

Living with hereditary cancer

*The experiences of Swedish MEN1 patients and Norwegian
BRCA1/2 mutation positive men*

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Scientific environment

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Summary

Background

During the past two decades there has been an increasingly focus on cancer risk reduction using genetic tests and family history to identify persons with increased risk of developing cancer. Depending on the genetic condition, persons at significantly increased risk may be identified and then enrolled into long term surveillance programs. This is the case for patients with Multiple Endocrine Neoplasia type 1(MEN1) where nearly 100% develop symptoms. Others may be identified as having a slightly increased cancer risk, but no management strategies are made available for them. This is the current clinical practice for Norwegian men identified with a mutation in breast cancer gene 1(BRCA1) or breast cancer gene 2 (BRCA2). Limited research interest has been paid to researching the psychosocial issues of these patient groups, the MEN1 patients and men with BRCA1/2 mutations.

Aims

The overall aim of this thesis is to explore and describe the experiences of two patient groups living with high and slightly increased risk for hereditary cancer.

Material and methods

Qualitative semi-structured interviews had been performed with 29 MEN1 patients recruited through a specialty clinic in Sweden (Study 1). The data were analyzed in line with Giorgi's phenomenological method. To learn about male experiences in hereditary breast and ovarian cancer syndrome (HBOC) families, a systematic review of existing psychosocial research on this topic was performed, and a thematic analysis was utilized (Study 2). Further, 15 BRCA1/2 mutation positive men participated in two successive in-depth interviews, and seven female partners participated in the second interview (Study 3). These participants were recruited through two departments of Clinical Genetics in Norway. A phenomenological

lifeworld approach was utilized, and the in-depth interviews were analyzed using Georgi's phenomenological method.

Results

The MEN1 patients with high increased risk described mixed feelings about the clinical follow-up program. They experienced decent care from their health care providers but they still had unmet informational needs. Their genetic condition was associated with pain, job insecurity and feelings of guilt towards their children. They also experienced short-term perspective in future planning due to fears that their condition might worsen. However, they had adjusted to their situation and described a change in their priorities and values. They also defined themselves as healthy.

A review of the literature regarding men in hereditary breast and ovarian cancer (HBOC) families describes women as playing the leading role in communicating genetic information in the family. Men's decision to seek genetic counseling and testing is said to be out of family duty or as an obligation to their children. Men are described as suffering from intrusive feelings due to unresolved grief and to use avoidance as a coping strategy. Previous reports describe men's feelings of guilt towards their children and other family members. Men's genetic test results may have an impact on familial relationships and reproductive decisions.

The Norwegian men identified as BRCA1/2 mutation positive experienced strong emotional reactions after disclosure of their test results including fear of developing cancer. The men also felt responsible for other family members' health, and described an unmet need of risk information regarding their own and relatives' potential cancer risk. Due to fear of being stigmatized most participants felt it important to keep the genetic information private. Many had not informed their children about the family mutation mainly because of their young age, or because they knew that their offspring were struggling with difficult life events. Participants also considered it difficult to discuss their test results or health related information with other males, and they perceived females as their social and emotional support.

Conclusion

People's feelings and understanding of genetic risk does not seem to depend on the numeric risk estimate. The results from this study pinpoint the need for counseling and follow-up strategies for both MEN1 patients and for male BRCA1/2 mutation carriers.

Health care providers may have an impact on how these patients deal with their condition, and the patients may also profit from closer contact with community health care. There is also a need for future research regarding the psychosocial issues for MEN1 patients and BRCA1/2 mutation positive men.

List of papers

Paper I

Strømsvik, N., Nordin, K., Berglund, G., Engebretsen, LF., Hansson, MG., Gjengedal, E. Living with Multiple Endocrine Neoplasia Type 1: Decent Care-Insufficient Medical and Genetic Information A Qualitative Study of MEN1 Patients in a Swedish Hospital. *Journal of Genetic Counseling* 2007 Feb; 16(1):105-17.

Paper II

Strømsvik, N., Råheim, M., Øyen, N., Gjengedal, E. Men in the women's world Of hereditary breast and ovarian cancer—a systematic review. *Familial Cancer: Volume 8, Issue 3(2009), Page 221-9.*

Paper III

Strømsvik N, Råheim M, Øyen N, Engebretsen LF, Gjengedal E. Stigmatization and male identity: Norwegian males' experience after identification as BRCA1/2 mutation carriers. *Journal of Genetic Counseling: Volume 19, Issue 4 (2010), Page 360-70.*

Paper IV

Strømsvik, N., Råheim, M., Gjengedal, E. Cancer worry among Norwegian male BRCA1/2 mutation carriers. Manuscript submitted.

List of abbreviations

BRCA1: Breast cancer gene 1

BRCA2 : Breast cancer gene 2

HBOC : Hereditary breast and ovarian cancer syndrome

HRQoL: Health related quality of life

MEN1 : Multiple Endocrine Neoplasia type 1

PGD: Preimplantation genetic diagnosis

PND: Prenatal diagnosis

PRCA: Prostate cancer

QoL: Quality of life

WHO: World Health Organization

Glossary

Carrier: An individual who has a recessive, disease-causing gene mutation at a particular locus on one chromosome of a pair and a normal allele at that locus on the other chromosome; may also refer to an individual with a balanced chromosome rearrangement. This concept is also used for heterozygotes for autosomal dominant conditions when the condition is mild, variable or late in onset [1, 2].

Gene: The basic unit of heredity, consisting of a segment of DNA arranged in a linear manner along a chromosome. A gene codes for a specific protein or segment of protein leading to a particular characteristic or function [1].

Mutation: Any alteration in a gene from its natural state; may be disease-causing or a benign, normal variant [1].

Penetrance: The proportion of individuals with a mutation causing a particular disorder who exhibit clinical symptoms of that disorder; most often refers to autosomal dominant conditions [1].

List of appendices

Appendix 1: Certificate of acceptance from the Swedish Regional Scientific Ethics Committee

Appendix 2: Information letter to the Swedish MEN1 patients

Appendix 3: Interview guide for the Swedish MEN1 patients

Appendix 4: Certificate of acceptance from the Norwegian Regional Scientific Ethics Committee

Appendix 5: Certificate of acceptance from the Norwegian Data Inspectorate

Appendix 6: Information letter to BRCA1/2 mutation positive men and their partners

Appendix 7: Informed consent form for Norwegian BRCA1/2 mutation positive men

Appendix 8: Informed consent form for partners of Norwegian BRCA1/2 mutation positive men

Appendix 9: Interview guide for the Norwegian BRCA1/2 mutation positive men

Appendix 10: Certificate of acceptance from the Norwegian Regional Scientific Ethics Committee to keep the data until 31.12.11.

1. Introduction

Healthcare is increasingly focused on risk reduction, and in recent years there has been a drive for cancer genetic risk assessment where genetic tests and family history have made it possible to identify persons at increased risk for hereditary cancer. This knowledge may lead to preventative interventions where persons at risk are enrolled in follow up programs, as is the case for persons with Multiple Endocrine Neoplasia type 1 (MEN1). This is a rare genetic condition where nearly 100% develop symptoms [3], and persons at risk are therefore enrolled into follow-up programs already from a very young age. Little is known about MEN1 patients' experiences of living with high genetic risk of disease, and their experiences of being involved in a long-term follow-up program. Persons with slightly increased risk for cancer may also be identified, without any management strategies available for them. This is the case for male BRCA1/2 mutation carriers. There has been little research interest in the psychosocial issues regarding these men, and there is also a lack of risk management strategies and guidelines for genetic counseling for BRCA1/2 mutation carriers [4]. The focus of this thesis is to explore and describe the experiences of two patient groups living with high and slightly increased risk for developing cancer.

Clinical practice in these fields may benefit from new knowledge in relation to genetic counseling and testing.

1.1.1 Multiple endocrine neoplasia type 1 (MEN1)

Multiple Endocrine Neoplasia type 1 (MEN1) is an autosomal dominant disease caused by a germline mutation in the MEN1 localized to chromosome 11q13 [5]. Although this condition often is regarded as a treatable endocrinopathy, MEN1 is regarded as a cancer syndrome due to lack of effective prevention for associated malignancies [6]. This condition is characterized by parathyroid hyperplasia, duodeno-pancreatic endocrine tumors, and anterior pituitary adenoma. These cancer forms may be present in the same patient or in multiple family members [7]. Parathyroid adenomas are the most common feature, and are present in 90% of the

cases. In approximately 50%-75% of the cases pancreatic islet cell tumors are seen [8]. There is also evidence that other endocrine and nonendocrine neoplasm may be common in MEN1. In addition to skin tumors foregut carcinoid, tumors in the central nervous system, leiomyomas and lipomas are described [6]. Each child of an individual with a mutation in the MEN1 gene has a 50% chance of inheriting the disease-causing mutation. Symptoms may develop already from the age of five, and the risk of developing disease (penetrance) is nearly 100% increasing with age [3]. By the age of 30-40, most affected individuals will have developed symptoms. There is however variation in where tumors are localized, onset age, and clinical aggressiveness [9]. Persons identified with MEN1 are offered regular life-long surveillance as it is important to identify and treat possible new hormonal disturbances before serious illness develops [10]. Advances in knowledge from surgical and pharmacological interventions have lead to improved clinical management [6].

1.1.2 Hereditary breast and ovarian cancer (HBOC)

Hereditary breast and ovarian cancer (HBOC) is one of the most common hereditary cancer syndromes in the Western world [8]. In Norway 2700 women develop breast cancer and 450 are diagnosed with ovarian cancer annually [11]. Of these cases approximately 5 to 10 % of breast cancer and ovarian cancer are due to a hereditary predisposition. In 50 % of the genetic cases, mutations of the BRCA1 or BRCA2 (located on 17q and 13q respectively) genes may be involved [12, 13]. Both men and women have a 50% risk of inheriting a cancer susceptibility mutation if one of their parents has a mutation. In cases where the family-specific mutation is known, family members may be identified as mutation positive or negative. The penetrance (i.e. the cumulative risk) is not complete, and variable risk estimates regarding lifetime female risk of developing breast and/or ovarian cancer are reported. These risk estimates vary depending on if they are derived from affected family-ascertained studies or population ascertained studies [8]. There is also a great variation in the prognosis of the cancer developed [14-16]. The female risk estimates also vary between BRCA1 and BRCA2, and there is a broad variation among carriers [17]. The lifetime risk (up

to 70 years) for breast cancer is estimated to be 44-78% and 18-54% for ovarian cancer for women with a mutation in BRCA1. The cancer risk in women caused by a mutation in BRCA2 is reported to be somewhat lower [18, 19].

Other studies suggest lifetime risk estimates for developing breast cancer to be between 43 and 95%, and an additional risk of developing ovarian cancer up to 60% [12]. Four common Norwegian founder mutations located in BRCA1 are estimated to confer a risk for breast and/or ovarian cancer up to 80-88% at age 70. In the southwestern part of Norway there is a high prevalence of three local founder BRCA1 mutations, resulting in a higher incidence of HBOC in this region than in the rest of the country [20]. A risk management program including annual mammography and magnetic resonance imaging (MRI) is available for female BRCA1/2 mutation carriers in Norway. Bilateral salphingo oophorectomy is recommended from the age of 35. Prophylactic mastectomy is also available [21].

Male BRCA1/2 mutation carriers also have slightly increased cancer risk, but the implications on males are still uncertain. A lifetime risk of 6% to 7% of developing breast cancer is described in male BRCA2 mutation carriers. The cumulative risk of prostate cancer (PRCA) is said to be 20% before age 80 [22]. It is also suggested that BRCA1/2 mutation carriers may develop a particularly aggressive PRCA [23, 24], and greater risks for pancreatic, gastric and hematologic cancers compared to non-carriers are reported. The risk for colorectal cancer and melanoma is not clear [4]. It is suggested that PRCA cancer may be detected at an early stage by target screening of BRCA1/2 mutation positive males [23, 24]. However, there is a lack of genetic counseling and risk management strategies for these men [4].

1.2 Genetic counseling

Families with hereditary cancer syndromes may seek or be referred for genetic counseling and testing.

1.2.1 History of genetic counseling

The intention of the early activity of providing genetic advice was to prevent certain genetic conditions in the society [2]. It is said that the strong tradition of nondirectiveness in modern genetic counseling developed as a reaction to the eugenic tradition established by Charles Davenport in 1910 [25]. This early tradition represented a dark period from the 1920s and during the Second World War. Over the years genetic counseling has developed into a communication process which also deals with the entire family. In 1947 the modern concept of genetic counseling was established by Sheldon Reed, and by 1951 ten genetic counseling centres were established in the USA. These centres focused their activity on the medical, psychological and social aspects of counseling [25, 26].

In 2001, due to the relatively short existence of genetic counseling in the Norwegian and Swedish health care system, the first Masters Degree program of health science in genetic counseling was established at the University of Bergen, Norway. In Sweden the first genetic counselors completed their training in 2005 at Uppsala University. However, locally trained genetic counselors have been working in both Norway and Sweden for two decades. Genetic counseling practice varies between the two countries depending on differences in education and legislation. Genetic services are funded by the National Health Service in both countries, theoretically allowing for equal access to genetic counseling and testing.

1.2.2 Definition of genetic counseling

Numerous definition of genetic counseling exists, but most of the modern definitions of genetic counseling are based upon Fraser's definition from 1974 [27] (p. 637).

“Genetic counseling is a communication process which deals with the human problems associated with the occurrence, or the risk of occurrence, of a genetic disorder in a family. This process involves an attempt by one or more appropriately trained persons to help the individual or family (1) comprehend the medical facts, including the diagnosis, the probable course of the disorder, and the available management; (2) appreciate the way heredity contributes to the disorder, and the risk

of recurrence in specified relatives; (3) understand the options for dealing with the risk of recurrence; (4) choose the course of action which seems appropriate to them in view of their risk and their family goals and act in accordance with that decision; and (5) make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder.”

The current genetic counseling encompasses other aspects than merely providing information about disease or hereditary conditions in general [28]. One aim of genetic counseling is to achieve empowerment [29] which refers to people’s ability to mobilize and strengthen their resources, and neutralize those forces that could lead to feelings of helplessness [30]. There are educational, emotional and ethical aspects involved in the process of genetic counseling [31], and previous evidence pinpoints that the supportive function of genetic counseling can be of greater value for some clients compared to the informational component [32, 33].

1.2.3 Professionals in Norway and Sweden

In Norway and Sweden genetic counseling is performed by both genetic counselors and medical doctors with a speciality in medical genetics. In this thesis the term counselor is used synonymously for both professions.

In line with Fraser’s definition of genetic counseling [27] the genetic counseling in Norway and Sweden is performed by appropriately trained persons. In order to empower the individual and the family to understand the medical facts, the probable course of the disorder and available management, the counselors are skilled in dealing with these issues. Such counseling and familial evaluation for possible hereditary cancer syndrome takes place in a clinical genetics department. This process requires team work, involving medical geneticists and genetic counselors. In addition, the patients with significantly increased risk are offered surveillance programs supervised by specialized clinical health professionals depending on the management program. Genetic counseling is mandated prior to predictive testing by Norwegian law[34]. Such counseling includes options for testing and surveillance. This may contribute to making the best possible adjustment to the actual familial cancer syndrome.

1.2.4 Norwegian laws regulating genetic counseling

The Norwegian “Biotechnology Act” was introduced in 1994, and revised in 2003. This law mandates genetic counseling prior to, during and following predictive, presymptomatic or carrier testing. The law also protects persons from genetic discrimination and prevents insurance companies and employers from making use of genetic information [34]. In the time frame (2000-2001) when data in Study 1 were collected, Swedish law was less comprehensive than the Norwegian legislation [35], and fewer genetic tests were regulated by Swedish law. The Norwegian law does however not mandate genetic counseling prior to diagnostic testing. According to this legislation, the genetic counseling should be performed by genetic counselors and medical doctors with a speciality in medical genetics.

According to Norwegian legislation, all persons approaching the health care system are defined as patients [36]. In this thesis both symptomatic MEN1 patients and male BRCA1/2 mutation carriers will be referred to as patients accordingly.

2. Theoretical perspective and previous research

2.1 Health and quality of life

The present study aims at exploring and describing the experience of two patient groups living with high and slightly increased risk for hereditary cancer. Quality of life (QoL) and the concept of health are important when exploring human experiences in health research. QoL and health are complex phenomena. QoL is related to, for instance, happiness, well-being, realizing one's potentials etc, including an evaluation of one's life as a whole. In quality of life research it is important to explore subjectivity, as only the persons themselves are able to judge the quality of their lives [37]. The concept of QoL has a normative element. Furthermore, it relates to a measurement of how an individual experiences life at a particular moment e.g. when suffering from a genetic condition or living with a genetic vulnerability [38]. Also, the quality of life (QoL) may be closely related to a view of health as a holistic property of a person. The concept of health also has a normative component which concerns a person's general ability to realize his or her plans of life or to fulfil vital goals in life [39]. The research in health and QoL are rooted in two main traditions: Surveys measuring QoL with predefined definitions and operational questionnaires and the qualitative tradition: Interview studies based on subjective meaning and interpretation in which the phenomenological life-world tradition is rooted.

The World Health Organization (WHO) regards health to be more than absence of infirmity and diseases, and includes physical, mental and social well-being in their view of health [40]. Later approaches to studies of health and QoL are inspired by this definition, naming it "health related quality of life" [41] The distinction between health and QoL may however sometimes become vague as the concepts health status, functional status and QoL are used interchangeably [42, 43]. The concept of Health Related Quality of Life (HRQoL) refers to measures to investigate how patients experience their situation, and concerns psychosocial aspects that are usually not explored in the traditional medical research[44]. Health related research measures of QoL have become important features, and refers to physical, social, psychological

and existential aspects which may be affected during disease and treatment [45]. When individuals undergo a change in their health state, a response shift caused by changes in internal standards may have vital importance. Cognitive, behavioural and affective issues are involved in the process of adjusting to the change in their health status, and may have an impact on assimilating illness.

Three different outcomes in this adjustment are described [45, 46]. In the first case helplessness, frustration and depression may occur because the affected person remains focused on controlling the uncontrollable disease or condition. Consequently their perceived QoL will be worse than prior to the change in their health status. The second outcome described is a response shift caused by changes in internal standards. A changed sense of purpose in life may be developed and could result in a modification in the conceptualization of QoL. As such, the experience of QoL would be at a similar level as before the changed health status. Finally, the third possible outcome is to maintain a sense of internal control by changing focus to manageable aspects in life and seeking positive role models in how to adjust to the new health status, or creating a new sense of purpose in life. These changes may induce a response shift that results in changed values and a change in the conceptualization of QoL. This may lead to an experience of similar or better QoL compared to perceived QoL prior to the change in health status [45, 46].

2.1.1 Antonovsky's salutogenic model of health

Aaron Antonovsky was a sociologist focusing on medical sociology. His work concerned the relationship between stress, health and well-being. In order to create or maintain health and well-being his salutogenetic model is focusing on identifying patients' health resources and capacities, within the patient him-/herself as well as in his/her surroundings, rather than on disease [47]. This is in line with the aims of genetic counseling, which aims at achieving empowerment [29, 30] by strengthening people's resources and their ability to mobilize and neutralize those forces that could lead to helplessness. Antonovsky developed his salutogenic model during his study of menopause in Israeli women who had survived concentration camps in the Second World War. In spite of their traumatic experiences these women were in surprisingly

good health. His salutogenic model called Sense of Coherence develops during childhood and adolescence, and new knowledge suggests that it develops and increases throughout the life [48]. The salutogenic model comprises three dimensions: comprehensibility, manageability, and meaningfulness.

Comprehensibility relates to whether the experienced internal and external stimuli are perceived as structured, predictable, and explainable. Manageability concerns the individuals perceived resources to deal with stressful situations or disease. The main dimension in Antonovsky's theory is the experiences of meaningfulness which is the most important issue in creating well-being and health. Important lifetime aspects for achieving meaningfulness are interpersonal relationships, existential issues, activities, and employment. It is essential that individuals participate in shaping their own future, otherwise these aspects of life will be lost over time if they are not invested in or experienced as meaningful [47]. The theory refers to a generic understanding of how Sense of Coherence may be developed and sustained, thus leading to coping and health. This salutogenic model has shown strong positive correlations to perceived health, mental health and QoL [48], and studies of several different populations relates Sense of Coherence to QoL [49].

2.1.2 Risk

This study is focusing on the experiences of persons living with high and slightly increased risk of developing cancer. In the latest decades it has been an increased focus on risk factors for healthy persons [50]. Evidence suggests that individuals have problems quantifying their risk [51]. There is however also evidence suggesting that persons may have a tendency to overestimate their risk because "high risk" is associated with access to follow-up programs they otherwise would not be entitled to. Previous research suggests some evidence that high risk estimation may have adverse consequences for psychological health. However, this evidence is inconsistent [51]. It is also argued that a common mistake in risk communication is to convert results from group levels into an individual level [52], and that risk interventions among healthy individuals may have undesired consequences like introducing uncertainty into healthy people's lives [53, 54].

Risk assessment and communicating risk information are essential in genetic counseling [33, 55], and it is important to understand how individuals perceive their genetic risk [51]. The individual subjective feeling of risk does frequently conflict with the objective risk estimates communicated by the genetic counselor [33]. According to Sivell et al. [51] feelings of risk is based on personal experience and thereby hard to quantify. Risk perception is described to be influenced by three main areas: contextual factors, the nature of potential outcome and numeric probability [33]. The first main area that might have an impact on risk perception is said to be the contextual factors like family history and the prevalence of the actual condition in the population [33]. Sivell et al. [51] regard contextual factors as past experiences, family history, environmental factors, occupation, diet and stress/worry to also influence perceived risk. The second main factor is the nature of potential outcome which relates to the individual perceived severity of the actual condition. According to Sivell et al. [51] risk perception for numerous conditions seem to be influenced by the personal experiences of the actual disease, and the treatment of the condition. The third main factor that effects perceived risk is the individual perceived pre-existing numeric probability influence on risk perception. However, an objective numeric probability provided during genetic counseling may modify the perceived subjective probability for illness. Also, risk perception may change over time if there is an alteration in the context, especially if additional family members develop disease [33].

2.2 Previous psychosocial research in MEN1 patients and men in HBOC families

2.2.1 MEN1 patients

One study regarding QoL in MEN1 patients was identified [56]. Berglund et al. monitored the same twenty-nine MEN1 patients included in Study 1 using questionnaires at an in-hospital stay and six months later at home. Psychosocial outcome measures such as anxiety, depression, intrusion and avoidance changed only marginally between the hospital stay and later at home. The findings describe that 70% of the participants were defined as pessimists, and patients who have a high

burden of disease and treatment showed an increase in depression levels. They also scored lower on the General Health and Social Functioning scale than population-based norm values. It is suggested that MEN1 patients who suffer from severe disease and treatment should be offered psychosocial support [56].

2.2.2 Men in HBOC families

Few studies had been published regarding male experiences in HBOC families where the study focus had been solely on men. Hallowell et al. published three papers from the same study where in-depth interviews with 17 men (five BRCA1/2 carriers and 12 non-carriers), eight partners and four adult children were performed [57-59]. Results from this study describe men's understanding of their role in transmitting BRCA1/2 mutations [57], and how male decision-making regarding predictive testing for BRCA1/2 mutations may be influenced by females [58]. One paper describes males' different strategies for disclosure of genetic information to their children varying from total openness to total secrecy [59]. A qualitative study from McAllister et al. [60] describes fear of developing cancer, and concern for daughters amongst twenty-two men in breast cancer families [60]. Lodder et al. explored the emotional implications of genetic testing in twenty-eight males and their partners with interviews and questionnaires. Only four men were identified as mutation carriers, and a large variation of psychological reactions in these men were reported [61]. Adverse psychological reactions amongst twenty-six men undergoing genetic testing for BRCA1/2 were reported by Daly et al. [62]. Dudok de Wit et al. [63] also explored the experiences, process and outcome of genetic testing for BRCA1 in four males. Results from this study describe men's tendency to deny and avoid discussing their emotions and the presence of hereditary cancer in the family [63]. The largest male population explored is reported in a study from Liede et al. [64] where more than half of the fifty-nine BRCA1/2 mutations positive males reported intrusive thoughts regarding their own cancer risk. The motivation for genetic testing was however concern for their daughters [64].

Other studies deal with both male and female experiences in HBOC families, where males or gender issues are commented separately. Ormondroyd et al. [65]

interviewed thirteen widows or blood relatives from deceased BRCA1/2 positive males where the mutation was detected after the men's death. All relatives believed that such results should be communicated to relatives, and many felt that these results had been beneficial for themselves [65]. Two quantitative studies were performed by Smith et al. and included both males and females in HBOC families. The first of these studies focused on the familial context of genetic testing for BRCA1, and this study reports that male mutation carriers experienced significantly more distress if they were first tested in the family. Males identified as mutation negative also experienced distress if their siblings were identified as mutation positive [66]. The second study from Smith et al. concerns fertility intentions after testing for an identified BRCA1 mutation. The results indicated that mutation positive men, in contrast to the women, are likely to want additional children [67]. In a qualitative study d'Agincourt-Canning explored gender issues, responsibility and disclosure of genetic information among males and females undergoing testing for BRCA1/2 [68]. A review from the same author focuses on genetic testing and gender in relation to testing for hereditary cancer [69]. These studies conclude that communicating genetic information seems to be a gendered activity where women play the leading role. Another quantitative study measures changes in family functioning after genetic testing for a BRCA1 mutation [70]. This study reports a negative effect on males' perceived family cohesion in relation to personal history of cancer or care giving responsibility for female relatives with cancer. Anxiety and some coping resources may also influence on family cohesion.

2.2.3 Summary of previous research

It is a lack of knowledge concerning the psychosocial issues regarding MEN1 patients, as only one study was identified. Results from this study indicated a need for psychosocial support among these patients. It is therefore of vital importance that more studies are performed. There is a need for both qualitative and quantitative studies on how these patients experience their situation.

It also appears to have been little research interest in the experiences of male BRCA1/2 mutation carriers. The sparse available studies regarding males in HBOC families report fear of cancer, emotional reactions, avoidance, concern for daughters and difficulties in communicating genetic risk information. Effect upon family cohesion is also described. In the few available studies on men in HBOC families, the participation rate of mutation positive males was low. Far more mutation negative than mutation positive men participated in these studies. As such, very limited knowledge is available regarding BRCA1/2 mutation positive men. Further studies are therefore needed in order to provide a deeper understanding of BRCA1/2 mutation positive men's experiences.

3. Aims of the study

3.1 The overall aim

The overall aim of the study was to explore and describe the experience of two patient groups living with high and slightly increased risk for hereditary cancer.

3.1.1 Secondary aims

To explore and describe the experiences of Swedish male and female MEN1 patients (Study 1/Paper I).

To conduct a systematic review of the literature to explore and describe the existing psychosocial studies of male experiences in HBOC families (Study 2/Paper II).

To explore and describe the experiences of male BRCA1/2 mutation carriers in Norway (Study 3/Paper III&IV).

4. Methods

Three different studies were performed in order to respond to the overall aim presented above.

4.1 Presentation of studies

Table I

<p>Study 1: Qualitative research interviews with Swedish male and female MEN1 patients</p> <p>Semi-structured interviews</p> <p>Interviews performed by Swedish psychologists</p>	<p>Analysis: Giorgi`s phenomenological method</p>
<p>Study 2: A review of existing knowledge about men in HBOC families</p>	<p>Analysis: Thematic analysis</p>
<p>Study 3 : A phenomenological lifeworld approach</p> <p>In-depth interviews with Norwegian BRCA1/2 mutation positive men</p> <p>Interviews performed by the principal investigator</p>	<p>Analysis: Giorgi`s phenomenological method</p> <p>Narrative approach</p>

4.1.1 Swedish MEN1 patients (Study 1)

The first aim was to explore and describe the experiences of Swedish male and female MEN1 patients. These patients have a very high risk of developing cancer, and were all included in follow-up programs. None of the participants had attended genetic counseling. This study was part of a larger Swedish study focusing on health-related QoL and hereditary cancer. In this study, the interview guide were rooted in the moral philosopher Griffin's theory about well-being [71]. According to this theory, the concept of well-being is defined as a state of possessing those elements one would desire if rational and informed. According to Griffin four prudential values constitute essential aspects of a person's overall quality of life; I) the ability to enjoy a certain sense of autonomy, not merely being victim of circumstances beyond one's control; II) the enjoyment of pleasure, life should not contain only pain and suffering; III) the enjoyment of a certain level of deep personal relationships, and; IV) the enjoyment of having accomplished something in life, making an imprint [71]. These prudential values aid in achieving QoL, and are in line with components identified in quality of life surveys [38]. It is essential to notice that every individual chooses an individual combination of these values [71].

4.1.2 A systematic review of men in HBOC families (Study 2)

The second aim of this study was to conduct a systematic review of the literature to explore and describe the existing psychosocial studies of male experiences in HBOC families. Methods for reviewing trials are well developed [72, 73]. However, few methods for synthesis of non-experimental or qualitative evidence are available [72]. In our study it was essential to include all available qualitative and quantitative research evidence due to the limitation in available studies. Some approaches are described to be suitable for the purpose of integrating qualitative and quantitative research evidence. Four broad groups of these approaches are described: narrative, qualitative, quantitative and Bayesian [74]. In this study a qualitative approach was utilized in order to integrate qualitative and quantitative research evidence. In line with this approach, the quantitative evidence was converted into a qualitative textual form, and a thematic analysis was used in this transformation by identifying concepts

or key findings [74].

4.1.3 Norwegian BRCA1/2 mutation positive men (Study 3)

The third aim of this study was to explore and describe the experience of male BRCA1/2 mutation carriers in Norway. A phenomenological lifeworld approach was chosen to respond to this aim.

The lifeworld concept was developed during the phenomenological movement as part of Edmund Husserl's critique of the "totalization of natural science as a governing ideal for science in general, and the view that it had a general superior method to attain truth" [75] (p. 30). According to Husserl this totalization runs the risk of a dehumanized science, thus creating a crisis of confidence as to the human quest about the meaning of human existence [76]. As Dahlberg et al. put it, Husserl wanted to "reinstiate the everyday world as the foundation of science" [75] (p. 31). Lifeworld, then, is partly outlined as the un-escapable foundation for knowing anything at all about the world, partly as an object for exploration itself [77]. Thus, the lifeworld means "the concrete everyday reality which we encounter and relate to, that of which we cannot depart, and which is shared by others [77] (p. 31, translated from Norwegian). A lifeworld perspective in the health sciences implies qualitative research methods that are governed by openness towards the complexity and variety of meanings and values in everyday life. Further, it entails the lived experience's character of cognitions and emotions, perceptions and sensations, as well as sociality [78] (p. 38).

The focus in this qualitative study was to explore and describe human experience of living with cancer risk. A phenomenological approach makes it possible to place the patients' lived experiences at the heart of the investigation, as well as doing so in a systematic and thorough manner. It provides specific strategies for data collection and analysis [79]. In a lifeworld approach, data collection is often performed through face-to-face in-depth interviews [80]. In this manner, valuable aspects of and insight in, for instance the phenomenon of quality of life, may be added. In Study 3 qualitative in-depth interviews were performed, and Giorgi's four step

phenomenological method was used in the analysis of the interview texts. However, the strong philosophical foundation of phenomenological oriented research in the health sciences has not been further explicated in the interpretations of the findings.

The intention of the phenomenological thinking is to go back to the things themselves [81]. By entering the lived world of the phenomena of study interest and ask for the participants' descriptions in their actual situations, one may gain a deeper understanding. The present experience is always related to past and future experiences [82], as outlined in phenomenology. As such, the participants' earlier experiences from cancer in the family, and future perspectives are essential for understanding their present lived experiences. In this sense, it is based on the understanding of time as lived experiences focusing on the individual story describing the specific context, but simultaneously recognizing patterns in spite of variations [83]. In addition, we are all part of the lifeworld and perceive and explore the experiences of others from a subject position. It is essential to be aware that as researchers we are always already intertwined in the lifeworld, and are thereby bound to subjectivity [84, 85]. In this case, the subject position of a genetic counsellor, the principal investigator. The experience and knowledge about living with hereditary cancer risk is part of the fundament for exploring the participants' experiences. This is also a position to challenge consciously underway, in order to be open in the encounters with the participants.

A narrative approach was utilized in Study 3 (Paper IV) to gain a deeper contextual insight into what was identified as the main structure in this study. By focusing on each individual's specific story, this approach makes it possible to grasp the participants' own understanding of their situation [83]. As a narrative story traditionally is regarded as a meaningful whole containing a beginning, middle and an end, following this structure may open up possibilities to describe the meaningful whole from the participants' perspective. By following each participant's storyline we are able to describe lived time by concretising how the present is coloured by past experiences and expectations of the future. At the same time as we are able to

understand (describe) the individual story in context, we also may recognize patterns in spite of variations.

4.2 Participants

This thesis contains data collected from qualitative semi-structured interviews with Swedish MEN1 patients and in-depth-interviews with Norwegian BRCA1/2 mutation positive men.

4.2.1 Swedish MEN1 patients (Study 1)

The first aim of the study was to explore and describe the experiences of Swedish male and female MEN1 patients. The participants were recruited through a specialist ward for MEN1 patients in Sweden. Ninety percent of all Swedish MEN1 patients come to this particular hospital ward on a regular basis. Written information and an invitation to participate in the study were sent together with an appointment time to the clinical follow-up program. As this study was part of a larger study, the participants were also monitored with questionnaires in the same timeframe and location. Results from these questionnaires are described elsewhere [56]. The participants were included according to the following criteria;

- They should have a mutation detected or clinical symptoms of MEN1
- They should be Swedish speaking
- They should have no present known psychiatric disease and/or drug abuse
- They should have no identified distant cancer metastasis

During a one-year time period in 2000-2001, 16 men and 13 women (29/36) were included in the study. Five declined participation, and two were not invited to participate due to recent diagnosis. They ranged in age from 28-85 years and 25 had undergone prior surgical treatment. Nine had Interferon or chemotherapy treatment. None of the participants had attended genetic counseling at the time of the interviews. All were included in follow-up programs on a regular basis. The analysis of the qualitative interview started in March 2005.

4.2.2 Norwegian BRCA1/2 mutation positive men (Study 3)

The third aim of the study was to explore and describe the experience of Norwegian

male BRCA1/2 mutation carriers. The participants were recruited through two departments of Clinical Genetics at University Hospitals in Norway in 2008. They were included according to the following criteria;

- They were men older than 18 years and able to read and understand Norwegian
- They were identified as BRCA1 or BRCA2 mutation positive
- It was more than six months since the disclosure of their test results

Invitation letters and written information were sent from the two departments to 43 BRCA1/2 mutation positive males in 19 different families. The authors were not a part of this process. The invitation letter also included a postage paid envelope with direct contact information for the principal investigator. The males who wanted to participate in the study returned the consent form, and the principal investigator contacted them by phone. In order to obtain knowledge about male and female communication and family dynamics, their current partners were also invited to participate in the study. No reminders were sent to those who did not respond to the invitation letter. A total of 15 BRCA1/2 mutation positive men from 12 different families and seven female partners participated in the study. The males ranged in age from 26 to 73 years (Mdn=51). One was diagnosed with cancer after the disclosure of his test result. This information was not known when he was included in the study and came to our attention during the first interview.

All the males had attended genetic counseling both prior to genetic testing and at the disclosure of their test results as required by Norwegian law. Two to six years had elapsed since the men received their test results and none of the participants had further genetic counseling after the disclosure of their test results. None of the participants were enrolled in follow-up programs at the time of the interviews.

4.3 Data collection

In this thesis data collection has been performed by qualitative research interviews (Study 1 and 3) and through literature search (Study 2).

Qualitative interviews were performed in order to learn about the participants' experiences of living with hereditary cancer risk. This is described to be a suitable

method for learning about persons lived experiences [80, 86]. According to Kvale [80] a professional research interview involves a specific technique of questioning, and is said to be semi-structured. He states that it is not an open conversation, nor highly structured questionnaire. The interview is conducted according to an interview guide containing themes, and may also include certain concrete questions [80]. The aim of a qualitative interview is to grasp the participants' experiences as complete as possible by describing and understanding the meaning of central themes in the participants' lives [80, 87]. However, this may not always be easy, and many difficulties may occur during the interview. Issues like reticence to talk, or the tendency to talk about everything but the phenomena of interest may occur. In these situations it is legitimate to lead the participant back to the subject in focus. It is important to distinguish between "directing" and "leading" the participant. In these cases "directing" refers to guiding the participant to talk about the phenomena of interest. "Leading" however, refers to the researchers attempt to get the participant to express particular issues desired and thereby biasing the data [87].

4.3.1 Swedish MEN1 patients (Study 1)

The individual interviews were performed by two Swedish psychologists on the day of arrival to the hospital ward. As this study was part of a larger QoL study, the participants were also monitored with questionnaires in the same timeframe and location. Results from these questionnaires are described elsewhere [56]. An interview guide based upon Griffin's theory [71], validated in a pilot study on an empirical views of life, [88] was utilized in the individual interviews. In addition the participants were encouraged to expound on issues important to them. Semi-structured questions also explored the participants' experiences of living with the condition in the family, the consequences upon daily activities and participating in a clinical follow-up program. The interviews lasted on average one hour, and were recorded and fully transcribed. The principal investigator received both the tapes and the written transcripts.

4.3.2 A systematic review of men in HBOC families (Study 2)

Data collection in the review study was performed by searching in Pubmed, Cinahl, Embase, PsycINFO and Cochrane Library. The search terms used were: “Genetic counseling” and “cancer risk” and “males”, “risk perception” and “neoplasm” and “males”, “risk management” and “counseling” or “counselling” and “males”. The first searches were performed in January 2007. Eight studies regarding males only in HBOC families were identified and included in the study. Due to the limited sample, six studies where males or gender differences in HBOC families were commented separately were also identified and included. New searches using the same search terms were performed in 2008.

Studies were included according to the following criteria:

- Studies regarding males only in HBOC families
- Studies where males or gender differences in HBOC families were commented separately

Studies describing both males and females but where men were not commented separately, were not included in the study.

Eight studies regarding males only in HBOC families and six studies describing males or gender differences were identified. A total of 14 qualitative and quantitative methods studies conducted from 1996 to 2007 were identified and included.

4.3.3 Norwegian BRCA1/2 mutation positive men (Study 3)

Two separate in-depth interviews were performed in 2008 with a time interval from two to five weeks. The interviews were performed by the principle investigator, and took place in a local Clinical Genetics Department or at another location preferred by the participants. Only the males were included in the first interview, and their current partners were invited to participate in the second interview. This was done in order to obtain knowledge about male and female communication and family dynamics. In seven cases the two interviews were performed with the male only, and seven female partners participated in the second interview. One participant was not able to participate in the second interview for practical reasons. Between two to eight years had elapsed after the disclosure of their test results. An interview guide developed by the research group was utilized (see Appendix 9). The interviews lasted on average

40 minutes. Due to technical problems in one interview notes were taken. All other interviews were recorded and fully transcribed. The transcriptions were performed by trusted administrative staff at one of the Clinical Genetics departments and validated by the principal investigator.

4.4 Analysis

Giorgi's phenomenological approach was used to analyse the data in Study 1 (paper I) and Study 3 (paper III and IV). In study 3 transcripts from both interviews were analysed simultaneously in order to get a complete overview over the participants' stories. A thematic theoretical analysis was utilized in Study 2 (paper II).

In Study 1 both structured and semi-structured questions have been utilized. In the analysis only the responses from the semi-structured questions were taken into account as very limited information was obtained from the responses from the structured questions.

4.4.1 Giorgi's phenomenological analysis

The data were analysed in accordance with Giorgi's four step analysis [81]:

- The first step was to get a grasp of the whole by reading the text thoroughly several times, and the tapes from the interviews were listened through repeatedly. Especially in Study 1 where the interviews had been performed by others than the principal investigator, it was important to grasp nuances in the communication between the interviewers and the participants. Some of the interview transcripts were also read by co-authors. However, according to Giorgi the person analyzing the data need not have been the interviewer [87]. In study 2 B it was important to get a complete overview over the participant's descriptions by reading both interviews simultaneously. It was also essential to grasp the differences between the men's perspective and their female partner's experiences.
- This made the basis for the next step where the attention was drawn to each participant and each interview was read again in order to discriminate meaning units. In this step the text was broken down to manageable units, and the focus

was on the experiences of living with increased risk of developing cancer. It was important according to Giorgi that the discriminations were done spontaneously, and a mark was made in the data when a shift in meaning was identified. Giorgi recommends using a professional perspective in this process of analysis [81], and the principal investigator's experience and understanding of hereditary cancer as a genetic counselor was guiding in this part of the analysis. The perceived meaning unit discriminations were defined when the researcher became aware of a change of meaning toward a concrete description, and one co-author participated in this process. The focus was on the participant's experiences after learning about their mutation status and their experiences of living with a genetic condition. This procedure is defined to be science in the context of discovery instead of science in the context of verification, and the attention was aimed at catching what was important to the participants [81, 87].

- According to Giorgi, the third step is the heart of the analysis [87]. By returning to the early descriptions now delineated into meaning units, the everyday language of the meaning units was transformed into professional terminology with the attention on the participant's experiences. It was a tension between the general description and the concrete situations described by the participants. In this step the process and the concrete formulations were discussed between the authors. The intention of phenomenology is to create a general description by going through the concrete story, striving to bring forth what was important to the individual participant in living with hereditary cancer risk [81].
- In the last step of the analysis the transformed meaning units were synthesized into a consistent description regarding the individual participant's experience. In this process all transformed meaning units were considered. It is however difficult to describe a general structure based upon only one instance, and therefore variations across individuals were made. Several subjects create larger variations and improve the ability to notice what is essential at the level

of the phenomenon. Special structures might however be important, and could sometimes rely on one single subject.

The data program NUD*IST (Nonnumeric Unstructured Data Indexing Searching and Theorizing) computer software was used to organize and analyze the interviews.

4.4.2 Thematic theoretical analysis

In Study 2 a thematic theoretical analyses was utilized. As only limited studies regarding men in HBOC families were available, both qualitative and quantitative studies were included. A thematic analysis is known to be applied across different theoretical approaches, and is regarded as suitable in converting quantitative data into a qualitative form [73]. This analysis is also regarded as suitable in areas where few studies are available [89]. The data were analyzed in accordance with the six steps analysis described by Braun and Clarke [89];

- Initially, the articles were read and re-read in order to become familiar with the data. Notes were taken and resumes from all the papers were written. The main impression from the papers was discussed with two co-authors.
- Secondly the initial codes from the data were produced. In this process of analysis it was a constant moving back to the first step reading the papers again in order to secure that the findings in the studies was correctly understood. In this part of the analysis the papers concerning men only were first coded. Next, the same procedure was performed with the papers dealing with men and women where the males were commented separately. Concepts or key findings from the quantitative studies were extracted and coded verbally in order to transform these into a qualitative textual form as described by Pope et al. [73].
- In the third step the different codes were sorted into potential themes. In order to integrate the qualitative and quantitative evidence, the codes from the quantitative studies were also developed into potential themes.
- Fourthly, the themes were reviewed, securing that all the codes from the data had been taken into account.

- In the fifth step the themes were defined and named. In this part of the analysis, the formulations of the concrete themes were developed.
- Finally, the report was written. However, writing the paper was a continuous process moving back and forth between the various steps in the analysis. During the entire process of the thematic analysis, the coding of data and the formulation of the concrete themes was discussed between the authors.

4.4.3 Narrative approach

In order to gain a deeper contextual insight into the main structure in Study 3, a narrative approach was chosen. This approach makes it possible to focus on the individual story [83] and describes the specific context, but simultaneously recognizes patterns in spite of variations. In most interviews the initial question, asking the participants to tell how they became aware of the family mutation and their decision to perform genetic testing generated a long narrative story. The interviews were listened through once more, this time focusing on the fourth core theme as a story. In order to create meaning from experience or to describe human experience [90], individuals may organize non-systematic encounters into coherent stories [91]. These narrative stories are described to contain a beginning, middle and an end [92]. The study of the participants' responses as narratives and the effort to empower these males are also closely related [93]. One important way to understand and give meaning to individuals is to organize experiences into a narrative form [93]. By letting the participants speak in their own "voices" they are more likely to tell stories [93]. In this case the narrative stories contribute to the understanding of their own experiences as BRCA1/2 mutation positive.

5. Ethics

Confidentiality in research is an important issue. In order to protect the participants' privacy, anonymity was ensured during the process of data analysis and presentation of the results. Private data that might identify the participants were not reported.

5.1.1 The researcher's role

According to Kvale [80] three ethical aspects are described; scientific responsibility, relation to the subjects, and researcher independence [80]. The researcher uses him-or herself as an instrument for obtaining knowledge in interviews. It is therefore important that the researcher has the sensibility to identify ethical issues and the ability to act appropriately upon these issues. In this study the principal investigator has been conscious about referring the participants in Study 3 to genetic counseling after the interviews in order to avoid the role of a genetic counselor. It was also important to be aware of too close interpersonal interactions with the participants to maintain a professional researcher's view. In the study of the Swedish MEN1 patients, the principal investigator was not in contact with the participants.

5.1.2 Swedish MEN1 patients (Study 1)

Approval for this study was obtained through the local Research Ethics Committee at the Swedish University hospital (see Appendix 1). An invitation letter with information was sent together with the time appointment to the clinical follow-up (see Appendix 2). At their arrival at the clinic they decided if they wanted to participate or not. Voluntary participation and their right to withdraw from the study were described in the invitation letter. It was also pinpointed that their potential refusal to participate in the study would not have any consequences for their medical treatment. The participants were also asked for permission to review data from their medical records. The individual interviews were performed by two psychologists. The principal investigator received the interview transcripts and the tapes. These data have been kept safe and unavailable to others.

5.1.3 Norwegian BRCA1/2 mutation positive men (Study 3)

The study was approved by a Regional Scientific Ethics Committee and the Norwegian Data Inspectorate (see Appendix 4-5). The participants received an information letter together with the invitation to participate in the study (see Appendix 6). Voluntary participation and their right to withdraw from the study were pinpointed. No reminders were sent to those who did not respond to the invitation. Written informed consent was requested and obtained for all participants and their partners. Two separate consent forms were obtained in cases where their current partner participated (see Appendix 7-8). The written transcripts and tapes from the interviews have been kept secured unavailable to others, and will be deleted after the study is completed. The Regional Scientific Ethics Committee has permitted that these data may be kept until 31.12.11(see Appendix 10).

All participants were offered additional genetic counseling in one of the departments of Clinical Genetics after the interviews were completed. Ten participants attended genetic counseling after the interviews, and an additional three wanted a new genetic counseling session later in time. If some of the participants experienced strong emotional reactions after the interviews, a psychologist familiar with genetic issues was available for the participants. None of the participants accepted this offer. Some of the males were still in the process of integrating the knowledge in their lives when the interviews were performed. The interviews might influence upon this process. Also, the topics discussed in the interviews included sensitive information, and it was important to respect the participants' personal boundaries. According to Fog [86] it is always a balance between only scraping the surface and passing the others "borders".

6. Results

The main results from the four papers in this thesis are presented below.

6.1 Living with Multiple Endocrine Neoplasia. Decent Care-Insufficient Medical and Genetic Information (Paper I)

The first aim of the study was to explore and describe the experiences of Swedish male and female MEN1 patients. Four main categories and several subcategories were identified; (1) the mixed feelings of being in a follow-up program, (2) the effect of MEN1 upon daily activities, (3) coming to terms with the condition, and (4) uncertainty concerning the future.

The findings indicate that most of the participants have adjusted to their situation. They experienced decent care but lack of information in the clinical follow-up program. Needs for informative communication and better access to test results were also expressed. The genetic condition had impact on their everyday life by causing pain, job insecurity, and feelings of guilt. Despite suffering from physical and psychological symptoms, they described themselves as being healthy. However, they expressed a change in priorities after developing MEN1 or learning about their personal risk. Due to uncertainty regarding their physical condition, the participants also described a short-term perspective in future planning. This study concludes that these patients are in need of medical and genetic information, and they should have access to genetic counseling.

6.2 Men in the women's world of hereditary breast and ovarian cancer – a systematic review (Paper II)

The second aim of the study was to conduct a systematic review of the literature to explore and describe the existing psychosocial studies of male experiences in HBOC families.

A systematic review of the sparse previous evidence identified two main themes; (1) women's influence and (2) the psychological impact on men. Women are described to influence male decision-making and to play the leading role in communicating risk information in the family. Several studies pinpoint that men's decision to seek genetic counseling and testing is considered as an obligation to their children or a family duty. Wives are described to take responsibility for informing family members, including children, and males address a need to learn how to communicate genetic information. With respect to psychological impact, males are said to suffer from intrusive feelings stemming from unresolved grief and use avoidance as a coping strategy. Previous research also describes feelings of guilt because they might have passed on the family mutation to their children. The men also felt guilty if their relatives were identified as mutation positive and they themselves turned out to be mutation negative. The review reports that males would use the genetic test results for reproductive decisions, and describes impact on familial relationships.

6.3 Stigmatization and male identity: Norwegian males' experience after identification as BRCA1/2 mutation carriers (Paper III)

The third aim of the study was to explore and describe the experience of male BRCA1/2 mutation carriers in Norway in order to gain deeper understanding of their situation. Two successive in-depth interviews were performed with 15 males. Seven female partners participated in the second interview. Four core themes were identified, and this paper presents three of the themes: (1) strong feelings after identification as a mutation carrier, (2) difficulties in communicating, and (3) hope and thoughts for the future. The participants experienced anxiety, feelings of sadness and unfairness after the disclosure of their unfavourable test results. Feelings of loneliness and disappointment were also described. Due to fear of being stigmatized, most participants felt it important to keep the genetic information private. They also described difficulties in communicating with other men about health related issues and emotional reactions, and preferred to discuss these issues with women. Many had not informed their children about the family mutation mainly because of their young

age, or because they knew that their children were struggling with other difficult life events. In some cases their wives communicated the genetic risk information to their children. Family secrets were revealed during the genetic testing process, initiating emotional reactions new questions. Some of the participants learned that they had additional sisters. The participants expressed hope for the future and believed in future medications for preventing cancer development. Primarily, however, the men hoped that their children had not inherited the mutation. Religious beliefs and hope of meeting their deceased relatives after death were present in some of the stories.

6.4 Cancer worry among Norwegian male BRCA1/2 mutation carriers (Paper IV)

The data for this paper is collected from the same interviews as described in paper III. This paper presents the fourth core theme: Fear of cancer development. This was the main finding in the study, and two narrative patterns represent typical features: (1) fear for their own health, including fear of developing cancer and (2) negative feelings of responsibility for other family members' health. The participants' narrative stories started when they learned about the family mutation. In the middle they described the process of genetic counseling and testing and their emotional reactions. The end of the story was described to be their present situation at the time of the interviews.

The first narrative pattern describes how the disclosure of the participants' unfavourable test resulted in fear of developing cancer and a need for additional genetic risk information. Emotional reactions due to their test results were expressed, and need for emotional and informational support some time after the disclosure of their mutation status was described. Being aware of possible cancer symptoms had become a part of their everyday-life after learning about their mutation status. At the time of the interviews, the participants also questioned whether the future might reveal additional knowledge regarding male risk. The second narrative pattern describes the men's feelings of responsibility for other family members' health. The participants expressed that concern for their children was their main motivation for

genetic testing when they became aware of the family mutation. After learning about their mutation status, the men experienced deep concern for their children and siblings, in particular daughters and sisters. Feelings of guilt were also expressed especially in relation to daughters. Worries for cancer risk amongst young grandchildren were also described. Questions and thoughts regarding actual risks and risk reduction options for their female relatives had become part of their everyday life.

7. Discussion

This chapter is divided into three parts: methodological considerations; general discussion of the findings and possible implications for clinical practice.

7.1 Methodological considerations

The overall aim of the study was to explore and describe the experience of two patient groups living with high and slightly increased risk for hereditary cancer. Different methodological approaches have been utilized in order to respond to the overall aim of the study. This thesis includes analysis of semi-structured qualitative interviews with Swedish MEN1 patients performed by persons other than the principal investigator, a systematic review of the psychosocial studies regarding males in HBOC families, and two successive qualitative in-depth interviews with Norwegian male BRCA1/2 mutation carriers.

In Study 1 the findings are referred to as main categories and in Study 2 and 3 as themes. However, in light of the learning process during the studies in this thesis, the findings in Study 1 also should have been referred to as themes. According to Morse [94] the terms categories and themes are sometimes used almost interchangeably in completed research. It is however important to distinguish between these two concepts. A category is described to be a collection of similar data which makes it possible to identify and describe the characteristics. The category itself may also be defined, compared and contrasted with other categories. Broader categories may be divided into smaller categories (subcategories) [94].

A theme is defined to be a meaningful “essence” that runs through the data [94] (p. 727), and captures something vital in the data related to the research question [89]. It also represents some patterned response or meaning in the data [89]. As the findings in Study 1 are in line with the definition of themes, it should also have been referred to as themes.

7.1.1 Swedish MEN1 patients (Study 1)

The interviews in this study contained originally both structured and semi-structured questions. The inclusion of structured interviews must be understood in the context of the larger study. However, the structured questions brought little new knowledge, and the inclusion of these in the first place may be questioned. The structured part of the interviews was not included in the analysis. Vital information was however obtained from the semi-structured questions in the study, as they were open and facilitated spontaneous, lively and unexpected answers. In qualitative interviews access to the participants' stories and experiences is obtained through dialogic conversation [80, 95]. In this study the participants' experiences may have been more extensively explored. On the other hand, the Swedish researchers wanted to highlight aspects already included in the larger study. 29 participants may also be regarded as a large sample size in qualitative research. According to Giorgi all data collected have to be analyzed [87], and the length of the interviews made it manageable to analyze all data.

One issue to discuss is possible loss of non-verbal communication as the interviews were performed by other persons than the principal investigator. However, the principal investigator had access to the tapes and the transcripts, and listened through the tapes carefully. On the other hand, having another researcher analyzing the interview data might have brought new insight into the study. Also, according to Giorgi the person analysing the transcripts need not have been the interviewer [87]. He also suggests that some of the liveliness in the dialogue could be helpful to the researcher during analysis, and attended to by listening to the interview records. There are a cultural and language differences between Sweden and Norway. The interviews were carried out by Swedish interviewers with Swedish participants, and the analysis was performed by Norwegians. There are also differences in medical and genetic clinical practice and legislation. However, having the Swedish researchers who performed the interviews as co-authors contributed to confirm the understanding.

It is also important to notice that at the time of the interview only 22 % of the participants had an identified MEN1 gene mutation. The low number of mutation positive participants is in contrast to other studies in the same timeframe who report a detection rate of 85-95% for MEN1 in families with suggestive clinical features [96, 97]. Included participants have, however, been diagnosed with MEN1 either through meeting clinical criteria or through genetic testing. Our study did not specifically explore if there were differences in how patients experienced their situation or in how they experienced follow up between these two groups.

7.1.2 A systematic review of men in HBOC families (Study 2)

Due to the limitation in available studies, both qualitative and quantitative studies were included in the review. As such, no common quality assessment tool has been utilized and the quality of the included studies has therefore not been evaluated. It is underscored that the results from the studies are presented differently depending on if they derive from qualitative or quantitative studies [74]. Quantitative studies report results from numeric data based on questionnaires, while qualitative research provides rich descriptions and understanding [98]. This issue may have had an impact on the analysis in this study. However, some approaches have been described as suitable to integrate qualitative and quantitative research evidence [74] e.g. thematic analysis as used in our case.

7.1.3 Norwegian BRCA1/2 mutation positive men (Study 3)

A process was initiated during the first interview, and some participants had discussed genetic and familial issues with close family members when they returned to the second interview. Interestingly, new information appeared in the second interview on several levels. This was mainly an advantage in the cases where the male participated alone in the two interviews. However, in some cases where their female partners participated in the second interview, their partners added information about the participants which was embarrassing for the men. For ethical reasons this has not been described in the papers.

Most of the male BRCA mutation carriers had many questions regarding their own

and their family situation when they came to the interviews. In some cases it was important to respond to the most urgent questions before the interview started. If new questions appeared during the interview, the tape recorder was turned off when answering questions in order to distinguish between the interview situation and the response to their questions. As the principal investigator performing the interviews is a genetic counselor, it was crucial to distinguish between this role and the role of being a researcher. Otherwise the research interview could easily have turned into a therapeutic interview. It is important to distinguish between a qualitative research interview and a therapeutic interview [80]. The purpose of the research interview is to obtain knowledge of the phenomena investigated. Observed changes in the interviewed person are described to be a side effect. In contrast, the therapeutic interview seeks for changes in the patient, and knowledge acquired in this situation is a side effect of helping the patient [80].

In this study it was important to focus on the research situation. At the same time, the participants had an unmet need for information and counseling. It is essential to notice that a process was initiated in the first interview leading to new information about family members or additional questions from the participants when they returned to the second interview. This was particularly present in the seven cases where the males participated without their partners present in the second interview. All participants were offered genetic counseling sessions between the interviews or after both interviews were completed. These counseling sessions were performed by others than the principal investigator. Several of the participants expressed gratitude for having been invited to participate in the study. They also questioned whether health professionals deliberately held back genetic risk information regarding males.

7.1.4 Reliability and validity

Reliability in qualitative studies is regarded as the trustworthiness of the procedures and the data generated, and is also a necessity for the validity in a study [99]. The validity of a study refers to the degree that a method investigates what was the intention to investigate [80]. According to Malterud [100] the internal validity in qualitative research asks whether the study investigates what it was meant to, whereas

external validity asks in what contexts the findings can be applied [100] (p. 484). Possible threat to validity in qualitative studies may be caused by researcher's bias like selective data collection or interpretation based on personal perspectives [101, 102]. Familiarity with the particular phenomena investigated may be either an advantage or a drawback, or even both. Being familiar with the phenomena investigated may open the possibility for losing important information by overlooking nuances [101]. On the other hand, being familiar with the investigated subject makes it easier to identify relevant questions to ask, as well as less necessary for the researcher to intervene unnecessarily in the dialogue by asking questions in order to clarify. In this study the principal investigator is a genetic counselor with long standing experience in counseling for cancer. Two co-authors outside of the field of genetic counseling have read some of the interview transcripts, and participated in the process of analyzing the data. Also, the interviews with the Swedish MEN1 patients were performed by others than the persons analysing the data. This may indicate valuable distance, but also less knowledge about the situations where the data was produced.

Another way of enhancing validity by avoiding researchers' bias in descriptive phenomenological research is the use of bracketing, a term first described by Husserl [103]. This relates to the researchers attempt to suspend their own experience, judgement and beliefs. This claim might be difficult, if not, impossible, to fulfil, but the validity of the results from the study may be increased if the process of bracketing means reflecting consciously and openly on these issues and described by the researcher [101]. In Study 1, the person analysing the data did not participate in the development of the interview guide or in the interviews. As MEN1 is a rare condition, both the interviewers and the principal investigator had little clinical experience with these patients, which may be considered an advantage as well as a drawback. Furthermore, the researcher was very conscious about the knowledge obtained during the work of the review paper (Study 2), when starting Study 3. This consciousness was based on the awareness of not jumping into conclusions or restraining openness when starting Study 3. The understanding of a phenomenon

includes both openness and the researcher's pre-understanding [75]. In this study it was important to be aware of the researcher's background as a genetic counsellor, and it was essential to balance restraining and using pre-understandings. Also, in this study two successive interviews were performed, and the principal investigator listened to the transcripts from the first interview prior to the second interview. In this manner it was possible to verify that information obtained in the first interview was understood correctly, and the participants had the opportunity to add new information. Also, new information not described earlier appeared in the second interview.

Technical accuracy in recording and transcribing is also said to increase reliability [80]. In Study 1, the verbal transcripts and the tapes were made available for the principal investigator, who investigated the transcripts carefully while listening to the tapes. In Study 3 the transcriptions were performed by two trusted administrative staff, but the tapes were listened to by the principal investigator and the transcripts were checked simultaneously. Technical problems occurred in one interview, and notes were taken. All other interviews were recorded and fully transcribed. However, it is important to be aware of the transformation and reduction occurring from the richness of verbal and non-verbal information in the interview situation from tapes to transcripts [93]. In order to recall the non-verbal signals like laughter and cry from the interviews in the analysis, the principal investigator listened to the tapes repeatedly when analysing the transcripts.

During the entire process of analysis in Study 1 and 3, one co-author guided the process. Another co-author also participated in vital discussions during this process in Study 3. In Study 2, a thematic theoretical analysis was performed. The identified themes and the defining of the concrete formulations of the themes were discussed between the authors during the entire research process. Verbatim examples of the participants' comments were used in the results sections in Study 1 and 3. This is also said to enhance the reliability. It is however important that the examples reflect the general responses generated, and not simply picking the most vivid quotations [101].

It is also suggested that letting another researcher follow the analysis to enhance reliability may reduce jumping to conclusions. This might however also be questioned because the reduction and search for variation is part of the phenomenological analysis and are based on the researcher's reflection [81]. Generally, the researcher (s) must take responsibility for the analysis and the interpretations of core meanings.

Reliability may be enhanced by using computerized data analysis packages [101]. In Study 1 and 3 the data program NUD*IST (Nonnumerical Unstructured Data Indexing Searching and Theorizing) was used to organize and analyze the interviews. This data program made it possible to move back and forward between the interview transcripts, the preliminary themes and the transformed meaning units. It also made it possible to trace prior steps in the analysis. The qualitative studies included in this thesis have small sample sizes. It has been said that small sample sizes in the reporting in qualitative studies have given the impression that the results have little application to other populations [98]. More relevant than reducing the question about transferability to sample size is questions related to detailed and contextualised descriptions, development of clinically useful insights and/or concepts, interpretations of core meanings according to relevant theory, and the level of abstractions reached in the analysis. All of this depends on the quality of the research material as well as the analysis. Also, the vital distinction between internal and external validity in quantitative research is not essential when the aim of the research is not mainly generalizability to populations [104]. Malterud [100] defines the external validity of qualitative research as: "*The findings from a qualitative study are not thought of as facts that are applicable to the population at large, but rather as descriptions, notions, or theories applicable within a specified setting*" [100] (p. 486). An important question in our case is for instance concerning what Kvale [80] terms pragmatic validity, namely if genetic counselors find knowledge from our studies relevant and useful in their clinical practice.

7.2 General discussion of the findings

The overall aim of this study was to explore and describe the experience of two patient groups living with high and slightly increased risk for hereditary cancer. The results from both patient groups will be discussed simultaneously in this section. Even though the interviews designs of the two patient groups differ, and the qualitative interviews were performed by different interviewers, both studies still give insight into the participants' experiences of living with hereditary cancer.

The MEN1 patients experienced good care, but insufficient information in the clinical follow-up program. They also described pain, job insecurity, and feelings of guilt towards their children. A change in values and short-term perspective in future planning after learning about their condition was also expressed. The literature review identified females in HBOC families to play the leading role in all genetic activity in the family, and men's decision to seek genetic counseling and testing as a family duty. Men are said to suffer from feelings of guilt, intrusive feelings due to unresolved grief and to use avoidance as a coping strategy. Their genetic test results may have an impact on familial relationships and reproductive decisions. The Norwegian BRCA1/2 mutation positive men in this study experienced strong emotional reactions including fear of cancer, responsibility for other family members' health and an unmet need for risk information. They also kept the genetic information private and perceived females as their social network.

Findings from the studies in this thesis indicate that risk perception and emotional reactions do not seem to depend on estimated percentage risk. This is in line with previous evidence suggesting that it is difficult to interpret the patients' understanding of their risk level [105]. Information about future risk may also bring insecurity into people's lives [54, 106] and become a source of anxiety and worry [107, 108]. However, genetic counseling is described to improve the accuracy of perceived risk without increasing the fear of cancer [109, 110]. The MEN1 patients were in need of genetic information which could have been communicated to them through genetic counseling. Males identified as BRCA1/2 mutation positive currently

thought to be at low cancer risk not included in follow-up programs may be vulnerable, as they also seem to experience need for emotional or informative support. In the present study we learned that these men experienced cancer worries after learning about their mutation status. Their anxiety and need for risk information may be caused by their lack of enrolment in risk management program or other regular clinical contact, in contrast to the MEN1 patients who were enrolled in a follow-up program on a regular basis. However, this study also adds knowledge about high risk persons mixed feeling of being included in a follow-up program.

In contrast to the BRCA1/2 positive men, MEN1 patients had not attended genetic counseling prior to the genetic test. Genetic testing for MEN1 is regarded as a diagnostic test if the patients have symptoms, and the Norwegian and Swedish law does not mandate genetic counseling prior to and following diagnostic testing [34]. As such, these patients may be enrolled into follow-up programs without receiving any genetic counseling both in Norway and Sweden. Testing their relatives with no symptoms will however be considered as predictive testing, requiring genetic counseling according to the law [34]. Questions arise as to whether it is acceptable that persons suffering from symptoms are not entitled to the same information as their healthy siblings prior to a genetic test.

In this study it has been described that male's genetic test results may have an impact on reproductive issues. This is in line with previous evidence suggesting that genetic risk information may have an impact on decision making processes [111]. Both the Swedish MEN1 patients and the Norwegian BRCA mutation carriers also expressed feelings of guilt towards their children and concern for their offspring's future health [112-114]. In some countries prenatal diagnosis (PND) and preimplantation genetic diagnosis (PGD) for inherited cancer syndromes are discussed [115]. In these discussions it seems to be difficult to reach a consensus on what conditions that should give access to PND and PGD. However, according to Norwegian legislation [34] this option has so far not been available for families with inherited cancer predispositions. None of the Norwegian and Swedish participants in this study mentioned this option during the interviews. In a potential future ethical debate it

might also be drawn a distinction between the two patient groups related to the difference in the objective risk and severity in these two conditions.

Study 2 described low rate of participation among men in HBOC families [116], and avoidance as a coping strategy amongst men was reported in some of the reviewed studies [116]. Studies report higher anxiety levels among cancer patients who declined genetic testing compared to those receiving test results regardless of the test results. Also persons who did not want to receive their test results were at risk for poorer psychological health [51, 117]. These findings are explained by a way of coping through avoidance [118]. We learned from reviewed studies [116] that women may have an influence on the men's decision to request genetic testing [116]. This might cause pressure on males that otherwise would not perform a genetic test interrupting their intention of coping through avoidance.

Risk perception may be influenced by factors like family history, the perceived nature of the potential outcome and the subjective numeric probability. The subjective perceived risk may however be modified during counseling [33]. Studies have shown that even though genetic counseling improves the accuracy of risk perception, it is still inaccurate after the counseling session [119, 120]. We learned that the male BRCA mutation carriers who had attended genetic counseling prior to the testing and at disclosure of test results also experienced need for risk information in line with the MEN1 patients who had never attended genetic counseling. According to Austin [33], the effect of risk communication in genetic counseling at a group level might be questioned. She suggests that by reflecting back to the patient issues like family history, the perceived severity of the disease and the pre-existing perceived risk during genetic counseling, the counselors should enable the patients to become more aware of factors that may influence their subjective risk perception [33].

The findings from our study also add knowledge about BRCA1/2 mutation positive men's fear of cancer and need of risk information after the disclosure of their test results as well as their feelings of loneliness. Even though their level of cancer risk

did not trigger access to medical follow-up on a regular basis, they still had educational and informational needs. They also described need of support in how to cope with their own and other family members' risk. As many participants were identified with Norwegian founder mutations with high penetrance [20], and lived in areas where these founder mutations are frequent in the population, many had experienced cancer and death in female family members. It is said that personal experience with the severity of the actual disease may influence on how individuals perceive their risk [33, 51]. Also population prevalence of the actual condition in the population may influence on risk perception [33]. Previous evidence suggests that individuals are primarily concerned with the emotional or supportive elements of genetic counseling and are seeking support and ways to cope with their risk [32, 51]. One aim in genetic counseling is to aid in empowerment [29]. Support in how to cope with their risk, may empower them to deal with their situation.

Both MEN1 patients and male BRCA1/2 mutation carriers experienced feelings of guilt, and being responsible for other family members' health. They also experienced psychological pain and problems with communicating their test results to their children and other family members. Both patient groups experienced their future as unsafe and unpredictable, particularly regarding risk of future disease. It is reported that cancer worry is associated with a need for more information [121], and it might be questioned whether their need for information enhanced both patient groups fear of disease. Previous evidence suggests that coping strategies may have a significant impact on health among persons at risk [122] and that patient education is important to mobilize and strengthen the individual resources in humans [30]. This corresponds well with one of Griffin's prudential values for QoL of not being victim of circumstances beyond one's control [71]. According to Antonovsky's Sense of Coherence (SOC) model a necessity for experiencing life as meaningful is to have some influence over one's own future and fate [47]. Vital in the SOC model is also the concept of comprehensibility which refers to whether human experiences are perceived as structured, predictable, and explainable, and is essential in coping with health related issues. Informational and emotional support may be crucial to both

patient groups in order to enhance comprehensibility and thereby empower them to deal with their situation.

Both patient groups living with high and slightly increased risk experienced a change in their health status due to disease or mutation status. Response shift is described to be a change in self-evaluation due to changes in health status [45]. This concept is rooted in the quantitative tradition of measuring QoL, and is thereby not in line with terminology rooted in the phenomenological tradition. However, the participants in this study described changes in their health status which may be associated with the response shift model. Both groups described a change in their lives after receiving their unfavourable test results or being diagnosed with a genetic condition. The physical healthy BRCA1/2 mutation positive men changed their focus and became more focused on possible cancer symptoms. MEN1 patients however, where many suffered from severe physical symptoms due to their condition, described having adjusted to the situation by changing their values. According to their new values, they considered themselves as healthy despite of physical symptoms. This is in line with the response shift model which is defined as a change of the individual subjective experience of QoL due to changes in internal standards, values and the perception of QoL [46]. However, individuals also have cognitive, affective and behavioural strategies like coping, social comparison and social support, goal recording, reframing of expectations and spiritual practices that may be involved in adapting to new situations [46]. According to Antonovsky, change of values may also be connected to the experience of meaningfulness [47].

In contrast to the MEN1 patients, the BRCA1/2 mutation positive men had not changed their internal standards or values in order to adjust to the situation when two to six years had elapsed since the males received their unfavourable test results. This difference may be due to the change in the perception of their health status from the identity of healthy into a person at risk, and “the source” of their children`s risk. Also, no available surveillance was made available for these men. In contrast, many of the MEN1 patients had suffered from clinical symptoms for many years without

receiving proper medical care at their local hospitals. Being diagnosed with MEN1 resulted in inclusion into a follow-up program which may have improved their QoL. According to the response-shift model, the BRCA1/2 mutation positive men were not able to maintain a sense of internal control after learning about their mutation status, and their perceived QoL may have been reduced. This is in line with findings amongst persons with increased risk of inheriting a mutation in p53, another gene involved with a hereditary cancer syndrome, where cancer worry was associated with lower QoL and increased perceived cancer risk. [123]. Information about the men's BRCA1/2 mutation status may have been experienced as a threat to the male identity facing a potential uncontrollable situation. It is said that masculine health is associated with a position of control and invulnerability [124].

The BRCA1/2 mutation positive males' problems in coping with this situation may also be due to lack of social network. From the findings in Study 2, we have learned that males in HBOC families seemed to be less able to communicate their BRCA1/2 test results than women [125, 126], and might have limited social support. In Study 3 we learned that men rarely discussed their mutation status or other health related issues with other men [113], and preferred to communicate with women in these matters. It is said that open communication regarding hereditary cancer and partner support may protect against hereditary cancer distress [127]. Social support may also be essential in dealing with disease-related stress [122], and lack of support and protective buffering were associated with greater distress among women testing for BRCA1/2 [128]. It is described among persons testing for Huntington disease that special attention should be paid to networks during genetic counseling, as persons with limited social network might be more vulnerable to depression [129]. This is in line with one of Griffin's prudential values for QoL which pinpoints the importance of a certain level of deep personal relationships [71]. This view is also consistent with the concept of manageability which is another constituent in Antonovsky's theory referring to individuals' ability to perceive available resources [47].

In contrast to the MEN1 patients, the BRCA1/2 mutation positive men appeared physical healthy since they had no visible signs or symptoms of their condition. Still they kept the information about their mutation status private, and had no contact with the health care system on a regular basis. Their desire to keep the genetic information private, may also be due to the fact that men in general tend not to make use of the health care system in the same manner as women [130]. Health care providers could however have represented a social network, and thereby have been perceived as available resources. The MEN1 patients included in a follow up program were diagnosed with a genetic condition, and many had physical symptoms. In contrast to the BRCA1/2 mutation positive men, they also met with others patients in the same situation in the specialty hospital ward, and were able to share information and experiences. However, even though the MEN1 patients experienced good care, they still were in need of medical and genetic information [112]. Their need of information was often related to test results which were not available when they left the hospital ward after their regular follow-up. These test results were closely related to an uncertain future with regard to potential development of disease.

Living with increased risk of developing cancer may be regarded as a chronic condition. According to the World Health Organization (WHO) the self management of patients with chronic disease should be strengthened [131]. In order to cope effectively with their condition on a daily basis, these patients must be provided with adequate tools and knowledge. In this way male BRCA1/2 mutation positive and MEN1 patients should be empowered to cope with their situation after having received information about a genetic vulnerability, or developed symptoms of illness. It is said that if risk information should be effectively utilized in health care management, the genetic information needs to be communicated outside the genetic services [132]. One way to provide these patients access to information and support networks is to increase contact and collaboration between the genetic departments in hospitals and the community health care. This does however require that the community health care is equipped with sufficient knowledge. Health issues suggested to improve collaboration between different levels of care have been

emphasized by the National Health Plan for Norway (2007–2010) [133]. Patients in our studies have experienced lack of knowledge when they addressed questions to their local GP [114]. This is also in line with findings amongst women in HBOC families [134]. In this study we have learned that some MEN1 patients had been ill for several years without receiving the proper diagnosis at their local hospitals. They did not receive the proper diagnosis and care before they were admitted to the special hospitality ward [112]. Also, these patients pessimistic outlook reported by Berglund et al. [56] seem to be related to difficulties in coping with an uncertain future, due to lack of information that could have been provided to them by their local GP.

Another reason for the reluctance to contact their local GP regarding their genetic condition might be fear of genetic discrimination. Both MEN1 patients and male BRCA1/2 mutation carriers feared that this genetic information might harm themselves or their children [112]. It is said that genetic discrimination may cause psychological distress [135] and could prevent people from genetic testing [136]. It is also reported that in addition to insurance companies, persons perceived genetic discrimination coming from health care providers, family, or other social or health domains [137, 138].

Several male BRCA1/2 mutation carriers received advices during genetic counseling to keep their mutation status private [113]. This advice may contribute to maintain their feelings of loneliness [113]. Their fear of being stigmatized also seemed to prevent them from addressing these questions with their community health care providers. There was however differences in how the two patient groups addressed their health related problems with health care professionals. MEN1 patients had contact with health professionals who had special knowledge about their condition on a regular basis, whilst the male BRCA1/2 mutation positive felt abandoned after the disclosure of their test results, and experienced lack of genetic knowledge amongst their GP's. Besides, they were also considered healthy as long as no symptoms have occurred, in contrast to MEN1 patients where almost all develop symptoms. Besides, health- care providers may not regard breast cancer as a male disease [64], and men

in HBOC families are often excluded from studies concerning psychological distress because of their low cancer risk [139-141].

It is vital that both patient groups regard their local GP's as available resources. The population density in Norway and Sweden is low, and many of the MEN1 patients may live far from the specialty hospital ward. The male BRCA1/2 mutation positive men have in most cases no contact with the genetic departments after the disclosure of their test results. In both patient groups a change with regard to their context of risk perception may occur if additional family members develop cancer. The participants risk perception may therefore change accordingly over time, and it is essential that both patient groups have available resources in their local areas.

7.3 Clinical implications

Our studies indicated that both patients with high and slightly increased risk of developing cancer are in need of educational and emotional support. The results from this study also pinpoint the need for counseling strategies, guidelines and follow-up programs for both patients diagnosed with MEN1 and male BRCA-1/2 mutation carriers. MEN1 patients despite being included in a follow-up program for many years are in need of genetic and medical information. This may also be due to lack of genetic counseling as none of the MEN1 patients in the study had attended such consultations. These patients should have access to genetic counseling even in cases where the test is diagnostic and counseling is not mandated by law. MEN1 patients pointed out that they often were unable to understand the content of medical test results performed in the hospital sent to them by mail, causing an uncertain future. Therefore, results from their medical test results should be provided to them either by phone or face to face in order to ensure that they understand the information. Their local GP's should also have been included in providing these test results.

Most of the BRCA1/2 mutation positive men accepted the offer for additional genetic counseling after the interviews. It is important to be aware of their need for emotional

support and ways to cope with their risk as this is said to have greater importance in the genetic counseling sessions than purely informational aspects [32, 51]. This may indicate a need for additional genetic counseling sometime after the disclosure of the test results. It would be essential to offer support on how to share genetic risk information with children and other family members. Although they themselves do not have very high risk of developing cancer, they experienced responsibility for other family member's health, in particular their daughters. Information about risk reduction options and surveillance programs for women should also be included in genetic counseling sessions for BRCA1/2 mutation positive males as many of the participants questioned this issue. The findings in this study also pinpoint that males do not communicate about genetic risk or health issues in the same manner as women [125, 142].

Male BRCA1/2 mutation carriers questioned their potential cancer risk, and wanted to receive information on a regular basis as they expected knowledge to improve in the future. There has been a change in the surveillance program for BRCA1/2 positive women as knowledge improves, and hopefully the understanding and management of male risk will also improve in the future. Recent evidence shows that PSA screening detects clinically significant prostate cancer in BRCA1/2 mutation positive men compared to the non-carrier control group [143]. There is also evidence to support that these men tend to develop a more aggressive cancer [143]. This raises the question on whether or not a surveillance program for male BRCA1/2 mutation carriers should or can be established in Norway.

One should be aware of both patient groups' feelings of being stigmatized, and health care providers should focus on how to prevent the patients' feelings of stigma. These patients might also profit from closer contact with community health care providers. The findings in this study also pinpoint the need for counseling strategies regarding risk information and strategies for empowering persons with both high and slightly increased risk of cancer to cope with their genetic condition. Health care providers may have a significant influence upon how persons with MEN1 and male BRCA1/2

mutation positive male cope with their genetic risk. The patients should be provided with adequate tools and knowledge to cope effectively with their condition on a daily basis. Better contact and collaboration between the clinical genetic departments and the local health care providers should be established in order to provide better care for these patients. So far, there are no international guidelines for counseling strategies for MEN1 patients or male BRCA1/2 mutation carriers. This is also reflected in the sparse available studies. Manner in which risk information is provided and timing of such information is important. It is said that genetic counselors should not use words like “high or low chance” in their clinical practice because individuals experience and perception and contexts may be different [33, 144]. Several genetic counseling sessions may be necessary in order to obtain optimal information about their actual situation for both these patient groups. The way these patients are counselled should also be evaluated.

In order to develop new guidelines, research findings must be implemented into clinical practice. Systematic reviews or research syntheses are essential in transferring research evidence between researchers and healthcare decision-makers [145]. It is however pinpointed that it is important to distinguish between research evidence as knowledge-support providing general background information and evidence for decision-support in a particular context [73]. Health care providers working in this field must also have sufficient skills about research methodology to transform research findings into clinical practice [146]. So far, there has been little research interest for the psychosocial issues for both these patients groups, and more studies are needed to provide insight about their experiences.

7.4 Implications for future research

The present findings raise new research questions. Further studies are needed to provide optimal care for both MEN1 patients and men seeking genetic counseling for hereditary breast and ovarian cancer. Future studies should explore how patients with MEN1 might profit from genetic counseling, and whether or not genetic counseling may have positive influence in dealing with their condition. Studies regarding their

informational and emotional needs in the follow-up program should also be conducted.

Further exploration on male emotional reactions including cancer fear after being identified as BRCA1/2 mutation positive should be conducted on other populations with both qualitative and quantitative study designs. Studies should also explore the impact on male social network and how genetic counseling may empower males to cope with their situation. One should also investigate the impact on partner's participation in the genetic counseling sessions. Research should be performed on the effect of follow-programs, and how health care providers may empower these patients to cope with their situation.

8. Conclusions

Feelings and understanding of genetic risk does not seem to depend on the numeric risk estimate. The results indicate that patients with both high and slightly increased risk of developing cancer are in need of educational and emotional support.

- Health care providers may have a significant influence upon how persons with MEN1 and male BRCA1/2 mutation positive male cope with their genetic risk on a daily basis. Patients with slightly increased risk, such as BRCA1/2 mutation positive men, with no indication for access to medical follow-up may have an unmet need of information.
- MEN1 patients described change in their personal values in order to adjust to their situation. This was not described among male BRCA1/2 mutation carriers and these men had not adjusted to their new health status.
- MEN1 patients' clinical follow-up program seems to play an essential part in these patients' lives, but they still described a need for genetic and medical information. They also had to deal with physical and psychological pain, lack of control over the progression of the disease and were facing an uncertain future. However, most patients had adjusted to living with the condition in their everyday life. These patients should have access to genetic counseling in the same manner as persons seeking predictive genetic testing.
- According to the sparse available previous evidences regarding men in HBOC families, these men worry about their own and their daughters' health, and are emotionally affected by the experiences of cancer amongst female relatives. Women are said to have an influence on male decision-making regarding genetic testing, and seem to play the leading role in communicating genetic information in the family. More research is needed about psychosocial consequences.

- Male BRCA1/2 mutation carriers experienced strong emotional reactions after learning about their mutation status, including fear of developing cancer and feelings of responsibility for other family members' health. Their needs of information were inadequately served. There is a need for counseling and follow-up strategies for BRCA1/2 mutation positive men. Contact with local health care providers should be established after the disclosure of their test results.

This study adds valuable insight into the experiences of two patient groups where little previous evidence exists.

9. References

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Original papers

