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**PARTICIPATION RATES IN CF CARRIER TESTING:
Need for information or Convenience of testing?**

by
Annie Youn, B.A.

A thesis submitted to
the Faculty of Graduate Studies and Research
in partial fulfilment of
the requirements for the degree of
Master of Arts

Department of Psychology

RUNNING HEAD: CF Carrier Testing

Carleton University
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July 5, 1996

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ABSTRACT

As the Human Genome project rapidly sequences the human genetic code, DNA predictive testing has become a clinical reality. Individuals at risk of certain genetic diseases may now be provided with unprecedented preventative options. The discovery of the Cystic Fibrosis (CF) gene in 1989 was met with enthusiasm as it was anticipated that the public would actively seek out CF carrier testing for their future family planning decisions. However, contrary to these expectations, recent research has reported poor test participation amongst the high risk population (i.e., family history of CF). The aim of the present study was to expand on previous investigations by exploring the influence of personal factors which may predict who seeks carrier testing and why. It was hypothesized that decisions to undergo carrier testing would be influenced by (a) high levels of knowledge; (b) favourable attitudes towards testing; (c) low levels of perceived negative affect resulting from testing; and (d) higher preferences for hypothetical outcomes of testing which involved avoidance of a CF birth. This hypothesis was tested on four distinct populations each with different experiences with CF and CF Carrier Testing. 1) *Obligate Carriers*: 49 parents of children with CF; 2) *Tested*: 59 individuals with a family history of CF (i.e., high risk) who had previously been carrier tested; 3) *Not-Tested*: 98 high risk un-tested individuals; and 4) *General Population*: 59 members of the general public with no known family history of CF. The expectation was that those groups who had previously undergone carrier testing (i.e., Obligate Carrier and Tested) would be distinct on decision making factors from those who had not been tested (i.e., Not-Tested and General Population). The results demonstrate that decision making factors do not discriminate between the carrier testing

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ABSTRACT

As the Human Genome project rapidly sequences the human genetic code, DNA predictive testing has become a clinical reality. Individuals at risk of certain genetic diseases may now be provided with unprecedented preventative options. The discovery of the Cystic Fibrosis (CF) gene in 1989 was met with enthusiasm as it was anticipated that the public would actively seek out CF carrier testing for their future family planning decisions. However, contrary to these expectations, recent research has reported poor test participation amongst the high risk population (i.e., family history of CF). The aim of the present study was to expand on previous investigations by exploring the influence of personal factors which may predict who seeks carrier testing and why. It was hypothesized that decisions to undergo carrier testing would be influenced by (a) high levels of knowledge; (b) favourable attitudes towards testing; (c) low levels of perceived negative affect resulting from testing; and (d) higher preferences for hypothetical outcomes of testing which involved avoidance of a CF birth. This hypothesis was tested on four distinct populations each with different experiences with CF and CF Carrier Testing. 1) *Obligate Carriers*: 49 parents of children with CF; 2) *Tested*: 59 individuals with a family history of CF (i.e., high risk) who had previously been carrier tested; 3) *Not-Tested*: 98 high risk un-tested individuals; and 4) *General Population*: 59 members of the general public with no known family history of CF. The expectation was that those groups who had previously undergone carrier testing (i.e., Obligate Carrier and Tested) would be distinct on decision making factors from those who had not been tested (i.e., Not-Tested and General Population). The results demonstrate that decision making factors do not discriminate between the carrier testing

decisions of the high risk groups. That is, Obligate Carriers, Tested and Not Tested individuals are similar in knowledge, affect, attitudes and preferences. In addition, virtually all the participants in the Not-Tested group (98%) chose to be tested with the study. Therefore, despite the fact that the Not Tested group was previously informed and in favour of testing, they did not come forward for testing prior to the study. In contrast, the General Population group demonstrated significantly lower levels of knowledge and unfavourable views towards testing, yet recent research has reported moderate to high test participation amongst the general public. Upon closer examination, it appears that participation in CF carrier testing is not accurately predicted by the proposed decision making factors. Instead, opportunistic testing protocols which involve active recruitment of individuals has been shown to artificially inflate demand for testing. Therefore, these findings indicate that participation in genetic testing may not indicate a need for information by the client, nor can it provide an accurate assessment of success for carrier screening programs. In conclusion, the present study proposes that examination of the process involved in genetic testing decisions may provide a more accurate measure of demand for testing.

**PARTICIPATION RATES IN CF CARRIER TESTING:
Need for information or Convenience of testing?**

BACKGROUND

Genetic diseases are no longer perceived as rare single gene disorders, such as, Sickle Cell Anemia, Tay Sachs and Cystic Fibrosis. Other more "common" diseases such as Alzheimer's, heart disease and various cancers, are now known to be caused by both genetic predisposition and environmental susceptibility (multifactorial) (Science council of Canada, 1991). It has been estimated that 1 in 20 Canadians will experience a gene-related impairment, disability or handicap by the age of 25 and that more than half the population will develop a multifactorial disease during their lifetime (Science Council of Canada, 1991). With the multi-billion dollar Human Genome Project ambitiously sequencing the human genetic code, disease genes are being cloned at an unprecedented rate (U.S. Congress, 1992).

Not only is new DNA information being rapidly compiled, but it is also being eagerly introduced into everyday medical practice (U.S. Congress, 1992). Recent advances in molecular genetics continue to uncover the etiology of many diseases and develop the technology to predict the likelihood of disease onset. Thus, prophylactic treatment options have become a reality to those at high risk (i.e., positive family history) for certain genetic diseases and unprecedented reproductive options are now available to high risk prospective

parents. Moreover, innovative experimental treatments such as gene therapy have been introduced for those affected with certain inherited illnesses and may offer the possibility of a cure (Porteous and Dorn, 1993; Colledge, 1994; Crystal, 1992).

Notwithstanding these developments, predictive DNA testing may not be the medical panacea it is often perceived to be. In reality, although disease genes may be identified, curative or prophylactic treatment(s) may not yet be available. Therefore, in the absence of treatment options, DNA molecular diagnostics simply provide genetic information. This is the case in current genetic testing for Huntington's disease which determines whether or not an individual will develop this late onset degenerative illness (Codori and Brandt, 1994; Wiggins et al., 1992). Because there are no known preventative medical interventions for Huntington's, an individual who tests positive must live with the knowledge that the disease will one day manifest itself. In some cases, availability of prophylactic measures may not be ideal or desirable. For example, current preventative treatment options for women found to carry a familial breast cancer gene mutation (BRCA1 or BRCA2) (Hall et al., 1990; Easton, Bishop, Ford, Crockford and Breast Cancer Linkage Consortium, 1993) include radical bilateral mastectomy, oophorectomy, chemotherapy (e.g., Tamoxifen) and radiation therapy, which are often accompanied with side effects and health risks (see Lerman and Croyle, 1994; Struwing, Lerman, Kase, Giambarresi and Tucker, 1995; Claus, Risch and Thompson, 1994). Therefore, in some cases, disease prevention at all costs may not be desirable.

Americans, and 1 in 90,000 for Asians (Beaudet, 1992).

CF is caused by a defect in the Cystic Fibrosis Transmembrane conductance Regulator (CFTR) gene which causes the exocrine glands to malfunction (Lewis, 1994). These glands are responsible for the normal production of sweat, mucus, tears, saliva, digestive juices and other secretions. However, the CF gene mutation causes CF patients to produce 1) excessive amounts of histologically normal secretions in the tracheobronchial glands; 2) abnormally thick and sticky secretions causing obstruction of the lumen by viscid material (pancreas, intestinal glands, intrahepatic bile ducts, gallbladder and submaxillary glands; and 3) secretions with excessive electrolyte concentration. These abnormal and excessive secretions lead to chronic obstructive pulmonary disease and pancreatic exocrine deficiency.

As a result, CF patients suffer from frequent lung infections and malnutrition which steadily worsen eventually leading to death in early adulthood (Canadian Task Force on the Periodic Health Examination, 1991; Beaudet, 1992; Lloyd-Still, 1983).

The severity of CF varies between patients. Children with mild cases may not be diagnosed until their early teens while those with severe cases may not live past infancy. The average CF patient usually passes through their first 5 years with few symptoms other than poor weight gain and foul smelling bowel movements. By the time they are in school, children with CF must undergo daily treatment which includes: chest physiotherapy (i.e., postural drainage, percussion, vibration and assisted coughing) to clear the lungs of mucus; antibiotics to ward off lung infections; and vitamins and enzymes to increase their nutritional uptake. Adolescents must battle more aggressively with weight loss by following

beliefs and behaviourally implemented (Surh et al., 1992), it has not yet been established *why* some individuals choose to be tested. The purpose of this research study was examine current DNA predictive testing for Cystic Fibrosis (CF) in order to determine who participates in carrier testing and why.

CYSTIC FIBROSIS CARRIER TESTING

Cystic Fibrosis (CF) is an ideal model for this research project for several reasons: First, CF is the most common lethal autosomal recessive gene disorder amongst Caucasians of European descent affecting 1 in 2500 births and where 1 in 25 individuals are CF carriers. Second, the morbidity/mortality of CF may be comparable to many diseases. Therefore, the findings of genetic testing decisions may be generalizable to other genetic testing programs. Third, CF carrier testing has recently become available to those with a family history of CF (high risk) and widespread population CF carrier screening is being explored.

What is CF?

CF is the most common lethal autosomal recessive disorder in Caucasians. Incidence rates in North America and Britain have been customarily estimated at 1 in 2500 births (Brock, 1995; Wilfond and Fost, 1990; Canadian Task Force on the Periodic Examination, 1991). However, reported incidence rates in Canada are closer to 1 in 2927 births (Canadian Task Force on the Periodic Health Examination, 1991). Incidence rates vary according to the cultural, ethnic and racial background of the population (Wilfond and Fost, 1990). For example, small tight knit French communities such as the Saguenay-Lac-St-Jean region in Quebec report a higher incidence rate of 1 in 891 affected births (Rozen et al., 1991). Also, risk estimates for affected births are 1 in 5,000 for Jews, 1 in 17,000 for African

Americans, and 1 in 90,000 for Asians (Beaudet, 1992).

CF is caused by a defect in the Cystic Fibrosis Transmembrane conductance Regulator (CFTR) gene which causes the exocrine glands to malfunction (Lewis, 1994). These glands are responsible for the normal production of sweat, mucus, tears, saliva, digestive juices and other secretions. However, the CF gene mutation causes CF patients to produce 1) excessive amounts of histologically normal secretions in the tracheobronchial glands; 2) abnormally thick and sticky secretions causing obstruction of the lumen by viscid material (pancreas, intestinal glands, intrahepatic bile ducts, gallbladder and submaxillary glands; and 3) secretions with excessive electrolyte concentration. These abnormal and excessive secretions lead to chronic obstructive pulmonary disease and pancreatic exocrine deficiency.

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high energy, protein and fat diets while continuing to take vitamins and animal enzymes to compensate for further loss of pancreatic enzyme activity. At the same time, obvious breathing problems and dangerous infections are managed with a variety of antibiotics making the total number of daily pills required close to 50. Most teens spend 2 hours a day in physiotherapy, go to monthly medical appointments, and are usually admitted to the hospital 2 to 3 times a year. Later in early adulthood, most CF patients are no longer able to work as respiratory functioning rapidly deteriorates and hospital stays are more frequent. Eventually in their 30s, most patients die from respiratory failure after a prolonged hospital stay (see Lloyd-Still, 1983; Canadian Task Force on the Periodic Health Examination, 1991; Beaudet, 1992).

There has been little evidence of psychosocial sequelae as the majority CF patients enjoy a normal, active childhood and adolescence. Previous research has shown that children with CF are similar to their same aged counterparts in terms of depression and anxiety (Drotar, Doershuk, Stern, Boat, Boyer and Mathews, 1981; Cappelli, McGrath, Heck, MacDonald, Feldman and Rowe, 1989); hopelessness and self-concept (Kashani, Barbero, Wilfley, Morris and Shepperd 1988); and self-efficacy (Cappelli et al., 1989). However, adolescents with CF report stress due to their family's reaction to their illness (Cappelli et al., 1989). This stress appears to escalate in adulthood, as patients indicate a reduction in the amount of satisfaction with their family's acceptance of their change in lifestyle (Shepherd et al., 1990). There is also an increasing trend towards depression in adulthood (Pearson, Pumariega and Seilheimer, 1991).

What is a CF Carrier?

All humans possess two CF genes, one from each parent. A CF Carrier is someone who has inherited one normal and one mutated CF gene (heterozygote). In North America, it is estimated that 1 in 25 Caucasians in the general population are CF carriers (Beaudet, 1992). CF Carriers are completely asymptomatic because their normal CF gene compensates for their mutated gene. However, they have a 50% chance of passing on their mutated CF gene to their offspring. CF is inherited in a recessive pattern, therefore if both parents are carriers, they have 1 in 4 chance of having a child affected with CF. Thus, a person *affected* with CF has two mutated CF genes inherited from each of their parents (homozygote). Parents of individuals affected with CF are called "Obligate Carriers" as they both must carry a CF mutation to have conceived an affected child.

What is CF Carrier Testing?

In 1989, Lap-Chee Tsui cloned the most common CF mutation labelled as $\Delta F508$ (Kerem et al, 1989; Riordan et al. 1989; Rommens et al., 1989). The $\Delta F508$ mutation accounts for roughly 75.8% of Caucasian carriers in North America and Great Britain (Beaudet, 1992; Kerem et al, 1989; Lemna et al., 1990). Other less common mutations (i.e., G542X, G551D, R1553X and N1303K) have also been isolated which account for additional 8.7% carriers raising the detection rate to approximately 84.5% (Beaudet, 1992). It has been estimated that over 500 rare unknown CF mutations account for the remaining 15.5% (Beaudet, 1992). It is important to note that these estimates do not apply to other geographic regions or ethnic groups. For example, the $\Delta F508$ mutation accounts for a lower percentage of carriers (30% to 55%) among French, Spanish, Italian and Ashkenazic

Jewish populations (Rozen et al., 1991; Claustres et al., 1993; Ober et al., 1992; Super and Schwartz, 1992 and Estivill et al., 1989).

Therefore, DNA carrier testing for CF is 100% specific such that those who are found to carry known CF mutations are CF carriers (i.e., no false positives) (Williamson, 1993; Beaudet, 1992; Brock, 1995). However, current testing is only sensitive enough to detect 85% of carriers. At an 85% detection rate (see Figure 1), 1 in 15 couples in the general population are given results such that only one partner is detected as a carrier (carrier risk is 1), while the other is given a low but not zero carrier risk (approximately 1/600). Therefore, their combined risk of having a CF child is 1 in 2400 ($1 \times 1/600 \times 1/4$). This is a relatively small reduction in their risk as their estimated risk prior to testing was 1 in 2500 ($1/25 \times 1/25 \times 1/4$). Consequently, this couple may require significant genetic counselling as their fears of having a child affected with CF may not be allayed and could be somewhat elevated as one partner has been positively identified as a carrier. The lack of test sensitivity places significant stress and pressure onto the genetic counselling community to provide adequate genetic information and promote informed patient decision making. However, these problems would be substantially reduced if the detection rate were to be increased to 99%, then 98% of carrier couples would be accurately identified and assigned a more refined risk estimate of having an affected child (approximately 1 in 9814) (Beaudet, 1990, 1992; Wilfond and Fost, 1990). Of note, the current detection rate of the DNA laboratory utilized for the present study has reached approximately 90% which accounts for the 10 most common mutations in the Ottawa-Carleton area (Surh and Cappelli, 1992).

Insert Figure 1 about here

The actual CF carrier DNA test procedure involves taking a blood sample by venipuncture or buccal (cheek) cell sample by mouthwash or buccal swab. DNA is extracted from these samples and tested for common CF mutations. If the client has no known family history of CF (i.e., general population), they are tested for the most common identified CF mutations. If they test positive, they are CF carriers. If they test negative, they are given a residual carrier risk estimate of approximately 1 in 160 (Beaudet, 1992; Wilfond and Fost, 1990). Therefore, even though their a priori carrier risk (1 in 25) has been significantly reduced, they still have a “low but not zero risk” of carrying an unidentified rare CF mutation.

Carrier testing can be more accurate in the high risk population. However, the calculation of risk estimates may not be as straightforward. Prior to testing, high risk blood relatives are assigned Mendelian inheritance carrier risks where the risk for siblings is 2 in 3, aunts/uncles is 1 in 2 and first cousins is 1 in 4 (Lewis, 1994). The accuracy of the DNA carrier test for a high risk blood relative may approach 100% if: a) CF mutation(s) have been identified in the CF patient and/or their parents; and b) the relative is either a first (i.e., parent or sibling) or second (i.e., grandparent or aunt/uncle) degree relative to the affected relative. Basically, the more information about the familial mutation(s) carried by the CF Patient and their parents, the better the accuracy. In fact, even if the CF patient

possesses one or more unknown CF mutations, further DNA testing by linkage analysis may still be able to refine carrier risks of a high risk relative. Briefly, linkage analysis involves examining the DNA pattern (i.e., haplotype) around the high risk blood relative's CF gene and comparing it to the pattern found in the CF patient (Lewis, 1994; Beaudet, 1992). If the high risk blood relative has a different haplotype, their a priori carrier risks may be slightly reduced. However, in reality, mutation and/or haplotype analyses are not always definitive or informative (Beaudet, 1992). Therefore, some high risk relatives are also provided with indefinite "low risk" test results.

What is CF Prenatal Testing?

Before the CF gene was identified, health care professionals were only able to offer high risk prospective parents with Mendelian inheritance probabilities of having an affected child. These risk estimates were rarely sought out because most parents of CF patients (80%) were unaware of their previous family history of CF prior to the birth of their affected child (Watson, Marchant and Bush, 1992; Williamson, 1993). Furthermore, accurate prenatal testing was not available at that time limiting the usefulness of risk estimates.

Prenatal testing began in 1983 using microvillar intestinal enzymes (MIE) screening which examines MIE levels in the amniotic fluid at 17 to 18 weeks (U.S. Congress, 1992; Beaudet, 1992). However, this test is accompanied by high false-positive (2%) and false negative (8%) rates making it an unpopular choice for both physicians and patients (U.S. Congress, 1992; Beaudet, 1992). Consequently, in the absence of any other reliable

preventative interventions, previous research has found that 45% to 65% of parents of CF children have opted to have one partner sterilized to avoid future CF births (Evers-Kiebooms, Denayer and Van den Berghe, 1990; Wertz, Janes, Rosenfield and Erbe, 1992; Kayback et al, 1984).

With the discovery of the CF gene, fetuses affected with CF can now be reliably detected in utero using Chorionic Villus Sampling (CVS) or Amniocentesis (Dick, 1996; Heckerling and Verp, 1991; U.S. Congress, 1992). Both methods are vast improvements over MIE screening because DNA testing of the fetal sample can be 100% specific and 100% sensitive when the parents mutations have been identified (Williamson, 1993). In terms of patient preference between the two tests, CVS has the advantage of early detection as it may be performed in the first trimester (9 to 12 weeks) which is several weeks before amniocentesis (16 to 18 weeks) (Dick, 1996; Heckerling and Verp, 1991; U.S. Congress, 1992). However, CVS is also accompanied by higher risks of spontaneous abortion (2.4% to 6.2%) when compared to amniocentesis (0.7% to 1.7%). Moreover, it has been recently reported that CVS is associated with risks (0.03%) of fetal limb defects such as transverse limb and digital deficiency (Dick, 1996).

Implications of CF Carrier Testing

In light of the prevalence of CF and the high incidence of carriers, identification of the CF gene has widespread health care implications. On an individual level, carrier status may affect a person's life choices such as mate selection, marriage and/or pregnancy. Similarly, carrier couples may consider other reproductive options prior to pregnancy such as artificial

insemination, adoption, choosing not to have children and preparing for the birth of a child with CF. In addition, carrier couples may choose to undergo prenatal testing in order to determine whether they should continue or terminate an affected fetus once pregnant. Carrier testing may also have more distant family planning effects such that individuals undergoing testing may be obtaining information which may ultimately affect their children's and/or grandchildren's family planning decisions. On a larger population based scale, widespread testing may reduce the incidence of CF, thereby lessening the medical and financial burdens of this disease.

HIGH RISK CARRIER TESTING VS. POPULATION CARRIER SCREENING

In spite of these medical and social implications, the lack of test sensitivity has prompted North American health organizations to put forth practice recommendations limiting access to CF carrier testing (Caskey, Kaback and Beaudet, 1990; Workshop on Population Screening for the Cystic Fibrosis Gene, 1990; Canadian Task Force on the Periodic Health Examination, 1991). The consensus in Canada and the United States is that widespread general population screening is premature and carrier testing should only be offered to those with a family history of CF (i.e., high risk population). In contrast, the general accord in Great Britain is to implement general population screening through hospital clinics and family practitioners' offices on a research basis. Once the detection rate is increased, North American organizations concede population testing should be implemented (Caskey et al., 1990; Modell, 1993; Workshop on the Population Screening for the Cystic Fibrosis Gene, 1990). However, it is unclear at which point the detection rate will be sufficiently sensitive to organise widespread screening as recommendations vary from 90% to 99% (Wilfond and

Fost, 1990; Beaudet, 1990; Workshop on Population Screening for the Cystic Fibrosis Gene, 1990).

Nonetheless, Health care professionals across the globe have been engaged in a debate over *who* should be offered CF carrier testing. Opponents of population screening argue that the test is not yet sensitive enough to provide reasonable risk estimates to all individuals (DeBraekeleer and Melancon, 1990; Stewart, 1989; Wilfond and Fost, 1990; Beaudet, 1992, 1990). The imperfect detection rate necessitates comprehensive genetic counselling as past screening programs have demonstrated the potential for discrimination and stigmatization when test information is poorly communicated and/or understood (Roberts, 1990; McGourty, 1989; Beaudet, 1990). Some researchers question the value of population screening at this time stating, "What would be the psychological effect of the speech 'You may be a CF carrier, but we cannot yet confirm whether you carry another mutation; we will check later!' How are we to qualify such 'counselling' from an ethical point of view? A feeling of 'genetic insecurity' could cause misleading reproductive choices" (DeBraekeleer and Melancon, 1990, p.580).

However, widespread genetic counselling is not yet attainable as there is a shortage of clinical geneticists and genetic counsellors to adequately educate the public (Roberts, 1990). For example, Wilfond and Fost (1990) explain that population testing in the United States would identify over 8 million carriers. Therefore, even if only 3 million prospective parents were tested per year, 651,000 counselling hours would be needed. Currently in the United States there are qualified genetic counsellors and geneticists. This means that

providing genetic counselling for CF alone would occupy 17 weeks a year for every counsellor. The situation in Canada is similar as there are only 130 board certified genetic counsellors with only 6 new graduates per year.

Notwithstanding these concerns, opponents of widespread carrier *screening* of the general population are in favour of providing individual carrier *testing* to high risk blood relatives. Advocates of high risk carrier testing feel that this population will be better serviced because (a) test results can be 100% accurate when familial mutations have been identified; (b) current genetic counselling resources can cope with the potential demand from this population; and (c) high risk carrier screening is more cost-effective as fewer individuals need to be tested to detect a large number of carriers (Workshop on Population Screening for the Cystic Fibrosis Gene, 1990; Beaudet, 1992).

On the other hand, proponents of population screening argue that it is unethical to withhold genetic testing from those who may benefit from it. They assert that "...if the medical profession is truly concerned about the well-being of the community in its care, and if it has the technical ability to offer some reduction in the risk of having an affected child, it will find the energy to overcome the inevitable organizational and social problems in delivering a suitably designed program" (Brock, 1990, p.164-165). Advocates argue that limiting carrier testing to high risk relatives bypasses the vast majority of carrier couples (80%) who are either unaware that they have/had a blood relative with CF or have a CF mutation that has gone undetected in their family (Rowley, Loader, Levenkron and Phelps, 1993; U.S. Congress, 1992; Modell, 1990).

DEMAND FOR CF CARRIER TESTING

The swift recommendations of national health organizations restricting testing to the high risk population in North America were not only due to the imperfect detection rate and genetic counselling limitations. Population testing was also postponed due a lack of preparation by the medical community for the anticipated influx of requests for carrier testing (Roberts, 1990). That is, despite the fact that health professionals could foresee the day when the CF gene would be identified (Stewart, 1989; Dodge, 1988), there was no existing infrastructure for testing of this scale nor were there guidelines for appropriate genetic counselling (Caskey et al., 1990; U.S. Congress, 1992). Therefore, given the expected demand and lack of restrictions, private DNA labs in the United States promptly began organizing for widespread testing (Wilfond and Fost, 1990; Roberts, 1990), thereby opening up a new multi-billion dollar industry. Consider, for example, if only 2.4 million newly wed couples (or approximately 5 million people) in the U.S. are tested every year. At \$200 per DNA carrier test, private labs could generate a billion dollars in sales per year (Wilfond and Fost, 1990). This threat lead health officials to quickly place a voluntary moratorium on widespread screening so that they could take policy measures to ensure that testing would be offered responsibly (Roberts, 1990).

The assumption of public health care administrators and private DNA industry leaders was that the availability of testing would lead to an immediate and overwhelming response by the public to seek testing. The prevailing attitude was that it was only a matter of time before the public would demand testing after being educated through popular lay publications such as "Cosmopolitan" or Redbook" (Roberts, 1990). Moreover, it was

proposed that legal action against physicians who did not offer the test would coerce other health care professionals into offering the test to all their clients (Rowley et al., 1993; Super, 1993; Roberts, 1990). Therefore, given these concerns, CF consortiums were formed and pilot projects were readily funded in order to investigate the scope of the public's response to testing (Langfelder, Juengst and Thompson, 1992).

Demand for testing by high risk relatives was not addressed in these discussions, instead it was largely assumed that the high risk population would enthusiastically seek testing because of their higher carrier risk (Workshop on population screening for the Cystic Fibrosis gene, 1990; Super et al., 1994). Moreover, it was presumed that relatives would have more experience and greater knowledge of the disease and its inheritance and would take measures to avoid a CF birth.

Interestingly, recent research has demonstrated that high risk relatives are not taking up the offer for carrier testing. An American study reported only 4.1% participation among first degree (i.e., parents and siblings) and second degree (i.e., aunts/uncles, cousins) high risk blood relatives of CF patients (Sorenson, DeVellis, Cheuvront, Callanan and Talton, 1994).

They concluded that test uptake was low due to lack of knowledge regarding testing and an inability to pay for the test. Similarly, a Canadian study conducted by Surh, Cappelli MacDonald, Mettler and Dales (1994) found less than 10% of the high risk adult population came in for testing at an Ottawa area hospital. They also attributed the low uptake to lack of knowledge of the CF carrier test, however, they did not find that testing covered under a universal health care plan attracted significantly more high risk relatives. Surh et al. (1994)

further speculated that low participation rates among high risk relatives may be the result of personal factors such as low self-perceived risk and a belief that testing is not personally useful.

If low participation rates amongst the high risk population reflect traditional medical barriers to testing such as knowledge (Deber, 1994) and cost(s) (Sorenson et al, 1994; Bernhardt, 1991) then public education campaigns (see Myers, Bernhardt, Tambor and Holtzman, 1994) and subsidised testing may make genetic services more accessible to those who want it. However, if poor test participation rates reflect personal factors and preferences for different outcomes of testing then the genetics community must re-assess their current focus on the provision of genetic testing services. If current high risk CF Carrier Testing programs are not sought out by high risk relatives who may potentially benefit most from it, the question to debate may not be "who to test?" (i.e., population versus high risk screening) but "why do people choose to be, or not to be, tested?" It is imperative to determine what motivates individuals to seek carrier testing as factors which predict testing behaviour may provide important information in terms of unique genetic counselling issues, target populations and test accessibility. Similarly, factors which predict who does not seek testing may shed light on social and ethical issues such as the perception of disease prevention and the provision of predictive DNA information in the absence of a cure. It is likely that these complex micro and macro issues are not unique to CF carrier testing and may be generalizable to other inherited diseases as genetic testing becomes more common place in standard medical care.

MOLECULAR TESTING DECISION MAKING MODEL

In order to examine the influence of traditional testing barriers (such as knowledge) and personal factors on CF carrier testing decisions, the present study utilized Drs. Cappelli and Surh's model for Molecular Testing Decision Making (1992). This model goes beyond previous research which has made a leap from assessing attitudes towards testing to measuring participation rates in testing with the assumption that favourable attitudes and decisions to be tested reflect demand for genetic testing. The present model proposed that carrier testing decisions were influenced by 1) *knowledge* regarding the disease and the carrier test; 2) *affect* resulting from testing; 3) *attitudes* towards carrier testing; and 4) *preferences* for different hypothetical carrier test and reproductive outcomes (e.g., abortion of an affected fetus) (Figure 2).

Insert Figure 2 about here

I. Knowledge

Lack of knowledge is seen as a common barrier to new medical tests (Deber, 1994). Clearly, those who are unaware of the availability of a test and its purpose will not come forward for testing. Thus, it follows that proper dissemination of test information is a crucial element of test accessibility.

Traditionally, the onus is placed on health care professionals to inform their patients of their risk(s) for diseases as well as new technological advances and treatments that may be

available (Deber, 1994). However, in the case of hereditary genetic disorders such as CF, health care professionals may encounter difficulties when educating and informing their patients as genetic testing is often only available to those with a family history of the illness. Consequently, health care professionals must be able to accurately identify their patients who may be at high risk for passing on a defective gene and disseminate test information to them. This is a challenging task as (1) it is difficult for physicians to single out at risk patients as most individuals are unaware of their positive family history of CF (Watson, Marchant et al., 1992; Williamson, 1993); (2) physicians themselves tend to have poor knowledge of the genetic disease, its inheritance and testing (Kenen and Schmidt, 1978; Faden et al., 1994; Rowley et al., 1993); and (3) even if the family physician was aware of a person's risk through genetic testing of another family member, they cannot disclose personal information of one family member to another without breaching patient confidentiality. Thus, in genetic testing the onus to disseminate information is shifted onto family members who have previously undergone testing to communicate their test result to other family members and inform them of their risk.

Current clinical practice for CF carrier testing follows this pattern of information dissemination where the CF patient and/or their parents (Obligate Carriers) are responsible for advising blood relatives of their increased carrier risk and the availability of the carrier test (Surh et al., 1994; Super et al., 1994; Denayer, Evers-Kiebooms, DeBoeck and Van den Berghe, 1992). It is further expected that high risk relatives, regardless of their own carrier test decisions and/or carrier test results will continue to disseminate testing information to other blood relatives (Surh et al., 1994; Super et al., 1994; Denayer et al.,

1992). Therefore, given that CF patients and Obligate Carriers are the primary source of genetic information, it is crucial that they be fully informed.

Following this traditional test recruitment procedure, Surh et al. (1994) provided thorough genetic counselling to 99% of CF patients and/or their parents attending the two Ottawa-Carleton region CF clinics and encouraged them to tell their high risk blood relatives that testing was available and free of charge. Despite these efforts, less than 10% of relatives came in for testing over a four year period. It is possible that insufficient or incorrect knowledge of CF and CF carrier testing may have posed barriers for high risk individuals seeking testing.

Past research has unequivocally found that although Obligate Carriers have a good understanding of the CF disease process and its treatment, they have a tenuous grasp on the genetic aspects of CF such as carrier risks and/or recurrence risks (i.e., 25% chance that they will have another child affected with CF) (Hames, Beesley and Nelson, 1991; Wertz et al., 1992; Miller and Schwartz, 1992; Kaback et al., 1984; Wolff et al., 1990). Similarly, second degree family members (i.e., grandparents, aunts and uncles) demonstrate fair knowledge of the disease, but only 22% could correctly identify their risk of being carriers (i.e., 1 in 2) and only 28% knew their risk of having a child with CF (Denayer et al., 1992).

Risk estimates are inherent in the provision of information regarding CF carrier testing (Vlek, 1987). Therefore, understanding of these risk estimates is crucial for informed

patient decision making. It has been proposed that low knowledge of carrier risks demonstrated by high risk relatives may be the result of a lack of understanding of mathematical concepts such as probabilities, fractions, odds and/or ratios. As a result, misunderstanding and/or misinformation of carrier risks may inhibit relatives from coming forward for testing. A study conducted by Chase et al (1984) found that these mathematical concepts used in predictive testing are often poorly understood. For example, 28.4% of pregnant women undergoing alpha-fetoprotein screening responded incorrectly to the question "What does 1 out of 1000 mean to you?" such that the majority of women overestimated the risk and 19.5% thought "1/1000" was equivalent to "1 in 10". These findings are not surprising as proportions and ratios have been shown to be poorly understood amongst high school students and difficult concepts to grasp even later in adulthood. Both students and adults have demonstrated difficulty transforming fractions into their equivalent percentages and visa versa. Also, subjective assessment of percentages appear to be consistently perceived as greater than their proportion equivalents (Kessler and Levine, 1987). Unfortunately, reliable and valid alternatives to numeric risks have not been established (Lippman-Hand and Fraser, 1979). Therefore, genetic counsellors face the challenge of imparting genetic risk information in a manner which is easily and accurately understood by individuals seeking genetic testing.

Problems regarding information dissemination may be exacerbated as high risk relatives take on the role of informant and pass this information along to other blood relatives. Similar to a telephone line, test information may be forgotten, omitted or become distorted from the original genetic counselling session. Past research has shown that not only do

previously tested individuals have a poor understanding of CF carrier testing (Fanos and Johnson, 1995), they frequently forget and/or misinterpret their own test result (Sorenson et al., 1994). Inaccurate recall of test results is most likely due to the fact that carrier testing is not yet 100% sensitive. As a result, the majority of clients are provided with risk estimates (e.g., 'your risk of being a CF carrier is low but not zero') as opposed to definitive results (e.g., 'you are a CF carrier'). These risk estimates are problematic as Watson, Mayall, Lamb, Chapple and Williamson (1992) found that some clients do not remember their test results 3 months after testing despite being informed verbally and in writing. That is, only 57% of participants who were found to be at "low risk" correctly recalled their result, 21% incorrectly assumed their risk was zero, and the remaining 22% were unsure. Surprisingly, even individuals who are given unambiguous *positive* test results have been shown to misunderstand and/or demonstrate poor recall of their test result (Bekker, Denniss, Modell, Bobrow and Marteau, 1994; Evers-Kiebooms, Denayer, Welkenhuysen, Cassiman and Van den Berghe, 1994).

If test information has not filtered down to all high risk relatives, those who have not already undergone testing may be similar to the general population who have been shown to have low knowledge of CF and its inheritance (Williamson et al., 1989; Decruyenaere, Evers-Kiebooms, Denayer and Van den Berghe, 1992). Despite consistent media attention in North America (Goldbloom, 1995) and public awareness campaigns in the U.K. and U.S. (U.S. Congress, 1992; Clayton et al., 1996) knowledge of CF does not go beyond name recognition for most members of the general population (Watson, Mayall et al., 1991; Watson, Williamson and Chapple, 1991). In a survey of 385 adult social science students,

Decruyenaere et al. (1992) found that although 59% of respondents claimed that they had *heard* about CF, only 38% could identify at least one feature of the disease. Also, those who claimed to have heard of CF were equally as uneducated regarding its inheritance as those who had not heard of CF. This low knowledge of CF and CF carrier testing amongst the general population may have serious implications for the genetics community in terms of the provision of adequate genetic counselling services should widespread testing become available in North America.

In sum, previous research has demonstrated that the high risk population have higher knowledge of the CF disease process and its inheritance when compared with the general population. However, both groups have little understanding of CF carrier risks. The present study expanded on earlier studies investigating level of knowledge regarding CF and its influence on carrier testing decisions by: 1) using a more comprehensive survey which explores three distinct areas of knowledge (disease process, CF carrier test and CF carrier risks); and 2) comparing the high risk and general populations to directly examine specific differences in knowledge.

II. Affect

Lack of knowledge regarding genetic testing may cause serious emotional difficulties for those undergoing testing. Poor understanding and recall of information provided in genetic counselling may lead to misunderstanding of test results which in turn have been shown to cause undue self-stigmatization, anxiety and depression for some tested individuals (Marteau, 1989, 1992; Roberts, 1990; Alper et al., 1994). Moreover, if the general public is also

uninformed there is a dangerous potential for stigmatization and discrimination against those found to be carriers (Science Council of Canada, 1991; U.S. Congress, 1992; Markel, 1992; Wilfond and Fost, 1990; Roberts, 1990). On the other hand, if widespread screening programs are implemented with clear counselling objectives, the genetics community can effectively provide genetic services to those who request it. The Sickle Cell Anemia and Tay-Sachs screening programs of the 1970s are ideal examples of the relationship between thorough genetic counselling and negative affect resulting from testing.

The Sickle Cell Anemia trait is an autosomal recessive disorder most prevalent amongst American blacks with an incidence rate of 1 in 625 and a carrier rate of 1 in 13 (Science Council of Canada, 1991). This potentially fatal disease produces an abnormal type of haemoglobin which inhibits blood circulation (Kenen and Schmidt, 1978). The discovery of the Sickle Cell Anemia marker was met with great enthusiasm in the U.S. which promptly lead to widespread population testing for sickle cell anemia carriers (Roberts, 1990). Seventeen states hastily mandated that all African Americans be carrier screened, while some went so far as to make testing a pre-requisite to school admission or issuance of a marriage licence (Wilfond and Fost, 1990). In their zeal to implement population screening, health officials failed to adequately inform the general public on the disease, carrier test and possible impact of the results. Consequently, extensive stigmatization and anxiety ensued as individuals who were found to be carriers also mistakenly believed that they were affected by the disease (Roberts, 1990). Confidentiality had also been breached allowing some public and private sector agencies to discriminate against carriers by denying them employment and/or life insurance (Wilfond and Fost, 1990). To compound these

problems, prenatal screening was not yet available, therefore the only preventative measure available to prospective parents was to abstain from having children. This suggestion arose suspicions of racism and eventually lead to legal charges against the state (Roberts, 1990).

Tay-sachs is an autosomal recessive disorder which is common amongst Ashkenazi Jews where 1 in 3600 infants are affected and 1 in 30 individuals are carriers (Science Council of Canada, 1991). Tay-Sachs is a degenerative disorder that affects the neurological system, causing blindness, mental retardation, and death in early childhood (Kenen and Schmidt, 1978). In contrast to Sickle Cell Anemia screening, testing did not start until the community and religious leaders had been sufficiently informed such that they could serve as additional educators to the public. Consequently, the public had a solid understanding of the disease, its inheritance and their carrier risks prior to testing. Therefore, there was minimal confusion regarding the purpose or the results of the test. In addition to proper counselling, the Tay-sachs program was successful because (a) screening targeted individuals of child-bearing age who have been shown to be highly motivated for this type of testing (Abramovsky, Godmilow, Hirschhorn and Smith, 1980; Emery, Raeburn, Skinner, Holloway and Lewis, 1979); (b) testing took place at convenient times and places for the target group (e.g., in synagogues during off-hours such as Sunday afternoon); and finally, (c) prenatal testing for Tay-Sachs was available (Roberts, 1990; Wilfond and Fost, 1990).

The Genetics Community has heeded warnings for genetic discrimination, stigmatization and psychosocial sequelae as evidenced by the Sickle Cell Anemia Screening disaster and

other genetic screening programs (U.S. Congress, 1992). As well, elements of the Tay Sachs screening program which contributed to its success have been recognized. CF researchers acknowledge that "the emergence of increasingly powerful scientific and diagnostic tools such as DNA probes, will not allow clinical geneticists to avoid the social implications of human genetics. In our view, medical geneticists need to consolidate their best insights of the past, so that they can be prepared to contribute to the development of improved and informed ethical guidance for the complex problems of the future" (Wertz and Fletcher, 1988, p.817). In line with this concern, psychosocial genetics has become one of the fastest growing bodies of medical genetics research (Harper, 1993).

Historical examples of stigmatization resulting from genetic testing has provided insight into psychosocial issues which are unique to DNA predictive testing. Research in this area has outlined the distinct psychological consequences for autosomal dominant gene disorders (i.e., affected heterozygotes) versus recessive gene disorders (i.e., asymptomatic heterozygotes). Obviously, DNA predictive testing for dominant gene disorders has direct health implications for the client. For example, Huntington's disease is a dominant gene lethal progressive brain disorder which causes choreiform movement disorder, dementia and affective disturbances at around age 40 eventually leading to death by age 55 (Codori and Brandt, 1994). In anticipation of the discovery of DNA markers, health care providers actively debated the pros and cons of offering this insidious predictive information in the absence of a cure. Researchers feared that positive test results could lead to depression, suicide, family turmoil, divorce and survivor guilt (Kessler, 1987; Kessler, Field, Worth, and Moshbarger, 1987). Also, those found to carry the gene might be discriminated against

by insurance companies or employment agencies. In addition, Marteau (1989) warns of the possible psychological effects resulting from false positives of dominant gene genetic testing. She found that even when individuals are reassured that they do not carry the gene - after they had been falsely informed that they did carry it, they are reported to be depressed and have a lower state of general health when compared to a normative sample. Marteau (1989) explains, 'once the seeds of doubt have been sown they seem to be difficult to remove'.

On the other hand, test results may give clients the opportunity to plan for their future, reconsider their family planning and end the upset and worry associated with not knowing their genetic risk (Codori and Brandt, 1994). In fact, subsequent studies have found that individuals who have undergone testing report that, despite feelings of worry, guilt and disappointment, they do not regret their decision to be tested and indicated that the benefits of testing outweighed the drawbacks (Codori and Brandt, 1994; Tibben, Vliss and Niermeijer, 1990). Moreover, longitudinal studies have found that those who test negative show significant progressive decreases in psychological distress associated with testing. Whereas, those who test positive do not show any increase or decrease in their distress over a 1 year period (Wiggins et al., 1992). Thus, it appears that these recent findings may allay the substantial fears of those opposed to DNA testing for Huntington's disease. Nonetheless, it is important to note that the views and reactions of participants in these studies may not be representative of the Huntington's population as they had all voluntarily elected to undergo predictive testing. Therefore, it remains unknown why some affected individuals did not pursue testing and, in particular, what their perceived affective reactions to a positive test result might be.

Past carrier testing programs for recessive gene disorders (such as Sickle cell anemia and Tay-Sachs) have forced the medical community to recognize that genetic breakthroughs must be combined with solid social support. Thus, much of the recent research on CF carrier testing has focused on possible negative affect resulting from testing from the perspective of individuals and couples undergoing testing. Studies examining the psychosocial sequelae of carriers has unequivocally found that although positive test results initially evoke feelings of anxiety and worry, they quickly subside. Two studies conducted in Montreal high schools have reported modest anxiety amongst youth who received positive test results, however anxiety had dissipated one year after testing (Kaplan, Clow and Scriver, 1991; Lippman-Hand, Perry, Mandel and Cartier, 1985). Similarly, general population adults tested at a health clinic reported that receiving positive test results caused initial surprise, anxiety, worry and depression, but eventually dissipated after three to six months (Bekker et al., 1994; Watson, Mayall et al., 1992).

Studies examining affective changes amongst pregnant women in the general population undergoing CF carrier testing have also found decreases in negative affect, however decreases in anxiety appear to be contingent on their spouse's negative test result and not on the passage of time (Mennie et al., 1992; Livingstone et al., 1994; Miedzybrodzka et al., 1995). In addition, it appears that levels of anxiety and inadequacy are further elevated during the time in which their partner is awaiting his test result (Mennie et al., 1992). This peak in anxiety demonstrated by both partners is avoided in "Couple Screening" programs (Wald, 1991) where prospective parents are given their combined risk estimate of having an

affected child. In couple screening, both partners provide DNA samples, however, only one sample is tested initially. If the test is negative, the couple is given a risk of 1 in 9000 of having an affected child. If the test is positive, then the partner's DNA sample is carrier tested and the *couple's* risk is further refined. Because individual carrier test results are unknown, members of the couple are never left in the state of uncertainty which may cause interim anxiety and worry (Livingstone et al., 1994; Miedzybrodzka et al., 1995).

In sum, psychosocial research has taken a prospective view of changes in affect due to carrier testing. By examining the short term (Watson, Mayall et al., 1992; Bekker et al., 1994) and long term psychological reactions (Evers-Kiebooms et al., 1994) of those who have undergone testing, the genetics community has been reassured that genetic testing does not cause any lasting psychosocial consequences. Unfortunately, these findings yield limited insight as to the relationship between affect and decisions to be carrier tested. When considering genetic testing decisions, researchers have yet to address the potential for anticipated anxiety or negative affect to act as a deterrent to testing. For example, if one believes that receiving a positive test result will lead to feeling of anxiety and depression, it is possible that they will not seek out testing. To date investigators have not explored the hypothetical emotional reaction to receiving a positive carrier test result and its relation to testing decisions.

Consequently, the present study contrasted the anticipated affective reactions of individuals who had not yet been carrier tested with the actual reactions of previously tested individuals to determine (a) if individuals who have *not* been carrier tested have a realistic view of the

psychosocial sequelae involved with finding out one is a carrier and (b) how their view may affect their subsequent carrier testing decisions. In addition, to address the findings of previous research, clinical affect measures of depression and anxiety were administered to investigate if already tested members of the high risk population demonstrate residual negative affect 6 months to 5 years after testing.

III. Attitudes

After the CF gene was cloned, attitudes towards CF carrier testing became a popular topic in CF genetic screening research. In keeping with the population screening debate, researchers have attempted to assess the opinions of high risk and general populations regarding CF carrier testing. Overall, the findings indicate that both groups appear to approve of the provision of CF carrier testing. Acceptance rates of CF carrier testing amongst the high risk population range from 79% to 100% (Watson, Williamson et al., 1991; Watson, Marchant et al., 1992; Conway, Allenby and Pond, 1994; and Miller and Schwartz, 1992). Similarly, 75% to 90% of the general public feel that carrier testing should be available (Cobb, Holloway, Elton and Raeburn, 1991; Watson, Williamson et al., 1991; Ten Kate and Tijnstra, 1989; Williamson et al., 1989; Decruyenaere et al., 1992; Clayton, et al., 1996). However, realizing that attitudes towards testing for others may not translate to individual's attitude towards testing for themselves, investigators have further examined attitudes towards testing by asking participants to indicate their personal view of carrier testing for their own reproductive information. Again, the high risk population appears to highly regard carrier testing as 74% to 91% would consider testing for themselves (Denayer, et al., 1992; Wolff et al., 1990; and Watson, Williamson et al.,

1991). In contrast, general population surveys have reported that only 54% to 77% would request testing for themselves (Watson, Williamson et al, 1991; Ten Kate and Tjijmstra, 1989; and Decruyenaere, et al., 1992). Therefore, notwithstanding the fact that the general population feels that carrier testing should be offered, fewer report that they would actually take up the offer for themselves.

Unfortunately, it has not yet been established why fewer of the general population would seek testing for themselves. Attitudinal studies have typically asked some form of the questions, "Do you think CF carrier testing should be available to those who want it?" and/or "Would you consider being carrier tested for CF?" Researchers have yet to examine views on perceived benefits of testing such as, increased family planning options, gaining peace of mind, or ending the uncertainty surrounding their carrier status, or the perceived drawbacks of carrier testing such as, testing would make me worry unnecessarily, "ignorance is bliss" or its best not to meddle with God's plan.

In addition to the lack of detail in past attitudinal surveys, very few studies have specifically examined the views of high risk relatives, not including Obligate Carriers and CF patients (Wolff et al., 1990). In fact, only two attitude studies have investigated this subset of the high risk population (Denayer, et al., 1992; Wolff et al., 1990), whereas three studies have been conducted with Obligate Carriers (Watson, Marchant et al., 1992; Conway, et al., 1994; and Miller and Schwartz, 1992) and one with affected adult CF patients (Conway, et al., 1994). Although these initial attitude studies have consistently shown that most high risk relatives are in favour of testing, it is important to specifically assess their perception of

the advantages and disadvantages of carrier testing of those high risk relatives who are currently targeted by testing programs across North America. It can also be argued that views of the Obligate Carriers and adults affected with CF are distinct as they are less likely to personally benefit from carrier testing.

In sum, attitudinal research in CF Carrier Testing has been limited for two reasons. First, research questions have narrowly focused on the intention of high risk and general populations to seek carrier testing. Therefore, there is little evidence which specifically explores possible advantages and disadvantages of CF carrier testing which may have contributed to their view. Second, previous attitudinal research has mostly surveyed the opinion of the general population. As a result, the attitudes of those who may currently benefit from testing (i.e., high risk population) have been neglected. In response to these shortcomings, the present study closely assessed the views of both high risk and general population individuals regarding possible pros and cons of carrier testing and how they may affect carrier testing decisions.

IV. Preferences

Knowledge barriers, perceived and actual affective consequences, attitudes and self perceived risk explore the question “who goes for CF carrier testing?” Examination of these factors will lend understanding to the *process* of carrier testing decisions. Correspondingly, in order to evaluate “why people go for testing” it is important to assess their preference for possible *outcomes* of testing. Outcomes of CF carrier testing can be conceptualized along a continuum starting with the actual carrier test result, then prenatal

test result, and finally, reproductive outcomes (e.g., abortion of a fetus affected with CF). In contrast to the previous section which outlined the attitudinal research for CF carrier screening, the following sections discuss the measurement of less tangible and more long-term outcomes associated with actual reproductive decisions resulting from CF carrier testing.

Research assessing views towards prenatal testing have not yet been thoroughly examined. Nonetheless, previous findings indicate that high risk and general population individuals have positive attitudes towards prenatal testing. Specifically, when asked a general question assessing their approval of the procedure, acceptance rates ranged from 56% to 94% in the high risk population (Denayer, et al., 1992; Wolff et al., 1990; Watson, Williamson et al., 1991; Kaback, et al., 1984; Watson, Marchant et al., 1992; Wertz, Janes et al., 1992; Conway et al., 1994; Miller and Schwartz, 1992; and Evers-Kiebooms et al., 1990) and 75% to 96% in the general population (Cobb, et al., 1991; Watson, Williamson et al., 1991; Decruyenare, et al., 1992; and Watson, Mayall et al., 1991). However, upon closer examination, framing effects were evident such that when individuals are asked their approval of prenatal testing - without mention of future family planning or pregnancies - they tend to report favourable views ranging from 73% to 92% acceptance amongst high risk relatives (Denayer et al., 1992; Watson, Williamson et al., 1991; Watson, Marchant et al., 1992; Al-Jader et al., 1990; Conway et al., 1994) and 86% to 96% in the general population (Cobb et al., 1991; Watson, Williamson et al., 1991). However, when Obligate Carriers who are planning on having children are asked to imagine being in a pregnant state, only 58% report that they would opt for prenatal diagnosis (Wolff, et al., 1990; and

Evers-Kiebooms et al., 1990). Similarly, only 56% of high risk relatives (excluding Obligate Carriers and affected adults) who were currently planning a family would go for prenatal testing (Wolff, et al, 1990). The general population also demonstrates this decreasing trend as 75% reported they would use prenatal diagnosis when imagining that both parents were carriers (Decruyenaere et al., 1992). Therefore, it is not clear from previous research that those with a positive attitude towards prenatal testing will actually undergo testing once in the pregnant state.

In the same way, studies investigating attitudes towards abortion have found that the family planning situation in which participants were placed has a significant influence on their likelihood to abort for CF. Framing some form of the question, "would you have an abortion to avoid having a child with CF?" in actual reproductive situations leads to a lower likelihood of terminating an affected fetus. Specifically, two high risk studies found that only 26% of those currently planning to have children (Wertz, Janes et al., 1992) and 28% of those imagining that they (or their partner) were pregnant (Wolff et al., 1990) were willing to terminate a CF fetus. Yet, when high risk individuals are asked about their likelihood of abortion without any mention of pregnancy or family planning, 58% and 44% (Watson, Williamson et al., 1991; Watson, Marchant et al., 1992, respectively) indicate that they would abort for CF. The same pattern is found amongst general population studies as only 25% of pregnant women would abort for CF (Watson, Mayall et al., 1991), in contrast 62% of general population individuals who indicate that they would abort for CF (Watson, Williamson et al., 1991).

In sum, examination of the previous descriptive research which has investigated the likelihood of prenatal testing and abortion must be interpreted with caution. If research questions are posed without any reference to family planning stages, then acceptance rates for genetic testing and abortion may be inflated.

Past CF research has typically focused on three areas: 1) attitudes towards carrier testing; 2) prenatal testing; and 3) abortion with the assumption being that those who have a positive attitude towards carrier testing will opt for prenatal testing and abortion, if necessary. As a result, there is little information regarding other reproductive options such as choosing not to have any biological children or letting nature take its course and risk having a child with CF. Only a few studies have examined the likelihood of not having any children. Overall, 36% to 45% of both high risk and general population individuals indicated that they would choose not to have any children, regardless of family planning status (Watson, Williamson et al., 1991; Decruyenaere et al., 1992; and Ten Kate and Tijnstra, 1989). In contrast, 64% of Obligate Carriers surveyed indicated that they would choose not to have any more children (Watson, Marchant et al., 1992). Interestingly, only one study has examined having a CF child as a specific reproductive option. Unfortunately this study only surveyed Obligate Carriers who are clearly a unique group in terms of their views towards having and caring for a child with CF. They found that 44% of Obligate Carriers would continue with an affected pregnancy, 28% would abort, and 28% were undecided (Wertz, Janes et al., 1992).

Thus, previous research on the likelihood of seeking out particular reproductive outcomes is biased by the framing of questions in relation to family planning status. In addition, very few studies have examined people's views on other possible reproductive options such as having a child with CF or choosing not to have any children. In response to these shortcomings, the present study examined the most common reproductive outcomes resulting from CF carrier testing by placing individuals within hypothetical scenarios which included: birth of a healthy baby, abortion of a CF fetus, birth of a baby affected with CF, and choosing not to have any children. In order to determine the desirability of these outcomes, the present study elicited "preference" values, where preference is defined as "the level of satisfaction or desirability that a person associates with a particular health state (e.g., chronic angina), treatment process (e.g., hemodialysis), duration of treatment or illness, or level of participation." (Health Services Research Group, 1992, p.859). Assuming that preferences are a measurable construct (see James, 1993; Frisch and Clemen, 1994), preference values such as "utilities" (see below) may provide an estimate of the individual's likelihood of using, or not using, their test result towards a particular reproductive outcome.

Utility Theory and Rationale

The present study elicited specific preference values called utilities. Utilities are based on a theory of rational decision making under conditions of uncertainty. Briefly this theory proposes that if a person's choices conform to a certain set of axioms developed by von Neuman and Morgenstern, then they will maximize their expected utility for an outcome.

Use of utilities in health related research has gained more popularity in recent years. Utilities have been applied to the review of prenatal testing such as chorionic villus sampling and amniocentesis (Heckerling and Verp, 1991) and hormone replacement therapy (Holmes et al., 1987). However, most of its applications have been in terms of economic evaluations such as phenylketonuria (PKU) neonatal screening (Bush, Chen and Patrick, 1973), tuberculin screening (Bush, Fanshel and Chen, 1972), in vitro fertilization (Goeree, Labell and Jarrell, 1993), and cholecystectomy (Bass et al., 1994). Nonetheless, the use of utility theory in Genetic testing is both novel and unique. The following sections describe the methods of utility assessment used in the present study and introduces some new measurement issues which pose distinct challenges to eliciting preferences such that they are intuitive with respect to their clinical application.

While utilities may have become more common place in medical decision making literature, controversy over its use in medical decision making and health related policy support has grown along side. Proponents of utility theory often note that utility scores are generalizable across disorders because they are measured on a common scale (ranging from perfect health (1.0) to death (0.0)). Therefore, they are ideal for costing and policy investigations which must decide how to allocate the diminishing pool of health care dollars to different health care areas (Kaplan, 1993; Steinwachs, 1989). Investigators have also claimed that utility values may be easily compared across evaluators such as patients, relatives of the patients, and health care providers (review Feeny and Torrance, 1989). Moreover, some utility advocates assert that utilities of individuals imagining hypothetical health states are similar to those utilities of those actually living with in the disease state

(Feeny and Torrance, 1989). Finally, the fact that utilities are based on the von Neumann and Morgenstern theory of rational decision making under uncertainty (von Neumann and Morgenstern, 1947) has also maintained its credibility amongst many health researchers.

In contrast, opponents of utility theory state that utility measurements are not highly precise. Standard deviations greater than 0.20 are commonly reported, yet, at the same time, changes in utilities of ± 0.10 have been proposed to be clinically significant (Feeny and Torrance, 1989; Deyo and Patrick, 1989). Some recent studies have not supported the generalizability of utility values as hypothetical estimates of a health state are often perceived as worse than those patients who have/are experienced the state (Lomas, Pickard and Mohide, 1987; Holmes et al., 1987). Also, in terms of administration, utility assessments are highly structured which necessitates detailed interviews conducted by highly trained personnel (Feeny and Torrance, 1989). In addition, certain methods of utility elicitation have been described as cognitively taxing (Feeny and Torrance, 1989). More importantly, the axioms on which the theory was built have not only come under fire, but have been shown to be frequently violated (Fishburn, 1988; Bell and Farquhar, 1986).

Given the growing popularity of utility measures in health care, it was proposed to explore the appropriateness and applicability of utility theory in the context of genetic testing. Utility measurement appeared to be suited to preference measurement for genetic testing outcomes for several reasons. First, it involves decision making under conditions of uncertainty. Second, it incorporates the concept of risk when assessing choices. Third, it may serve as a patient decision aid as it forces clients to consider specific reproductive

outcomes. In terms of the method of utility measurement, there is no “gold standard” for eliciting patient and public preferences for disease health states. Yet, elicitation of utilities using the Standard Gamble method (see below) has become increasingly popular because it is based on von Neumann and Morgenstern’s solvability axiom (Furlong, Feeny, Torrance and Barr, 1990). Thus, despite the fact that the use of utilities in the present study was exploratory, it was proposed that these specific preference values might provide a better indication of what reproductive options individuals are interested in pursuing and how their preferences for these outcomes might affect their decision to be carrier tested.

Utility Measurement

According to von Neumann and Morgenstern’s theory there are 5 axioms that define rational behaviour (see Torrance and Feeny, 1989; Dawes, 1988; Yates, 1990). First, when comparing pairs of alternatives (e.g., A_1 vs. A_2) the individual must either prefer one alternative to the other or is indifferent between them. Second, the individual’s preferences and indifferences are transitive (e.g., A_1 is preferred to A_2 , and A_2 is preferred to A_3 , then A_1 is preferred to A_3). Third, compound lotteries (i.e., lotteries in which the pay off is another lottery) may be broken down into simple lotteries using probability calculus. Fourth, if two lotteries involve the same two alternatives, then the one in which the more preferred alternative has the higher probability of occurring is the preferred lottery. Fifth, if A_1 is preferred to A_2 , and A_2 is preferred to A_3 , then there exists a lottery involving A_1 and A_3 such that the person is indifferent between that lottery and receiving A_2 with certainty. Assuming that individuals follow these axioms, they are said to maximize their expected utility for desired outcomes when faced with decision making under uncertainty.

For the present study, outcomes of interest were derived from a decision tree (Figure 3). In this case, the decision tree branched out into the various test decisions, test outcomes, reproductive decision making and reproductive outcomes related to CF Carrier Testing. Reproductive options taken from the decision tree were then described in hypothetical scenarios called “health states”. Five health states specific to CF carrier testing were developed (Appendix A). Three health states examined reproductive outcomes where the participant was asked to imagine: (a) the birth and lifelong care of a child with CF, (b) choosing not to have children, and (c) abortion of a fetus prenatally diagnosed with CF. In contrast, two additional scenarios described carrier test results where: (a) both partners are identified as CF carriers with a 1 in 4 chance of having a child with CF; and (b) one partner is a CF carrier (i.e., mutation detected) and one partner has a low but not zero risk of being a carrier (i.e., mutation not detected).

Insert Figure 3 about here

In accordance with the trend in the literature, the present study elicited utility values using rating scales and the standard gamble method (Furlong et al., 1990). However, as it has been argued that ratings do not provide cardinal (interval) utility measures, the present study elicited ratings using a visual analogue scale more as a means to familiarize the participant with the health states than as a measurement of preference (Furlong et al., 1990). After

participants had ordered the health states according to their relative desirability, anchors of the scale (i.e., the best and worst case scenarios) were used in the presentation of the Standard Gamble lotteries.

The Standard Gamble method involves two hypothetical choices, A and B. Choice A involves a gamble between two outcomes, perfect health occurring at probability (p) versus death occurring at probability ($1-p$). Choice B involves an intermediate health state which falls between perfect health (1.0) and death (0.0) and occurs with 100% certainty. Participants must choose between Choice A and Choice B at varying probabilities until they are indifferent between the two. The probability (p) at this "indifference" point represents the utility score for the health state in choice B (Furlong et al., 1990; Feeney and Torrence, 1989; Torrance, 1987). For example, if one is indifferent between a gamble which includes a 90% (p) chance of perfect health and a 10% ($1-p$) chance of death in Choice A with a 100% certainty of lifelong daily dialysis in Choice B, then their utility for dialysis is .90.

Traditionally, the utility scale ranges from perfect health to death. This continuum is appropriate for disorders which directly affect the health of the participant such as heart disease or breast cancer. In these cases, patients must often weigh increments in quality of life due to new treatments or procedures with the likelihood of death. In contrast, carrier testing decisions do not impact on the physical health of the individual undergoing testing as carriers are asymptomatic. Instead, carrier testing may have implications for their quality of life as *caregivers* of a sick child and the quality of life that child. Therefore, given that

utilities for carrier testing reflect the perspective of the parent regarding the impact of the disease on the child, gambles which involve the conventional health self/death anchors do not make clinical sense. That is, it is highly unlikely that a parent would choose any probability of their own death over the birth of a sick child. As a result, the present study modified the approach to incorporate health states specific to reproduction (such as abortion of a CF fetus) by redefining the utility scale such that the upper limit represented the birth and care of a healthy baby (1.0) and a lower limit represented the birth and care of a baby with severe physical and mental impairments (0.0). This revised scale was designed to reflect the clinical equivalent of the conventional scale for health states involving a "third person" (i.e., my baby's health). Similar modifications to the utility scale have also been performed in previous decision analysis investigations which examine preferences for prenatal testing procedures (i.e., amniocentesis and chorionic villus sampling) (Pauker and Pauker, 1987, 1977; Heckerling and Verp, 1991). In these studies scales ranged from having an unaffected child (1.0) to having an affected child (0.0).

Similarly, utilities for two health states specific to genetic test information were also elicited. Therefore, the utility scale was again modified such that the upper limit was perfect health and the lower limit was an anxious/depressed state. Eliciting these carrier test information health states on this scale more closely reflected the clinically relevant gamble.

In summary, previous research has narrowly focused on abortion as the primary reproductive outcome resulting from CF carrier testing. Clearly, other reproductive outcomes need to be assessed as attitudinal studies have reported low acceptance of abortion

amongst the high risk and general populations. The present study elicited utilities in order to evaluate the preference values of three common reproductive outcomes (i.e., have a baby with CF, abort a fetus with CF, and choose not to have any children) and two reproductive outcomes (i.e., one partner is a carrier and both partners are carriers). It was proposed that utilities for these health states would provide a more accurate indication of an individual's likelihood to seek out carrier testing as well as how they may use their test results in their future family planning.

RESEARCH OBJECTIVE:

As discussed in the preceding sections, past research in CF carrier testing has concentrated on assessing the demand for testing from a population perspective. That is, researchers have focused their interests on the general population in order to evaluate demand for testing with the intent of developing a suitable screening program given the imperfect detection rate and the threat of psychosocial consequences. Within this rush for general population pilot testing, research specifically examining the high risk population were set aside as it was expected that test participation amongst this group would be high. However, Surh et al.'s (1994) findings clearly demonstrate that carrier testing was not as widely received as the medical community expected as a mere 10% of eligible high risk relatives presented for carrier testing.

Overall, review of the literature suggests two areas in need of attention in CF carrier testing research. First, at the time this project was originally conceptualized, Surh et al. (1994) were the only investigators that had assessed actual test uptake amongst the high risk

population. The purpose of their study was to investigate *who* was presenting for testing (i.e., their relationship to the affected individual). The present study expanded upon this early research to assess reasons *why* high risk individuals choose to be, or not to be, carrier tested and *how* they may (or may not) use their test results in their future family planning. Second, previous research has limited their investigations to either the general population *or* the high risk population (which has usually been comprised of Obligate Carriers). Therefore, researchers have not specifically compared the views of these groups. If carrier testing programs may soon be opened up to the general population, similarities and/or differences between the groups may dictate how, or if, carrier screening should be offered. Specifically, given the findings of Surh et al. (1994), if high risk relatives who are (a) currently targeted by screening programs and (b) at higher risk for being carriers demonstrate poor participation in testing, then it is possible that screening programs targeted at the general population may also demonstrate low demand. Therefore, the present study contrasted these groups in order to assess their respective views on carrier testing as well as their carrier testing decisions.

The present study examined the influence of factors in the Genetic Testing Decision Making Model on carrier testing decisions (Surh et al., 1992). This model suggests that decisions to undergo carrier testing are influenced by: 1) higher levels of knowledge regarding CF and CF carrier testing; 2) less negative affect associated with testing; 3) more favourable attitudes towards testing; 4) higher preferences for health states which involve avoiding a CF birth (i.e., abortion of a fetus with CF, choosing not to have children, one carrier, and both carrier health states).

These factors were compared amongst the following four groups: 1) *Tested*: comprised a sample of high risk relatives who had previously presented for testing on their own volition in Surh et al.'s (1994) study. 2) *Not-Tested*: comprised a sample of high risk relatives who did *not* go for testing in the earlier study, but were recruited by the present study. 3) *General Population*: comprised a sample of individuals who do not have a prior family history of CF and thus, were not previously carrier tested. 4) *Obligate Carriers*: comprised a sample of parents of children with CF who had been carrier tested in Surh et al.'s (1994) study.

The inclusion of the Tested and Not-Tested groups addressed the issue of demand amongst the high risk population. That is, by contrasting those who previously came in for testing with those who did not, it was possible to explore the influence of knowledge barriers as well as affective, attitudinal and preference factors on carrier testing decisions. Likewise, the inclusion of the General Population group addresses the second issue of demand across the high risk groups and the general population. Comparisons between the two populations were conducted to assess if the expected demand for testing amongst the general population warrants all the attention it has been receiving in the literature.

The rationale for the inclusion of the Obligate Carrier group was more involved. Obligate Carriers were of interest because they comprised the largest segment of the high risk population that had previously come forward for testing. Also, because they were the entry point into many high risk families, it was important to evaluate their views on carrier testing

as they were ultimately responsible for disseminating test information to other high risk family members. Therefore, it is conceivable that their position on the decision making factors may have influenced the views of other high risk relatives - tested or not. At the same time, it was expected that some of the views of the Obligate Carriers may be distinct as they did not come forward for testing to determine their carrier status. Contrary to the other high risk groups, the results of carrier testing for Obligate Carriers may have allowed them to determine whether or not they carried identified CF mutations and therefore, could benefit from prenatal testing. Also, information received from their carrier test may have been sought out for the benefit other family members interested in testing for themselves. It was further expected that Obligate Carriers would have a distinct perspective on preferences for reproductive health states involving the birth and abortion of a baby with CF. Given their extensive experience with the disease, their preferences were predicted to be the most accurate reflection of the quality of life of a child with CF. Yet, at the same time, it was anticipated that their views on abortion were likely to be negative as they are currently caring for a child with CF. In sum, despite the uniqueness of the Obligate Carriers, assessment of the high risk population would be incomplete without accounting for their views.

According to the proposed Genetic Testing Decision Making model and the composition of the groups, the following hypotheses were tested:

Hypothesis 1: Knowledge

It was hypothesized that those with higher levels of knowledge regarding CF and CF carrier testing would be more likely to undergo carrier testing. Therefore, high risk individuals in

the Obligate Carrier and Tested groups, who had previously sought out carrier testing, would demonstrate higher levels of knowledge than the Not-Tested and General Population groups.

Hypothesis 2: Affect

It was hypothesized that those who anticipated high levels of negative affect resulting from a positive carrier test result would be less likely to seek out carrier testing. Therefore, the anticipated affective reactions of the Not-Tested and General population groups would be similar and demonstrate high levels of perceived negative affect. Whereas, the actual affective reactions of the Obligate Carriers and carriers in the Tested group would be similar and demonstrate low levels of perceived negative affect.

It was further hypothesized that the Obligate Carrier and Tested groups would *not* demonstrate elevated levels of anxiety and depression as they had been tested 6 months to 5 years prior to the study. Therefore, they would report normal levels of anxiety and depressive symptomatology similar to the Not-Tested and General Population groups.

Hypothesis 3: Attitudes

It was hypothesized that those with more favourable attitudes towards testing would be more likely to undergo carrier testing. Therefore, high risk individuals in the Obligate Carrier and Tested groups would demonstrate more favourable attitudes towards testing than the Not-Tested and General Population groups.

Hypothesis 4: Preferences

It was hypothesized that those who undergo carrier testing would report higher preferences for health states which involved finding out one's carrier status (i.e., one carrier, both carriers) and abortion of a fetus detected with CF. Conversely, it was expected that those who did not undergo testing would indicate higher preferences for having a child with CF or choosing not to have any children.

Secondary analyses:

It was expected that a certain percentage of the Not-Tested population would opt for carrier testing. Based on Surh et al.'s (1994) previous findings, it was estimated that a small percentage (approximately 10%) of those approached would be tested. As a result, it was proposed to conduct further comparisons of the Not-Tested group to determine if those who requested testing were significantly different on decision making factors from those who did not.

METHODS

Participants:

All participants were of reproductive age (i.e., 18-50 years) as this group has been shown to be the most likely to seek out genetic counselling for their family planning (Abramovsky et al., 1980; Emery et al., 1979). Also, in order to accommodate the English questionnaires and semi-structured utility interview, participants were either English speaking or bilingual.

A total of 265 participants comprised the following four groups:

1. '*Obligate Carrier*' group included 49 parents of at least one child affected with CF who is currently attending either the pediatric (Children's Hospital of Eastern Ontario - CHEO) or adult (Ottawa General Hospital - OGH) multidisciplinary CF clinics. Individuals who met the inclusion criteria were randomly selected from a comprehensive list provided by the clinic administrators.
2. '*Tested*' group included 59 high risk individuals who had been previously carrier tested. Because all DNA testing for the Ottawa-Carleton region is conducted through the Molecular Diagnostic Lab at CHEO, a complete list was available of individuals who had received genetic counselling and carrier testing (via blood sampling) between six months to five years prior to the present study. Individuals who met the inclusion criteria were selected from this list for possible participation in the study.
3. '*Not-Tested*' group was comprised of 98 high risk individuals who had *not* been previously carrier tested. It was proposed that this group would be further sub-divided into two groups, those who opted for testing and those who did not. Due to issues of confidentiality and the concerns of the CHEO Ethics committee, these individuals could

only be recruited via family members who had been previously carrier tested at CHEO.

Therefore, members of the Obligate Carrier and Tested groups were asked to provide the names, addresses and phone numbers blood relatives who met the inclusion criteria and resided within a 2 hour radius of Ottawa. It was stressed that the project was interested in *all* blood relatives, regardless of their intention to be carrier tested.

Obligate Carriers and Tested group members were informed that if the blood relative inquired how the study obtained their personal information, the research assistant would be obliged to disclose their name.

4. '*General Population*' group was comprised of 59 individuals who had no known family history of CF. Names of potential participants were provided by the Medical Records Department at CHEO. General Population participants were matched to the Obligate Carriers such that an unaffected '*General Population*' child was matched on gender and age with an affected '*Obligate Carrier*' child. Also, only parents of children admitted for an acute problem (e.g., fracture) were selected for possible inclusion in this group.

Procedure

As shown in Figure 4, potential participants in all four groups were initially mailed an introductory letter (Appendix B) which outlined the rationale of the study and time commitment required. Approximately one week later, they received a semi structured phone call from a research assistant who provided more information on the study and asked if they were interested in participating (Appendix C). If they chose not to participate, then reasons for refusal were requested. If they agreed to participate, the research assistant arranged for a one hour face-to-face interview to take place at the convenience of the

participant. Participants were also mailed the Genetic Testing for CF Survey which they were instructed to complete at their leisure anytime prior to the interview. The Not-Tested and General Population groups completed form A of the survey (Appendix D), while the Obligate Carriers and Tested groups completed form B (Appendix E). All interviews began with a short description of the study and its purpose followed by the informed consent (Appendix F). Then, Genetic Testing for CF surveys were collected and any questions regarding survey items were answered. Next, measures of depression and anxiety were assessed using the BDI (Appendix G) and STAI (Appendix H).

Insert Figure 4 about here

At this point, the procedure for those who had previously undergone testing (i.e., Obligate Carrier and Tested) varied from those who had not been tested (i.e., Not-Tested and General Population). Since the Obligate Carrier and Tested groups had already undergone genetic counselling and carrier testing 6 months to 5 years prior to the study, they immediately completed the Utility Assessment (Appendix I). At the end of the interview, participants were asked for the names, addresses and phone numbers of blood relatives living in the area and their consent to contact them for the study. These individuals were contacted for possible inclusion in the study.

In contrast, following the administration of the BDI and STAI, the Not-Tested and General Population groups were provided with a 20-30 minute semi-structured genetic counselling session developed by a Clinical Geneticist and Genetic Counsellor at CHEO (Appendix J). The session was designed to ensure informed decision making and covered the following topics: CF disease description, minimal basic genetics, CF genetic inheritance pattern, CF carrier risks, test sensitivity and DNA sampling procedures. Participants' questions and concerns regarding CF and CF carrier testing were answered at this time, however, if they requested further information they were referred to a qualified Genetic Counsellor at CHEO. After genetic counselling, the Not-Tested and General Population groups then completed the Utility Assessment. At the end of the interview, participants in the General Population were posed the hypothetical question, "If carrier testing were available to you right now, would you choose to be tested?" In contrast, members of the Not-Tested population were offered actual carrier testing using a buccal swab procedure (see DNA Sampling and Testing section below). Those who opted for testing signed a DNA consent form (Appendix K). Finally, similar to the Obligate Carriers and Tested groups, Not Tested participants were also asked for names, addresses and phone numbers of other untested blood relatives in the area.

Instruments:

1. Genetic Testing for CF (Survey A and B)

This 23 page questionnaire was developed by Drs. L. Surh and M. Cappelli (1992) to evaluate attitude, affect, knowledge, and behaviours associated with CF carrier testing. The structure and content of the questionnaire was determined by previous attitudinal

questionnaires regarding carrier testing, recent studies, and clinical experience. Survey A (Appendix D) was designed for individuals who had not yet been carrier tested, while survey B (Appendix E) was designed for individuals who had already been carrier tested. Forms A and B are identical with the exception of a few items which are not applicable to individuals who have already been tested. Also, the tense of many questions differ as survey A assesses anticipated reactions and behaviours associated with testing, whereas survey B assesses the actual reactions and use of test results.

Both surveys contain 4 subscales which measure knowledge of CF and CF carrier testing (9 items), affect associated with carrier test results (7 items), attitudes towards carrier testing (9 items) and behaviours following testing (7 items). Scale reliability analysis yielded Cronbach's alphas of 0.75, 0.82, 0.83, and 0.74 for each subscale, respectively. Three specific hypotheses were tested and confirmed in order to measure concurrent validity, (1) anticipated family planning behaviour was correlated with a positive attitude toward genetic screening ($r=0.56$; $p<.001$), (2) individuals reported significantly less pleasant feelings with respect to a hypothetical positive carrier test result scenario than a negative carrier test scenario ($t = 16.08$; $p<.001$), and (3) individuals considering screening had significantly less negative attitudes and more positive behaviours (e.g., encouraging other family members to be tested) when compared with individuals who did not consider testing ($t = 4.52$; $p<.001$ and $t=2.50$; $p<.01$, respectively).

2. State-Trait Anxiety Inventory - STAI

The State-Trait anxiety inventory by Spielberger (Appendix H) is one of the most prevalent

anxiety inventories in the literature. It is comprised of 40 items, 20 which measure state anxiety (i.e., how I feel right now at this very moment) and 20 which measure trait anxiety (i.e., how I generally feel). Two forms of the inventory have been published, form X and form Y. The more recent version, form Y, will be used in the present study. Although the two forms are highly correlated (e.g., 0.96 -0.98 for college norms), form Y is recommended because of its superior psychometric properties. Form Y norms are based on the responses of 1838 working adults of the Federal Aviation Administration (1387 males vs. 451 females). The alpha coefficients for the state and trait scores are reported as 0.93 and 0.91, respectively. Test-Retest of form Y was determined using 357 high school students at 30 days and 60 days. The reliability coefficients for trait anxiety were 0.71, 0.68 for males and 0.75, 0.65 for females, respectively. Coefficients for the state scale were 0.62, 0.51 for males and 0.34, 0.36 for females, respectively (Spielberger, Gorsuch, Lushene, Vagg and Jacobs, 1983).

3. Beck Depression Inventory - BDI

This popular 21-item scale (Appendix G) asks the adult to choose the best description of how they have been feeling over the past 8 days (Beck, Ward, Medelson, Mock and Erlbaugh, 1961). Norms for the BDI are based upon a sample of 529 normal adults. Scores may be classified into four categories, none, mild, moderate, and severe depression. Factor analysis has revealed the following factors, (1) vital depression comprised of fatigability, loss of appetite, somatic preoccupation, weight loss, difficulty sleeping, and loss of libido; (2) self-debasement consisting of self-dislike, sense of failure, expectation of punishment, and guilty feeling; (3) pessimism-suicide consisting of pessimism and suicidal wishes; and

(3) indecision-inhibition comprised of indecision and work inhibition (Beck, 1967). Internal consistency was reported as .86 or .93 with a Spearman-Brown correction (Beck and Beamesderfer, 1974; Beck, 1967; see also Beck, Steer, and Garbin, 1988).

4. CF Utility Assessment

A decision tree illustrating possible processes and outcomes regarding CF carrier testing was developed by Drs. L. Surh and M. Cappelli (1992) (Appendix L). From this tree, five outcomes of interest to the study were selected for the Utility Assessment. Three outcomes involved reproductive consequences including birth of a CF baby (CF Baby), abortion of a CF baby (Abortion) and choosing not to have any children at all (No Baby). The remaining two outcomes involved carrier test results where one partner of a couple is found to be a carrier (One carrier) and both partners of a couple are found to be carriers (Both carriers). These outcomes were subsequently described in hypothetical “health state” scenarios which depicted the outcome and then asked the reader to imagine living the rest of their life in that state.

Five additional health state scenarios were required for the “Standard Gamble” utility assessment method. As described earlier, utilities are usually elicited using the conventional “healthy self - dead self” anchors. However, hypothetical reproductive health states used in the present study (e.g., CF baby) did not put the participant’s physiological health at risk. Instead, health states used in the present study affected the health of the participant’s hypothetical child and the participant’s emotional well-being with respect to their hypothetical carrier status. Therefore, in order to provide realistic lotteries for the Standard

Gamble the anchors of the utility scale were modified such that participants were never gambling with their own life or death (Appendix M). Specifically, participants weighed the reproductive health states against the birth of a healthy child (Healthy Baby) with a physically and mentally impaired child (Very sick baby). Similarly, for carrier status health states the participant gambled against their perfect health (healthy self) with living in an state of anxiety and depression (anxiety/depression).

For ease of understanding and administration, health state scenarios were designed to be comprehensive yet concise. Therefore, all health states were presented on small cards with descriptions in “bullet” form. However, because the morbidity and mortality of CF varies from patient to patient, a CF disease description illustrating the lifespan of the average CF patient (Appendix J) was read by all participants in order to supplement the CF Baby health state scenario. Of note, all written materials used in the utility assessment were reviewed for readability, accuracy and sensitivity (i.e., political correctness) by a focus group comprised of 8 parents of CF children and 4 adult CF patients as well as staff members of the CF clinics.

Prior to doing the Standard Gamble, participants were instructed to carefully read through each of the Health State descriptions, imagine spending the rest of their life in that state, then rate the health state on the “Feeling Thermometer” (see Appendix N for design specifications) which is essentially a visual analogue scale ranging from 0-100. This was done so that the participant could familiarize themselves with the health state scenarios and their relative preference for each state.

Finally, utility values were elicited by the Standard Gamble method using a visual aid called the “Chance Board” (see Appendix O for design specifications). The Chance Board presents participants with two choices, Choice A and Choice B. In Choice A, there is a lottery between the highest rated health state scenario with probability (p) of occurring and the lowest rated scenario with a probability of $(p-1)$. In Choice B there is no lottery - instead, if chosen, it is 100% certain to occur. Participants are presented with varying probabilities of these health states and must gamble between the two choices until they are indifferent. For example, assuming that participants rated the reproductive health states such that Healthy Baby was the highest and Very sick baby was lowest, they would be presented with a gamble similar to that illustrated in Appendix P.

DNA Sampling and Laboratory Tests

DNA sampling for the Not-Tested group involved a painless buccal swab procedure. Participant's handled all the unsealed test materials and performed the procedure on themselves in order to avoid sample contamination. Using a sterilized cotton swab (q-tip) participants were asked to rub the inside of their cheeks for approximately 45 seconds to collect buccal cells, then place the swab in a sterilized eppendorf tube and seal it tightly. The research assistant then delivered the sample to the Molecular Diagnostic Lab at CHEO for testing. Test results were provided to the research assistant approximately eight weeks later by a genetic counsellor. It was the research assistant's responsibility to disclose the test result to the participant first over the phone and then in a detailed letter mailed to their home. The research assistant also met with the participant two weeks later for follow-up.

In addition, with the participant's permission, their family physician was also notified by letter which included the DNA laboratory report.

Actual DNA testing entailed conducting seven separate PCR reactions (Eisenstem, 1990) to test for the following CF mutations: $\Delta F508$ (Kerem et al., 1989), $\Delta I507$ (Kerem et al., 1990), three exon 11 mutations (G551D, G542X, S549N) (Cutting et al., 1990), three exon 4 mutations (621+1 G>T, R117H, 55delA, 711+1G>T) (Zielenski et al., 1991), as well as haplotyping (Beaudet, Feldman, Fernbach, Buffone and O'Brien, 1989) with XV2C and KM19. The inclusion of mutations for the French Canadian population (Rozen et al., 1991) reflected their representation of 40% within the Ottawa-Carleton catchment population. Overall carrier detection in this population has been 90% with both haplotype and mutation analyses (Surh et al., 1994).

RESULTS:

A total of 344 individuals were approached to participate in the study of which 265 accepted, yielding an overall participation rate of 77%. Within the groups, fewer of the Obligate Carriers (65%) participated when compared to the Tested (85%), Not-Tested (84%) and General Population (72%). This may be due to the fact that Obligate Carriers in the Ottawa-Carleton region have been widely surveyed and are frequently approached for research studies. Overall, the majority of individuals who did not participate indicated that they did not have enough time, whereas only 10% (8/88) of individuals approached expressed that they were not interested in participating in the study.

In terms of recruitment for the Not-Tested population, preliminary analyses revealed that only 13% (27/206) of the entire high risk population did not provide names of family members. Of these individuals, 63% (17/27) stated that their relatives lived outside a 2 hour radius of Ottawa and thus were ineligible for the study, 19% (5/27) preferred to contact their relatives directly and provide the study's phone number, 7% (2/27) stated that their relatives would not be interested, 7% (2/27) indicated that CF was a taboo subject and 1% (1/27) refused to provide any names. In depth analyses of who provided names, how many names, their relationship to the affected individual, and their decision to participate are beyond the scope of this paper.

Interviews for the study were arranged at a time and place of the participant's convenience. Consequently, the vast majority of home visits (approximately 95%) took place in the evening.

at the participant's home

Family Planning and Demographics

The groups did not differ on gender, level of education, language and income (Table 1). Yet, strong similarities between the Obligate Carriers and General Population were found on other variables. Chi-square tests indicated that members of both groups already had children, were likely to be married and were older than the Tested and Not Tested groups. These similarities may be attributed to the recruitment procedure for General Population participants. As described earlier, members of the General Population were selected such that their child matched the age and gender of a corresponding affected child belonging to a member of the Obligate Carrier group (see methods). Thus, the Obligate Carrier and the General Population groups would be similar in terms of age, parity and marital status.

Also, there appeared to be more variability in the types of religions amongst the Obligate Carrier and General Population groups, whereas the Tested and Not Tested groups were predominantly Catholic. This may reflect the fact that the prevalence of CF is higher in the French Canadian population (Rozen et al., 1991; Cloutres et al., 1993) which is also known for its strong affiliation with the Catholic religion.

Examination of demographics which discriminated between the groups revealed that there was a significant relationship ($\chi^2(2, 250) = 3.36$; $p = .37$) between the participant's religion and their attitude towards testing such that those who were separated or divorced ($n = 10$) were more likely to have a positive attitude towards testing ($\bar{X} = 40$, $sd = 3.3$) than those

who were married ($n=214$) ($X=36$, $sd=5.2$). However, due to the large difference in sample sizes, the effect of religion on attitudes could not be determined.

In addition, the family planning variable which inquired about plans for having children within the next two years had a significant relationship on affect and attitude subscales. Specifically, those who were planning on having children in the next two years ($n=162$) were more likely to perceive negative affect associated with being a carrier ($X=22$, $sd=4.9$) than those who were not ($n=42$) ($X=19$, $sd=4.5$) ($t(202)=2.95$; $p=.004$). Similarly, participants who were planning more children ($n=201$) ($X=36$, $sd=5.1$) had a significantly less favourable attitude towards testing ($t(252)=-2.35$; $p=.019$) than those who were not planning on having children ($n=53$) ($X=37$, $sd=5.1$). Consequently, this family planning variable was entered into the overall affect and attitude subscale analyses as a covariate.

Insert Table 1 about here

1. Knowledge of CF and CF Carrier Testing

The hypothesis that the Obligate Carrier and Tested groups would demonstrate higher levels of knowledge when compared with the Not-Tested and General Population groups was confirmed. The overall percentage correct score was significantly different across the groups ($F(3, 261) = 59.04$, $p < .000$). Post-hoc multiple comparisons revealed that mean knowledge scores were also significantly different between each of the groups such that the

Obligate Carriers performed the best, followed by the Tested group, the Not Tested group, and the General Population (Tukey α , $p < .05$) (Table 2). Individual knowledge items were also descriptively evaluated using Chi-square tests to assess participants' specific understanding of the CF Disease Process, CF Carrier Test and CF Carrier Risks. Significant differences were found on all items using a conservative alpha level to account for multiple tests and reduce experimenter wise error such that the conventional level of .05 was divided by the total number of questions within each of the three categories (χ^2 (3, 265); $p < .01$). It is noteworthy that the General Population consistently had the lowest number of participants responding correctly to each of the knowledge items.

Insert Table 2 about here

II. Affect

In contrast to the hypothesis that the Not-Tested and General Population groups would demonstrate high levels of anticipated affect, statistically significant differences were found between the hypothetical reaction of the General Population and Not Tested groups (Table 3). The findings indicated that members of the General Population were more likely to react with negative affect than those in the Not-Tested group (ANCOVA: $F(1,144)$ 23.2; $p < .000$). Of note, univariate analyses revealed a significant relationship such that those individuals who already had children were more likely to demonstrate negative affect when compared to those without children ($t(202)=2.93$; $p < .01$). This covariate (i.e.,

have children vs. do not have children) was not found to be significant in the overall ANCOVA ($F(1,144) = 0.572$; ns). Individual items of the affect subscale were also descriptively analysed by collapsing the 5-point Likert scale into the following categories: very likely/likely, neutral and unlikely/very unlikely. Chi-square tests found that the General Population group were more likely to perceive anxiety, depression, anger and stigmatization upon receiving a hypothetical positive carrier test result when compared with the Not-Tested group ($\chi^2 (1, 157); p < .000$). The General Population also demonstrated a trend towards the increased likelihood of feelings of hopelessness ($\chi^2 (1, 157); p < .05$).

In contrast, recall of the actual emotional reaction experienced by Obligate Carriers and carriers within the Tested group did not reveal any significant differences in their overall affect score ($t(55) = 0.695$; ns) nor were there any significant differences when the individual affect subscale items were analysed with a Chi-square test ($\chi^2 (2, 59)$; ns). Although, there was a trend such that Obligate Carriers were more likely to feel hopeless when compared with the carriers in the Tested group ($\chi^2 (2, 59); p < .05$).

Insert Table 3 about here

As expected, clinical measures of anxiety (STAI) and depression (BDI) did not reveal significant differences in affect between the groups (MANOVA: $F(9, 265) = 0.96$, ns) (Table 4).

Insert Table 4 about here

III. Attitudes Towards Carrier Testing

Analysis of participant's attitudes towards carrier testing illustrated further distinctions between the General Population and the high risk groups (i.e., Obligate Carrier, Tested and Not-Tested) contrary to the original hypothesis (Table 5). It appears that when evaluating the overall pros and cons of carrier testing, the General Population has a less favourable attitude towards carrier testing when compared to the high risk groups (ANCOVA: $F(3,249) = 15.53; p < .000$). Similar to the affect subscale, a significant relationship was found between those who had children versus those who did not and their attitudes towards carrier testing. Specifically, those with children were more likely to have a less favourable attitude compared to those without children ($t(252) = -2.357; p < .05$). In spite of this, the effect of having children was not significant in the overall ANCOVA ($F(3,249) = 0.185; ns$).

Descriptively it was found that the vast majority Obligate Carriers perceive that test results will provide them with important family planning information when compared to those in the other high risk groups and the General Population ($\chi^2(6, 265) = 21.5; p < .001$). Similarly, while 34% of the General Population indicated that testing may cause more worry than it is worth ($\chi^2(6, 265) = 43.1; p < .001$), the majority of individuals in the high

risk groups stated that testing would provide “peace of mind” ($\chi^2 (6, 265) = 41.1; p < .001$) regardless of the outcome of the test. The low self-perceived risk of the General Population was also evident as 41% stated that they believed that carrier testing was not necessary for them ($\chi^2 (6, 265) = 82.2; p < .001$).

Insert Table 5 about here

V. Preferences for CF Health States

In contrast to the hypothesis that preference values would discriminate between those who had been tested with those who had not, ratings for CF carrier testing health states taken from the visual analogue scale (Feeling Thermometer) were not significantly different between the groups (MANOVA: $F(15,326) = 1.23; ns$) (Table 6). However, significant group differences were found for the utility values of those same health states (MANOVA: $F(15,258) = 1.86; p < .05$). Subsequent univariate analyses detected significant differences for the CF baby health state in which Obligate Carriers had a higher preference for having a child affected with CF (ANOVA: $F(3,257) = 6.37; p < .000$; Tukey $a (p < .05)$). Despite the fact that both ratings and utilities were to provide a preference value for the CF health states, they were shown to be poorly correlated with each other (Table 7).

Insert Tables 6 and 7 about here

CF Carrier Test Participation

Following the interview, participants within the Not Tested population who indicated that they would like to be tested were offered testing. Unexpectedly, 98% (96/98) of the Not Tested group were subsequently tested. Only two participants refused testing because they did not have any children and were surgically sterilized. It had been originally suggested that secondary analyses would be conducted in order to assess any differences between the Not-Tested participants who opted for testing versus those who did not. In contrast, 63% of the General Population said they would consider testing at the end of the interview.

High Risk Relationship to the Affected Relative

Further comparisons of the Tested and Not-Tested groups revealed a significant relationship such that the Tested group was comprised of mostly siblings to the affected patient (33%). Whereas, nearly half the Not-Tested group (49%) was comprised of cousins of the affected patient (Figure 5). Therefore, high risk relatives who were previously tested at the hospital on their own volition were more likely to be members of the CF patient's nuclear family (first degree relative), whereas high risk relatives who participated in the present study - and were subsequently tested - were made up of more distantly related third degree relatives (i.e., cousins). Representation from second degree relatives (i.e., aunt/uncles) was similar between the groups.

Insert Figure 5 about here

DISCUSSION

With the cloning of the CF gene in 1989, health care professionals are now able to detect CF carriers (Beaudet, 1992). This discovery has opened the door to unprecedented reproductive options for those at risk of having a child affected with CF. For many in the medical community, availability of CF carrier testing seemed to lead a straightforward path from the identification of CF carriers to a reduction in the incidence rate of CF (Williamson, 1993; Super et al, 1994; Clarke, 1991). Thus, it was largely assumed that this new test would be actively sought out by individuals, regardless of whether they had a positive family history of CF. In fact, predicted demand was so high that National health care organizations placed a voluntary moratorium on testing due to a lack of genetic counselling guidelines and DNA laboratory standards (Caskey et al., 1990; Workshop on Population Screening for the Cystic Fibrosis Gene, 1990; Canadian Task Force on the Periodic Health Examination, 1991). In North America, it was unanimously agreed that pilot research assessing the demand of the general population for screening was required, while carrier testing would be offered to those with a family history of CF as it was assumed that they would not only seek out their carrier status, but would use the test information in their future family planning.

Ironically, six years later, it appears that the vast majority of the high risk population is *not* coming forward for testing (Sorenson et al., 1994 and Surh et al., 1994), while general population pilot studies have reported moderate to high uptake in their carrier screening programs (Harris et al., 1993 ; Miedzybrodzka et al., 1995). Results of attitudinal research

also run counter to the observed participation rates as studies have reported that fewer of the general population would consider testing for themselves (Decruyenaere et al., 1992; Watson, Williamson et al., 1991; TenKate and Tjnnstra, 1989) when compared to the high risk population (Denayer et al., 1992; Wolff et al., 1990; Watson, Williamson et al., 1991).

In response to these incongruent findings, the present study explored genetic testing decision making factors (i.e., knowledge, affect, attitude and preferences) of individuals who had previously undergone CF carrier testing (i.e., Obligate Carriers and Tested) and those who had not (i.e., Not-Tested and General Population). The aim of the study was to assess the influence of these factors on carrier testing decisions and participation in CF carrier testing.

Contrary to the stated hypotheses, the Not-Tested population were not impeded by knowledge barriers as they demonstrated better than average knowledge of CF and CF carrier testing. In addition, they indicated realistic levels of perceived negative affect resulting from testing, had positive attitudes towards carrier testing, and reported similar preferences for CF health states as the other previously tested high risk groups (i.e., Obligate Carriers and Tested groups). Therefore, in direct contrast to previous expectations, high risk relatives - previously tested or Not-Tested - appear to be a homogenous group. Moreover, prior to genetic counselling and meeting with the research assistant - 84% of the Not-Tested high risk population had previously been informed of CF carrier testing and 98% would consider carrier testing for themselves. Subsequently, 98% agreed to be tested when offered by the study.

If the high risk groups are similar in terms of genetic testing decision making factors, then why didn't the Not-Tested group seek out carrier testing at the same time as the Obligate Carriers and Tested groups? The following sections discuss the possibility that the high participation rate amongst the Not-Tested group may not be entirely due to hypothesized differences on testing factors. Instead, test participation may have been artificially inflated by the convenience factors associated with the recruitment and testing methods used in the present study.

On the other hand, responses of the General Population were consistent with the stated hypotheses which predicted that they would demonstrate low levels of knowledge, perceive more negative affect resulting from testing, less favourable attitudes, and higher preferences for abortion of a CF fetus. Implications for these findings are also discussed below.

Breaking the knowledge barrier

Lack of knowledge is often seen as a significant barrier to medical testing and is widely used as an explanation for low participation rates (Deber, 1994). Thus, in an attempt to reduce and/or eliminate knowledge barriers in genetic testing, CF researchers have examined the efficacy of different methods/mediums of providing genetic information (e.g., written vs. video) (Clayton et al., 1995; Livingstone, Axton, Mennie, Gilfillan and Brock, 1993; Williamson et al., 1989) as well as evaluating current genetic counselling services (Evers-Kiebooms and Van den Berghe, 1979; Abramovsky et al., 1980). These studies have increased the understanding of the clinical genetics community in terms of the

provision of genetic counselling to those who come in for testing.

However, this new understanding is of little practical value if those who may benefit from testing are unaware of available genetic counselling and/or testing services. This may be the case in high risk carrier testing programs as test information is traditionally disseminated from Health Care Providers to CF Patients and/or Obligate Carriers, who then inform other blood relatives. It is important to establish if there is a breakdown in information dissemination and where it occurs. Specifically, is genetic information not being effectively communicated by health care providers to the CF Patient and Obligate Carriers? And /or, do CF Patients and Obligate Carriers have difficulty providing information to other family members?

The results clearly support the hypothesis that individuals in the Obligate Carrier and Tested groups were more knowledgeable regarding CF, carrier testing and carrier risks than the Not-Tested and General Population groups. Therefore, these findings appear to indicate that previous genetic counselling of the Obligate Carriers and Tested individuals was effective. Nonetheless, Obligate Carriers outperformed the Tested group in terms of their overall knowledge. Examination of the individual items reveals that the Obligate Carriers' knowledge is higher with respect to the daily care of a CF patient. This may be expected given the roles and responsibility of the parent as caregiver and treatment provider. Moreover, these findings are consistent with past research which has found that Obligate Carriers are generally more knowledgeable than other high risk relatives regarding the disease process (Hames et al., 1991; Wertz, Janes et al., 1992; Miller and Schwartz, 1992;

Kaback et al., 1984; Wolff et al., 1990).

Yet, despite their impressive understanding of CF and carrier testing, Obligate Carriers and Tested individuals demonstrated poor recall of the general population's carrier risk (1/25) as well as their own carrier result which they received 6 months to 5 years prior to the study. Poor recall of carrier test results has been reported by previous research which has suggested that individuals who have undergone carrier testing tend to dichotomize test results as either positive (i.e., carrier) or negative (i.e., non-carrier) (Watson, Mayall et al., 1992; Bekker et al., 1994). Thus, those who are at low risk (i.e., not found to carry any detectable mutations) falsely believe that they are *not* carriers as opposed to having a reduced risk of being a carrier. Notwithstanding these findings, it is surprising that 35% of Obligate Carriers and 69% of the Tested group did not know their correct carrier risk especially in light of their high level of knowledge on all other items. This striking finding may be due to the fact the knowledge item which inquired about their carrier risk (number 8) read as follows, "What do you think is your chance of being a CF carrier?" Because the Obligate Carrier and Tested individuals had previously been carrier tested, they often expressed confusion as to whether this question was referring to what they thought their carrier risk was *before* testing as opposed to their actual test result. In retrospect, this question should have read, "What is your risk of being a carrier based on your carrier test result?"

Examination of the level of knowledge amongst the Not-Tested group reveals that they were well informed of CF and carrier testing prior to genetic counselling. Thus, it would appear

that genetic information is, in fact, being filtered down from Obligate Carriers and/or Tested individuals to Not-Tested high risk relatives. Although, the performance of the Not-Tested group was significantly lower than the Obligate Carriers and Tested groups, it is important to note that Obligate Carriers and Tested participants had had the opportunity to speak directly with a genetic counsellor regarding testing. Moreover, it is interesting to note that the Not-Tested group demonstrated poor performance on the items which contained specific information usually disclosed during genetic counselling such as their estimated carrier risk, general population carrier risks and DNA sampling procedure.

In sum, performance of the Not-Tested group on the knowledge items was significantly higher than the General Population but less than the Tested group and Obligate Carriers. This is in spite of the fact that they had not previously undergone genetic counselling, and in contrast to the expectation that they fell victim to knowledge barriers. Therefore, in contrast to recommendations for educational campaigns targeted at the high risk population (Fanos and Johnson, 1995; Sorenson et al., 1994), the present findings demonstrate evidence of high knowledge for the high risk Not-Tested population.

As expected, the General Population demonstrated the lowest performance on CF and carrier testing knowledge items when compared to the high risk groups. Nonetheless, their responses to individual knowledge items showed that more than two thirds of the General Population knew that CF affected the lungs and digestive system, was inherited, and knew what a carrier was. Yet, only a third had heard about CF carrier testing prior to filling out the Genetic Testing for CF survey. Therefore, it appears that lack of knowledge regarding

the availability of the carrier test may pose a significant barrier to testing for the General Population.

Influence of Perceived Negative Affect

The hypothesis that members of the Not-Tested and General Population groups might perceive similar negative affect associated with a positive carrier test result was not supported. The results illustrate that the General Population group anticipated significantly higher levels of anxiety, depression, anger and stigmatization after receiving a hypothetical positive carrier test result than the Not-Tested group. Conversely, as expected, the actual affective experiences of the Obligate Carriers and Tested individuals were similar. Interestingly, comparison of the Not-Tested group's anticipated reaction with the Obligate Carrier and Tested groups' actual reaction suggest that Not-Tested relatives may have a more realistic view of the emotional impact of being found to be a carrier. Therefore, these similarities amongst the high risk groups appear to indicate that it was unlikely that possible negative affect associated with positive test results inhibited them from coming in for testing.

However, the General Population's responses illustrate a significant misperception between their hypothetical reaction and the actual experience of carriers. Evers-Kiebooms et al (1994) also found that their mixed sample (both high risk and general population) described hypothetical carriers as less happy, more afraid, more angry, weaker, less healthy, more marked, less active, feeling more shocked, worse, more ashamed and more guilty than non-carriers. In contrast, the reactions of actual Carriers and Non-Carriers to their actual test

result indicated that Carriers do not demonstrate more negative feelings regarding their carrier status. Instead, Non-Carriers were found to feel more positive emotions such that they felt better, more unafraid, stronger, more relieved, happier and more pleased. Similarly, Bekker et al. (1994) found that although carriers tended to be surprised about their positive carrier status upon receipt of test result and 3 months later, they do not report feelings of depression, guilt, worry or upset at pre-testing or post-testing. Whereas, reports of the Non-Carriers at pre and post reveal happy, pleased and relieved reactions. Thus, there is new evidence emerging that does not support long-term negative affect of carriers, but has demonstrated positive affect amongst non-carriers. Consequently, it is possible that individuals considering testing may also be influenced by positive emotions associated with being a non-carrier than negative emotions of being a carrier. Although this was not supported by the findings of the present study, it is noteworthy that approximately 1 in 5 members of all groups indicated relief upon receiving a positive carrier test result.

It has been proposed that "Psychosocial Genetics" is emerging as the newest discipline in Genetics research (Harper, 1993). However, studies in this area have mainly focused on examining the short and long term psychosocial sequelae associated with genetic testing. It has been clearly demonstrated that although positive carrier test results cause initial rises in self-reported anxiety and depression, these emotions subside after 3 to 6 months (Watson, Mayall et al., 1992; Bekker et al., 1994). In keeping with the hypothesis regarding long term affective consequences, observed scores on the BDI and STAI in the present study did not discriminate between the groups in terms of depressive or anxiety related symptomatology. Moreover, group means for previously tested individuals (i.e., Obligate

Carrier and Tested groups) indicate that levels of depressive symptoms and state/trait anxiety are within the normal range - supporting the findings of earlier research.

Importance of Attitudes

Thus far, the results have indicated that the vast majority high risk Not-Tested individuals had previously heard about carrier testing and had adequate knowledge regarding the disease, its inheritance and the carrier test. Moreover, they do not appear to associate negative feelings with being a carrier of the CF gene. Therefore, it may follow that they did not present for testing because of unfavourable attitudes towards carrier testing for CF. It was hypothesized that perhaps the Not-Tested group perceived little value in being carrier tested as information regarding their carrier status would not affect their future family planning. However, the results clearly demonstrate that attitudes of the Not-Tested group were similar to those individuals who had previously come in for testing (i.e., Obligate Carrier and Tested). Therefore, despite the fact that all high risk groups demonstrated similar views on the pros and cons of CF carrier testing, those in the Not-Tested group did not previously come forward for testing but were tested when approached by the present study.

In contrast, consistent with the stated hypothesis, the General Population group indicated less favourable attitudes towards testing. Specifically, they reported that testing was not necessary for them, was unlikely to give them "peace of mind" and may cause them to worry unnecessarily. Yet, despite these negative views, 60% indicated that carrier testing would help them with their family planning. Past attitudinal research has performed only

shallow investigations of attitudes therefore, similar contradictions have not yet been reported. However, recent findings regarding carrier test participation appear to conflict with past attitude studies. The attitudinal research in CF Carrier testing has unequivocally demonstrated favourable attitudes towards this new type of testing, whether it be for the use of the respondent (Denayer et al., 1992; Wolff et al., 1990) or for the availability of testing to general public (Watson, Williamson et al., 1991; TenKate and Timstra, 1989; Decruyenare et al., 1992). Yet, actual participation in CF carrier screening programs have widely varied for both the high risk and general population studies (see below for discussion on participation rates). The implicit expectation from the medical community was that attitudinal research conducted on the general population would provide an indication of the actual demand for carrier testing and thus, be highly correlated with participation rates. With the results of these initial pilot studies now available, researchers are having difficulty consolidating their attitudinal findings with actual test uptake. Clearly, the expected link between attitudes towards DNA predictive testing and actual genetic testing behaviour is not as straightforward as once thought.

These findings have important implications for past and future attitudinal studies in genetic testing. It is well known that the relationship between attitudes and behaviours is tenuous at best (Baron and Byrne, 1987). Social psychology research has aptly demonstrated that although attitudes towards certain health outcomes may be reported as favourable, actual behaviours associated with the desired outcome(s) may be contradictory and/or counterproductive (Ajzen and Fishbein, 1980). Popular examples of this paradoxical relationship include, attitudes towards obtaining a healthy lifestyle vs actual diet and

exercise regiments, and reducing cancer risks vs. smoking habits (Ajzen and Fishbein, 1980). Explanations for these incongruent findings have been provided by social psychological theories such as cognitive dissonance and reactance theory (see Baron and Byrne, 1987).

Yet, notwithstanding the predictive limitations of attitudinal research, it is important to assess the views of the public regarding new DNA predictive testing. With new disease genes being cloned at an unprecedented rate, it is crucial to establish the value of this new type of testing from the perspective of the client and not just from other stakeholders such as medical staff and political officials. Review of the CF carrier screening literature illustrates that attitudinal research has only skimmed the surface in terms of evaluating attitudes towards testing. Most studies have employed uninvolved investigations of attitudes consisting of one or two questions inquiring about the acceptability of testing. Closer examination of the pros and cons of testing in the present study indicate that overall, the high risk populations perceive more benefits to carrier testing and the general population perceives more drawbacks.

Preferences

Utilities were incorporated into the decision making model so as to provide a more accurate measure of anticipated or potential use of CF carrier test results towards a particular reproductive outcome. It was proposed that the elicitation of preference values would address the three major shortcoming of previous research. Specifically, 1) investigators have not yet adequately examined the reproductive views of the high

risk population; 2) investigations of the likelihood using test results towards a specific reproduction outcome have been limited to descriptive methods; and 3) researchers have focused on abortion as the sole outcome of carrier testing, therefore, there is a lack of information regarding the desirability of other reproductive options. It was expected that preferences would provide an estimate of the individual's value associated with possible reproductive options related to carrier testing and insight as to the intended family planning and reproductive behaviours. Specifically, it was hypothesized that high preferences for abortion and carrier test results would indicate a desire to undergo carrier testing, while high preferences for a child with CF or no children indicate refusal of CF carrier testing.

Contrary to the stated hypothesis, yet consistent with past research, Obligate Carriers appear to be less likely to abort for CF than those in the General Population (Miller and Schwartz, 1992; Wertz and Janes, 1992; Miedzybordzka, 1995). This may be expected as Obligate Carriers have experienced the unique joys and challenges of caring for a child with CF. It has been suggested that to endorse abortion for CF may somehow negate the value of their current affected child (Denayer et al., 1992; Evers Kiebooms et al., 1990; Al-Jader, Goodchild, Ryley and Harper, 1990). Whereas, the General Population has been shown to have little knowledge of CF and possibly very little experience with CF. Therefore, they may have overestimated the morbidity associated with the CF disease.

Another significant difference was found between the Obligate Carriers and the General Population such that the latter group indicated that they had a lower preference for the scenario in which one partner was detected as a carrier and the other was at low risk of being a carrier. This finding further illustrates the negative value that the General Population places on being a carrier. As discussed earlier, the General Population demonstrated lower knowledge, higher perceived negative affect and less favourable attitudes towards carrier testing prior to genetic counselling than the high risk groups. Yet, utilities were assessed after genetic counselling, therefore, it would appear that, even once informed, the General Population perceives less value in pursuing carrier testing.

More importantly, utilities followed the same pattern as the previous decision making factors such that there were no significant differences between the high risk groups. Thus, high risk relatives who came in for testing on their own volition (i.e., Obligate Carriers and Tested) have the same preference for reproductive and carrier status outcomes than those who did not come in for testing (i.e., Not-Tested). Closer examination of the mean utility values reveals that abortion of a CF fetus is the least desirable outcome across all the groups. However, Obligate Carriers would prefer to have a child affected with CF than have no children at all. In contrast, the Tested, Not Tested and General Population groups' utilities indicated that they would prefer to have no children at all over having a child with CF. Again, this differentiation of the Obligate Carriers is most likely due to the fact that they have direct experience with the disease and may provide the most mindful estimates of the quality of life of a patient

with CF.

Unfortunately, utility values may not have provided accurate measures of which reproductive outcomes individuals may seek in their future family planning. These findings should be interpreted with caution as the present study has 1) confirmed theoretical limitations of utility theory in terms of violation of the axioms; 2) demonstrated a number of practical limitations regarding the involved administration of the utility assessment; and 3) proposed clinical limitations of the utility measurement as a reliable and valid measure of quality of life or patient decision aid. These areas of concern are discussed in the 'Limitations of the study' section (see page103).

Family Planning and Demographic Factors

Differences amongst the groups in terms of demographic factors revealed some similarities between the Obligate Carrier and General Population groups. These similarities were most likely due to the selection procedure for the General Population involved matching with the Obligate Carriers, these two groups were distinct in terms of age, parity and marital status when compared with the Tested and Not Tested participants. The findings also indicated that Tested and Not Tested participants were predominantly Catholic. It was suggested that because of the prevalence of French Canadians in the Ottawa-Carleton region and reflected the popularity of the Catholic religion among this segment of the population.

Carrier Test Decision

In pursuit of the reasons *why* individuals seek out carrier testing, it was proposed that the Not Tested group would be sub-divided into those participants who chose to be carrier tested with the study and those who did not. Unexpectedly, 98% of the high risk Not-Tested group indicated in the Genetic Testing for CF survey that they would consider being carrier tested prior to meeting with the research assistant. Similarly, after the provision of genetic counselling, 98% opted for carrier testing when asked during the interview. Consequently, there was no variance within this group to perform subsequent analyses to assess the predictive power of the factors associated with carrier testing decisions. However, the fact that almost all Not-Tested individuals requested carrier testing is an important finding which aptly illustrates the influence of genetic testing decision making factors involved external factors which were justifiably not included in the initial model. These factors are discussed in the following sections.

Carrier Testing: Good intentions, low priority

The Not-Tested group indicated they had previously heard about testing and were concerned about their risk of being a carrier prior to meeting with the research assistant. In addition, they demonstrated high knowledge, realistic levels of perceived negative affect resulting from carrier testing and favourable attitudes towards carrier testing similar to the Tested group (as well as the Obligate Carriers). Moreover, nearly 100% of the group requested testing with the present study. Therefore, these findings provide support of the influence and direction of the decision making factors in the model. However, it was hypothesized that the Not Tested group did not come forward for testing prior to the study because they

were different from the Tested group on these factors.

If the groups were similar on the decision making factors, what stopped the Not Tested group from coming forward for carrier testing prior to the study with members of the Tested group? Subsequent investigation revealed two important distinctions between the groups. First, the Tested group was recruited for carrier testing using a traditional (passive) recruitment protocol in which information regarding the carrier test and its availability was dissemination via CF patients and their parents. Therefore, those high risk relatives who were interested in testing had to contact the hospital to arrange for a genetic counselling session followed by blood sampling. In contrast, Not-Tested participants were actively recruited by the research assistant with the help of other family members. This labour intensive research protocol also included home visits in the evenings and non invasive testing using buccal swabs.

Second, members of the Tested group were more likely to be closely related to the affected patient (i.e., siblings). Whereas, the Not-Tested group was comprised of more distantly related blood relatives (i.e., first cousins). Thus, it would appear that the closer the relationship to the affected patient, the more likely the high risk individual will seek out carrier testing on their own volition. On the other hand, the more distant the relationship to the affected, the less likely that they will seek out carrier testing.

Participation rates: Is bigger better?

The results appear to indicate that when carrier testing programs are designed to

accommodate the client, test participation will increase. That is, if you remove the inconvenience factors associated with testing, more people are likely to be tested. Although the present study did not specifically investigate inconvenience factors, it is possible that preparations for testing such as arranging an appointment, taking time off work, finding a babysitter or transportation and parking may erect testing barriers. Knowledge, affect, attitudinal, and preference factors indicated that the Not-Tested group were well informed and were considering testing for themselves. Therefore, it appears that testing *decisions* are distinct from testing *behaviours*.

Recent research has reported participation rates for high risk and general population groups in either the top ($>75\%$) or bottom ($<25\%$) quartiles (Table 8). In contrast to the proposed influence of decision making factors on carrier testing decisions, review of the literature reveals four procedural patterns which significantly influence carrier test participation: First, studies which employ active recruitment have higher uptake rates than those using a passive recruitment protocol. Second, studies using less invasive DNA sampling procedures tend to yield to higher test uptake. Third, studies comprised of pregnant women report consistently high participation. Fourth, when general population samples are provided with thorough genetic counselling, participation rates fall. Whereas participation rates of high risk samples are consistently high regardless of the comprehensiveness or brevity genetic counselling. The following sections discuss the research implications active recruitment and non-invasive DNA sampling, as well as the ethical, medical and political implications of targeting pregnant populations and modifying genetic counselling.

Insert Table 8 about here

Procedural biases

Active vs. Passive recruitment

Active recruitment studies include those in which clients were sought out and contacted by a recruiter (i.e., researcher, physician or family member) and testing was performed either (a) in the client's home/school by a researcher or by the client, or (b) during a previously scheduled medical appointment for reasons other than carrier testing. For the high risk population, the results of the present study support those of Super et al. (1994) which demonstrate that active recruitment procedures yield participation rates approaching 100%. Conversely, active recruitment in non-pregnant general population studies has yielded lower participation rates such that when individuals are opportunistically approached in a clinic waiting room by researcher, 66% and 70% opt for testing if it can be done immediately (Watson, Mayali et al., 1991; Bekker et al., 1993, respectively). However, if the participant is approached in the same manner but must arrange a specific appointment for testing, participation rates drop to 25% (Bekker et al, 1993).

Active recruitment for general population CF carrier screening programs have often based in the offices and waiting rooms of general practitioners (GP). These settings are not ideal for carrier screening as they are not conducive to the provision of adequate genetic counselling. Genetic counselling in general population studies has often been provided by

physicians who have been shown to be poorly informed regarding the disease process and the implications of testing. A study conducted four years after the discovery of the CF gene revealed significant shortcomings in GPs knowledge of CF and its incidence, which are key elements of genetic counselling. Specifically, the top four incorrect answers included the following: current average at death of CF patients (75% incorrect); incidence of CF in Caucasians (more than 50% incorrect); differential sex incidence of CF (50% incorrect); and most couples at risk had a positive family history (39% incorrect) (Rowley et al., 1993).

Moreover, some active recruitment studies have allocated short time limits of less than 10 minutes for genetic counselling (Harris et al., 1993; Menne et al., 1992). To put this in perspective, the current clinical practice of most hospitals in the province of Ontario has been to provide formal counselling sessions of 60 minutes for genetic testing (Surh et al., 1995). Clearly, 10 minutes of genetic counselling is insufficient for informed decision making, especially in light of the findings of previous knowledge surveys (Chase et al., 1984) which illustrate that most individuals have difficulty with the most basic mathematical properties needed to comprehend genetic testing risk estimates.

Another reason why the provision of genetic testing services should not be left in the hands of GPs is that historically physicians have been directive in terms of patient decision making (Deber, 1994). Directiveness of health care providers in relation to genetic testing has only recently been addressed. Rowley et al. (1993) describe their research on the possible bias of physicians regarding genetic testing, "we are assessing the degree of understanding of

the woman at the time she accepted the offer of screening and whether the physician recommended or merely offered it" (p.265). Physicians are also often perceived as authority figures by their clients and thus, may inadvertently exert some influence over their patient's decisions. This may be a significant concern as Clayton et al. (1996) found that 70% of general population respondents thought that their GPs favoured testing

In addition, physicians' priorities for the provision of CF Carrier screening are questionable as they have been shown to be economically motivated. In a recent U.S. survey, 124 prenatal care providers indicated that would only offer testing if a) it was free of cost for their patient; and b) payment was available for their services (Rowley et al., 1993). Physicians have also voiced logistical concerns such as the time required to answer patients' questions regarding testing. However, it is of note that none of the physicians expressed concern about the imperfect test sensitivity, false reassurance of those testing negative or the possibility of those testing positive encountering discrimination (Rowley et al., 1993). Another significant business concern for physicians is the fear of litigation for wrongful birth. A review of audio recordings between ObGyns and their clients over the age of 38 revealed that amniocentesis was presented as "the sensible thing to do". In fact, for two women who declined the test, the doctor actively attempted to dissuade them having gone so far as to provide inaccurate risk figures (Marteau, Kidd, Cook, Michie, Johnston, Slack and Shaw, 1991)

Physicians have demonstrated a reluctance, not only to participate in carrier testing trials (Rowley et al., 1993), but also to educate themselves on available genetic tests. For

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or medical, a decrease in the incidence of CF due to the onset of carrier testing programs is unlikely because (a) population screening programs are not cost effective as the cost of a CF birth avoided is more than the lifelong care of a CF patient, and (b) feedback from past screening programs have not provided evidence which indicates that individuals are actually avoiding CF births.

Cost-effectiveness of screening:

Although calculating a dollar amount for the life of an individual is an insidious task, it has become a necessary evil in today's fiscally conservative environment. The lifetime health care costs for the average CF patient are exorbitant. A pilot study recently conducted at CHERO calculated that the average cost¹ per CF patient ranges between \$10,000 and \$75,000 per year (based on drugs, hospitalization, lab tests, physician fees, support staff, and social care costs) (Surh et al., 1992). Therefore, based on the current average lifespan of CF patients, the lifetime health care costs range from \$300,000 to \$2,250,000. In fact, the combined costs for occasional inpatient care (where 40% of patients require annual hospitalization for at least 1 week) and continuous outpatient care have been found to be disproportionate to the number of CF patients (Colten, 1990). Therefore, a reduction in the incidence of CF is particularly desirable from an economics perspective.

However, considering that a reduction in the incidence of CF births involves carrier screening, prenatal testing and therapeutic abortions, not to mention genetic counselling prior to each of these procedures, our current health care system simply cannot sustain the

were required to schedule specific appointments for genetic counselling and DNA sampling appointments. Both high risk (Surh et al., 1994; and Sorenson et al., 1994) and general population studies (Clayton et al., 1996; Bekker et al., 1993; Watson, Mayall et al., 1991) have reported low participation rates (1% to 17%) when using this form of recruitment. Reasons for non-participation have only been assessed by two studies. An American study found that over one third of their general population participants feared that if they were found to be carriers they might lose their health insurance, while less than one sixth thought that testing was meddling with God's plan (Clayton et al., 1996). These findings demonstrate that the cost of the actual test may not be a major barrier to testing. However, lack of security in terms of long term health care coverage will most likely be a significant liability of U.S. genetic screening programs. In contrast, a Canadian study examining high school students reported that 27% of those who chose not to be tested indicated a lack of interest, while 29% failed to complete or return the DNA testing consent form (Mitchell et al., 1993). It has been suggested that widespread population carrier screening would be most effective if targeted at the high school population as the majority of students have not yet made decisions regarding marriage and/or pregnancy. However, these results demonstrate that genetic testing may not be sought out due to low motivation and self-perceived risk amongst this young population.

Invasiveness of DNA sampling

For the most part, past research has conducted DNA sampling via mouthwashes and buccal swabs (Table 8). These are the preferred methods for the researchers as research assistants do not need to be specially trained in venipuncture and testing can be done by the

participant. In fact, in some studies, buccal cell sampling totally eliminated the need for a research assistant as testing kits are distributed and returned by mail (Super et al., 1994). Participants also appear to prefer buccal sample methods as they are painless and less obtrusive alternatives to conventional blood sampling by venipuncture. To date, only three studies have employed blood sampling, two of which also utilized a passive recruitment procedure. As a result, both reported low uptake rates of $< 1\%$ and $< 10\%$ (Clayton et al., 1996; and Surh et al., 1994, respectively). In the former study, 25% of respondents said that they would be more willing undergo carrier testing for CF if the procedure involved a buccal swab as opposed to venipuncture (Clayton et al., 1996). The third study involved the active recruitment of high school students (Mitchell et al., 1993). Although this study yielded higher participation rates (42%) using blood sampling procedures, 27% of those who refused to participate did so out of fear of the blood test. In fact, in a subsequent study which employed the same recruitment procedure but used buccal swab sampling, participation rates shot up to 70% (Kaplan et al., 1992). Therefore, these findings may indicate that participation rates will rise using active recruitment along with blood sampling, however, test participation will be optimized if DNA test is less invasive.

Supply Push vs. Demand Pull

Carrier testing during pregnancy

Some researchers are of the view that carrier testing decisions are most appropriately dealt with during pregnancy. In fact, the clinical reality of most genetic testing centres is that individuals do not come forward for testing until they are in the pregnant state (Brock, 1995). This phenomena was demonstrated by a couple in the present study from the Not

Tested group Due to a lack of DNA on both of their buccal swabs (this occurred in approximately 10% of the total samples) they were requested by the research assistant to either a) visit a blood drawing laboratory of their choice; b) come into CHEO for blood work; or c) arrange for another appointment with the research assistant to perform another buccal swab. This couple opted to go to their local laboratory and have them forward their samples. Over the next 7 weeks the research assistant made follow-up phone calls to inquire if they were still interested in carrier testing as the study had not yet received their samples. Although the couple consistently expressed interest in finding out their carrier status, they did not visit a blood lab and were considered as "drop-outs" of the study. Surprisingly, approximately one year later, the couple contacted the study to see if they could still be tested and promptly came in to CHEO for blood work. As it turns out, the couple had recently become pregnant and wanted to establish the risk of CF for their unborn child.

Previous research has clearly demonstrated that pregnant women and their partners report very favourable attitudes towards carrier testing and prenatal testing (Watson, Mayall et al., 1991; and Miedzybrodzka et al., 1995). Moreover, participation in CF carrier testing is high (70% to 90%) when offered to this population (Harris et al., 1993; Miedzybrodzka et al., 1995; Livingstone et al., 1994; Mennie et al., 1992; and Watson, Mayall et al., 1991) (Table 8).

Notwithstanding favourable attitudes, "impressive" uptake rates, or even the clinical reality of genetics laboratories, according to health care professionals and patients, pregnancy is

not the ideal time for carrier testing. A survey of pregnant women found that although the majority chose to undergo prenatal testing, most indicated that had they been offered the choice they would have chosen to be tested prior to pregnancy (Mennie, Gilfillan, Compton, Liston and Brock, 1993). Therefore, although carrier and prenatal test uptake amongst the pregnant general population may reflect a genuine need for information, reproductive options are limited during pregnancy and decision making may be rushed due to time constraints on terminations. Clarke (1991), a clinical geneticist, spoke candidly in his editorial about the aftermath of hasty reproductive decisions and his disapproval of carrier testing during pregnancy. He describes the "emotional anguish, guilt and depression" which ensued after some women had terminated an affected pregnancy which lead to their refusal of prenatal testing in subsequent pregnancies.

In addition, the view of most GPs (36%) and family planning health care providers (61%) is that carrier testing is best done before marriage and/or family planning. More importantly, when asked how they felt about testing during pregnancy, only 3% of GPs and 2% of family planning staff felt testing should be offered at this time (Watson, Williamson et al., 1991). Similarly, 43% of high risk individuals, 52% family planning clinic attendees, 42% school pupils preferred testing *prior* to marriage and/or planning a family. Unfortunately, they were not asked for their opinion of carrier testing during pregnancy (Watson, Williamson et al., 1991). These findings were also supported by Clayton et al. (1996) who reported that 74% of general population thought that the best time for carrier testing was prior to pregnancy, whereas only 2% thought that it was best to be tested during pregnancy. Similarly, Decruyenaere et al. (1992) found little support (2%) for testing

during pregnancy in their general population sample.

Comprehensiveness of Genetic Counselling

The notion that knowledge barriers inhibit carrier test participation has been challenged by non-pregnant general population studies which have employed in-depth genetic counselling.

In the present study General Population participants were provided with a 30 minute genetic counselling session. Prior to the session, it was determined that knowledge of CF and CF carrier testing amongst this group was low and only 35 of the 59 participants (59%) considered being carrier tested. Yet, after genetic counselling, only 2 of the General Population participants changed their mind and would consider being tested. This suggests that participation in carrier testing programs is not likely to increase significantly after comprehensive genetic counselling. Similarly, Clayton et al. (1996) found that participants who watched a video tape of genetic counselling information were more likely to refuse testing versus those participants provided with written genetic counselling material (i.e., pamphlet). The authors suggested that viewing of the video tape may have more effectively communicated genetic information and, more importantly, the notion of "choice" in carrier testing decisions (Clayton et al., 1996). Thus, it does not appear that the provision of thorough genetic counselling to the general population will substantially increase participation. In fact, the present findings indicate that genetic counselling may actually *decrease* participation in genetic testing.

On the other hand, knowledge of CF and CF carrier testing has been shown to be high amongst the high risk Not-Tested population. Thus, it is unlikely that the quantity or

quality of genetic counselling would affect carrier testing decisions in this population. This is supported by the two high risk studies which utilized active recruitment procedures. In the present study, all high risk Not-Tested participants were provided with thorough face-to-face genetic counselling based on the clinical standards used at CHEO. In contrast, high risk participants in Super et al. (1994) study were informed using information/testing kits which were distributed by Obligate Carriers and other previously tested high risk relatives. High risk un-tested relatives simply had to read through the information package, complete the mouthwash procedure and mail their sample to the study. Participants who were found to be low risk were mailed a "reassuring" letter. In the cases where couples were tested, they were mailed a "very assuring" letter if they were at low risk (i.e., one or no carriers) or invited to set up a counselling appointment if they were both carriers. Consequently, only 1% (15/1563) of the sample (i.e., carrier couples) had any contact with the researchers or clinical genetics staff. Thus, despite these genetic counselling differences, 98% of high risk relatives in *both* studies participated in carrier testing. One implication of these findings may be that the high risk population is sufficiently educated regarding carrier testing and may only require written information (i.e., pamphlet) on carrier testing as opposed to actual face to face genetic counselling.

In summary, participation rates amongst the high risk and general populations may be manipulated through recruitment (i.e., active vs. passive) and/or DNA sampling methods (i.e., buccal cell vs. blood). Moreover, test participation may also be inflated by targeting sensitive pregnant populations and/or with the use of directive or inadequate genetic counselling by physicians/researchers. Consequently, it is clear that high participation rates

do not indicate demand for test information. Instead, it appears that participation rates are a function of test convenience and the above methodological confounds. Given these significant influences, if participation rates are used as a measure of demand for testing and program success they will be inaccurate at best and misleading at worst.

Objectives of CF Carrier Screening programs

If knowledge, affect, attitudes and preferences can not testing *behaviour* and participation rates can be easily manipulated, what outcome will determine the demand, usefulness and effectiveness of current genetic services? Marteau suggests that "to evaluate any service we must first define its objective" (1994, p.1468). Unfortunately, the objectives of CF Carrier screening have not been specifically outlined (DeBrakeeler and Melancon, 1990). Although, most health care professionals and medical organizations carefully interpret the desired outcomes of carrier testing as increased reproductive options, yet it remains unclear whether there exists an implicit goal toward decreasing the incidence of CF births. Towards this end, researchers may further assume that individuals who undergo carrier testing will go on to *use* their test results towards the avoidance of CF in future generations. Therefore, it follows that there may be two implicit objectives of CF carrier screening programs: 1) to identify as many carriers as possible, or 2) prevention of CF births.

Objective 1: Identify as many carriers as possible

The previous discussion of participation rates would dictate that the most effective way to increase the number of carriers detected would be to actively recruit pregnant participants using mouthwash samples to collect DNA from buccal cells while providing minimal genetic counselling. Unwittingly, the researchers of two recently developed carrier testing

protocols. Sequential (Miedzybrodzka et al., 1995) and Couple Screening (Wald, 1991) tested their programs under these conditions. Both programs were designed to a) maximize participation rates and b) cut down on the overhead costs of widespread screening. The Sequential or two-step method involves initially testing one partner and if that partner is positive then testing the other partner (Livingstone et al., 1994). In this way, both members of the couple are provided their individual carrier test results as well as their combined risk.

In contrast, Couple Screening involves drawing DNA samples from both partners at the same time. However, only one sample is initially tested and, if positive, the second sample is tested. The distinction between these methods is that partners tested using the couple method are only given their combined risk having an affected child (Wald, 1991). In this way, couple screening programs can further reduce their genetic counselling resources (both cost and personnel) as they only provide counselling to carrier couples (as opposed to individuals) while identifying a large number of carriers. Both methods have been presented as highly successful programs as participation rates have been reported at 90% and 90% for sequential screening and couple screening, respectively (Miedzybrodzka et al. 1995).

Unfortunately, the solicitation of carrier testing participants has not always been this unintentional. Williamson et al. (1989) have been actively researching the demand for carrier testing amongst the general population in Great Britain. They, not unlike other investigators, often cite their participation rates as an indication of the success of their population screening program(s). However, in the interest of attracting participants, they explain, "The genetics of recessive illness is relatively difficult to understand, since the

carrier parents are not only unaffected, but may even be healthier than homozygote normals' (Williamson, 1993). In this statement they are referring to the somewhat inconsequential fact that CF carriers are more resistant to cholera due to balanced polymorphism (Lewis, 1994). (This means that carriers of a CF mutation have an evolutionary advantage over non carriers due to natural selection such that they have enough of a genetic defect which prevents the cholera toxin from taking hold.) Fortunately, cholera is no longer perceived as a deadly epidemic, therefore, it is misleading to present carriers in this favourable light.

Objective 2: Prevention of CF births

Because CF carrier testing is inherently linked with issues of abortion, latent objectives for reducing the incidence of CF will clearly cause controversy over the provision of testing (Raeburn, 1994, Beaudet, 1990). Public health genetic testing objectives state that the aim of carrier screening programs is to provide information and options (Marteau, 1994). Yet, at the same time policy objectives have been economically tied with reducing the incidence of genetic illness as suggested by the popularity of costing studies (U.S. Congress, 1992; Kaplan, 1993). Surprisingly, it appears that some members of the medical community are more likely to "call a spade, a spade" as the Royal College of Physicians of London indicated in their report on prenatal diagnosis and genetic screening that prevention is a primary professional goal (Clarke, 1991). Super et al. also support this view in their concluding statement, "The ultimate aim must be to have the most ideal treatment possible available to a smaller and smaller pool of affected people . as part of the global effort to conquer this and similar diseases" (1994, page 1467). From either point of view, political

or medical, a decrease in the incidence of CF due to the onset of carrier testing programs is unlikely because (a) population screening programs are not cost effective as the cost of a CF birth avoided is more than the lifelong care of a CF patient, and (b) feedback from past screening programs have not provided evidence which indicates that individuals are actually avoiding CF births.

Cost-effectiveness of screening:

Although calculating a dollar amount for the life of an individual is an insidious task, it has become a necessary evil in today's fiscally conservative environment. The lifetime health care costs for the average CF patient are exorbitant. A pilot study recently conducted at CHEO calculated that the average cost¹ per CF patient ranges between \$10,000 and \$75,000 per year (based on drugs, hospitalization, lab tests, physician fees, support staff, and social care costs) (Surh et al., 1992). Therefore, based on the current average lifespan of CF patients, the lifetime health care costs range from \$300,000 to \$2,250,000. In fact, the combined costs for occasional inpatient care (where 40% of patients require annual hospitalization for at least 1 week) and continuous outpatient care have been found to be disproportionate to the number of CF patients (Colten, 1990). Therefore, a reduction in the incidence of CF is particularly desirable from an economics perspective.

However, considering that a reduction in the incidence of CF births involves carrier screening, prenatal testing and therapeutic abortions, not to mention genetic counselling prior to each of these procedures, our current health care system simply cannot sustain the

cope with it. Similarly, in the present study, the burden of CF for the caregiver and quality of life for the child were assessed using preference values (ratings and utilities). Notwithstanding the significant shortcomings of utility measurement, both ratings and utility values indicated that the life of a child affected with CF is more preferable than the abortion of a CF fetus.

Implications of Supply "Push"

"Since the splitting of the atom, everything has changed except our way of thinking, and thus, we drift towards unparalleled catastrophe."

- Albert Einstein

What are the implications of the medical and political establishments "pushing" genetic testing upon society? Best case scenario is that individuals who may otherwise never have been tested subsequently benefit from testing (in one way or another). Screening programs which are guilty of targeting sensitive populations and providing insufficient or biased genetic counselling may tacitly couch their screening mandate within these terms (Dodge, 1990; Brock, 1990). Yet, it is not enough to "hope for the best" in relation to genetics. If Einstein's warning is to be heeded, then health care professionals should "expect the worst" and act accordingly.

It is difficult to imagine what the worst case scenario for genetic screening would entail. Historically, the Sickle Cell Anemia screening program is often cited as the biggest disaster in genetic screening (U.S. Congress, 1992; Roberts, 1992; Markel, 1992). As outlined

of prenatal diagnosis, however, only 43% would have an abortion. Similarly, Watson, Williamson et al. (1991) reported that 90% of relatives of CF sufferers would request prenatal testing, however, 58% would abort an affected fetus and 42% would not or were unsure. Thus, although it appears that carrier testing will provide prospective parents with important information, it is not clear that the incidence of CF will be significantly decreased as a result of the availability of prenatal testing and abortion.

Because CF carrier testing has been available for almost 6 years now, past research has been able to track the actual reproductive outcomes of carrier couples (Table 9). Including the present day, eight separate screening programs have collectively tested 13,489 individuals, detected 916 carriers, 24 carrier couples and 18 high risk pregnancies (Super et al., 1994; Mennie et al., 1992; Harris, et al., 1993; Livingstone et al., 1994; Watson, Mayall et al., 1991; Bekker et al., 1993 and Wald, 1991). Of these pregnancies, ten were healthy, seven were affected with CF and one was unknown. In total, six of the CF fetuses were terminated and one was carried to term. Unfortunately, due to the small number of couples faced with reproductive decisions, it is not possible to extrapolate any kind of pattern for the current outcomes of CF carrier screening programs. In reality the only way to measure the *actual* use of carrier test results towards avoiding a CF birth is through unwieldy longitudinal studies which prospectively examine the life decisions of huge numbers of individuals as they progress through mate selection, pregnancy, prenatal testing and abortion.

Insert Table 9 about here

The only prospective study of this kind was conducted in 1974 in Orchememos, a small farming village in Greece (Stamatoyannopoulos, 1974). In Orchememos, 23% of the population were Sickle cell anemia carriers with an incidence rate of 1 in 100 affected births. At this time, two thirds of marriages were still arranged by parents. Therefore, a team of physicians provided genetic counselling and carrier testing to members of the village with the intent that carrier status would become a consideration in marriage negotiations. Seven years later, the physicians re-visited the village with the expectation that the number of carrier marriages would be reduced. However, there were still the same number of carrier/carrier matings and no reduction in the incidence of Sickle Cell Anemia. Meanwhile, the screening program had introduced a new stigmatized health state, such that carriers were perceived as 'defective' and less desirable in terms of marriage partners. Although the results of this study may not be generalizable to other geographic areas or ethnic populations, it illustrates the potential for psychological harm of carriers without generating any societal "good" in the form disease reduction.

As the detection rate for CF carriers increases, it is the intention of the medical community to widen their audience to include members of the general public (Caskey, Kaback and Beaudet, 1990; Workshop on Population Screening for the Cystic Fibrosis Gene, 1990;

Canadian Task Force on the Periodic Health Examination, 1991). This day may be fast approaching as detection rates as high as 91.2% have been reported in certain areas (Clautres et al., 1993). However, as time marches on, the face of CF is also rapidly changing. Within the past two decades, CF has gone from a lethal disease of infancy, to a lethal disease of adulthood. The prognosis for children born with CF has never been better than it is today. New pharmaceutical treatments and medical interventions have provided reason for optimism for new CF parents. Moreover, CF therapy was previously limited to symptomatic intervention but now molecular research has led to new therapeutic alternatives such as aerosolized recombinant human DNases and novel uses of sodium channel blockers (see Surh et al., 1992). These developments and others could potentially halt, or even cure, the disease. Although these new treatments are highly experimental, at a minimum they provide hope for CF families and evidence that CF researchers are working towards a cure.

Given these medical advancements and lack of evidence that current carrier testing leads to a reduction of CF, Conway et al., (1994) pose the question "Is genetic screening in such a scenario justified?" In a study of general population adults, Decruyenaere et al. (1992) found that - after genetic counselling - only 5% of adults in the general population believed that they would not be able to care for an affected child. Closer examination of responses revealed that along a continuum of care ranging from "I could not manage" (score = 1) to "It would be easy to manage" (score = 7), scores were clustered about the middle such that only 1% and 5% of responses were for the low and high burden extremes, respectively. Also, Denayer et al (1992) found that only 7% of high risk aunts and uncles reported that they thought the burden of raising a child with CF would be so great that they could not

cope with it. Similarly, in the present study, the burden of CF for the caregiver and quality of life for the child were assessed using preference values (ratings and utilities). Notwithstanding the significant shortcomings of utility measurement, both ratings and utility values indicated that the life of a child affected with CF is more preferable than the abortion of a CF fetus.

Implications of Supply "Push"

"Since the splitting of the atom, everything has changed except our way of thinking, and thus, we drift towards unparalleled catastrophe,"

- Albert Einstein

What are the implications of the medical and political establishments "pushing" genetic testing upon society? Best case scenario is that individuals who may otherwise never have been tested subsequently benefit from testing (in one way or another). Screening programs which are guilty of targeting sensitive populations and providing insufficient or biased genetic counselling may tacitly couch their screening mandate within these terms (Dodge, 1990; Brock, 1990). Yet, it is not enough to "hope for the best" in relation to genetics. If Einstein's warning is to be heeded, then health care professionals should "expect the worst" and act accordingly.

It is difficult to imagine what the worst case scenario for genetic screening would entail. Historically, the Sickle Cell Anemia screening program is often cited as the biggest disaster in genetic screening (U.S. Congress, 1992; Roberts, 1992; Markel, 1992). As outlined

earlier, this autosomal recessive gene disorder is most prevalent amongst African Americans. Widespread screening programs which targeted this population were hastily implemented by the medical community in the 1970s with little genetic counselling resources. Moreover, the U.S. government inappropriately mandated that 1) all African Americans be tested prior to issuing a marriage license; 2) all school-aged children in urban areas - where, suspiciously, the vast majority of African Americans lived - be tested; and 3) that carriers be separated from non-carriers as they were falsely labelled as infectious (U.S. Congress, 1992; Roberts, 1992; Markel, 1992). Consequently, public misconception, prejudice and subsequent discrimination of carriers was rampant. For example, Linus Pauling, nobel prize winner and controversial scientist, was quoted as recommending ludicrous preventative measures. He advocated that "There should be tattooed on the forehead of every young person, a symbol showing possession of the sickle cell gene [so as to prevent] two young people carrying the same seriously defective gene in single dose from falling in love with one another" (as cited in Markel, 1992, p.213). Clearly, discriminatory measures were not this radical, although, Sickle cell carriers were denied insurance, employment and entrance into the U.S. air force academy (U.S. Congress, 1992).

Markel (1992) traces the evolution of stigmatization and discrimination from biblical times where the separation of the "healthy" from the "sick" are well documented in descriptions of leper colonies. Those with leprosy were ostracised from communities and essentially placed in quarantines. In its strictest sense, quarantine has been defined by medical historians as "any societal attempt at 'marking off' or 'the creation of a boundary to ward

off a feared biological contaminant lest it penetrate a healthy population'" (Markel, 1992, p.210). This way of thinking spawned the eugenics movement which first manifest itself in the form of immigration restrictions between 1880 and 1924 in the U.S. The Johnson-Reed Act effectively eliminated immigration of Russian and Polish Jews, Italians, and Central Europeans because "as a whole, [they] present a higher percentage of inborn socially inadequate qualities (e.g., insanity, feeble-mindedness, dependency, criminal behaviour, deformities, tuberculosis, etc.) than do the old stocks (e.g., Nordics, Anglo-Saxons, etc.)" (Laughlin, H.H., expert witness testimony as cited in Markel, 1992, p.210). Similarly, Canadian Eugenicists lobbied to influence policy development and legislation to prevent the immigration of races deemed physically and/or mentally incompetent. For example, an act passed in 1910 defined undesirable immigrants as "mental defectives (including epileptics, idiots, the feeble-minded, imbeciles, and the insane); physical defectives (including the dumb and blind); and people with "loathsome" diseases or those deemed a risk to public health" (Science Council of Canada, 1991, p. 78).

In Canada, direct control of reproduction by the state began in 1928 when the United Farmers of Alberta passed the Sexual Sterilization Act. This act would allow for the sterilization of the institutionalized mentally ill upon the approval of a Eugenics board and with the consent of the patient or their guardian (Science Council of Canada, 1991). Subsequently, in 1937 the Albertan government felt that it was no longer necessary to get the consent of the patient or guardian and would sterilize the mentally ill based solely on the recommendation of the Eugenics board. British Columbia followed suit in 1933 with their Sexual Sterilization Act. This act stated "[persons] likely to beget or bear children who by

reason of inheritance would have a tendency to serious mental disease or mental deficiency" could be recommended by the heads of mental institutions to be sterilized (Science Council of Canada, 1991, p. 76). Sterilization of "imbeciles" continued for 44 years until these acts were repealed by the governments of Alberta and British Columbia in 1972. By this time, 2822 individuals had been "approved" for sterilization in Alberta alone - 25% of which were Natives or Metis who only accounted for 2.5% of the population. Records for sterilizations in British Columbia are not available, however, it has been estimated that a few hundred individuals were sterilized during this time (Science Council of Canada, 1991).

History lessons have illustrated the cruel reality of discrimination and stigmatization of the disadvantaged. It seems only recently that society has adopted more enlightened views of the disabled, thereby opening the new realm of "political correctness". The move towards integration of the disabled into society has allowed many individuals to expand their previously sheltered world consisting of workshops and special schools (Kenen and Schmidt, 1978), while at the same time disproving unfounded stereotypes. This modern day attitude is packaged as one of compassion for the disadvantaged. However, it appears that this compassion does not translate for those who are found to carry defective genes such as Sickle cell anemia. Some investigators are now debating whether the discovery of deleterious genes created a new form of discrimination for individuals detected as "genetic cripples" (Markel, 1992; Kenen and Schmidt, 1978; and Clarke, 1991). This is a dangerous proposition as geneticists now estimate that each individual carries four to eight recessive disease genes that have gone undetected as mutant alleles not yet been identified (Kenen and Schmidt, 1978).

Re-Defining "Success" in CF Carrier Testing

Research for CF carrier screening began with an attempt to determine whether testing programs should be opened up to the general population. As such, demand for carrier testing was assessed by attitudinal studies which concluded that attitudes towards carrier testing were favourable across both the high risk and general populations. Thus, under the assumption that favourable attitudes will lead to positive testing behaviours, test uptake for CF carrier screening programs should have been high. However, observed participation rates varied widely. In particular, initial participation amongst the high risk population was unexpectedly low (Surh et al., 1994; Sorenson et al., 1994). Therefore, the present study examined the question "why do people get tested?" or, more specifically, "what factors predict testing decisions?" The overall finding of the study is that although knowledge, attitude, affect and preferences may predict testing decisions, they do not predict testing behaviour amongst the high risk population. Rather, the use of convenience factors such as active recruitment and non-invasive DNA sampling will ensure high participation in genetic testing. The present study has made the argument that high participation does not indicate a "need" on the part of the client for the test information, nor does it mean that those tested will take measures to avoid having a child with CF.

The present study argues that a 'successful' CF carrier screening has little to do with participation rates or a reduction in the incidence rate of CF. Instead, 'successful' DNA predictive testing programs should be defined as those in which genetic testing decisions are informed (knowledge), consistent with one's beliefs (attitudes) and behaviourally implemented (behaviours). Investigators have addressed knowledge and attitudinal issues,

therefore, it follows that the next step in this area should be to examine intended behaviours. Thus, if individuals could provide an accurate estimate of the likelihood that they would take action towards specific reproductive outcomes, then it may be possible to determine *how* people use the test result.

If the findings of previous attitudinal research are any indication of their predictive power for subsequent behaviours, then it is unlikely responses to questions such as “how do you intend to use your test result?” will accurately indicate actual reproductive behaviour. In fact, Watson, Mayall et al. (1992) conducted a follow-up study of members of the general population who were found to be carriers. Responses regarding their family planning at pre and post-testing (42% vs. 33%, respectively) or their request for prenatal diagnosis (70% vs. 78%, respectively) remained unchanged. However, when considering abortion, 20% said ‘yes’ prior to receiving their test result, whereas 36% said ‘yes’ after receiving their test result. These findings illustrate the effect of uncertainty on attitudes. It is natural that when choosing between competing options, additional pieces of information will influence decisions. Thus, it is quite possible that these same individuals might change their assessment of abortion if they knew their spouse’s carrier status or the results of prenatal tests.

It was proposed that utilities elicited in the present study would provide a better indication of the desirability of the reproductive outcomes resulting from carrier testing. Unfortunately, the present study has demonstrated that utility scores are subject to serious theoretical, practical and clinical limitations when used in the context of genetic testing (see

page 103). Consequently, it is argued that they are poor indicators of preference and are unlikely to provide an accurate indication of subsequent behaviours. However, even if utility values provided an accurate estimate of the individual's preference for the particular health state, they may not answer the right question.

A shift in research questions was required from population screening studies which examined "who to test?" (i.e., high risk versus general population). Thus, the present study explored the question "why do people get tested?" (i.e., genetic testing factors or convenience of testing). Given that participation in testing can be easily manipulated, the question to now ask is "how do people intend on using their test results in their future family planning?" In this way, individuals may be provided with the necessary medical and emotional support towards the desired outcome. For example, those who are most likely to pursue a therapeutic abortion to avoid having a child affected with CF may be provided with sufficient information regarding the availability, benefits, limitations and implications of carrier testing and prenatal testing. Similarly, those who are most likely to choose not to have any biological children or let nature take its course may also be in need of support and referrals to other resources. Therefore, if the appropriate question involves following individuals through their genetic testing decisions (i.e., carrier test for self and partner? prenatal test?) then it is of little value to assess their preferences for health states which may involve outcomes that they would never consider.

If the key to understanding carrier testing decisions lies in a person's behaviour, then the ideal method of research would entail a prospective investigation of individuals as they pass

through their mate selection and reproductive decisions. As shown in Table 9, seven separate studies have tested a total of 13,489 individuals, identifying only 18 high risk pregnancies (Super et al., 1994; Menne et al., 1992; Harris, et al., 1993; Livingstone et al., 1994; Watson, Mayall et al., 1991; Bekker et al., 1993 and Wald, 1991). Clearly, it is not feasible to follow a large number individuals throughout their testing decisions and test results to explore whether the few carrier couples detected follow through on their intended use of their test results. In essence what is required is an investigation of the *process* of genetic testing decisions in order to explore an individual's decisions along the decision tree (Appendix Q), without having to actually behaviourally implement these decisions. The shortcoming of this and other studies is that they have focused on the beginning (i.e., carrier testing decision) and end points (i.e., reproductive outcomes) of the tree.

Paradigm shift:

Ajzen and Fishbein's (1980) theory of reasoned action may provide the framework from which researchers in this area can better predict the individual's behaviours through the process of genetic testing decisions (Appendix R). This model suggests that an individual's behaviour can be predicted from a) their own attitudes towards the outcome; b) their preference for that outcome; c) their attitudes towards the behaviour associated with the outcome; and d) their intention to take action towards the outcome. In addition, this theory accounts for the influence of the opinions of significant others as well as the weight that the individual places on their opinion. For example, an individual's likelihood of seeking out an abortion might involve attitudes associated with the decision to have an abortion (e.g.,

my decision to have an abortion is good/bad), attitudes towards the procedure (e.g., my decision to have an abortion is harmful/beneficial), and their intention to go for the procedure (e.g., I intend or do not intend to have an abortion). Then the influence of significant others is factored in (e.g., my partner thinks that my decision to have an abortion is good/bad) as well as the importance of their opinion (e.g., generally speaking, how much do you want to do what your parents think you should do).

This model is particularly appealing for addressing the questions of 'use' of test results throughout the decision tree as it incorporates the views of others in the decision making process. Past research by Wertz et al. has noted the influence of significant others on the future reproductive decisions of Obligate Carriers. Specifically, attitudes of Obligate Carriers towards intentions to use prenatal diagnosis of CF (Wertz, Janes et al., 1992) or abortion (Wertz, Rosentfield et al., 1991) were dependent upon the approval of their siblings, spouse and parents. It may also be interesting to investigate the magnitude of the influence of health care professionals and determine if it detracts from the individual's own motivations for testing.

In summary, the results of the present study have demonstrated that attitudes towards carrier testing are poor predictors for testing behaviour. Rather, it appears that convenience of testing obscures the need for information or the perception of benefits resulting from testing. Therefore, a shift towards exploring intended behaviours may be necessary to assess demand for testing. However, shallow investigations which pose questions such as "would you consider abortion?" do not appear to accurately predict reproductive

behaviours. Fortunately, Ajzen and Fishbein's theory of reasoned action may provide more insight into this question by assessing the views of the participant, their perception of societal norms and their significant others throughout their genetic testing decisions.

Methodological Limitations of the study

As described earlier the use of utilities in genetics is novel and unique. It was proposed that utility assessment might provide an estimate of preference for different carrier testing outcomes and predict carrier testing decisions. Utilities were appealing because they incorporated risk and uncertainty in their assessment, thereby making them well suited to genetic testing decision making. However, it appears that utilities may not be assessing the right question as they force individuals into the end points of the decision tree using artificial scenarios. As a result, individuals must assign preferences for living in a health state which they may not ever consider. Therefore, utility assessment focuses on specific health state outcomes and therefore does not yield any insight into the process of genetic testing decisions. In addition throughout the study several theoretical, practical and clinical limitations of utility theory and assessment became evident. These shortcomings are described in the following sections.

Theoretical limitations of Utility Theory: Violation of the axioms

As described earlier, utility theory is based on von Neuman and Morgenstern's set of axioms defining rational decision making which have been under fire for many years (Fishburn, 1988). The two traditional examples of violation of the axioms have been aptly demonstrated by Allais' Paradox and Ellsberg's Paradox (Dawes, 1988, Yates, 1990). Both illustrate the rigidity of the axioms and prove that individuals do not always choose options which will maximize their expected utility (Dawes, 1988). The

following discussion outlines three common violations of specific axioms demonstrated by participants in the present study indicating: 1) it is clear that choices for certain options can not be considered as absolute as defined by the transitivity axiom; 2) indecision amongst choices can not be written off as indifference as dictated by the comparability axiom; and 3) health states used as 'anchors' according to the solvability axiom have been shown to be subjective and thus, arbitrary.

1. Transitivity

This axiom states that if $A \succ B$ and $B \succ C$, then $A \succ C$. Justification of this axiom is based on the danger that individuals who are shown to violate it may become "money pumps". Dawes (1988) aptly illustrates the effect of intransitivity and money pumps using the following example: Suppose that Nora preferred hard liquor over wine, wine over beer and yet, beer over hard liquor. As a result, she should be willing to pay some amount of money to trade a less preferable drink for a more preferred drink. Now suppose that Donna offered Nora some wine. Because Nora prefers hard liquor to wine, she should be willing to pay Donna something to have hard liquor instead. Subsequently, Nora should be willing to pay something to have beer in the place of the hard liquor, and finally willing to pay for the substitution of wine for beer. This would mean that Nora would have paid for the privilege of ending up with the alternative she was given in the first place. By repeating this cycle indefinitely, Nora would pay an indefinite amount to get nowhere.

Unfortunately, violations of transitivity were common in the present study. It is estimated that approximately one in ten respondents expressed inconsistent preferences when rankings of health states taken off of the visual analogue scale were compared with utility values elicited using the Standard Gamble technique. For example, on the visual analogue scale a participant may have ordered the health states such that having a CF baby more desirable than having no children at all, which was more desirable than having an abortion. Then later in the utility assessment, they may indicate that having an abortion is better than a CF baby, which is better than not having any children.

In some cases, violations of transitivity were somewhat inconsequential as health states may have been only rated one or two points apart on the visual analogue scale. This closeness in ratings may have indicated that the health states were similar in desirability. Thus, it is possible that these respondents were indifferent to the choices which means that the transitivity axiom does not apply. However, violations also occurred when health states were rated as being distinctly different in terms of desirability. In these cases, the research assistant queried the participant to determine the actual preference ranking of the health states in question. Some participants chose to change their previous rating of the health state such that their utilities for those states were consistent. While others did not change their previous ordering as they maintained that preference values measured by the visual analogue scale were based on the assessment of all of the health states. Whereas, utility values were elicited within the boundaries of the anchors within the lottery (e.g., healthy baby - very sick baby). Therefore, preferences for health states in this context were explained as being distinct

This intransitivity speaks to some of the problems associated with these two methods of assessing preferences. Although rating scales have been used to simply aid in the administration of the Standard Gamble utility assessment, they should, in theory, yield similar rankings of the health states. However, as Dawes points out, “choices are, after all, not made repeatedly, but in a particular context. A choice between two alternatives does not have to be one by which the individual is bound for all time and in all circumstances” (1988, p.156).

2. Comparability:

This axiom states that if A and B are in the alternative set S, then either $A \geq B$ or $B \geq A$ or both, in which case $A \approx B$. It is postulated that when an individual must choose between two choices, they will have a preference for one over the other. However, it is also possible that in some cases an individual will be indifferent between the two choices. For example, I may prefer beef to chicken, but I am indifferent between chicken and fish. Using this illustration the axiom appears straightforward, yet consider choices that participants were faced with in the present study. For example, I obviously prefer having a ‘healthy baby’ to having a ‘very sick baby’, but how do I compare the experience of having a very sick child to aborting a fetus affected with CF? Within this gamble, participants must weight their preference for choosing the lottery between a healthy and sick child against the certainty of having an abortion. For the majority of individuals, this gamble left them to decide between the lesser of two undesirable options. It was observed that many of those participants who had

demonstrated difficulty making a decision for any gamble they stated that they were indifferent between the two options. Some participants even voiced their displeasure with being confronted with some gambles and stated that they could not decide between the two. Yet, when queried (according to the utility assessment protocol) most participant in this situation would indicate that they were indifferent.

Therefore, it would appear that when decisions amongst choices are difficult for participants, they are more likely to indicate that they are indifferent between the choices. It was observed that for some participants, health states were incomparable and yet, if pressed for their preference they were more likely to indicate that they were indifferent. In sum, this axiom may inappropriately place a preference value on a health state based on a participant's justifiable inability to choose between two options.

3. Solvability:

This axiom states that for all A , B , and C in S , if $A \succ B \succeq C$, then there exists a probability p such that $B \approx (ApC)$. Basically, this means that there is some way of combining probabilities of the occurrence of A and C such that an individual is indifferent from choosing B or this combination (Dawes, 1988). The Standard Gamble method of utility assessment is often cited as the closest thing to a 'gold standard' because it is build upon this axiom (Wakker and Stiggelbout, 1995). It assumes that 'A' in this case would be 'perfect health' and 'C' would be 'death'. Yet, philosophically speaking can humans imagine living in a state of perfect health? Likewise, how do we conceptualize death? Moreover, can we make the assumption

that these intangible states are equivalent for all individuals? Clearly, the answer is no. Descriptions of perfect health and death used in the present study were taken from an established standard gamble protocol (Furlong et al., 1990). The death scenario involved an "immediate and painless death [where] you die today without any more pain or pleasure than you have already experienced". For many individuals this was not their worst case scenario, nor was it considered the worst way to die. Similarly, the 'very sick baby' scenario was not always considered the worst case scenario in relation to the other reproductive options. In fact, approximately one third of the respondents (93/265) ranked one of the other reproductive scenarios as their lowest anchor.

Previous studies have also documented health states which are perceived to be worse than death (Knaus, Wagner and Lynn, 1991, Mold, Looney, Viviani and Quiggins, 1994; Solomon, Glick, Russo, Lee and Schulman, 1994). In fact, several proponents of utility theory have even proposed different methods for dealing with quantifying states worse than death such as 1) equating those states to death (i.e., assigning them a value of 0) (Surh et al, 1996); 2) assigning them a value of -1 (Torrance, Boyle and Horwood, 1982); or 3) linearly transforming them into a negative value (Patrick, Starkes, Cain, Uhlmann and Pearlman, 1994). Thus, it is clear that the lower limit (origin) of the utility scale is not well grounded.

Practical limitations of Utility Assessments

Prominent proponents of utility assessment have noted the cognitive demands placed on the participant when eliciting utility values using the Standard Gamble method (Feeny and Torrance, 1989). Participants in the present study confirmed this finding as many

expressed difficulty in completing the utility assessment. It was not uncommon for participants to express frustration (46%) or confusion (16%) with the standard gamble procedure. However, it was interesting to note that most participants (90%) indicated that they felt that their responses accurately reflected their preferences for the health states. This may be explained by the fact that, unlike the scores on the rating scale, utility values derived from the standard gamble were not provided. That is, preferences for health states could be easily read off the rating scale, therefore, an individual knew what their score was for each health state. In contrast, utilities elicited from the standard gamble board were never disclosed by the research assistant. Instead, participant's simply revealed their choices for different lotteries from which their utility value was calculated. Therefore, it is *highly* unlikely that a participant would know that, for example, if they chose 100% chance of having a child with CF over a lottery in which they had a 90% chance of having a health baby and 10% chance of having a very sick baby, that their subsequent utility for having a child with CF was .90. Consequently, self-report of their beliefs that their responses revealed their preferences may have been based upon rating scale preference values and not their standard gamble utilities.

Low correlations between the rating scale preference values and the standard gamble utilities were observed for all health states with the exception of the CF baby scenario in which ratings were moderately correlated with utilities. The results demonstrated that there is a negligible relationship between preference values elicited using a visual analogue scale and the standard gamble method. In theory, both measures should yield comparable preference values, although it has been suggested that ratings are not

considered to be on an interval scale (Furlong et al., 1990). Yet, taken at face value, the rating scale is designed such that individuals rate their relative desirability of hypothetical scenarios from best to worst. Ideally, these values would provide an indication of their preference for these outcomes as well as their likelihood of seeking out these outcomes relative to each other. In contrast, the standard gamble does not pit the scenarios against each other. Instead, preference values are elicited from how much risk an individual is willing to take to avoid an undesirable outcome (e.g., birth of a very sick baby). Therefore, the direct comparison of the scenarios with each other is lost as scenarios are only evaluated against anchors (i.e., healthy baby - very sick baby). Thus, it is possible that these differences between the measures account for the low correlation between two preference values.

Previous research on gallbladder treatments has supported these findings. In a recent study, Bass et al. (1994) found that ratings of health states were also poorly correlated with utility values and voiced their concern over using these scaling techniques interchangeably. A subsequent response to their study by Bowe (1995) proposed that these discrepant findings may be due to a response bias in which participants are more 'risk averse' such that they are unwilling to accept any chance, or less chance, of receiving the worse case scenario (i.e., lower anchor). The phenomenon of 'risk aversion' has been reported to lead to a higher valuation of outcomes when measured against perfect health and death yielding a concave utility function (see Birnbaum, 1992; Wakker and Stiggelbout, 1995)

Clinical limitations of Utility Preference Values

In terms of practical limitations of utilities, risk aversion can be especially misleading for a) the physician who uses utility values as an indication of patient preferences and subsequent patient decision making and b) the policy maker who uses these inflated values for cost-utility analyses and subsequent policy making. If the patient is risk averse (i.e., if they have a strong disutility for the lower anchor) then they will report inflated utility values. Thus, in the case of the clinician, they might be more inclined to opt for a treatment which is not as desirable as the patient might have indicated. Similarly, cost-utility analysis may be skewed such that different treatments may appear to be uniformly desirable, therefore policy makers will opt to fund the least expensive treatment. However, actual preferences for the treatments may have been lower had they not been measured against some probability of the lower anchor (traditionally defined as death).

Moreover, it has been suggested that changes in utility values of $\pm .10$ are clinically significant (Feeny and Torrance, 1989). Yet, large standard deviations are common in utility measurement (Bass et al., 1994). Standard deviations of health state utilities in the present study were in the 0.30 range for all health states, with the exception of the carrier test scenario where one partner is detected as a carrier and the other is at low risk. In this scenario, standard deviations ranged from .13 to .26. This wide variability in utility scores detracts from the sensitivity of the measure as a research tool and clinical decision making aid.

Potential Biases of a Pre-Selected Sample:

The caveat of investigating the high risk population is that it is not possible to obtain a true random sample (Denayer et al., 1992; Super et al., 1994). Issues of confidentiality dictate that high risk un-tested relatives must be recruited via CF patients, Obligate Carriers, and/or high risk individuals who have previously come in for carrier testing. Similarly, in the present study, names of potential members of the Not-Tested group were provided by Obligate Carriers, Tested individuals and sometimes from Not-Tested members already seen by the study. In other words, participants comprising the Not-Tested group were pre-selected by other high risk individuals who had previously undergone testing. Although research assistants specifically asked for all names of other relatives in the area, these family recruiters may have had their own agendas when selecting the names of potential participants for the study. Because these recruiters decided to be tested themselves, they may be biased towards only selecting those relatives that have favourable views towards testing and would choose to be tested with the study. Furthermore, it is possible that the study would not gain access into families who feel that CF is a taboo subject and thus, have propagated the "web of silence" throughout the family. Likewise, it is possible that because the research assistant was obliged to disclose how (i.e., from whom) the study got their name, some family recruiters may not have provided the names of relatives with which they have precarious relations or irregular contact. These potential biases could have skewed the data such that high risk Not-Tested relatives recruited for the study would be more informed and have more preferable attitudes towards testing.

Denayer et al. (1992) also ran into this recruitment dilemma with their high risk sample. Although they admitted that the dependence on the co-operation of CF families to provide names may have created a small bias. They found that 70% of family members gave names of other relatives. They postulated that the remaining 30% may not have provided names because they had either lost contact with family members or CF was taboo within the family. In the present study, 87% of high risk relatives were willing to provide names of other family members, while 63% of those who did not provide names did so because they lived outside the boundaries of the study. Therefore, it would appear that most high risk relatives, notwithstanding their potential for biased recruitment, allow entry into their families.

However, entry into a family does not necessary mean full disclosure of names of relatives. Although high risk participants provided the names of some potential participants, they may not have provided the names of *all* potential participants. The present study attempted to gather detailed information on the participants' family tree (pedigree) which included the age, location and carrier status (if available) of all relatives. However, this was often a difficult task as: 1) some participants could not provide information on closely related relatives such as first cousins; 2) participants from the same families provided inconsistent family trees and/or 3) participants were unwilling to spend the extra time (ranging 15 to 30 minutes - depending on the size of the family) to map out their family tree. Thus, not only were the pedigree data potentially inaccurate, but further analyses would be involved and were beyond the scope of the present study.

Thus, an important piece of the pie is missing in this and other high risk studies. The combined efforts of Surh et al's previous study (1994) and the present study have assessed the views of high risk relatives. However, as almost all the participants in the present study were tested and all those in the previous study were tested (Surh et al., 1994), the views of those who have *not* been tested have yet to be assessed. Is it enough to assume that *all* high risk relatives suffer from inconvenience factors? And that if testing were provided to all potential high risk relatives that they would *all* choose to be tested? As shown in Figure 6, many of the un-tested high risk relatives in the Ottawa-Carleton area have not yet been surveyed. Moreover, totals presented for the high risk population are gross estimates as they do not include families that did not participate in the present study, the initial study (Surh et al., 1994) or newly diagnosed CF families (i.e., families who have recently had a child with CF who did not have a family history of CF).

Insert Figure 6 about here

One final limitation of the present study was that approximately three quarters of the study sample had either finished their family planning or were not planning on having children within the next two years. Consequently, reproductive issues were not a concern for a large part of the sample. Previous attitudinal research has demonstrated the effect of framing questions in terms of family planning decisions yields lower acceptance rates when

compared with questions referring to general opinions without reference to reproductive status. In the present study, many participants expressed an interest in carrier testing, although it may have been for their children's, and in some cases, their grandchildren's family planning.

Future research:

Opportunistic testing has been demonstrated to have a strong influence on testing behaviours. Future research should investigate distinct inconvenience factors such as taking time of work, finding a babysitter, transportation and parking costs in order to determine if these activities limit access to testing or rather if their elimination actively promotes and solicits certain testing behaviours. Understanding of convenience factors will aid in the provision of genetic services without going so far as to "push" genetic testing on those who may have little interest in using the test results towards their future family planning. This important addition to the genetic testing decision making model is illustrated in Figure 7.

Insert Figure 7 about here

In addition, the present study suggested that investigators shift the focus of their research question(s) from assessing attitudes towards outcomes (i.e., what do you think about abortion for CF?) and preferences for outcomes (i.e., what is your preference for aborting a fetus affected with CF?) such that they explore the likelihood of individuals to seek out

different reproductive options based on their attitudes, societal norms and intended behaviours. Therefore, those individuals seeking certain outcomes are provided with the necessary resources and support towards their desired reproductive outcome. Application of the Reasoned Action theory may identify those individuals who are most likely to benefit from genetic (carrier and prenatal) testing. As a result, this model may not only provide an accurate indicator of demand or “need” for genetic testing, but may also ensure that genetic services are informed, consistent with one’s beliefs and behaviourally implemented.

Conclusions

Advances in molecular genetics have opened up new debates concerning the medical, ethical, social and legal implications of widespread genetic testing. The cloning of the CF gene has provided experts from these fields with a model to examine the provision of new genetic services. To this end, past research has strived to assess the demand for CF carrier testing in order to ensure that screening programs are effective. Yet, accurate estimates of demand have alluded researchers due to unforeseen external influences such as convenience factors. Consequently, genetic services have been shown to be “pushed” upon those who may not have otherwise been tested and/or who may not want or need to be carrier tested.

The present study argued that the effect of genetic testing decision making factors such as knowledge, affect, attitude and preferences on carrier testing choices may be obscured by the influence of opportunistic carrier testing protocols. Paradoxically, individuals at high risk of being CF carriers are informed, have positive attitudes about testing and are interested in finding out their carrier status, yet they do not seek out testing. On the other

hand, members of the general population with a lower carrier risk, are uninformed, have less favourable views about testing, but are readily tested if the test is actively offered. Thus, recent research has clearly demonstrated that decisions to be carrier tested may be easily manipulated. As a result, the use of participation rates as a measure of demand for testing by the individual or program success in carrier screening has the potential to be dangerously misleading, especially in the case of dominant gene (e.g., Huntington's Disease) and susceptibility gene screening (e.g., breast and colon cancer).

In an attempt to develop the *ideal* population genetic testing model, research in this area has been enthusiastic, and as a result, too "active" in their recruitment for screening programs. After six years of high risk carrier screening, it is evident that the CF experience is not ideal. However, it is suggested that a more thorough assessment of an individual's need for genetic information through the examination of the process of decision making will make it a better model.

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Table 1

Family Planning and Demographics

	<u>Obligate Carrier</u> (n = 49)	<u>Tested</u> (n = 59)	<u>Not-Tested</u> (n = 98)	<u>General Population</u> (n = 59)	χ^2
<hr/>					
	<i>Family Planning</i>				
Have children	100%	64%	65%	100%	44.72***
Will have child(ren) in next 2 years	10%	27%	28%	24%	5.9
	<i>Demographics</i>				
Age^a	M 39 SD (7.0)	34 (8.3)	33 (7.8)	36 (6.4)	F = 8.09***
Gender:					
Male	45%	34%	34%	42%	2.67
Female	55%	66%	66%	58%	
Education:					
High School	35%	26%	31%	19%	10.32
College	46%	44%	41%	50%	
University BA	4%	2%	6%	2%	
University MA	13%	20%	17%	22%	
University PhD	2%	9%	5%	7%	
Language:					
English	75%	78%	83%	91%	8.11
French	23%	17%	14%	5%	
Both	2%	5%	3%	4%	
Other	0%	0%	0%	0%	
Religion:					
Catholic	39%	65%	63%	41%	19.83**
Protestant	44%	20%	22%	26%	
Other	17%	15%	15%	33%	

Table 1 (continued)

Family Planning and Demographics

	<u>Obligate Carrier</u> (n = 49)	<u>Tested</u> (n = 59)	<u>Not-Tested</u> (n = 98)	<u>General Population</u> (n = 59)	χ^2
Marital Status:					
Single	0%	20%	19%	0%	29.44***
Married or Common-Law	92%	75%	78%	100%	
Separated or Divorced	8%	5%	3%	0%	
Income:					
< \$20,000	5%	2%	5%	4%	20.2
\$20,000-\$39,000	33%	25%	16%	21%	
\$40,000-\$59,000	7%	16%	18%	11%	
\$60,000-\$79,000	38%	39%	21%	32%	
\$80,000-\$99,000	7%	10%	23%	19%	
> \$100,000	10%	8%	18%	13%	

Note. ** $p < .01$ ***; $p < .001$

^a ANOVA ($F(3,261) = 8.09; p < .000$). Tukey a (at $p < .05$) Obligate Carriers are older than the Tested and Not-tested groups.

Table 2

Knowledge of CF and CF Carrier Testing

Knowledge Items:	Percent correct				χ^2 (3, 265)
	Obligate Carrier (n=49)	Tested (n=59)	Not-Tested (n=98)	General Population (n=59)	
Before today, I have heard of CF Carrier Testing ^a	100	100	84	36	99.13***
CF Disease Process:					
CF is a disease affecting lungs and digestive system	98	100	95	73	36.62***
On average, individuals with CF live until adulthood	96	81	71	42	41.89***
CF patients usually need treatment every day and are less able to have children because of their disease	86	53	35	27	45.56***
CF Carrier Test:					
The cause of CF is an inherited illness	88	88	88	68	13.34**
A CF "carrier" is someone who does not have CF but who could have a child with CF	100	93	90	66	33.16***
CF "carriers" are diagnosed by a blood test	65	73	47	34	22.43**
CF Carrier Risks:					
If there is no family history of CF, the chance of being a carrier is 1 in 25	53	25	19	2	41.02***
If both partners are carriers the chance their unborn child will have CF is 1 in 4	94	92	78	34	69.37***
Knew their approximate carrier risk	65	31	14	5	61.42***
					F (3, 261)
Overall percent correct ^b	M 82.76	70.62	59.64	38.98	67.17***
	SD (14.50)	(15.50)	(17.00)	(19.50)	

Note. ** $p < .01$, *** $p < .001$

^a Not included in the overall percent correct calculation

^b Tukey α ($p < .05$); Obligate Carriers > Tested > Not-Tested > General Population

Table 3

Hypothetical and actual emotional reactions to carrier test results.

HYPOTHETICAL			
Anticipated emotion on being told that they are a CF carrier			
	General Population (n = 59)	Not-Tested (n = 98)	χ^2 (2, 157)
Happy^a	0%	1%	0.59
Relieved	16%	19%	0.28
Anxious	74%	44%	13.9**
Depressed	55%	25%	24.45***
Angry	51%	18%	20.15***
Hopeless	9%	7%	6.48*
Labelled/Abnormal	14%	6%	15.92***
Total Affect Score:^b	M 23.8 SD (3.78)	19.7 (4.54)	F (1,144) - 23.21***
ACTUAL			
Recalling emotions after receiving a positive carrier test result			
	Obligate Carrier (n = 41)	Tested (n = 18)	χ^2 (2, 59)
Happy	5%	0%	2.07
Relieved	32%	17%	2.20
Anxious	55%	41%	1.20
Depressed	50%	33%	1.69
Angry	40%	6%	7.58
Hopeless	30%	0%	6.92*
Labelled/Abnormal	10%	6%	0.37
Total Affect Score:	M 21 SD (6.08)	19.8 (4.73)	t (55) - 0.695

Note. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

^a Individual items were collapsed into three categories (very likely/likely, neutral or unlikely/very likely) for the χ^2 analyses such that percentages indicate those who were very likely or likely to feel these emotions.

^b Total Affect scores were calculated using the full 5 point scale. The higher the score, the higher the negative affect. Maximum score = 35.

Table 4

Depression and Anxiety Inventories

Clinical Measure	Obligate Carrier (n=49)		Tested (n=59)		Not-Tested (n=98)		General Population (n=59)		F (9, 265)
	M	SD	M	SD	M	SD	M	SD	
BDI ^a	4.9	(4.1)	5.8	(4.6)	5.1	(4.9)	4.9	(4.3)	0.96
STAI ^b - Trait Anxiety	47.4	(7.1)	49.2	(7.9)	47.1	(8.4)	48.6	(6.5)	
STAI - State Anxiety	45.5	(7.2)	45.6	(6.3)	43.9	(6.7)	44.7	(5.6)	

Note.

^a BDI maximum score = 63. Scores below nine represent depressive symptomatology within the normal range.

^b STAI trait and state scores have been converted into standardized T-scores.

Table 5**Attitudes towards Carrier Testing**

Attitude Items:	Percent of participants who agree ^a				χ^2 (6, 265)
	Obligate Carriers	Tested	Not-Tested	General Population	
	(n = 49)	(n = 59)	(n = 98)	(n = 59)	
Pros:					
Testing will help me make decision about my family planning	94	78	72	60	21.5***
Testing would give me peace of mind	65	83	67	33	41.1***
Testing would lead to a cure for CF	51	69	73	71	31.4***
CF Carriers should have their children tested	94	83	84	81	7.30
Cons:					
It's better to let nature take its course	12	7	9	12	13.31*
Testing would make me worry unnecessarily	14	7	21	34	41.3***
It's better not to know	10	3	4	7	20.12**
Testing is too much trouble	0	0	0	2	19.05**
I believe that testing is not necessary for me	19	3	5	41	82.2***
					F (2, 252)
Overall attitude score^b					
M	36.38	38.37	36.73	32.22	17.69***
SD	(5.28)	(4.83)	(4.49)	(4.66)	

Note. * $p < .05$; ** $p < .01$; *** $p < .001$

^a Percentage agreement based on those who strongly agree or agree with the statement

^b Total is calculated from the full 5-point Likert scale such that the higher the score the more favourable the attitude towards testing. Maximum score = 30. Tukey a (at $p < .05$) General Population score is significantly lower than the Obligate Carrier, Tested and Not Tested

Table 6

Preferences for CF Health States

Health State Description	Obligate Carrier (n = 49)		Tested (n = 59)		Not-Tested (n = 98)		General Population (n = 59)	
	M	SD	M	SD	M	SD	M	SD
<i>Ratings</i>								F (15,326)
Abortion	21 (26)		22 (24)		24 (24)		23 (23)	1.23
CF Baby	45 (28)		33 (22)		29 (24)		32 (21)	
No Baby	34 (27)		33 (28)		34 (28)		29 (26)	
One Carrier	69 (22)		71 (24)		71 (19)		71 (21)	
Both Carriers	45 (26)		43 (24)		41 (21)		41 (24)	
<i>Utilities</i>								F (15,258)
Abortion	0.24 (0.35)		0.29 (0.36)		0.36 (0.35)		0.31 (0.36)	1.86*
CF Baby ^a	0.64 (0.32)		0.48 (0.34)		0.44 (0.33)		0.38 (0.29)	
No Baby	0.56 (0.35)		0.52 (0.37)		0.59 (0.34)		0.47 (0.32)	
One Carrier ^b	0.87 (0.13)		0.79 (0.23)		0.79 (0.23)		0.73 (0.26)	
Both Carriers	0.66 (0.34)		0.62 (0.32)		0.58 (0.32)		0.56 (0.31)	

Note. * $p < .05$ ^a ANOVA, $F(3, 257) = 6.37, p = .000$. Tukey α ($p < .05$) = Obligate Carrier > General Population, Not Tested^b ANOVA, $F(3, 258) = 3.46, p = .017$. Tukey α ($p < .05$) = Obligate Carrier > General Population

Table 7**Correlations between Visual Analogue Scale and Standard Gamble Utilities**

<i>Ratings vs. Utilities</i>	
<hr/>	
Abortion	0.492**
CF Baby	0.144*
No Baby	0.121
One Carrier	0.181**
Both Carriers	0.274**

Note. * $p < .05$; ** $p < .01$

Based on total sample $N = 265$

Table 8

Previously reported participation rates for CF Carrier Testing

	Recruitment Procedure	DNA Test Method	% Uptake
HIGH RISK STUDIES			
<i>Active Recruitment:</i>			
Youn, A. (present study)	Testing done at a time and place of the participant's convenience; ~95% evening home visits	Buccal swab	98%
Super et al., (1994)	Information packages with mouthwash samples distributed by Obligate carriers, no direct contact for counselling, testing or follow-up	Mouthwash	91-98%
<i>Passive Recruitment:</i>			
Surh et al., (1994)	Individuals contact hospital for genetic counselling and testing appointment	Blood	< 10%
Sorenson et al., (1994)	Individuals contact hospital for appointment for genetic counselling and testing	Not specified	4%
GENERAL POPULATION STUDIES			
<i>Active Recruitment:</i>			
Harris et al., (1993)	During antenatal visits by physician	Mouthwash	90% *
Miedzybrodzka et al (1995)	Antenatal couple screening and stepwise screening	Mouthwash	90% *
Livingstone et al., (1994)	Couple screening; sample brought to antenatal visit	Mouthwash	76% *
Mennie et al., (1992)	Mailed letter and leaflet; phone contact by midwife; testing arranged during antenatal clinic appt.	Mouthwash	73% *
Watson et al., (1991)	Approached by researcher in family planning clinic; testing available	Mouthwash	87% *
	Approached by researcher in general practice waiting room, immediate testing available	Mouthwash	66%
Bekker et al., (1993)	Approached by researcher in clinic waiting room; immediate testing available	Mouthwash	70%
	Approached by researcher in clinic waiting room; testing by appointment	Mouthwash	25%
Mitchell et al., (1993)	High school students: Genetic Counselling in class; testing at school one week later	Blood	42%

Table 8 (continued)

Previously reported Uptake rates for CF Carrier Testing

	Recruitment Procedure	DNA Test Method	% Uptake
<i>Passive Recruitment:</i>			
Clayton et al., (1996)	Signs and letters in clinical and non clinical sites	Blood	< 1
Bekker et al., (1993)	Leaflet given in clinic waiting room, immediate testing available	Mouthwash	17%
	Mailed letter; testing by appt.	Mouthwash	12%
	Mailed letter with Leaflet; testing by appt	Mouthwash	9%
Watson, Mayall et al., (1991)	Mailed letter; testing by appt	Mouthwash	10%
Note. *Pregnant women comprised all or part of the sample			

Table 9

Literature review of the actual "use" of CF Carrier Test Results

	<u>Number Screened</u>	<u>Carriers Detected</u>	<u>Carrier Couples Detected</u>	<u>No. of Pregnancies</u>	<u>Outcome after Prenatal Dx</u>
<i>High Risk Studies</i>					
Super et al., (1994)	1563	450	15	9	4 Healthy 1 CF 3 Aborted 1 Unknown*
Youn, A. (present study)	98	33	0	--	--
<i>General Population Prenatal Studies</i>					
Mennie et al., (1992)	3165	111	4	4	3 Healthy 1 Aborted
Harris et al., (1993)	446	11	1	1	1 Healthy
Livingstone et al., (1994)	5922	238	4	4	2 Healthy 2 Aborted
<i>General Population Studies</i>					
Watson, Mayall, et al., (1991)	1000	29	0		-
Bekker, et al., (1993)	957	28	0		--
Wald, N. (1991)	338	13	0	-	--

Note, * refused prenatal diagnosis

Figure 1

CF Carrier Detection at 85% Sensitivity

Figure 2

Proposed Research Model for Genetic Testing Decision Making

Decision Making Factors:

Note. Reproduced with permission from Surh and Cappelli, 1992

Figure 3

Decision Tree for CF Health States

Figure 4

Experimental Design and Procedure

Note. : populations from which the group sample was selected
: groups of the study

Figure 5**Relationship to the affected relative**

Figure 6**Ottawa-Carleton High Risk Population**

APPENDIX A

HS

You are a perfectly well individual.

HS

- You are a perfectly well individual
- This means that you are in a constant state of complete physical, mental, and spiritual well-being.
- Think about living the rest of your life in this state

DS

You die an immediate death.

DS

- You die an immediate painless death
- This means that you would die today without any more planning, pleasure, or suffering than you have already experienced

CF

Birth of a CF baby.
(with physical problems)

CF

- You (or your partner) give birth to a baby with CF.
- Your child has normal intelligence but has physical problems which may limit some activities.
- Despite frequent sick days, your child goes to school and eventually to work.
- Despite needing daily intensive treatment, you face the usual joys and challenges of parenting.
- In their 30's, your child dies from CF.
- Think about living the rest of your life with this experience.

HB

Birth of a healthy baby.

HB

- You (or your partner) give birth to a healthy baby.
- You face the usual joys and challenges of parenting.
- Think about living the rest of your life with this experience.

AB

You proceed with the abortion of an unborn CF baby.

AB

- Prenatal testing shows that your unborn baby has CF
- You have an abortion rather than continuing with this pregnancy
- Think about living the rest of your life with this experience

MC

You (or your partner) have a miscarriage.

MC

- You (or your partner) have a miscarriage early in pregnancy
- You realize a miscarriage usually is because the unborn baby would not have lived
- You (or your partner) may experience periods of sadness and loss, perhaps depression
- Think about living the rest of your life with this experience

VSB

Birth of a very sick baby.
(with mental and physical problems)

VSB

- You (or your partner) give birth to a baby with severe mental retardation and physical problems.
- His/her treatment includes large amounts of drugs and many hospital stays
- Your child cannot go to school or work.
- In their 30's, your child dies from complications.
- While some parents appreciate the special joys in caring for such children, many others are unable to care for this child and place him/her in a group home.
- Think about spending the rest of your life with this experience.

NB

X

No children at all.

NB

X

- To avoid having a very sick baby (severe mental retardation and physical handicaps), you and your partner decide **not** to have any children.
- Think about living the rest of your life with this decision

NN

Neither one of you are CF carriers.

NN

- You and your partner decide to be tested to see if you are CF carriers.
- Test results show that neither one of you are CF carriers
- You understand that under these circumstances you will not have a child affected with CF.
- Think about living the rest of your life with this information

NP

Test results show that one of you is a CF carrier and the other has a low risk of being a carrier.

NP

- You and your partner decide to be tested to see if you are CF carriers.
- Test results show that one of you is a CF carrier and the other has a low (but not zero) risk of being a CF carrier.
- You understand that under these circumstances it is extremely unlikely that you will have a child affected with CF.
- Think about living the rest of your life with this information.

PP

Both are CF carriers.

PP

- You and your partner decide to be tested to see if you are CF carriers.
- Test results show that you are **both** CF carriers.
- Although being a CF carrier does not affect your own health , there is a 1 in 4 (25%) chance your child will be affected with CF.
- Think about living the rest of your life with this information

AN

You are almost always fretful, angry, irritable, anxious, or depressed for the rest of your life.

AN

- You are almost always fretful, angry, irritable, anxious, or depressed for the rest of your life.
- You recall time and place more slowly than others as judged by relatives and/or friends for the rest of your life.

Children's Hospital of Eastern Ontario Hôpital pour enfants de l'est de l'Ontario

100 Smyth - Ottawa, Ontario K1H 8L2 - Tel: (613) 738-3230

APPENDIX B

Introductory Letter

Carrier testing for cystic fibrosis (CF) has recently been available in Ontario. However, we have little information on how individuals feel about carrier testing, how they used this information, or how they plan to use this information. Furthermore, the effects of carrier testing for the individual and society is not well known.

The purpose of this project is to gather information from different groups of individuals, including yourself, family members who have or have not received carrier testing, and people from the general population. We would like to understand your attitudes and feelings towards carrier testing and how test results are or will be used. This would take about an hour of your time for an interview.

The results of this study will help us to improve our diagnosis of CF, and aid in developing better ways to help people understand this new type of testing. A research assistant, _____ will contact you in the next week to explain the project and to ask if you would be willing to participate in the study. The study involves a brief survey and an interview to be arranged at your convenience. All answers will be kept confidential.

You are under no obligation to participate in this study. All information will be kept confidential. If you agree to participate, you can withdraw from the study at any time. Please note that your decision will not affect the current or future care received by any family member at the Children's Hospital of Eastern Ontario or Ottawa General Hospital.

Should you have any questions before our call, please feel free to contact us at (613) 738-3230.

Sincerely,

Linda Surh, M.D., Ph.D.
Director, DNA Diagnostic Laboratory

Mario Cappelli, Ph.D.
Psychologist

APPENDIX C

TELEPHONE PROTOCOL OF SUBJECT RECRUITMENT BY RESEARCH CO-ORDINATOR

Hello My name is _____ and I am the research coordinator on the Cystic Fibrosis Genetic study This call is a follow-up to the introductory letter we mailed approximately 1 week ago. Have you received the letter?

(IF NO, briefly outline letter in Appendix B)

(IF YES, continue) I would like to give you more information about the project and ask if you would be willing to participate

CF carrier testing has recently become available in Ontario However we have little information on how individuals feel about carrier testing, how they used this information, or how they plan to use this information Furthermore, the effects of carrier testing for the individual and society is not well known

The purpose of this project is to gather information from different groups of individuals including yourself, family members who have or have not received carrier testing, and people from the general population on attitudes and feelings towards carrier testing and how test results are used

All information collected will be held strictly confidential You can withdraw from the study at any time and this will not affect current or future care at the Children's Hospital of Eastern Ontario or Ottawa General Hospital

We are asking about an hour and twenty minutes of your time If you agree to participate I will mail out a short questionnaire which will take you approximately 20 minutes to complete In addition, I would like to schedule an appointment at a time and place which is convenient for you This could be in the morning, afternoon, or evening and at your home or at CHEO for a more detailed interview This visit will take approximately 1 hour

Will you be willing to participate?

(IF YES Arrange appointment_____)

(IF NO Determine reasons for declining, i.e. uninterested, too busy, self-perceived carrier risk is low)

February 17, 1994

Number

SURVEY A

GENETIC TESTING

FOR

CYSTIC FIBROSIS (CF)

GENETIC TESTING FOR CYSTIC FIBROSIS (CF)

We would like you to participate in a study by the Children's Hospital of Eastern Ontario. The study is about genetic screening for the disease, cystic fibrosis (CF).

A new genetic test is available which lets people know if they carry a CF disease gene. We are interested in your opinions concerning genetic testing for CF and how useful you might find the test results. The information you provide to us in the attached questionnaire will help us to better understand people's views about CF genetic testing. Your opinions will help to improve our service in the future.

It should take about 20 minutes of your time. Your responses will be kept strictly confidential.

Please keep this survey until you meet with the research assistant.

For information:

Dr. Linda Smith or Dr. Mark Carter
Medical Genetics Study
Children's Hospital of Eastern Ontario
401 Somerset St.
Ottawa, Ontario K1H 8L2
(613) 737-7222

Before you begin, remember that you do not have to answer any questions you would rather not answer.

1 The following questions refer to the disease known as cystic fibrosis or CF. For each statement, circle one letter only, by choosing the single best answer from each list provided.

1 Cystic fibrosis (CF) is

- a a disease causing breast cysts
- b a disease affecting muscle control
- c a disease affecting lungs and digestive system
- d a rare type of bone disease
- e don't know

2 The cause of CF is

- a a virus illness
- b an inherited illness
- c a toxic medicine taken during pregnancy
- d a genetic accident during pregnancy
- e don't know

3 A CF "carrier" is

- a someone who has only mild symptoms of CF
- b someone who does not have CF but who could have a child with CF
- c someone who does not have CF disease now but will develop it later
- d all of the above
- e don't know

4 CF carriers are diagnosed by

- a their chest problems (i.e. asthma, colds)
- b a "sweat" test
- c a blood test
- d All of the above
- e Don't know

5 On average, individuals with CF live

- a until infancy
- b until childhood
- c until adulthood
- d people with CF live a normal lifespan
- e don't know

6 If there is no family history of CF, the chance of being a CF carrier is

- a 4 out of 4 (100%)
- b 1 out of 4 (25%)
- c 1 out of 25 (4%)
- d very low risk but not zero
- e no risk
- f don't know

7 Imagine that your neighbour and his pregnant wife find out that they are both CF carriers. What is the chance of their unborn child having CF?

- a 4 out of 4 (100%)
- b 1 out of 4 (25%)
- c 1 out of 25 (4%)
- d very low risk but not zero
- e no risk
- f don't know

8 What do you think is your chance of being a (CF carrier)?

- a 4 out of 4 (100%)
- b 2 out of 3 (67%)
- c 1 out of 4 (25%)
- d 1 out of 8 (12%)
- e 1 out of 25 (4%)
- f very low risk but not zero
- g no risk
- h don't know

How concerned are you about your own chance of being a CF carrier (as indicated in question 8)?

- a not at all concerned
- b slightly concerned
- c moderately concerned
- d very concerned
- e extremely concerned

The following statements are about the possible effects of CF disease

- (i) CF patients usually need treatment every day
- (ii) There is a cure for some CF patients
- (iii) CF patients are less able to have children because of their disease

Please indicate the true statement or statements by choosing one of the following answers

- a only (i)
- b only (ii)
- c only (iii)
- d (i) and (ii)
- e (ii) and (iii)
- f (i) and (iii)
- g (i), (ii) and (iii)

In the following sections, there is information given to assist you in answering the specific questions. Please DO NOT GO BACK to previous questions or change your answers

To help with the following questions, here is some information about CF:

- (1) CF disease is caused by having two CF genes
- (2) A CF carrier is a person who does not have the disease but does have one CF gene and one normal gene
- (3) If two CF carriers have a child, then that child has a 1 out of 4 chance (25%) of having the disease (i.e. the chance of that child getting a CF gene from each parent)

The following are some general questions about testing for cystic fibrosis carriers, also referred to as "CF genetic testing".

(i) Before today, have you heard about CF carrier (genetic) testing?

- YES ☐
- NO ☐

(ii) If YES, from whom and/or where did you hear? *(you may check more than one)*

- ☐ Parents
- ☐ Brothers/Sisters
- ☐ Aunt/Uncles
- ☐ Spouse/Partner
- ☐ Cousins
- ☐ Friends
- ☐ Family Doctor
- ☐ Genetic Counsellor
- ☐ Media (e.g. TV, radio, newspapers)
- ☐ CF Foundation
- ☐ Scientific literature
- ☐ Other (please specify) _____

12 (a) Would you consider having (F genetic testing? ☐ YES ☐ NO

(b) If YES, why? (you may check more than one)

- ☐ To find out my chance of being a carrier
- ☐ To find out my children's chance of being carriers
- ☐ To find out my siblings' chance of being carriers
- ☐ To find out other family members' chance of being carriers
- ☐ To learn more about CF
- ☐ To help research
- ☐ To help find a cure
- ☐ Other (please specify) _____

(c) If NO, why not? (you may check more than one)

- ☐ I have no known family history of CF
- ☐ I have finished my family
- ☐ I do not want to have children
- ☐ Other (please specify) _____

13 Which person(s) might influence your decision to have (F genetic testing? (you may check more than one)

- ☐ Parents
- ☐ Brothers/Sisters
- ☐ Aunts/Uncles
- ☐ Spouse/Partner
- ☐ Cousins
- ☐ Friends
- ☐ Family Doctor
- ☐ Genetic Counsellor
- ☐ No one, it is my choice
- ☐ Other (please specify) _____

14 What situation(s) might influence your decision to have CF genetic testing?

- ☐ Family member found to be a CF carrier
- ☐ Family member diagnosed with CF
- ☐ Marriage
- ☐ Pregnancy
- ☐ No situation would influence my decision
- ☐ Other (please specify) _____

15 How do you think you would use the information from the CF genetic test? (you may check more than one)

- ☐ For my family planning
- ☐ For my children's family planning
- ☐ For my siblings' family planning
- ☐ For other family members' family planning
- ☐ To prepare for the birth and care of a child with CF
- ☐ Spouse/Partner selection
- ☐ Have my spouse/partner tested
- ☐ I would not use the information from the CF genetic test
- ☐ I don't know how I would use the information
- ☐ Other (please specify) _____

16 (a) Would you tell anyone else about the availability of CF genetic testing?

YES ☐ NO ☐

(b) If YES, who would you tell? (you may check more than one)

- ☐ Parents
- ☐ Brothers/Sisters
- ☐ Aunt's/Uncles
- ☐ Cousins
- ☐ Spouse/Partner
- ☐ Friends
- ☐ Acquaintances (e.g. coworkers, neighbours)
- ☐ Couples who are planning to have children
- ☐ Anyone with a family history of CF
- ☐ People who ask
- ☐ No one
- ☐ Other (please specify) _____

(c) If YES, why would you tell? (you may check more than one)

- ☐ To encourage them to be tested
- ☐ For their information
- ☐ For their family planning
- ☐ To help research
- ☐ May lead to a cure
- ☐ Other (please specify) _____

(d) NO, why not? (you may check more than one)

- ☐ No chance to do so
- ☐ Don't know enough about CF genetic testing
- ☐ Don't want to encourage others to get tested
- ☐ Don't want to be seen as promoting
- ☐ Other (please specify) _____

17 What do you think might be the advantages of CF genetic testing?
(you may check more than one)

- ☐ Information about my carrier status
- ☐ End worry and uncertainty
- ☐ Family planning
- ☐ Prenatal testing
- ☐ Spouse/Partner selection
- ☐ Early detection of CF
- ☐ Prevent CF births in the future
- ☐ Help Research
- ☐ Lead to a cure
- ☐ I do not know of any advantages
- ☐ Other (please specify) _____

18 What do you think might be the disadvantages of CF genetic testing?
(you may check more than one)

- ☐ People who are carriers may be labelled or treated differently
- ☐ Emotional upset
- ☐ People may restrict themselves from having children
- ☐ It may lead to abortion
- ☐ Testing is expensive
- ☐ It's better not to know
- ☐ Other (please specify) _____

III Here are some opinions that people have about CF genetic testing. For EACH of the following statements, please circle your own level of agreement.

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
	1	2	3	4	5
19 Testing would make me sorry unnecessarily	1	2	3	4	5
20 Testing could lead to a cure for CF	1	2	3	4	5
21 It's better not to know	1	2	3	4	5
22 Testing is too much trouble	1	2	3	4	5
23 Testing will help me make decisions about family planning	1	2	3	4	5
24 I believe that testing is not necessary for me	1	2	3	4	5
25 Testing would give me peace of mind	1	2	3	4	5
26 It's better to let nature take its course	1	2	3	4	5
27 CF carriers should have their children tested	1	2	3	4	5

II Imagine that your test results show you are a CF carrier. For EACH of the following statements, please indicate how likely you are to:

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5
28 Keep the test results to yourself	1	2	3	4	5
29 Try not to think much about the test results	1	2	3	4	5
30 Tell your relatives about your test results	1	2	3	4	5
31 Tell your partner about your test results	1	2	3	4	5
32 Encourage your partner to be tested	1	2	3	4	5
33 Tell your family doctor about your test results	1	2	3	4	5
34 Tell your children about your test results	1	2	3	4	5

1

Again imagine that you have just been informed that you are a CF carrier. Here are some feelings people have expressed after they received similar test results. For EACH of the following feelings, please circle the ONE NUMBER that best indicates how you might feel

	Very Likely 1	Likely 2	Neutral 3	Unlikely 4	Very Unlikely 5
35 Anxious	1	2	3	4	5
36 Depressed	1	2	3	4	5
37 Happy	1	2	3	4	5
38 Relieved	1	2	3	4	5
39 Angry	1	2	3	4	5
40 Hopeless	1	2	3	4	5
41 Embarrassed or Awkward	1	2	3	4	5

17

Imagine that your test results show you are not a CF carrier. For EACH of the following statements, please indicate how likely you are to:

	Very Likely 1	Likely 2	Neutral 3	Unlikely 4	Very Unlikely 5
42 Keep the test results to yourself	1	2	3	4	5
43 Try not to think much about the test results	1	2	3	4	5
44 Tell your relatives about your test results	1	2	3	4	5
45 Tell your partner about your test results	1	2	3	4	5
46 Encourage your partner to be tested	1	2	3	4	5
47 Tell your family doctor about your test results	1	2	3	4	5
48 Tell your children about your test results	1	2	3	4	5

171 Again, imagine that you have just been informed that you are not a CF carrier.
For EACH of the following feelings, please circle the ONE NUMBER that indicates
how you might feel

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5

49	Anxious	1	2	3	4	5
50	Depressed	1	2	3	4	5
51	Happy	1	2	3	4	5
52	Relieved	1	2	3	4	5
53	Angry	1	2	3	4	5
54	Hopeless	1	2	3	4	5
55	"Labelled" or "Abnormal"	1	2	3	4	5

172 Imagine that your risk (or chance) to be a CF carrier has been lowered from 1:20 to 1:200 (i.e. 5% to 0.5%). Therefore, you have a very low risk, but not zero, for being a CF carrier. For EACH of the following statements, please indicate how likely you are to

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5

56	Keep the test results to yourself	1	2	3	4	5
57	Try not to think much about the test results	1	2	3	4	5
58	Tell your relatives about your test results	1	2	3	4	5
59	Tell your partner about your test results	1	2	3	4	5
60	Encourage your partner to be tested	1	2	3	4	5
61	Tell your family doctor about your test results	1	2	3	4	5
62	Tell your children about your test results	1	2	3	4	5

1A

Again, imagine that you have a very low risk, but not zero, for being a CF carrier. For EACH of the following feelings, please indicate the ONE NUMBER that best indicates how you might feel.

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5
63 Anxious	1	2	3	4	5
64 Depressed	1	2	3	4	5
65 Happy	1	2	3	4	5
66 Relieved	1	2	3	4	5
67 Angry	1	2	3	4	5
68 Horrified	1	2	3	4	5
69 Labeled as "Abnormal"	1	2	3	4	5

X

The following questions deal with how you **THINK** you would use the test results for planning your own family:

70 (a) Would the test results affect your family planning decisions? YES ☐ NO ☐

(b) If YES in what way? (you may check more than one.)

☐ I would get more information about CF

☐ I would have my partner tested

☐ I would not marry a carrier

☐ I would use a more effective birth control method

☐ I would consider adoption

☐ I would consider artificial insemination or egg donor

☐ For my partner would go for prenatal testing

☐ I would not have any more children

☐ If both myself and my partner are carriers

☐ I would consider abortion

☐ Other (please specify) _____

71 (c) If NO why not? (you may check more than one.)

☐ I am probably not a carrier

☐ I would prefer to let nature take its course

☐ I have finished my family

☐ I do not want any children

☐ Religious reasons

☐ For my partner is already pregnant

☐ Any child is worth the risk

☐ Other (please specify) _____

V/

Imagine that both you and your partner are CF carriers and that your future children are at risk for having CF disease. For each of the following items, please indicate how these test results might alter your family planning decisions.

	Very Likely 1	Likely 2	Neutral 3	Unlikely 4	Very Unlikely 5
--	------------------	-------------	--------------	---------------	--------------------

- 71 Use a more effective birth control method 1 2 3 4 5
- 72 If pregnancy occurs, go for prenatal or genetic testing of the unborn child 1 2 3 4 5
- 73 Reduce the number of children I plan to have 1 2 3 4 5
- 74 Consider adoption 1 2 3 4 5
- 75 Consider abortion 1 2 3 4 5
- 76 Consider artificial insemination or egg donor 1 2 3 4 5
- 77 Would not alter my family planning 1 2 3 4 5

V//

Remember you do not have to answer any questions that you would rather not answer. All responses will be kept confidential.

For the following questions, mark the appropriate box ☐ or fill in the blank.

- 78 What is your postal code?
- 79 What is your sex? Male ☐ Female ☐
- 80 What is the highest grade or level of education that you have completed?
☐ Less than high school
☐ Completed high school
☐ Trade certificate diploma
☐ Some college
☐ Some university
☐ Community college diploma degree
☐ University Bachelors degree
☐ University Masters degree
☐ Doctorate

- 81 What year were you born? 19 (Year)

82 What language do you speak most often in the home?

- ☐ English
☐ French
☐ Other

Specify _____

85 (a) Do you have any children?

YES ☐ NO ☐

83 What is your religion?

- ☐ Roman Catholic
☐ Protestant
☐ Jewish
☐ No religious preference
☐ Other

Specify _____

	SEX		Year of birth	Affected with CF?
	Male	Female		
1	☐	☐	19 ☐	Yes ☐ No ☐
2	☐	☐	19 ☐	Yes ☐ No ☐
3	☐	☐	19 ☐	Yes ☐ No ☐
4	☐	☐	19 ☐	Yes ☐ No ☐

84 What is your current marital status?

- ☐ Single
☐ Married or Common-law
☐ Separated
☐ Divorced
☐ Widowed

86 Is it possible you will have children in the next two years?

YES ☐ NO ☐ UNCERTAIN ☐

87 (a) What is your current occupation?

- ☐ Looking for work
☐ Student
☐ Retired
☐ Homemaker
☐ Currently employed as _____
☐ Other

Please specify _____

88 Number of years worked per week

☐

88 What is your family income per year? (If married or common-law, state the combined income of you and your partner.)

- ☐ Under \$10,000
☐ \$10,000 to 19,999
☐ \$20,000 to 29,999
☐ \$30,000 to 39,999
☐ \$40,000 to 49,999
☐ \$50,000 to 59,999
☐ \$60,000 to 69,999
☐ \$70,000 to 79,999
☐ \$80,000 to 89,999
☐ \$90,000 to 99,999
☐ \$100,000 or above

THANK YOU FOR TAKING THE TIME TO ANSWER OUR QUESTIONS.

If you have any questions or comments, please feel free to contact us at (613) 738-3286

Please keep this survey until you meet with the research assistant.

February 19, 1994

Number

GENETIC TESTING FOR CYSTIC FIBROSIS (CF)

We would like you to participate in a study by the Children's Hospital of Eastern Ontario. The study is about genetic screening for the disease, cystic fibrosis (CF).

A new genetic test is available which lets people know if they carry a CF disease gene. We are interested in your opinions concerning genetic testing for CF and how useful you might find the test results. The information you provide to us in the attached questionnaire will help us to better understand people's views about CF genetic testing. Your opinions will help to improve our service in the future.

It should take about 20 minutes of your time. Individual responses will be kept strictly confidential; your name will not appear with the responses you give.

Please keep this survey until you meet with the research assistant.

SURVEY B

GENETIC TESTING

FOR

CYSTIC FIBROSIS (CF)

For information:

Dr. Linda Surn or Dr. Mario Cappelli
c/o Molecular Genetics Study
Children's Hospital of Eastern Ontario
401 Smith Road
Ottawa, Ontario K1H 8L1
Telephone: (613) 738-3286

Before you begin, remember that you do not have to answer any questions you would rather not answer.

1 The following questions refer to the disease known as cystic fibrosis or CF. Choose the single best answer from the list provided. Circle one letter only for each statement.

1 Cystic fibrosis (CF) is

- a a disease causing breast cysts
- b a disease affecting muscle control
- c a disease affecting lungs and digestive system
- d a rare type of bone disease
- e don't know

2 The cause of CF is

- a a virus illness
- b an inherited illness
- c a toxic medicine taken during pregnancy
- d a genetic accident during pregnancy
- e don't know

3 A CF "carrier" is

- a someone who has only mild symptoms of CF
- b someone who does not have CF but who could have a child with CF
- c someone who does not have CF disease now but will develop it later
- d all of the above
- e don't know

4 CF "carriers" are diagnosed by

- a their chest problems (i.e. asthma, colds)
- b a "sweat" test
- c a blood test
- d All of the above
- e Don't know

5 On average, individuals with CF live

- a until infancy
- b until childhood
- c until adulthood
- d people with CF live a normal life span
- e don't know

6 If there is no family history of CF, the chance of being a CF carrier is

- a 4 out of 4 (100%)
- b 1 out of 4 (25%)
- c 1 out of 25 (4%)
- d very low risk but not zero
- e no risk
- f don't know

7 Imagine that your neighbour and his pregnant wife find out that they are both CF carriers. What is the chance of their unborn child having CF?

- a 4 out of 4 (100%)
- b 1 out of 4 (25%)
- c 1 out of 25 (4%)
- d very low risk but not zero
- e no risk
- f don't know

8 What is your chance of being a CF carrier?

- a 4 out of 4 (100%)
- b 2 out of 3 (67%)
- c 1 out of 4 (25%)
- d 1 out of 8 (12%)
- e 1 out of 25 (4%)
- f very low risk but not zero
- g no risk
- h don't know

9 How concerned are you about your own chance of being a CF carrier (as indicated in question 8)?

- a not at all concerned
- b slightly concerned
- c moderately concerned
- d very concerned
- e extremely concerned

10 The following statements are about the possible effects of CF disease

- i) CF patients usually need treatment every day
- ii) There is a cure for some CF patients
- iii) CF patients are less able to have children because of their disease

Please indicate the true statement or statements, by choosing one of the following answers

- a (i) only
- b (ii) only
- c (iii) only
- d (i) and (ii)
- e (ii) and (iii)
- f don't know

In the following sections, there may be information given to assist you in answering the specific questions. Please **DO NOT GO BACK** to previous questions or change your answers.

11 To help with the following questions, here is some information about CF:

- (1) CF disease is caused by having two CF genes
- (2) A CF carrier is a person who does not have the disease, but does have one CF gene and one normal gene.
- (3) If two CF carriers have a child, then that child has a 1 out of 4 chance (25%) of having the disease (i.e. the chance of that child getting a CF gene from each parent)

The following are some general questions about testing for cystic fibrosis carriers, also referred to as "CF genetic testing".

12 (a) Before today, have you heard about CF carrier (genetic) testing?

YES ☐ NO ☐

(b) If YES, how did you hear? Or, if you have had CF gene testing, how did you find out where to go? (you may check more than one)

- ☐ Parents
- ☐ Brothers/Sisters
- ☐ Aunts/Uncles
- ☐ Spouse/Partner
- ☐ Cousins
- ☐ Friends
- ☐ Family Doctor
- ☐ Genetic Counsellor
- ☐ Media (e.g. T.V., radio, newspapers)
- ☐ CF Foundation
- ☐ Scientific Literature
- ☐ Other (please specify) _____

2) Have you told anyone else about the availability of CF genetic testing?

YES ☐ NO ☐

(b) If YES, who did you tell? (you may check more than one)

- ☐ Parents
☐ Brothers/Sisters
☐ Aunts/Uncles
☐ Cousins
☐ Spouse/Partner
☐ Friends
☐ Acquaintances (e.g. coworkers, neighbours)
☐ Couples who are planning to have children
☐ People with a family history of CF
☐ People who asked
☐ Other (please specify) _____

(c) If YES, why did you tell? (you may check more than one)

- ☐ To encourage them to be tested
☐ For their information
☐ For their family planning
☐ To help research
☐ May lead to a cure
☐ Other (please specify) _____

(d) If NO, why not? (you may check more than one)

- ☐ No chance to do so
☐ I don't know enough about CF genetic testing
☐ I don't want others to ask about my test results
☐ It is not my place to bring it up
☐ Other (please specify) _____

III

Here are some opinions that people have about CF genetic testing. For EACH of the following statements, please circle your own level of agreement.

		Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
		1	2	3	4	5
13	Testing would make me worry unnecessarily	1	2	3	4	5
14	Testing could lead to a cure for CF	1	2	3	4	5
15	It's better not to know	1	2	3	4	5
16	Testing is too much trouble	1	2	3	4	5
17	Testing will help me make decisions about family planning	1	2	3	4	5
18	I believe that testing is not necessary for me	1	2	3	4	5
19	Testing would give me peace of mind	1	2	3	4	5
20	It's better to let nature take its course	1	2	3	4	5
21	CF carriers should have their children tested	1	2	3	4	5

22 Circle the **one** statement that best fits your own (F) carrier result. Follow the instructions that the arrow ($\Rightarrow$) indicates

A I **AM** a CF carrier $\Rightarrow$ Do Sections IV & V (PINK Only)

B I **am NOT** a CF carrier $\Rightarrow$ Do Sections VI & VII (YELLOW Only)

C I have a **very low** but **not zero** risk for being a CF carrier $\Rightarrow$ Do Sections VIII & IX (GREEN Only)

D I don't know $\Rightarrow$ Answer **ALL** the following sections

11 Answer this section if you are a **CF carrier**.

Your test results show you are a **CF carrier**. For EACH of the following statements, please indicate how likely you are to:

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5

23 Keep the test results to yourself

24 Try not to think much about the test results

25 Tell your relatives about your test results

26 Tell your partner about your test results

27 Encourage your partner to be tested

28 Tell your family doctor about your test results

29 Tell your children about your test results

3 OF/DE 3

PM-1 3 1/2" x 4" PHOTOGRAPHIC MICROCOPY TARGET
NBS 1010a ANSI/ISO #2 EQUIVALENT

PRECISIONSM RESOLUTION TARGETS

Answer this section if you are a CF carrier.

Here are some feelings other people have described after being told their test results. For EACH of the following feelings, please circle the ONE NUMBER that best indicates how you felt.

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5

10 Anxious	1	2	3	4	5
11 Depressed	1	2	3	4	5
12 Happy	1	2	3	4	5
13 Relieved	1	2	3	4	5
14 Angry	1	2	3	4	5
15 Hopeless	1	2	3	4	5
16 Labeled or Abnormal	1	2	3	4	5

Answer this section if you are not a CF carrier.

Your test results show you are not a CF carrier. For EACH of the following statements, please indicate how likely you are to

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5

17 Keep the test results to yourself	1	2	3	4	5
18 Try not to think much about the test results	1	2	3	4	5
19 Tell your relatives about your test results	1	2	3	4	5
20 Tell your partner about your test results	1	2	3	4	5
21 Encourage your partner to be tested	1	2	3	4	5
22 Tell your family doctor about your test results	1	2	3	4	5
23 Tell your employer about your test results	1	2	3	4	5

Go to Section X

177 Answer this section if you are not a CF carrier

Here are some feelings other people have described after being told their test results. For EACH of the following feelings, please circle the ONE NUMBER that best indicates how you felt.

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5

44 Anxious

45 Depressed

46 Happy

47 Relieved

48 Angry

49 Hopeless

50 "Labelled" or "Abnormal"

Go to Section X

178 Answer this section if your test result showed you have a very low risk, but not zero, for being a CF carrier.

Your test results show that you have a very low risk, but not zero, for being a CF carrier. EACH of the following statements, please indicate how likely you are to:

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5

51 Keep the test results to yourself

52 Try not to think much about the test results

53 Tell your relatives about your test results

54 Tell your partner about your test results

55 Encourage your partner to be tested

56 Tell your family doctor about your test results

57 Tell your children about your test results

IX Answer this section if your test result showed you have a very low risk, but not zero, for being a CF carrier.

Here are some feelings other people have described after being told their test results. For EACH of the following feelings, please circle the ONE NUMBER that best indicates how you felt.

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5
58 Anxious	1	2	3	4	5
59 Depressed	1	2	3	4	5
60 Happy	1	2	3	4	5
61 Relieved	1	2	3	4	5
62 Angry	1	2	3	4	5
63 Hopeless	1	2	3	4	5
64 "Labelled" or "Abnormal"	1	2	3	4	5

Go to Section X

X

The following questions deal with how you THINK you would use the test results for planning your own family.

65 (a) Would the test results affect your family planning decisions?

YES ☐ NO ☐

(b) IF YES, in what way? (you may check more than one)

- ☐ I would get more information about CF
- ☐ I would have my partner tested
- ☐ I would not marry a carrier
- ☐ I would use a more effective birth control method
- ☐ I would consider adoption
- ☐ I would consider artificial insemination or egg donor
- ☐ I (or my partner) would go for prenatal testing
- ☐ I would not have any more children if both myself and my partner are carriers
- ☐ I would consider abortion
- ☐ Other (please specify) _____

(c) IF NO, why not? (you may check more than one)

- ☐ I am not a carrier
- ☐ I would prefer to let nature take its course
- ☐ I have finished my family
- ☐ I do not want any children
- ☐ Religious reasons
- ☐ Any child is worth the risk
- ☐ Other (please specify) _____

56

(a) Have you used the information from your CF Genetic Testing?

YES ☐ NO ☐

(b) If no, please go to question 67

(c) If yes, I have used the information for (you may check more than one)

- ☐ Family planning for my children
☐ Family planning for my relatives
☐ Preparation for the birth and care of a child with CF
☐ Other (please specify) _____

57

(a) Will you use the information from your CF Genetic Testing?

YES ☐ NO ☐

(b) If no, please go to question 68

(c) If yes, I will use the information for (you may check more than one)

- ☐ Family planning for my children
☐ Family planning for my relatives
☐ Preparation for the birth and care of a child with CF
☐ Other (please specify) _____

58

If you said NO to questions 65, 66 AND 67, please indicate your reason(s) for getting tested (you may check more than one)

- ☐ Curiosity about my chance to be a carrier
☐ Convenience of the testing procedure
☐ Help research
☐ Pressure from family members
☐ Pressure from family doctor
☐ Other (please specify) _____

V

Imagine that both you and your partner are CF carriers and that your future children are at risk for having CF disease. For EACH of the following items, please indicate how these test results might alter your family planning decisions:

	Very Likely	Likely	Neutral	Unlikely	Very Unlikely
	1	2	3	4	5
66 Use a more effective birth control method	1	2	3	4	5
69 If pregnancy occurs, go for prenatal or genetic testing of the unborn child	1	2	3	4	5
70 Reduce the number of children I plan to have	1	2	3	4	5
72 Consider adoption	1	2	3	4	5
73 Consider abortion	1	2	3	4	5
74 Consider artificial insemination or egg donor	1	2	3	4	5
75 We will not alter my family plans	1	2	3	4	5

XII Remember you do not have to answer any questions that you would rather not answer. All responses will be kept confidential.

For the following questions, mark the appropriate box ☐ or fill in the blank.

76 What is your postal code?

77 What is your sex? Male ☐ Female ☐

78 What is the highest grade or level of education that you have completed?

- ☐ Less than high school
- ☐ Completed high school
- ☐ Trade certificate/diploma
- ☐ Some college
- ☐ Some university
- ☐ Community college diploma degree
- ☐ University Bachelors degree
- ☐ University Masters degree
- ☐ Doctorate

79 What year were you born? 19 (Year)

80 What language do you speak most often in the home?

- ☐ English
- ☐ French
- ☐ Other

Specify

81 What is your religion?

- ☐ Roman Catholic
- ☐ Protestant
- ☐ Jewish
- ☐ No religious preference
- ☐ Other

Specify

82 What is your current marital status?

- ☐ Single
- ☐ Married or Common-law
- ☐ Separated
- ☐ Divorced
- ☐ Widowed

Feeling Thermometer

(Present CI Disease Description)
(Display Thermometer and cards)

For this interview we would like to obtain your views about various hypothetical scenarios which we will call health states. I would like you to imagine spending the rest of your life in the health state described on these cards. We will assume that you will live an additional 40 years. Thus, all of the health states in these descriptions will last for 40 years, and will be followed by a natural death. Unless otherwise stated, you are able to see, hear and speak normally for your age, you are able to walk, bend, lift and climb normally for your age, you are generally happy and free from worry, you recall time and place normally for your age, you eat, bathe and dress yourself normally for your age, you are free of pain and discomfort, and you are able to have children with a fertile spouse. To make this task a little easier we will use the Feeling Thermometer.

The thermometer measures your preferences for different health states. The more desirable or preferable you feel a health state to be, the closer it should be to the top of the thermometer. The less desirable or preferable you feel a health state to be, the closer it should be to the bottom of the thermometer. The cards have a description of the health state on both sides. On one side there is a detailed description and on the other side is a brief summary.

Begin with these two health states (HS, DS), they are usually placed at 0 and 100. After carefully reading both sides of each card, place the arrow for the card which describes perfect health on the thermometer scale at 100. The arrow for the card which describes the lowest level of health is usually placed at 0.

(adjust if necessary)

(if the subject cannot decide where to place dead self because they think there are worse things than dying and immediate painless death, tell them to begin with placing it at zero. They can always change it's location once they read the other

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APPENDIX F

CONSENT FORM

I, _____, have had the project on "CF Carrier Testing" explained to me by _____ I have received the written information which also outlines the project and a copy of this consent. I understand that my participation is totally voluntary. If I decide not to participate or if I withdraw my participation during the study, even after signing this consent, I am free to do so. My actions or those of my family will in no way influence the way I or any member of my family will be treated at the Children's Hospital of Eastern Ontario.

I understand that this project could take a few years before the results will be fully known. All my responses will be kept confidential and my name will not be used.

I can withdraw from the study at any time and this will not affect current or future care at the Children's Hospital of Eastern Ontario or Ottawa General Hospital.

If I have any questions about this research, I can call Dr. Marie Cappella or Dr. Linda Smith at the above number.

Signature of Subject

Date

Signature of Witness

Date

UNABLE TO FILM MATERIAL ACCOMPANYING THIS THESIS (I.E.
DISKETTE(S), SLIDES, MICROFICHE, ETC...).

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Appendix G Beck Depression Inventory - BDI

Appendix H Spielberger State-Trait Anxiety Inventory - STAI

These appendicies have been removed due to copyright materials

Utility Assessment

On behalf of the research team I would like to thank you for agreeing to participate in this study. This study is being conducted at CHED by Dr. Linda Surh, director of the DNA Diagnostic Laboratory and Dr. Mario Cappella, Clinical Psychologist.

This study is examining people's views about carrier screening for Cystic Fibrosis in order to attempt to understand what people think about this procedure. Your participation is important in helping to plan our current and future research and treatment activities.

All information is confidential and anonymous. All questions in this interview deal with your opinions. There are no right or wrong answers, and opinions often differ on these matters. You do not have to explain any of your answers, and they will not be questioned.

Your answers and participation will not go on any records or files, and nothing you say will be repeated to anyone. If we should come to a question you would rather not answer, just let me know and we will skip it.

Just to give you a brief summary of what is to follow:

There are 3 parts to this interview:

- 1 The first will be for you to complete 3 (4) short pen and paper questionnaires.
- 2 The second part will consist of ordering different scenarios.
- 3 In the third part of the interview we will be asking you to make decisions based on the scenarios in part 2.

Feeling Thermometer

(Present CF Disease Description)

(Display Thermometer and cards)

For this interview we would like to obtain your views about various hypothetical scenarios which we will call health states. I would like you to imagine spending the rest of your life in the health state described on these cards. We will assume that you will live an additional 40 years. Thus, all of the health states in these descriptions will last for 40 years, and will be followed by a natural death. Unless otherwise stated, you are able to see, hear and speak normally for your age, you are able to walk, bend, lift and climb normally for your age, you are generally happy and free from worry, you recall time and place normally for your age, you eat, bathe and dress yourself normally for your age, you are free of pain and discomfort, and you are able to have children with a fertile spouse. To make this task a little easier we will use the Feeling Thermometer.

The thermometer measures your preferences for different health states. The more desirable or preferable you feel a health state to be, the closer it should be to the top of the thermometer. The less desirable or preferable you feel a health state to be, the closer it should be to the bottom of the thermometer. The cards have a description of the health state on both sides. On one side there is a detailed description and on the other side is a brief summary.

Begin with these two health states (HS, DS), they are usually placed at 0 and 100. After carefully reading both sides of each card, place the arrow for the card which describes perfect health on the thermometer scale at 100. The arrow for the card which describes the lowest level of health is usually placed at 0.

(adjust if necessary)

If the subject cannot decide where to place dead self because they think there are worse things than dying and immediate painless death, tell them to begin with placing it at zero. They can always change it's location once they read the other

health states!

We will repeat this procedure for the remaining descriptions. There will be ten in all and the thermometer may get a bit crowded. You may shift the arrows on the thermometer at any time before we record your scores.

Please read both sides of these cards carefully (* *place detailed side up* *) and place the matching arrows on the thermometer scale somewhere between the top and the bottom, depending upon how you feel about each description. Please ignore the colour of the arrows and consider the health states together. That is, don't separate the left from the right or red from white.

The distances between the arrows should represent how much better or worse you feel one type of health is when compared to the others. That is, the closer 2 arrows are the more similar you find the health states in terms of desirability. Similarly the further away the two arrows are the more different you find the health states in terms of desirability. No two arrows can be placed at the same point on the thermometer.

(In the event that any other state(s) are ranked below dead self

Refer to the state(s) and ask

"Does this mean that you consider 40 years living in this state(s)
as worse than dying an immediate painless death?"

Record response in booklet)

Are you satisfied with your results? Now that you can see the results, are there any changes you would like to make?

(Pause until respondent indicates satisfactory completion of any revisions)

We are now ready to record your answers. Starting from the top of the

thermometer and working towards the bottom, would you please read me the letters on each arrow and read me the number on the thermometer. Please leave the arrows on the thermometer.

(Record scores on the response sheet.)

Thank you. We are finished with the Feeling Thermometer but we will continue using the same cards.

(leave thermometer beside subject)

(Record the time it took the subject to complete the feeling thermometer task in response booklet. Gather the cards in the subjects ranking, highest on top, lowest on bottom. This will facilitate their arrangement in the standard gamble section. Leave the arrows attached to the thermometer, place the thermometer aside and get the chance board.)

Chance Board

In life we are often forced to make decisions under conditions of uncertainty. These decisions can lead to good or bad outcomes. This last section of the interview will require you to make decisions similar to those of people undergoing CF carrier screening.

This last section consists of seven separate questions. For each question I will present you with two choices and ask you to choose the one you would prefer. One choice will involve a risk and the other choice will be certain. The amount of risk will be changed until we find out how much risk you will take to avoid the certain choice. Please remember that your decisions should represent what is best from your point of view. In order to make the task easier to understand we will use an aid similar to a probability board which we call the Chance Board. This is simply a tool we use to measure how people make decision under conditions of uncertainty.

(Place the chance board on the table.)

We call this a **Chance Board** because it indicates the chance or probability of a certain event occurring. As you can see the top part of the board is labelled **Choice A**.

(Point finger at Choice A.)

The bottom part of the board is labelled **Choice B**.

(Point finger at Choice B.)

Choice B is fairly simple because it describes only one form of health and in the event that this option is chosen, this form of health is certain to occur. If something is certain to occur, it is equal to a 100% chance or probability.

Choice A, however, is a little more complex because if it is chosen there are two

possible results, the best form of health or the worst form of health. The chances of each of these results occurring are indicated by the numbers appearing above each result.

To make these ideas a little clearer, let's run through an example. Let us assume that you are thinking of buying a car. You now have 2 choices, Choice A and Choice B.

(Point to Choice A and Choice B)

Choice A represents buying a reliable new car and Choice B represents buying a reliable used car. Which would you choose? Choice A or Choice B, or are they equal?

I have now changed choice A to show that there is a 10% chance that you will purchase a reliable new car but there is a 90% chance that you will purchase a lemon. Choice B is still you purchase a reliable used car. Which would you choose, Choice A, Choice B, or are they equal?

If they choose:

Choice B = Move the wheel to 90/10, continue...

Choice A = Prompt:

Do you mean you would prefer to have a 90% chance of
buying a lemon rather than buying a used
car?

No = Repeat choices on board.

Yes = Ask:

If choice A was 100% chance of buying a
lemon, do you think this would be better than,
equal to, or worse than buying a used car?

Better = Negative

Equal = 0.00

Worse = 0.05

Example 2: (begin by 100% choices)

Let us assume you have been involved in an accident which has damaged your kidneys. You now have 2 choices, Choice A and Choice B.

(Point to Choice A and then Choice B.)

Choice A

(Again, point to Choice A.)

represents a kidney transplant operation that has a 90% chance of full recovery to perfect health.

(Point to 90 and pink area of circle.)

However, there is also a 10% chance that you will die on the operating table.

(Point to 10 and blue area of circle.)

Your second choice, Choice B represents no operation but you can be 100% certain that for the rest of your life, you will have to go to the hospital 3 times a week, every week, to have your blood cleansed.

(Point to Choice B section.)

One way of thinking about this is, on average, for every 100 people who choose A, the operation, 90 will recover to perfect health but 10 will die on the operating table. Another way of thinking about it is, the chances of full recovery are 90% with a 10% chance of dying.

Do you understand the way the two choices will be described and how the Chance Board works?

(Continue--find utility for dialysis if they do not understand)

OUTCOME STATES

(If the subject has a different lower anchor than VSB go to section AA)

(Set wheel to 100 and 0)

Let's work through the first question carefully together.

Please read over each description, tell me when you are finished and we will begin.

(Wait for respondent to indicate they are ready.)

We are now ready to begin.

(Ask subject to decide which health state is worse for them. (intermediate state versus VSB))

As you can see Choice A, is a 100% chance of Healthy Baby and zero chance of Very Sick Baby. Choice B is 100% certainty of (insert appropriate intermediate state). Which would you choose, Choice A, Choice B, or are they equal?

If they choose:

Choice A = Move the wheel to 10/90, continue...

Choice B = ?

Equal = 1.00

Now I've changed Choice A to show that there is a 10% chance of a Healthy Baby and a 90% chance of a Very Sick Baby. Choice B, is 100% certainty of _____

Would you pick A or B now, or are they equal?

B = Move wheel to 90/10, continue...

Equal = Mark response(0.10), go to next health state.

A = Prompt:

"Do you mean you would prefer to have a 90% chance of a Very Sick Baby rather than living in the state of health described on the card in Choice B?"

No = Repeat choices on board.

Yes = "If choice A was a 100% chance of a Very Sick Baby

do you think this would be better than, equal to, or worse than living the rest of your life in choice B?

Mark response.

Better = Negative

Equal = 0.00

Worse = 0.05

The board now shows Choice A to be a 90% chance of a Healthy Baby with a 10% chance of a Very Sick Baby and Choice B remains the same as before Which choice would you prefer, choice A or choice B, or are the two choices equal?

A = Move wheel to 20/80, continue...

B = Mark response (0.95) and state, "Thank you that ends this question" Go to next health state.

Equal = Mark (0.90) and state "Thank you, that ends this question" Go to next health state.

Now I've changed Choice A, to a 20% chance of a Healthy Baby with an 80% chance of a Very Sick Baby. Choice B, is 100% certainty of Which choice would you prefer, or are the two choices equal?

A = Move wheel to 80/20, continue..

B = Mark response (0.15) and state, "Thank you that ends this question" Go to next health state.

Equal = Mark (0.20) and state "Thank you, that ends this question" Go to next health state.

ect...

INFORMATION STATES

(If the subject's lower anchor is different than Anxious/Depressed, go to section BB)

I have changed choice A so that the gamble is now between your own health and a state of Anxiety/Depression.

(Do 1/1 and 4/4 utilities.)

HEALTHY SELF DEAD SELF

(If the subject's lowest anchor is something other than Dead Self, go to section CC)

Begin at 100.

I have changed choice A so that the gamble is now between perfect health and death. There is now a 10% chance that you will be perfectly healthy but there is a 90% chance that you will die. Choice B is a 100% certainty that you are almost always fretful, angry, irritable, anxious, or depressed.
etc...

(do VSB)

WHAT IS A CF CARRIER?

Inherited characteristics - such as eye colour and hair colour - are passed from parents to their children through genes. Everyone possesses two copies of every gene: one copy comes from the father, and one from the mother.

CF is caused by a changed gene on chromosome 7. The disease is present when a child receives two copies of this changed gene, one from each parent.

Any person with one copy of the changed CF gene, and one copy of an unaffected gene, is a CF carrier. Carriers are not themselves affected by cystic fibrosis. However, if their partner is also a carrier, then each child they produce has a 1 in 4 chance of having CF.

CF DISEASE DESCRIPTION

In the beginning your baby will seem healthy, however, you will begin to notice certain persistent signs of illness such as less playfulness, some coughing, and foul smelling bowel movements. You may need to give pills to your child many times a day. Your child will occasionally need to stay in the hospital (i.e. once a year). You will, however, be able to enjoy many of the joys of parenthood, with allowances made for the illness.

Imagine that the symptoms steadily progress. As a teenager your child is often tired, has a poor appetite, and has a constant cough. In addition to needing more medication, there is now a need for more frequent hospital stays (i.e. 2-3 times a year) and physical therapy to clear your child's lungs. You find that you are spending an increasing amount of time caring for your child. There is, however, still some time for normal family activities.

In their 20's, your child's activity level becomes severely limited so that he/she cannot work. Hospital stays are more frequent. Your child is taking as many as 40 pills a day and friends notice obvious signs of weight loss and breathing problems. In their 30's your child may die from CF after a prolonged hospital stay.

Throughout your child's lifetime there will be no intellectual impairment but there may be some social and emotional difficulties related to the disease.

At times, many parents may feel sadness and distress dealing with the additional responsibilities of caring for their CF child. In spite of this, some parents find hidden strengths in themselves and appreciate the special joys in caring for such children.

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APPENDIX K

CONSENT FORM FOR CF MOLECULAR TESTING AND FOLLOW UP ASSESSMENTS

I _____ request that an attempt be made by molecular (DNA) testing to assess whether I am a carrier of the gene for cystic fibrosis

I understand that this analysis is to be performed on a swab from my mouth

I understand that my results are confidential, but that they may be used in the interpretation of results for other members of my family

I understand that the data generated by this analysis will be assembled in to a report and explained to me by a geneticist or genetic counsellor. In approximately 2 weeks after receiving feedback on my test results, the Research Coordinator will contact me to complete the questionnaires and interview from the "CF Carrier Testing Project". This will be repeated again in approximately 6 months

All my responses will be kept confidential and my name will not be used. I can withdraw from the study at any time and this will not affect current or future care at the Children's Hospital of Eastern Ontario or Ottawa General Hospital

Signature _____

Date _____

Witness _____

Date _____

APPENDIX 1

DECISION TREE FOR HIGH RISK PREGNANT SCREENING OF CARRIER TESTING

* used in Ranking Scale
** used in Standard Gamble

Figures indicated based on observed or preliminary data

INDIVIDUAL

CUPLE

Partner Not Tested (SS)

Test Positive
[+] (SS)**

Carrier
Testing
YES

YES

Couple Test
Positive [++]
(SS)**

Prenatal
Test NO

25

Partner Tested

Carrier
Testing

CF Child

25

Other
Reproductive
Options

YES

CF P. Addition AT

Pregnancy

NO

Low Risk

1:60 to 1:25

Test Negative
[-] (SS)**

Healthy Child

True Negative-Healthy Child

Couple
Test Negative [S+]

25

25

True Negative

Healthy Child

Healthy Child

Healthy Child

Appendix M

Standard Gamble Anchors

APPENDIX IV

FEELING THERMOMETER BOARD SPECIFICATIONS

Scale 1:4

SCALE: 1 cm. = 1 inch.

- NOTES:
- ① lime green coloured translucent film overlay.
 - ② cut-out sections to display LIFE A numeric and graphical probability display.
 - ③ cut-out section for gripping probability wheel.
 - ④ designers' initials (surnames).
 - ⑤ dotted lines depict transparent plastic "parking permit" envelopes.
 - ⑥ arrow suggests direction in which "wheel" be rotated.
 - ⑦ background provided by white bristol board.
 - ⑧ all lettering, arrows and lines are printed in black.
 - ⑨ after all printing, colouring and trimming (including cut outs) are complete laminate entire faceplate with transparent plastic film which is subsequently trimmed to one-eighth inch of faceplate edges.

CHANCE (STANDARD GAMBLE) BOARD BACKPLATE SPECIFICATIONS

Scale: 1 cm = 1 inch

- Notes:
- 1 backplate may be any colour or material but should be stiff and have sufficient strength to support the chance wheel using a grommet;
 - 2 grommet is not centrally located;
 - 3 no lettering or graphics are required;
 - 4 lamination is optional and depends on material used.

(choice "A" is Perfect Health vs. Death.

"B" is utility measurement state)

Appendix P

Example of a reproductive health state standard gamble

Appendix Q

Process of CF Carrier Testing Decisions

Note: Adapted from U.S. Congress, Office of Technology Assessment, 1992

Appendix R

Ajzen and Fishbein's Model of Reasoned Action

Note. Arrows indicate the direction of influence.
Taken from Ajzen and Fishbein, 1980

END

1 8 0 6 9 7

FIN