EXPERIENCES OF INDIVIDUALS LIVING WITH HEREDITARY NON-POLYPOSIS COLORECTAL CANCER (HNPCC) IN FAMILIES WITH AN EXON 8 DELETION MUTATION: A MODIFIED GROUNDED THEORY STUDY

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Experiences of Individuals Living with Hereditary Non-Polyposis Colorectal Cancer (HNPCC) in Families with an Exon 8 Deletion Mutation: A Modified Grounded Theory Study

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Abstract

Hereditary non-polyposis colorectal cancer (HNPCC) is an autosomal dominant condition that predisposes individuals to colon and other cancers. Genetic testing is available to families with known mutations. Limited insight exists on situational and contextual factors influencing genetic testing, as well as the reaction to and acceptance of one`s results. An original qualitative study used grounded theory methodological to explore the meaning of genetic testing for HNPCC, to develop a greater understanding of the psychosocial and behavioural impact for carriers and non-carriers, and to identify relevant information to facilitate the provision of counseling programs for both individuals and families. A substantive theory, *Confronting and Accepting the Challenges of Living in Families with Genetic Linked Diseases*, emerged from the data analysis. This theory is defined by three major thematic categories – living in families with a strong history of cancer, becoming aware of genetic testing and living the process, and struggling to adjust.

Most of the participants in the original study were from families with the intron 5 splice site of the MSH2 gene. These individuals had participated in genetic testing eight to ten years prior to being interviewed. With the identification of an additional MSH2 mutation, exon 8 deletion, family members were now available to be interviewed closer to the time of genetic testing. A modified grounded theory study was subsequently conducted with these individuals by this researcher. The purpose of the current study was to augment the conceptualizations leading to the substantive theory generated in the original study.

The findings indicated that the genetic testing event was viewed narrowly in comparison to the larger life context. The importance of lay inheritance beliefs became integral to shaping the meaning of genetic testing. Family experiential knowledge emerged as a major factor in shaping risk perceptions and emotional readiness. The impact of these experiences requires careful assessment before genetic testing. Pre-test genetic counseling enhanced cognitive processing of results, but unexpected emotional reactions occurred in relation to extensiveness of familial cancer, beliefs about inheritance, coping abilities, and family communication. Attention needs to be given to the impact of subjective feeling states on the testing process. The psycho-emotional impact of knowing one's HNPCC status can impede successful coping long-term. Being open to and having family support emerged as being significant. Timing and sites of recommended cancer screening were variable amongst physicians, suggesting the value of accurate timely information flow. For carriers reaching the affected stage, access to health care becomes increasingly significant.

In conclusion, clinicians and families need to think longitudinally about the course of HNPCC illness with normative landmark transitions and constantly changing demands to help individuals achieve a sense of resilience and maintain an optimal quality of life. Nurses are poised to prioritize, coordinate, and provide psychological and emotional support to HNPCC families.

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Table of Contents

Abstract ii

Acknowledgements iv

List of Figures viii

CHAPTER 1 1

Introduction 1

Background and Rationale 3

Significance and Problem Statement 5

Purpose and Research Questions 7

CHAPTER 2 8

Literature Review 8

The Lead-In Period 9

Familial Experiential Context 9

Risk Perceptions and Pre-genetic Testing Engagement 11

Summary 13

The Genetic Testing Period 14

Decision-Making for and Engagement in Genetic Testing 14

Reactions and Adjustment to Receipt of Test Results 21

Family Communications About Cancer Risk 23

Summary 25

The Post Genetic Testing Period 27

Psychosocial and Emotional Adjustment 27

Behavioral Adjustment 35

Summary 38

CHAPTER 3 40

Methodology 40

Research Design 40

Predictive Genetic Testing 43

Population and Participant Recruitment 44

Procedure 47

Interview Schedule 48

Ehtical Considerations 49

Data Analysis 50

Trustworthiness of the Study 51

Credibility 51

Dependability 52

Confirmability 52

Transferability 53

CHAPTER 4 54

Results 54

Descriptive Profile 54

Conceptual Model 55

HNPCC Families with Exon 8 Deletion Mutation 58

Living in Families with a Strong History of Cancer 58

Becoming Aware of Genetic Testing and Living the Process 64

Struggling to Adjust 77

Discussion 90

CHAPTER 5 93

Discussion 93

Living in Families with a Strong History of Cancer 93

Becoming Aware of Genetic Testing and Living the Process 96

Struggling to Adjust 99

Interactive Effects 102

CHAPTER 6 105

Limitations and Implications 105

Limitations 105

Clinical Implications 106

Nursing Implications 112

References 115

APPENDIX A: Cover Letter and Brief Overview of Research Study 125

APPENDIX B: Consent Form 128

APPENDIX C: Interview Schedule 134

APPENDIX D: Ethical Approval 136

List of Figures

Figure 1: Flow Chart of Sampling Plan 44

Figure 2: Confronting and Accepting the Challenges of Living in Families with Genetic-Linked Diseases 55

CHAPTER 1

Introduction

Hereditary non-polyposis colorectal cancer (HNPCC) is an autosomal dominant syndrome associated with one of five germ-line mutations (hMSH2, hMLHI, PSM1, PMS2 and hMSH6) that predisposes individuals to colon and other associated cancers (Lynch, Lynch, Lynch, & Attard, 2008). Autosomal dominant means that only one parent needs to pass the abnormal gene for HNPCC onto offspring for them to inherit the syndrome. The syndrome is characterized by early age of cancer onset and carries a significant lifetime risk for colorectal cancer (CRC) (80%-90%), endometrial cancer (40-60%), and ovarian cancer (12-15%) (Lynch et al., 2008). It is also associated with an increased risk of kidney, gastric, urothelial cancer, biliary tract, small intestine, brain and skin tumours (Aarino et al., 1999; Chung & Rustgi, 2003; Green et al., 2002; Stuckless et al., 2007).

Individuals from families with a known HNPCC gene mutation are encouraged to participate in at-risk testing upon reaching the age of informed consent. Genetic testing will determine individual family member's risk status for the condition but not if or when it will surface. Defining features of the HNPCC syndrome are incomplete penetrance (not all mutation carriers will develop a cancer) and variable expressivity (carriers develop different cancers at different ages) (Brodersen, Sutton, Goff, Hodgson, & Thomas, 2004; Lindor et al., 2006; Stuckless et al., 2007). Following genetic testing, carriers are alerted to the importance of continuing or initiating screening for the prevention and early detection of associated cancers, while non-carriers can be relieved from the burden of

unnecessary screening (Aarino et al., 1999; Lin et al., 1998; Lynch & Chapelle, 2003; Vasen et al., 1998).

The full extent and specifics of the psychosocial and behavioural impacts of genetic testing for HNPCC on individuals and families are still unknown despite the expanding research base in this area. Limited insight also exists on how personal understandings of hereditary based cancer and situational and contextual factors influence an individual's decision making prior to and following genetic testing for HNPCC (Bleiker, Hahn, & Aaronson, 2003; Marteau & Weinman, 2006; McAllister, 2002, 2003; Meiser, 2005; Murakami et al., 2004). An important contextual factor that seems to buffer the impact of genetic testing on family members is strong and open communication patterns (Rolland & Williams, 2005; van Oostrom et al., 2007a). Currently, researchers and theorists are placing more emphasis on exploring how variations in the family context may impact short- and long-term adjustment for those at risk for HNPCC (Gaff, Collins, Symes, & Halliday, 2005; Koehly et al., 2003; Lim, Macluran, Price, Bennett, & Butow, 2004; McAllister, 2002; Mesters, Ausems, Eichhorn, & Vasen, 2005; Peterson et al., 2003; Rolland & Williams, 2005).

Overall, the results of systematic reviews and meta-analyses of both controlled and uncontrolled trials on the psychological and behavioural effects of genetic testing for familial cancers suggest that genetic testing has no major effect on an individual's level of general anxiety or cancer-specific worry (Bleiker et al., 2003; Braithwaite, Emery, & Walter, 2004; Meiser, 2005). In fact, prospective data specific to the HNPCC population suggest decreases in general anxiety and cancer-specific worry by the three and six-month time points post-genetic testing. Despite this favourable evidence, researchers note

the dearth of knowledge in the area of genetic testing for HNPCC and recommend that more extensive research be conducted to determine its true effects on the individual and the family unit in both the short- and long-term. Many advocate for the use of a qualitative approach (Bleiker et al., 2003; Marteau & Weinman, 2006; McAllister, 2001; Riper, 2005).

Background and Rationale

Previous studies on genetic testing for cancer conditions have primarily focused on hereditary breast and HNPCC populations. Studies on HNPCC have mainly attempted to gain greater insight into the factors that relate to decision making around genetic testing and the psychosocial and behavioural impacts of this experience in the short-term. Study findings concur that such psychological factors as personal cancer worry and perceived high risk for the disease, as well as concern for children and close family members, positively impact interest and engagement in genetic testing (Braithwaite et al., 2004; Claes, Denayer, Evers-Kiebooms, Boogaerts, & Legius, 2004; Claes et al., 2005; Meiser et al., 2005).

There is also emerging evidence on the relevancy of the family context for shaping risk perceptions in the pre-genetic testing phase and influencing acceptance of and adjustment to genetic test results (d' Agincourt-Canning, 2005; Kenen, Arden-Jones, & Eeles, 2003; McAllister, 2001, 2002; Shiloh, 2006). Nevertheless, study findings generated by standardized scales indicate minimal psychological and emotional harm from genetic testing for both carriers and non-carriers. The findings also suggest that anxiety and distress levels rise briefly at the time of genetic testing and usually subside

within a year after testing for carriers (Aktan-Collan, Haukkala, Mecklin, & Kaariainen, 2001; Braithwaite, Emery, & Walter, 2004; Claes et al., 2004; Claes et al., 2005; Meiser, 2005).

Study findings also suggest that there are a range of complex concerns not being considered in the assessment of an individual's overall adjustment to genetic testing. Coping strategies, experiential knowledge about cancer risk in the family, the development of risk perceptions during the years prior to testing, and family impacts appear to have significant effects on adjustment in the long-term (Braithwaite et al., 2004; Heshka, Palleschi, Howley, Wilson, & Wells, 2008; Meiser, 2005). Studies evaluating the behavioural outcomes of testing are largely quantitative and focus on screening rates among carriers post-testing. Yet there is a growing body of research highlighting the barriers to screening adherence and the importance of the health care system in facilitating this for carriers (Geary et al., 2007; Lindor et al., 2006; Lynch et al., 2008).

Nevertheless, what appears to be absent is reliable and valid measures for assessing important factors, such as the years spent living in a high-risk family, that shape individuals' willingness to engage in genetic testing and how they experience the process. Equally important is the limited research conducted on individual and family adjustment years after testing. The studies designed to assess short- and long-term adjustment use standardized scales for measuring outcomes such as anxiety, depression and self-efficacy, yet there are only a few designed to measure factors specific to genetic testing for cancer syndromes (Balmana, Stoffel, Emmons, Garber, & Syngal., 2004; Pieterse et al., 2005). More substantive theory development, through the use of grounded theory methodology,

is needed to provide a database for generating reliable and valid operational measures of key factors believed to exert a mediating and moderating impact on overall adjustment (Coyle & Williams, 2000; Gilgun, 1992, 2004; McAllister, 2001; Way et al., 2008). More importantly, in order to ensure that individuals, families and health care professionals have a full understanding of the implications of genetic testing for HNPCC, it is imperative that we explore the full scope of the experience including the many years preceding and following the genetic testing event.

Significance and Problem Statement

A large case control study conducted in the provinces of Ontario (ON) and Newfoundland (NL) examined the genetic epidemiology of CRC and its psychosocial component, investigating the impact of genetic testing for HNPCC both quantitatively and qualitatively (Way et al., 2008). The results of the initial quantitative study suggested that personal characteristics such as time since HNPCC testing, age, gender, family frequency of CRC, and affected and non-affected status did not have a significant impact on lifestyle changes, adjustment difficulties or emotional status following genetic testing. Interestingly, participants with a greater CRC presence in the family were less likely to experience such negative emotions as cancer worry and guilt.

A follow-up qualitative study was designed to explore the meaning of genetic testing for HNPCC, to develop a greater understanding of the psychosocial and behavioural impact for carriers and non-carriers, and to identify relevant information to facilitate the provision of counseling programs for both individuals and families (Way et al., 2008). A substantive theory entitled, *Confronting and Accepting the Challenges of*

Living in Families with Genetic Linked Diseases, emerged from the data analysis. This theory is defined by three major thematic categories – living in families with a strong history of cancer, becoming aware of genetic testing and living the process, and struggling to adjust. It proposes that living in families with a strong history of cancer and becoming aware of genetic testing and living the process exert both a direct and an indirect effect on adjustment to a HNPCC carrier or non-carrier status. It also conjectures that each construct exerts a separate and interactive effect on quality outcome.

Most of the participants in the original qualitative study had undergone genetic testing eight to ten years prior to being interviewed. Targeted individuals were from the 12 families with a known germline mutation on the mismatch repair MSH2 gene – splice site of intron 5 which results in exon 5 deletion (Green et al., 2002; Stuckless et al., 2007). However, during the course of the study, further analysis of other high-risk families resulted in the identification of a second MSH2 gene mutation – deletions of exon 8 in five families. What this meant for the larger research study is that family members were potentially available to the research team who had experienced genetic testing more recently. This discovery also coincided with changes noted in the prevalence of other types of cancers in these families. Exon 8 deletion mutation family members were being counselled to pay particular attention to other cancers, such as kidney and urothelial cancers. The health system had also integrated genetic counselors into the provincial medical genetics program. Thus, new referrals for genetic testing for HNPCC were now being offered information and advice from both the geneticist and genetic counselors. It was necessary to capture the experiences of individuals more recently tested for HNPCC in order to confirm the substantive theory.

CHAPTER 2

Literature Review

Research in cancer and genetics has identified several mutations associated with the development of HNPCC. Close to 1000 HNPCC families have been recognized worldwide and many other families at risk are being followed clinically every day. The identification of a genetic mutation provides an opportunity for individuals in high-risk families to confirm their cancer risk and to engage in preventative and early detection screening programs to help control disease progression. Research to date suggests regular screening decreases morbidity and mortality (Bleiker et al., 2003; Jarvinen et al., 2000). Nevertheless, very little is known about what it is like to live with knowledge of a hereditary link to cancer in the family. Health care professionals need to be confident that providing cancer risk information to individuals has minimal psychosocial and emotional impact in the short- and long-term.

Research on genetic testing for HNPCC is largely quantitative, although a few qualitative studies provide a richer representation of the experience. This literature review explores the entire genetic testing experience (i.e., the lead-in, actual and post-test periods). First, it provides an overview of research studies conducted on the lead-in period to genetic testing for hereditary cancer. Second, it explores the actual genetic testing period, which includes the preparation for and reaction to the receipt of test results and the perceived level and quality of communication within families following confirmation of a HNPCC gene mutation. Finally, it provides a discussion of key issues

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in the post-test period. Specifically, the discussion will focus on the impact on the family and others, screening practices, and the need to confront new issues beyond the self.

The Lead-in Period

The lead-in period refers to the months and years prior to genetic testing for hereditary cancer. For some individuals, the period is marked by significant family losses from cancer followed by the notion that one could also be at risk. For others, family losses from cancer are less pervasive and therefore little thought is given to one's personal risk status. Although few studies explore the years prior to testing in-depth, the importance of events occurring during this time for full engagement in the genetic testing process are recurring themes in the literature (Bleiker et al., 2003; McAllister, 2002, 2003; McAllister, Davies, Payne, Nicholls, Donnai, & MacLeod, 2007; McCann et al., 2009).

Familial Experiential Context

The relevancy of the family context for shaping individuals' beliefs about cancer transmission and what implications this might have personally has been recognized as important in the development of risk perceptions for genetic-based diseases. Several studies have focused on developing greater insight into the meaning and importance of this context for facilitating acceptance of the genetic link to cancer and willingness to engage in the genetic testing process. It is conjectured that the impact of the family context can be quite variable for different individuals depending on their closeness to and degree of involvement with cancer illness in family members, and/or personal

experiences with cancer (d' Agincourt-Canning, 2005; Kenen, et al., 2003; McAllister, 2001, 2002; Shiloh, 2006).

In a qualitative study of women's experiences with hereditary breast and ovarian cancer, d' Agincourt-Canning (2005) concluded that participants' conceptualizations of personal risk seemed to be informed by two types of knowing – emphatic and embodied. Emphatic knowing is defined as a continuum of knowing that is informed by stories relayed to a person by others and/or close/distant encounters with family members who have or have had cancer. Embodied knowing is defined in terms of how cancer and its treatment are experienced within the self. The frequency and intensity of encounters with or the stories about others are conjectured to have far-reaching implications for individuals' understandings and knowledge of cancer. As well, personal experiences with cancer tend to augment pre-existing knowledge and understandings derived from prior encounters with or memories of others' experiences with cancer.

An important aspect of perceived risk for cancer, which is grounded in a familial/personal experiential base, is that it is continuously evolving, albeit in a non-linear manner. As such, each new encounter with cancer in other family members or on a personal level rekindles what lies dormant during disease-free periods. What is conjectured to be salient for risk constructions is how one interprets the meaning of these experiences for the self (Way et al., 2008). In a qualitative study of women with a family history of hereditary and ovarian cancer, Kenen et al. (2003) found that risk perceptions were constructed by piecing together family cancer experiences in a highly selective manner from story fragments vaguely remembered and/or secret stories unearthed while searching for answers. Significantly, interpretations of a particular family's cancer history

seemed to be more important in shaping risk perceptions than actual familial cancer patterns.

McAllister's (2002) theory of engagement captures the process of engaging in risk for HNPCC. The degree of engagement in HNPCC risk is conjectured to vary over time in relation to the level of cognitive and emotional involvement with the family's history of cancer. At any point in time, individuals fall along a continuum marked by disengagement or partial/intense engagement. Individuals are more likely to evidence partial engagement with their risk if they are ignorant of the family history, have impersonal knowledge of this history, have sporadic experiences with cancer in family members, or live in families where cancer is a taboo. McAllister (2002) suggests that the degree of engagement with HNPCC risk is a function of the openness of discussions about the family history in response to the unfolding of cancer events.

Risk Perceptions and Pre-genetic Testing Engagement

Risk perception takes on new meaning when an individual is first introduced to the idea that the cancer observed or experienced in one's family is potentially due to genetic factors. Several authors noted a discrepancy between knowing about the family history of cancer and thinking about the possibility that this might be inherited versus becoming informed about the potential genetic link and understanding how this could impact personal risk perceptions for the disease (McAllister, 2003; Reeve, Owens, & Winship, 2000). Study findings suggest that individuals whose lives are affected by familial cancer seek explanations about possible causal factors.

Many families at risk for HNPCC tend to use rudimentary inheritance patterns to seek answers to and to cope with their own potential risk status (Kenen et al., 2003; McAllister, 2002, 2003; Targum, 2000). In many instances, individuals tend to overestimate their risk, which may in part be attributed to the closeness and severity of cancer episodes experienced in the family. In contrast, individuals tend to underestimate risk if they perceive the family cancer as not severe or they are unaware of its presence. Either way, awareness and experiential knowledge play a significant role in the development of personal risk perceptions and hence may have a strong influence on coping strategies to deal with the event (McAllister, 2001).

Carlsson and Nilbert's (2007) and McAllister's (2003) qualitative inquiries demonstrate the importance of awareness of hereditary cancer in the family for engagement in HNPCC risk and, ultimately, the genetic testing process. Carlsson and Nilbert found that many study participants reported being suspicious of hereditary cancer long before confirmation of the HNPCC presence in the family. For many, it triggered the unexplained worry about cancer in the family that had been discussed over the years amongst parents and grandparents. Significantly, individuals unaware of the cancer hereditary link were overwhelmed by the news. McAllister (2003) described how family members develop narratives around their risk status to enable them to cope with the interaction of lay theories of inheritance, ideas about luck, past coping strategies and conviction about carrier status as a means of dealing with the decision to become involved in genetic testing. Assessment of the development of personal risk status and related coping abilities are important to consider in determining a person's emotional readiness for testing.

Beyond awareness of hereditary cancer prior to testing, experiential knowledge is another factor influencing the emotional readiness of individuals presenting for genetic testing for HNPCC. Carlsson and Nilbert (2007) noted that individuals who had cared for close family members reported experiencing emotional difficulties when first presented with the option of genetic testing for HNPCC. Similarly, McAllister (2002) noted that individuals who struggle with painful memories of having cared for and lost close family members may resist becoming engaged with their HNPCC risk. As this author noted, accounts of cancer stories are not just reflections of the past linked to emotions, but rather are post hoc justifications for beliefs and actions about a possible mutation carrier status. Past cancer experiences seem to be inextricably linked to coping strategies in complex ways.

Summary

It seems apparent that awareness of family history, anxiety and worry, experiential knowledge and development of risk perceptions and coping strategies are all important factors that need to be considered in assessing individuals' emotional readiness for genetic testing. The importance of how these factors relate to one another in the evolution of events during the many years preceding testing becomes increasingly relevant to the impact of genetic testing for HNPCC. Currently, the literature fails to address the influences of living in a family with hereditary cancer on accepting the need for genetic testing for HNPCC and moving through the testing process.

The lead-in period for genetic testing needs further exploration to determine how living in a family with an extensive cancer history influences individuals' reactions to the

ideas of HNPCC and genetic testing. Furthermore, we need greater insight into how a familial cancer history influences the meaning of cancer illness for the self and/or the development of personal risk perceptions. Finally, more information is required about how risk perceptions for future disease states influence acceptance of and adjustment to genetic test results in the short- and long-term. These components require more in-depth analysis using a broader conceptualization of the lead-in period to genetic testing for HNPCC.

The Genetic Testing Period

The genetic testing period refers to the preparation for the testing and counseling process, reactions and adjustment to the receipt of results, and willingness to communicate the findings of genetic testing patterns within families. Studies on the genetic testing period focus on evaluating the counseling process, the reactions and short-term adjustment to learning about one's carrier status and the importance of communication within families (Bleiker et al., 2003; Braithwaite, Emery, Walter, Prevost, & Sutton, 2006; Meiser, 2005; van Oostrom et al., 2006b).

Decision-Making for and Engagement in Genetic Testing

A number of studies have been conducted on decision making around genetic testing, with many suggesting it is largely a cognitive process. Etchegary's (2004) review revealed that many of the studies in this area are descriptive, while a few researchers have used social cognition theory and, more recently, grounded theory to further discern how and why individuals decide to undergo genetic testing for HNPCC. All of the study

findings indicate that the decision-making process is intrinsically linked to the development of a healthy appreciation for ones' personal risk.

Descriptive findings. Early descriptive studies on the decision to test focused primarily on extrapolating what factors motivate an individual to engage in the genetic testing process. Perceived risk of being a carrier, belief that cancer in the family is hereditary, the ability to handle the emotional aspects of testing, and the psychosocial effects that carrier status would have on other family members were found to be associated with the motivation to test (Bleiker et al., 2003; Meiser, 2005).

Bleiker et al.'s (2003) review highlighted study findings on risk perceptions and motivations for genetic testing over the previous decade. An important finding was the significant influence of subjective risk as opposed to objective risk on genetic testing decision-making. Subjective risk is shaped by the family history of cancer, psychological distress and coping strategies, and family communications. As perceived susceptibility for cancer is often overestimated, it is conjectured that individuals seek genetic testing to reduce uncertainty, confirm the need for preventive actions, determine their children's risk, and plan for the future. Meiser's (2005) and Etchegary's (2004) reviews of the literature on genetic testing for HNPCC and breast/ovarian cancer support Bleiker et al.'s (2003) findings.

Higher education, younger age, being married, previous involvement with genetics services and less advanced stage of CRC have also been found to be predictive of a greater intention to test. However, some researchers have found that the frequency of intrusive thoughts about CRC being hereditary seems to be a stronger correlate of

intention to test (Esplen, Urquhart, Butler, Gallinger, Aronson, & Wong, 2003; Esplen et al., 2007; Hadley et al., 2003; Kinney et al., 2000; Lerman et al., 1999). Meiser (2005) also found that intention to engage in genetic testing appears to be more consistently associated with psychological factors than socio-demographic factors.

Despite consistent findings on interest in and intention to participate in genetic testing, concerns exist about the reliability of these early studies. Specifically, the use of single items to measure distress, worry, and intrusive thoughts and/or standardized scales not validated in populations with genetic-based diseases compromises the reliability and validity of the results (Bleiker et al., 2003; Braithwaite et al., 2006; Broadstock, Mitchie, & Marteau, 2000; Heshka et al., 2008; Meiser, 2005; van Ostroom, 2006a, 2006b). As well, even though high rates of interest are reported, this does not necessarily translate into high levels of engagement in genetic testing for HNPCC. Discrepancies may be due to change in knowledge about HNPCC, risk perceptions, perceived benefits, or the risks and limitations of genetic education and counseling (Claes et al., 2004; Coyle & Williams, 2000; Heshka et al., 2008).

Besides the research findings on motivators of genetic testing, a number of quantitative studies have investigated the psychosocial and emotional status of individuals prior to actually participating in the process (Bleiker et al., 2003; Braithwaite et al., 2006; Meiser, 2005). As noted previously, perceived risk for cancer is highly variable and heavily influenced by personal factors and the family condition (d' Agincourt-Canning, 2005; Kenen, et al., 2003; McAllister, 2001, 2002; Shiloh, 2006). Nevertheless, for the most part, psychosocial and emotional states do not reach clinical

levels during the pre-test period (Bleiker et al., 2003; Braithwaite et al., 2006; Meiser, 2005).

There is also some support for a strong association between elevated risk perceptions and higher levels of psychological distress (Bleiker et al., 2003; Carlsson, Bjorvatn, Engebretsen, Berglund, & Natvig, 2004; Claes et al., 2005; Esplen et al., 2003). There is also some evidence suggesting that greater perceived social support (Carlsson & Nilbert, 2007; Esplen et al., 2007) greater self-efficacy (Carlsson & Nilbert, 2007) and more positive coping styles (Claes et al., 2005; Esplen et al., 2007) decrease distress levels.

Genetic counseling is designed to improve disease prevention by providing genetic risk information to those at risk. During HNPCC counseling sessions individuals are given information about the ongoing characterization of the condition, the variability of the disease, the benefits and limitations of testing, potential impacts on personal relationships and goals, and options for risk reduction through screening (Brodersen et al., 2004; Lindor et al., 2006; McAllister, 2003; McAllister, Payne, MacLeod, Nicholls, Donnai, & Davies, 2008b; Stuckless et al., 2007). Individuals are also counseled on how to communicate test results to others and are given supportive counseling options (van Oostrom et al., 2006a, 2006b, 2007).

At present, clinical genetics services operate primarily under the principles of a knowledge sharing approach. The focus of counseling is on providing information about cancer inheritance and susceptibility, gene identification and the meaning of results largely from a Mendelian perspective. That is, individuals are counseled first about their risk for having the HNPCC gene mutation and second on their CRC and extracolonic

cancer risks (Aarnio et al., 1999; Jarvinen et al., 2000; Lynch et al., 2008). McAllister, Payne, MacLeod, Nicholls, Donnai, and Davies (2008a) noted there is very little evidence that accurate information or risk figures per se are necessarily valued by patients.

Theoretical insights. Social cognition models depict relationships between knowledge, beliefs, attitudes, and behavior. It is conjectured that decision-making is based on beliefs and consideration of these beliefs can help predict future health behavior. As HNPCC offers individuals a measure of disease control through preventative screening regimes, the application of these models are deemed to be valuable for identification of factors that relate to the decision to test (Etchegary, 2004; Marteau & Weinman, 2006; Shiloh, 2006).

Shiloh's (2006) theoretical review of genetic counseling applies self regulation theory to the decision to test. The theory proposes that illness representations, defined as people's perceptions of and beliefs about an illness, mediate the relationship between health threats and reactions to them. Identity of the threat, cause, timeline, consequences and controllability are key aspects. It is also proposed that the genetic testing decision-making is underpinned by factors such as family influence, perceived benefits and health care professional influences. Illness representations evolve over time based on personal experiences with disease and social/cultural information acquired through various social sources. It follows that personal experiences with a genetic disease are major determinants of its representation and the decision to test.

Marteau and Weinman (2006) similarly applied self-regulation theory to explain decision making and behavioral responses to learning about one's carrier status. These

researchers highlighted that the decision to test and subsequent participation in screening depends on a range of factors, which include perceptions about threat, the likeliness of screening to reduce the threat and one's ability to engage in screening. The authors concluded that, although studies to date indicate consistent uptake of testing, few if any, have found support for appropriate increases in surveillance behavior following genetic counseling.

With self-regulation theory, emphasis is placed on the cognitive process in shaping the development of risk perception. Marteau and Weinman (2006) recommend further investigation of what motivates testing by focusing on enhancing the cognitive aspects of how information is presented to individuals and how the representation is translated into a behavioral response. In contrast, qualitative evidence suggests that genetic testing is also an emotional process and further research is needed to explore the emotional aspects as a means of elucidating a broader picture of the influences on the decision to test.

Qualitative findings. Quantitative studies have documented the importance of both cognitive and emotional factors in determining a person's readiness for testing (McAllister et al., 2007; van Oostrom, 2006a; 2006b). However, the focus in these studies remains on the individual to the exclusion of the family context. Qualitative studies have explored the importance of the level of awareness of hereditary cancer, anxiety prior to testing, experiential knowledge, risk perceptions and coping strategies in shaping individual readiness for and reactions and adjustment to genetic test results

(Carlsson & Nilbert, 2007; McAllister, 2002, 2003; McAllister et al., 2007; Reeve et al., 2000).

Emotional readiness for predictive genetic testing for a variety of diseases has become increasingly the focus of qualitative inquiries. Reeve et al., (2000) qualitative study identified awareness of hereditary cancer in the family as an important part of one's emotional readiness for testing. All participants spoke of the long-standing recognition of a family link with bowel cancer. For many, it was long before the idea of a cancer genetic link was even considered in the medical field. Participants in this study had an overall positive attitude toward taking part in testing and adjusted well to news of their carrier status. These findings suggest a healthy awareness of a cancer genetic link is an important part of positive adjustment to genetic testing results.

McAllister (2002) also suggested that engaging in genetic testing may be difficult due to past experiences. Many of the participants in her study described painful memories and emotional experiences with cancer diagnoses and /or death of a parent or close family members at an early age. These experiences seemed to play a key role in the decision making process.

Anxiety and worry have also been exhibited amongst participants presenting for gene testing. Carlsson and Nilbert (2007) found that some of their participants reported feeling tense and worried before testing, postponing originally scheduled appointments, and/or needing time to mentally prepare before scheduling counseling sessions. Other participants discussed how emotions related to a hereditary predisposition to cancer were suppressed and how coping strategies, such as denial, projection, and distraction, were employed to spend less time reflecting on the awareness of the genetic defect. In short,

the findings highlighted the complexity of feeling states prior to genetic testing that often extended beyond the self to other family members.

Reactions and Adjustment to Receipt of Test Results

Studies that have investigated reactions to genetic testing seek to determine whether or not it causes significant psychological harm (Bleiker et al., 2003; Braithwaite et al., 2006; Meiser, 2005). Particular attention has been given to measuring such cognitive and affective states as perceived health and risk for cancer, distress, anxiety, depression, guilt, worry, fear of cancer/death, and intrusive and avoidant thoughts. Other areas of focus include such health outcomes as attitudes toward the future, psychological well-being, life satisfaction, and health-related quality of life (HRQOL). Significantly, limited research exists on evaluating the effectiveness of genetic counseling sessions for reducing the psychological sequelae surrounding genetic testing. Bleiker et al. (2003) noted that the positive impact of genetic counseling on decreasing psychological distress and enhancing risk perceptions remains unconfirmed.

Despite consistent and favorable findings on psychological responses to testing, concerns exist about the reliability and validity of quantitative findings that rely on standardized measures (Coyle & Williams, 2000; McAllister et al., 2007). Several authors emphasize the need for qualitative methodologies to highlight the scope of emotional effects in the short- and long-term, as well as theory generation to capture the psychosocial processes involved with genetic-based diseases (Bleiker et al., 2003; Marteau & Weinman, 2006; McAllister, 2001; Riper, 2005). In fact, a couple of qualitative inquires have already provided new insights into the complexity and

variability of emotional effects on individuals and families (Carlsson & Nilbert, 2007; McAllister et al., 2007).

McAllister's (2002) theory of engagement seeks to explain how the degree of engagement at the time of genetic testing influences reactions to test results. Engagement is proposed to be a continuous process that fluctuates over time and with the unfolding of family cancer-related events. McAllister (2002) conjectured that the process varies according to the blend of cognitive and emotional factors. For example, individuals who are intensely engaged appear to accept their carrier status more quickly, whereas those partially engaged experience some anxiety in the early post-test period.

In a qualitative inquiry focusing on the psychological impact of predictive genetic testing for HNPCC, Reeve et al. (2000) found that the genetic testing event is viewed by many participants as a normal progression in ones' search for answers to what is happening or had happened to the family. Many of the study participants also commented upon the emotional benefits (i.e., level of protection provided by screening). Although distress was minimal, there were reports of worry and concern for the children, especially concerning their willingness to follow recommended screening protocols.

In summary, although studies have consistently shown that anxiety and distress levels rise and fall over the course of the genetic testing period and appear manageable in the short-term, the qualitative evidence suggests that the depths of the emotional aspects to testing are not yet fully explored. The use of a knowledge sharing approach in genetic counseling practice may also be ignoring many of the emotional concerns of family members at risk. These findings give credence to the emerging evidence that awareness and experiential knowledge are key components of emotional readiness and reactions to

testing for HNPCC. No doubt recent literature indicates the need to assess emotional readiness and possible reactions to genetic testing during pre-counseling sessions. However, the extent to which these findings have influenced practice remains unclear.

Family Communications about Cancer Risk

Another key factor in the genetic testing process is the role of family communications. Communications in families about HNPCC and genetic testing are just beginning to be understood (Gaff et al., 2005; Koehly et al., 2003; Mesters et al., 2005; Peterson et al., 2003). Many of the studies are qualitative and descriptive in nature and employ the use of semi-structured interviews. Some of these studies have explored communication patterns, motivations about disclosure, and/or reactions of family members to information on HNPCC and genetic testing (Gaff et al., 2005; Mesters et al., 2005; Peterson et al., 2003).

The importance of communication within families about HNPCC and genetic testing cannot be understated. In most cases, the proband, or first person in the family recognized as being at risk by the health care system, carries the burden of informing other family members about HNPCC and genetic testing. Difficult family relationships, fear of potential rejection and protective factors, such as the unwillingness to alarm others may hinder the communication process and prevent family members from disclosing information about HNPCC and genetic testing. Non-disclosure has the potential to place family members at an increased risk for HNPCC when they could be following recommended screening protocols (Koehly et al., 2003).

Study findings demonstrate that information about the identification of an HNPCC gene mutation is most often perceived as a private family matter and not something to be openly announced to others. Communications about the genetic risk for disease are occurring either within the immediate family or with select extended family members (Gaff et al., 2005; Mesters et al., 2005; Peterson et al., 2003). Both women and men report telling children and their siblings about their HNPCC genetic testing result within the first 48 hours of testing. If the children are considered to be too young, many are choosing to postpone discussions until they are older (Gaff et al., 2005; Mesters et al., 2005; Peterson et al., 2003).

Only a few individuals report that they told extended family members about their results in the immediate post-test period. In many cases, it takes years to inform all family members across generations. The challenge here is that the information about risk and cancer status among multiple family members is constantly changing and therefore communication on the matter is an ongoing process (Gaff et al., 2005; Mesters et al., 2005; Peterson et al., 2003).

Motivations for disclosure amongst family members include moral obligation and anticipatory regret. Study findings indicate that disrupted and tense family relations impede disclosure. Importantly, if individuals experience negative reactions on their first attempt to inform others about the genetic link, they tend to be reticent about doing so again (Gaff et al., 2005; Mesters et al., 2005).

Van Oostrom et al. (2006a) reported changes in second-degree relationships in their study on family impacts. Carriers and non-carriers reported difficulty talking about hereditary cancer and emotional distance. Commentary on the context of difficult

situations or conflicts with respect to genetic testing include differences in attitudes towards testing (i.e., those engaging versus declining) and the tendency of certain family members to impose secrecy on the topic, both within and outside the family network.

Moreover, the presence of external cues is an important factor influencing disclosure among family members. If health care professionals verbally stressed the importance of communicating this information, it surfaced as an important motivator to get the word out to other family members. Also the number of fatal cancers in the family emerged as being a very relevant motivator for disseminating news of HNPCC and genetic testing (Gaff et al., 2005; Mesters et al., 2005; Peterson et al., 2003).

Carlsson and Nilbert's (2007) study also revealed important themes on communications within families. All participants discussed the importance of understanding and conveying information about the results. Once they became aware of the hereditary cancer risk, they expressed a desire to advocate, support and engage other family members to seek information and become involved with screening surveillance programs. Nevertheless, many participants expressed difficulty knowing what to do with relatives with whom they have had very little contact. As well, some participants were concerned about telling others if they felt ill-equipped to deal with different reactions to the news. In some instances, old disputes and new aggressions arose when the hereditary cancer was confirmed, whereas in other situations relationships improved.

Summary

The findings from earlier studies suggest that emotional experiences immediately prior and in the short-term following testing are manageable. However, the reliability of

many of these studies has been questioned. More recent studies have found that the emotional experience of genetic testing for HNPCC is a broad and more intense experience that extends backward in time to the years prior to testing. Dealing with cancer illness in close family members and coping with multiple family losses have important implications for readiness for genetic testing and reactions and adjustment to test results in the short- and long-term.

Other studies suggest that those more aware of the cancer hereditary link and/or those with more difficult memories associated with cancer in the family have little difficulty making the decision to test. In some instances they are more prepared (Reeve et al., 2000). Meiser's (2005) review of 15 studies on participants testing for hereditary cancer confirmed this finding. The review concluded that those who had personal and family experiences with cancer are more likely to undergo genetic testing than those who decline. Hereditary cancer awareness and experiences in the years prior to testing appear to have significant import for the process, as do risk perceptions and coping strategies.

Communication within families about HNPCC and genetic testing is an essential consideration for genetic counseling services. Most often the burden rests with a carrier affected by the disease. Clearly the family dynamics and personal relationships have the potential to interfere with timely communication of information putting family members at risk. How best to support the individual who becomes the designated communicator still needs to be determined.

The Post-Test Period

The post-test period refers to long-term adjustment following confirmation of a carrier or non-carrier status for HNPCC. For most, the period is marked by struggling to cope with personal and family issues, and adhering to recommended screening protocols and follow-up when abnormalities are detected. Studies exploring adjustment are largely quantitative and focus on the personal psychological and behavioural impacts shortly after genetic testing. Significant gaps exist in this literature, including personal and family challenges over time, the support and information mechanisms needed by carriers and their families to buffer these challenges, and how experiences with the health care system can facilitate or impede effective disease management.

Psychosocial and Emotional Adjustment

Meta analyses and literature reviews indicate that there is minimal psychological harm associated with undergoing genetic testing for HNPCC. Prospective studies suggest that distress levels rise slightly for carriers immediately in the post-test period and return to baseline levels within a year, but decrease immediately for non-carriers and remain relatively stable during the follow-up period (Aktan-Collan et al., 2001; Claes et al., 2004; Claes et al., 2005; Murakami et al., 2004). Despite these positive results, there are reliability and validity concerns around the use of single items to measure psychological outcomes of genetic testing (e.g., depression, anxiety, distress, cancer worry, etc.) and few of the standardized instruments measuring outcomes have been validated in populations with genetic-based diseases (Bleiker et al., 2003; Braithwaite et al., 2006; Broadstock et al., 2000; Heshka et al., 2008; Meiser, 2005; van Ostroom, 2006a, 2006b).

The following review is divided into two major sections. First, quantitative and qualitative study findings from HNPCC populations are discussed. Second, a discussion is presented on recent theoretical/conceptual models for guiding research inquiries that focus on long-term adjustment of individuals and families with genetic-based diseases.

Descriptive findings. Heshka et al. (2008) reviewed 30 randomized control trials and prospective studies on the perceived risks, and psychological and behavioural impacts of genetic testing for hereditary disease. For the majority of studies, the perceived risk of HNPCC in carriers was lower one year after testing compared to pretest levels. Furthermore, no overall differences were detected in outcomes evaluated (i.e., general distress, anxiety, depression, and disease specific worry) between carriers and non-carriers. Finally, most study findings failed to detect any of the anticipated negative psychological outcomes.

Several authors noted that there is limited empirical evidence to make any definite conclusions about long-term psychosocial effects (d' Agincourt-Canning, 2005; Bleiker et al., 2003; Braithwaite et al., 2006; Heshka et al., 2008; Kenen et al., 2003; Meiser, 2005). Bleiker et al.'s (2003) review article on risk perceptions after testing suggests that knowledge of an increased probability of developing a life-threatening condition long before its onset can be quite burdensome, given that the options for managing risk are currently limited. This review also noted that there is a significant amount of speculation about the existence of survivor guilt among those who do not carry the gene mutation. The findings suggest that non-carriers report feeling guilty about receiving good news and inadequate about helping others in the family who are dealing with a carrier status

and/or cancer onset. Hence, the psychosocial impacts apply to both carriers and non-carriers.

The findings from qualitative studies suggest that there is a range of complex concerns not being considered regarding overall psychological adjustment to a carrier status. Major influencing factors include differences in personal understandings of perceived risk and coping ability with respect to maintaining a positive mindset and feeling in control of the disease. Researchers concur that experiential knowledge and development of risk perceptions related to living with hereditary cancer and individual coping strategies are all important factors post-genetic testing. How these factors relate to one another and respond to the evolution of events during the years preceding testing becomes increasingly relevant for psychosocial and emotional well-being following genetic testing for HNPCC. Finally, more information is required about how risk perceptions for future disease states influence acceptance of and adjustment to genetic test results in the short- and long-term (d' Agincourt-Canning, 2005; Kenen et al., 2003; McAllister, 2001, 2002).

Several studies have been designed to explore potential factors that may moderate the distress levels of individuals post-genetic testing. Although distress levels tend to fall within healthy ranges for HNPCC carriers, van Oostrom et al. (2006b) found that the familial context had a significant effect. Specifically, individuals who had a parent affected by cancer at a young age and were exposed to a greater number of first-degree relatives affected by cancer tended to evidence higher levels of distress following genetic testing. Similar findings have been reported by other researchers (Erblich, Bovbjerg, & Valdimarsdottir, 2000; Esplen et al., 2003).

In a recent prospective study covering a one year period, Shiloh, Koehly, Jenkins, Martin, & Hadley (2008) investigated the distress levels of individuals classified as high monitors (i.e., hyper vigilant over potential health threats and active information-seekers about ways to buffer them). These authors found that high monitors evidenced more distress in the pre-test period and upon receiving indeterminate or positive results about their HNPCC carrier status. The researchers also cautioned that high monitors generally experience greater distress in response to critical events that threaten their well-being. That is, individuals who fall into this group tend to perceive greater personal risks and experience more intrusive ideation and encode events as catastrophic. On the positive side, high monitors may also experience greater emotional benefits from genetic testing (i.e., high monitors tend to be more positive about their ability to control their cancer risk if they adhere to recommended screening protocols). Importantly, levels of distress and depression diminished over time and appeared to be a function of elevated levels prior to genetic testing.

Besides the individual, genetic testing for HNPCC impacts the total family system. McInerney-Leo (2005) examined changes in cohesion, expressiveness and conflict in close family relationships with individuals undergoing genetic testing. Most study participants felt that family relationships became closer due to the genetic testing process. In contrast, two Belgian studies by Claes et al. (2004) and Claes et al. (2005) evaluated the impacts of genetic testing on family relationships in samples of carriers and non-carriers. Study findings revealed a large variation between carriers' and non-carriers' perceptions. Only a very small percent of non-carriers (6%) reported negative changes in

partner relationships, whereas a significant proportion of carriers (40%) reported a negative change in relationships with their children.

van Oostrom et al.'s (2006a) prospective study evaluated the psychological impact of genetic testing on the entire family unit. Significantly, HNPCC carriers reported more positive changes in family relations than non-carriers. Many of the carriers reported feeling closer to partners and siblings, improved relations with children, greater understanding and support from parents, and improved communication towards second degree relatives. A smaller number of carriers reported negative relationship changes, including greater emotional distance, guilt feelings about having passed on the mutation to their children, secrecy, strained communication around hereditary cancer or genetic testing, and diminished support. In the final analysis, families rated as "enmeshed–chaotic" or "disengaged–rigid" at baseline reported more adverse consequences in relationships. Participants who felt constrained in communicating about the hereditary cancer and less supported at baseline reported more frequent adverse effects on relationships and greater family difficulties in the post-test period.

van Oostrom et al. (2003) conducted a long-term follow-up study of female carriers and non-carriers tested for hereditary breast/ovarian cancer. Although no significant differences were detected between carriers and non-carriers on distress and cancer worry one and five years after genetic testing, both groups showed a significant decrease in anxiety and depression at the one year mark, but a steady increase in these levels at the five year follow-up. The most significant predictor of long-term cancer-related distress and cancer worry was hereditary cancer-related distress at baseline or pre-test disclosure. The second most significant predictor for targeted outcomes at five years

follow-up varied. Having children less than 15 years of age at baseline was predictive of cancer-related distress, and knowing one or more relatives who died of breast and/ovarian cancer was predictive of cancer worry. Long-term distress and cancer-specific worry was also associated with less open family communications about the test result and more doubts about the validity of test findings. In contrast, changes in relationships with relatives emerged as a significant predictor of distress, whereas greater perceived risk of breast cancer was a significant predictor of worry (van Oostrom et al., 2003).

In a later study of families with BRCA1/2 and/or HNPCC, van Oostrom et al. (2007) explored significant predictors of hereditary cancer-related distress. During regression analysis the most significant predictor of distress was pre-test distress levels. Other predictors in the model were complicated grief or unresolved losses, number of first-degree relatives affected, more intense emotional representations and non-carrier status. The authors concluded that individuals who have clinical levels of distress at baseline seem to be more in need of psychological support in the short- and long-term.

Theoretical insights. One of the most significant gaps in the literature on the long-term impact of genetic testing is the absence of a well-developed conceptual/ theoretical base to guide research inquiries in this area (Biesecker & Erby, 2008; McAllister et al., 2008a; Rolland & Williams, 2005). Using a grounded theory design, McAllister et al. (2008a) proposed a framework for exploring patients continued need for genetic services after testing to maintain the benefits associated with going through the process. Empowerment was the overarching theme. Empowerment was defined as a belief system that allowed a person to take control of their lives and feel responsibility for

their decisions in the post-test phase. Individuals felt that genetic testing allowed them to make life decisions in an informed way and gave them sufficient information about the condition, including risks to the self and other family members. It helped them make effective use of the health care system, gave them the ability to look to the future and feel hope for a fulfilling life. This study identifies the importance of feeling in control of the disease, a desire for hope for the future, the need for accurate risk information and the role of the health care system.

A frequently identified problem is the conceptual ambiguity around the full meaning of adaptation for individuals with a confirmed HNPCC gene mutation, as well as their families. One relatively recent attempt to reduce this gap is the work by Biesecker and Erby (2008). The authors highlighted that an individual's adaptation to a genetic test result has typically been studied as a finite outcome. This approach is valid provided relevant observable indicators can be identified. More importantly, adaptation may be viewed as an evolving process such that at any one point in time an individual can be assessed as being more or less adjusted. This view highlights the reality of the ups and downs associated with a persistent personal and/or family cancer threat. In keeping with these two approaches, the authors suggest there is a clear need for a multidimensional outcome measure capable of assessing levels of adaptation to living with a genetic condition at a given time point. Such a measure should incorporate intrapersonal and interpersonal outcomes of the process and include cognitive and emotional responses to having HNPCC.

Another attempt to rectify this conceptual gap is the work by Rolland and Williams (2005). The authors propose a biopsychosocial model that highlights some of

the developmental challenges associated with having a genetic condition that has a high probability for cancer onset. This model provides a useful framework to guide inquiries into potential issues/challenges confronting individuals as they move from the pre-symptomatic phase through disease onset through treatment modalities and follow-up.

One study was identified that relied on the Rolland and William's (2005) developmental model to examine adaption over a four year period in a sample of individuals tested for hereditary breast and ovarian cancer. Hamilton, Williams, Skirton, and Bowers (2009) uncovered four concepts in the long-term adaptation phase of living with genetic knowledge over time. Participants acknowledged the strain imposed on family relationships after testing and what individual members did to try and counteract it. Some participants spoke about becoming empowered as a result of knowing their carrier status (e.g., increasing screening, seeking support and education, and considering or acting upon prophylactic measures to offset risk). Other participants became more uncertain and developed a sense of mistrust over their bodies. Participants also made conscious choices to adopt healthy lifestyle habits and gather further knowledge about the condition and related screening. Many felt a positive aura, a new lease on life and luckier than other family members who did not have this opportunity and had already succumbed to the disease. Finally, adjustment in the long-term also meant dealing with concerns for the next generation, as mothers described struggles with what to tell offspring and how and when to tell it. Importantly, adjustment was defined by personal and family impacts over time and was marked by the need for support and follow-up.

Behavioural Adjustment

Only a limited number of studies have identified behavioral adjustment in the post-genetic testing phase as an important area for research inquiry (Braithwaite et al., 2006; Bleiker et al., 2003; Heshka et al., 2008; Meiser, 2005). In addition, most of this research tends to be quantitative and more concerned about screening adherence rates than barriers to and/or facilitators of timely access to screening tests and follow-through from diagnostic testing to treatment and ongoing surveillance. There is a growing body of qualitative evidence which suggests that health care in itself can be a significant barrier to individual and family willingness to follow recommended protocols for HNPCC. Specific reference has been made to such things as ineffectual co-ordination, non-person centered care, limited provider knowledge and expertise, and inadequate provider/clinician communication skills, among others.

The few research studies that have focused on the behavioural aspects of adjustment to genetic testing provide insight into screening recommendations, adherence rates, and patient preferences for support in helping with disease management (Bleiker et al., 2003; Braithwaite et al., 2006; Etchegary, 2004; Heshka et al., 2008; Marteau & Weinman, 2006; Meiser, 2005; Vasen, 2007). Although most study findings suggest that carriers regularly engage in screening protocols to identify early HNPCC cancer onset, the evidence is less clear on the exact scope of these protocols and the frequency intervals between screening procedures (Heshka et al., 2008; Lindor et al., 2006; Lynch et al., 2008; Schmeler et al., 2006; Schroy, Glick, Robinson, & Heeren, 2007; Vasen, 2007). More importantly, there is limited insight into potential barriers to regular screening (e.g., personal, informational, logistical, and health care system-related barriers).

It is well-documented that regular colonoscopy surveillance leads to the detection of cancer in its early stages and results in an overall positive impact on survival for HNPCC carriers (Dove-Edwin, Sasieni, Adams, & Thomas, 2006; Green et al., 2002; Jarvinen et al., 2000; Pylvanainen, Kairaluoma & Mecklin, 2006; Stuckless et al., 2007). Despite these positive findings concerning the impact of regular screening on morbidity and mortality, there continues to be controversy over the age of initiation and time intervals between colonoscopy and the scope and frequency of extra colonic screening for effective HNPCC management (Lindor et al., 2006; Lynch et al., 2008; Schroy et al., 2007; Vasen, 2007).

Lindor et al.'s (2006) systematic review explored the recommendations regarding HNPCC cancer screening and prevention during the past decade. Current evidence fully supports colonoscopy for carriers every one to two years beginning at age 20-25 and annual endometrial sampling through trans-vaginal ultrasound of the uterus and ovaries starting at age 30-35. In addition, because of the excess of transitional cell carcinoma of the uro-epithelial tract, urinalysis and cytology must be initiated between 25-35 years of age. For those who develop CRC a subtotal colectomy is favoured.

There are also reports of the efficacy of prophylactic hysterectomy and oophorectomy for HNPCC carriers. Defining an optimal screening regime for HNPCC remains a challenge as the types, frequency and age of screening initiation vary according to family history, age of onset, number of family members affected and the mutation involved (Lindor et al., 2006; Lynch et al., 2008).

Research conducted on compliance and predictors of screening behaviour for CRC patients, highlights that physical discomfort may act as a deterrent to adhering to

necessary screening regimes. Several authors also suggest that emotional consequences, such as concerns about the effectiveness of screening protocols, and fear of negative findings, and the cumulative effect of having so many of these tests over time need to be considered as real barriers to maintaining screening regimes (Becker, Kraft, Southwell, & Jorgesen, 2000; Neilson & Whynes, 1995; Pylvanainen et al., 2006).

Study findings also indicate that individuals and families are in need of system and provider supports to facilitate adherence to screening protocols and disease management over time (Geary et al., 2007; Lindor et al., 2006; Lynch et al., 2008). HNPCC families require ongoing health care supports, not only to facilitate adherence to screening regimes, but to support the ongoing challenges posed by cancer onset, new information and ongoing testing of other family members (Griffin et al., 2007; McAllister et al., 2008b). In a recent qualitative study, McAllister et al. (2008b) identified five areas that patients and health care providers deem important for long-term clinical genetic services. Participants wanted local and accessible services, open access and follow-up, coordinated, tailored family care, a quality patient-clinician relationship, and time to talk. Effective support requires knowledgeable physicians and genetic counselors, educated patients, and readily available clinical cancer genetics services (Lindor et al., 2006; Lynch et al., 2008).

Oftentimes individuals at risk for CRC receive insufficient and inconsistent information on the timing and expectations of screening, yet there needs to be an established flow of up-to-date screening and treatment protocols for HNPCC (Hadley et al., 2003; Lynch et al., 2008). Study findings indicate that primary care physicians, specialists, genetics personnel and other health care providers have an important role to

play in improving and sustaining adherence to screening in those at risk for HNPCC (Lindor et al., 2006; Lynch et al., 2008; McAllister et al., 2008b; Stormer, Hodgson, & Kavalier, 2004). A multidisciplinary approach to HNPCC has been suggested (Geary et al., 2007).

The reality of maintaining comprehensive screening practices over time in accordance with updated guidelines may be more of a challenge than is known and needs further examination (Braithwaite et al., 2006; Collins, Meiser, Ukoumunne, Gaff, St. John, & Halliday, 2007; van Oostrom et al., 2006a). More specifically, the value and importance of follow-up of carriers and non-carriers during the adjustment phase by clinical genetics is apparent in the literature.

Summary

Overall, the empirical evidence from quantitative studies demonstrates that there are minimal psychosocial and behavioural effects from genetic testing in the short-term. The presence of a comparable database on the long-term psychosocial effects for both carriers and non-carriers of HNPCC is quite limited. Importantly, adjustment after testing has been viewed as an ongoing process occurring on personal and family levels. Consideration may need to be given to past coping styles and experiences with cancer illness and loss in the family, as the impact that these factors have on the acceptance of and adjustment to one's test results have yet to be fully realized.

Research findings also identify the impact testing has on the larger family system in some instances making relationships more cohesive and in others causing significant strain. New theoretical insights conjecture that adjustment should also be viewed as an

ongoing process that takes place over time in the face of the constant cancer threat. Models highlight the importance of developmental challenges and family system approaches to guide inquiries exploring adjustment over the long-term.

The need for ongoing support has been recognized to help those tested to adhere to extensive, ever-changing and lifelong screening regimes for effective disease management and to assist other family members to embrace and act on the new knowledge. Primary care physicians, specialists, genetics personnel and other health care providers have an important role to play in facilitating and helping sustain adherence to screening. HNPCC familial cancer registries and family information services are believed to be effective mechanisms for facilitating ongoing communication with individuals and families at risk for this syndrome.

CHAPTER 3

Methodology

The focus of this chapter is on describing the qualitative methodology used in the current study to explore the psychosocial processes emerging from exon 8 deletion family members' descriptions of how they were experiencing HNPCC in their families. The original study used grounded theory methodology to: (1) explore the meaning of predictive DNA testing for individuals in families at risk for developing colorectal cancer and related-cancers due to intron 5 splice site mutation on exon 5 or deletions on exon 8, and (2) develop a greater understanding of the psychosocial and behavioral impact of genetic testing on individuals who were confirmed carriers or non-carriers of HNPCC. The current study was an extension of the larger qualitative study and, thus, used a modified grounded theory methodology.

Research Design

The following section describes the methodology used to guide the inquiry into the problem under focus in the current study. It might be helpful for the reader if a brief description was provided of grounded theory versus modified grounded theory.

Grounded Theory as Method

Grounded theory methodology provides a highly systematic method of analyzing, interpreting, and categorizing qualitative interview data into substantive social theory about the dominant social processes of a given phenomenon (Streubert Speziale &

Carpenter, 2003). Glaser and Strauss (1967) are credited with the original development of grounded theory methodology. Based on the principles of symbolic interactionism, a grounded theory approach proposes that how individuals and families respond to an event is related to their existing meaning structures. Exploring how the event is processed on a cognitive, emotional, and behavioural level, within these existing meaning structures, helps reveal coping and adjustment strategies used over time (Chenitz & Swanson, 1986; Glaser & Strauss, 1967).

Grounded theory functions under the principles of induction, commonality, and conceptualization which are maintained by its key feature - the constant comparative method of analysis. This method requires a simultaneous data collection, coding, and analysis within and across interview data to reveal theoretical categories, properties and descriptors and the conceptualization of social theory. Substantive coding and memoing, which uses words of the interviewees themselves, further corroborates findings. Theoretical and purposive sampling facilitates the representativeness of the data and ensures that there is a relevant range of experience. According to Glaser and Strauss (1967), rigor is enhanced as the information pertinent to the emerging theory comes directly from the data. Therefore, the theory generated is grounded in the data.

Researchers increasingly employ the use of qualitative data to substantiate health experiences, as it is provides the richest evidence for planning health care (Gilgun, 1992; Morse, 1994). Many interested in understanding and explaining the experience of genetic testing for HNPCC have used qualitative research, with some using grounded theory as a means to build substantive theory directly from the experiences of family members who have undergone the process (McAllister, 2001). The main advantage of this method is

that the resulting theory and its various hypotheses can be empirically tested and used to aptly guide clinical practice in the area of cancer genetics.

Modified Grounded Theory

A modified grounded theory approach to data collection was chosen for stage 2 of the larger qualitative study. The decision to use a modified as opposed to a pure approach was dictated by the emergent questions that seemed to be unanswered by the original study. Thus, the focus of the current study was on expanding the theoretical and empirical base on how personal understandings of hereditary based cancer and situational and contextual factors influence an individual's decision-making. In the original qualitative study (stage 1), the primary focus of data collection was on the purposive selection of individuals from families with the intron 5 splice site mutation on exon 5, with a lesser emphasis on individuals in families with exon 8 deletion. The rationale for this was the presence of a larger pool of potential participants from families with the intron 5 splice site mutation on exon 5. As the original study drew to a close, the research team questioned the importance of time since the discovery of the family-based gene mutation and the family context, especially relations and supportive structures.

For the current study, there was a deliberate selection of individuals from families with the exon 8 deletion. As well, the theoretical sampling logic used in the final stages of the original qualitative study meant that greater attention needed to be placed on family clusters of carriers and-non-carriers of HNPCC, and carriers with and without cancer. The specifics of the participant recruitment are detailed in a subsequent section.

Predictive Genetic Testing

Predictive DNA testing is offered to individuals with a family history of CRC who are referred to the cancer genetics service by family physicians or specialists (gastroenterologist, surgeon or oncologist). All exon 8 deletion participants were first assessed by a geneticist or genetic counselor to be at high risk for HNPCC based on the Amsterdam I and II and/or Bethesda criteria (Merg, Lynch, Lynch, & Howe, 2005). That is, participants who were deemed to be 50% risk for inheriting the MSH2 mutation were entered into a counseling program to prepare them for predictive DNA testing.

Once participants were informed of their risk individually or during family sessions, a follow-up counseling session was held with them to determine their interest in undergoing genetic testing for HNPCC. In addition to being counseled on the benefits and risks associated with genetic testing for HNPCC, participants are reminded of the known implications of carrier status, such as more frequent and extensive screening for the self, increased risk for offspring as well as insurance and psychosocial effects. As all study participants opted for testing, blood samples were collected and forwarded to a clinical molecular genetics lab for analysis.

Following genetic testing, carrier or non-carrier results were reported in face-to-face individual/family counseling sessions. In most cases, a supportive person was present. A follow-up letter summarizing the results of the counseling session was sent to the participants and their physicians. Clinical screening programs were adjusted according to the results. Genetic testing was also offered to the probands children and siblings who had reached the age of maturity (i.e., 18 years of age).

Population and Participant Recruitment

The target population for the initial quantitative survey was restricted to individuals from high risk families registered in the Medical Genetics Program of Newfoundland, who had DNA testing for HNPCC and had received or were waiting for test results. The eligible population consisted of carriers and non-carriers from families with a confirmed MSH2 mutation on intron 5 (12 families) and exon 8 (5 families) (Stuckless et al., 2007). With the exon 8 mutation identified more recently (early 2000's) than the intron 5 mutation (early 1990's), there was a larger cohort available from the latter group for research purposes when data collection commenced in 2004.

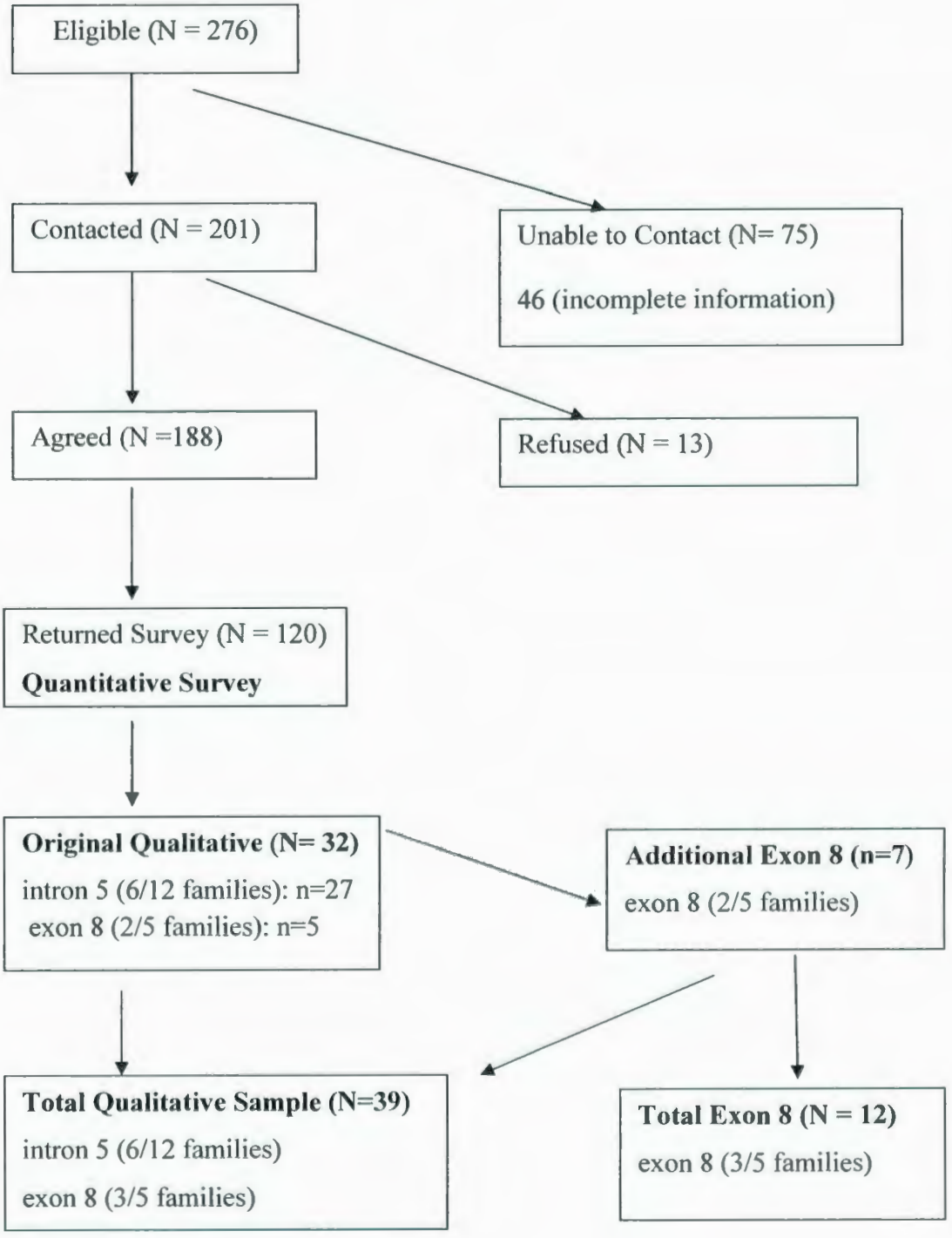
A total of 276 individuals were identified for possible contact (i.e., exclusion of presumed positives, obligate carriers and unknowns). From this group, 75 individuals could not be contacted (i.e., 46 due to incomplete information and 29 unable to reach after multiple attempts). Contact was subsequently made with 201 individuals; 188 of whom agreed to receive study materials. Of the original consenting group, 120 returned completed questionnaires and signed consent forms (see Figure 1).

Data collection for the original qualitative study occurred from late 2004 to the early 2007. For this study, a purposive sample was derived from the 120 respondents to the quantitative survey who indicated an interest in further research. In this case, purposive sampling refers to the selection of individuals known to this researcher from the earlier quantitative study and considered to be good informants. Theoretical sampling indicated that common themes were emerging after completion of 18 interviews and first-level coding (i.e., substantive codes). Interviewing was temporarily stopped and the

constant-comparative method of analysis applied to the data sets. A family meaning context (i.e., shared/different experiences and/or reactions and similar/variant timelines) emerged during the in-depth analysis and coding of the first 18 transcripts. In addition, meaningful differences were emerging between carriers and non-carriers of HNPCC (i.e., perception of screening protocols and time to cancer diagnosis, variant coping mechanisms, implications for children) and those affected and unaffected with cancer (i.e., intensity of reactions, burdensome versus sense of resilience). As a result of these insights, the foci shifted to purposive selection of an additional 14 HNPCC carriers from family pedigrees with and without a cancer diagnosis (see Figure 1).

In the original qualitative study, five of the thirty-two participants had been tested for the exon 8 deletion mutation. Importantly, late in the qualitative analysis, length of time since the discovery of the family-based gene mutation for HNPCC and the availability of and actual involvement in genetic testing appeared to have significant impacts on individual and family perceptions of the experience. The importance of family context and meaningful differences between carriers and non-carriers and carriers affected and unaffected by cancer had emerged in the original study. Thus, purposive sampling was used to ensure equal representation of individuals from these groups. From early to late 2007, an additional seven individuals were recruited from the exon 8 deletion families.

Figure 1. Flow Chart of Sampling Plan



The final sample consisted of three family groupings of four individuals – six carriers, six non-carriers; four affected and eight unaffected. The large volume of narrative data generated by the 12 exon 8 deletion family participants was sufficient to represent the experiences of those more recently tested for HNPCC and did not alter existing categories (Sandelowski, 1995). Thus, a final sample of 12 participants from families with the exon 8 deletion mutation was used to augment and confirm the proposed model.

Procedure

Potential participants from exon 8 deletion families were identified by the research team from the same population eligible for the original study. Due to the psychosocial nature of the research and related risks, those with a known previous diagnosis of anxiety, depression, mental illness or substance abuse were excluded. Those who had previously been involved in quantitative research in this area and had indicated a willingness to be involved in further research were first contacted by phone to ascertain whether or not they were willing to receive a package of information on the study. Information packages included a cover letter and a brief summary of the study (see Appendix A), and two copies of the consent form (see Appendix B). Individuals who required further information on the study were encouraged to contact the researcher either through local or toll free numbers. Subsequent contact was made within two weeks of the mail out to ascertain patients' willingness to be interviewed. Interviews were scheduled at a mutually agreed upon time.

Interview Schedule

Informed, written consent was obtained prior to the first interview and participants were asked for their permission to be audio-taped. In-depth, semi-structured interviews were conducted using the interview schedule designed for the qualitative study (see Appendix C). Although the schedule items were used to guide the interview process, additional questions generated by the ongoing data analysis were also integrated into subsequent interviews. After analysis of the first two interviews, major content areas were identified to further guide the interview process. For example, participants highlighted the struggle to deal with losses, the prolonged impact it had on them and close family members, and their search for greater meaning, understanding, and certainty. The rich descriptions of experiences that led them to the possibility of a cancer genetic link were subsequently used as probes for interviewing additional participants.

The initial interviews also provided detailed descriptions about the impact of the genetic testing experience and adjustment challenges for both carriers and non-carriers. For example, some of the non-carriers portrayed the genetic testing experience as a non-event and described a healthy adjustment to learning their HNPCC risk status, while some carriers felt shock and disbelief. These variations in descriptions that occurred according to carrier status were noted and teased out during subsequent interviews. The second interview took place approximately six months after the first to provide participants with a summary of their interview and to obtain feedback on its interpretation.

Ethical Considerations

Approval to conduct the proposed research study was granted from the Human Investigation Committee (HIC), Memorial University of Newfoundland (see Appendix D). Ethical considerations for participants and the data generated were clearly identified and discussed during the consent procedure.

Participants were interviewed in the place most convenient for them and their privacy was ensured. During the first interview, participants were made aware of the potential risks and benefits of participating in the study. They were also given the choice of terminating the interview. However, this option was not utilized by any of the participants. Given the personal and sensitive nature of cancer and genetic information, there was an additional consideration for the protection of privacy and confidentiality of specific genetic test results and cancer episodes among family members during the interview process.

Participants were informed that all information collected would be described in a manner that would prevent identification of the source. Also, no direct benefits were anticipated and they were free to withdraw from the study at any time without having to give a reason, nor would their participation affect any future aspect of care.

Appropriate measures were taken to ensure that the confidentiality of all data was maintained. All tapes and transcriptions were coded and kept in a locked location. A database of names and matching codes was also stored under password protection accessible only to this researcher. The tapes and transcriptions will be maintained until the final publication phase of this study and subsequently destroyed five years following this phase.

Data Analysis

Data analysis proceeded in several phases with the constant-comparative method of analysis being integrated in the process. Taped interviews were transcribed verbatim, checked for accuracy and then perused independently by the two member research team. The focus was on interpreting the meaning of words and sentences through reading and rereading of each transcript. Beginning after the first interview, the researcher and thesis supervisor independently coded the lines of the transcripts as appropriate, according to the substantive coding and themes established by the original conceptualization. This served two purposes. First, it allowed the researchers to become immersed in each narrative and to construct interpretive summaries. Second, it helped to identify further probes and questions. Regular debriefing sessions were held to compare independent transcript coding and achieve consensus on the identity of the constructs and properties.

Additionally, each transcript was perused for major thematic content related to the major constructs already developed in the original model. Challenges posed for individuals and their families at different time periods (i.e., pre, during and post-genetic testing) were also identified. This information was also used to construct interpretive summaries. Validity was assured by having two researchers construct independent interpretive summaries of each transcript and achieve consensus on the final versions. Participants were given an opportunity to read, or receive a verbal presentation on their interpretive summaries. All participants confirmed their interpretive summaries, adding a further element of credibility to the findings.

All lines of each participant transcript were then reinterpreted and built as in the original study in the form of a family narrative, which facilitated further comparisons

between the original family groupings and new ones. Differences were confirmed between carriers and non-carriers as well as those affected and unaffected with cancer in accordance with intensity of reactions, length of exposure and burden versus resilience. The importance of time since testing to the length of the awareness period and its significant impact on the process was established by exon 8 deletion participants. Views on screening protocols, timelines to diagnosis, short- and long-term coping mechanisms and implications for children were also confirmed by this new data.

In addition to the validity and reliability features of this work, other qualitative principles were maintained. They were credibility, dependability, confirmability, and transferability.

Trustworthiness of the Study

Credibility

Credibility measures how vivid and faithful the description of the phenomena is and provides the standard for judging their truth value (Streubert Speziale & Carpenter, 2003). Family members at high risk for HNPCC and who participated in genetic testing are considered to be the experts and therefore are the most credible sources of information. A qualitative study is considered credible when the participants recognize the descriptions and interpretations of the experience as their own (Sandelowski, 1986, 1995). The credibility of the study's findings was enhanced by having two researchers independently prepare an interpretive summary of each participant's interview and then

reaching consensus on the content. At the final step interpretive summaries were reviewed with participants to seek additional clarification and confirmation.

Dependability

Dependability measures how stable the data are over time or across situational contexts (Streubert Speziale & Carpenter, 2003). Dependability of the findings was established by validating model constructs and properties with additional members from the exon 8 families accessed in the original qualitative study, as well as recruiting individuals from new families with the exon 8 deletion. Another way in which dependability was enhanced was selecting family members from variant age groups, primary cancer sites, and lengths of time since genetic testing.

Confirmability

Confirmability refers to the ability of an independent researcher to follow the decision trail as conveyed by the study findings (Streubert Speziale & Carpenter, 2003). That is, the method and findings must provide an audit trail for other researchers to follow in an understandable and predictable manner. This was accomplished in two ways: (1) the ease experienced by this researcher in using the coding and analysis process outlined in the first study to confirm model constructs and properties with the data received from other members of families with the exon 8 deletion mutation, and (2) the ability of other researchers reading the study results to follow the logic of the interpretations and conclusions.

Transferability

Transferability refers to the applicability of the results to other related groups (Streubert Speziale & Carpenter, 2003). This study set out to augment and confirm the experiences of those family members who were tested for the intron 5 splice site MSH2 mutation on exon 5 eight to ten years ago. The results of the exon 8 deletion family members, who were tested more recently, are therefore applicable to those tested previously. As well, this model is being tested for transferability in those who have been tested for another genetic condition, including arrhythmogenic right ventricular cardiomyopathy (ARVC), increasing the transferability of this study's findings. Current study findings will now be presented in the following chapter.

CHAPTER 4

Results

The findings are presented in four sections. The first section presents a summary of participant characteristics. The second section presents an overview of the conceptual model, *Confronting and Accepting the Challenges of Living in Families with Genetic Linked Diseases*, derived from the original grounded theory study. The third section summaries the findings on each major construct of the model from individuals in families with the exon 8 deletion mutation. The final section presents a brief discussion on how the study findings confirm the major tenets of the original conceptual model and augment its properties and descriptors.

Descriptive Profile

Most of the 12 study participants were female (75%) and had at least one child (91.67%). All had a partner and were part of three distinct family units. The average age of participants at the time of the study was 50.17 years (SD = 7.81; range 42 to 66). All of the participants lived in families with a strong history of colorectal and extracolonic cancers and had experienced cancer onset in a parent. This event occurred for most of them (58.3%) in childhood (< 13 years) or adolescence (13 to 20 years).

Study participants took part in genetic counseling and received their test results between 2002 and 2004. The sample was equally divided between HNPCC carriers and non-carriers. The mean time from receipt of test results to the initial qualitative interview was 2.26 years (SD = 1.27), with a range between .08 and 3.75 years. Most of the carriers

had reached the affected stage at least once (66.67%) at the time of the study. The cancer type varied with three carriers experiencing one primary site (CRC, endometrial or skin) and one carrier with two primary sites (endometrial and kidney).

Conceptual Model

The conceptual model proposes a broad theoretical representation of the psychosocial and behavioural impacts of genetic testing for HNPCC from the lead-in through genetic testing to the post-test periods. This theoretical representation illuminates significant influences beyond genetic testing by casting light on factors which have been given only cursory attention in the literature.

The first construct, *living in families with a strong history of hereditary cancer,* describes the phase prior to genetic testing for HNPCC. It depicts what it is like to live within a family with an ominous cancer presence and to eventually awaken to the idea that these cancers could be hereditary. The second construct, *becoming aware of genetic testing and living the process*, outlines how family members decide to become involved in genetic testing, react to being informed about their carrier status, perceive the supportiveness of genetics personnel, understand their risk, and are willing to communicate genetic testing findings within and outside the family network.

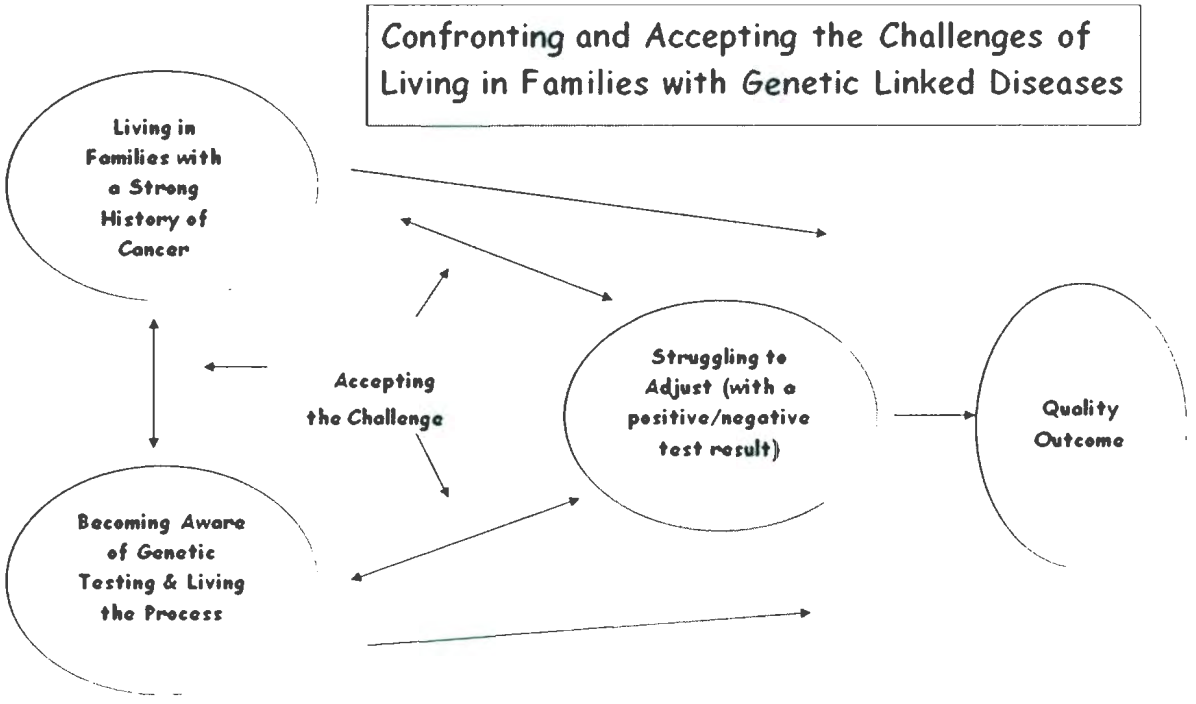
The third construct, *struggling to adjust*, describes the personal and family challenges following genetic testing for HNPCC. Consideration is also given to significant personal and family factors that may facilitate or impede overall adjustment in the short- and long-term. Most important among these are the extensiveness of screening protocols, cancer occurrences/recurrences in the self and others, the effectiveness of

screening and treatment modalities, and the receptivity of children to becoming involved in genetic testing and, ultimately, screening.

The first two constructs, living in families with a strong history of hereditary cancer and becoming aware of genetic testing and living the process, are conjectured to exert a direct impact on each other and a direct and indirect impact on struggling to adjust (see Figure 2). It is also proposed that accepting the challenge is the unifying thread that links the constructs, signifying that a change in one area has repercussions for other areas. For example, as children awaken to the idea of a cancer genetic link in the family, more family members reach the affected stage, or family relations become more disrupted with loss, individuals may or may not accept the challenge to seek answers about their own HNPCC risk and, even if they do so, may not cope well with either their carrier status or disease management.

Finally, all three constructs are believed to exert a direct impact on quality outcome, which is seen as an evolving state. The third construct, struggling to adjust, is also conjectured to mediate the effects of living in a family with a strong history of cancer and becoming aware of genetic testing and living the process on quality outcome.

Figure 2. Confronting and Accepting the Challenges of Living in Families with Genetic Linked Diseases



HNPCC Families with Exon 8 Deletion Mutation – Model Findings

The discussion of findings is organized according to each major construct of the model. The content of each construct is, in turn, divided in terms of its defining properties.

Living in Families with a Strong History of Cancer

Data from the interview transcripts of exon 8 deletion participants confirmed the first construct of the model. The first construct refers to the lead-in period of the genetic testing process and consists of two properties: (1) struggling with multiple losses – conflicting emotions, and (2) searching for meaning/understanding/certainty.

Struggling with multiple losses – conflicting emotions. This property captures how family members deal with increased cancer incidence and prevalence as well as early losses of close relatives from the disease. Most participants were familiar with the strong presence of cancer in the family. For some, the awareness of a likely hereditary component to colorectal cancer had been passed down from previous generations: "She [mother] would say, 'Live as long as you could just like you are and you'll get a longer time out of it because it [colon cancer] is in our family'."

The stories relayed by several participants highlight what life is like when one is forced to endure the prolonged suffering of a close family member who never seems to escape the disease. The continuous onslaught of cancers creates a cumulative effect and compounds the level of uncertainty. One participant's recounting of her mother's cancer recurrences over a 30 year period captures the sentiments of others: "It [cancer] has

almost had ten year increments really when you think about it. Every ten years she [mother] has been faced with a cancer diagnosis."

The high cancer presence in the family and early losses from cancer had significant emotional effects on participants. For many of them, events with the greatest impact were recalled most vividly, recanted in detail and sometimes evoked strong emotional reactions. One participant, who was a health care provider, spoke about how difficult it was caring for her mother: "I can remember rubbing her back and feeling everywhere and thinking how many times have I done this to someone else and it was [very difficult]." Another participant, who was very close to her brother, described how difficult it was being vigilant and supportive while he endured so much pain and suffering before dying at 38 years of age: "[Six years] he [brother] went through hell. That's all I can call it."

As participants encountered more and more cancer in the family, the disease increasingly took on a fatalistic meaning. There was a dawning of sorts that this disease, although not yet discussed in terms of genetics, was something passed down from one generation to another. The following quotes illustrate this:

> And we watched our grandparents or great grandparents go down in the ground. That was it because of cancer this deadly, this monster. There is no controlling this monster. That's it.

> Once you had this colon cancer thing or whatever it was … if you were in the family and you were the one that had [cancer], we didn't call it a gene or anything, you didn't stand a chance anyways. This is the way we felt.

Against this fatalistic background many participants believed that it was just a matter of time before cancer would surface. Two siblings tried to prepare themselves and significant others for this eventuality:

> It's like whenever something would happen in our family … with my sisters and my mother and father, my cousins or whatever, we would talk on the phone, and we would say I guess we're next. You know you're just like little ducks, and you're the next one; ticked off type thing.

> I've always felt personally that if I got out of this world not having cancer I was a very lucky person. So deep down … since I've been twenty-ish, I've always thought well somewhere, some day, some how they're going to say, me.

When cancer surfaced on a personal level, the disease assumed new meaning for the self and one's offspring. Younger participants seemed to struggle more with the psychological and physical sequelae of managing the disease. One female spoke about the emotional difficulties that she experienced when diagnosed with endometrial cancer at 40 years of age.

> She [gynecologist] did my hysteroscopy and five days later I get a call. I had clear cell carcinoma which is very aggressive and it was in one of the polyps that the ultrasound was showing as a small fibroid. ...So anyway that was it. It was a real roller coaster after that.

For individuals, with non-HNPCC cancers on the unaffected side of the family, the potential for interactive effects played havoc with their ability to grasp their perceived personal risk. One participant commented on how her son believed that he could be at increased risk for both HNPCC cancers and prostate cancer: "My son at age 40, bless his heart, he feels like he got a double whammy now where his father just had prostate cancer at 65."

The extended period of cancer occurrences and losses within families also had the potential to disrupt family relations and decrease the number of members available for support. Although most families remain unchanged, some relations are weakened while others are strengthened. It seems that younger family members may have to make greater adjustments. Participants from two separate families were in their early to late teens when first exposed to cancer in a parent: "I think our life just kind of revolved around Mom was sick and we had to kind of do things, certain things she couldn't, and you know I think it just became a way of life"; "She [sister] wasn't in school [when mother diagnosed]. We all had to take our turn automatically you know cleaning the house, doing the dishes and chores. We all had to pick up our slack and help out."

Searching for meaning/understanding/certainty. The awakening period prior to confirmation of a genetic link was shaped by the level of awareness of cancer in the family. Although most participants had been exposed to a relative with cancer during pre-adolescence, it was not until their 20s and 30s when cancer recurred in a parent or surfaced in other family members that they developed a greater appreciation for its hereditary nature. In many cases, family physicians and specialists alerted members to the need to be vigilant about the disease:

> All this cancer and I mean I am impressionable at 20 [years of age]. The doctors were saying, "I think people should be watched here". This is just not our family doctors. I guess they [specialists] knew so many of the family. … You know my cousins, my uncles, my aunts. So they could see what was really going on here.

Due to previous cancer events in close relatives (mother, father, brother or sister), screening was sometimes initiated before formal awareness of a genetic link. One male participant initiated screening upon learning about his potential high risk for cancer: "Up until the time that I found out that I wasn't the gene carrier, I mean I had the colonoscopies done every two years."

Conversely, participants who were not exposed to cancer illness in a parent or close family relative until mid-life were not aware of the full extent of its presence. This meant a shorter awareness period going into genetic testing. One female participant noted that it was only when her mother was diagnosed with cancer at 67 years of age that she started looking for answers: "It must be then with Mom [cancer] that we actually made

the connection to think okay there's something wrong here."; "We started looking for information for a family tree. We knew that there were still lots of cancer there but actually how much [we didn't know]."

For participants who suspected a hereditary basis for the familial cancer, the availability of genetic testing for HNPCC was a welcome relief for their growing concern. One female participant captured the generally high level of acceptance and readiness of most family members to become involved in genetic testing:

> Our reaction to that [availability of genetic testing for HNPCC] was again there would be no big surprise because of living in my family with cancer for a long time. … There was no discussion, like, maybe we should, maybe we shouldn't. That didn't enter into the picture. Yes we will do this.

Summary. It was apparent from participants' stories that living in a family with a strong history of cancer shaped personal beliefs, vulnerabilities and rudimentary hereditary understandings. The impact of familial cancer experiences on personal risk perceptions seemed to be even more dramatic for those exposed at younger ages. For the most part, these individuals were more accepting of a genetic link and the necessity for regular screening prior to genetic testing. Certainly acceptance of one's high-risk status was a significant motivator behind an individual's decision to test.

Becoming Aware of Genetic Testing and Living the Process

The data from exon 8 deletion participants also supported the second construct of the model. The second construct focuses on the actual genetic testing period and is defined by three properties: (1) moving closer to puzzle completion, (2) the meaning of genetic testing, and (3) communicating with others.

Moving closer to puzzle completion. The lead-in period is a key component of genetic testing. Participants' willingness to become involved in the process was heavily influenced by motivational and risk perception factors, family members' acceptance, and the perceived availability of formal and informal supports.

Genetic testing provided participants with an opportunity to bring greater certainty to personal risk status and, ultimately, to future generations. For many of them, it was now possible to find answers to why so many family members were suffering and dying from cancer: "To say that we will find out what's going to happen [concerning cancer risk], knowing made a big difference. Just the anticipation of knowing, well we are finally going to know." For others, genetic testing came as a surprise. Despite only becoming aware of the possible hereditary link as relatives reached the affected stage, these participants were also able to appreciate the benefits of genetic testing. One man described the benefits as such: "I came with the frame of mind that it [genetic testing] might not do me any good. But then again I'm still only a young man, 46 years old. It may do me good."

A significant motivational force was the desire to protect children and grandchildren from the disease. One woman's comments captured the sentiments of

many others: "My thing was that I have seven children and God knows how many grandchildren I'm going to have so this might help my family." Because of the obvious implications for future generations, it was difficult for study participants to understand why some family members chose not to become involved in genetic testing. Several participants were of the opinion that those refusing were not making wise choices. One female non-carrier expressed concern that their children could be at risk: "Well I don't think [Uncle 1's daughter's son] did because he got cancer, he just assumes he got the gene anyway."

Time frames between the offering of genetic testing, blood submission and the availability of results varied across families. Some members are informed of the possibility of genetic testing early in the identification process, submit blood for testing, and then wait for a prolonged period before the family's HNPCC mutation is uncovered and individual results become available. Other members are informed of genetic testing closer to gene mutation identification and thus receive their results in a more expedient fashion. Most participants described the wait-time as an unwanted distraction: "From the time that the blood was drawn until I actually got the result, I shouldn't say [it] didn't make a difference to me whether it was negative or positive, because it certainly does. But the waiting was worse."

The meaning of genetic testing. This property captures participants' reactions to test results, perceptions of support from genetic personnel, understandings of the implications of their HNPCC status, and perceptions of the benefits and liabilities of genetic testing. Processing of information received about one's carrier status occurs on

both cognitive and emotional levels. What surfaced as significant for acceptance of one's HNPCC status was existing beliefs about inheritance patterns within families.

Some participants relied on beliefs about inheritance to speculate about who would most likely inherit the gene mutation. Gender, physical characteristics, and mannerisms surfaced as important factors. One participant believed the family's cancer was much more prevalent among females: "That's the way it presented in my mother's family, every single girl had cancer, not one of the boys. Now since then, one [male] has but he is in his 70's. You know you do not count that." Another participant believed that physical likeness to the affected parent was relevant. "Even before I knew my results, you base things on well my sister is more like my father than I am. I am more like mom. So my sister is more likely to have this gene and not me."

Although lay beliefs about cancer inheritance have very little scientific relevance, coincidental mannerisms helped some participants speculate about more susceptible family members. One woman commented on what she observed or what was reported to her about family members who had colon cancer.

> My mother had to have well water. My brother had to have well water. This is the connection to colon cancer. Like they just knew it and they all died in July, every one of them. … That's not medical related, but that's how my family has dealt with it.

Despite feeling well prepared to receive genetic testing results, some carriers, and to a lesser extent non-carriers, experienced unexpected emotional reactions. A disconnect

seemed to exist between understanding what their HNPCC results meant on a cognitive level and accepting them on an emotional level. The emotional fallout is most likely due to the lengthy period of being exposed to cancer in the family prior to genetic testing.

One carrier commented that genetic testing had somehow given her an additional burden because of so much uncertainty about the future: "It [HNPCC carrier] left me with this really eerie sense that there is always something just over that little left shoulder of yours. It is just that one little thing that you had to carry around somewhere." Another female carrier commented on the anger she experienced and how surprised she was to be having such a negative reaction:

> I went in there totally prepared for a positive result. I knew what was in front of me. I knew what it meant. I never second guessed myself once. ... I was adamant I wanted to know but the instant that I knew I wished I didn't. ... I remember driving out from [main city] like totally angry thinking oh for the love of God is there a real need for this. I was really surprised at myself for having that reaction.

This same person continued to have periods of doubt concerning the utility of genetic testing and oscillating feeling states for a protracted period of time post-testing: "I would say, 'what did I get this [genetic testing] done for.' I wish I never knew I really did. There are still times that I feel that way ... I guess I'll be going through cycles."

For the most part, non-carriers of HNPCC experienced a sense of closure to the life-long uncertainty of developing cancer. As well, they benefitted from not having to endure frequent colonoscopies and other recommended screening protocols. Their

comments conveyed an uplifting experience – a sense of relief, lifting of a burden, and to a degree a new lease on life. One non-carrier commented: "It made me feel better too, right …when I found out I didn't have it because it was going to make them [my children] feel better."

There was also a downside to being a non-carrier in a family with a high incidence of cancer and losses from this disease. As certain participants noted, although they were spared having to contend with the disease personally and/or passing it on to their offspring, they still carried the emotional burden of knowing about other close members' status and: "You're negative but then you feel bad for the rest of the family. …I have to be honest I cried for [Brother 1]."; "I worry a lot about my sisters. … And every time she [younger sister] gets something wrong, I'm wondering, you know."

Most participants were generally satisfied with the support received from genetic counselors immediately following receipt of test results. One participant commented: "They [genetics personnel] were excellent, I must say. It was really good, really understandable." With privacy issues an important consideration for some, a couple of participants noted that the genetic counselor was able to be supportive while maintaining confidentiality concerning the status of other family members.

> She [genetic counselor] wouldn't disclose anything about my sister and I can understand that. She is such a sweet lady you know – very mild and leads up to the situation. I mean there is nothing that she springs on you.

> I sat there and she [genetic counselor] come out and sat down and started explaining everything to me. [I thought], "I guess there's something here somewhere in a minute she'll tell me [my result]." That's all; I didn't get upset or anything. She said, "[Name] your test is good, right." I said, "That's great." She gave me a hug.

In order to facilitate greater understanding and acceptance of the information conveyed during receipt of results, genetic counselors asked participants to bring support persons with them. Nevertheless, two sisters had to convince the counselor of the merits of receiving their results at the same time.

> She [the genetic counselor] was really kind of saying to me, "Well may be it shouldn't be your sister. … [I said], "Well if she doesn't come with me, I am not going. [Ha, Ha]…my sisters were the only ones that I really felt confident enough that no matter what it [result] was, well we were going to have to deal with it for the years to come too.

On another level this participant understood the ramifications of being in a situation where one was positive and the other negative. She commented thus: "I think it would have been guilt at that point [if one were positive and the other negative]. I am happy for me but I am sad for you, so what do I do?"

An important outcome of the genetic testing process is the decision-making that occurs subsequent to the receipt of results. Arguably individuals who test positive are

under considerable strain at this point, especially in the absence of personal signs and symptoms of cancer. Nevertheless, optimal well-being in the short- and long-term is contingent upon balancing the plusses and minuses of preventive actions to delay cancer onset and progression.

Adequate understanding of one's risk for developing colorectal and other cancers following genetic testing is important for both carriers and non-carriers of the HNPCC gene mutation. For the most part, non-carriers understood that their cancer risk was the same as the general population. Nevertheless, some of them continued to feel vulnerable, which seemed to be a function of general cancer worry: "We still got the chance of the general population. With genetic testing well, it will just tell you if your odds are any higher to get this certain type. But to me I'm in a risk [category] anyway." Another part of non-carriers continued vulnerability stemmed from worry over children. One non-carrier indicated that it was still a good idea to have the children tested or at least screened on a regular basis: "I have my children who are not positive getting tested [screened]. They don't care."

All of the carriers generally had a very good understanding of their increased risk for colorectal and related cancers, as well as the importance of following recommended screening. A couple of siblings admitted that they could not remember all of the specifics relayed to them by the geneticist/genetic counselor, but did note that the written documentation received helped clarify things: "She [geneticist] did go over that [risk percentage for different HNPCC cancers]."; "I don't think we actually retained a lot of it. ...We have letters with that." In order to promote better understanding of her HNPCC risk, one participant sourced a website for further information: "I remember the first time

when I looked at the website and saw the stats. You have an 80% chance – geeze that's not real good odds."

Due to the variable expressivity of the disease across families, some participants had a more comprehensive understanding of their cancer risk than others. In families where colorectal cancer dominated, some female carriers underestimated their risk for other cancers. One participant discounted the merit of annual endometrial screening.

> They had given me a list of screening. I have been doing it. Of course not as they would say. … This transvaginal ultrasound, I never had that done. Who does go off and get that done every once a year or so? And this CA125, well who goes and gets that done? The colonoscopy, yes, because I don't forget. From the time I was born we talked about [it], we had colon cancer. … It wasn't the ovarian, it wasn't the skin; it was colon cancer.

Finally, there is a well defined cognitive and emotional processing that occurs among family members that helps them sort out the positive and negative aspects of receiving genetic testing results for HNPCC. Knowing that you are an HNPCC carrier provides a reality check for all carriers with some becoming more motivated to adopt healthy lifestyle habits than others. One person had this to say: "The writing is on the wall, you wake up, and you say to yourself don't be drinking too much. …start living a healthy life." Another carrier who was motivated to screen regularly benefited from the early detection of cancer: "I'm glad it is being done. … I would not be here if it wasn't for the screening process."

One of main plusses of knowing one's HNPCC risk status is forewarning. Carriers are alerted to the importance of maintaining screening to promote early detection of the disease. One carrier saw the benefit of seeking medical attention for early warning signs that may have been ignored in the past:

> I think that once you know that you have the gene, it will affect you to the point that if you get an ache or pain that is probably the first thing that is going to come to your mind which will probably send you to a doctor quicker than if you were not.

Other carriers recognized that knowledge of their risk status would benefit current and future generations and they hoped their involvement in predictive testing would one day lead to the HNPCC gene mutation being repaired.

> It would be wonderful to know that somewhere down the road, that little drop of blood that we gave played a key role in figuring out what in the name of God went terribly wrong. If we can get that mutation fixed, vaccine, anything, I'm all for that.

A downside to being aware of one's carrier status is not knowing when cancer will occur, what organ it will attack, how severe it will be, or how responsive it will be to treatment. One female carrier had this to say:

> It [confirmed carrier for HNPCC] doesn't necessarily mean that I'm going to pop off anytime soon but chances are I don't think I'll live a real long life, I don't. I guess that's why it's so important to me not to be spending my time running around the health care [system] and that now.

Another carrier questioned the true benefits of genetic testing for HNPCC and regular screening when both fail to alter the outcome.

> My cousin that passed away... her son …knew of every test that was available that she should have done. She started with ovarian and then it was all through her body. But she lived several years and it still ended up to be the same thing – died from colon cancer. So you really wonder if the results [death] are the same what's the good of genetic testing.

Non-carriers also had a mixture of positive and negative feelings about knowing their HNPCC status. One female participant summed up her feelings:

> I thought it was great first. Trying to keep that oral fleet down was terrible. I was thinking, "Wow I don't have to do that now for another few years and I'm really feeling good." Then I got home and I thought about it … "Is this a good thing or is it not a good thing?" Before I was getting it [colonoscopy] every year …. Now I'm thinking, "Hum, it's like it was a crutch, and now that crutch is gone." So I just watch myself a little bit more carefully.

Communicating with others. Family dynamics play a very important role in deciding who becomes privy to information about HNPCC risk and genetic testing. Within exon 8 deletion mutation families, differences exist in how willing individuals are to be open about their HNPCC status to close and distant family members. The level of disclosure to the children was often guarded, with participants remaining highly sensitive to the potential for negative reactions.

Obvious differences existed in how carriers and non-carriers communicated with their children and other members of their social networks. For non-carriers, the results were favourable and the news about their status was communicated in a swift and uplifting fashion. One female participant felt a great sense of relief and excitement and openly shared the good news with others: "Our daughter came home that afternoon because she had been at university [and I told her I was negative]. My best friend, I called her because she was waiting as well. We were all really happy about it."

For carriers, there was a general tendency to engage in greater deliberation and discussion about when and how to inform their children. Many of them struggled with how much information to convey to their children and at what age. One carrier felt that her children were too young to be told and chose a more reactive approach to gauge their level of readiness. She believed that their exposure to cancer illness in family members would naturally stimulate inquiries about HNPCC and genetic testing.

> Well it was a year or so after I knew my results that it came up in conversation with mom where my children [were present] about having this genetic testing

> done. When I went home my daughter asked me, "Did you have that done?" I felt she was 11 or 12 years old and my son is three years older and they were both sitting there and I didn't feel the need to lie and I said, "Yes I did." So it was just kind of quiet and I said, "I did have it done and mom is positive."

An important emotional barrier was perceived reactions of the children to knowledge of their parent's carrier status. One female participant used an individualized approach to communicate with her two children. The child who was receptive was informed of her carrier status right away: "I gave it [information sheet from genetic counselor] to my son. He called her [genetic counselor] and of course hence he went out and had his testing done." Knowing that the other child would be less receptive, she chose a more guarded approach. As expected, the daughter was opposed to genetic testing and decided not to share this information with her two adult children: "But with my daughter I couldn't give it [information sheet] to her because she wanted no part of it [genetic testing]."

The responsibility of communicating to children may create additional psychological burdens for carriers. Many carriers are unsure of any formal mechanisms available to help them with this task. One male participant expressed concern over his inability to convince his children about the seriousness of the HNPCC risk.

> My 22 year old daughter [is able to see the benefits]. My son is not [going for genetic testing]. … Because he's not going to be able to do this, do that. I keep telling him no, that's not true. He's 21…. How do I educate them [children]? I can

> only talk to them, I mean I can't force or drag them in here.

Another female carrier expressed a need for assistance in order to effectively communicate information about the HNPCC risk in the family to her children.

> They [daughter and son-in-law] had a lot of questions for me that I couldn't answer. I need someone now to tell me the answers to the questions so that I can tell them. ...It is a big problem for me.

Close family ties and open communication patterns helped facilitate disclosure about the HNPCC risk in the family. Overall, it appeared that information sharing about HNPCC was greater among immediate than extended family members. One participant who had an affected sister was aware of her battles with cancer, but less certain about the details of his uncle's family: "I don't know if my [paternal] Uncle 3 had cancer when he died I can't remember what he had. Some of his children died with cancer [first cousins on paternal side]." A non-carrier from a close-knit family noted that physical distance did not hamper their discussions.

> I have cousins who are still being tested because there were so many of us .... Even though they are on the mainland, we still see each other. ...we still have contact through their parents. ...We still know what's going on in their lives.

What is troubling here is that the policy of reliance on family members to communicate

with one another about the risk of HNPCC and the importance of genetic testing may not be prudent if they are not provided with access to formal psychological supports: "We do talk about it [HNPCC testing] but it's hard for us to sit around and talk about it because my brother just lost his daughter 17 years old. So it's hard to even bring up that topic now."

Even in the presence of strong family supports, carriers and non-carriers sometimes concealed information about genetic testing from others. All of the siblings in one family tried to protect their mother from additional burden: "At that point mom knew that I tested positive but I had not had the conversation with her. Had she asked me I would not have lied. I just felt that she had tackled enough in her lifetime."

Summary. Exon 8 deletion participants viewed genetic testing as an opportunity to bring greater certainty into their lives. Importantly, the amount, intensity and level of awareness about familial cancer influenced how individuals made decisions around genetic testing. Support from geneticists and genetic counselors prior to and during the process were deemed valuable. Nevertheless, the real work of emotionally adjusting to one's results occurs at the individual and family levels. Amidst the positive and negative aspects of knowing one's personal risk status is communicating this information to other family members. It is through such communications that a full understanding of the causal factors for the cancer and what can be done to modify one's risk becomes known.

Struggling to Adjust

The third construct, struggling to adjust, focuses on the period after genetic

testing. It is defined by two major properties: (1) coping with HNPCC risk – personal and family challenges, and (2) identifying and addressing barriers to successful coping – engaging in recommended screening protocols, dealing with cancer onset, and accessing cancer care in a timely fashion.

Coping with HNPCC risk. This property captures two key aspects of coping – personal acceptance and family burden. The presence of the HNPCC gene mutation in families has significant implications for, not only confirmed carriers, but also non-carriers. Overwhelming demands on individual family members can threaten the entire system's ability to cope and adapt in an effective manner. The family's ability to adjust is influenced by the cohesiveness of its structure and communication patterns within and between units. Carriers' acceptance of their status, willingness to be proactive in disease management, and receptivity to the giving and receiving of support are also important to successful adjustment in the short- and long-term.

All of the study participants reiterated the importance of maintaining a positive attitude toward one's carrier status, cancer onset and the usefulness of treatment. For the carriers, the emotional toll of waiting for the disease to recur or manifest itself for the first time ebbed and flowed in response to one's inner strength and the perceived supportiveness of family and friends. A couple of individuals, who had not reached the affected stage, spoke about how difficult it was to remain positive with so much cancer all around them:

> Yes many are touched by it [cancer]. And some are way younger than her [mother] and some are like a shock – 'Wow, how could this person be so healthy and how did this happen?' I think that has to play on your mind.
>
> They [children] just lost their cousin, 17 years old. How do they deal with that? We're finding it difficult to deal with and not only that we watched her die. She just didn't die we watched her melt away.

The carriers who had reached the affected stage articulated how they attempted to stay positive and rise above the conflicting emotions posed by the illness. One carrier commented on how a second bout of cancer weakened her outlook and caused her to reflect on the uncertainty of her future.

> I don't sit and dwell. Yes we all do; especially last year when I got sort of down and I got cancer again. …What else is going to happen to me now? Oh God, when is it going to break out next."

Nevertheless, she was cognizant of the importance of staying positive and relied on self talk to build up her inner strength: "I have to survive. I have to carry on and you can't dwell. I kind of have to give myself a little smack now and then and say smarten up, you know get on with it, it's life."

Another affected female carrier spoke about how she struggled to remain positive when cancer was literally all around her at home and at work.

> I think because of my diagnosis and because of mom's situation [terminal cancer], and probably because I'm in a health care setting, it seems like not a day goes by that I'm not dealing with cancer and counseling people and arranging tests. I think sometimes you run out of steam because you are always keeping up the positive attitude.

This person stressed the importance of being mindful of one's high-risk status, but not allowing it to control you: "I try my best to live by it [positive attitude]. Cancer has such a weight associated with it. We all need to dwell at a certain point, and it's important to do that but we can't facilitate it."

Still another affected carrier coped most effectively by avoiding any thoughts of cancer for most of the year. Her comments suggest that because she was having great difficulty adjusting, she preferred to only acknowledge things during annual screening: "I need to compartmentalize it. ...Like I said about the one stop shopping, once a year I'll admit it, kind of thing. The rest of the year denial is a lovely thing, I can just forget about it."

Although non-carriers experienced tremendous personal relief from not being at-risk, they still retain the burden of having to interact with and, in some instances, provide care to carriers. Their level of burden is a function of the strength of established relationships and being willing to sustain close ties with carriers. One non-carrier provided insight into why she continued to struggle to maintain a positive attitude as

other family members received confirmation of their carrier status and/or reached the affected stage:

> Since I've had this wonderful news that I don't have the mutation, two of my younger cousins are now having problems. One had his colon removed not for cancer but because he had so many polyps .... His sister a few months later has bilateral lung cancer – she's 36 years old .... So like you go along in this family and you're thinking .... It's not just off there in the distance; it's right up there in your face all the time.

The impact of testing positive for the HNPCC gene mutation is not restricted to the individual receiving the news, but also influences spouses, children and other family members. In some families, the presence of a cohesive structure enabled members to rally around the latest person to become a confirmed carrier or to develop cancer. When a person is the first one in his/her generation to be diagnosed with cancer, it is sometimes difficult to share the news with other members so as not to negatively impact them. This seems to be especially difficult when the contributing parent is still alive and the affected person has young children who could be also at risk.

> When I think of all the people I had to tell [about my cancer]. No offence to my mom, you know my son was the hardest. That was the toughest for me. But the second person, even more than my husband, was my mom only because I knew

> what she was going to feel like. I knew what that experience was going to be for her. But I handled it well I think.

This participant also discussed how, over the years, family members became more familiar with individual strengths and weaknesses and who could or could not be called upon in different situations: "We all have different roles that we do very well. We've kind of learned through the years where we excel. We are all not good at everything."

All of the carriers spoke about the comfort of knowing that there is at least one person in their social or family network available to them to discuss their fears and concerns. Two female carriers highlighted the importance of having someone there as needed.

> She [female cousin] has been a great source of strength for all of our family – for myself and my sister because we're you know close to [Cousin 1]. She called me this morning to see how I am .... See she's really supportive.

> The one cousin who I know has also tested positive, he's gone through a lot ... had his colon removed. We were never very close but like now we call each other. I guess it's kind of that ... even though I haven't gone through what he's gone through we've become closer.

In contrast, other families were more conscious of an individual's need for privacy and time to assimilate the information about his/her carrier status or recent health

threat. Participants from these families tried to maintain a healthy distance while leaving the door open to provide support.

> We do talk about it but it's hard for us to sit around and talk about it. Because okay let's give you an example, my brother just lost his daughter 17 years old. So it's hard to even bring up that topic now. If we can get a year or so off without tragedy, we probably will sit down.

Although some non-carriers felt that it was a challenging experience dealing with hereditary cancer in the family, they did acknowledge that it helped forge closer relationships in some instances. The following quote illustrates this: "I think actually it has made our family a lot closer. Well, we are very close with my mother's siblings, and I think it is because everyday well it could be anybody. And you just need to be there for them."

A final aspect of coping focuses on having to confront new issues for the self and for one's offspring. A great source of worry and concern for carriers was the possibility of or actually having passed on the HNPCC gene mutation onto their children. One affected carrier with several children prayed that none of them would carry the gene mutation. "I was praying that they all would be negative. …But I said, what are the chances of that? …Usually its split down the middle, isn't it?" Carriers also worry about their children's ability to accept their potential risk and, if necessary, adjust to screening requirements. One carrier commented thus: "I can say this, that when my children are tested and one of them is positive, I think that it will affect me way more than my being a

carrier."

The guilt of knowing that one may have passed the germ-line mutation for HNPCC onto one's children and grandchildren is a source of constant worry and concern. One affected carrier, who endured a lifetime of watching close relatives suffering from cancer and eventually succumbing to the illness, struggled to overcome the sense of responsibility toward her children, grandchildren and nieces/nephews.

> Now I look at my grandchildren. It never leaves me, yeah it never leaves me. The guilt never leaves me.

> And the guilt stays each time I see my niece, each time I see her little girl. … Each time I see my sister-in-law, you know I mean I'm not a morbid person. … It hits and I think of it and then it's gone again. We do have our good times, I don't mean I'm going around crying all the time, I'm not.

Identifying and addressing barriers to successful coping. A major part of adjusting to life as an HNPCC carrier is following recommended screening protocols. While many family members adapt well to the negative aspects of the preparations and procedures, others encounter difficulties that threaten continued participation. This property focuses on the barriers and facilitators to actively engaging in recommended screening protocols and accessing supportive health care providers and services.

Many of the carriers had endured a long period of screening prior to identification of the gene mutation in their families. For some, it was more of the same, but for others it

became more of a challenge. While discussing the pros and cons of screening, some of the carriers highlighted the physical and emotional challenges of disease management. One woman spoke about the emotional trepidation experienced during the lead-in time to a colonoscopy: "I cry. It's just as well to tell the truth, I cry. I'm weeks before thinking about it and I'm dreading it. I'm dreading the day that the test [will come]." A second carrier discussed some of the physical barriers to adherence:

> I had had a horrendous experience with my last colonoscopy which was the first one done by a new person to me. [Specialist 1] had always done it before and I hadn't had a problem. This other one was absolutely horrendous. I would never, ever go through that again.

The increased scope of required procedures following confirmation of one's HNPCC status was also viewed as a major deterrent to full screening. One carrier described in detail how her life was significantly altered by the acceptance of the true requirements of HNPCC screening:

> I was thinking what has changed, because I was getting screened before. Then I thought well I was kind of getting half screened before. I was doing the scope thing. I was having my transvaginal ultrasounds done, and since that I've had a total abdominal hysterectomy so all that's gone. ...The things that I had decided not to do before because I considered they would be really uncomfortable and not

> high enough on the priority list, I have now had those done as well. So I have changed.

This participant expressed a strong desire for a more normal life: "So a part of me is thinking, okay I know why it's being done, the other part is thinking, I don't want to be at this. I just want to be a normal person."

As more cancers surface in HNPCC families which are conjectured to be associated with the syndrome, there is heightened concern over the extensiveness of monitoring. Participants were asked to think about possible ways to help make screening practices more user-friendly and potentially increase screening. One carrier highlighted the importance of knowing that someone is close-by to help buffer some of the logistic barriers to screening: "We're lucky that I do have my sister and my brother and [female cousin] .... So if I have major test or something I would probably go to [her house] and stay the night." Another carrier noted the importance of having a personal system in place to keep track of appointments and scheduling needs:

> I know that if I don't keep track [screening appointments may be missed]. ...I got my sheet at home and its all different colours. Because every year I have it [colonoscopy] done, I check it all off. The next year, I use a different colour.

One carrier recognized the element of self-responsibility in all this, even in the presence of formal supports.

> Well it's called survival too, you know because if you don't look after your health, no one else will. No matter how many friends or family or doctors you have in your life, they are so busy doing all their aspects of their lives that if you don't look after [it], and wait for them to call you, forget it.

Besides needing a personal system of reminders, there is an even greater need to have access to health care providers to help facilitate understanding of the various screening procedures and test results. One female participant commented: "I don't know this terminology. I say to [younger sister], "What's this that I had done with [urologist]?" I know what I need done but I [need to understand the results]."

Carriers stressed the importance of having access to formal supports to facilitate understanding of what is needed to manage their condition, greater continuity among all health care providers, and timely access to care. One key aspect of this was interacting with supportive caregivers, most especially knowledgeable physicians with good interpersonal skills. What carriers desired more than anything else was receiving consistent, accurate and up-to-date information about screening protocols for colorectal and associated cancers. One carrier commented thus: "You want to be informed [about the implications of new information] because you want to protect yourself and you want to protect your family." Many carriers and their families express a lack of familiarity with the health care supports that they should seek for help as they continue to manage the disease.

Some participants encountered family physicians unfamiliar with the specifics of HNPCC. This can be quite unsettling for individuals who rely on physicians to help them

with disease management: "The other guy [family physician] she [mother] asked him if it [kidney and lung cancer] could be related [to HNPCC] and he didn't even know anything about it." In contrast, encounters with specialists were generally positive because they seemed to be more informed about HNPCC. One carrier recalled that her urologist made a tentative plan to add more screening pending confirmation of her carrier status:

> Where I've been having those problems the past couple of years with my bladder, [urologist] said, 'Now if you turn out to be positive, with what you have done [genetic testing for HNPCC] let me know because there is another test I need to do for you.' So he was interested. I guess its life, you know, some people [physicians] know a little more.

Gaps were also identified in continuity of health care and informational inconsistencies across specialty areas. One carrier noted that when colonoscopies fail to detect signs of cancer future testing may be extended beyond one year. The variable screening protocols recommended by physicians may potentiate or lessen the challenges confronted by carriers and thus facilitate or impede adjustment.

> Not only the surgeon that's doing the screening, but I'm seeing this a little more often from a clinical standpoint, I'm getting one doctor, even if the scope is negative saying okay we will do her in a year. And the next one done by another guy will come and say even though she's positive, they are clear and we'll do them in two to three years.

In collaboration with specialists, a few participants found ways to streamline the screening process and decrease the number of appointment days. One participant commented on how working with providers to coordinate scheduling and receipt of results ensures greater continuity of care, while decreasing the number of visits with different providers: "Actually it [breast screening] had been done with another physician. So I figured leave it with her [Specialist 2] as opposed to going back to my family physician. I'm no worse off; I'm still making another trip."

Study participants also made suggestions about system changes that could help them better manage HNPCC in the family. Particular emphasis was placed on the importance of resolving identified gaps with genetic testing services and what health care services are necessary to support the management of this condition. Many have successfully forged their own linkages in the health care system and commented upon ways to improve the efficiency of individual and family HNPCC management.

> There should be like a little package. This is what I can give to my family doctor so that he is aware and here is a list of doctors that we have and once you picked these [specialists] notify [genetics] and we can refer the rest of your family there.

> I would like to have one stop shopping, [Ha, ha, ha] I would. Because it seems like I'm running around doing this all, and I don't want this, I don't need this. I know why it's necessary to a point. ...If I could just once a year grease and oil get everything done now. Go away, I'll let you know when I have a problem or I'll come back in a year.

Summary. Personal and family challenges in the short- and long-term period following genetic testing interfered with the coping abilities of both carriers and non-carriers. The ability to maintain inner strength and a positive mindset against the cancer threat of HNPCC became an important coping strategy for carriers. Effective coping was measured in terms of one's acceptance of HNPCC status and willingness to adjust screening regimes according to cancer risk. Besides the self, carriers experienced ongoing guilt, worry and concern associated with potentially/actually passing on the gene mutation to children and grandchildren.

For non-carriers, the burden of care assumed for family members ,who had the gene mutation and had or not reached the affected stage, was contingent upon the cohesiveness of the family unit, the openness of communication patterns and the individual's willingness "to be there" as needed. Finally, most carriers felt that meaningful contact with formal supports was needed to help coordinate, create consistency and facilitate timely access to health system services. Carriers also valued up-to-date and consistent information from all health care providers.

Discussion

The conceptual model, *Confronting and Accepting the Challenges of Living in Families with Genetic Linked Diseases*, presents a broad framework for the genetic testing experience and elucidates the importance and complexity of the lead-in period, while revealing the importance of the presence of comprehensive supports during the short- and long-term adjustment period following testing. Data from the interview transcripts of the exon 8 deletion participants confirmed many aspects of the original

conceptual model and, in addition, helped clarify and reduce overlap among certain key properties defining the major constructs.

The first construct, living in families with a strong history of hereditary cancer, was confirmed by the exon 8 deletion mutation participants. Despite the commonalities observed in the stories of participants from HNPCC families, not everyone was equally aware of or influenced to the same degree by cancer in the immediate family. For those most aware, there was a strong sense of fatalism toward the disease, limited surprise by the suggestion of a hereditary basis, and greater willingness to become involved in screening prior to genetic testing.

The second construct, becoming aware of genetic testing and living the process, was also confirmed by participants in the current study. This construct is comprised of three defining properties – moving closer to puzzle completion, meaning of genetic testing, and communicating with others. Accepting the need for genetic testing for HNPCC was heavily influenced by prior lived experiences and perceived high risk for the self and one's offspring. Participants' descriptions conveyed variable levels of awareness about the extensiveness of familial cancer and personal experiences with a close family member who developed cancer and survived it or succumbed to it.

The meaning of genetic testing seemed to be a function of the adequacy of cognitive and emotional processing of information conveyed about one's test results. The degree of concurrence between existing beliefs about inheritance patterns and genetic testing results emerged as a significant factor in promoting acceptance and understanding of one's risk, and greater willingness to adjust one's health behaviors accordingly. Prior to the current study, existing beliefs about inheritance and developing greater awareness

of genetic linkages to disease was categorized as a separate property. However, based on the findings from exon 8 deletion participants, it was possible to develop a greater appreciation of how lay beliefs about inheritance were integral in shaping the meaning of genetic testing results.

The third property of the second construct, communicating with others, captures the level of difficulty in disclosing personal risk status to other family members. Disclosure seemed to vary depending upon closeness of family relatives, prior levels of awareness about the potential genetic link and normal styles of communication in the family. This property was also reaffirmed by the exon 8 deletion participants.

The third and final construct of the model, struggling to adjust, captures the oscillating feeling states of carriers and non-carriers in response to what was happening around them, as well as the barriers/facilitators of successful coping with HNPCC. Each time participants achieved a sense of stability something seemed to surface to potentially undermine their well-being and threaten their ability to cope. A second property of this construct is the importance that individuals attach to recognizing the barriers and facilitators of adequate disease management. An important barrier/facilitator is the perceived responsiveness of the health care system to families with a confirmed HNPCC presence. A key player in this system is family physicians. Physicians must have up-to-date information on this condition as well as preventive and treatment modalities in order to provide effective and timely care. This construct was further confirmed by the exon 8 deletion participants.

CHAPTER 5

Discussion

This chapter discusses the experiences of participants from exon 8 deletion mutation families according to the three constructs from the model – *Confronting and Accepting the Challenges of Living in Families with Genetic Linked Diseases*. As noted in the previous chapter, study findings confirm and augment the model, its constructs and properties. The current study's findings also contribute to existing research and clinical findings presented in the literature. A summary will be presented at the end highlighting the separate and interactive effects of the model constructs on quality outcomes.

Living in Families with a Strong History of Cancer

The first construct captures the *experiential context of cancer* for individuals who belong to HNPCC families. Within this context, risk perceptions for the self and others are formed and rudimentary ideas about a possible hereditary cancer link take shape and develop. At some point in time, steps are taken by immediate or extended family members, the self or a family physician/specialist to initiate contact with genetics personnel to explore the idea that the cancer patterns observed within and across generations is being passed down. Subsequently, contact is made with someone in the family by a geneticist/genetic counselor to initiate the process of profiling the family cancers. Based on these initial findings, individuals who have or have had cancer are notified and requested to become involved in genetic testing for HNPCC.

Individuals who are exposed to cancer in a parent or close relative at a young age often struggle with ideas of becoming affected with cancer themselves. The fatalistic meaning of cancer for the self is contingent upon how much suffering the affected person endured or whether or not s (he) succumbed to the illness. Many stories were told about how unsettling these experiences were for children, siblings and other family members. Comparable findings about the relevancy of the family context for shaping personal risk perceptions about cancer and its potential genetic transmission have been reported in the literature (d'Agincourt-Canning, 2005; Kenen et al., 2003; McAllister, 2001, 2002; Shiloh, 2006).

What is somewhat unique about the current study's findings is the importance of the quality of family relations in helping shape personal risk perceptions. Although McAllister (2002, 2003) highlights the importance of open family communications about cancer in influencing a person's degree of engagement with HNPCC risk, there is no specific reference to how the pervasive incidence of cancer and subsequent losses may strengthen or weaken family relations. In instances where family relations were strengthened (being there and providing support where possible), there seemed to be a greater awareness of the need to be more attentive to what was happening to the self and, eventually, greater acceptance of one's personal risk. Conversely, when family relations were weakened (continuous avalanche of cancer onset and death diminished the capacity of the family support network), there was more of a fatalistic risk perception that took shape (i.e., powerless to change or alter what is in store for the self health wise).

Individuals moved to a higher level of awareness concerning their personal risk for cancer when informed by a family member and/or family physician or were contacted

by a geneticist/genetic counselor. At this time, they were alerted to the potential hereditary nature of the disease and the implications of this on a personal level. Participants reacted differently to being informed about their potential risk with some experiencing surprise and others receiving confirmation of their worst fears. Several researchers have found evidence to support the cognitive and emotional movements that occur at the individual and family levels when there is a formal acknowledgement of the fact that the cancer in the family could be due to hereditary factors (Kenen et al., 2003; McAllister, 2002, 2003; Reeve et al., 2000; Targum, 2000).

The decision to become involved in genetic testing for HNPCC is different for everyone as it is heavily influenced by the familial context and individual risk perceptions. Personal willingness to accept the possibility of being at high risk for cancer is exemplified by actions taken to learn more about the hereditary nature of the disease and to engage in preventative screening. Another important influencing factor surrounding an individual's willingness to engage in preventative screening and the genetic testing process is the openness of communication within the family and the general acceptance of the importance of knowing one's actual risk for the disease.

The findings from relevant research studies concur that many families at risk for HNPCC tend to use rudimentary inheritance patterns to seek answers to and to cope with their own potential risk status (Kenen et al., 2003; McAllister, 2002, 2003; Targum, 2000). In many instances, individuals tend to overestimate their risk, which may in part be attributed to the closeness and severity of cancer episodes experienced in the family. In contrast, individuals tend to underestimate risk if they perceive the family cancer as not severe or they are unaware of its presence.

The literature suggests that cancer risk perception takes on new meaning when an individual is first introduced to the idea of a family genetic link. The family experiential knowledge base is an important factor influencing the emotional readiness of individuals presenting for genetic testing for HNPCC. Carlsson and Nilbert (2007) noted that individuals who had cared for close family members reported experiencing emotional difficulties when first presented with the option of genetic testing for HNPCC. Similarly, McAllister (2002) noted that individuals who struggle with painful memories of having cared for and lost close family members may resist becoming engaged with their HNPCC risk. Past cancer experiences seem to be inextricably linked to coping strategies in complex ways.

Becoming Aware of Genetic Testing and Living the Process

The second construct of the model captures participants' experiences with genetic testing for HNPCC (i.e., prior counseling for, actual involvement in, and immediate and short-term reactions to receipt of results). Although genetic counseling sessions served to enhance individuals' understandings of what might or might not be in store for them post-testing, many of the participants in the current study were not prepared emotionally for their test results. The apparent disconnect between understanding on a cognitive level and emotional acceptance was partially due to the extensive familial cancer presence, personal and family beliefs about inheritance that impeded healthy processing of information conveyed from the Mendelian perspective, personal coping abilities, and openness of communication among members about cancer in the family.

Support for the greater impact of subjective feeling states and lay beliefs about inheritance patterns on family members' motivation to become involved in genetic testing and initial reactions to, as well as adequate understanding of, test results is referenced in the research literature on genetic-based diseases (Bleiker et al., 2003; Etchegary, 2004; McAllister, 2002; Meiser, 2005). These findings seem to be more developed in qualitative studies and the theoretical literature than in the quantitative study findings. Significantly, certain authors suggest that genetic counseling may not alter risk perceptions due to the prolonged exposure to familial cancer conditions, ingrained beliefs about inheritance, psychological states, and coping abilities (Brain et al., 2005; McAllister, 2002, 2003). What the findings from the current study and the literature imply is that genetic counselors should pay as much attention to subjective feeling states as to how well the individual is processing the information being conveyed about genetic testing for a HNPCC gene mutation. Important to consider are the intensity and extensiveness of prior experiences with cancer in the family and/or on a personal level, as well as an individual's overall emotional well-being and coping abilities.

The interview transcripts of study participants served as constant reminders of the narrowness of the genetic testing event in comparison to the larger context of their lives prior to and following genetic testing. Nevertheless, the literature continues to attach great importance to the factors influencing the uptake of, as well as immediate reactions to, the genetic testing event (Aktan-Collan et al., 2001; Bleiker et al., 2003; Meiser, 2005). Despite being sufficiently motivated to become involved in genetic testing for personal clarity of risk and to know the potential risk for the next generation, there was a general sense of ambivalence concerning the merits of their actions.

As the current study's findings suggest there are wide discrepancies in both carriers and non-carriers reactions to their test results. Some participants described the additional burden that knowing entailed (i.e., not knowing when cancer will occur, what organ it will attack, how severe it will be, or how responsive it will be to treatment). With most of the evidence quantitative in nature, study findings suggest that there is minimal psychological and emotional harm from knowing one's HNPCC risk (Bleiker et al., 2003; Braithwaite et al., 2006; Claes et al., 2005; Heshka et al., 2008; Meiser, 2005). Nevertheless, the current study's findings suggest that the psycho-emotional impact of knowing can become a major impediment to successful coping in the short- and long-term.

One of the ways in which understanding and acceptance is conveyed in the immediate post-testing period is in terms of how willing individuals are to engage in thinking about reasonable strategies/actions to help offset their risk. The current study's findings suggest that the information provided by genetic counselors was used to empower some participants to action. In contrast, other participants used this information to reinforce their need to be more selective in choosing screening programs that were more reasonable and manageable. In some instances this was due to how the individual perceived/actual dominance of one type of cancer over another (colon versus endometrial) and emotional or cognitive barriers to accepting the potential for variable expressivity across family clusters and/or multiple primaries in one person. Although not directly addressed in this manner, the theoretical insights gleaned from the relevancy of social cognition theory for research inquires into genetic-based diseases, especially the

interactive effects among multiple factors (e.g.,knowledge, belief, attitude, and behavior) reinforce study findings (Etchegary, 2004; Marteau & Weinman, 2006; Shiloh, 2006).

The current study's findings also indicate that many of the participants felt inept about conveying the news of the HNPCC gene mutation within the family to others, especially children. The barriers/facilitators to sharing news about the HNPCC risk in the family highlighted by study participants included the openness of communication in the family as well as the perceived supportiveness of immediate and extended family members. Comparable study findings have been reported in the literature on both the difficulties experienced in disclosing information about HNPCC and genetic testing (Carlsson & Nilbert, 2007; Esplen et al., 2007; Gaff et al., 2005; Hamilton et al., 2009; Koehly et al., 2003; Mesters et al., 2005; Riper, 2005) as well as barriers to open communication and ways to overcome them (Beeker et al., 2000; Neilson & Whynes, 1995; Peterson et al., 2003; Pylvanainen et al., 2006).

Struggling to Adjust

The third construct focuses on the long-term adjustment of individuals and families following confirmation of the presence of the HNPCC gene mutation. Adjustment post-genetic testing is best described as an evolving state that ebbs and flows in response to critical events that are person or other-centered. In the current study, participant's ability to maintain a positive attitude was heavily influenced by the challenges posed by extensive screening protocols, new onset of cancer in the self or other close family members, the perceived/actual burden of belonging to these families, the perceived/actual barriers to accessing care in a timely fashion, and the perceived

supportiveness of health care providers and the health care system in facilitating ready access to care. Biesecker and Erby (2008) highlight the importance of viewing adjustment as a multidimensional construct, with many potential interacting factors altering its presentation at any point in time.

In the current study, both carriers and non-carriers oscillated between positive and negative feeling states. Many of them spoke about their search for stability, ongoing struggles to create a meaningful context for the self and other family members, and attempts to build inner strength. Past coping strategies were taxed, not only by personal issues, but also by the demands of thinking about and providing care to other family members affected by the disease. Superimposed on this was mounting worry and concern for younger family members who could be potentially at-risk for HNPCC. Although existing literature provides limited insight into the depth and scope of the long-term struggles of individuals living within HNPCC families, several authors acknowledge that their complexity is shaped by the interaction of experiential cancer-based knowledge from the past and present as well as individual coping styles (Bleiker et al., 2003; d'Agincourt-Canning, 2005; Kenen et al., 2003; McAllister, 2001, 2002).

Several authors note that there is limited empirical evidence to make any definite conclusions about long-term psychosocial effects (Bleiker, 2003; Braithwaite et al., 2006; d' Agincourt-Canning, 2005; Heshka et al., 2008; Kenen et al., 2003; Meiser, 2005). The familial experiential context , such as having a parent affected by cancer at a young age or being exposed to a greater number of first-degree relatives affected by cancer, appeared to be associated with higher levels of distress following genetic testing (Erblich, et al., 2000; van Oostrom et al., 2003, 2007). As well, many researchers concur that

experiential knowledge and development of risk perceptions related to living with hereditary cancer and individual coping strategies are all important factors post-genetic testing (d' Agincourt-Canning, 2005; Kenen et al., 2003; McAllister, 2001, 2002). Nevertheless, few findings exist on the extensive personal processing that occurs in both carriers and non-carriers in the months and years following testing. The existing research base also provides limited insight into how both HNPCC carriers and non-carriers struggle to create a meaning context, attempt to maintain a steady state in the face of personal issues, and cope with the demands of providing support to others in the family network.

A significant finding from the current study was the relative importance attached to the presence of supportive others within the family – someone to share the burden of concern and care with – as well as the openness of carriers, affected and unaffected, to receive support from others. The value of the strength and stability of family support systems for facilitating positive coping and adjustment at the individual and family level is receiving increased attention in the research literature on genetic-based diseases (Hamilton et al., 2009; Rolland & Williams, 2005; van Oostrom et al., 2003; van Oostrom et al., 2007).

Although carriers were involved in screening prior to genetic testing, many of them highlighted additional challenges post-testing. The most important of these related to inconsistencies among providers concerning the extensiveness and frequency of required screening procedures for cancers, growing concerns about the intrusiveness of lifelong screening, increasing problems accessing formal supports (e.g., healthcare

providers with adequate knowledge) and lessening certainty about the presence of a supportive health care system to help facilitate effective HNPCC management.

Several authors confirm the continued controversy over the suitable time intervals for colonoscopy and the appropriate scope and frequency of screening for related cancers in the management of HNPCC (Lindor et al., 2006; Lynch et al., 2008, Schroy et al., 2007; Vasen, 2007). Similarly, the research evidence supports the potential negative impact of the procedures themselves and growing concerns/fears about procedure findings on long-term adherence to recommended protocols (Beeker et al., 2000; Madlensky , Esplen, & Goel, 2004; Pylvanainen et al., 2006; Wagner et al., 2005). The growing importance of timely access to physicians/specialists with the requisite knowledge and skill base as well as a supportive health care system with ready access to diagnostic procedures has been identified by other researchers (Braithwaite et al., 2006; Collins et al., 2007; Geary et al., 2007; Griffin et al., 2007; Hadley et al., 2003; Lindor et al., 2006; Lynch et al., 2008; McAllister et al., 2008b; van Oostrom et al., 2006a).

Interactive Effects

The conceptual model, Confronting and Accepting the Challenges of Living in Families with Genetic Linked Diseases, presents a broad framework for the pre, during and post-genetic testing period. Its three constructs (i.e., living in families with a strong history of cancer, becoming aware of genetic testing and living the process, and struggling to adjust to a positive/negative test result) are conjectured to exert a separate and interactive effect on each other in response to evolving challenges in one or more of them. The major unifying thread connecting the constructs is defined as accepting the

challenge (e.g., testing and willingness to know personal status, living in families with cancer with a personal carrier or non-carrier status, enduring or finding strength from engaging in screening protocols, etc.). A couple of examples are needed to illustrate how this manifests itself within individuals and families.

Individuals are present in all HNPCC families who need support services whether living alone or do not have strong family support structures. Other individuals who have a strong history of cancer in their families are struggling to cope with the implications of all of this for the self and others. Regardless of their personal affected status, they are dealing with a wide range of emotional and psychological issues that require therapeutic intervention if they are to develop a strong sense of resilience and maintain an optimal quality of life.

The other significant finding is the negative impact that genetic testing for cancer-related diseases is having on available health care resources. As long as HNPCC carriers are healthy, there is no problem with accessibility. In contrast, when these individuals move to the affected stage, the time between one screening and the next is very important to them physically and emotionally. When accessibility and timeliness pose problems, this has important implications for an individual's ability to adjust psychologically and emotionally.

Equally important, is the fact that physicians need to be more informed, not only about the presence of the HNPCC gene mutation in families, but also the multiple vulnerable sites for cancer and variant penetrance rates in families. What this means for families is importance of encouraging individuals to keep up-to-date on new developments in this area and reinforce with other members the importance of

maintaining recommended screening schedules, especially when confronted with conflicting information about appropriate times and screening sites amongst physicians.

One relevant model has surfaced since the original conceptualization of accepting the challenges. Importantly, Rolland and Williams (2005) have explicated the importance of the psychosocial impacts of developing a genetic disease based on the likelihood of developing the condition. These authors suggest that when a gene mutation is highly penetrant, the patient and family must absorb the certainty that the disease will occur. They have categorized HNPCC as a "variable likelihood" disease and therefore it carries that variable penetrance and, hence, variable likelihood of psychosocial consequences. The concept of time phases provides a way for clinicians and families to think longitudinally about the course of an illness as an ongoing process with normative landmark transitions and changing demands.

CHAPTER 6

Limitations and Implications

Limitations

The purpose of this research study was to augment and confirm the conceptual model proposed in the original qualitative study and as a result the model constructs and properties served as a guide for the data analysis process. Using the model in this fashion was the main limitation in this study as there was an anticipation to reveal findings that were consistent with the model's conceptualization, increasing the risk of researcher bias. Nevertheless, the researcher was aware of this study limitation and remained cognizant of the potential for bias, while reading and coding the transcripts and analyzing them for content. The findings from the exon 8 deletion participants did confirm the model. However, participants did highlight new information that served to augment model properties reducing overlap and enhancing areas of significance, which minimized the bias potential.

A second limitation of this study was the use of newly obtained data in combination with data obtained from exon 8 deletion participants from the original study. This meant five of the 12 interviews had been independently reviewed, coded and rated as part of the original study analysis and therefore received additional attention and scrutiny increasing the risk of bias. Nevertheless, all 12 interviews were analyzed under the context of the exon 8 deletion participant grouping using the same data analysis process and each transcript was reviewed for major themes by two independent

researchers to enhance rigor. Participant confirmation of interpretive summaries also added further credibility to the findings.

Finally, a common limitation for many studies on the genetic testing experience is the purposeful selection of participants from individuals who have been through the genetic testing process. These are the individuals that provide the richest and most relevant data, yet they have also received the benefits of genetic counseling and likely have had and will report healthy experiences with testing. Nevertheless, study findings may be considered more trustworthy as participants in this study felt comfortable and provided genuine detailed information on their actual experiences prior to, during and following genetic testing. Also sampling was guided by the emerging content and the model constructs and properties and a range of experiences was revealed offsetting the risk of bias associated with purposeful selection.

Clinical Implications

With the increased availability of genetic testing for hereditary cancer conditions, health care professionals must have the appropriate knowledge to assist individuals and families with disease management. Findings from this study have clinical implications that serve to enhance the provision of genetic counseling, genetic testing and overall management of individuals and families with HNPCC.

The impact of the experiential context of cancer for individuals who belong to HNPCC families cannot be understated. Experiences with family cancer significantly influence one's level of awareness, formulation of risk perceptions and coping abilities for managing the disease. The variation and complexity of individual and family

experiences from living with HNPCC necessitates an individualized approach to the provision of genetic services. Consideration must be given to all aspects of the HNPCC condition, including the experiential impact of living in these families and the genetic testing process, as well as the short- and long-term adjustment to genetic test results and the concomitant formal and informal support requirements. Assessment tools are not yet available, but are required to effectively monitor and clinically manage individuals with hereditary cancer conditions. Clinical tools will allow health care professionals to assess an individual's level of preparedness, potential reactions to and support needs for undergoing genetic testing for HNPCC. Meanwhile, genetics personnel should be alerted to some of the more significant psycho-emotional needs of individuals and families undergoing genetic testing for HNPCC.

Not everyone is equally aware of or influenced to the same degree by the cancer that presents in the immediate family. For those most aware, often due to exposure to cancer in a parent or close relative at a young age, there may be a greater sense of fatalism towards the disease. Importantly, the outlook for the self and for others seems to vary depending on the degree of suffering and whether or not the parent or close relative with HNPCC succumbed to the disease. An individual's outlook is an important factor shaping their sense of controllability of the disease. Genetics personnel need to be alert to variant levels of awareness of cancer in the family and the closeness of relatives affected by the disease as this influences comprehension, acceptance and emotional readiness to become informed of one's HNPCC risk status.

The quality of the family relations is also significant in shaping risk perceptions for HNPCC. When family cancer experiences strengthen family relations there seems to

be a greater appreciation of one's high-risk status and the need to be more attentive to one's health. Conversely, when cancer weakens family relations there seems to be decreased awareness, lesser appreciation of being high risk and more negative outlook about being able to control the disease. Assessing family functioning in relation to the HNPCC events can help shed light on an individual's level of awareness and acceptance of high-risk status. Knowledge gained from this assessment can help genetic personnel identify those with strong and weak family support structures. Strong family structures suggest the presence of sufficient resources to help buffer stress and facilitate understanding and acceptance of carrier or non-carrier status. Conversely, weak family structures should indicate to genetics personnel that there is a need to provide additional cognitive and emotional support regarding risk and disease prevention.

Genetics personnel must also remain cognizant of the fact that full acceptance of the challenge to engage in testing often occurs over time at an individual's personal pace. Time may be required to assimilate and adjust to the high risk information and even more time to weigh the risks and the benefits of engaging in the process. It is also important to consider the age of those engaging in genetic testing for HNPCC, as younger individual's in their teenage years or early adulthood are not always fully aware of the extent of cancer in the family and often are only introduced to it by health care professionals. Younger individuals may also require additional psychological, emotional and informational support.

Genetic counseling relies heavily on a Mendelian knowledge-sharing approach often emphasizing the cognitive aspects of testing and focusing on percentage of risk for colon and associated cancers, and related screening information. Nevertheless, there is

growing support for further integration of strategies to assess and support the emotional aspects of testing in the short- and long-term adjustment phase. Study findings indicate that many participants were unprepared for how they reacted emotionally to being informed of their HNPCC status. The apparent disconnect between understanding on a cognitive level and emotional acceptance of the results seems intimately related to the extent of family cancer, beliefs about inheritance, personal coping abilities and openness of communication in families in complex ways. Genetics personnel need to be cognizant of the subjective feeling states of individuals presenting for genetic testing and how well they are processing the information communicated to them. It is important also for counselors to consider the impact of past family cancer experiences on possible emotional reactions to the results of genetic testing. This event is an emotional one for many individuals and adequate emotional processing may require immediate and/or more intense short- or long-term psychological support. Individuals need to be given an opportunity to explore feelings and understandings openly and in a supportive environment. Contact to assess psycho-emotional support needs should continue in the short- and long-term periods after testing.

Participants in this study were clear that the genetic testing event itself is narrow when compared to the larger context of their lives both before and after the testing event, with many describing a sense of ambivalence concerning the merits of taking part in genetic testing. Health care professionals need to embrace a broader conceptual view of being at risk for HNPCC. Being at risk is a condition that affects the individual and the family with both requiring support and management over time. Genetic testing for HNPCC is one event along a continuum of lifelong disease management. The years prior

to and following the event are very significant to HNPCC families in terms of psychosocial and emotional impact and require further study and exploration. Health care professionals need to understand that even though patients accept and adjust to their HNPCC status, they may not always view it as a beneficial process over the long-term. In fact the impact of knowing one's results can impede successful coping. Information provided by genetics personnel may empower some individuals to act and embrace the demands of additional screening, while others are more selective in what they are willing and able to take on. Personal beliefs about inheritance, emotional and cognitive barriers to accept the range of cancer screening requirements may influence how individuals plan to proceed with screening after testing. Genetics personnel need to assess lay beliefs about HNPCC and explore how past experiences with cancer among loved ones influence and create existing beliefs because they are likely to provide clues to actual screening uptake.

The burden of communication about hereditary cancer and testing for all family members at risk often rests with one individual, who is most often the one diagnosed with HNPCC or has been identified as a carrier. This burden requires further assessment as there are many important considerations around duty to tell, and how and when to inform others. Many study participants expressed a lack of confidence in relaying genetic test results especially to children and family members with whom they have had very little contact. This finding suggests that individuals need continued support after testing to help them communicate with other family members. Families with less cohesion and decreased perceived support require greater assistance and support to ensure adequate disclosure of at-risk information.

There are many challenges after testing to maintain a positive attitude in the face of lifelong screening. Screening is viewed as burdensome and there is fear regarding the potential onset of new cancer onset in the self or others. Accessing care in a timely fashion is a concern and some individuals may need someone to help them navigate a complex health care system. Nurses in genetics and in the community are poised to help carriers navigate the health care system. Nurses need to advocate for HNPCC carriers to promote access to screening and to ensure communication of screening results by family physicians and specialists.

Concerns were also raised by participants about being able to continue with lifelong screening due to increasing problems with accessing formal supports, especially physicians. Most importantly, concerns were expressed about health care system barriers that interfere with the need for extensive and timely screening. Screening adherence is challenging, cumulative, and requires support at the family, social, and healthcare system level. Health care providers need to ensure access to screening. The family physician plays a crucial role in the management of HNPCC and together with nurses need to improve coordination of screening regimes. These findings also suggest that individuals want ongoing contact with health care providers in order to receive up-to-date information about HNPCC and its management. Long-term follow-up and support by the health care providers in genetics is necessary.

Carriers and non-carriers describe a constant search for stability as they continue to adjust to life after testing. Many highlighted the struggle to create a meaningful context for the self and others and build inner strength. The search for new coping strategies was apparent as participants spoke of the demands of thinking and providing care to other

family members, as well as mounting worry and concern for younger family members, who may also be at risk. Supportive families made a difference as individuals had someone available to share the burden – openly discussing and disclosing fears and concerns while deriving emotional and psychological support. Further study is required on the social and family support needs and benefits for those with genetic-based disease. Nurses are poised to play an important role in the follow-up and support of individuals and families living with HNPCC.

Nursing Implications

Nurses are often the first point of contact whether in the community or acute care setting for individuals at risk for hereditary cancer conditions and as such must embrace the specific needs of this new group of patients. As such, nurses must have adequate knowledge about the basics of genetics and genetic-linked diseases. Individuals with a confirmed genetic link are at higher risk for cancer onset than those of the general population. Care for individuals with a high risk for cancer conditions is largely preventative. Nevertheless, the context of being in a high-risk family and actually being a carrier of a cancer gene mutation has significant lifelong physical, psychosocial and emotional impacts.

Nurses must have up-to-date knowledge of the Amsterdam I and II criteria as well as the Bethesda guidelines that outline HNPCC risk in order to be alerted to patients who are at increased risk for this disease. Nurses also need to pay attention to young people who present with cancer, as well as individuals with a family history of CRC, and consider their potential HNPCC risk. Nurses should also assess the family structure,

patterns of communication and functional capacity in terms of how they influence one's awareness of the possibility of hereditary cancer risk as part of the decision to refer patients to genetic services.

HNPCC carriers need to be supported by nurses in their screening efforts. They require navigation through the health system, timely follow-up and coordination to help them manage likely cancer events. As episodes of cancer appear, nurses need to be aware of the increased psycho-emotional needs of carriers, non-carriers and their families and provide support and referral as necessary. Nurses must also be prepared to provide education on appropriate and ever-changing screening recommendations as they encounter individuals at risk for HNPCC.

Nurse educators need to incorporate advances in cancer genetics into nursing curricula to provide students with the knowledge of this ever advancing field. Patients who have undergone genetic testing have made the decision to live life knowing about their carrier or non-carrier status. As patients, these individuals have a more precise knowledge of cancer risk and therefore present in the health system as a unique population. Nursing education must prepare students for the range of patient perspectives that come with advances in genetics and technology.

Nurse researchers must continue to make contributions, through qualitative and quantitative study, to advance knowledge of the care and management of HNPCC and genetic testing. The long-term adjustment phase requires further prospective inquiry specific to those living with a known HNPCC carrier status. The role of social and family support for carriers and on carriers after testing remains largely unexplored and nurse

researchers are uniquely poised with expertise and well-developed theory on family and health systems to further advance knowledge in this area.

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Appendix A

Cover Letter and Brief Overview of Research Study

22 March 2004

Dear

Thank you for agreeing to review the materials associated with the qualitative component of the research study on individuals' experiences with genetic testing for hereditary colorectal cancer. We are asking people to share their experiences in a face to face interview in order to explore more deeply their thoughts and feelings surrounding genetic testing.

Enclosed you will find a summary of the study and two consent forms for review at your convenience. If you require more information about the study and the extent of your involvement, please contact Jackie Stokes at 777- 6738 or the toll free number at 1-888-908-4988. Jackie is the research co-ordinator for both the quantitative and qualitative components of this study. She will be contacting you in 3 to 4 weeks to confirm your interest in participating in the qualitative phase.

We appreciate your cooperation. We hope the answers you provide will help enhance the care of future patients and families.

Yours sincerely,

Christine Way, PhD
Principal Investigator
NL Colorectal Cancer Study

Brief Overview of Research Study

Title: Psychosocial and Behavioral Impact of Predictive DNA Testing on Hereditary Colorectal Cancer

Investigators: Dr. Christine Way, Dr. Mary Jane Esplen, Dr. Jane Green, Robert Meadus and Jackie (Stokes) Fiander

Objectives of the study:

1. To explore the meaning of genetic testing for individuals at risk for developing hereditary colorectal cancer.

2. To develop a greater understanding of the impact of genetic testing for colorectal cancer on individuals who receive positive or negative results.

3. To identify relevant information that will facilitate the provision of counseling programs to more adequately address the needs of individuals belonging to families with documented hereditary colorectal cancer.

Rationale for the study:

Limited research has been conducted on the impact of genetic testing for individuals at risk for hereditary colorectal cancer. Genetic testing provides an opportunity to more precisely predict an individual's risk of developing these cancers. Still, with the ability to predict or anticipate health threats may come fear, worry, and distress. Also, there is limited insight into how such testing influences screening and health practices.

Brief description of the study:

The proposed study will attempt to capture individuals' experiences with genetic testing for hereditary colorectal cancer in NL families. Each participant will be asked to participate in two interviews. During the first interview, which will last approximately 60 to 90 minutes, the interviewer will focus on your experiences with genetic testing, your reasons for considering genetic testing, and the impact of test results on you and your family. In the second interview, you will be asked to confirm a summary of the main points addressed in the first interview and provide any additional information that may help facilitate our understanding of your experience.

Procedure for obtaining consent:

A written, informed and witnessed consent will be obtained prior to the first scheduled interview.

Proposed staring date: 06/01/04

Appendix B

Consent Form

October 2003

Faculty of Medicine, Schools of Nursing and Pharmacy of Memorial University of Newfoundland; Health Care Corporation, St. John's; Newfoundland Cancer Treatment and Research Foundation

Consent to Take Part in Health Research

TITLE: **Psychosocial and Behavioral Impact of DNA Predictive Testing for Hereditary Non-Polyposis Colorectal Cancer (HNPCC)**

INVESTIGATOR(S): Dr. Christine Way (709-777-6872), Dr. Mary Jane Esplen (416-340-4736), Dr. Jane Green (709-777-6242), Robert Meadus (709-777-6716) and Jackie (Stokes) Fiander (709-777-6738)

SPONSOR:

You have been asked to take part in a research study. It is up to you to decide whether to be in the study or not. Before you decide, you need to understand what the study is for, what risks you might take and what benefits you might receive. This consent form explains the study.

The researchers will:

- **discuss the study with you**
- **answer your questions**
- **keep confidential any information which could identify you personally**
- **be available during the study to deal with problems and answer questions**

If you decide not to take part or to leave the study this will not affect your normal treatment.

1. Introduction/Background:
   You are being asked to participate in a research study of individuals receiving genetic testing for colorectal cancer. Very little is known about how people experience this type of testing or how test results may or may not influence their decision to participate in recommended screening or treatment programs. This information may help improve the quality of genetic counseling services available to individuals and their families.

   1. Purpose of study:

   The purpose of this study is to explore individuals' experiences with genetic testing for colorectal cancer and perceptions of recommended screening programs. The

study has the potential to increase our understanding of difficult aspects of these experiences, and provide useful information on how counseling services can be improved to address individual needs.

2. Description of the study procedures and tests:
You are being asked to participate in two interviews which will be conducted at a place and time that is convenient for you. Interviews will be audiotaped (with your permission). Tapes will be transcribed word for word and used solely to help the interviewer recall the details of your conversation.

During the first interview you will be asked to reflect upon your experiences with genetic testing and describe any thoughts and feelings that you may recall about it. You will also be asked to comment upon the least and most helpful aspects of any information given to you about your test results and recommended screening programs.

Within a three to four week period, you will be given an interpretive summary of the first interview and arrangements made for a second interview. During the second interview you will be asked to confirm whether or not the interpretive summary accurately reflects your experiences with genetic testing, and provide any additional information that you may consider important for clarifying your experiences.

4. Length of time:

The first interview will take approximately 60 to 90 minutes, and the second about 30 minutes. Both interviews should be completed within two months.

5. Possible risks and discomforts:

It is possible that during the interview you may reflect upon some difficult moments associated with genetic testing. This may cause you to experience some anxiety and discomfort about disclosing your thoughts and feelings. You may refuse to answer any interview questions, and terminate the interview, as well as your participation in this study, at any time. The interviewer may also terminate the interview and refer you back to your genetic counsellor if it is determined that you could benefit from additional counselling services.

All information that you provide will be kept strictly confidential, secured in a locked file, and accessible only to the research team. Your name will not appear on the audiotape or written copy, and any names that you might mention during the course of the interview will be removed from the transcribed texts.

6. Benefits:

   It is not known whether this study will benefit you.

7. Liability statement:

   Signing this form gives us your consent to be in this study. It tells us that you understand the information about the research study. When you sign this form, you do not give up your legal rights. Researchers or agencies involved in this research study still have their legal and professional responsibilities.

8. Questions:

If you have any questions about taking part in this study, you can meet with the investigator who is in charge of the study at this institution. That person is:

Dr. Christine Way: (709) 777 – 6872

Or you can talk to someone who is not involved with the study at all, but can advise you on your rights as a participant in a research study. This person can be reached through:

Office of the Human Investigation Committee (HIC) at 709-777-6974
Email: hic@mun.ca

Signature Page

Study title: **Psychosocial and Behavioral Impact of DNA Predictive Testing for Hereditary Non-Polyposis Colorectal Cancer (HNPCC)**

Name of principal investigators: Dr. Christine Way and Dr. Mary Jane Esplen

To be filled out and signed by the participant:

Please check as appropriate:

I have read the consent [and information sheet]. Yes { } No { }
I have had the opportunity to ask questions/to discuss this study. Yes { } No { }
I have received satisfactory answers to all of my questions. Yes { } No { }
I have received enough information about the study. Yes { } No { }
I have spoken to Dr. _____ and he/she has answered my questions Yes { } No { }
I understand that I am free to withdraw from the study Yes { } No { }

- at any time
- without having to give a reason
- without affecting my future care [student status, etc.]

I understand that it is my choice to be in the study and that I may not benefit. Yes { } No { }

I agree that the study doctor or investigator may read the parts of my hospital records which are relevant to the study. Yes { } No { }

I agree to take part in this study. Yes { } No { }

_____ _____ _____
Signature of participant Date

_____ _____
Signature of witness Date

To be signed by the investigator:

I have explained this study to the best of my ability. I invited questions and gave answers. I believe that the participant fully understands what is involved in being in the study, any potential risks of the study and that he or she has freely chosen to be in the study.

_____ _____
Signature of investigator Date

Telephone number: _____

Appendix C

Interview Schedule

Interview Script

We are interested in your experiences with genetic testing for hereditary colorectal cancer from the time you first learned about the testing right up to now. We would like for you to take some time to reflect upon these experiences and share with us your perceptions of the genetic testing process as you saw it. You can share any thoughts, feelings, and ideas about your experiences. Feel free to talk about whatever comes to mind.

Examples of Probes/Questions to Facilitate the Interview

3. Could you think back to when you first learned that you were eligible for genetic testing for hereditary colorectal cancer and what that meant to you then?

4. Can you recall a significant personal experience around genetic testing for hereditary colorectal cancer that left a lasting impression in your memory? If so, when and how did this experience occur? How important was it for you at the time? Do you believe that it is still important? (Probes: Are you able to identify any particular experiences that left you feeling good/bad about things/yourself? Can you recall a significant event that reinforced/diminished your confidence about how well prepared you were to deal with the results and potential problems/needs in a comprehensive manner?)

5. How do you feel about genetic testing and hereditary colorectal cancer in general? What are some of the positives? Negatives?

6. How has this experience changed the way you look at things/life?

7. How has this experience influenced your relationships with other family members?

8. How would you rate the overall genetic testing experience? Are there particular aspects of these services that could be improved? What measures would you like to see implemented/changed that could potentially improve the quality of genetic testing services? (Probes, if not mentioned: Access to community resources, such as diagnostic facilities, specialists, genetic counselors, hospitals, etc.; access to other sources of information).

9. Are there any other comments or thoughts that you would like to share with us about your experiences with genetic testing for hereditary colorectal cancer?

Appendix D

Ethical Approval