72)	0.47	3.1*	7.57(1,46)**
Subjective Norm	3.83(3.84)	0.74	4.25(4.24)	0.62	3.6*	
Perceived Behavioural Control	3.20(3.2)	0.70	3.13(3.12)	0.79	1.29(ns)	
Anticipated Negative Affect if decided not to have test	2.53(2.53)	0.70	2.71(2.72)	0.69	0.66(ns)	
Anticipated Negative Affect if positive result	2.08(2.09)	0.52	1.92(1.89)	0.43	4.5**	
Anticipated Negative Affect if negative result	1.06(1.06)	0.20	1.06(1.07)	0.19	0.53(ns)	
Anticipated Positive Affect if negative result	2.74(2.76)	0.56	2.96(2.96)	0.73	1.05(ns)	
Perceived Benefits	3.69(3.70)	0.58	4.08(4.05)	0.72	5.32**	7.49(1,32)**
Perceived Barriers	2.50(2.5)	0.70	2.29(2.29)	0.63	3.91**	
Perceived Susceptibility	3.44(3.44)	0.78	3.82(3.85)	0.91	2.2(ns)	
Perceived Severity	3.55(3.56)	0.71	3.29(3.24)	0.85	2.45	
Uncertainty	3.97(3.98)	0.68	4.20(4.15)	0.59	2.71*	
Worry	9.55(9.55)	2.36	10.14(10.15)	2.73	3.84*	
Anticipated Reassurance GT compared with FOB	2.38(2.37)	0.94	2.39(2.45)	1.10	1.23	
Anticipated Reassurance GT compared with colonoscopy	3.03(3.04)	1.03	2.89(2.87)	1.17	0.48	
Anxiety	6.18(6.17)	3.93	5.89(5.95)	3.55	7.39***	
Depression	2.74(2.79)	2.8	2.93(2.63)	3.08	9.23***	

***p<0.001
**p<0.01
*p<0.05

The overall multivariate analysis of covariance showed a difference between groups (Pillai's Trace $F=1.75(18, 194)$, $p<0.05$). Levene's test of the equality of error variances, showed that overall there were few significant differences in the variance between the two groups. The exception to this was the measure of attitudes ($F=9.04(1,213)$, $p<0.01$) and perceived benefits ($F=5.014(1,213)$, $p<0.05$). Using the Welch procedure, the results remained substantially the same, indicating that the heterogeneous samples did not have an undue effect on the MANCOVA.

The analysis failed to demonstrate higher levels of intent in those people who have had cancer, with high levels of intent in both groups (mean = 4.47(asymptomatic group), mean =4.64 (colon cancer group)). People who have had cancer reported more positive attitudes towards having a genetic test ($F= 3.1$, $p<0.05$). There was a significant difference in subjective norms, with affected individuals perceiving important others to be more in favour of them having a test than people who have not had cancer ($F= 3.6$, $p<0.05$). People who had had cancer anticipated less negative affect in response to a positive genetic test($F= 4.5$, $p<0.01$). People who had had cancer could see more benefits to testing ($F= 5.3$, $p<0.01$) and fewer barriers ($F= 3.9$, $p<0.01$) but did not perceive themselves as more susceptible and did not rate colon cancer as any less severe than those who had not had colon cancer. People who had had cancer were more likely to want to reduce medical uncertainty by having any tests available ($F= 2.7$, $p<0.05$); they also worried more about developing cancer again in the future ($F= 3.8$, $p<0.05$). People who had had cancer reported being less anxious ($F= 7.4$, $p<0.001$) and less depressed ($F= 9.2$, $p<0.001$) in general than people who had not had cancer.

8.6 Discussion

This study explored the influence of past experience (have versus not had cancer) on intentions to have and opinions of genetic testing. Despite the small sample size, the study found support for most of the hypotheses that were outlined initially. In accordance with these hypotheses, people who have had cancer are generally more favourably disposed towards genetic testing, perceive fewer barriers to testing and anticipate fewer or less major emotional consequences of testing. This supports the view of the clinical collaborators on the study that genetic testing is likely to be viewed more favourably by people who have had cancer.

There were some findings that did not concur with the hypotheses. People who had had colon cancer did not report significantly greater perceptions of their susceptibility or lower perceived severity or the perception of fewer benefits. The hypothesised higher perceived behavioural control was also not supported. All participants believed that they had a large degree of control over the decision whether to have a genetic test. This level of control is likely to be unrealistic for those who have not had cancer, as they can only have the genetic test if affected family members also have the test. Despite the support for the majority of the hypotheses, and the more favourable attitudes and subjective norms of those who had had colon cancer, this did not translate into the predicted significantly higher intent to have a genetic test. These findings are discussed below.

In the initial analysis, background information on the participants was compared by group to determine which, if any, factors other than psychological factors varied by cancer status. The people who had already had cancer were older and did report poorer health, however there was no difference in working status. The reason for the age difference between the groups could be because cancer tends to have an onset in middle or old age even in people at high risk, so young people are less likely to have cancer, even if they carry a genetic mutation. The difference in numbers attending school beyond 16 may also be a reflection of this age difference, as people were less likely to pursue further education forty years ago. These background variables were then entered into a multivariate ANOVA which explored the effect of cancer status on psychological variables.

The differences between those who had and not had cancer on measures of attitudes and subjective norm were significant, with people who have had cancer holding more favourable evaluations and perceiving others to be more in favour of genetic testing than those who had not had cancer. It is interesting that these differences are not reflected so strongly in the measure of intent that is held to be determined by these measures. There was a high level of intent to have genetic testing in people who have had colon cancer which is perhaps unsurprising, as they may perceive it as helping them and their family gain more information about early prevention. Their intent however was not significantly different from those of people of comparable risk who had not had colon cancer. This is likely to be due to the near ceiling effect in both groups, with the majority of people being in favour of testing.

One area of possible concern in offering testing is the high perceived norms in favour of genetic testing in those who have had cancer compared with those who have not. This may represent a perceived support from the family or a projection of their own beliefs onto others. It may alternatively be due to a perceived pressure to have the test from other family members who also intend to learn of their own risk. Genetic testing is currently only available through an affected family member, this may lead to real or apparent pressure on those affected to have the test so that others in the family can also benefit from this knowledge. This may be an important area to be aware of when counselling affected individuals about having a genetic test. Future research should also explore in more detail the possible reasons for this high level of perceived norms in favour of testing.

There was no significant difference in perceived behavioural control, despite those who have had cancer having objectively greater actual control over whether they have the test, as their decision is not dependent on others agreeing to also have the test.

As anticipated, those who have had cancer believed that they would experience fewer negative reactions if they were found to be gene carriers. This indicates that these people might not find testing evokes as many emotions as a person would with no personal cancer history. This supports the view of the collaborating physicians that that for people who have had cancer, a positive result will have less of an effect. These people have previously survived cancer, so have a greater understanding of the disease, there is less 'fear of the unknown'. Affected individuals may have themselves anticipated this result on the basis of their previous cancer history, and medical personnel have probably prepared them for the fact that this is the likely outcome. With a strong family history, the occurrence of a colon cancer in an individual is often presumed to be due to a mutated gene, however it is important to remain open minded, as most colon cancers are sporadic, and these do occur in high risk families.

There were no differences on the other measures of anticipated affect, with both groups reporting high negative affect if they decided not to have the test, low negative affect for a low risk result and high positive and surprised feelings if they did not carry an at risk gene. The variances for all these measures were homogeneous, indicating that not only did the two groups hold similar views, but the distribution of these views was also similar.

Within the health belief model there was only one difference in the directions predicted, however other aspects were not demonstrably different between the two groups. People who had already had cancer perceived more benefits in having genetic testing. This was contrary to that predicted as many of the benefits (screening, motivation for healthy lifestyle, more aware of early symptoms) would, it was hypothesised, have occurred when the person experienced the cancer. The perceived barriers to testing for people who have had colon cancer were, as predicted, less. These individuals will already have some insight into how they and their family will cope with the threat of cancer, so these are less of a concern. Insurance is already likely to be weighed against them due to their personal history of cancer, so this additional confirmation of risk may not have as much actuarial significance. According to the health belief model the higher perceived benefits and lower perceived barriers should lead to greater intent to have the test in people who have had cancer.

The results for perceived susceptibility and severity were in the direction hypothesised (people who have had cancer see themselves as more at risk of cancer, but see cancer as less severe). The differences failed to reach significance, possibly due to the small sample sizes in the group that had had colon cancer. Within the framework of the health belief model, these trends would nearly cancel each other out, if one were using an additive model. Although those who have had cancer perceive colon cancer as less severe (a disincentive for testing), they perceive themselves to be at greater risk (an incentive to have the test) and vice versa for those who have not had cancer. Using a threshold approach to the measurement of threat[1] (assuming that the perceived severity in both groups is above the threshold) those who have had cancer should be more inclined to have the genetic test, as their perceived susceptibility is higher, however this is not significant. Both groups perceive the severity of colon cancer to be above the midpoint (3), however neither, on average, rate it as very severe (in relation to other diseases, and in terms of its curability and impact on life). Despite this possible minimisation of the severity of colon cancer, it can probably be assumed that the severity would be above that of a threshold, and the person would perceive colon cancer as a threat if they perceive themselves to be susceptible.

[1] The threshold approach to the measurement of threat (Weinstein 1988) indicates that perceived severity is a dichotomous variable, either it is high enough to prompt the need for action, or it is not. Once perceived severity has exceeded this threshold, an even greater level of perceived severity will not have any more effect.

People who have had cancer also varied from those who have not on a number of other psychological variables. Those who have had cancer were more likely to dislike medical uncertainty. This is likely to be both a cause and an effect of surviving colon cancer. These people are among the minority of colon cancer suffers who have survived colon cancer, although with the gene mutation they may develop subsequent tumours. Their survival may be in part due to their vigilance in detecting colon cancer, which may in turn have been due to a disposition in favour of seeking medical knowledge and certainty, rather than ignoring risks. The experience of having not developed cancer may have reinforced the need for screening and testing, so that they can be sure that the cancer will not reoccur in the future. There were no differences between the groups in the perception of the reassurance of genetic testing compared with current clinical screening.

Those who had had cancer reported being more worried about developing cancer in the future but reported less depression and general anxiety. Anxiety and depression were measured using the HADS, which is designed to be independent of the effects of concurrent physical illness. The mean levels of anxiety approached the clinical cut-off for 'possible anxiety' (HADs) in both groups, 35% of the whole population reported levels of anxiety which were above the clinical criteria for either possible or probable anxiety, only 10% reported similar figures for depression. This indicates that both groups are potentially vulnerable, and whilst not excluding testing, clinicians should be aware of the psychological state of participants in genetic testing programmes.

8.6.1. Statistical considerations

This analysis suffered from small samples of people who had had cancer, which may limit the scope of the findings. This is unfortunately unavoidable, due to the poor survival rate from colon cancer, additionally there is likely, at any one time, to be more young unaffected individuals registered, as this includes all participants who are asymptomatic carriers. Those people who have had cancer may be to some extent unusual, as they have survived a cancer that is usually fatal. This is likely to be either due to their own vigilance and awareness, or due to the screening programme. The MANCOVA is particularly affected, as this deletes missing values in a listwise manner, and adopts a more stringent level of testing than a one way ANOVA (to reduce the chances of a type 1 error). By adopting this strategy, the chances of a type 2 error are increased, and there may indeed be more differences between these two groups of

individuals than these analyses suggest. In addition the small sample size precluded regression analyses due to the power required for such statistical approaches.

8.7. Conclusion and Next Study

The studies have thus far explored issues surrounding genetic testing in people with a family history of colon cancer. The focus of the investigation now broadens to include a wider variety of individuals and the implications of genetic testing for them. The subsequent studies will investigate differences associated with being at risk for breast cancer as compared to colon cancer, and the effect that objective risk has on the intention to undergo genetic testing, using a general practice sample.

Chapter 9

Comparison with General Practice Sample

9.1 Introduction

The comparative aspects of the study were designed to investigate how valid it is to generalise the findings of a study in one narrowly defined population to a wider range of people, or extrapolating findings from people at risk of one disease to people at risk of other disorders. So far the focus has been solely on those people who have already been aware of colon cancer, for whom testing would have particular meaning and applicability. People who have had colon cancer, people who are from high risk groups, and people whose spouses are affected have all been asked their views. In the final two comparative studies the exploration extends to encompass people from a much wider population. This study includes people who may have never thought about colon cancer, or genetic testing, people from a general practice sample.

Previous studies have also explored intention to have a genetic test and correlates of this intention in general population samples (Smith & Croyle 1995; Croyle & Lerman 1993; Croyle, Dutson et al 1995; Graham, Logan et al 1998). Some of these studies have taken the approach that tests are likely to be widely available at some point in the future (e.g. Smith & Croyle 1995). Others adopt the view that intent to have a genetic test in a general population sample is not desirable as it will use valuable resources inappropriately (Graham et al 1998). Although both perspectives have some merit they miss an important factor which is the differences between the views of the general population and those of people at high risk of cancer. There may be no differences, the differences may be simply quantitative (degree of intent to have a genetic test etc) and/ or they may be qualitative (a general practice sample may intend to have or not have a genetic test for different reasons from a high risk sample). These areas will be explored in this study.

Previous studies have indicated that level of objective risk is associated with intention and uptake of genetic testing (e.g. Valdimarsdottir et al 1999), but these studies have not explored whether the correlates of intention differ in people at lower risk of the disease. In this study, by examining not only the influence of objective risk on intent to have a

genetic test, but also the predictors of intent, it will be possible to establish whether objective risk just influences intent, or whether it acts at more levels in the emerging model to explain intent.

Research is needed to determine how comparable a model of intention derived from a population group would be in a clinical sample. If the populations show little difference in terms of the determinants of their intention to have a genetic test, or these differences are simply moderated by the decreased risk, then research in a non clinical sample could be of benefit. If the differences are more qualitative, and intention to have a genetic test in people who have no family history is influenced by different factors to those influencing intent to have a genetic test in people with a family history, then comparisons would be more problematic.

The comparison is difficult because in these studies, the participants from the database at St Marks are all aware of their family history and are receiving screening, so differences could be due to their contact with the clinic. To explore whether this might have an effect, the clinic sample will be divided into two groups - those at high / moderate risk and those at lower risk. As the step increase between these two groups is approximately equal to the difference between the general practice and the lower risk clinical sample, a difference due to actual risk should be linear. The pattern of responding and the variance explained by the lower risk clinic group should be approximately midway between that found in the high risk group and in the general practice group.

Genetic testing for colon cancer is still in its infancy, and it is unlikely that an accurate genetic test will emerge for the general population in the near future. Nevertheless, determining intent to have a test in this sample will indicate the likely demand for this and other tests from populations other than those who have approached clinics. It also indicates the general acceptability of genetic tests to the general population, establishing the societal norms for this new type of medical diagnosis. In the future these tests may become more widely applicable, so that even people who have no family history may be helped by the detection of environmentally prompted mutations in the same genes which also predispose to hereditary colon cancer.

9.2 Aims

The aim of this study was to explore the influence of actual risk on psychological factors associated with genetic testing for colon cancer. Three groups will be compared, those regarded by the clinic as being at high risk, those regarded as being a lower risk, and a general practice sample. If the actual risk is an important factor then there will be an approximately linear relationship between these groups, as their level of risk of colon cancer is also approximately linear. If instead it is an effect due to the fact that those at risk are under surveillance, then the largest difference will be between those registered with St Marks and those not registered with St Marks.

9.3 Hypotheses

- People from the general practice group compared to the other groups will:
  - Be less likely than the high risk and low risk groups registered with St Marks to intend to have a genetic test, as they will regard it as less relevant to their circumstances. Although the general practice group is not at much lower risk than those people with just one affected family member, any people registered on the database have at some point viewed themselves as being at risk.
  - Hold less positive attitudes, subjective norms and lower perceived behavioral control.
- The correlates of intention will be similar across all the groups, consistent with the hypothesis that there are similar factors underlying intentions to have a genetic test, regardless of risk category.

9.4 Method

9.4.1. Procedure

The general practice comparison group were all recruited from a single GP practice in North West London (West Hampstead). The study utilised a postal survey design, sent to all patients who were randomly selected to receive a questionnaire. The pack included a freepost envelope for the return of the questionnaire, and a letter from the GP involved and UCL. This questionnaire was based on the main study reported in Chapter 4, and where appropriate, similar wording was used to facilitate direct comparisons between the samples. The questionnaire used can be found in Appendix A. All participants for whom data is reported here were asked their opinions about genetic testing for colon

cancer. The procedure for the collection of data from the people with a family history of colon cancer sample is reported in Chapter 4.

9.4.2. Materials

The initial preparation of the combined data set involved identifying comparative questionnaire measures, and harmonising the coding categories. Only those questions that were directly comparable were used. The measures included in this study were – intention to have a genetic test; attitude towards having a genetic test; subjective and normative beliefs; perceived behavioural control; and attitude towards medical uncertainty. These items have been described in Chapter 4. Unfortunately due to the incompatible nature of the risk evaluation questions it was not possible to examine differences in perceived susceptibility. Other variables that had been measured in the colon cancer study were not measured in this study. The evaluation of benefits and barriers to testing will be examined in a detailed way between the samples on an individual item basis.

9.4.3 Participants

The general practice sample was randomly drawn from a GP's database, with the conditions that the individuals were between 18 and 60, free from breast or colon cancer and stratified by gender. One part of this study explored attitudes towards genetic testing for breast cancer however this data will not be explored in this thesis. The subject pool consisted of 200 women and 200 men sent questionnaires about colon cancer. From this original sample 60 (15 %) of the questionnaires (36 male, 24 female) were returned recipient unknown. From the remaining sample of those who were presumed to have received the questionnaire, 168/340 (49.4%) returned completed questionnaires, (41% of men and 57% of women). People were excluded if they reported one or more family members affected by colon cancer, 14 cases were excluded on this basis, 5 males and 9 females. The total sample size for this group was 154.

The samples for the colon cancer groups were as specified in Chapter 4. In these samples there were 219 people with just one first degree relative over 45(lower risk), and 218 with one or more affected first degree relatives, or one or more affected under the age of 45 (higher risk). As fewer variables were used in this study, cases were not

screened out if they had missing data, but were simply excluded statistically from any analysis for which there was missing data for that case.

For the purposes of this study, individuals from the GP's dataset were excluded if they reported any family history of colon cancer as it was not possible to assign a clinical risk criterion comparable to that used in assessments at the Family Cancer Clinic based on available information. For simplicity, analyses examined the differences between just three groups – those at moderate to high risk of dying from colon cancer (**high and moderately high risk groups in study 1**); those at a slightly increased risk (**lower risk group in study 1**); and those at population risk (**no affected relatives**). Participants were excluded from all groups if they reported having had cancer as proportionately more of the people on the colon cancer database had experienced cancer, so the study was only examining predictive genetic testing. The moderate to high risk group is the most likely to be offered a genetic test. Those at slightly increased risk or from the general practice are unlikely to be offered testing in the near future.

9.4.4. Statistical analyses

The first analysis explored whether there were any reported health or demographic differences between the three groups using a series of chi-squared analyses, and one-way ANOVAs for those variables that were on a linear continuous scale. Any variables that did differ across the groups were then entered as co-variates in a multivariate analysis of variance to determine whether there were any differences in responses to the psychological variables between the people in the three risk groups. Responses to the specific benefit and barrier items were then compared across the three groups using an ANOVA. Finally correlates of intent were modelled using linear regressions, one model was derived for each of the three risk groups and the orders of importance and the proportions of the variance explained were compared across the groups.

9.5. Analysis

9.5.1. Demographic Differences

The groups were examined with respect to the demographic differences between them. Although there was no hypothesized effect of demographic variables, these were examined so that they could be entered as covariates in subsequent analyses (Table 9.1).

Table 9.1 Comparison between groups for demographic and risk variables

Variable	General practice	Lower Risk – one affected FDR over 45	Higher risk – more than one affected FDR or one under 45	Significance Levels
		Frequency (%)		χ^2 , p
General Health				
Poor	4 (2.7)	8 (3.7)	3 (1.4)	
Fair	21 (14.1)	32 (14.8)	28 (12.9)	
Good	86 (57.7)	116(53.7)	126(58.1)	
Excellent	38 (25.5)	60 (27.8)	60(27.6)	3.192 ns
Gender				
Male	65 (42.2)	73 (33.5)	63(29.0)	
Female	89(57.8)	145(66.5)	154(71)	7.02 p<0.05
Marital Status				
Married/ cohabiting	81 (52.6)	174 (81.3)	165 (76.4)	
Not married	73(47.4)	40(18.7)	51 (23.6)	39.95 p<0.001
Affluence				
Working / retired	132 (86.8)	149 (68.0)	159 (72.9)	
Not working	20 (13.2)	70 (32.0)	59 (27.1)	17.36 p<0.001
Own home	71 (47.0)	195 (89.0)	192 (89.3)	
Renting home	80 (53.0)	24 (11.0)	23 (10.7)	117.11 p<0.001
1 or more cars	116 (75.3)	206 (94.5)	202 (92.7)	
No car	38 (24.7)	12 (5.5)	16 (7.3)	38.54 p<0.001
Summary score				
0 –affluent	44 (29.5)	127 (58.3)	136 (63.3)	
1	77 (51.7)	78 (35.8)	64(29.8)	
2	24 (16.1)	12 (5.5)	12 (5.6)	
3 – less affluent	4 (2.7)	1 (0.5)	3 (1.4)	50.72 p<0.001
Age				
18-34	78 (51%)	22 (10.2)	40 (18.5)	
34-49	43 (28.1)	97 (44.9)	81 (37.5)	
49+	32 (20.9)	97 (44.9)	95 (44.0)	89.54, p<0.001
Children				
No children	117(77.0)	40 (18.5)	54 (25.0)	
One or more	53 (23)	176 (81.5)	162 (75.0)	150.5 p<0.005

There were a large number of differences between the groups on demographic measures. The main source of this difference was the comparison of the general practice sample with the other two groups. The general practice sample contained more men, were less likely to be married or co-habiting, reported lower affluence, were younger and had fewer children.

These factors, with the exception of age and number of children, have not been found to be correlated significantly with intention in the studies of these datasets. These factors were controlled for in subsequent analyses because the large differences in these variables between the datasets may have an impact on the dependent variables. As

entering all three affluence indices would have led to a greater drop in power, the contributing variables (employment status, housing tenure and car ownership) were added together to form a summary variable.

9.5.2. Differences between groups on psychological variables

The groups were compared on psychological variables, controlling for the demographic differences between the groups that emerged in the initial analysis. In this sample there were few participants who had missing data for demographic variables but complete data for the psychological variables, so controlling for the demographic variables did not cause a large drop in power. The drop in cases caused by entering the co-variates were 6 cases in group 1, 3 cases in group 2 and 3 cases in group 3. The analysis was therefore a multivariate analysis of co-variance, controlling for gender, marital status, age, children and deprivation (Table 9.2).

Table 9.2. MANCOVA - controlling for gender, marital status, age, children and deprivation.

	General Population (1) N=128		Colon cancer – low risk (2) N=189		Colon cancer –high risk (3) N=191		F (7,500)	Post hoc
	Mean (Marginal)	SD	Mean (Marginal)	SD	Mean (Marginal)	SD		
Intent	4.00 (4.1)	1.10	4.32 (4.28)	0.84	4.45 (4.43)	0.72	4.66***	1:2, 1:3
Attitude	3.88 (3.92)	0.99	4.13 (4.1)	0.99	4.47 (4.47)	0.69	8.36***	1:3, 2:3
Norms	3.34 (3.41)	0.89	3.70 (3.66)	0.71	3.81(3.8)	0.75	6.12***	1:2; 1:3
PBC	3.34 (3.27)	0.75	3.36(3.39)	0.85	3.34 (3.37)	0.87	2.0	ns
Uncertainty	3.50 (3.52)	0.68	3.80(3.79)	0.78	3.93 (3.93)	0.73	5.86***	1:2, 1:3

***p<0.001
**p<0.01
*p<0.05

The overall MANCOVA was significant, (Pillai's Trace, $F(10,994)=4.09$, $p<0.001$). The analysis of equality of variances showed that all the variables, with the exception of uncertainty, had heterogeneous variances across the three groups. The results were therefore checked using the Welch procedure, which did not reveal any differences in the significance of the results. The Games Howell post hoc tests revealed that the general practice group, compared with those with a family history of colon cancer, report lower mean intention to have a genetic test; lower perceived norms that they should have a genetic test and lower levels of dislike of uncertainty with regard to medical tests. The general practice sample, and the lower risk group of individuals with a family history of colon cancer, reported significantly less positive attitudes towards

genetic testing than did those people at high risk of developing colon cancer. Adjusting for covariates had little impact on the means, and the outcome, indicating that the most significant differences were probably those due to the differences between being a GP patient and a person registered on a high risk family cancer database. The significant results show a linear pattern.

Despite these differences, the mean level of intention in the general practice sample is still above the middle value of 3, so on average these participants reported that they would probably have a genetic test. Attitudes towards testing, norms and dislike of uncertainty are also above the midpoint. This indicates that most people in the general practice sample think that testing is a good idea, most think others would also think it is a good idea, and that it is best to act to reduce medical uncertainty.

9.5.3. Microanalysis of responses to specific belief measures.

The responses to specific questions about perceived benefits or barriers to having a test were examined in detail using a multivariate analysis of variance, controlling for demographic covariates (gender, marital status, age, children and deprivation) (Table 9.3).

Table 9.3 Responses to specific belief measures

Variable	General Population (1) N=126		Colon cancer – low risk (2) N=195		Colon cancer – high risk (3) N=209		F (7,522)	Location of difference
	Mean (Marginal)	SD	Mean (Marginal)	SD	Mean (Marginal)	SD		
Know whether at high risk	3.8(3.86)	0.91	3.91(3.89)	0.79	4.03(4.02)	0.80	2.03*	1:3
Know whether children at high risk	3.15(3.21)	1.00	3.54(3.52)	0.87	3.7(3.68)	0.96	4.96***	1:2, 1:3
Have trouble getting life insurance/ mortgage	2.91(2.9)	0.96	3.01(3.02)	0.88	2.99(2.99)	0.91	1.38	
Motivate to healthier lifestyle	3.61(3.69)	1.10	3.66(3.64)	1.01	3.62(3.6)	1.00	1.24	
Can have more regular screening	3.83(3.91)	0.83	3.62(3.59)	0.81	3.68(3.66)	0.89	1.31	
Can decide about surgery	3.7(3.7)	0.96	3.21(3.2)	0.96	3.24(3.25)	0.99	3.59***	1:2, 1:3
Will worry constantly	2.76(2.76)	1.11	2.65(2.67)	1.03	2.57(2.57)	0.96	4.36***	
Upset members of family	2.13(2.19)	0.92	2.28(2.26)	1.01	2.13(2.11)	0.98	1.09	

***p<0.001
**p<0.01
*p<0.05

The overall MANCOVA was significant (Pillai's Trace, $F(16, 1032)= 3.075$, $p<0.001$). The variances were homogeneous between the groups for all the variables. Games Howell post hoc tests revealed that the people in the general practice sample thought the genetic test would give them less information about their own risk than those at high risk. The general practice sample thought that they would learn less about their children's risk than the other samples did, but that the result would help them to decide about having surgery more than the other groups did. Neither post hoc tests, nor planned comparisons were able to localise the difference on the measure of whether the results would lead to more worry. The results are in the direction that people from the general practice anticipated worrying more than people from the colon cancer database did.

9.5.4. Correlates of intent to have a genetic test

These analyses have highlighted the differences between the groups, showing that people who have a lower objective risk are less likely to intend to have a genetic test than people who are at greater risk are. This is in the direction hypothesised. The analyses do not, however, indicate whether the same underlying variables are driving the intent to have a genetic test across the groups, or whether different constructs are important at different risk levels.

To determine whether the correlates of intention are the same in the different samples linear regressions were used. Initial analyses of correlation co-efficients identified significant correlates of intention (Table 9.4) – attitudes, subjective norm, uncertainty, gender, age and whether a person has children or not. These were examined on a group by group basis. In some groups there were significant correlations with the variables whereas in other groups there was no association. All these correlates were entered into hierarchical linear regressions calculated for each group separately (Table 9.5). Linear regressions were used instead of ordinal regressions, as the first study (Chapter 4) demonstrated that linear equations produce substantially similar results. In addition the general practice sample was more heterogeneous in their responses to the dependent variable, so the violation of the normality assumption was not so great in this group.

Measures were entered in steps, with the theory of reasoned action first followed by perceived behavioural control (although this was not significantly correlated with intention it was entered for completeness of the theory of planned behaviour); attitude towards uncertainty; gender, age and number of children.

Significant models emerged for all the three groups of participants, with the same three variables contributing significant variance. In the general practice sample the theory of reasoned action explained 51% of the variance in intention ($F(2,129) = 68.7$, $p<0.001$, adjusted $R^2 = 0.508$); in the low risk group it explained 56% of the variance in intention ($F(2,188) = 120.3$, $p<0.001$, adjusted $R^2 = 0.557$); and in the higher risk group it explained 53% of the variance in intention ($F(2,189) = 108.16$, $p<0.001$, adjusted $R^2 = 0.53$). There was no support for the inclusion of perceived behavioural control in the final model. Attitude towards medical uncertainty explained an additional 1.7%; 4.4% and 2.1% of the variance in the three groups respectively. None of the demographic variables explained variance in addition to that already accounted for by the other correlates. Across all groups high intent was associated with positive attitudes, subjective norms in favour of testing, and dislike of medical uncertainty.

In the general practice sample and the high risk sample, attitudes was the most important correlate, followed by subjective norms and then attitude towards uncertainty. In the lower risk group of people with only a moderate family history of colon cancer, dislike of uncertainty was marginally more significant in the final equation than subjective norms.

In these analyses therefore, support was found for the importance of the theory of reasoned action across all three risk levels. The final equations for all three samples were significant. In the general practice sample 52% of the variance was accounted for ($F(7,124) = 21.4$; $p<0.001$; adjusted $R^2 = 0.521$). In the lower risk sample of people at risk of colon cancer 60% of the variance was accounted for ($F(7,183) = 41$; $p<0.001$; adjusted $R^2 = 0.596$). In the high risk sample 55% of variance was explained ($F(7,184) = 33.93$; $p<0.001$; adjusted $R^2 = 0.547$).

The three data sets were then pooled and dummy variables created to represent the groups and the interactions between the groups and the individual variables. These dummy variables and the interaction terms were entered into an analysis after the original blocks of variables. The interaction terms were not significant, and neither was the final F change statistic ($F(14, 495) = 0.79$ $p=0.68$). This indicates that there was no difference between the model that emerged from the reference group (general practice sample) and the two at risk groups.

Table 9.4 Correlates of intent to have a genetic test.

		Correlates of intent								
		General practice			Low Risk – one affected FDR over 45			High risk – more than one affected FDR or one under 45		
		r	p	n	r	p	n	r	p	n
Step 1	Attitude	0.66	<0.001***	143	0.70	<0.001***	200	0.66	<0.001***	201
	Subjective Norm	0.64	<0.001***	150	0.649	<0.001***	208	0.57	<0.001***	212
Step 2	Perceived Behavioural Control	0.08	0.34	151	-0.07	0.31	213	-0.05	0.47	211
Step 3	Uncertainty	0.58	0.001***	150	0.60	<0.001***	207	0.44	<0.001***	205
Step 4	Gender	-0.17	0.03*	154	-0.07	0.31	215	-0.027	0.70	214
	Age	0.09	0.26	153	-0.013	0.85	214	0.192	0.005**	214
	Children	0.1	0.24	152	-0.02	0.77	215	0.209	0.002**	213

Table 9.5 Linear regression of intent onto correlates of intent

		Linear regression of intent onto correlates of intent											
		General practice				Low Risk – one affected FDR over 45				High risk – more than one affected FDR or one under 45			
		Final Beta	R^2	Adjusted R^2	R^2 change (sig^n)	Final Beta	R^2	Adjusted R^2	R^2 change (sig^n)	Final Beta	R^2	Adjusted R^2	R^2 change (sig^n)
Step 1	Attitude	0.42***	0.516	0.508	0.516***	0.44***	0.561	0.557	0.561***	0.41***	0.534	0.529	0.534***
	Subjective Norm	0.29***				0.24***				0.33***			
Step 2	Perceived Behavioural Control	0.04	0.516	0.504	0	-0.24	0.562	0.555	0.001	-0.07	0.538	0.53	0.004
Step 3	Uncertainty	0.17*	0.533	0.518	0.017*	0.26***	0.606	0.598	0.044***	0.16**	0.559	0.549	0.021**
Step 4	Gender	0.03	0.547	0.521	0.014	0.068	0.61	0.596	0.004	-0.12	0.563	0.547	0.005
	Age	-0.08				-0.07				0.049			
	Children	0.11				0.013				0.043			

9.6. Discussion

This comparison was designed to explore the differences between the intent to have a genetic test in those for which this intention was appropriate, and those for whom the test is currently inappropriate (those with no family history of colon cancer). This will show whether the intentions and beliefs held by an at risk group are quantitatively and/ or qualitatively different from those held by the general population. Does the intention follow from being at risk, or is it due to a more basic human desire to know the possible future?

The general practice sample was contacted through a G.P. database based in North London. There were a number of demographic differences between these groups. In the general practice sample there was a larger proportion of men than in the clinic groups, this may reflect the sampling approach. The general practice sample was stratified by gender, with equal numbers of questionnaires sent to men and women, whereas the sample at increased risk of colon cancer was drawn at random from a database, with no stratification by gender. This resulted in respondents having a similar gender bias as the registry from which the sample was drawn.

The general practice sample was also younger, less likely to be married, less likely to have children and were less likely to have material assets. These differences were controlled for in the subsequent analysis. The most likely explanation for all the differences is the geographical locations sampled. The general practice sample was derived from a GP list in a small geographical area of North West London (West Hampstead area). This area is approximately 5 miles from central London, and has good public transport links, including three train lines and frequent bus services.

The individuals registered on the St. Mark's database reside in a much more diffuse area than those on the GP database. The majority of St. Mark's patients reside in the North Thames area (encompassing London North of the River Thames, Essex, Herts, Bucks and Bedfordshire), however people are registered from throughout the UK. The higher proportion of people renting in West Hampstead is likely to be due in part to the high cost of housing in London. The

lower proportion of car ownership is likely to be due to a lower dependency on private transport due to the good public transport available. The GP sample is also younger, less likely to be married and less likely to have children. This means that they may not have as much capital as the other groups, but also they may be more mobile and so less likely to want to purchase their accommodation, and less likely than a family to have need of a car. These factors were included as co-variates in the subsequent analysis. These demographics indicate as well that although the sample was drawn from a 'non-clinical' group - (ie a group for whom colon cancer is not salient), they are not representative of the population of the UK, therefore their views may differ from those which would be expressed by a truly random national or international population sample.

In the examination of beliefs about genetic testing, there were a number of significant differences between the groups, primarily between those from the general practice and those with a family history (regardless of strength of family history). This supports the first hypothesis that it is having registered as being at risk which more important than actual risk. The adjusted means however do follow a linear pattern, indicating that the effects are also linked with increasing levels of clinical risk, as was found in the previous studies. The strength of intent to have a genetic test, and the covariates of intent (attitudes, subjective norms and attitude towards uncertainty), were also lower in the general practice sample. Although people in the general practice sample reported lower intentions to have a genetic test, the mean response was still that they probably would have a test, despite there being no familial risk of colon cancer.

This high level of intent to have a genetic test reveals that there is a strong desire even in those without risk indicators to learn of and plan for future illness. If this high level of intent led to referrals to specialist clinics, not only for colon cancer but also for other forms of cancer, there would be insufficient resources to assess the referrals. There is a need, therefore, to increase GPs' knowledge and understanding of genetic risk to provide pre-referral screening in primary care, to ensure appropriate referrals to secondary services. Means by which this can be achieved are already being explored, and include the introduction of computer based assessment within GP surgeries.

There were differences in the beliefs held by the different groups. The general practice sample thought that they would learn little about their own or children's risk. This may indicate that perceived risk was not such an important factor in determining their intent, as it was for those at high risk. The general practice sample however did think that the information from a test would be more helpful in deciding about surgery. The higher anticipated levels of worry in this group indicate another potential problem if genetic testing were to be offered on a wider basis. The high risk individuals have been aware of the potential risk that they may have a predisposition to colon cancer, and have developed coping strategies. A high risk result will not be completely unanticipated, although may still be surprising. In the general practice sample a high risk result is still possible, as new mutations must occur at some point in the germ line, but for them the impact may be greater, as there is less preparation for this result.

There were no differences across the three groups on the significant correlates of intention to have a genetic test (attitudes, subjective norms and dislike of uncertainty) this supports the last hypothesis. Although there may be differences in the strengths of intention and its correlates, the same factors are important in deciding whether to have a genetic test despite the different risk levels. The differences are therefore quantitative rather than qualitative.

9.7 Conclusions and Next Study

Genetic testing for colon cancer, whether in a population with colon cancer, an asymptomatic population at risk of colon cancer or a general practice sample, raises similar issues, and generates similar responses. In the next study comparisons will be made with women at risk of breast cancer to explore whether these similarities are unique to the issue of testing for colon cancer, or whether it is possible to make more generalised statements about the reasons for and the implications of genetic testing for other disorders.

Chapter 10

Breast Cancer Comparative Study

10.1 Introduction

In the near future there is likely to be a rapid expansion in the range of diseases for which it is possible to offer a predictive genetic test. Although each disease will have unique issues, it is important to determine general predictors that can be used in planning new services and in the introduction of legislation. For this reason the final study will compare the women participating in study 1 with women who participated in a study using the theory of planned behaviour to predict intention to have a genetic test for breast and ovarian cancer.

As discussed in Chapters 1 and 2, there are distinct differences between the two types of cancer, which make the decision to have a genetic test different in each case. One difference is the differential impact of carrying a genetic mutation on men and women. As discussed in Chapter 5, research into the impact of breast cancer cannot be extrapolated to accurately predict how a man may react faced with a similar threat (e.g. developing prostrate cancer). To assist the comparison, this study will only focus on the women in each cohort, so that gender effects are eliminated.

Another factor is the different screening options offered to people carrying genetic mutations. Currently in the UK mammograms are available to women at risk of breast cancer, however these may have limited application in pre-menopausal women, and rapid developing cancers may be missed between screening. A woman via self-examination can however, often detect breast cancer at a treatable stage. In addition tamoxifen may play a prophylactic role in preventing breast cancer, similar chemopreventive options for colon cancer are still in development. Colonoscopies can be effective at detecting colon cancers at very early stages, regardless of age, however they do carry a small risk of bowel perforation. Detection of colon cancer by the patient is only possible through observation of symptoms, which usually occur at an advanced stage.

If a test is negative, again the implications are different. Women found not to carry a gene predisposing to breast cancer will still be eligible for the national breast screening service. In the UK, unlike the USA, there is no screening programme recommended for the general population to reduce the risk of colon cancer, although various options have been piloted. People found to be at population risk of colon cancer lose the right to receive screening, for some people this might be an issue.

Despite these differences, both diseases are serious illnesses, which benefit from early treatment and detection. The penetrance of predisposing genes is similar for breast cancers caused by BRCA1 or 2 and for colon cancers caused by HNPCC mutations. The procedures for detection of genetic mutations are similar and the diagnosis of either disease is likely to have a large impact on the recipient of the news. By determining the similarities and differences between these two cancers in terms of the decision to have a genetic test and the likely impact of the news will begin to establish a model which can be applied and modified to other cancers and other genetic disorders. This will then provide a framework from which future investigations can develop thus furthering the psychological understanding of factors surrounding testing for genetic disorders.

10.2 Aims

The aim of this study is to establish the similarities and differences in views of genetic testing between women at high risk of developing colon cancer and women at high risk of developing breast/ ovarian cancer.

10.3 Hypotheses

- Compared with the other groups women attending primarily for genetic testing for breast cancer will

1. Be more likely to intend to have a genetic test.
2. Consequently have more positive attitudes, subjective norms, and higher perceived behavioural control.

- Both groups of women attending the Regional Genetics service will

1. Have had more worries about cancer in the previous month than the women on the bowel cancer database. The women attending the regional genetics service may be concerned about their forthcoming appointment, and may have unrealistically high

perceptions of their risk, which may be reduced in their appointment. The women on the bowel cancer database are existing patients who have already been placed on a surveillance protocol aimed at detecting pre-malignant colonic lesions (polyps) or early cancers. The initial appointment and subsequent screening programme may act to reassure these women. In addition the majority of these women do not have an impending appointment.

2. rate a genetic test for breast cancer more favourably than the other cohort rate a test for colon cancer due to a higher level of publicity and awareness surrounding breast cancer and genetic testing for breast cancer. In addition research has revealed that those who attend a clinic because of concerns about their own breast cancer risk are more interested in testing than those already on clinic registries (Geller et al1999)
3. be more likely to see the genetic test as an opportunity to have increased surveillance and preventative measures, compared with those already on the surveillance regime for colon cancer.

- The women who have the greatest intent to have a genetic test will anticipate more negative emotions if they do not have a test, and will anticipate fewer negative emotions if they receive a positive result based on the previous study.

- The socio-cognitive and psychological variables will have a similar degree of correlation with intent across both diseases, consistent with the hypothesis that there are similar underlying factors driving the decision to take a genetic test for colon cancer and breast cancer, and by extrapolation, genetic tests for other diseases. There may, however, be additional disease-specific factors that also influence intention.

10.4 Method

10.4.1 Procedure

The breast cancer comparison group were all recruited from a Regional Genetics Centre with a catchment area of South London and the South East. The data used in this study were collected by a postal questionnaire sent to all women who were given an appointment with a genetic counsellor to discuss their family history of breast and/or ovarian cancer. The questionnaire was returned prior to this first appointment. The study was part of a longitudinal study investigating the uptake and impact of genetic testing, however only the initial responses will be discussed here. The colon cancer study was

developed with consideration to the breast cancer study, and where appropriate similar wording of questions were used, to enable the direct comparison of the two groups. The procedure for the collection of data from the colon cancer sample was detailed previously (Chapter 4).

10.4.2 Materials

The initial preparation of the combined data set involved identifying comparative questionnaire measures, and harmonising the coding categories. Only those questions that were directly comparable were used, however the wording on all of the questions was specific to the index cancer for which the participants had sought medical advice. The measures included in this study were:- intent to have a genetic test; attitude towards having a genetic test; subjective normative beliefs; perceived behavioural control; anticipated affect; cancer worry; anxiety and depression (HADS); perception of likelihood of carrying a genetic mutation (1 item) and perception of likelihood of being offered a test (1 item). With the exception of the last two items, descriptions of the reliability of these scales can be found in Chapter 4. Perception of likelihood of carrying a gene was assessed using the question '*How likely do you think it is that you carry a gene which increases your chances of developing ____ cancer' (extremely likely, fairly likely, unsure, fairly unlikely, extremely unlikely).* Perception of likelihood of being offered a test was assessed by the question *'How likely do you think you are to be offered the genetic test when it becomes available?' (extremely likely, fairly likely, unsure, fairly unlikely, extremely unlikely).*

The analysis of risk was problematical due to the differing incidence of colon cancer and breast cancer in the general population. Participants therefore had a different comparative risk for either condition. Three broad risk bands were adopted based on the clinical evaluation of risk:-

- **High risk group** - this group included all the women in the high risk for colon cancer group from study 1 (risk 1 in 2/ 1 in 3) and women with an estimated risk of 1 in 2 or 1 in 3 of developing breast cancer.
- **Moderate risk group** - this group included all the women in the moderate risk for colon cancer group from study 1 (risk 1 in 6 to 1 in 12) and women with an estimated risk of 1 in 4 to 1 in 6 of developing breast cancer.

- **Low risk group** - this group included all the women in the lower risk for colon cancer group from study 1 (risk 1 in 17) and women with an estimated risk of less than 1 in 6 of developing breast cancer.

10.4.3 Participants

This study only included the women from the colon cancer study to exclude the possibility of gender acting as a confounding variable.

The women who were recruited at the Regional Genetics Centre were asked in the questionnaire what their primary reason was for attending for genetic counselling. The women were compared on their responses to this question, comparing those who reported that their main reason was to have a genetic test, with all the other women at risk of breast cancer. The rationale for this comparison was a concern that the people contacted in study 1, examining interest in genetic testing for colon cancer, were all part of an existing research database of people with a family history of colon cancer. These people were registered for the purpose of regular screening via colonoscopy or faecal occult blood testing, they were not attending primarily for genetic testing. The presence of individuals in the breast/ovarian sample attending primarily for genetic testing may bias other analyses. The results indicated that there were indeed differences between these two sub-groups of women at risk of breast cancer (Appendix B). Subsequent analyses compared these two groups of women at risk of or who had had breast cancer with the women at risk of or who had had colon cancer.

There were 338 women in the colon cancer sample (for response rates see Chapter 4). 16 cases had been deleted from the database due to a large percentage of missing summary values (>20% missing). There were 323 women in the breast /ovarian cancer sample (74 of whom said genetic testing was their primary reason for wanting genetic counselling). 7 of the cases had been deleted from the database because more than 20% of the summary values were missing. 81 cases were deleted because they did not attend the clinic session; therefore they may not be comparable with the women at risk of colon cancer who were all clinic attendees.

10.4.4 Statistical analyses

The first analysis explored whether there were any reported health or demographic differences between the three groups of women using a series of chi-squared analyses, and one-way ANOVAs for those variables that were on a linear continuous scale. These demographic differences were then entered as co-variates in a multivariate analysis of variance to determine whether there were any differences in responses to the psychological variables between the three groups of women. Responses to the specific benefit and barrier items were then compared across the three groups using an ANOVA. Finally correlates of intent were modelled using a linear regression. Two regression equations were derived, one for the women at risk of colon cancer and one for the women at risk of breast/ovarian cancer but who were not attending the clinic primarily to have a genetic test. Correlates of intention were not explored in the third group (those attending primarily for a genetic test) as the numbers of people in this group were insufficient, so any analysis would have much lower levels of power than is found in the other two groups.

10.5 Analysis

10.5.1. Demographic Differences

The groups were examined with respect to the demographic differences between the women. Although there is no hypothesis that there will be demographic differences, these were examined so that they could be entered as covariates in subsequent analyses (Table 10.1).

Table 10.1 Comparison between groups for demographic and risk variables

Variable	Colon Cancer (1)	Breast Cancer not GT (2)	Breast Cancer GT (3)	Significance Levels
	Frequency (%)			χ^2 , p
General Health				
Poor	14 (4.1)	17 (6.9)	6 (8.2)	
Fair	51 (15)	55 (22.2)	13 (17.8)	
Good	192 (56.6)	120 (48.4)	36 (49.3)	
Excellent	82 (24.2)	56 (22.6)	18 (24.7)	9.16 (6) ns
Marital Status				
Married/ cohabiting	266 (78.9)	180 (72.3)	52 (70.3)	
Not married	71 (21.1)	69 (27.7)	22 (29.7)	4.62 (2) ns
Religion				
Protestant	211 (62.8)	164 (66.1)	44 (59.5)	
Catholic	50 (14.9)	31 (12.5)	12 (16.2)	
Jewish	19 (5.7)	1 (0.4)	3 (4.1)	
Other	7 (2.1)	9 (3.6)	2(2.7)	
None	49 (14.6)	43 (17.3)	13 (17.6)	14.7 (8) ns
Working status				
Retired	56 (16.6)	58 (23.3)	13 (17.8)	
Not working	65(19.2)	25 (10.0)	5 (6.8)	
Part time	107 (31.7)	72 (28.9)	31 (42.5)	
Full time	110 (32.5)	94 (37.8)	24 (32.9)	19.57 (6) p<0.01
Qualifications				
None	53 (15.7)	72(28.9)	23 (31.1)	
Some	284 (84.3)	177 (71.1)	51 (68.9)	17.91 (2) p<0.001
Cancer Status				
Not had index cancer	315 (93.2)	220 (88.4)	53 (71.6)	
Had index cancer	23 (6.8)	29 (11.6)	21 (28.4)	28.9 (2) p<0.001
Risk group				
Low risk	150 (45.2)	28 (14)	11 (24.4)	
Moderate Risk	61 (18.4)	101 (55.2)	21 (46.7)	
High Risk	121 (36.4)	71 (35.5)	13 (28.9)	82.8(4) p<0.001
	N Mean (sd)			F (d.f), p
Age	338 47.72 (11.07)	249 40.12 (12.23)	74 41.46 (10.34)	34.01(2, 658), p<0.001*
Children	338 1.8 (1.17)	245 1.63 (1.3)	68 1.87 (1.16)	1.95(2, 648) ns

* Women completing the colon cancer survey were significantly older than the women attending the Regional Genetics Service concerning breast cancer.

The analysis shows that there are significant differences between the three groups on a number of variables. More of the women at risk of colon cancer (group 1) were not working and more of the women in group 3 have part time employment. Women in group 1 however were more likely to have qualifications than women in group 3. The women in the first group (colon cancer) were significantly older than the other groups.

There were no differences between the groups on perceived general health, marital status, religion or number of children.

In the analysis of actual risk and personal cancer history there were a number of differences. The women who were attending for counselling because they intended to have a genetic test were more likely to have had the index cancer than the other two groups. The remaining women attending for counselling were more likely to have had breast cancer than the other women were to have had colon cancer. There were differences in the levels of predicted risk, with more women in the breast cancer groups having a moderate predicted likelihood of cancer, and more women in the colon cancer group having a lower clinical likelihood. The proportion of high risk individuals in the three groups is similar.

Those demographic variables that differed significantly between groups (working status, qualifications, cancer risk and age) were entered as covariates in the subsequent analysis of social-cognitive variables and other psychological variables.

10.5.2 Differences between groups on psychological variables

10.5.2.1 Analysis of variance controlling for working status, qualifications, cancer status, risk group and age.

The analysis was conducted in SPSS 9, using group as the main factor, and psychological variables as the dependent variables (Table 10.2).

Table 10.2 MANOVA controlling for working status, qualifications, cancer status, risk group and age.

Variable	Colon Cancer (1) N= 281		Breast Cancer not GT (2) N= 164		Breast Cancer GT (3) N= 34		F (7,471)
	Mean (Marginal)	SD	Mean (Marginal)	SD	Mean (Marginal)	SD	
Intent	4.38 (4.37)	0.78	4.25 (4.27)	0.88	4.82 (4.86)	0.39	3.49***
Attitude	4.27 (4.28)	0.87	4.21 (4.19)	0.91	4.68 (4.71)	0.46	5.5***
Subjective Norm	3.77 (3.77)	0.76	3.84 (3.84)	0.78	4.25 (4.25)	0.58	5.59***
Perceived Behavioural Control	2.87 (2.85)	0.40	2.98 (3.01)	0.72	2.90 (2.92)	0.69	2.26*
Anticipated Negative Affect if decided not to have test	2.41 (2.45)	0.65	2.53 (2.47)	0.67	2.93 (2.9)	0.79	5.45***
Anticipated Negative Affect if positive result	2.19 (2.21)	0.54	2.23 (2.21)	0.54	1.84 (1.81)	0.47	3.51***
Anticipated Negative Affect if negative result	1.09 (1.11)	0.25	1.16 (1.13)	0.39	1.3 (1.27)	0.61	3.97***
Anticipated Positive Affect if negative result	2.53 (2.55)	0.61	2.54 (2.50)	0.74	2.71 (2.70)	0.74	3.55***
Worry	9.81 (10.09)	2.62	12.49 (12.1)	3.26	13.68 (13.3)	3.94	20.49***
Likely to carry gene	3.74 (3.79)	0.82	3.62 (3.54)	0.79	4.03 (4.02)	0.8	9.18***
Likely to be offered test	3.41 (3.43)	0.82	3.33 (3.3)	0.74	3.71 (3.73)	0.84	8.35***
Anxiety	6.61(6.85)	3.99	7.20 (6.8)	4.33	6.79 (6.49)	3.49	1.71 ns
Depression	3.1 (3.1)	3.06	2.89 (2.88)	3.15	3.38 (3.35)	3.33	2.69*

***$p<0.001$
**$p<0.01$
*$p<0.05$

The overall MANCOVA was significant (Pillai's Trace $F(26,920) = 5.37$, $p<0.001$). Due to the inclusion of covariates it was not possible to carry out post hoc analyses on the adjusted means, however the means were examined to determine the likely location of the effects. This was also explored using post hoc tests, but excluding the co-variates, to indicate likely locations of difference in the adjusted means. Most of the differences between the groups appeared to be between the women who wanted genetic counselling so that they could have a genetic test (group 3) and the other two groups. The women in group 3 reported higher intent to have a genetic test, more positive attitudes and more favourable subjective normative beliefs. Women in this group (in comparison to the other groups) also anticipated more negative affect if they did not have a genetic test, less negative affect if they received a positive result, and more positive and negative affect if they received negative results. This group also reported more cancer worry, believed they were more likely to be offered a test than the other groups, and compared with group 2 were more likely to believe that they carried a gene that increased their chances of breast cancer.

Women at risk of breast cancer, but who did not specifically intend to have a genetic test, reported somewhat less depression than those at risk of colon cancer, and substantially less than those at risk of breast cancer but specifically intending to have a genetic test. There were no differences between the groups on their perception of behavioural control or levels of anxiety.

10.5.2.2. Microanalysis of responses to specific belief measures

It was also possible to compare the responses on more specific questions, detailing perceived benefits or disadvantages to having a genetic test. This was conducted using a multivariate analysis of variance (Table 10.3).

Table 10.3 Responses to specific belief measures.

Variable	Colon Cancer (1) N=329		Breast Cancer not GT (2) N=233		Breast Cancer GT (3) N=62		F (2,698)	Location of difference
	Mean	SD	Mean	SD	Mean	SD		
Know whether at high risk	4.05	0.77	4.02	0.87	4.37	0.77	4.78**	(1/3); (2/3)
Know whether children at high risk	3.72	0.95	3.68	0.97	4.1	0.84	4.92**	(1/3); (2/3)
Have trouble getting life insurance/ mortgage	2.98	0.86	3.07	0.97	3.13	0.97	1.08ns	
More aware early symptoms	3.98	1.04	4.21	0.89	4.37	0.87	6.33**	(1/2)
Can have more regular screening	3.71	0.87	4.01	0.87	4.06	0.87	9.76***	(1/2); (1/3)
Can decide about surgery	3.24	0.98	3.62	1.06	3.68	0.94	11.68***	(1/2); (1/3)
Will worry constantly	2.62	0.97	2.77	0.95	2.39	0.98	4.28*	(1/3)

***$p<0.001$
**$p<0.01$
*$p<0.05$

In this analysis those women who state that their primary reason for attending for genetic counselling is to have a genetic test (group 3), are more likely to agree that testing will mean that they will know about their own and their children's risk of cancer. The women who are at high risk of colon cancer are less likely than the other women to see genetic testing as an opportunity to be more aware of early symptoms and to have regular screening. They are also less likely to use it to decide about surgery.

10.5.2.3 Correlates of intent to have a genetic test.

The previous analyses have demonstrated that there are few differences on psychological variables between women registered at risk of colon cancer, and those attending genetic counselling who do not state that having a genetic test is their primary motive. The data were then examined to determine the intercorrelations between

variables, and more specifically the primary correlates of intent to have a genetic test for the different types of cancer. Bivariate Pearson correlations were run to determine the intercorrelation of variables in the different groups (Appendix B).

The pattern of correlations was similar in all the groups, however many of the correlations failed to reach significance in the smallest group (women who were attending the clinic primarily to have a genetic test). In the other two groups intent was associated with:- attitudes, subjective norms, anticipated affect if decided not to have the test, anticipated affect if test is positive, perceived likelihood of carrying mutated gene and perceived likelihood of being offered a genetic test. In addition there was an association between intent and perceived behavioural control in the group of women at risk of colon cancer. These variables were all also intercorrelated. There was also a significant correlation between anticipated affect, perceived likelihood of carrying a mutated gene and measures of cancer worry, anxiety and depression.

Subsequent hierarchical multiple linear regression analyses were run to determine the relative contribution of psychological variables in explaining variance in intent in groups 1 and 2. Group 3 was too small to conduct the analyses, due to the small sample size relative to the number of variables. Measures were entered into the model in steps, with the theory of reasoned action variables entered initially, followed by perceived behavioural control, anticipated affect, other psychological variables, and finally clinical risk and personal cancer history (Table 10.4). This is in the same order as they were entered in study 1.

In this analysis a significant model emerged at the first step in the analysis of both groups. In the women at risk of colon cancer, the theory of reasoned action explained 52% of the variance in intent ($F = 152.99$, $p<0.001$, adjusted $R^2 = 0.515$). In the women at risk of breast cancer it explained more variance in intent (58%); ($F = 128.15$, $p<0.001$, adjusted $R^2 = 0.58$). People were more likely to intend to have the test if they had positive attitudes towards the test, and if their subjective normative beliefs supported testing. Perceived behavioural control did not explain any additional variance in either of the two groups of women.

In both samples anticipated affect if they decided not to have a test contributed significantly to the explanation of variance in intent. Participants who believed they would experience a high level of negative affect if they did not have the test were more likely to intend to have a test. In the colon cancer sample women were more likely to intend to have a test if they anticipated a low level of negative affect if they tested positive. Overall, however this block of four variables did not produce a significant change in R^2. In the breast cancer sample women were more likely to intend to have a test if they anticipated a low level of negative affect if they tested negative. The addition of the block of anticipated affect variables explained 3.4% significant additional variance in intent.

The fourth block entered (Cancer worry, perceived likelihood of carrying mutated gene, perceived likelihood of being offered test) did not explain any additional variance in either of the populations studied, either as individual items or as a block of items. Among the women at risk of colon cancer, low clinical risk was associated with lower intent to have a genetic test, this explained a significant additional 1.7% variance in intent in this group. Low clinical risk and personal cancer history explained no additional variance in the group of women at risk of breast cancer.

The final equations for both subsamples were significant, accounting for 54% of the variance in intent in the colon cancer subsample ($F = 28.4$, $p<0.001$, adjusted $R^2 = 0.535$) and 60% of the variance in intent in the breast cancer subsample ($F = 23.97$, $p<0.001$, adjusted $R^2 = 0.6$). Examination of the regression diagnostics did not show any cases that had particular influence on this result.

The unstandardised regression co-efficients were then compared between men and women. These analyses indicated that there was no significant difference between men and women in the relative strengths of the predictors.

Table 10.4 Correlates of intention to have a genetic test

		Correlates of intent						Linear regression of intent onto psychological variables							
		Group 1(colon cancer)			Group 2 (breast cancer)			Group 1 (colon cancer)				Group 2 (breast cancer)			
		r	p	n	r	p	n	Final Beta	R^2	Adjusted R^2	R^2 change (sig^n)	Final Beta	R^2	Adjusted R^2	R^2 change (sig^n)
Step 1	Attitude	.665	.000***	320	0.737	.000***	281	.427***				.531***			
	Subjective Norm	.612	.000***	338	0.635	.000***	304	.318***	.519	.515	.519***	.245***	.585	.580	.585***
Step 2	Perceived Behavioural Control	.167	.002**	337	0.038	.513	302	.024	.519	.514	.001	-.041	.586	.579	.001
Step 3	Anticipated Negative Affect if decided not to have test	.383	.000***	329	0.403	.000***	291	.102*				.154*			
	Anticipated Negative Affect if positive result	-.339	.000***	327	-0.305	.000***	286	-.099*				-.085			
	Anticipated Negative Affect if negative result	-.065	.239	326	-0.053	.368	285	-.010				-.058*			
	Anticipated Positive Affect if negative result	.104	.060	328	0.07	.229	293	.041	.534	.522	.015	-.145	.620	.605	.034**
Step 4	Cancer Worry	.062	.260	337	0.073	.204	304	-.080				.029			
	Likely to carry gene	.247	.000***	339	0.155	.007**	305	.052				-.014			
	Likely to be offered test	.202	.000***	339	0.26	.000***	306	.005	.537	.521	.004	-.043	.623	.601	.003
Step 5	Cancer History (0-not had; 1- had)	.053	.328	337	-0.014	.80	307	-.061				.056			
	Assessed risk	.111	.043*	331	-0.036	.58	233	-.126*	.554	.535	.017**	-.025	.626	.600	.003

10.6 Discussion

This comparison study utilised data from a study of outpatients attending a regional genetics service for the assessment of risk of breast/ ovarian cancer. Although there are some differences between the groups in terms of route of entry to the study (established clinic list versus new attendees), the main difference is the potential illness (colon cancer versus breast / ovarian cancer). These diseases have a similar penetrance in a high risk population. Colon cancer is more reliably detected by current screening practice (colonoscopy versus mammography), however there is a poorer prognosis, as it is often not treated early enough.

There were a number of demographic differences between the women recruited from the different sources. There were apparently contradictory differences between the groups on measures of work status and qualifications. More of the women at risk of colon cancer (group 1) were not working, however they were also more likely to have qualifications. As all of the respondents are women, one possible explanation is that the more qualified women are married to more qualified men, so only one person in the household needs to work. More of the women in group 3 have part time employment, which is often poorly paid and often requires fewer qualifications. It is difficult to draw any conclusions about levels of deprivation in this sample, as there are no other comparable indicators of deprivation that the data sets share.

The age difference, with women at risk of colon cancer being six years older, may be explained by considering the likely times of first presentation to the Family Cancer Clinic. These women were recruited from an established screening database and may have first presented to the clinic for assessment over 10 years previously, this would mean that their age of first presentation might be similar to that found in the other groups, although this data was not available.

The difference in the cancer incidence is likely to be due to a number of reasons concerned with sampling. Higher rates in women specifically intending to have genetic testing may be due to referrals for this purpose from oncologists, who have discussed their family's genetic risks, and have suggested that they discuss having a genetic test. The higher rates of cancer in the breast cancer groups compared with women at risk of colon cancer may be because the prognosis for breast cancer is better than that for colon cancer; women affected with colon cancer are more likely to have died.

The difference in levels of clinical risk is in part because the group at risk of colon cancer contains a large number of women recruited specifically for a study of (FOB) screening in lower risk individuals. These women may not have normally been referred for genetic counselling and do not meet the general guidelines for inclusion on the Family Cancer Clinic database. The disproportionate numbers of women at lower risk of colon cancer may have had an impact on the subsequent analyses in which this factor is controlled for, as there is a much larger number of responses on which to base the statistical adjustment of the effect.

The main differences were not between the women at risk of colon cancer and those at risk of breast cancer, but between the women who attended specifically to have a genetic test for breast cancer compared with all the other women. Those women who were specifically intending to have a genetic test held significantly more positive intentions, attitudes and subjective normative beliefs. Their anticipated emotional reactions also were in the direction to support their intention to have a genetic test. These women have already formed an intention to have a genetic test, and their other cognitions support this intention. These differences expand the observation that the source of participants influences the degree of participation (Geller et al 1999). Participants attending following recruitment specifically for genetic testing research protocols show higher levels of intent and participation than those recruited via pre-existing patient registries (Geller et al 1999; Crauford et al 1989). This must be considered when comparing levels of intent across existing studies.

When the two groups of women at risk of breast cancer are compared together against those at risk of colon cancer, the only differences are that women at risk of breast cancer are more worried, and perceive more control over having a test. Women at risk of either type of cancer therefore hold similar positive beliefs about genetic testing, however those who attend genetic counselling specifically to have a genetic test are more in favour of testing.

The most important difference between the groups was the level of cancer worry. Those women at risk of colon cancer reported much lower levels of concern than those at risk of breast cancer. This may be due to a number of reasons. Firstly many of the women even in the moderate risk group are at a lower absolute risk of developing colon cancer than the women at moderate risk in the breast cancer cohort. Despite this when only those at highest risk are compared, there is still a significant difference. The other

reasons concern the circumstances surrounding entry to the study. The women at risk of colon cancer have been registered with the family cancer clinic in some circumstances for a number of years, whereas the women at risk of breast cancer are anticipating perhaps their first contact with services for people with a genetic risk of cancer. The prospect of the appointment itself may have heightened their concern, alternatively their motivation for the contact may be due to increased concern about their risk of cancer prompted by other factors, such as media coverage of genetics and breast cancer. In assessments of cancer worry in the time prior to a clinic visit, compared with measures taken immediately and 9 months after the clinic visit, it has been demonstrated that worry decreases following the visit (Brain, Gray, France et al 2000). The differences between the two samples may be due to the timing of the questionnaire measures, comparing new patients who have no risk assessment and existing patients who have had a limited risk assessment through the screening service (high, moderate, low).

A third possible reason for the difference is that all of the women at risk of colon cancer are offered regular screening. This may serve to reassure them about their risk, whereas many of the women at risk of breast cancer will not have received screening at this stage until their clinical risk is established.

This explanation was supported by the finding that women at risk of breast cancer were more likely to see testing as a way of ensuring more screening and deciding about surgery than those at risk of colon cancer. The women at risk of colon cancer are either receiving regular colonoscopies or FOB tests, and are probably already aware of the symptoms of colon cancer. The women attending for counselling concerning breast cancer may not have had screening previously, and so may see a genetic test as being a prerequisite for regular screening.

Currently regular screening for both colon cancer, and breast/ovarian cancer is available to people at high risk free of charge without the need for genetic evidence of risk. The differences in considering surgery may in part be explained by the medical profession's greater readiness to accept mastectomies and oophrectomies as an appropriate prophylactic treatment. The consideration of prophylactic colectomies is more complex due to the important role of the colon in daily life, however partial resections of the bowel have been proposed by some experts (Lynch et al 1999).

There appear to be few differences in the measures by group, however this does not indicate whether there are differences between the groups in correlates of intention. Although they may hold similar beliefs, the same beliefs may not be important for determining intentions in the different groups. Due to the small numbers of people explicitly requesting counselling in order to have a genetic test for breast cancer this group was excluded from this analysis. Regressions predicting intentions showed support for the importance of the theory of reasoned action in explaining variance in intent in both samples. The evidence did not support the additional value of perceived behavioural control in explaining intentions in either group. Anticipated affect was more significantly associated with intent among women at risk of breast cancer, and clinical risk was more important in explaining intent among women at risk of colon cancer. The decision to have a test for breast cancer may be based on more emotional factors, but the decision to have a test for colon cancer on perceived or actual risk of cancer.

When unstandardised beta values were compared there were no significant differences, indicating that the models were substantially the same in both groups. This gives support to the possibility that there is an underlying common model which explains intention to have a genetic test in both colon cancer and breast cancer.

10.7 Conclusions

The similarities between the groups examined in these comparison studies are greater than the differences, indicating that there is a common underlying influence on intent to have a genetic test, which crosses risk levels and disease models. Most of the differences that have been noted could be attributed either to these influences or to differences in recruitment of participants across the studies. There are high levels of intent to have a genetic test in all populations examined, and in all of them the theory of reasoned action explains between 51% and 58% of the variance in intent. The differences between groups appear to be in terms of degree of effect, rather than different underlying structures associated with intent formation. These findings should be explored further in other cancers and other genetic predispositions to determine whether similar mechanisms underlie all decisions to have genetic tests. The long-term effects of genetic testing for different types of cancers will be explored in the continuing follow-up of the breast and colon cancer samples.

Chapter 11

Conclusions

11.1 Main findings

This thesis has explored the role of social cognition models in intention formation with respect to genetic testing for cancer. This issue has been explored in various groups of individuals defined by risk or type of cancer.

Two main themes were explored in this thesis. The first theme was the determination of the associates of intention to have a genetic test for colon cancer in people with a known family history but no personal history. One framework adopted in this study was the theory of planned behaviour. This model was explored in two parts, the original theory of reasoned action, and the addition of perceived behavioural control to form the theory of planned behaviour. The outcome variable was intention to have a genetic test. Technical problems involved with genetic testing limited the investigation of behaviour and effects. Support was found for the role of the theory of reasoned action in explaining intention, however perceived behavioural control did not explain any additional variance. The structure of the theory was questioned in the follow-up study conducted a year later, particularly the direction of influence of attitudes, subjective norms and intent. The results indicated that there might be a feedback mechanism with the model having a bi-directional rather than a unidirectional nature.

It has been suggested that the theory of planned behaviour would be enhanced by adding anticipated affect where the decision is one which may result in different affect states depending on the choice made. It was hypothesised that this may be important in genetic testing, as the action of having a genetic test is one which cannot be reversed, and a person, once having received a test result, cannot revert to a state of not knowing. Support was not found for the contribution of anticipated affect in these analyses.

The theory of planned behaviour and anticipated affect were compared with the health belief model. Although the theory of planned behaviour consistently explains more variance in intention than the health belief model, perceived susceptibility is inadequately measured by the theory of planned behaviour. As genetic testing has an emphasis on risk determination and is only appropriate for people with a strong family

history indicative of a genetic trait, perceived susceptibility was hypothesised to be an important additional determinant of intention. The analyses did not support this hypothesis, and no additional role of perceived susceptibility was found to be associated with intention beyond that explained by the theory of planned behaviour. There was an effect of general risk group however, categorised by clinical risk. This indicates that objective risk is more predictive of intent than perceived risk. This may indicate that the individual level assessment of perceived risk, (in part based on numerical estimates) may have been inaccurately reported. People who are told that they are at 'high risk' by clinical judgement may use this as a factor in deciding whether to have a genetic test or not, without being able to put an accurate numerical figure on their risk.

Other components of the health belief model were also measured, but when their influence on intention was considered, the proportion of variance explained was less than that explained by the theory of reasoned action. In the final regression model however, benefits and barriers were found to explain unique variance in addition to that explained by attitudes and subjective norms. The theory of planned behaviour includes similar concepts - behavioural beliefs as determinants of attitudes - however this study indicated that such beliefs might also have an independent influence on intention.

The addition of a measure of attitudes towards medical uncertainty explained additional variance in intention, indicating that there may be a role for personality assessment in the prediction of intention. Higher intent was found in people who dislike uncertainty. This was measured using a constructed scale that was specific to medical tests, rather than uncertainty in general. The specificity was important, as the association had only once previously been tested, in a general population sample (Croyle et al 1995). Considering the strength of this association, introducing more general personality scales into the study of intention to have a genetic test may lead to a greater understanding of the role of personality factors in determining both intention and attitudes.

The analysis of future intentions has indicated that people intend to use genetic risk information to reassure themselves about the future. This involves seeking additional screening if a genetic mutation is found, and adopting a healthier lifestyle. Other plans include making financial arrangements, however few people intended to use a test result to influence childbearing plans. A low-risk result would probably not lead to a more unhealthy lifestyle, however fewer people would seek financial security. Most people

would still want to continue with a screening regime even if their risk of cancer was significantly reduced.

In the second study the influence of gender on intent to have a genetic test was examined. There was no difference between men and women's levels of intent to have a genetic test to detect a predisposition to colon cancer, there were differences in the predictors of this intent though. In men most of the components of the two social cognition models used emerged as significant predictors of intent to have a genetic test, the exception being perceived severity of cancer. The only other significant predictor was attitude towards uncertainty. In women only three components (attitudes, subjective norms and perceived barriers) of social cognition models were significant predictors, however anticipated reassurance, number of children and objective risk were all also significant predictors. Women also anticipated experiencing more emotional reactions to genetic testing. More detailed analyses revealed no significant differences in the strength of the individual predictors of intention for men and women.

This study has found support for the findings of Struewing et al (1995b) that men and women differ in their reasons for wanting testing and their anticipated emotional reactions. No support was found for different levels of intent between the genders. This indicates that either there is no difference, or the men in this study differ from those in the population of men at risk contacted by previous studies. The clinical implications of this study are that men appear to base their intention to have a genetic test on cognitive factors, whereas in women a more diverse range of factors are considered- fewer cognitive factors but more family factors and anticipated screening implications.

The following two studies both questioned the structure and the determinants of the components of the theory of reasoned action. In Chapter 6 the stability of the factors measured was examined one year later. In this study it was revealed that rather than attitudes and subjective norms being the determinants of intent, it was possible that a feedback mechanism was operating, and there was a dynamic relationship between the variables. This study has highlighted the need for further research into the stability and causal relationships within the theory of reasoned action.

When partners of high risk individuals were questioned about genetic testing in the next study they were found to hold broadly similar views about genetic testing as the high risk individual. They saw their partner being at lower risk than their partner's own

perceived or actual risk, they also saw themselves as having less control over the decision to have a test, and anticipated fewer emotional consequences. These findings indicate that partners are likely to agree with their partner's decisions, however it will be important to explore the impact of testing on spouses and marriages. This study also revealed that subjective norms are more closely related to a person's own intent than to the actual views of the person to whom the question refers. This raises interesting questions about the nature of subjective norms and whether such questions actually measure intent.

The next group of people compared with the high risk sample was people from the same database who not only had a family history of colon cancer, but also a personal history of colon cancer. This is an area that has received little attention, but there were a number of differences found between the two groups. Although there was no significant difference in levels of intent to have a genetic test, people who had had cancer held more positive attitudes, subjective norms, anticipated lower negative affect if found to carry a genetic mutation, perceived more benefits and fewer barriers to testing, reported higher levels of wanting to reduce uncertainty, worried more about developing cancer, were less anxious and less depressed than the asymptomatic group. This long list of differences indicates that predictive testing is perceived very differently from confirmatory genetic testing. The implication of this study brings into question the findings of those studies that have not differentiated between affected and unaffected participants (Struewing et al 1995b, Wagner, Moslinger et al 2000, Lerman, Hughes et al 1998, Lerman, Hughes, Trock et al 1999). The small sample size limited this study, however it is clear that genetic tests have different meanings for people who have not had colon cancer than for people who have had colon cancer.

In the next comparison study, a general practice sample was contacted via a general practitioner's list. Although this sample still reported high levels of intent to have a genetic test, their reported intent was much lower than either of the two at risk groups. Norms and attitude towards uncertainty followed a similar pattern. Attitudes towards testing were also less positive in the general practice sample, although this time a linear relationship emerged, with more positive attitudes being associated with higher risk levels. This study replicated the high level of intent to have a genetic test found in general population studies, but also demonstrated that this level is not as high as that found in a high risk sample. The regression analysis showed that with these measures

the predictors of intent in the three groups were the same. This means that general population samples are likely to provide a similar pattern of responses, at least on these measures, but their actual levels of intent are lower. This means that other studies utilising a general population sample may produce results that can be generalised to a high risk sample. This is important because it means that researchers can question a general population sample, at least initially, so high risk populations are not put under an undue research burden.

The final comparison study explored whether a common model could be fitted to intention to have a genetic test for either breast cancer or colon cancer. The results of this study indicated that indeed a similar model might be appropriate, at least in women. The study, however, did highlight the impact that reason for seeking genetic counselling has on responses to the questionnaire. Those women who specifically requested testing so that they might have a genetic test differed significantly, not only from the women at risk of colon cancer, but also those at risk of breast cancer. This emphasises the impact that the recruitment frame might have on the responses obtained to questions, and the need to consider all findings in studies of genetic testing in relation to the method by which the participants were recruited.

Overall these studies have shown that the degree of intention does vary across groups, but the structure of the associations between intention and its correlates is similar across groups. The theoretical and practical implications of some of these findings will now be explored in more depth.

11.2 Theoretical implications

The theory of reasoned action explained a large amount of variation in intent in all the studies, however the follow-up study challenged the accepted structure of the model. The model as traditionally viewed is a unidirectional model, with attitudes and subjective norms determining intention, and intention determining behaviour. The follow-up study indicated that, rather than intention changing over time, attitudes and subjective norms had become more aligned with intent. This finding implies that there may be a feed-back mechanism within the theory of reasoned action, which means that intentions, once formed, may influence attitudes and subjective normative beliefs as well as being determined by these factors.

The study of spouses also raised issues about the nature of subjective normative beliefs. These beliefs are held to be subjective perceptions of what others would think about the individual behaving in a certain way. The assessment of individual cognitions indicated that there is a stronger relationship between a person's subjective norm and their own intention than between their subjective norm and an actual norm. The weak relationship between subjective norms and actual norms may be because people had little idea of what significant others would actually want them to do. Participants may have inferred others' views from their own intention: 'I want to do this so other people would also want me to do it'. This indicates that in this situation subjective norms may be an indirect measure of intention, rather than a representation of actual norms. This finding may be because genetic testing is a novel behaviour that is rarely discussed. Most people would know or guess accurately how significant others might view their engagement in behaviours such as smoking and exercise, even if their views were different from their own beliefs. For example, parents may be perceived to disapprove of smoking, even if the individual holds a positive attitude towards smoking. Genetic testing is a relatively novel behaviour, and many people may not know what others would think about it, the only evidence that they have is their own intent and attitudes, and a belief that significant others would hold similar beliefs.

Whereas the studies have revealed a number of possibilities about the influence of the theory of reasoned action on intention and vice versa, little has been revealed about perceived behavioural control. This concept showed only small differences between groups of participants, and did not explain any variance in addition to that explained by other factors. The general level of perceived control, although not high, indicated that people felt that they had some control over whether they had a genetic test or not. This perception of control however was not associated with intention.

Despite the lack of association with intention, the role of behavioural control in genetic testing cannot be dismissed. In the original conceptualisation of perceived behavioural control it was seen as a proxy for actual control, which it was assumed could not usually be measured (Ajzen 1988). Therefore there are two facets - perceived control and actual control. Whereas perceived control has played little role in the formation of attitudes, actual control has been almost the sole determinant of behaviour in this study. Despite the high levels of intention, virtually no participants underwent genetic testing during this study due to technical problems in isolating genetic mutations in the research group.

Without the identification of mutations for each family, genetic testing, and the receipt of a test result is not possible. The intention to have a test and perceived control over the behaviour was high, but without actual control the psychological 'determinants' of behaviour had no impact on the situation of the participants.

The strength of the theory of reasoned action was not increased with the addition of anticipated affect, except in the case of women with breast cancer, however it was increased with the addition of a personality measure of attitude towards uncertainty. This variable is likely to be important in tests that reduce uncertainty, with some people wanting to limit the amount of uncertainty experienced, whereas others prefer to live with uncertainty.

11.3 Practical Implications

The practical implications of testing for clinical practice have also been explored in this thesis. The discovery of high levels of intent to have a genetic test in this sample has confirmed reports from North America that many people intend to have a genetic test for colon cancer if offered it, both in the high risk population and in the general population. Although in the case of Huntington's disease, high intent did not translate into high uptake of testing, initial indications are that uptake of testing for cancers is quite high (although still lower than intent) (Aktan-Collan, Mecklin, Jarvinen et al 2000b; Lerman, Schwartz, Lin et al 1997).

The applications of the theory of planned behaviour to genetic testing, beyond explaining intention, are currently limited. It is not currently appropriate to plan interventions to encourage the uptake of genetic testing, whilst the options for prevention and cure of colon cancer remain surgical and clinically invasive. There are currently no recommendations for those testing positive for a genetic mutation, beyond those given to high risk individuals pre testing. The advent of preventive medication for colon cancer, such as tamoxifen for breast cancer, and lifestyle recommendations concerning diet, may prompt the need for interventions to persuade people to have a genetic test, rather than simply continuing with current care strategies. In breast cancer, the lack of reliable screening programmes for young women found to be at risk, mean that in this cancer too, a non-directive approach to decision making concerning genetic testing is desirable. In the near future, however this position is likely to change,

therefore the identification of attitudes and subjective norms as the main correlates of intent can inform interventions when these are appropriate.

Within the population who chose to have a genetic test, new issues are raised for clinical practice. Initial indications from this study show that most people do not anticipate many negative feelings if they are found to carry a mutation. Until these people are followed up, caution must be exercised in the management of people who believe that they will not experience many negative feelings, as these people may be unprepared for the impact that genetic knowledge may bring.

In this population, and in other clinics offering screening to people at high risk, a common issue may be the reluctance to relinquish colonoscopic screening if a low-risk result is obtained. In the UK there is currently no national screening programme for colon cancer, although a trial of flexible sigmoidoscopy (Atkin, Hart, Edwards et al 1998) has taken place and piloting is underway for FOB testing. The lack of a national screening programme means that a person receiving a low risk result is classified as having a population risk of colon cancer, and is no longer offered colonoscopy screening. In the current NHS it is not financially viable to offer genetic testing, and continue to offer screening to those found to be at low risk. In addition a colonoscopy is clinically invasive, and as most sporadic cancers are found in the distal colon, a colonoscopy is not required to detect most cancers.

Most of the respondents in the initial survey expressed the desire to continue with screening even if a test showed they were at low risk of developing colon cancer. It is possible that this view would be moderated with improved education and counselling. This has however been an issue for people at risk of FAP (Michie et al 1996), so it is likely to also remain an issue for this sample. One possible strategy might be the offer of a flexible sigmoidoscopy once the individual reaches the age at which they are likely to be at risk of sporadic colon cancer. This would reduce unnecessary interventions, whilst still offering those at low risk the protection of appropriate screening. One reason for the reluctance to give up screening could be the anticipated regret if screening was stopped, and then later a colon cancer developed. In this situation, not only have they endured unpleasant colonoscopies in their early life, but also they have still succumbed to the disease that they fear. As, on average, one in twenty of those who are found to be at low

risk will develop a sporadic colon cancer, this anticipated regret is not unfounded, appropriate screening may be sufficient to ameliorate this situation.

The impact of genetic testing on the insurance industry is also of concern in the consideration of this issue. The current insurance system is based on actuarial data concerning projected risks for certain groups of individuals. Within this system, a person who knows of their own risk, but does not reveal it to an insurance company, is regarded as a liability, and increases the possibility of a claim without an appropriate increase in cover. This would have an impact on the cost of subsequent cover for others. The revelation of a known genetic risk to an insurance company, however, may lead to the applicant being unable to obtain life or health insurance.

A recent government committee decided to permit insurance companies to use genetic test results for Huntington's disease (Genetics and Insurance Committee 2000), a test which has been shown to accurately predict the development of disease. This ruling means that an insurance company can ask for existing test results, but cannot request an applicant to undergo testing. Failure to reveal a test result would invalidate any insurance obtained under these circumstances.

For cancer the picture is less clear, as test results for most cancers indicate simply a predisposition to cancer, not a definitive evaluation of the likely development of cancer. Additionally in cancer the time scale of the development of the disease is less clear even than in the case of Huntington's disease. The result of a genetic test for cancers is not yet required to be revealed, however some insurance companies currently ask whether any genetic tests have been conducted, but they cannot request results. For people at high risk of cancers, it is not yet clear whether insurance companies will reduce the premiums for those found to be at high risk who adhere to a regular screening regime which significantly reduces their risk of developing cancer.

In the survey many people stated that they would make more financial plans if a genetic test showed they were at high risk, however few considered that they would find it difficult to obtain insurance. This desire for financial security if the result shows they are at high risk will confirm insurance companies' concerns that people will seek additional cover if they know they are likely to develop cancer. Currently the approach taken by genetic counsellors is to educate prospective candidates about the implications for insurance, and advise them to seek insurance pre-testing based on their pre-testing

risk. Even this approach may challenge the current system of insurance, as it leaves the possibility that test candidates may take out large premiums prior to testing, only to cancel them if the result shows they are at low risk. The implications for insurance of the new genetics are considerable, with few simple solutions.

11.4 Limitations of studies

11.4.1 Scope of thesis

The scope of the thesis was to explore psychosocial issues surrounding genetic testing for colon and breast cancer, in different groups of people, to determine the appropriateness of established health behaviour models and other variables in explaining intention to have a genetic test. This thesis has employed a broad perspective, exploring the interaction of a number of different variables across different groups of individuals. The breadth of the study has meant that the exploration is not as deep as may have been accomplished if a single model (e.g. the theory of planned behaviour) had been employed. The researcher's desire to conduct a detailed investigation must be balanced against the demands placed on volunteer participants. The limitations on the length of the questionnaire mean that invariably some topics that emerge as important in the analysis could have been explored in more detail if additional pertinent questions had addressed certain emergent findings.

For example, in retrospect a more detailed analysis of the motivation to comply to other's wishes may have provided greater clarification of the issues surrounding subjective normative beliefs, and the relationship between subjective norms, normative beliefs and motivation to comply could have been investigated in more depth. The aim of the thesis, however was to explore reasons for intending to have a genetic, not just limited to the theory of planned behaviour. The breadth of information obtained in this study has provided some interesting insights into the issues surrounding genetic testing.

11.4.2 Participants

Using of different methods of recruiting the participants limited the generalisability of the comparison studies, particularly the comparison of those at risk of colon cancer and those at risk of breast cancer. At the start of the study, few people were attending for genetic testing for colon cancer at the same regional genetics centre from where the women at risk of breast cancer were recruited. The availability of the cohort registered

on a screening programme for colon cancer provided an ideal opportunity to conduct a large-scale investigation. This group included people who may not request to be seen by a genetic counsellor, but who are still concerned about their health. Compared with other studies however there were a large number of people who were good candidates for genetic testing.

In determining the likely intent in a population at high risk of colon cancer most recruitment approaches are problematic. People attending for genetic counselling are likely to include a disproportionate number intending to have a genetic test, as they are aware that such a test is possible. Approaching FDRs of people currently affected is likely to target a population with a high level of concern about cancer, but as only 5-10% of colon cancers are hereditary, most participants with only one affected relative would not meet the criteria for genetic testing. A sample of the general population would require a high level of recruitment to contact enough people to comprise a study. The recruitment of people from a high-risk screening programme (although limiting generalisation to the entire population of people at risk), has the advantage of contacting a population that is stable, for which clinical risk is well established, and which is likely to contain people with varying views of genetic testing.

Finally, the population studied was limited by its lack of ethnic diversity. The clinic from which the main sample was drawn was relatively homogeneous, and this was reflected in the study. This does prompt questions about the accessibility of clinic provision to ethnic minorities. Although over 6% of the sample reported that they were Jewish, this distinction was not made in the analyses as this was reported in relation to their religious affiliation, not necessarily ethnic origin. In addition it was not possible to distinguish between those of Ashkenazi Jewish origin (who are at particularly high risk) and those of other Jewish origin by this question.

11.4.3 Different questionnaires

As will be noted in the examination of the questionnaires in Appendix 1, there is a discrepancy between the questions asked of participants. Wherever possible similar wording was employed, however there are differences, and this means that the same variables could not be compared across all the groups of participants. Each study had different focuses, which explain some of the differences, as the studies were designed to 'stand alone' as well as to be included in a larger analysis.

11.4.4 Follow-up of participants

The principally cross-sectional nature of the data limits the value of the studies reported in exploring important issues associated with genetic testing, such as the actual uptake of testing, and the impact of testing on both emotions and behaviour. This unfortunately was unavoidable due to problems with the location of genetic mutations in research samples, which due to the protocol employed by the clinic, were assessed before clients were contacted to decide whether they intended to undergo clinical genetic testing. Clinical testing means that the person gives a blood sample with the intention of receiving a result as opposed to the research testing conducted on the blood of most affected people registered on the database, for which no result is given. This limitation will be addressed in the continuing follow-up of the participants of this study.

11.5 Future directions

The immediate future direction of this study is the follow-up of the participants of this baseline assessment who are offered a genetic test. Over time it will be possible to determine the effect that choosing to have a test or not, and the different possible test outcomes, will have on emotional and behavioural outcome measures. The provision of genetic tests should be associated with appropriate psychological support. Studies of people undergoing testing for Huntington's disease have provided little cause for concern, however the anticipated wider uptake of tests for cancer means that more vulnerable people may be exposed to this information. The longitudinal study of emotional impact will provide the information required to determine the likely long term implications for this and other groups of people undergoing testing for colon cancer.

In addition to the emotional implications, attention must be paid to the behavioural implications. The cross-sectional data indicate that learning information about genetic risk, whether indicating high or low risk, will lead to healthier lifestyles, and diets. This lifestyle change may be particularly important for people who are found to be at high risk. It is important to determine whether these changes do occur spontaneously, or whether more intensive interventions may be required if the link between diet and the development of cancer is demonstrated in high-risk populations. The effect of test results on other aspects of people's plans will also be explored, specifically seeking further financial security.

In more general terms there should be a focus on the study of intentions and uptake in other groups where interventions to prevent cancer may be more important than screening - for example lung cancer. In people at risk of lung cancer, the major determinant of final risk is whether the person is exposed to carcinogens such as tobacco smoke. As genetic tests are increasingly being developed to identify those most predisposed to different illnesses, health psychologists will have a greater role to play. Initially the focus of attention will be, as in the follow-up phase of this study, the impact that risk information has in itself on healthy and unhealthy behaviours.

For lung cancer the rates of smoking reduction in those found to be at high risk will be an important outcome measure, as this will have the main effect on the development of cancer. In addition to the study of those found to be at high risk, those found to be at low risk should be followed to determine whether this information results in false reassurance, as the person may still be at risk of other smoking related diseases such as heart disease. Following these initial studies the effectiveness of focused interventions will need to be assessed, to help people to reduce their risks. Ultimately it may be possible to screen individuals comprehensively prior to the establishment of health behaviours, to advise of likely health risks. The impact that this information has on young people will also need to be studied.

In addition to the study of individuals, there is also a need for a more systemic approach to the issue of genetic testing, considering not only the high risk person, but also their immediate blood relatives (including their children), partners, and the impact on the wider society. These issues have been explored to a limited extent in this study, however there is a need for a more detailed analysis of the impact on different people influenced by an individual's choice to have a test. A genetic test is not just a personal one, but also a familial one. The potential ethical conflicts could be explored by adopting a more systemic analysis, for example if an adult child intended to have a test for a known familial mutation, but their parent chose not to know, the parent's genetic status might be revealed if the child is tested. The implications of these decisions should be explored in more detail.

On a theoretical level the investigation has also raised issues primarily in relation to the structure of the theory of planned behaviour. Future directions for this model should involve longitudinal studies of the changes and influences on components of the model

over time. Such studies should determine whether there is a feedback mechanism by which intention and behaviour also affect attitudes, not only based on experience, but also on cognitive evaluation.

The issue of the role of subjective normative beliefs also deserves more attention. Are the beliefs actually based on assessment of other's actual beliefs, or are they an indirect way of measuring a person's own intention? The true nature of subjective norms will influence the way that they should be regarded in the theory of planned behaviour, at least in respect of relatively novel behaviours. The role of 'supportive norms' should also be explored. In many relationships the knowledge that a partner will support whichever decision is made will encourage the person to follow their own intention, whilst not engaging his or her partner's active evaluation of the desirability of the test.

Whilst this study has found support for the theory of reasoned action in explaining intention, there is a need for the measured evaluation of the likely impact of this finding. In the clinical setting, learning that a person is more likely to intend to have a genetic test if they hold a positive attitude towards testing (whilst of theoretical importance) may not be as important as the knowledge that they are likely to request post-testing screening regardless of test outcome. In the utilisation of models it is important to consider the likely practical implications to maintain a theory-practice link in the development of health psychology as a distinct discipline.

This thesis has investigated the role of social cognition models and other factors in the formation of intentions to have genetic testing for colon cancer and breast cancer. Support has been found for the role of the theory of reasoned action in explaining intention, with the additional consideration of demographic factors, clinical risk, perceived benefits and barriers to testing and individual disposition to situations of uncertainty. The formation of intention in individuals appears to be similar across groups divided by risk level or disease model. Other factors have also emerged as important - the role of the stage in life, the numbers of children and anticipated actions following receipt of a genetic test result. A number of statistical methodologies have been applied to this issue to provide a broad understanding of genetic testing as applied to colon cancer, and compared with genetic testing for breast / ovarian cancer.

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APPENDICIES

APPENDIX A - Copies of Questionnaires

APPENDIX B - Additional Analyses

APPENDIX C - Criticisms of Previous Studies

APPENDIX D - Ethical Approval

APPENDIX A – QUESTIONNAIRES

COVERING LETTER, PATIENT INFORMATION LEAFLET, AND QUESTIONNAIRE FOR INITIAL SURVEY

Imperial Cancer
Research Fund

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02 June 1998

Dear

As you know, various research projects are in progress to try to establish more about the inherited aspects of bowel cancer and you have already kindly given a blood sample for part of this research.

I would now like to ask for your help with two other research studies both of which will help in different ways with our understanding of hereditary bowel cancer and how to help people to deal with it.

The first is about diet. We know that although genetics plays a part in the development of bowel cancer, there are other factors involved as well. Diet is one of these and we would like to investigate the effect of different diets on the development of polyps in the bowel. To assist with this research, we invite you to fill in the enclosed food diary. As you will see this involves a description of everything you eat over a seven day period. Details on how to complete the diary are given inside the front cover. When you have completed it please return it to the family cancer clinic at St Mark's in the **brown** prepaid envelope.

The second research study involves finding out how people feel about the idea of genetic testing for bowel cancer. Researchers from the ICRF Health Behaviour Unit at University College London have put together a detailed questionnaire about this which I enclose together with an information sheet explaining the research. When you have completed the questionnaire, please return it to the health behaviour unit at University College in the **white** prepaid envelope.

Thank you very much for taking the time to complete both the food diary and the questionnaire. Your responses will be really helpful to us.

With best wishes
Yours sincerely

Sheila Goff
Clinical Nurse Specialist
Family Cancer Clinic

Attitudes towards genetic testing in cancer

Patient Information Leaflet
CONFIDENTIAL

Genetic testing is a new medical development which will give doctors and patients the opportunity to know how likely they are to develop certain diseases in the future. This knowledge will ensure that the most appropriate advice is given to people to help them stay healthy. At the moment genetic tests are still being developed for many illnesses, including bowel (colon) cancer. As part of this development, it is important to know what people, who might one day have such a test, think about genetic testing and how they might react to finding out information about their likelihood of developing diseases.

Bowel cancer is one of the diseases for which a genetic test is currently being developed. This questionnaire has been sent to you because you are currently registered with the ICRF Family Cancer Clinic at St Marks as having one or more family members with bowel cancer. Some families may soon be able to have a genetic test which simply involves family members having a blood test. The results of this blood test would then tell doctors how likely each family member is to develop bowel cancer, and some other cancers.

We want to hear from people who have different views about testing, so we are inviting people to complete this questionnaire whatever they think about genetic testing. It should take you no more than half an hour to complete. The questionnaire asks you some questions about bowel cancer, then about genetic testing, and then some more general questions. When you have completed the questionnaire, please return it in the postage paid envelope provided. We will be contacting some people in the future, to monitor how attitudes change over time, and may ask some people if they have a partner or spouse who would also be willing to participate at a later stage. Completion of this questionnaire does not commit you to participate at subsequent stages of the study.

The questionnaires will be marked by computer, and the results assessed by researchers from University College London. Each person's questionnaire will be coded to ensure that your answers are anonymous. The researchers cannot influence your treatment, however, if you have any questions about treatment you can contact the hospital or raise them at your next appointment. If you have any questions about the questionnaire please contact the principal researcher (Naomi Steggles (0171 391 1701)). The results of your questionnaire will only be used for research purposes, and will not be available to anyone outside of the study.

All proposals for research using human subjects are reviewed by an ethics committee before they can proceed. This proposal was reviewed by Harrow Research Ethics Committee and the Joint UCL/UCLH Committees on the Ethics of Human Research. You do not have to take part in this study if you do not want to. If you decide to take part you may withdraw at any time without having to give a reason. Your decision whether to take part or not will not affect your care and management in any way. Return of the completed questionnaire will be taken as consent to participate in this study.

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ICRF HEALTH BEHAVIOUR UNIT

University College London
2-16 Torrington Place
LONDON WC1E 6BT

&

ST MARKS ICRF FAMILY CANCER CLINIC

Study of attitudes about inherited bowel (colon) cancer and genetic testing

This questionnaire is about your general health and feelings and your attitudes towards bowel cancer and genetic testing. Please read the patient information leaflet on the reverse of this page before completing this questionnaire.

All your responses are confidential and will not affect your treatment. By answering the questions you are not committing yourself to having any treatment or investigation.

Please answer ALL the questions in this questionnaire as accurately as you can. If you are not sure about an answer, please guess. Most questions require you to tick the box next to the answer you wish to give, or to circle a number. The form should take about 30 minutes to complete.

Please try to ensure that part of your tick is inside the appropriate box. If you make a mistake, do not worry, just clearly indicate which answer you wish to give.

Thank you for your help

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Section 1. General Health

Firstly please answer these questions about your general health and well being.

Would you say that for someone of your age, your health in general in the past six months has been:

excellent ☐ good ☐ fair ☐ poor ☐

About how many times have you been to your GP in the past six months? ☐☐ *times*

Section 2. Bowel cancer risk and current screening

Please tick just one box for each question

Have you ever had any of the following screening procedures?

a) Testing for blood in the faeces (faecal occult blood test/ haemoccult/ stool test) Yes ☐ No ☐ Dont' know ☐

If yes, how often?
only once ☐ every 3-5 years ☐ every 1-3 years ☐ more than once a year ☐

b) Colonoscopic examination (examination of bowel by camera) Yes ☐ No ☐ Don't know ☐

If yes, how often?
only once ☐ every 3-5 years ☐ every 1-3 years ☐ more than once a year ☐

Some people who think they may be at increased risk of bowel cancer say they would consider the following options. Please tick a box for each part of this question to show whether you would do these things.

a) Have regular tests for blood in the faeces?
no, definitely not ☐ no, probably not ☐ unsure ☐ yes, probably ☐ yes, definitely ☐

b) Have regular colonoscopic examinations?
no, definitely not ☐ no, probably not ☐ unsure ☐ yes, probably ☐ yes, definitely ☐

If you have had bowel cancer in the past, please answer the following questions in terms of your chances of developing bowel cancer again. If you have not had bowel cancer please answer the questions in terms of your chances of developing this cancer at some time. *(If you do not know please guess the answer)*

It is likely that at some point in my life I will get bowel cancer
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

What would you say are the chances of a person in this country developing bowel cancer at some time in their life?
1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 50 ☐ 1 in 75 ☐ 1 in 125 ☐

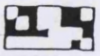
What would you say are *your* chances of developing bowel cancer?
1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 50 ☐ 1 in 75 ☐ 1 in 125 ☐

The following questions ask about how serious you think that bowel cancer is.

If I got bowel cancer my whole life would change
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

I think that bowel cancer is no more serious than other diseases
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Despite medical advances it is still difficult to cure bowel cancer
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐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Section 3: Your feelings about bowel cancer

If you have had bowel cancer in the past please answer the following questions in terms of your feelings about developing bowel cancer again. If you have not had bowel cancer please answer the questions in terms of your feelings about developing this cancer at some time in the future.

During the past month, how often have you thought about your own chances of developing bowel cancer?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

During the past month, how often have thoughts about your chances of getting bowel cancer affected your mood?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

During the past month, have thoughts about your chances of getting bowel cancer affected your ability to perform your daily activities?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

How concerned are you about the possibility that you might get bowel cancer someday?

not at all ☐ somewhat ☐ moderately ☐ very concerned ☐

How often do you worry about developing bowel cancer?

not at all ☐ occasionally ☐ frequently ☐ constantly ☐

How much of a problem is worrying about bowel cancer to you?

not at all ☐ somewhat ☐ definitely is ☐ severe problem ☐

Section 4: The genetic test

In a small number of families, it may be possible to carry out a genetic test to find out who has inherited a gene which increases their risk of developing bowel cancer, and possibly other cancers. At some point you may be offered such a test. If you have already had bowel cancer, having this gene would increase your risk of developing these cancers again. Your views on this might change, but we are interested in your current thoughts about having this genetic test. There are no right or wrong answers. (Your answers here will NOT affect whether or not you are offered the test at some point).

Have you talked with a genetic counsellor for advice about your risk of developing bowel cancer? Yes ☐ No ☐

Have any members of your family talked with a genetic counsellor for advice about their risk of developing bowel cancer? Yes ☐ No ☐ Don't Know ☐

Please read each of the following statements and tick the box next to the statement which best applies to you.

I've never thought about having the genetic test ☐

I'm undecided about having the genetic test ☐

I've decided I don't want to have the genetic test ☐

I've decided I do want to have the genetic test ☐

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Please circle a number between 1 and 5 for each part of this question to indicate what you think about having the genetic test

For me, having the genetic test would be	wise	1	2	3	4	5	foolish
For me, having the genetic test would be	desirable	1	2	3	4	5	undesirable
For me, having the genetic test would be	easy	1	2	3	4	5	difficult
For me, having the genetic test would be	good	1	2	3	4	5	bad

If I have the genetic test I will be certain about whether or not I am at high risk of developing bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test I will be certain about whether or not my children are likely to be at high risk of developing bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test I will have trouble getting life insurance or a mortgage

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test it would make me more aware of early symptoms of bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test it will motivate me to have a healthier lifestyle

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test I will be able to have more regular screening

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test it will help me decide about having surgery to prevent bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test it will make me worry constantly about getting bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test I may upset members of my family

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Thinking now about what other people in your life may think about genetic testing and you having a test, please tick the box which most closely describes how much you agree with these statements

Most people who are important to me would want me to have the genetic test

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

My partner would want me to have the genetic test

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐ Not applicable ☐

Most of my family would want me to have the genetic test

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Most of my friends would want me to have the genetic test

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If a test was available for them, most of my relatives would have it

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

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These statements ask about how much influence you think you have over whether you have a genetic test

I would like to have the genetic test but I don't really know if I can

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Whether or not I have the genetic test is entirely up to me

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

In general, how difficult do you think it would be for you to have the genetic test?

extremely difficult ☐ fairly difficult ☐ not very difficult ☐ not at all difficult ☐

How much control do you feel you have over whether or not you have the genetic test?

complete control ☐ a lot of control ☐ some control ☐ no control ☐

The next few questions ask you to think about how you might feel under various circumstances. Please tick the box for each part of the question which best describes how you might feel.

How might you feel if you *decided not to have* the genetic test? (please respond to each part of this question).

I would feel:	not at all	a bit	fairly	extremely
guilty	☐	☐	☐	☐
relieved	☐	☐	☐	☐
depressed	☐	☐	☐	☐
worried	☐	☐	☐	☐
regretful	☐	☐	☐	☐
forever wondering	☐	☐	☐	☐

How might you feel if you had the genetic test *and the result showed that you were at high risk of developing bowel cancer?* (please respond to each part of this question).

I would feel:	not at all	a bit	fairly	extremely
guilty	☐	☐	☐	☐
relieved	☐	☐	☐	☐
depressed	☐	☐	☐	☐
worried	☐	☐	☐	☐
surprised	☐	☐	☐	☐
regretful	☐	☐	☐	☐
that it was hard to believe	☐	☐	☐	☐
angry	☐	☐	☐	☐

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How might you feel if you had the genetic test *and the result showed that your risk of developing bowel cancer was no higher than the general population?* (please respond to each part of this question).

I would feel:	not at all	a bit	fairly	extremely
guilty	☐	☐	☐	☐
relieved	☐	☐	☐	☐
depressed	☐	☐	☐	☐
worried	☐	☐	☐	☐
surprised	☐	☐	☐	☐
regretful	☐	☐	☐	☐
that it was hard to believe	☐	☐	☐	☐
angry	☐	☐	☐	☐
happy	☐	☐	☐	☐

For the next questions please indicate how much you agree with the statements

A clear (low risk) genetic test would reassure me more than a clear haemoccult blood test

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

A clear (low risk) genetic test would reassure me more than a clear colonoscopy

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

The next questions ask under which circumstances you would want to have a genetic test

I would have the test if I knew that the cancer could definitely be prevented or cured Yes ☐ No ☐

I would have the genetic test if I knew there was a good chance the cancer could be prevented or cured Yes ☐ No ☐

I would have the genetic test even if the cancer could not be prevented or cured Yes ☐ No ☐

	definitely not								definitely yes
Would you like to have a genetic test when one is available?	1	2	3	4	5	6	7	8	9

These questions ask you what you think you would do if you found out the results of a genetic test

What would you do if you found out that you *were at high risk* of developing bowel cancer?

I would:	no, definitely not	no, probably not	unsure	yes, probably	yes, definitely
have more regular screening	☐	☐	☐	☐	☐
plan financially for the future	☐	☐	☐	☐	☐
not have any more children in case I pass the gene to them	☐	☐	☐	☐	☐
try to forget about it	☐	☐	☐	☐	☐
be more careful to avoid unhealthy food	☐	☐	☐	☐	☐
do all the things I've always wanted to do	☐	☐	☐	☐	☐
watch more carefully for signs of bowel cancer	☐	☐	☐	☐	☐
find a more fulfilling job	☐	☐	☐	☐	☐
try to adopt a healthier lifestyle	☐	☐	☐	☐	☐
make more plans for the future	☐	☐	☐	☐	☐

42993

What would you do if you found out that you *were not at high risk* of developing bowel cancer?

I would:	no, definitely not	no, probably not	unsure	yes, probably	yes, definitely
stop having screening	☐	☐	☐	☐	☐
plan financially for the future	☐	☐	☐	☐	☐
have more children	☐	☐	☐	☐	☐
not worry so much about eating unhealthy food	☐	☐	☐	☐	☐
do all the things I've always wanted to do	☐	☐	☐	☐	☐
still worry about getting bowel cancer	☐	☐	☐	☐	☐
find a more fulfilling job	☐	☐	☐	☐	☐
try to adopt a healthier lifestyle	☐	☐	☐	☐	☐
make more plans for the future	☐	☐	☐	☐	☐

How likely do you think it is that you carry a gene which increases your chances of developing bowel cancer?

extremely likely ☐ fairly likely ☐ unsure ☐ fairly unlikely ☐ extremely unlikely ☐

How likely do you think you are to be offered the genetic test when it becomes available?

extremely likely ☐ fairly likely ☐ unsure ☐ fairly unlikely ☐ extremely unlikely ☐

Would you have a genetic test, if you were offered it?

yes, definitely ☐ yes, probably ☐ unsure ☐ no, probably not ☐ no, definitely not ☐

These next questions ask you about how you feel about having medical tests in general. Please circle a number between 1 and 5 to show how much you agree with each statement.

	Strongly disagree				Strongly agree
I would rather have a medical test, and be certain about my future health, even if the result is bad news	1	2	3	4	5
I would like to know now if I am likely to be ill so I can get used to the news	1	2	3	4	5
If I didn't have a medical test I would always be wondering whether I was going to develop the disease	1	2	3	4	5
The relief I would get from a good result makes it worth the risk that the result is bad	1	2	3	4	5
I think it is tempting fate to ask questions about future illness	1	2	3	4	5
I would rather live with uncertainty, than find out I was going to develop a disease	1	2	3	4	5
Knowing the result of a medical test would mean I felt more in control	1	2	3	4	5
It is better to know that I will develop a disease, even if I can't prevent it	1	2	3	4	5

Section 5: About how you think and feel

Please read the 6 statements below and then tick the box under the most appropriate word(s) to indicate how you feel right now, at this moment.

RIGHT NOW:-	not at all	somewhat	moderately	very much
I feel calm	☐	☐	☐	☐
I am tense	☐	☐	☐	☐
I feel upset	☐	☐	☐	☐
I am relaxed	☐	☐	☐	☐
I feel content	☐	☐	☐	☐
I am worried	☐	☐	☐	☐

42993

Please read each of the items below, and tick the box next to the answer which comes closest to how you have been feeling in the past week

IN THE PAST WEEK I WOULD SAY THAT:

I feel tense or 'wound up'
most of the time ☐ a lot of the time ☐ time to time, occasionally ☐ not at all ☐

I still enjoy the things I used to enjoy
definitely as much ☐ not quite as much ☐ only a little ☐ hardly at all ☐

I get a sort of frightened feeling as if something awful is going to happen
very definitely and quite badly ☐ yes, but not too badly ☐ a little, but it doesn't worry me ☐ not at all ☐

I can laugh and see the funny side of things
as much as I always could ☐ not quite so much now ☐ definitely not so much now ☐ not at all ☐

Worrying thoughts go through my mind
a great deal of the time ☐ a lot of the time ☐ from time to time but not too often ☐ only occasionally ☐

I feel cheerful
not at all ☐ not often ☐ sometimes ☐ most of the time ☐

I can sit at ease and feel relaxed
definitely ☐ usually ☐ not often ☐ not at all ☐

I feel as if I am slowed down
nearly all the time ☐ very often ☐ sometimes ☐ not at all ☐

I get a sort of frightened feeling like 'butterflies' in my stomach
not at all ☐ occasionally ☐ quite often ☐ very often ☐

I have lost interest in my appearance
definitel ☐ I don't take as much care as I should ☐ I may not take quite as much care ☐ I take just as much care as ever ☐

I feel restless as if I have to be on the move
very much indeed ☐ quite a lot ☐ not very much ☐ not at all ☐

I look forward with enjoyment to things
as much as I ever did ☐ rather less than I used to ☐ definitely less than I used to ☐ hardly at all ☐

I get sudden feelings of panic
very often indeed ☐ quite often ☐ not very often ☐ not at all ☐

I can enjoy a good book or radio or TV programme
often ☐ sometimes ☐ not often ☐ very seldom ☐

Section 6:- About yourself

I am male ☐ female ☐
I am married/ living as married ☐ separated ☐ divorced ☐ widowed ☐ single ☐ in relationship (not co-habiting) ☐

How old are you? ☐☐ *years old*

How many children do you have? ☐☐

Which of the following best describes your ethnic background?
White ☐ Asian ☐ Black ☐ Other ☐ Do not wish to answer ☐

What religion would you say you were, if any? ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

In the last year, how often have you taken part in religious activities?
once a week or more ☐ once a month ☐ less than once a month ☐ not at all ☐

42993

Do you have a paid job or do any paid work?

No, retired ☐ No, not working at present ☐ Yes, part time ☐ Yes, full time ☐

Do you own or rent your own home?

Own it/ buying it ☐ Rent it ☐ Other ☐

Does your household have a car?

No ☐ Yes, 1 ☐ More than 1 ☐

Do you have any educational qualifications? Yes ☐ No ☐
(e.g. School Certificate, GCSEs, O'Levels etc)

How many years of full time education did you complete AFTER THE AGE OF 16? ☐☐ *years*
(please include any vocational training, two years part time counts as one year)

What would you say is your highest educational qualificaton?

Do you think that cancer might run in your family? Yes ☐ No ☐

If yes, How old were you when you first thought or were told that cancer might run in your family? ☐☐ *years*

Have you ever had bowel cancer? Yes ☐ No ☐

Have you ever had any other medical problems with your bowels? Yes ☐ No ☐

Do you have any problems with your bowels at the moment? Yes ☐ No ☐

Have you ever had any other form of cancer ? Yes ☐ No ☐

If yes, which type and how long ago

Thank you very much for completing this questionnaire, if you have any comments about genetic testing or this questionnaire, please use the space below.

Comments

COVERING LETTER, PATIENT INFORMATION LEAFLET, AND QUESTIONNAIRE FOR FOLLOW-UP SURVEY

Dear ,

Thank-you for your participation in the study on genetic testing, which you completed last year. We have enclosed a follow-up questionnaire that asks you more questions about genetic testing, and whether you have changed your mind since the last time we contacted you. We would appreciate it if you could complete and return this in the envelope provided.

We have also included a questionnaire for your spouse or partner to complete. We use the term partner to refer to anyone with whom you are living with as married, or with whom you are in a long-term relationship with. If you do not have a partner, please ignore this questionnaire. You may read the questionnaire before deciding whether you want your partner to complete it. Once your partner has completed it, they can return it in the envelope supplied for this purpose, so their responses are confidential.

If you have any questions then please contact me at the ICRF Health Behaviour Unit, University College London. My telephone number is 0171 209 6634.

Thank you for your continued participation in this study. Your responses will be really helpful to us.

With best wishes
Yours sincerely

Naomi Steggles

Draft

Section 1

In this section you will be asked whether you think anything has changed since the last time you completed a questionnaire.

Do you think that your attitude has changed towards having a genetic test? Yes ☐ No ☐ Don't Know ☐

If yes, are you more in favour, or more against having a test? more in favour ☐ more against ☐

Which of the following has made you change your mind?

talking to genetic counsellor	☐	My GP	☐
talking to my partner	☐	thinking about the test	☐
talking to my family	☐	illness of family member	☐
talking to friends	☐	my health	☐
something in the media	☐	other, please specify	

Would you say that for someone of your age, your health in general in the past six months has been:

excellent ☐ good ☐ fair ☐ poor ☐

About how many times have you been to your GP in the past six months? ☐☐ *times*

Do you have any problems with your bowels at the moment? Yes ☐ No ☐

If you have had bowel cancer in the past, please answer the following questions in terms of your chances of developing bowel cancer again. If you have not had bowel cancer please answer the questions in terms of your chances of developing this cancer at some time

It is likely that at some point in my life I will get bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

What would you say are the chances of a person in this country developing bowel cancer at some time in their life?

1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 50 ☐ 1 in 75 ☐ 1 in 125 ☐

What would you say are *your* chances of developing bowel cancer?

1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 50 ☐ 1 in 75 ☐ 1 in 125 ☐

If you have been given a different estimate of your risk, please write the figure below

I was told that my risk of developing bowel cancer is 1 in_____ or _____%

The following questions ask about how serious you think that bowel cancer is.

If I got bowel cancer my whole life would change

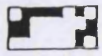
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

I think that bowel cancer is no more serious than other diseases

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Despite medical advances it is still difficult to cure bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐


Draft

Section 2: Your feelings about bowel cancer

If you have had bowel cancer in the past please answer the following questions in terms of your feelings about developing bowel cancer again. If you have not had bowel cancer please answer the questions in terms of your feelings about developing this cancer at some time in the future.

During the past month, how often have you thought about your own chances of developing bowel cancer?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

During the past month, how often have thoughts about your chances of getting bowel cancer affected your mood?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

During the past month, have thoughts about your chances of getting bowel cancer affected your ability to perform your daily activities?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

How concerned are you about the possibility that you might get bowel cancer someday?

not at all ☐ somewhat ☐ moderately ☐ very concerned ☐

How often do you worry about developing bowel cancer?

not at all ☐ occasionally ☐ frequently ☐ constantly ☐

How much of a problem is worrying about bowel cancer to you?

not at all ☐ somewhat ☐ definitely is ☐ severe problem ☐

Section 3: The genetic test

In a small number of families, it is possible to carry out a genetic test to find out who has inherited a gene which increases their risk of developing bowel cancer, and possibly other cancers. If you have already had bowel cancer, having this gene would increase your risk of developing these cancers again. What do you currently think about the genetic test?

Please read each of the following statements and tick the box next to the statement which best applies to you.

I'm undecided about having the genetic test ☐

I've decided I don't want to have the genetic test ☐

I've decided I do want to have the genetic test ☐

Please circle a number between 1 and 5 for each part of this question to indicate what you think about having the genetic test

For me, having the genetic test would be	wise	1	2	3	4	5	foolish
For me, having the genetic test would be	desirable	1	2	3	4	5	undesirable
For me, having the genetic test would be	easy	1	2	3	4	5	difficult
For me, having the genetic test would be	good	1	2	3	4	5	bad
For me, having the genetic test would be	beneficial	1	2	3	4	5	harmful

Draft

If I have the genetic test I will be certain about whether or not I am at high risk of developing bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test I will be certain about whether or not my children are likely to be at high risk of developing bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test I will have trouble getting life insurance or a mortgage

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test it would make me more aware of early symptoms of bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test it will motivate me to have a healthier lifestyle

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test I will be able to have more regular screening

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test it will help me decide about having surgery to prevent bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test it will make me worry constantly about getting bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If I have the genetic test I may upset members of my family

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Thinking now about what other people in your life may think about genetic testing and you having a test, please tick the box which most closely describes how much you agree with these statements

Most people who are important to me want me to have the genetic test

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

My partner wants me to have the genetic test

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐ Not applicable ☐

Most of my family wants me to have the genetic test

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Most of my friends want me to have the genetic test

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If a test was available for them, most of my relatives would have it

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

These statements ask about how much influence you think you have over whether you have a genetic test

Whether or not I have the genetic test is entirely up to me

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

In general, how difficult do you think it will be for you to have the genetic test?

extremely difficult ☐ fairly difficult ☐ not very difficult ☐ not at all difficult ☐

How much control do you feel you have over whether or not you have the genetic test?

complete control ☐ a lot of control ☐ some control ☐ no control ☐

Draft

The next few questions ask you to think about how you might feel under various circumstances. Please tick the box for each part of the question which best describes how you might feel.

How might you feel if you *decided not to have* the genetic test? (please respond to each part of this question). If you have already decided not to have the test, this will reflect how you feel about it now. If you want to have the test, the answers will reflect how you would feel if you did not have the test.

I would feel:	not at all	a bit	fairly	extremely
guilty	☐	☐	☐	☐
relieved	☐	☐	☐	☐
depressed	☐	☐	☐	☐
worried	☐	☐	☐	☐
regretful	☐	☐	☐	☐
forever wondering	☐	☐	☐	☐

How might you feel if you had the genetic test *and the result showed that you were at high risk of developing bowel cancer?*(please respond to each part of this question).

I would feel:	not at all	a bit	fairly	extremely
guilty	☐	☐	☐	☐
relieved	☐	☐	☐	☐
depressed	☐	☐	☐	☐
worried	☐	☐	☐	☐
surprised	☐	☐	☐	☐
regretful	☐	☐	☐	☐
that it was hard to believe	☐	☐	☐	☐
angry	☐	☐	☐	☐

How might you feel if you had the genetic test *and the result showed that your risk of developing bowel cancer was no higher than the general population?* (please respond to each part of this question).

I would feel:	not at all	a bit	fairly	extremely
guilty	☐	☐	☐	☐
relieved	☐	☐	☐	☐
depressed	☐	☐	☐	☐
worried	☐	☐	☐	☐
surprised	☐	☐	☐	☐
regretful	☐	☐	☐	☐
that it was hard to believe	☐	☐	☐	☐
angry	☐	☐	☐	☐
happy	☐	☐	☐	☐

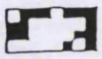
The next questions ask under which circumstances you would want to have a genetic test

I would have the test if I knew that the cancer could definitely be prevented or cured Yes ☐ No ☐

I would have the genetic test if I knew there was a good chance the cancer could be prevented or cured Yes ☐ No ☐

I would have the genetic test even if the cancer could not be prevented or cured Yes ☐ No ☐

	definitely not								definitely yes
Would you like to have a genetic test ?	1	2	3	4	5	6	7	8	9



How likely do you think it is that you carry a gene which increases your chances of developing bowel cancer?
extremely likely ☐ fairly likely ☐ unsure ☐ fairly unlikely ☐ extremely unlikely ☐

Would you have a genetic test if you were offered it?
yes, definitely ☐ yes, probably ☐ unsure ☐ no, probably not ☐ no, definitely not ☐

Section 4: About how you think and feel

Please read each of the items below, and tick the box next to the answer which comes closest to how you have been feeling in the past week

IN THE PAST WEEK I WOULD SAY THAT:

I feel tense or 'wound up'
most of the time ☐ a lot of the time ☐ time to time, occasionally ☐ not at all ☐

I still enjoy the things I used to enjoy
definitely as much ☐ not quite as much ☐ only a little ☐ hardly at all ☐

I get a sort of frightened feeling as if something awful is going to happen
very definitely and quite badly ☐ yes, but not too badly ☐ a little, but it doesn't worry me ☐ not at all ☐

I can laugh and see the funny side of things
as much as I always could ☐ not quite so much now ☐ definitely not so much now ☐ not at all ☐

Worrying thoughts go through my mind
a great deal of the time ☐ a lot of the time ☐ from time to time but not too often ☐ only occasionally ☐

I feel cheerful
not at all ☐ not often ☐ sometimes ☐ most of the time ☐

I can sit at ease and feel relaxed
definitely ☐ usually ☐ not often ☐ not at all ☐

I feel as if I am slowed down
nearly all the time ☐ very often ☐ sometimes ☐ not at all ☐

I get a sort of frightened feeling like 'butterflies' in my stomach
not at all ☐ occasionally ☐ quite often ☐ very often ☐

I have lost interest in my appearance
definitel ☐ I don't take as much care as I should ☐ I may not take quite as much care ☐ I take just as much care as ever ☐

I feel restless as if I have to be on the move
very much indeed ☐ quite a lot ☐ not very much ☐ not at all ☐

I look forward with enjoyment to things
as much as I ever did ☐ rather less than I used to ☐ definitely less than I used to ☐ hardly at all ☐

I get sudden feelings of panic
very often indeed ☐ quite often ☐ not very often ☐ not at all ☐

I can enjoy a good book or radio or TV programme
often ☐ sometimes ☐ not often ☐ very seldom ☐

Please read the 6 statements below and then tick the box under the most appropriate word(s) to indicate how you feel right now, at this moment.

RIGHT NOW:-	not at all	somewhat	moderately	very much
I feel calm	☐	☐	☐	☐
I am tense	☐	☐	☐	☐
I feel upset	☐	☐	☐	☐
I am relaxed	☐	☐	☐	☐
I feel content	☐	☐	☐	☐
I am worried	☐	☐	☐	☐

Please could you write in the space below the three main reasons why you would want a genetic test, with the most important reason first

I would like to have / not have the genetic test because:

Reason 1

Reason 2

Reason 3

Please could you write in the space below the three main reasons why you would not want a genetic test, with the most important reason first

Reason 1

Reason 2

Reason 3

Thank you very much for completing this questionnaire, if you have any comments about genetic testing or this questionnaire, please use the space below.

Comments

COVERING LETTER, PATIENT INFORMATION LEAFLET AND QUESTIONNAIRE FOR PARTNERS OF PEOPLE AT HIGH RISK OF COLON CANCER

Dear Sir/ Madam,

I am writing to invite you to participate in a study of interest in genetic testing in spouses and partners of people with a family history of colon cancer. This study is part of an on-going study to investigate what people think about genetic testing, and why people form certain opinions. With this letter you should have also received an information leaflet and a questionnaire. I would appreciate it if you would complete this and return it to me in the FREEPOST envelope supplied.

If you have any questions then please contact me at the ICRF Health Behaviour Unit, University College London. My telephone number is 0171 209 6634.

Thank you very much for taking the time to complete this questionnaire. Your responses will be very helpful to us.

With best wishes
Yours sincerely

Naomi Steggles
Principal Researcher

Attitudes towards genetic testing in cancer

Information Leaflet

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Genetic testing is a new and exciting medical development which will give doctors and patients the opportunity to know how likely they are to develop certain diseases in the future. This knowledge will ensure that the most appropriate advice is given to people to help them stay healthy. At the moment genetic tests are still being developed for many illnesses, including bowel (colon) cancer. As part of this development, it is important to know what people, who might one day have such a test, think about genetic testing and how they might react to finding out information about their likelihood of developing diseases. In addition it is important to see how this information may affect relationships, especially with partners, and how they feel they would react to knowledge about their partener's risk of disease.

Bowel cancer is one of the diseases for which a genetic test is currently being developed. This questionnaire has been given to you by your partner, because they are currently registered with the ICRF Family Cancer Clinic at St Marks as having one or more family members with bowel cancer. Some families may soon be able to have a genetic test that simply involves family members having a blood test. The results of this blood test would then tell doctors how likely each family member is to develop bowel cancer, and some other cancers.

We are asking people from families with a history of bowel cancer about their feelings about genetic testing, and are then asking their partners about what they think. We want to hear from you whatever you think about genetic testing. It should take you no more than half an hour to complete. The questionnaire asks you some questions about bowel cancer, about genetic testing, and some more general questions. In the questionnaire, we use the term partner to refer to your spouse or person with whom you have a significant relationship. There is an opportunity on the form for you to state the nature of this relationship, if you wish to. When you have completed the questionnaire, please return it in the postage paid envelope provided. This envelope is just for your questionnaire, and is confidential, your partner will not be told your responses.

The questionnaires will be assessed by researchers from University College London. Each person's questionnaire will be coded to ensure that your answers are anonymous. If you have any questions about the questionnaire please contact the principal researcher (Naomi Steggles (0171 209 6634)). The results of your questionnaire will only be used for research purposes, and will not be available to anyone outside of the study.

All proposals for research using human subjects are reviewed by an ethics committee before they can proceed. This proposal was reviewed by Harrow Research Ethics Committee and the Joint UCL/UCLH Committees on the Ethics of Human Research. You do not have to take part in this study if you do not want to. If you decide to take part you may withdraw at any time without having to give a reason. Your decision whether to take part or not will not affect your partner's care and management in any way. Return of the completed questionnaire will be taken as consent to participate in this study.

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ICRF HEALTH BEHAVIOUR UNIT

University College London
2-16 Torrington Place
LONDON WC1E 6BT

&

ST MARKS ICRF FAMILY CANCER CLINIC

Study of attitudes about inherited bowel (colon) cancer and genetic testing in spouses and partners

This questionnaire is about your attitudes towards bowel cancer and genetic testing for your partner or spouse. All your responses are confidential and will not affect your partner's treatment. You are free to withdraw from this study at anytime. On the other side of this sheet is an information leaflet explaining the study. Please read this BEFORE completing the questionnaire.

Please answer all the questions in this questionnaire as accurately as you can. If you are not sure about an answer, please guess. Most questions require you to tick the box next to the answer you wish to give, or to circle a number. The form should take about 30 minutes to complete.

Thank you for your help

In this questionnaire, we use the term 'partner' to describe the person with whom you have a significant relationship, who gave you this questionnaire. Please describe in the box below how you would describe your relationship, eg married, living together, etc

Section 1. Bowel cancer

Firstly we would like to ask you about how you view your own and your partner's risk of developing bowel cancer If you or your partner have had bowel cancer in the past, please answer the following questions in terms of your chances of developing bowel cancer again. If you or your partner have not had bowel cancer please answer the questions in terms of your chances of developing this cancer at some time.

It is likely that at some point in my life I will get bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

What would you say are the chances of a person in this country developing bowel cancer at some time in their life?

1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 50 ☐ 1 in 75 ☐ 1 in 125 ☐

What would you say are *your* chances of developing bowel cancer?

1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 50 ☐ 1 in 75 ☐ 1 in 125 ☐

What would you say are *your partner's* chances of developing bowel cancer?

1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 50 ☐ 1 in 75 ☐ 1 in 125 ☐

The following questions ask about how serious you think that bowel cancer is.

I think that bowel cancer is a serious disease

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

I think that bowel cancer is more serious than other diseases that I know

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Despite medical advances it is still difficult to cure bowel cancer

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

During the past month, how often have you thought about your partner's chances of developing bowel cancer?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

During the past month, how often have thoughts about your partner's chances of getting bowel cancer affected your mood?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

During the past month, have thoughts about your partner's chances of getting bowel cancer affected your ability to perform your daily activities?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

How concerned are you about the possibility that your partner might get bowel cancer someday?

not at all ☐ somewhat ☐ moderately ☐ very concerned ☐

How often do you worry about your partner developing bowel cancer?

not at all ☐ occasionally ☐ frequently ☐ constantly ☐

How much of a problem is worrying about bowel cancer to you?

not at all ☐ somewhat ☐ definitely is ☐ severe problem ☐

Draft

Section 2: The genetic test

At some point your partner may be offered the chance of having a genetic test to find out whether they have inherited a gene which increases their risk of developing bowel cancer, and possibly other cancers. If they have already had bowel cancer, having this gene would increase their risk of developing these cancers again. Your views on this might change, but we are interested in your current thoughts about your partner having this genetic test. There are no right or wrong answers. (Your answers here will NOT affect whether or not your partenr is offered the test at some point).

Have you talked with a genetic counsellor for advice about your partner's risk of developing bowel cancer? Yes ☐ No ☐

Have you talked with your partner about their risk of developing bowel cancer? Yes ☐ No ☐

Please read each of the following statements and tick the box next to the statement which best describes what you think about your partner having the genetic test (this might be different to whether they want the test or not)

- I've never thought about my partner having the genetic test ☐
- I'm undecided about whether I want my partner to have the ☐
- I've decided I don't want my partner to have the genetic test ☐
- I've decided I do want my partner to have the genetic test ☐

Please circle a number between 1 and 5 for each part of this question to indicate what you think about your partner having the genetic test

For my partner, having the genetic test would be	wise	1	2	3	4	5	foolish
For my partner, having the genetic test would be	desirable	1	2	3	4	5	undesirable
For my partner, having the genetic test would be	easy	1	2	3	4	5	difficult
For my partner, having the genetic test would be	good	1	2	3	4	5	bad
For my partner, having the genetic test would be	beneficial	1	2	3	4	5	harmful

If my partner has the genetic test I will be certain about whether or not they are at high risk of developing bowel cancer
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If my partner has the genetic test I will be certain about whether or not our children are likely to be at high risk of developing bowel cancer
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐ not applicable ☐

If my partner has the genetic test we will have trouble getting life insurance or a mortgage
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If my partner has the genetic test it would make me more aware of early symptoms of bowel cancer
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If my partner has the genetic test I will try to motivate them to have a healthier lifestyle
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If my partner has the genetic test it will make me worry constantly about them getting bowel cancer
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

If my partner has the genetic test it may upset members of our family
strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Draft

These statements ask about how much influence you think you have over whether your partner has a genetic test

Whether or not my partner has the genetic test is entirely up to them

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

In general, how difficult do you think it would be for your partner to have the genetic test?

extremely difficult ☐ fairly difficult ☐ not very difficult ☐ not at all difficult ☐

How much control do you feel you have over whether or not your partner has the genetic test?

complete control ☐ a lot of control ☐ some control ☐ no control ☐

If I asked my partner to have the genetic test, they would even if they didn't really want it

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

The next few questions ask you to think about how you might feel under various circumstances. Please tick the box for each part of the question which best describes how you might feel.

How might you feel if your partner *decided not to have* the genetic test? (please respond to each part of this question)

I would feel:	not at all	a bit	fairly	extremely
guilty	☐	☐	☐	☐
relieved	☐	☐	☐	☐
depressed	☐	☐	☐	☐
worried	☐	☐	☐	☐
regretful	☐	☐	☐	☐
forever wondering	☐	☐	☐	☐
angry	☐	☐	☐	☐
annoyed	☐	☐	☐	☐

How might you feel if your partner had the genetic test *and the result showed that they were at high risk of developing bowel cancer?*(please respond to each part of this question).

I would feel:	not at all	a bit	fairly	extremely
guilty	☐	☐	☐	☐
relieved	☐	☐	☐	☐
depressed	☐	☐	☐	☐
worried	☐	☐	☐	☐
suprised	☐	☐	☐	☐
regretful	☐	☐	☐	☐
that it was hard to believe	☐	☐	☐	☐
angry	☐	☐	☐	☐

How might you feel if your partner had the genetic test *and the result showed that their risk of developing bowel cancer was no higher than the general population?*(please respond to each part of this question).

I would feel:	not at all	a bit	fairly	extremely
guilty	☐	☐	☐	☐
relieved	☐	☐	☐	☐
depressed	☐	☐	☐	☐
worried	☐	☐	☐	☐
suprised	☐	☐	☐	☐
regretful	☐	☐	☐	☐
that it was hard to believe	☐	☐	☐	☐
angry	☐	☐	☐	☐
happy	☐	☐	☐	☐

Draft

The next questions ask under which circumstances you would want your partner to have a genetic test?

I would want them to have the test if I knew that the cancer could definitely be prevented or cured	Yes ☐	No ☐
I would want them to have the genetic test if I knew there was a good chance the cancer could be prevented or cured	Yes ☐	No ☐
I would want them to have the genetic test even if the cancer could not be prevented or cured	Yes ☐	No ☐

	definitely not								definitely yes
Would you like your partner to have a genetic test when one is available?	1	2	3	4	5	6	7	8	9

The next questions ask you what you think you would do if you were told the results of your partner's genetic test

What would you do if you found out that your partner *was at high risk* of developing bowel cancer?

I would:	no, definitely not	no, probably not	unsure	yes, probably	yes, definitely
encourage them to have more regular screening	☐	☐	☐	☐	☐
plan financially for the future	☐	☐	☐	☐	☐
not have any more children in case my partner passes the gene to them	☐	☐	☐	☐	☐
try to forget about it	☐	☐	☐	☐	☐
encourage them to avoid unhealthy food	☐	☐	☐	☐	☐
do all the things we've always wanted to	☐	☐	☐	☐	☐
watch more carefully for signs of bowel cancer	☐	☐	☐	☐	☐
leave my partner	☐	☐	☐	☐	☐
try to help them adopt a healthier lifestyle	☐	☐	☐	☐	☐
make more plans for the future	☐	☐	☐	☐	☐

What would you do if you found out that your partner *was not at high risk* of developing bowel cancer?

I would:	no, definitely not	no, probably not	unsure	yes, probably	yes, definitely
encourage them to stop having screening	☐	☐	☐	☐	☐
plan financially for the future	☐	☐	☐	☐	☐
have more children	☐	☐	☐	☐	☐
not worry so much about them eating unhealthy food	☐	☐	☐	☐	☐
do all the things we've always wanted to do	☐	☐	☐	☐	☐
still worry about getting bowel cancer	☐	☐	☐	☐	☐
leave my partner	☐	☐	☐	☐	☐
try toencourage them to adopt a healthier lifestyle	☐	☐	☐	☐	☐
make more plans for the future	☐	☐	☐	☐	☐

How likely do you think it is that they carry a gene which increases their chances of developing bowel cancer?

extremely likely ☐ fairly likely ☐ unsure ☐ fairly unlikely ☐ extremely unlikely ☐

How likely do you think they are to be offered the genetic test when it becomes available?

extremely likely ☐ fairly likely ☐ unsure ☐ fairly unlikely ☐ extremely unlikely ☐

Would you want them to have a genetic test, if they were offered it?

yes, definitely ☐ yes, probably ☐ unsure ☐ no, probably not ☐ no, definitely not ☐

Draft

These next questions ask you about how you feel about having medical tests in general, please circle a number between 1 and 5 to show how much you agree with the statement.

	Strongly disagree				Strongly agree
I would rather have a medical test, and be certain about my future health, even if the result is bad news	1	2	3	4	5
I would like to know now if I am likely to be ill so I can get used to the news	1	2	3	4	5
If I didn't have a medical test I would always be wondering whether I was going to develop the disease	1	2	3	4	5
The relief I would get from a good result makes it worth the risk that the result is bad	1	2	3	4	5
I think it is tempting fate to ask questions about future illness	1	2	3	4	5
I would rather live with uncertainty, than find out I was going to develop a disease	1	2	3	4	5
Knowing the result of a medical test would mean I felt more in control	1	2	3	4	5
It is better to know that I will develop a disease, even if I can't prevent it	1	2	3	4	5

Section 3: About how you think and feel

Please read the 6 statements below and then tick the box under the most appropriate word(s) to indicate how you feel right now, at this moment

RIGHT NOW:-	not at all	somewhat	moderately	very much
I feel calm	☐	☐	☐	☐
I am tense	☐	☐	☐	☐
I feel upset	☐	☐	☐	☐
I am relaxed	☐	☐	☐	☐
I feel content	☐	☐	☐	☐
I am worried	☐	☐	☐	☐

Please read each of the items below, and tick the box next to the answer which comes closest to how you have bee feeling in the past week

IN THE PAST WEEK I WOULD SAY THAT:

I feel tense or 'wound up'
most of the time ☐ a lot of the time ☐ time to time, occasionally ☐ not at all ☐

I still enjoy the things I used to enjoy
definitely as much ☐ not quite as much ☐ only a little ☐ hardly at all ☐

I get a sort of frightened feeling as if something awful is going to happen
very definitely and quite badly ☐ yes, but not too badly ☐ a little, but it doesn't worry me ☐ not at all ☐

I can laugh and see the funny side of things
as much as I always could ☐ not quite so much now ☐ definitely not so much now ☐ not at all ☐

Worrying thoughts go through my mind
a great deal of the time ☐ a lot of the time ☐ from time to time but not too often ☐ only occasionally ☐

I feel cheerful
not at all ☐ not often ☐ sometimes ☐ most of the time ☐

I can sit at ease and feel relaxed
definitely ☐ usually ☐ not often ☐ not at all ☐

I feel as if I am slowed down
nearly all the time ☐ very often ☐ sometimes ☐ not at all ☐

Draft

I get a sort of frightened feeling like 'butterflies' in my stomach
not at all ☐ occasionally ☐ quite often ☐ very often ☐

I have lost interest in my appearance
definitel ☐ I don't take as much care as I should ☐ I may not take quite as much y care ☐ I take just as much care as ☐

I feel restless as if I have to be on the move
very much indeed ☐ quite a lot ☐ not very much ☐ not at all ☐

I look forward with enjoyment to things
as much as I ever did ☐ rather less than I used to ☐ definitely less than I used to ☐ hardly at all ☐

I get sudden feelings of panic
very often indeed ☐ quite often ☐ not very often ☐ not at all ☐

I can enjoy a good book or radio or TV programme
often ☐ sometimes ☐ not often ☐ very seldom ☐

Section 6:- About yourself

I am male ☐ female ☐

How old are you? ☐☐ *years old*

Which of the following best describes your ethnic background?
White ☐ Asian ☐ Black ☐ Other ☐ Do not wish to answer ☐

What religion would you say you were, if any? ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

In the last year, how often have you taken part in religious activities?
once a week or more ☐ once a month ☐ less than once a month ☐ not at all ☐

Do you have a paid job or do any paid work?
No, retired ☐ No, not working at present ☐ Yes, part time ☐ Yes, full time ☐

Do you have any educational qualifications?
(e g. School Certificate, GCSES, O'Levels etc) Yes ☐ No ☐

How many years of full time education did you complete AFTER THE AGE OF 16? ☐☐ *years*
(please include any vocational training, two years part time counts as one year)

When did you find out that cancer might run in your partner's family?
when we first met ☐ before we got engaged/ lived together ☐ before we got married ☐ before we had children ☐

Other, please specify ☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐☐

How long have you known your partner? ☐☐ *years*

If you are married, how long have you been married? ☐☐ *years*

Thank you very much for completing this questionnaire

QUESTIONNAIRE FOR WOMEN AT HIGH RISK OF BREAST /OVARIAN CANCER

UMDS Guy's and St. Thomas's Medical and Dental Schools

Study of attitudes about inherited breast and ovarian cancer and genetic testing

You will shortly be coming to the Family Cancer Clinic at Guy's Hospital. This questionnaire covers aspects of your general health and feelings and also your attitudes to breast and ovarian cancer and genetic testing.

The questionnaire does not ask about your family history of cancer as the genetic counsellors in the clinic will discuss this with you.

All your responses are confidential to the psychologists on the study team and will not affect your treatment at the Family Cancer Clinic. By answering the questions you are not committing yourself to having any treatment or investigation.

Thank you for your help.

Code .....

Section 1: Your appointment at the Family Cancer Clinic

[1] Please tell us the date of your appointment at the clinic ...../...../.....

[2] Please give the date you are completing this questionnaire: ...../...../.....

[3] What is your main reason for attending the clinic?

.....

.....

.....

[4] In some cases, it is now possible to do a blood test to find out whether a person has inherited a gene that increases their risk of developing breast cancer and possibly also ovarian cancer. This test is referred to in this questionnaire as 'the genetic test'.

Had you ever heard of this genetic test? yes ☐ no ☐

Section 2: Breast and ovarian cancer risk

Please tick just one box for every question

[1] Have you ever had breast cancer? yes ☐ no ☐

[2] Have you ever had any other medical problems with your breasts? (e.g. lump, discomfort) yes ☐ no ☐

[3] Do you have any problems with your breasts at the moment? yes ☐ no ☐

[4] In the last six months, approximately how often have you examined your breasts?

more than once a day ☐	once every two weeks ☐	once every three months ☐
once a day ☐	once every month ☐	once during the last six months ☐
once a week ☐	once every two months ☐	not at all ☐

[5] Some women attending the Family Cancer Clinic say they would consider the following options. Please tick a box for each part of this question to show if you would do these things.

(a) Have regular mammograms (breast x-rays)?

no, definitely not ☐ no, probably not ☐ unsure ☐ yes, probably ☐ yes, definitely ☐

(b) Have regular breast examinations by a doctor or nurse?

no, definitely not ☐ no, probably not ☐ unsure ☐ yes, probably ☐ yes, definitely ☐

(c) Have a prophylactic mastectomy (a surgical operation to remove most of the breast tissue before cancer develops)? ***If you have had both your breasts removed please leave this item blank***

no, definitely not ☐ no, probably not ☐ unsure ☐ yes, probably ☐ yes, definitely ☐

(d) Have a prophylactic oophorectomy (a surgical operation to remove the ovaries before cancer develops)? *If you have had both your ovaries removed please leave this item blank*

no, definitely not ☐ no, probably not ☐ unsure ☐ yes, probably ☐ yes, definitely ☐

(e) Examine your breasts more often than you do?

no, definitely not ☐ no, probably not ☐ unsure ☐ yes, probably ☐ yes, definitely ☐

[6] Have you ever had ovarian cancer? yes ☐ no ☐

[7] What would you say the chances are of a woman in this country developing breast cancer at some time in her life? (please tick a box)

1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 75 ☐ 1 in 125 ☐

[8] What would you say the chances are of a woman in this country developing ovarian cancer at some time in her life?

1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 75 ☐ 1 in 125 ☐

If you have had breast or ovarian cancer in the past, please answer questions 9-12 in terms of your chances of developing these cancers again. If you have not had breast or ovarian cancer please answer the questions in terms of your chances of developing these cancers at some time.

[9] What would you say *your* chances are of developing breast cancer?

1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 75 ☐ 1 in 125 ☐

[10] Compared to other women of your age, how likely do you think you are to develop breast cancer?

much more likely ☐ a bit more likely ☐ about the same ☐ a bit less likely ☐ much less likely ☐

[11] Compared to other women attending the Family Cancer Clinic, how likely do you think you are to develop breast cancer?

much more likely ☐ a bit more likely ☐ about the same ☐ a bit less likely ☐ much less likely ☐

[12] What would you say *your* chances are of developing ovarian cancer?

1 in 2 ☐ 1 in 4 ☐ 1 in 12 ☐ 1 in 25 ☐ 1 in 75 ☐ 1 in 125 ☐

[13] What proportion of breast cancers would you say are inherited?

0% ☐ 5% ☐ 25% ☐ 50% ☐ 100% ☐ don't know ☐

[14] What proportion of ovarian cancers would you say are inherited?

0% ☐ 5% ☐ 25% ☐ 50% ☐ 100% ☐ don't know ☐

[15] If a woman carries a gene which increases her risk of developing breast or ovarian cancer what do you think would be the chance of her passing this gene to her child?

less than 5% ☐ 25% ☐ 50% ☐ 75% ☐ 100% ☐ don't know ☐

[16] What do you think would be the chance of a father passing the gene to his child?

less than 5% ☐ 25% ☐ 50% ☐ 75% ☐ 100% ☐ don't know ☐

Section 3: Your feelings about breast and ovarian cancer

If you have had breast or ovarian cancer in the past, please answer the following questions in terms of your feelings about developing these cancers again. If you have not had breast or ovarian cancer, please answer the questions in terms of your feelings about developing these cancers at some time.

Firstly about breast cancer:

[1] During the past month, how often have you thought about your own chances of developing breast cancer?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

[2] During the past month, how often have thoughts about your chances of getting breast cancer affected your mood?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

[3] During the past month, have thoughts about your chances of getting breast cancer affected your ability to perform your daily activities?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

[4] How concerned are you about the possibility that you might get breast cancer someday?

not at all ☐ somewhat ☐ moderately ☐ very concerned ☐

[5] How often do you worry about developing breast cancer?

not at all ☐ occasionally ☐ frequently ☐ constantly ☐

[6] How much of a problem is worrying about breast cancer to you?

not at all ☐ somewhat ☐ definitely is ☐ severe problem ☐

Secondly, about ovarian cancer:

[7] During the past month, how often have you thought about your own chances of developing ovarian cancer?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

[8] During the past month, how often have thoughts about your chances of getting ovarian cancer affected your mood?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

[9] During the past month, have thoughts about your chances of getting ovarian cancer affected your ability to perform your daily activities?

not at all or rarely ☐ sometimes ☐ often ☐ almost all the time ☐

[10] How concerned are you about the possibility that you might get ovarian cancer someday?

not at all ☐ somewhat ☐ moderately ☐ very concerned ☐

[11] How often do you worry about developing ovarian cancer?

not at all ☐ occasionally ☐ frequently ☐ constantly ☐

[12] How much of a problem is worrying about ovarian cancer to you?

not at all ☐ somewhat ☐ definitely is ☐ severe problem ☐

Section 4: The genetic test

At the Family Cancer Clinic you may be offered the chance of having the genetic test to find out whether you have inherited a gene which increases your risk of developing breast, and possibly ovarian, cancer. If you have already had breast or ovarian cancer having the gene would increase your risk of developing these cancers again. We realise that your views may change as a result of talking it over with the genetic counsellor, but we are interested in your current thoughts about having this genetic test. There are no right or wrong answers.

[1] Please read each of the following statements and tick the box next to the one statement which best applies to you.

I've never thought about having the genetic test ☐
I'm undecided about having the genetic test ☐
I've decided I don't want to have the genetic test ☐
I've decided I do want to have the genetic test ☐

So we can get some idea of what people take into account when making their decision about having the genetic test, please respond to the statements on the following few pages by ticking a box or circling a number. You may not have given it much thought but please try to answer the questions as best you can.

[2] Please circle a number between 1 and 5 for each part of this question to indicate what you think about having the genetic test.

(a) For me, having the genetic test would be	wise	1	2	3	4	5	foolish
(b) For me, having the genetic test would be	desirable	1	2	3	4	5	undesirable
(c) For me, having the genetic test would be	easy	1	2	3	4	5	difficult
(d) For me, having the genetic test would be	good	1	2	3	4	5	bad

[3a] If I have the genetic test I will be certain about whether or not I am at high risk of developing breast or ovarian cancer (please tick a box).

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[b] For me, being certain about whether or not I am at high risk of developing breast or ovarian cancer would be (please circle a number):

good 1 2 3 4 5 bad

[4a] If I have the genetic test I will be certain about whether or not my children are likely to be at high risk of developing breast or ovarian cancer.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[b] For me, being certain about whether or not my children are likely to be at high risk of developing breast or ovarian cancer would be:

good 1 2 3 4 5 bad

[5a] If I have the genetic test I will have trouble getting life insurance or a mortgage.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[b] For me, having trouble getting life insurance or a mortgage would be:

good 1 2 3 4 5 bad

[6a] If I have the genetic test it will help me to decide about having surgery to prevent cancer.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[b] For me, being helped to decide about having surgery would be:

good 1 2 3 4 5 bad

[7a] If I have the genetic test it will make me aware of any problems with my breasts before cancer develops.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[b] For me, being aware of any problems with my breasts before cancer develops would be:

good 1 2 3 4 5 bad

[8a] If I have the genetic test it will mean I will be able to have regular breast screening.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[b] For me, being able to have regular breast screening would be:

good 1 2 3 4 5 bad

[9a] If I have the genetic test it will make me worry constantly about getting breast cancer.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[b] For me, worrying constantly about getting breast cancer would be:

good 1 2 3 4 5 bad

Thinking generally about what other people in your life may think about genetic testing and/or having the test, please respond to the following statements:

[10] Most people who are important to me would want me to have the genetic test.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[11] If a test was available for them, most of my relatives would have it.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[12] I intend to have the genetic test.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[13] Has anyone in your family already had the genetic test?

yes ☐ no ☐ don't know ☐

[14] Have any members of your family had genetic counselling about inherited breast or ovarian cancer?

yes ☐ no ☐ don't know ☐

[15] How likely is it that the specific people listed below would want you to have the genetic test? Please respond to each item by ticking a box (please tick not applicable - N/A - only if you do not have such a person in your life, or if they are deceased).

	strongly agree	agree	unsure	disagree	strongly disagree	N/A
(a) My husband/partner would want me to have the test	☐	☐	☐	☐	☐	☐
(b) My children would want me to have the test	☐	☐	☐	☐	☐	☐
(c) My mother would want me to have the test	☐	☐	☐	☐	☐	☐
(d) My father would want me to have the test	☐	☐	☐	☐	☐	☐
(e) My sister (s) would want me to have the test	☐	☐	☐	☐	☐	☐
(f) My brother (s) would want me to have the test	☐	☐	☐	☐	☐	☐

[b] Concerning the decision about whether or not to have the genetic test, how much do you want to do what the people listed below want you to?

	very much	a fair amount	a bit	not at all	N/A
(a) I want to do what my husband/partner thinks I should	☐	☐	☐	☐	☐
(b) I want to do what my children think I should	☐	☐	☐	☐	☐

	very much	a fair amount	a bit	not at all	N/A
(c) I want to do what my mother thinks I should	❑	❑	❑	❑	❑
(d) I want to do what my father thinks I should	❑	❑	❑	❑	❑
(e) I want to do what my sister (s) thinks I should	❑	❑	❑	❑	❑
(f) I want to do what my brother (s) thinks I should	❑	❑	❑	❑	❑

The following factors may influence whether or not you can have a genetic test. The genetic counsellor will explain, not everyone can be tested. Please respond to all the statements below by circling a letter or ticking a box.

[16] How much do the following things apply to you? (please circle a number between 1 and 5 for each part of this question)

	definitely applies to me				definitely does not apply to me
(a) Not being able to find out who in my family has had cancer	1	2	3	4	5
(b) Not having a strong family history of breast or ovarian cancer	1	2	3	4	5
(c) Having no living relatives who have had breast or ovarian cancer	1	2	3	4	5
(d) Having no living relatives who have had breast or ovarian cancer who would be willing to be tested	1	2	3	4	5
(e) Having no living relatives who have had breast or ovarian cancer who are likely to be carrying the gene	1	2	3	4	5

[17] How likely is it that the following things would stop you from having the genetic test if you wanted to have it? (please circle a number between 1 and 5 for each part of this question):

	extremely likely to stop me				extremely unlikely to stop me
(a) Not being able to find out who in my family has had cancer	1	2	3	4	5
(b) Not having a strong family history of breast or ovarian cancer	1	2	3	4	5
(c) Having no living relatives who have had breast or ovarian cancer	1	2	3	4	5
(d) Having no living relatives who have had breast or ovarian cancer who would be willing to be tested	1	2	3	4	5
(e) Having no living relatives who have had breast or ovarian cancer who are likely to be carrying the gene	1	2	3	4	5

[18] How far do you agree with these two statements? (please tick a box)

(a) I would like to have the genetic test but I don't really know if I can.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

(b) Whether or not I have the genetic test is entirely up to me.

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

[19] In general, how difficult do you think it would be for you to have the genetic test?

extremely difficult ☐ fairly difficult ☐ not very difficult ☐ not at all difficult ☐

[20] How much control do you feel you have over whether or not you have the genetic test?

complete control ☐ a lot of control ☐ some control ☐ no control ☐

The next four questions ask you to think about how you might feel under various circumstances. Please tick the box for each part of each question which best describes how you might feel.

[21] How might you feel if you *decided not to have* the genetic test? (please respond to each part of this question)

I would feel:	not at all	a bit	fairly	extremely
(a) guilty	☐	☐	☐	☐
(b) relieved	☐	☐	☐	☐
(c) depressed	☐	☐	☐	☐
(d) worried	☐	☐	☐	☐
(e) regretful	☐	☐	☐	☐

[22] How might you feel if you *were told that you could not have* the genetic test? (please respond to each part of this question)

I would feel:	not at all	a bit	fairly	extremely
(a) guilty	☐	☐	☐	☐
(b) relieved	☐	☐	☐	☐
(c) depressed	☐	☐	☐	☐
(d) worried	☐	☐	☐	☐
(e) surprised	☐	☐	☐	☐
(f) regretful	☐	☐	☐	☐
(g) that it was hard to believe	☐	☐	☐	☐
(h) angry	☐	☐	☐	☐

[23] How might you feel if you had the genetic test and *the result showed that you were at high risk of developing breast or ovarian cancer?* (please respond to each part of this question)

I would feel:	not at all	a bit	fairly	extremely
(a) guilty	☐	☐	☐	☐
(b) relieved	☐	☐	☐	☐
(c) depressed	☐	☐	☐	☐
(d) worried	☐	☐	☐	☐
(e) surprised	☐	☐	☐	☐
(f) regretful	☐	☐	☐	☐
(g) that it was hard to believe	☐	☐	☐	☐
(h) angry	☐	☐	☐	☐

[24] How might you feel if you had the genetic test and *the result showed that your risk of developing breast or ovarian cancer was no higher than the general population*? (please respond to each part of this question)

I would feel:	not at all	a bit	fairly	extremely
(a) guilty	☐	☐	☐	☐
(b) relieved	☐	☐	☐	☐
(c) depressed	☐	☐	☐	☐
(d) worried	☐	☐	☐	☐
(e) surprised	☐	☐	☐	☐
(f) regretful	☐	☐	☐	☐
(g) that it was hard to believe	☐	☐	☐	☐
(h) angry	☐	☐	☐	☐

[25] How likely do you think it is that you carry the gene which increases your risk of developing breast or ovarian cancer?

extremely likely ☐ fairly likely ☐ unsure ☐ fairly unlikely ☐ extremely unlikely ☐

[26] How likely do you think you are to be offered the genetic test?

extremely likely ☐ fairly likely ☐ unsure ☐ fairly unlikely ☐ extremely unlikely ☐

[27] Would you have the genetic test, if you were offered it?

yes, definitely ☐ yes, probably ☐ unsure ☐ no, probably not ☐ no, definitely not ☐

[13] Worrying thoughts go through my mind

a great deal of the time ☐ a lot of the time ☐ from time to time but not too often ☐ only occasionally ☐

[14] I feel cheerful

not at all ☐ not often ☐ sometimes ☐ most of the time ☐

[15] I can sit at ease and feel relaxed

definitely ☐ usually ☐ not often ☐ not at all ☐

[16] I feel as if I am slowed down

nearly all the time ☐ very often ☐ sometimes ☐ not at all ☐

[17] I get a sort of frightened feeling like 'butterflies' in my stomach

not at all ☐ occasionally ☐ quite often ☐ very often ☐

[18] I have lost interest in my appearance

definitely ☐ I don't take so much care as I should ☐ I may not take quite as much care ☐ I take just as much care as ever ☐

[19] I feel restless as if I have to be on the move

very much indeed ☐ quite a lot ☐ not very much ☐ not at all ☐

[20] I look forward with enjoyment to things

as much as I ever did ☐ rather less than I used to ☐ definitely less than I used to ☐ hardly at all ☐

[21] I get sudden feelings of panic

very often indeed ☐ quite often ☐ not very often ☐ not at all ☐

[22] I can enjoy a good book or radio or TV programme

often ☐ sometimes ☐ not often ☐ very seldom ☐

We would like to know if you have had any medical complaints, and how your health has been in general over the past few weeks. Please tick the box next to the answer which you think most nearly applies to you.

HAVE YOU RECENTLY:

[23] Been able to concentrate on whatever you're doing?

better than usual ☐ same as usual ☐ less than usual ☐ much less than usual ☐

[24] Lost much sleep over worry?

not at all ☐ no more than usual ☐ rather more than usual ☐ much more than usual ☐

[25] Felt that you are playing a useful part in things?

more so than usual ☐ same as usual ☐ less useful than usual ☐ much less useful ☐

[26] Felt capable of making decisions about things?

more so than usual ☐ same as usual ☐ less capable than usual ☐ much less capable ☐

[27] Felt constantly under strain?

not at all ☐ no more than usual ☐ rather more than usual ☐ much more than usual ☐

[28] Felt you couldn't overcome difficulties?

not at all ☐ no more than usual ☐ rather more than usual ☐ much more than usual ☐

[29] Been able to enjoy your normal day to day activities?

more so than usual ☐ same as usual ☐ less so than usual ☐ much less than usual ☐

[30] Been able to face up to your problems?

more so than usual ☐ same as usual ☐ less able than usual ☐ much less able ☐

[31] Been feeling unhappy and depressed?

not at all ☐ no more than usual ☐ rather more than usual ☐ much more than usual ☐

[32] Been losing confidence in yourself?

not at all ☐ no more than usual ☐ rather more than usual ☐ much more than usual ☐

[33] Been thinking of yourself as a worthless person?

not at all ☐ no more than usual ☐ rather more than usual ☐ much more than usual ☐

[34] Been feeling reasonably happy, all things considered?

more so than usual ☐ about the same as usual ☐ less so than usual ☐ much less than usual ☐

Thank you very much for taking the time to complete this questionnaire

Please return it in the FREEPOST envelope as soon as possible to:

Alison Bish
UMDS/Guy's Hospital
Paediatric Research Unit
FREEPOST LON7797
LONDON
SE1 9BR

QUESTIONNAIRE FOR GENERAL PRACTICE SAMPLE CONCERNING PERCEPTIONS OF GENETIC TESING FOR COLON CANCER

Study of Attitudes about Genetic Testing for Inherited Bowel Cancer Predisposition

University College London
Health Behaviour Unit
Department of Epidemiology and Public Health
Brook House
2-16 Torrington Place
London WC1E 6BT

PARTICIPANTS' QUESTIONNAIRE

Code.....

INSTRUCTIONS FOR FILLING OUT SURVEY

This survey asks about your views about hereditary cancer and genetic testing. The aim of the study is to look at the attitudes and beliefs of the general public in regard to these issues.

We very much hope you will take part.

All the information you provide will be treated in the **strictest confidence.** No completed questionnaires will be passed to your General Practitioner and no individuals will be identified in any subsequent presentations or reports.

We would be grateful if you could return the completed questionnaire in the enclosed envelope by **20th December.**

Please answer the questions by ticking an appropriate box, by circling the appropriate number, or by writing in the answer as requested.

Example:

In my view, having the genetic test would be.....
(please circle one number)

wise ① 2 3 4 5 foolish

Some questions may look similar but each one is different Please answer every question as honestly as possible If you are unsure about how to answer a question, please guess your answer.

Although the questionnaire may, at first glance, look quite long, completing it should only take around 10-15 minutes of your time.

Thank you for your help.

SECTION 1 – ABOUT YOUR HEALTH

Q1.1 **Would you say that for someone of your age, your health in general in the past six months has been:**

Excellent ☐ Good ☐ Fair ☐ Poor ☐

SECTION 2 – YOUR FAMILY HISTORY OF CANCER

Q2.1 **Have any members of your family (blood relatives, not relatives by marriage) ever been diagnosed with cancer?**

	Yes	No	Don't know	If yes, please state age when diagnosed and type of cancer
Mother	☐	☐	☐	.....
Father	☐	☐	☐	.....
Mother's mother	☐	☐	☐	.....
Mother's father	☐	☐	☐	.....
Father's mother	☐	☐	☐	.....
Father's father	☐	☐	☐	.....

	Yes	No	Don't know	Not applicable	
Son(s)	☐	☐	☐	☐	.....
Daughter(s)	☐	☐	☐	☐	.....
Sister(s)	☐	☐	☐	☐	.....
Brother(s)	☐	☐	☐	☐	.....

Q2.2 **Have you ever been diagnosed with cancer?**

Yes ☐ No ☐

If yes, which type of cancer have you been diagnosed with?
(Please write in.)

.....

Q2.3 **Have you ever known anyone personally who has had bowel cancer?**

Yes ☐ No ☐

SECTION 4 – ABOUT YOUR INTEREST IN TESTING

A blood test identifying certain individuals as having a gene associated with a high risk of developing bowel cancer in their lifetime is currently available.

Q4.1 **Now vividly imagine that you are offered a genetic test for bowel cancer susceptibility at some point in the future. Would you choose to have the test?**

Yes, definitely ☐ Yes, probably ☐ Unsure ☐
No, probably not ☐ No, definitely not ☐

Please write down three reasons relevant to your decision whether to be tested.

Q4.2 Reasons *for* having a test:

1. .....
2. .....
3. .....

Q4.3 Reasons *against* having a test:

1 .....
2. .....
3. .....

SECTION 5 – YOUR VIEWS REGARDING GENETIC TESTING FOR BOWEL CANCER SUSCEPTIBILITY

Q5.1 **For me, having the genetic test would be:**
(Please circle one number for each part of the question.)

Wise	1	2	3	4	5	Foolish
Desirable	1	2	3	4	5	Undesirable
Beneficial	1	2	3	4	5	Harmful
Easy	1	2	3	4	5	Difficult
Good	1	2	3	4	5	Bad

Please indicate how much you agree or disagree with the following statements.

Q5.2 **If I had the genetic test, I would be certain about whether or not I am at high risk of developing bowel cancer.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.3 **If I had the genetic test, this would allow me to make childbearing decisions.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.4 **If I had the genetic test, I might upset members of my family.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.5 **If I had the genetic test, I would have trouble getting life insurance or a mortgage.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.6 **If I had the genetic test (which involves giving a blood sample), I would be afraid.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.7 **If I had the genetic test, I might be discriminated against at work.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.8 **If I had the genetic test, I would be certain about whether or not my children are likely to be at high risk of developing bowel cancer.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐
not applicable ☐

Q5.9 **If I had the genetic test, this would allow me to have more regular screening.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.10 **If I had the genetic test, this would motivate me to have a healthier lifestyle.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.11 **If I had the genetic test, this would help me decide about having surgery to prevent bowel cancer.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.12 **If I had the genetic test, it would make me worry constantly about getting bowel cancer.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Thinking now about what other people in your life may think about genetic testing and you having a test, please tick the box which most closely describes how much you agree with the following statements.

Q5.13 **Most people who are important to me would want me to have the genetic test.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.14 **My partner would want me to have the genetic test.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐
not applicable ☐

Q5.15 **Most of my family would want me to have the genetic test.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.16 **Most of my friends would want me to have the genetic test.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.17 **If a test were available for them, most of my relatives would have it.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.18 **Whether or not I had the genetic test would be entirely up to me.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q5.19 **In general, how difficult do you think would be for you to have the genetic test?**

extremely difficult ☐ fairly difficult ☐ unsure ☐ not very difficult ☐
not at all difficult ☐

Q5.20 **How much control do you feel you have over whether or not you have the genetic test?**

complete control ☐ a lot of control ☐ some control ☐ no control ☐

Q5.21 **How likely do you think it is that you carry a gene which increases your chances of developing bowel cancer?**

extremely likely ☐ fairly likely ☐ unsure ☐ fairly unlikely ☐
extremely unlikely ☐

Q5.22 **Would you be interested in having a genetic test for any other type of cancer?**

Yes ☐ No ☐

If yes, please specify which type of cancer and please give a reason why you would wish to be tested?
(Please write in.)

.....

.....

SECTION 7 – ABOUT YOUR VIEWS CONCERNING MEDICAL TESTS IN GENERAL

Q7.1 **I would rather have a medical test, and be certain about my future health, even If the result is bad news.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q7.2 **I would like to know now if I am likely to be ill so I can get used to the news.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q7.3 **If I didn't have a medical test I would always be wondering whether I was going to develop the disease.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q7.4 **The relief I would get from a good result makes it worth the risk that the result is bad.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q7.5 **I think it is tempting fate to ask questions about future illness.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q7.6 **I would rather live with uncertainty, than find out I was going to develop the disease.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q7.7 **Knowing the result of a medical test would mean I felt more in control.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

Q7.8 **It is better to know that I will develop a disease, even if I can't prevent it.**

strongly agree ☐ agree ☐ unsure ☐ disagree ☐ strongly disagree ☐

SECTION 8 – YOUR VIEWS AND FEELINGS ABOUT INHERITED BOWEL CANCER

Q8.1 **Compared to other men of your age, do you think your chances of developing inherited bowel cancer at some time in your life are:**

much lower ☐ lower ☐ about the same ☐ higher ☐ much higher ☐

Q8.2 **Do you think bowel cancer runs in your family?**

Yes ☐ No ☐

Q8.3 **Do you feel you may be at increased risk of developing any other inherited cancer(s)?**

Yes ☐ No ☐

If yes, please specify which type of cancer you feel you may be at risk from And give a reason.
(Please write in.)

.....

.....

Q8.4 **If you had to put a figure on it, what would you say are the chances of a man in this country developing inherited bowel cancer at some time in his life?**
(If you are unsure, please guess an answer.)

I think the chances of a man in this country developing inherited bowel cancer are 1 chance in _____.

Q8.5 **If you had to put a figure on it, what would you say are your chances of developing inherited bowel cancer at some time in your life?**
(If you are unsure, please guess an answer.)

I think my chances are about 1 chance in _____.

SECTION 9 – ABOUT YOURSELF

Q9.1 **Are you....**

Male ☐ Female ☐

Q9.2 **What is your age?**
(Please write in your age.)

.....

Q9.3 **How would you describe your marital status?**

Married	☐
Divorced	☐
Widowed	☐
Single	☐
Living with partner	☐

Q9.4 **Do you have any children?**

Yes ☐ No ☐

Q9 5 **Which of the following best describes your ethnic background?**

Black-African	☐
Black-other	☐
Irish	☐
White British	☐
White-other	☐
Indian	☐
Pakistani	☐
Asian-other	☐
Other	☐

.....

Q9 6 **What is your highest educational qualification** (e.g. GCSE, A level, degree)?
(Please write in.)

.....

Q9.7 **Do you have a paid job or do any paid work?**

No, retired	☐
No, not working at present	☐
Yes, part time	☐
Yes, full time	☐

Q9.8 **Does your household have a car?**

No	☐
Yes, one	☐
Yes, more than one	☐

Q9.9 **Do you own or rent your home?**

Own it / buying it	☐
Rent it	☐
Other	☐

Q9.10 **Thank you for completing all our questions. It may be that we would re-contact you to help in another aspect of this research programme. Would you be willing for us to approach you again?**

Yes, willing	☐→	please write in telephone number
No, would rather not be approached	☐→	skip to the end

Your telephone number:.....

THANK YOU FOR COMPLETING THE QUESTIONNAIRE.

PLEASE RETURN IT IN THE STAMPED ENVELOPE PROVIDED.

APPENDIX B

Additional Analyses

From Chapter 4

From Chapter 5

From Chapter 10

Chapter 4 - Intercorrelations between variables, asymptomatic people at high risk of colon cancer n=357

			Intent	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
2	Attitude	r	0.646																
		p	0.001																
3	Subjective Norm	r	0.604	0.535															
		p	0.001	0.001															
4	Perceived Behavioural Control	r	0.089	0.067	0.131														
		p	0.092	0.210	0.013														
5	Anticipated Negative Affect if decided not to have test	r	0.360	0.373	0.406	0.044													
		p	0.001	0.001	0.001	0.408													
6	Anticipated Negative Affect if positive result	r	-0.313	-0.287	-0.300	-0.146	-0.054												
		p	0.001	0.001	0.001	0.006	0.308												
7	Anticipated Negative Affect if negative result	r	-0.055	-0.070	0.008	-0.065	0.110	0.163											
		p	0.300	0.189	0.881	0.217	0.037	0.002											
8	Anticipated Positive Affect if negative result	r	0.142	0.140	0.141	0.007	0.323	0.150	-0.032										
		p	0.007	0.008	0.008	0.898	0.001	0.004	0.542										
9	Perceived Benefits	r	0.310	0.261	0.338	0.152	0.335	-0.033	0.068	0.238									
		p	0.001	0.001	0.001	0.004	0.001	0.531	0.202	0.001									
10	Perceived Barriers	r	-0.471	-0.367	-.485	-0.220	-0.112	0.436	0.070	0.104	0.012								
		p	0.001	0.001	0.001	0.001	0.034	0.001	0.185	0.050	0.823								
11	Perceived Susceptibility	r	0.159	0.210	0.176	0.046	0.266	-0.207	0.118	0.356	0.124	-0.042							
		p	0.003	0.001	0.001	0.391	0.001	0.001	0.026	0.001	0.019	0.426							
12	Perceived Severity	r	-0.010	0.024	0.080	0.064	0.149	0.188	0.094	0.217	0.116	0.038	0.086						
		p	0.854	0.653	0.133	0.228	0.005	0.001	0.075	0.001	0.028	0.469	0.104						
13	Uncertainty	r	0.548	0.444	0.453	0.131	0.362	-0.249	-0.052	0.068	0.308	-0.299	0.102	0.027					
		p	0.001	0.001	0.001	0.013	0.001	0.001	0.324	0.203	0.001	0.001	0.055	0.614					
14	Worry	r	0.052	0.090	0.145	-0.008	0.330	0.154	0.379	0.307	0.217	0.152	0.347	0.302	0.122				
		p	0.327	0.091	0.006	0.879	0.001	0.004	0.001	0.001	0.001	0.004	0.001	0.001	0.021				
15	Anticipated Reassurance GT compared with FOB	r	-0.231	-0.276	-0.145	0.058	-0.096	0.091	-0.077	-0.103	-0.162	0.020	-0.125	-0.064	-0.183	-0.154			
		p	0.001	0.001	0.006	0.277	0.071	0.087	0.149	0.051	0.002	0.700	0.018	0.231	0.001	-0.154			
16	Anticipated Reassurance GT compared with colonoscopy	r	-0.164	-0.204	-0.167	0.027	-0.092	0.051	0.034	0.058	-0.160	0.030	0.017	0.014	-0.181	-0.056	0.512		
		p	0.002	0.001	0.002	0.613	0.082	0.338	0.524	0.272	0.002	0.577	0.753	0.799	0.001	0.294	0.001		
17	Anxiety	r	-0.086	-0.061	-0.081	-0.031	0.122	0.254	0.222	0.125	-0.003	0.182	0.089	0.099	-0.059	0.418	0.025	0.067	
		p	0.105	0.253	0.129	0.564	0.021	0.001	0.001	0.018	0.951	0.001	0.093	0.062	0.267	0.001	0.642	0.205	
18	Depression	r	-0.008	-0.044	-0.088	0.013	0.076	0.150	0.246	0.033	0.035	0.093	0.048	0.162	-0.037	0.297	-0.005	0.025	0.659
		p	0.880	0.406	0.099	0.800	0.156	0.005	0.001	0.536	0.515	0.079	0.371	0.002	0.486	0.001	0.925	0.642	0.001

p<= 0.001; p<=0.05

Chapter 5 - Intercorrelations between anticipated affect individual items WOMEN n=247

	11	12	13	14	15	16	21	22	23	24	25	26	27	28	31	32	33	34	35	36	37	38
12	-0.162																					
13	0.442	-0.38																				
14	0.460	-0.77	0.556																			
15	0.523	-0.194	0.473	0.634																		
16	0.516	-0.129	0.424	0.57	0.693																	
21	0.14	0.192	0.13	0.132	0.07	0.054																
22	0.302	-0.102	0.347	0.292	0.247	0.132	-0.021															
23	-0.053	0.312	0.135	0.179	-0.02	0.133	0.301	-0.113														
24	-0.018	0.257	0.072	0.144	-0.012	0.112	0.202	-0.103	0.692													
25	0.056	0.151	-0.09	-0.025	-0.018	-0.06	0.212	-0.014	0.247	0.321												
26	-0.04	0.214	-0.153	-0.068	-0.032	-0.078	0.228	-0.205	0.376	0.287	0.196											
27	-0.015	0.247	-0.06	0.069	0.034	0.085	0.246	-0.073	0.370	0.361	0.539	0.351										
28	0.005	0.262	0.086	0.213	0.028	0.115	0.277	-0.042	0.509	0.426	0.291	0.320	0.507									
31	0.097	0.169	0.052	0.013	0.068	0.064	0.246	-0.044	0.096	0.132	0.059	0.119	0.110	0.122								
32	0.039	0.119	0.007	0.07	0.085	0.161	0.022	0.058	0.195	0.171	0.056	0.005	0.056	0.168	-.0010							
33	0.073	0.054	0.076	0.05	0.005	0.119	0.096	0.042	0.171	0.198	0.063	0.081	0.134	0.161	0.087	-0.214						
34	0.022	0.145	0.136	0.142	0.062	0.085	0.179	-0.015	0.141	0.204	-0.067	0.151	0.036	0.197	0.234	-0.191	0.249					
35	0.123	-0.051	0.228	0.232	0.157	0.265	0.040	0.018	0.091	0.059	-0.194	-0.025	-0.195	0.053	-0.009	0.163	0.105	0.085				
36	0.14	0.034	0.069	-0.021	0.132	0.097	0.046	0.109	-0.036	0.037	0.009	0.076	0.067	0.026	0.164	-0.178	0.277	0.356	0.035			
37	0.208	-0.052	0.286	0.242	0.125	0.275	0.182	-0.049	0.128	0.081	-0.064	0.027	0.003	0.036	0.034	-0.044	0.206	0.189	0.540	0.106		
38	0.166	-0.015	0.131	0.022	0.1	0.15	0.076	0.120	0.003	0.061	0.078	-0.038	.0781	.0902	0.194	-0.149	0.449	0.336	0.143	0.742	0.154	
39	0.069	-0.01	0.016	0.075	0.113	0.116	-0.030	0.060	0.125	0.108	0.046	-0.032	.0425	.0514	-0.194	0.527	-0.147	-0.250	0.213	-0.204	0.065	-0.088

KEY

Anticipated affect if not tested
11 guilty
12 relieved
13 depressed
14 worried
15 regretful
16 forever wondering

Anticipated affect if tested positive
21 guilty
22 relieved
23 depressed
24 worried
25 surprised
26 regretful
27 hard to believe
28 angry

Anticipated affect if tested negative
31 guilty
32 relieved
33 depressed
34 worried
35 surprised
36 regretful
37 hard to believe
38 angry
39 happy

Chapter 5 - Intercorrelations between anticipated affect individual items MEN n=110

	11	12	13	14	15	16	21	22	23	24	25	26	27	28	31	32	33	34	35	36	37	38
12	-0.129																					
13	0.566	-0.177																				
14	0.554	-0.060	0.693																			
15	0.642	-0.197	0.476	0.518																		
16	0.545	-0.169	0.490	0.609	0.616																	
21	0.096	0.177	0.088	0.043	0.040	0.173																
22	0.061	0.138	0.073	0.054	0.050	-0.161	-0.089															
23	0.040	0.175	0.142	0.140	-0.048	0.176	0.100	-0.226														
24	-0.043	0.167	0.064	0.162	0.015	0.183	0.107	-0.079	0.666													
25	-0.052	0.210	0.023	-0.064	-0.153	-0.070	0.158	0.107	0.162	0.177												
26	-0.054	0.230	-0.087	-0.046	0.031	0.008	0.147	-0.163	0.531	0.392	0.112											
27	-0.072	0.350	-0.016	-0.070	-0.022	0.060	0.224	-0.016	0.359	0.337	0.580	0.387										
28	0.058	0.143	-0.014	0.084	0.121	0.287	0.186	-0.222	0.485	0.318	0.169	0.324	0.323									
31	-0.024	-0.077	0.092	-0.002	0.059	0.087	-0.049	0.040	0.121	0.041	0.019	-0.014	0.158	0.046								
32	0.266	-0.042	0.229	0.349	0.337	0.463	-0.051	0.004	0.385	0.356	0.025	0.240	0.083	0.205	0.149							
33	-0.014	0.115	0.056	-0.001	-0.035	-0.062	0.176	0.024	-0.013	-0.070	0.012	0.018	0.041	0.057	-0.015	-0.273						
34	0.039	0.005	0.146	0.146	0.071	0.039	-0.031	0.049	0.110	0.061	-0.039	0.026	0.023	-0.042	0.087	-0.022	0.303					
35	0.226	-0.063	0.242	0.311	0.213	0.324	0.037	0.031	0.174	0.230	-0.253	0.167	-0.121	0.047	-0.026	0.334	-0.016	0.055				
36	-0.059	0.122	-0.004	-0.002	0.059	0.012	0.036	-0.036	0.027	0.041	-0.077	0.117	0.021	-0.002	0.317	-0.001	0.400	0.361	0.063			
37	0.223	0.108	0.168	0.221	0.083	0.288	0.119	0.025	0.173	0.186	-0.102	0.169	-0.013	0.011	-0.090	0.209	-0.085	0.080	0.601	0.060		
38	-0.014	0.115	0.056	-0.001	-0.035	-0.062	0.176	0.024	-0.013	-0.070	0.012	0.018	0.041	0.057	-0.015	-0.273	1.000	0.303	-0.016	0.400	-0.085	
39	0.232	-0.048	0.200	0.282	0.293	0.417	0.094	-0.050	0.402	0.336	0.023	0.258	0.082	0.302	0.085	0.625	-0.283	-0.131	0.307	-0.016	0.274	-0.283

KEY

Anticipated affect if not tested
11 guilty
12 relieved
13 depressed
14 worried
15 regretful
16 forever wondering

Anticipated affect if tested positive
21 guilty
22 relieved
23 depressed
24 worried
25 surprised
26 regretful
27 hard to believe
28 angry

Anticipated affect if tested negative
31 guilty
32 relieved
33 depressed
34 worried
35 surprised
36 regretful
37 hard to believe
38 angry
39 happy

Chapter 10

Preliminary analysis of data to determine grouping of breast cancer participants.

A multivariate analysis of variance compared those women for whom genetic testing was their main reason for wanting the appointment with the rest of the women in the breast cancer sample on a number of key variables. The key variables explored were intent, attitude towards genetic testing, subjective norm, perceived behavioural control, perceived likelihood of carrying a gene and cancer worry (table below). These variables were selected for their relevance to the theoretical basis of the study, and because these were hypothesed to be the variables most likely to vary. Women who have already decided that they would like to find out more about genetic testing are likely to hold more favourable views of genetic testing and may also be more concerned about their risk of developing cancer. The analysis showed that there were significant differences between the two groups of women on four of the six variables examined. On this basis it was decided that the subsequent analyses should divide these women into two groups. The subsequent analyses therefore compared women at risk of colon cancer (group 1), with women at risk of breast cancer who did not report that their main reason for wanting counselling was for a test (group2), and with women for whom their main reason for counselling was to have a genetic test (group3).

Comparison of women at risk of breast cancer on primary reason for wanting genetic counselling.

	Genetic testing is primary reason for counselling N= 64		Genetic testing is not primary reason for counselling N = 224			
Variable	Mean	SD	Mean	SD	F (1,286)	Sig^{n}. of F
Intent	4.86	0.39	4.29	0.85	27.33	0.001
Attitude	4.6	0.67	4.24	0.88	9.17	0.003
Subjective norm	4.23	0.60	3.88	0.76	11.21	0.001
Perceived Behavioural Control	2.99	0.69	3.04	0.70	0.24	0.63
Cancer Worry	12.72	3.93	12.46	3.29	0.29	0.59
Likely to carry gene	3.95	0.81	3.69	0.81	5.2	0.023

Intercorrelations between variables, asymptomatic women at high risk of colon cancer

	Intent		Intent	2	3	4	5	6	7	8	9	10	11	12
2	Attitude	r	0.665											
		p	0.001											
		n	320											
3	Subjective Norm	r	0.612	0.555										
		p	0.001	0.001										
		n	338	320										
4	Perceived Behavioural Control	r	0.167	0.169	0.220									
		p	0.002	0.002	0.001									
		n	337	318	336									
5	Anticipated Negative Affect if decided not to have test	r	0.383	0.379	0.426	0.156								
		p	0.001	0.001	0.001	0.005								
		n	329	313	329	328								
6	Anticipated Negative Affect if positive result	r	-0.339	-0.328	-0.319	-0.145	-0.140							
		p	0.001	0.001	0.001	0.009	0.012							
		n	327	312	327	325	323							
7	Anticipated Negative Affect if negative result	r	-0.065	-0.070	-0.006	0.002	0.097	0.178						
		p	0.239	0.219	0.920	0.976	0.083	0.001						
		n	326	310	326	324	321	322						
8	Anticipated Positive Affect if negative result	r	0.104	0.142	0.102	-0.084	0.218	0.088	0.058					
		p	0.060	0.012	0.064	0.131	0.001	0.115	0.297					
		n	328	312	327	326	321	322	323					
9	Worry	r	0.062	0.073	0.169	-0.057	0.326	0.112	0.324	0.289				
		p	0.260	0.190	0.002	0.300	0.001	0.043	0.001	0.001				
		n	337	320	337	335	328	326	325	326				
10	Likely to carry gene	r	0.247	0.278	0.234	0.041	0.268	-.0191	0.099	0.361	0.265			
		p	0.001	0.001	0.001	0.453	0.001	0.001	0.074	0.001	0.001			
		n	339	321	339	337	330	328	327	328	338			
11	Likely to be offered test	r	0.202	0.273	0.199	0.135	0.149	-.0098	-0.048	0.228	0.065	0.292		
		p	0.001	0.001	0.001	0.013	0.007	.0075	0.391	0.001	0.236	0.001		
		n	339	321	339	337	330	328	327	328	338	340		
12	Anxiety	r	-0.027	-0.072	0.015	0.056	0.134	.0228	0.217	0.113	0.468	0.146	-0.034	
		p	0.621	0.202	0.792	0.311	0.016	0.001	0.001	0.042	0.001	0.008	0.536	
		n	334	316	333	332	325	322	321	323	332	334	334	
13	Depression	r	0.002	-0.046	-0.037	0.016	0.070	0.159	0.208	0.031	0.303	0.159	-0.086	0.648
		p	0.973	0.413	0.505	0.769	0.211	0.004	0.001	0.578	0.001	0.003	0.116	0.001
		n	334	317	334	332	325	323	322	323	333	335	335	331

p<= 0.001; p<=0.05

Intercorrelations between variables, all asymptomatic women at high risk of breast/ ovarian cancer

	Intent		Intent	2	3	4	5	6	7	8	9	10	11	12
2	Attitude	r	0.723											
		p	0.001											
		n	366											
3	Subjective Norm	r	0.622	0.560										
		p	0.001	0.001										
		n	398	365										
4	Perceived Behavioural Control	r	0.065	0.115	0.209									
		p	0.196	0.029	0.001									
		n	394	363	393									
5	Anticipated Negative Affect if decided not to have test	r	0.390	0.371	0.420	0.002								
		p	0.001	0.001	0.001	0.971								
		n	379	355	379	376								
6	Anticipated Negative Affect if positive result	r	-0.297	-0.292	-0.099	-0.006	0.028							
		p	0.001	0.001	0.059	0.912	0.599							
		n	367	344	366	365	363							
7	Anticipated Negative Affect if negative result	r	-0.019	-0.060	0.022	-0.048	0.152	0.215						
		p	0.722	0.263	0.668	0.363	0.004	0.001						
		n	370	346	369	368	364	356						
8	Anticipated Positive Affect if negative result	r	0.093	0.080	0.153	-0.125	0.252	0.085	-0.049					
		p	0.069	0.134	0.003	0.015	0.001	0.106	0.344					
		n	381	355	380	378	375	365	369					
9	Worry	r	0.090	0.100	0.152	-0.053	0.381	0.120	0.213	0.268				
		p	0.072	0.056	0.002	0.296	0.001	0.022	0.001	0.001				
		n	397	365	396	392	378	366	369	380				
10	Likely to carry gene	r	0.193	0.182	0.215	-0.086	0.300	-0.156	0.045	0.335	0.211			
		p	0.001	0.001	0.001	0.087	0.001	0.003	0.388	0.001	0.001			
		n	399	367	398	394	381	369	372	383	398			
11	Likely to be offered test	r	0.295	0.263	0.301	0.243	0.226	-0.103	-0.038	0.105	0.068	0.388		
		p	0.001	0.001	0.001	0.001	0.001	0.048	0.461	0.040	0.175	0.001		
		n	399	367	398	395	381	369	372	383	398	400		
12	Anxiety	r	-0.024	-0.010	0.073	-0.094	0.293	0.258	0.190	0.118	0.509	0.168	-0.035	
		p	0.628	0.853	0.146	0.062	0.001	0.001	0.001	0.021	0.001	0.001	0.491	
		n	395	364	394	391	376	365	367	379	393	395	395	
13	Depression	r	0.061	0.039	0.107	-0.008	0.304	0.128	0.228	0.162	0.404	0.116	0.012	0.669
		p	0.229	0.456	0.033	0.879	0.001	0.015	0.001	0.002	0.001	0.021	0.811	0.001
		n	396	364	395	391	377	366	368	380	394	396	396	396

p<= 0.001; p<=0.05

Intercorrelations between variables, women at high risk of breast/ ovarian cancer – genetic testing not primary reason for counselling

	Intent		Intent	2	3	4	5	6	7	8	9	10	11	12
2	Attitude	r	0.737											
		p	0.001											
		n	281											
3	Subjective Norm	r	0.635	0.606										
		p	0.001	0.001										
		n	304	280										
4	Perceived Behavioural Control	r	0.038	0.113	0.206									
		p	0.513	0.058	0.001									
		n	302	280	301									
5	Anticipated Negative Affect if decided not to have test	r	0.403	0.389	0.460	0.026								
		p	0.001	0.001	0.001	0.655								
		n	291	274	291	289								
6	Anticipated Negative Affect if positive result	r	-0.305	-0.318	-0.125	-0.014	0.046							
		p	0.001	0.001	0.035	0.818	0.443							
		n	286	270	285	284	283							
7	Anticipated Negative Affect if negative result	r	-0.053	-0.086	0.029	-0.029	0.070	0.224						
		p	0.368	0.161	0.630	0.629	0.244	0.001						
		n	285	269	284	283	281	277						
8	Anticipated Positive Affect if negative result	r	0.070	0.088	0.174	-0.094	0.311	0.148	-0.070					
		p	0.229	0.143	0.003	0.110	0.001	0.012	0.241					
		n	293	275	292	291	289	284	285					
9	Worry	r	0.073	0.066	0.154	-0.091	0.324	0.141	0.168	0.323				
		p	0.204	0.271	0.007	0.114	0.001	0.017	0.005	0.001				
		n	304	281	303	301	291	286	285	293				
10	Likely to carry gene	r	0.155	0.174	0.180	-0.082	0.339	-0.146	0.088	0.385	0.230			
		p	0.007	0.003	0.002	0.153	0.001	0.013	0.137	0.001	0.001			
		n	305	282	304	302	293	288	287	295	305			
11	Likely to be offered test	r	0.260	0.268	0.291	0.234	0.263	-0.122	-0.012	0.145	0.082	0.381		
		p	0.001	0.001	0.001	0.001	0.001	0.038	0.845	0.012	0.151	0.001		
		n	306	283	305	303	293	288	287	295	306	307		
12	Anxiety	r	0.013	0.015	0.095	-0.105	0.307	0.236	0.141	0.168	0.514	0.169	-0.019	
		p	0.817	0.806	0.101	0.069	0.001	0.001	0.017	0.004	0.001	0.003	0.738	
		n	303	281	302	301	290	285	284	293	302	303	304	
13	Depression	r	0.065	0.040	0.124	0.001	0.294	0.122	0.150	0.195	0.407	0.118	0.017	0.672
		p	0.259	0.503	0.031	0.997	0.001	0.038	0.011	0.001	0.001	0.040	0.766	0.001
		n	304	281	303	301	291	286	285	294	303	304	305	304

p<= 0.001; p<=0.05

Intercorrelations between variables, women at high risk of breast/ ovarian cancer – genetic testing is primary reason for counselling

	Intent		Intent	2	3	4	5	6	7	8	9	10	11	12
2	Attitude	r	0.495											
		p	0.001											
		n	85											
3	Subjective Norm	r	0.450	0.193										
		p	0.001	0.077										
		n	94	85										
4	Perceived Behavioural Control	r	0.293	0.182	0.268									
		p	0.005	0.101	0.010									
		n	92	83	92									
5	Anticipated Negative Affect if decided not to have test	r	0.205	0.208	0.190	-0.045								
		p	0.055	0.063	0.076	0.680								
		n	88	81	88	87								
6	Anticipated Negative Affect if positive result	r	-0.095	-0.015	0.145	0.001	0.096							
		p	0.398	0.900	0.198	0.990	0.399							
		n	81	74	81	81	80							
7	Anticipated Negative Affect if negative result	r	0.090	-0.027	-0.028	-0.095	0.352	0.252						
		p	0.412	0.816	0.802	0.386	0.001	0.025						
		n	85	77	85	85	83	79						
8	Anticipated Positive Affect if negative result	r	0.240	0.037	0.061	-0.227	0.067	-0.140	0.007					
		p	0.024	0.743	0.572	0.035	0.540	0.212	0.951					
		n	88	80	88	87	86	81	84					
9	Worry	r	0.099	0.163	0.110	0.058	0.511	0.120	0.318	0.100				
		p	0.345	0.138	0.295	0.584	0.001	0.291	0.003	0.357				
		n	93	84	93	91	87	80	84	87				
10	Likely to carry gene	r	0.175	0.072	0.233	-0.082	0.059	-0.088	-0.117	0.149	0.114			
		p	0.091	0.514	0.024	0.435	0.588	0.436	0.286	0.167	0.277			
		n	94	85	94	92	88	81	85	88	93			
11	Likely to be offered test	r	0.244	0.067	0.205	0.327	-0.017	0.108	-0.152	-0.034	-0.026	0.303		
		p	0.019	0.543	0.048	0.001	0.876	0.337	0.164	0.754	0.806	0.003		
		n	93	84	93	92	88	81	85	88	92	93		
12	Anxiety	r	-0.199	-0.103	0.026	-0.065	0.303	0.354	0.353	-0.072	0.517	0.207	-0.056	
		p	0.058	0.356	0.807	0.545	0.005	0.001	0.001	0.510	0.001	0.047	0.599	
		n	92	83	92	90	86	80	83	86	91	92	91	
13	Depression	r	-0.010	-0.026	0.016	-0.027	0.328	0.184	0.441	0.041	0.389	0.081	-0.049	0.674
		p	0.927	0.813	0.876	0.802	0.002	0.103	0.001	0.707	0.001	0.443	0.647	0.001
		n	92	83	92	90	86	80	83	86	91	92	91	92

p<= 0.001; p<=0.05

APPENDIX C

Criticisms of Previous Studies

Breast Cancer- Papers

	Low level of objective risk	Study participants are related	Source of recruitment means participation rates difficult to ascertain	Report findings without clearly differentiating affected and unaffected	Dichotomise 'yes definitely' c.f. other responses
Lynch et al 1993	All at high risk	Yes - 32 people all from 1 family	Via one at risk family		N/A reported uptake
Lerman et al 1994	Yes - 87% only one FDR with ovarian cancer	Yes - 121 from 81 families	Via index patients (FDRs)	No	Yes
Lerman et al 1995	Yes - 90% only one affected FDR	Probably	Via index patients (FDRs)	No	N/A
Struewing et al 1995b	Moderate/ high risk	Yes - 140 from only 19 families	Registry	Yes	Yes
Lerman et al 1996	All high risk	Yes - 192 from only 13 families	Registry		N/A reported uptake
Hughes et al 1997	Yes – only 12% had two or more affected FDRs	?	26% via FDRs, 74% self-referred	No	N/A
Meiser et al 2000	80% at high risk, 20% at moderate risk	?	Genetic clinic attendees	Not stated	Yes
Philips et al 2000	Cancer patients- 41% no family history	?	Cancer registry	All affected	N/A
Metcalfe et al 2000	All high risk	Yes - 79 from up to 70 families	Cancer clinics	46 affected, 33 unaffected	N/A
Durfy et al 1999	Moderately high risk				
Geller et al 1999	Moderate/ high risk	No	Via FDRs on registry and via attendees at clinic	No	N/A reported uptake of counselling
Cappelli et al 1999	60 breast cancer patients 50 from population	?	Patients via oncologist. Population sample self-referred	Compared patients with population sample	Yes
Tambor et al 1997.	Yes - mainly no family history	No	Mammogram non- attenders	No	Yes:No
Valdimarsdottir et al 1999	Moderately high risk	No	Attending for regular mammography	No	N/A reported uptake
Wagner et al 2000	Carriers and non-carriers of mutation	Yes - 90 people from 35 families	Via registry	Yes	
Lerman et al 1997	High risk population	Yes - 149 people from 11 families	Via registry	Yes	N/A reported uptake
Lerman et al 1998.	At risk	Yes - 327 people from 33 families	Via registry	Yes	N/A reported uptake
Meijers-Heijboor et al 2000	Most at high risk	Yes - 682 people from 53 families	Via registry	No	N/A reported uptake

Colon cancer papers

	Low level of objective risk	Study participants are related	Source of recruitment means participation rates difficult to ascertain	Report findings without clearly differentiating affected and unaffected	Dichotomise 'yes definitely' c.f. other responses
Gritz, Vernon, Peterson et al 1999	Cancer patients – 32% had a family history	?	Via group of people already consented to give blood	No	N/A
Lynch, Watson, Shaw, et al 1999		Yes- 199 participants from 7 families			
Lerman et al 1996	Moderate risk level	44 people from 24 families	Via FDRs	No	Yes
Aktan-Collan, Mecklin, Jarvinen et al 2000b	At high risk	Yes – 446 participants from only 36 families	Via registry	No	N/A- Accept: decline
Kinney et al 2000	89% had only one affected FDR	?	Via affected FDRs and self-referred	No	Compared Interested vs Not interested/ unsure
Petersen et al 1999	At high risk	1373 from 650 families	Via cancer registry	No	Yes
Glanz et al 1999	Only 9% had more than one affected FDR	Controlled for family relationships	Via FDRs	No	Yes
Vernon et al 1999	All colon cancer patients	?	Via cancer clinic	No	Agree: disagree/ uncertain
Smith & Croyle 1995	General population sample	No	Random population sample	Mixed those with and without family history	Very interested: somewhat/not interested
Croyle & Lerman 1993	General population sample	No	Random population sample	No	No
Croyle, Dutson et al 1995	70 had family history, 201 no family history	No	Volunteer students	Mixed those with and without family history	No
Graham, Logan et al 1998	General population sample	No	Random population sample	No	No
Codori, Petersen, Miglioretti et al 1999	Moderate risk – 65% had two or more affected FDRs	258 people in 118 families	Via registry	No	N/A - Accept: decline
Lerman, Hughes, Trock et al 1999	High risk	208 people in only 4 families	Via registry	Yes	N/A - Accept: decline

APPENDIX D

ETHICAL APPROVAL FOR STUDY

HARROW RESEARCH ETHICS COMMITTEE
(Chairman Dr David Lubel)
Room 6BB 014
Northwick Park Hospital
Tel: 0181-869-2688
Fax: 0181-869-2174

NORTHWICK PARK & ST MARK'S
NHS TRUST
WATFORD ROAD HARROW
MIDDLESEX HA1 3UJ

5 October 1998

Miss A Steggles
Health Behaviour Unit
Brook House
2 - 16 Torrington Place
LONDON WC1E 6BT

Dear Miss Steggles

Ethical Submission No. 2447: Psychological aspects of genetic testing for hereditary non-polyposis colorectal cancer

The above project was approved by the Harrow Research Ethics Committee at its meeting on 5 October 1998. It would be appreciated if, in any future correspondence relating to this project or in any entry made in case-notes about procedures undertaken in the course of this study, you would refer to it as **EC 2273.**

Set out overleaf is the REC membership list which should, if applicable, be copied to the sponsoring organisation

The Committee wishes to remind all investigators of the importance of keeping General Practitioners informed of research work affecting their patients particularly when the patient's involvement continues after discharge from hospital.

Please note that all adverse events arising during the course of this study should be reported. These will be noted by the Chairman and reported to the Committee, but no acknowledgement will be sent or further correspondence entered into, except in those cases where the Chairman considers this to be warranted.

Yours sincerely

Brian Saperia
Secretary

UCL
HOSPITALS

The University College London Hospitals

The Joint UCL/UCLH Committees on the Ethics of Human Research

Committee A Chairman: Dr F D Thompson

Please address all correspondence to:
Mrs Iwona Nowicka
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Dr S Sutton
Reader in Social/Health Psychology
Health Behavioural Unit
Department of Epidemiology & Public Health
UCL
Brook Hous
2-16 Torrington Place

27 June 1998

Dear Dr Sutton

Study No: 98/0124
Title: The uptake and psychological impact of genetic testing for hereditary non-polyposis colorectal cancer

Your application was considered at the last Ethics Committee meeting on 25th June. We were basically happy but would have the following minor comments relating to the information sheet:

1. We wondered whether the word 'exciting' should be deleted from your opening paragraph.
2. We are not certain how clear it is that this study is voluntary, perhaps this should be emphasised in the information sheet.
3. We wondered whether it should contain the fact that in the future a partner may be asked to fill in a questionnaire.

Once you have addressed the above points your study can go ahead.

Please note that it is important that you notify the Committee of any adverse events or changes (name of investigator etc) relating to this project. You should also notify the Committee on completion of the project, or indeed if the project is abandoned. **Please remember to quote the above number in any correspondence.**

Yours sincerely

I. Thompson

FP Dr F D Thompson
Chairman

sut27jun/fdu/j1025/06/98