Mutation Carriers' Perspectives on Lynch Syndrome; self-concept and lived experiences.

Vendel Petersen, Helle

2012

Mutation Carriers' Perspectives on Lynch Syndrome

Self-concept and Lived Experiences

Helle Vendel Petersen

Doctoral dissertation
By due permission of the faculty of medicine, Lund University.
To be publicly defended in the Lecture Hall, Department of Oncology
Klinikgatan 7, Skånes Universitetssjukhus, Lund
at 14.00, Thursday December 6th, 2012

Faculty opponent
Professor Christoffer Johansen, Danish Cancer Society Research Center, Copenhagen, Denmark

Supervisors
Professor Mef Nilbert, MD,PhD
Christina Carlsson, RN, PhD

Organization
LUND UNIVERSITY

Department of Oncology
Institute of Clinical Sciences, Lund University
SE-221 85 Lund
Sweden

Author(s)
Helle Vendel Petersen

Document name
DOCTORAL DISSERTATION

Date of issue
December 6th 2012

Sponsoring organization
Copenhagen University Hospital, Hvidovre
The Danish Cancer Society

Title and subtitle

Mutation Carriers' Perspectives on Lynch Syndrome; Self-concept and Lived Experiences

Abstract

Lynch syndrome is a hereditary cancer syndrome that predisposes to several types of cancer, including colorectal cancer, endometrial cancer and ovarian cancer. Genetic testing for Lynch syndrome has been available since the mid-1990's, which implies that an increasing number of individuals live with knowledge of a high risk of cancer. Most individuals affected by Lynch syndrome experience increased levels of e.g. anxiety and distress after having learnt about a disease-predisposing mutation. In the majority of the individuals, the scores return to normal within 12 months. A smaller subset reports remaining high scores, which may indicate a need for psychosocial support. Global measures of may have a limited possibility to capture the psychological and social issues specifically associated with genetic testing and life at increased risk of cancer. This motivates our evaluation and application of more specific instruments related to the psychological impact from Lynch syndrome and our study of perspectives among healthy individuals at increased risk.

In *study I*, we evaluated the structure of the Lynch syndrome self-concept scale and its performance in three Lynch syndrome populations. The findings support the basic structure of the scale and its applicability in western populations.

Study II provides the first extended use of the Lynch syndrome self-concept scale through data collection from the entire Danish Lynch syndrome cohort. The results suggest that mutation carriers adapt well to the situation, though a subset reports adverse scores with a higher impact on self-concept.

In *study III*, sense of coherence (SOC) was assessed in individuals with Lynch syndrome and the data were correlated to self-concept. SOC scores in mutation carriers were similar to those in a general population. In the majority (76%), SOC and self-concept were in accordance. Discrepant subsets were identified, which likely reflects different aspects of finding life at increased risk difficult. Adverse scores on both scales, i.e. a low SOC and a high impact on self-concept, were reported by 10% of the individuals.

In *study IV*, the lived experiences among healthy mutation carriers in Lynch syndrome families were explored. The findings suggest that living with a high risk of cancer constitutes an act of balance, in which personal interpretation and family experiences combined with knowledge, contribute to how the individuals approach life at increased risk of cancer.

Key words
Lynch syndrome, psychological impact, self-concept, validity, sense of coherence, anxiety, lived experinces, questionaries phenomenology, interviews

Classification system and/or index terms (if any)

Supplementary bibliographical information

Language
English

ISSN and key title
1652-8220

ISBN
978-91-87189-62-3

Recipient's notes

Number of pages
122

Price

Security classification

Distribution by (name and address)

Mutation Carriers' Perspectives on Lynch Syndrome

Self-concept and Lived Experiences

Helle Vendel Petersen

LUND
UNIVERSITY

Faculty of Medicine
Department of Oncology
Lund University, Sweden

In collaboration with
HNPCC register, Clinical Research Center,
Copenhagen University Hospital, Hvidovre, Denmark

The family, presented on the cover of this thesis, is a Lynch syndrome family with 17 children. The picture was taken in 1953, when the family was gathered to celebrate the father's 65th birthday.

The picture is printed with permission from the family.

Contact information:,Clinical Research Center, Hvidovre Hospital, Kettegård allé, 2650 Hvidovre, DENMARK

Email: helle.vendel.petersen@hvh.regionh.dk

Faculty of Medicine
Department of Oncology, Lund University
ISBN 978-91-87189-62-3
ISSN 1652-8220

Printed in Sweden by Media-Tryck, Lund University
Lund 2012

Table of Contents

Original studies

This thesis is based on the following studies referred to in the text by their roman numerals:

I Petersen HV, Domanska K, Bendahl, PO, Wong J, Carlsson C, Bernstein I, Esplen MJ, Nilbert M. Validation of a self-concept scale for lynch syndrome in different nationalities. *Journal of Genetic Counselling; 2011 Jun;20(3):308-13.*

II Petersen HV, Esplen MJ, Ladelund S, Bernstein I, Sunde L, Carlsson C, Nilbert M. Limited impact on self-concept in individuals with Lynch syndrome; results from a national cohort study. *Familial Cancer; 2011 Dec;10(4):633-9.*

III Petersen HV, Ladelund S, Carlsson C, Nilbert M. Sense of Coherence and Self Concept in Lynch Syndrome. Submitted

IV Petersen HV, Nilbert M, Bernstein I, Carlsson C. Balancing life at risk of hereditary cancer -A phenomenological study of the long-term experiences of healthy carriers of Lynch syndrome. In manuscript

The studies were reprinted with permission from the publishers.

Contribution not included in the thesis but of relevance to the field:

Esplen MJ, Stuckless N, Gallinger S, Aronson M, Rothenmund H, Semotiuk K, Stokes J, Way C, Green J, Butler K, Petersen HV, Wong J. Development and validation of an instrument to measure the impact of genetic testing on self-concept in Lynch syndrome. *Clin Genet 2011; 80:415-23.*

Preface

Mapping of the human genome has made predictive genetic testing for various diseases possible. From a public health perspective, genetic testing provides opportunities for identification of individuals, in whom targeted interventions may prevent disease and cancer-related death. This development implies that a growing number of people live with knowledge of an increased risk of cancer.

Since genetic testing became possible concerns have been raised, among health care professionals as well as the public, whether information about an increased risk may be psychologically harmful, or whether it may rather be perceived as an advantage and possibility for intervention.

When individuals learn about a potentially increased risk of disease, principles of autonomy, beneficence, non-maleficence and justice must be met and ethical considerations regarding the individual's right "to know" and "not to know" are mandatory. Knowledge about the individual's perspectives and the short-term and long-term psychosocial impact from genetic testing is relevant in order to provide optimal support during counselling, diagnostic and surveillance for hereditary cancer.

Definitions

Definitions related to hereditary colorectal cancer:

FAP: Familial Adenomatous Polyposis

HNPCC: Hereditary Nonpolyposis Colorectal Cancer

Mismatch repair (MMR) genes: Genes responsible for the repair of DNA mismatches. When constitutionally mutated the MMR genes MLH1, MSH2, MSH6 and PMS2 cause Lynch syndrome

Principal component analysis (factor analysis): A statistical procedure that reduces a large set of variables into a smaller set of variables with common characteristics or underlying dimensions

Proband: The person within the family in whom a mutation is first verified

Self-concept: How we think about and perceive ourselves

Sense of coherence: A stress resource orientated concept that is thought to explain why some people stay well despite stressful situations and hardship

Definitions related to validity concepts:

Construct validity: The degree to which an instrument measures the construct under investigation

Content validity: The degree to which the items in an instrument adequately represents the universe of content

Convergent validity: An approach to construct validation that involves assessing the degree to which two measures of a construct are similar

Criterion validity: The correlation of a scale with some other measures of the trait or disorder under study

External validity: The degree to which the results of a study can be generalized to settings or samples others than the ones studied

Face validity: The extent to which an instrument indeed measures what it is supposed to measure

Internal consistency: The degree to which the subparts of an instrument all measure the same attribute or dimension, as a measure if the instruments reliability

Internal validity: The degree to which it can be inferred that the independent variable, rather than uncontrolled extraneous factors, is responsible for the effect observed

Reliability: The degree of consistency or dependability to which an instrument measures the attribute it is designed to measure

Background

Hereditary colorectal cancer and the Danish HNPCC register

In Denmark, almost 4000 individuals are annually diagnosed with colorectal cancer (www.DCCG.dk), which is one of the most common forms of cancer with a 5% risk in the general population (Anonymous, 2008). Colorectal cancer represents the third most common cancer type in both men and women and in Denmark (www.cancer.dk). Familial aggregation has long since been recognized (Lynch and Lynch, 2002). Epidemiological studies estimate that 20-30% of colorectal cancers are caused by hereditary factors, though only about 5% originate from a defined germline mutation (de la Chapelle A, 2005).

The Danish hereditary nonpolyposis colorectal cancer (HNPCC) register was established in 1991 at Hvidovre University hospital. Clinical geneticists, pathologists, surgeons and gynecologists contribute data to the register. Currently (October 2012) the register contains 2,600 families with suspected or verified hereditary colorectal cancer, of which about 1,600 are considered to be at increased risk (table 1) (Inge Bernstein, personal communication). To provide information to all Danes with suspected risk of hereditary colorectal cancer, the register was granted permission in 1997 to directly contact relatives of probands as an alternative to sharing information within the family. Relatives at risk are informed by mail and are invited to contact the register for genetic counseling.

Table 1. HNPCC and HNPCC-like families in the Danish register (October 2012)

Family type		**Families (n)**
Lynch syndrome families	Mutation verified	**251** **(931 individuals)**
Amsterdam I families	Three family members with CRC in two generations One < 50 years and one 1.degree relative to the others FAP excluded	**176**
Amsterdam II families	Like Amsterdam I, but now also including extra-colonic cancers	**28**
HNPCC suspected families	Two CRC in small family, one <50 years Two CRC and one adenoma or HNPCC related cancer Three CRC in a small family, one <50 years, not 1.degree relatives	**724**
Late onset families	As Amsterdam I, except none <50	**444**
Moderate risk families	One CRC <50 years Two CRC, none <50 years	**1,021**

CRC: Colorectal cancer

Genetic counselling

Individuals or families suspected of hereditary colorectal cancer should be referred for genetic counselling. From a public health perspective, the goal is to identify individuals at high risk of cancer in order to decrease morbidity and mortality. For the individual, the goal is to gain understanding of heredity and to adapt to the medical, psychological and familial implications of a genetic predisposition to disease. The individual needs to make informed decisions about genetic diagnostics and risk reducing strategies (Resta *et al.* 2006). The counselling process integrates establishment of a family history, verification of cancer diagnoses, risk estimates, education about the medical aspects of the condition and information about surveillance programs (Resta *et al.* 2006; Weissman *et al.* 2011). Genetic counselling is generally performed in two steps. The first session includes risk estimates, heredity and informed decisions about genetic testing. The second session typically deals with the test result and its implications and recommendations for surveillance (Trimbath and Giardiello, 2002).

Clinical guidelines related to genetic counselling generally emphasize issues related to information, education, clinical management and surveillance, but tend to give less attention to the psychological and psychosocial aspects of hereditary cancer (Butow and Lobb, 2004; Ellington *et al.* 2005; Resta *et al.* 2006). As genetic counselling aims to guide and support individuals and families with increased risk, understanding patients' perspectives and exploring the psychosocial dimensions of genetic counselling and testing are important (Bojesen *et al.* 2007; Trimbath and Giardiello, 2002).

Lynch syndrome

Historical perspective

Long before the identification of disease-predisposing mutations, families have been living with knowledge about a high cancer risk based on their family history. In 1895, the seamstress of Dr. Aldred Warthin told him that she was afraid of dying from cancer since several family members had been affected by cancer in the intestinal tract or in the genital organs. Dr. Warthin collected her family history and was the first to link gastrointestinal and gynaecological cancer to heredity when he in 1913 published a description of the family, which he called family G (Warthin A, 1985). The syndrome was rediscovered in the 1960's (Lynch and Krush, 1971b) when Dr. Henry Lynch revisited the family and described other similar families, and thereby confirmed the presence of dominantly inherited colorectal and endometrial cancer (Lynch and Krush, 1971a; Lynch and Krush, 1971b). In an early overview Dr. Lynch emphasized the importance that counselees recognize the potential personal and societal consequences of genetic testing, including its effect on psychological stress (Lynch *et al.* 1996).

In 1991, an international collaborative group agreed on the establishment of the Amsterdam criteria for uniformed classification of families with hereditary colorectal cancer (Vasen *et al.* 1991). The Amsterdam I criteria include three or more family members with histologically verified colorectal cancer, one of whom, should be a first-degree relative to the other two and at least two successive generations should be affected. At least one individual should be diagnosed before the age of 50 and familial adenomatous polyposis (FAP) should be excluded. Later, the criteria were broadened to the Amsterdam II criteria, which also include endometrial cancer, cancer of the upper urinary tract and cancer of the small bowel (Vasen *et al.* 1999). Though the Amsterdam criteria identify families with a high likelihood of Lynch syndrome, they cannot be used to exclude the syndrome since

many families escape detection, typically due to a few cases, small families or late age at onset. Among the Amsterdam positive families, only about half carry germline disease-predisposing mutations. Today, a combination of family history of cancer (pedigree) and histopathology/mismatch-repair (MMR) protein analysis is used to identify individuals suspected of HNPCC/Lynch syndrome. Lynch syndrome refers to families with a disease-predisposing MMR gene mutation and Familial Colorectal Cancer refers to families that met the Amsterdam criteria but do not show any MMR gene mutations (Vasen *et al.* 2007).

Genotype and phenotype

Lynch syndrome is estimated to cause 2-5% of colorectal cancer and around 3% of endometrial cancer (de la Chapelle A, 2005; Lynch *et al.* 2009). The syndrome is characterized by increased lifetime risks for several tumour types. The highest risks apply to colorectal cancer (50-80% risk), endometrial cancer (40-60% risk) and ovarian cancer (10-12% risk) (Koornstra *et al.* 2009; Patel and Ahnen, 2012; Quehenberger *et al.* 2005). Lynch syndrome-associated tumours develop at an earlier age with a mean age at onset of 45 years for colorectal cancer, 48 years for endometrial cancer and 40-45 years for ovarian cancer (Koornstra *et al.* 2009).

In 1993, the first germline mutations in the MMR genes *MLH1* and *MSH2* were linked to Lynch syndrome (Bronner *et al.* 1994; Fishel *et al.*1993; Lindblom *et al.* 1993). A few years later, mutations in the MMR genes *MSH6* and *PMS2* genes were also linked to the syndrome (Miyaki *et al.* 1997; Nicolaides *et al.* 1994). The MMR proteins are responsible for repair of errors that occur during DNA replication. Failure to recognize such errors allow for accumulation of mutations in repeated sequences, referred to as microsatellite instability (MSI). Likewise, mutations that occur in coding repeats will lead to somatic frameshift mutations that often affect cancer-associated genes. Mutations in *MLH1* account for 50% of the families, *MSH2* 40%, *MSH6* 7% and *PMS2* 1-2% (Peltomaki and Vasen, 2004). In Denmark, the *MLH1* and *MHS2* genes contribute to an equal fraction of cases, whereas *MSH6* mutations account for higher number (20%) of the families than described in other populations (Nilbert et al., 2009).

The different MMR genes are linked to somewhat different tumour spectra, with a predominance of colorectal cancer in *MLH1* mutant families, high risks of gynaecological cancer and a later age at onset of colorectal cancer in *MSH6* mutant families and a broader phenotype and an increased risk of extracolonic cancers in the *MSH2* mutant cases.

Surveillance

Colonoscopies effectively reduce morbidity and mortality from colorectal cancer in Lynch syndrome mutation carriers (Jarvinen *et al.* 2000; Vasen *et al.* 2010). Colonoscopies are recommended every 1-2 years starting from age 20-25. In Denmark, recommendations call for colonoscopies every second year from age 25. Due to the increased risk of endometrial cancer, women are recommended to undergo gynaecological surveillance annually, and in conjunction with abdominal surgery, prophylactic hysterectomy is an option after child-bearing age (Lindor *et al.* 2006; Vasen *et al.* 2007). Evidence for the benefit of gynaecological cancer surveillance is, however, lacking (Lynch *et al.* 2009). Endometrial cancer generally causes early symptoms of bleeding and is associated with a favourable prognosis, whereas ovarian cancer may be difficult to detect and has a worse prognosis (Evans *et al.* 2009; Stuckless *et al.* 2012).

Psychological aspects of hereditary cancer

Since predictive genetic testing for various hereditary diseases became possible in the early 1990's, the psychological aspects of pre-symptomatic genetic testing have been widely addressed, in particular in hereditary breast cancer and ovarian cancer (BRCA) and to some extend also in HNPCC/Lynch syndrome (table 2). The studies have focused on different aspects of genetic testing, e.g. risk perception, motivational factors, coping strategies, family history and short-term psychological effects from learning about hereditary cancer (Bjorvatn *et al.* 2007; Bjorvatn *et al.* 2008; Braithwaite *et al.* 2006; Broadstock *et al.* 2000; Codori *et al.* 2005; Esplen *et al.* 2007; Gritz *et al.* 2005; Hasenbring *et al.* 2011; Landsbergen *et al.* 2009; Meiser, 2005; Mikkelsen *et al.* 2009; Nordin *et al.* 2002; Shiloh *et al.* 2008). Few studies have, however, evaluated the long-term consequences of living with a high risk of hereditary cancer (Aktan-Collan *et al.* 2000; Bleiker *et al.* 2007; Gritz *et al.* 2005). The psychological impact from genetic testing has been assessed in various ways using a variety of different measures. Some of the most commonly used instruments used to measure anxiety are the hospital and depression scale (HADS) and the state trait anxiety inventory (STAI). For distress, the impact of event scale (IES), Center for Epidemiological Studies Depression scale (CES-D) and HADS have been widely applied. HADS and CES-D have been used to assess depression (Vadaparampil *et al.* 2005). Perceptions of different health beliefs related to hereditary colorectal cancer have been assessed using ratings on a Likert scale in relation to specific areas e.g. cancer worry, vulnerability and coping ability (Keller *et al.* 2002). The research area has been

influenced by the National Human genome Research Institute (NHGRI) that recommended the use of a core set of questionnaires developed by multidisciplinary teams for BRCA patients (Botkin *et al.* 1996).

The findings are fairly consistent and suggest that genetic diagnostics for Lynch syndrome leads to increased distress around the time of testing, but that the changes seem temporary with the majority of mutation carriers showing no adverse psychological effects 6–12 month after testing (Aktan-Collan *et al.* 2001;Braithwaite *et al.* 2006; Broadstock *et al.* 2000; Gritz *et al.* 2005; Meiser *et al.* 2004). Clinically relevant distress prior to and after genetic testing has been assessed in affected and unaffected individuals with BRCA1/2 and HNPCC and show that both internal and external factors affect the outcome. Such factors include pre-test level of distress, emotional illness, number of affected first-degree relatives, coping strategies and family communication, which may constitute predictors for post-test distress up to 6 month after disclosure (Meiser, 2005). Also, family system characteristics, in particular family communication and loss of close relatives have been shown to be of importance (Bartuma *et al.* 2012; McCann *et al.* 2009; Meiser, 2005). The prevalence of clinically relevant distress does not differ between individuals from BRCA1/2 and HNPCC families (Meiser, 2005). The psychological impact from genetic testing have by some investigators been found to depend more on the pre-test psychological distress than the test result itself (Gritz *et al* 2005; Meiser, 2005; Murakami *et al.* 2004; Sivell *et al.* 2008). The specific knowledge about the psychological impact of genetic testing the first year after receiving a cancer diagnosis is limited (Landsbergen *et al.* 2009).

Assessment of anxiety has been widely used in relation to the psychological impact from genetic testing in Lynch syndrome. Short-term as well as a long-term decrease in colon cancer anxiety and general anxiety has been shown, whereas state anxiety does not seem to differ between carriers and non-carriers 12 months after testing occurred (Aktan-Collan *et al.* 2001; Meiser *et al.* 2004).

Subgroups with an increased vulnerability have been identified. A minor group reports clinically relevant depression scores before and after genetic counselling (Esplen *et al.* 2003; Keller *et al.* 2002; Murakami *et al.* 2004). Carriers with lower education have reported significantly higher levels of anxiety and depression compared to carriers with higher education (Gritz *et al.* 2005). Individuals with higher levels of mood disturbance at baseline may be at risk of both short-term and long-term increased distress after genetic testing (Gritz *et al.* 2005). Younger individuals with low social support may be a at higher risk of anxiety, whereas individuals with low social support and poorer physical function seem to be more vulnerable to depression (Bjorvatn *et al.* 2007).

Table 2. Studies on psychological impact from Lynch syndrome (HNPCC)

Authors	Year of publica-tion	Area	Measurements and variables	Main findings and conclusions
Keller M et al.	2002	Impact on distress and perceptions related to genetic counselling in Lynch syndrome (HNPCC)	Anxiety and depression, impact of event, health beliefs, perception of risk, cancer worries, coping, attitude towards genetic testing and evaluation of counselling	An overall beneficial impact of comprehensive counselling. Distress and worries related to counselling declined. A substantial minority experienced increased worry and physical symptoms after counselling.
Esplen MJ et al.	2003	Experience of loss and distress in colorectal cancer patients undergoing genetic counselling	Family history, anticipated test result, psychological distress, anxiety and depression	A subgroup of colorectal cancer patients experience distress. Family history and losses related to cancer may be important factors of post-test adjustment.
Murikami et al	2004	Psychological distress after receiving a genetic test result	Major and minor depression, post traumatic stress disorder and acute stress disorder	Only history of major and minor depression was a predictor of distress 1 month after disclosure of test result.
Meiser B et al.	2004	Psychological impact of testing for Lynch syndrome (HNPCC)	Coping, impact of event, anxiety and depression	Predictive testing leads to psychological benefits among non-mutation carriers and no adverse psychological outcome in mutation carriers.
Meiser B et al Review	2005	Psychological impact of genetic testing: an update of the literature on hereditary breast and ovarian cancer	Uptake, predictors of uptake, psychological impact in general on affected and non-affected carriers, behavioural impact, risk factors for psychological distress	Unique impact of genetic testing for different types of hereditary cancer. Psychological benefits for non-mutation carriers, no adverse effects amongst mutation carriers. Benefits more clear-cut for HNPCC.
Gritz ER et al.	2005	Psychological impact from genetic testing for Lynch syndrome (HNPCC)	Depression, anxiety, cancer worries and perceived risk	No adverse long-tem psychological outcomes. Those with higher levels of baseline mood disturbance, low quality of life and lower social support may be at risk for both long and short-term increased distress.

Authors	Year of publica-tion	Area	Measurements and variables	Main findings and conclusions
Claea E et al.	2005	Stress evaluation one year after test. Delineate if pre-test variables were predictors of post-test distress and health – related behaviour	Coping, perceived impact of test result, illness perception, perceived control, cancer specific distress, general distress and health related behaviour	A wide range of distress levels. Mutation carriers had higher levels of cancer related distress one year after test. Mutation carriers were adherent to colonoscopies one year after test. In general, predictive testing does not seem to induce major psychological problems.
Codori AM et al	2005	Perceived risk and distress after genetic counselling for Lynch syndrome (HNPCC)	Perceived risk, distress, Lynch syndrome (HNPCC) related knowledge and beliefs about prevention	Risk overestimated. Risk perception change after counselling. Distress after counselling was positively related with baseline distress and anxiety symptoms.
Braithwaite D et al. Review and meta-analysis	2006	Psychological impact of genetic counselling for familial cancer	Risk perception, knowledge, anxiety, cancer specific worry, depression, and cancer surveillance	Genetic counselling improved knowledge, but did not alter risk perception. No adverse effect on affective outcomes.
Collons VR et al.	2007	Impact on individuals three years after genetic testing for Lynch syndrome (HNPCC)	Impact of event, depression and anxiety	Improved psychological measures in non-mutation carriers. No evidence of undue psychological distress in carriers.
Esplen MJ et al.	2007	Motivational factors and psychological functioning in cancer survivors undergoing genetic testing	Impact of event, anxiety, depression, social support and coping	Post counselling distress was predicted by less social support, escape-avoiding coping style and anticipation of becoming distressed.
Blieker E et al.	2007	Psychological distress and social issues after genetic testing in Lynch syndrome (HNPCC) families	Perceived risk, involvement of relatives, professional support, cancer specific distress, familial relationship, consequences for future planning and social issues	Four years after genetic testing, only a small minority of counselled reported clinically significant levels of distress, or significant familial or social problems.

Authors	Year of publica-tion	Area	Measurements and variables	Main findings and conclusions
Siglen E et al	2007	The influence from distress and SOC on anxiety and depression in hereditary cancer patients	SOC, impact of event, anxiety and depression	Association between cancer-related distress and symptoms of anxiety and depression. SOC significantly associated with anxiety and depression.
Bjorvatn C et al.	2007	Changes in anxiety and depressing over time among subjects attending genetic counselling for hereditary cancer	Anxiety and depression	Overall low levels of anxiety and depression at all times. Anxiety and depression declined over time. Higher age, self-efficacy and social support were associated with lower levels of depression.
Sivell S et al. Review	2007	Risk perception	Accuracy and likelihood of personal risk, lifetime risk, risk rating and risk perception in relation to psychological wellbeing	Anxiety before testing was a predictor of increased perceived risk. However perceived risk was not a predictor of anxiety.
Bjorvatn C et al.	2008	Anxiety and depression in individuals attending genetic counselling for hereditary cancer	Social support, self-efficacy, self-rated physical function, social support satisfaction with genetic counselling, levels of worries, anxiety and depression	Anxiety and depression declined over time. Social support, satisfaction with genetic counselling, physical function, and self-efficacy were related with lower levels of anxiety. Social support interacts with anxiety over time.
Mikkelsen E et al.	2008	Psychological consequences of genetic counselling (Breast and ovarian cancer mutation carriers)	Anxiety and depression, impact of event, quality of life	Genetic counselling does not reduce general anxiety, may alleviate cancer specific distress in women with a history of familial cancer, no adverse impact on anxiety depression and quality of life.

Authors	Year of publica-tion	Area	Measurements and variables	Main findings and conclusions
Shiloh S et al.	2008	Coping style in testing for HNPCC	Impact of event, depression and coping style	No long-term distress after genetic testing for HNPCC in most individuals. Time and coping style have effect on emotional reactions. Individuals with a high monitoring coping style were more distressed than low monitors.
Landsbergen K et al. Review	2009	Psychological impact from genetic testing in the first year of individual affected with colorectal cancer	Quality of life, physical and mental health related quality of life, overall perceived health, demands of illness, diagnostic reactions, adjustment to cancer, anxiety, depression, impact of event	Limitation in emotional and social function can persist up to one year after cancer treatment. Little is known about the psychological impact during the first year after diagnosis and very little is known about additional psychological effect of genetic testing during the same period.
Bjorvatn C et al.	2009	Intrusion and avoidance in individuals undergoing genetic investigation and counselling for hereditary cancer	Satisfaction with genetic counselling, level of worry, impact of event, physical function.	Subject with lower levels of self-efficacy at baseline and high level of worry immediate after genetic counselling seemed to be more vulnerable to both intrusion and avoidance.
Hadley DW et al.	2010	Psychological impact of genetic services through a cascade approach	Depression, worries about cancer and impact of event	Those family member, from the same generation as the first identified mutation (index person), who were tested closest to the index person experience less distress.
Hasenbring M et al.	2011	Psychological impact from genetic testing for Lynch syndrome (HNPCC): The role of cancer history, gender, age and psychological distress	Anxiety, general affective distress, impact of event, and cancer and Lynch syndrome (HNPCC) related beliefs	Genetic counselling for Lynch syndrome (HNPCC) leads to an overall reduction of anxiety. Cancer-affected younger men do not seem to reduce high anxiety levels after testing (small sample size).

Conceptual framework

The research presented in this thesis focuses on individuals in families with Lynch syndrome and integrates knowledge from natural sciences and lifeworld research. The conceptual framework presentation herein considers self-concept, salutogenisis and lived experiences in individuals with an increased risk of cancer.

The self and self-concept

Self-concept relates to how people think about and evaluate themselves and represents a psychological concept developed from research on the self (Markus and Wurf, 1987). Through an internal system of knowledge structures, referred to as schemas, experiences are stored in the long-term memory and constitute the cognitive foundation of purposive thoughts and actions. Self-schemas integrate and summarize an individual's thoughts, feelings and experiences about the self in a specific domain. Individuals are more likely to be attentive to information and process it more quickly when it is consistent with an established self-schema (Stein, 1995). Self-concept comprises several self-representations, but most self-theorists agree that it is a multi-dimensional, multi-faceted dynamic structure that can be regarded as a set or collections of images, schemas, conceptions, theories and goals (Markus and Wurf, 1987). Three classes of self-conceptions have been hypothesized: the "actual" self, the "ideal" self and the "ought" self. Discrepancy between any of these can induce a state of discomfort (Higgins, 1987). Discrepancy between the actual and the ideal self is associated with depression, whereas discrepancy between the actual and the ought self is related to anxiety (Higgins, 1987). Another dimension of the self-concept relates to beliefs about the self in the past, present and future. The perceptions of the self are considered powerful determinants of behavior (Markus and Wurf, 1987). In this sense, self-concept is viewed as dynamic and changing. Individuals with a positive self-concept are more apt at enduring stressful situations in life as opposed to those with a more negative perception of the self (Markus and Wurf, 1987).

Self-concept has been considered both an outcome and an explanatory variable related to the psychosocial aspects of cancer (Curbow *et al.* 1990). Information about a person's self can be experienced as threatening (Conkie-Rosell *et al.* 2000) and expression like "mutation" and "abnormal" may influence the way a person perceives themselves. Women tested negative for mutations have described "feeling normal for the first time" (Lim *et al.* 2004). Genetic information has been found to impact a person's self in hereditary breast cancer (Esplen *et al.* 2009b; Lim *et al.* 2004), but otherwise, research on self-concept related to heredity is limited to the area of prenatal diagnostics where comprehensive measures of self-concept have been used (Conkie-Rosell *et al.* 2000). Global measures of self-concept may be limited in capturing specific aspects of self (Markus and Wurf, 1987). Self-concept scales for BRCA1/2, FAP and Lynch syndrome have, however, been developed with the aim to measure the impact of genetic testing on the mutations carriers' self (Esplen *et al.* 2009b; Esplen *et al.* 2009a; Esplen *et al.* 2011).

Salutogenesis and sense of coherence

Salutogenesis is a stress resource orientated concept that has been applied in different cultural settings and subgroups. Salutogenesis is thought to explain why some people stay well despite stressful situations and hardship. The salutogenic concept focuses on orientation towards problem solving and capacity to use the resources available (Antonovsky A, 1987; Antonovsky, 1993; Lindstrom and Eriksson, 2005). Based on the salutogenic idea, sense of coherence (SOC) holds three nuclear components that reflect a person's ability to assess and understand stressful situation (comprehensibility) ability to find meaning in situations (meaningfulness) and capacity to use internal and external resources available (manageability) (Antonovsky A, 1987). A key element is the presence of resources available e.g. knowledge, intelligence, coping strategies, social support, ego identity and religion and a preventive health orientation (Antonovsky A, 1987; Antonovsky, 1993; Eriksson and Lindstrom, 2005). SOC does not refer to a specific coping strategy, but rather to factors, which across cultures provide a basis for successful coping (Antonovsky, 1993). The original SOC scale consists of 29 items. A shorter form with 13 items has been developed (Antonovsky, 1987; 1993; Lindstrom and Eriksson, 2005).

Individuals with a strong SOC are more likely to perceive a stressor as a challenge rather than a negative influence and to react more appropriately to stressful situations by way of using relevant personal coping strategies (Stankunas *et al.* 2009). SOC is positively correlated to mental health, quality of life, low depressive mode, high self-esteem and an optimistic life orientation (Eriksson and Lindstrom,

2006; 2007; Feldt *et al.* 2007; Idler and Benyamini, 1997). The concept of SOC is considered a health resource that influences quality of life. SOC may be mediated by a good perceived health (Eriksson and Lindstrom, 2007). SOC tends to increase with age and may be less stable than primarily assumed (Eriksson and Lindstrom, 2005).

Both the 13-item and the 29-item SOC scales have been widely validated and applied. The scales have shown satisfactory performance (Antonovsky, 1993; Eriksson and Lindstrom, 2006; Gili *et al.* 2006; Jakobsson *et al* 2004; Langius-Eklof *et al.* 2009; Lindmark *et al.* 2009; Siglen *et al.* 2007; Soderhamn and Holmgren, 2004). The scale is considered psychometrically sound with acceptable face validity and good construct validity and reliability (Antonovsky A, 1987; Antonovsky, 1993; Lindstrom and Eriksson, 2005).

Reflective lifeworld research and phenomenological research method

Phenomenology and hermeneutic philosophy provide strong foundations for human sciences and reflective lifeworld research. Phenomenology is not a single philosophy and has been described by several philosophers during the 18th century (Dahlberg K *et al.* 2010). Phenomenology can be defined as the study of structures of consciousness as experienced from the first-person point of view. In the phenomenological framework, humans are considered both biological infrastructures as well as bearers of consciousness (Giorgi, 2005). In the 19th century and the beginning of 20th century, logical empiricism was the dominating perspective in science. The German philosopher Edmund Husserl introduced a shift in the philosophic paradigm from things and nature towards human being and their world (Giorgi, 2005).

The phenomenological idea of “going to the things themselves” implies to do justice to the everyday experience. As researchers we should position ourselves in a way that things can show themselves to us. “Phenomenon” is a central concept within the phenomenology and can be understood as a matter, a thing or a part of the world. Phenomenology is thus the “science of phenomenon, and consequently the science of the world and its inhabitants”. Based on phenomenology a descriptive phenomenological research method has been developed. The purpose of the descriptive phenomenological research method is to investigate and describe a phenomenon as precisely as possible in terms of the meaning it has for those who experience it (Dahlberg *et al.* 2010; Giorgi, 1975; 2005; 2009; 2011).

Aims and design

Aims

The overall aims of this thesis were to evaluate the Lynch syndrome self-concept scale and to address perspectives from life with a high risk of cancer.

The specific aims were:

- To validate the structure of the Lynch syndrome self-concept scale and to evaluate its performance in different Western countries (*study I*).
- To evaluate self-concept in the entire Danish Lynch syndrome cohort (*study II*).
- To assess SOC in individuals with Lynch syndrome and to correlate the data to self-concept and to SOC in a general population (*study III*).
- To explore the lived experiences of healthy mutation carriers in Lynch syndrome families (*study IV*).

Design

This thesis is based on 4 studies: a validation study of self-concept in three Western countries (*study I*), a descriptive cohort study based on data from Danish individuals with Lynch syndrome (*study II*), a descriptive and comparative cohort study based on data from Danish mutation carriers and published data on SOC in a general population (*study III*) and an interview study with individuals from Lynch syndrome families (*study IV*).

Materials, informants and methods

The Lynch syndrome self-concept scale

The Lynch syndrome self-concept scale contains two subscales that reflect *stigma and vulnerability* (15 items) and *bowel symptom-related anxiety* (5 items) (Esplen *et al.* 2011). Sum scores range between 20 and 140. Whereas statements 1 and 2 are positive and consequently reversed in the analysis, the remaining 18 statements are negative. Responders are asked to indicate their agreement on a 7-point Likert scale or indicate the item as non-applicable. Sum scores range between 20 and 140 with higher scores linked to a greater impact on self-concept. The self-concept scale was translated into Danish according to recommended guidelines, including re-back translation and a bilingual panel to ensure preservation of the conceptual meaning. The bilingual panel consisted of 6 native Danish and English speaking persons from different age groups (Bonomi *et al.* 1996; Sousa and Rojjanasrirat, 2011).

The Lynch syndrome self-concept scale has shown promising psychometric properties with positive correlations to validating measures (Esplen *et al.* 2011). A positive correlation to the Impact of Event scale (Horowitz *et al.* 1979) supports the convergent validity and a weaker correlation with the Fear Questionnaire support discriminating validity (Van Zuuren, 1988). The scale has been found to have a high level of internal consistency with an inter-item correlation at 0.40 and a Cronbach's α at 0.93. We contributed to the evaluation of the test-retest reliability using data from 45 Danish mutation carriers. A high degree of reliability was found (intra-class coefficient of 0.92) supporting the use of the scale (Esplen *et al.* 2011). Further validation of the Lynch syndrome self-concept scale will later be presented and discussed as a part of this thesis.

The sense of coherence (SOC) scale

The SOC scale is a self-administered scale developed by Antonovsky (Antonovsky A, 1987; Antonovsky, 1993). Responders are asked to state their agreement on a 7-point Likert scale. For this study the 13-item version of the scale was chosen. Some statements are reversed to avoid extreme answering. The scale can be divided into three subscales though Antonovsky argued that the scale should be uses as a single concept (Antonovsky, 1993) The SOC scale has previously been translated into Danish (Due and Holstein, 1998), but in application, disagreement between the Danish and the English version was found for statement 11. We chose to re-translate this statement using a bilingual panel. The new version was in accordance with the Swedish version and was consequently chosen for *study III*.

Studies I-III

At the time of data collection for *studies I-II*, the Danish HNPCC register contained 180 Lynch syndrome families. Data were collected on two occasions; in May 2008 (n=262, response rate 80%) and in January 2009 (n=260, response rate 78%). In June 2011, we did a follow-up and collected data from mutation carriers identified after January 2009 (n=181, response rate 80%). In total, 522 eligible adults (>18 years of age) provided data. No significant differences regarding sex, time since testing, previous cancer and age were identified between responders and non-responders.

Self-reported data on self-concept were used for *studies I-III* and additional self-reported data on SOC was used in *study III*. Eligible participants were identified from the HNPCC register and information and questionnaires were sent by post including a letter of invitation and information about voluntary participation and the possibility to withdraw from the study at any time. Carriers were asked to return the questionnaires within two weeks if possible and one reminder was sent out. Return of the questionnaire was considered consent for participation. The questionnaires were coded with unique family numbers, which were kept separate from identifiable data during analysis.

Study I focused on validation of the self-concept scale. In addition to data from 404 Danish mutation carries, it also included data from 65 Swedish Lynch syndrome mutation carriers (mean age 49 years, 57% female) and secondary data from 107 Canadian mutation carriers (mean age 50 years, 55% female). The Canadian data have been used for the development of the Lynch syndrome self-

concept scale (Esplen *et al.* 2011), whereas the Swedish data have not previously been published.

Study II is a descriptive study on self-concept in Lynch syndrome and was based on data from 419 Danish mutation carriers (mean age 48 years (18-85), 52% female).

Study III is a descriptive and comparative cohort study based on self-reported data on self-concept and SOC from 345 Danish carriers of Lynch syndrome. These individuals represent part of the sample used in studies I-II, but for practical reasons the SOC questionnaire was only distributed in Western Denmark. SOC data in the Lynch syndrome cohort were compared to data from the general Danish population based on a publication containing five birth cohorts from 1975 (N=663), 1965 (N=663), 1940 (N=272), 1930 (N=270) and 1920 (N=438). Data on SOC in the general population were collected within the Danish longitudinal Health behaviour study in 1994 (Due and Holstein, 1998).

Study IV

Study IV represents an interview study based on individual interviews with healthy mutation carriers with long-term experience (minimum 3 years) from living with an increased risk of cancer. From the Danish HNPCC register 16 eligible mutation carriers (men and women in different age groups and with different time since genetic testing) were identified. The 16 mutation carriers were invited to participate by post or email and returned response letters for participation, whereupon 12 individuals were interviewed. The informants had a mean age of 48 years (range 31-69) and their mean time since genetic testing was 9.6 years (range 3-14).

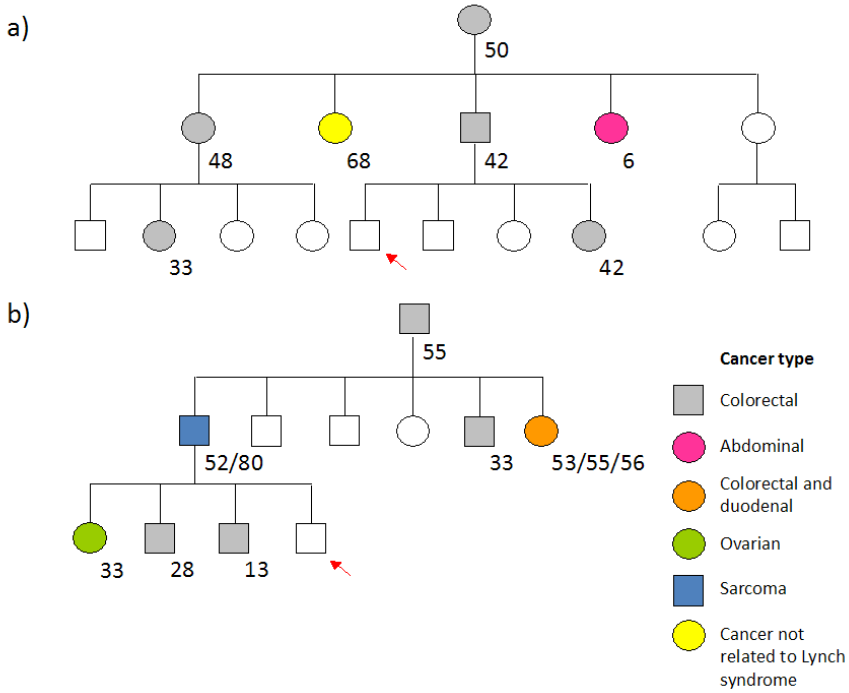

Figure 1. Examples of pedigrees of the families of participants in *study IV*. The nuclear family from an extended pedigree is presented. The arrows indicate the informant, and the numbers refer to the ages at diagnosis.

The interviews were performed by HVP, were audio taped and lasted 45–75 minutes. The interviews took place at a time and location chosen by the informants. Five interviews were performed at the research centre, five in the informants' homes and two at a local hospital close to the informants' homes. The interviews started with an open-ended question: "Tell me about life after you were told that you were carrying a mutation?". "Tell me more about…" is an example of follow up questions. Prior to the interviews there was some small talk to establish a relationship. Afterwards the informants were given the opportunity to reflect on the interview and ask questions.

Data analysis

Statistical analysis

Study I

Demographic differences between cohorts were evaluated using analysis of variance (ANOVA) for age. Differences in sex and previous cancer between cohorts were tested, using Pearson's chi square test. Analysis of variance was also used to test for differences in self-concept scale scores as a function of cohort, sex and cancer history. The significance level was set to 0.05. The 20 items were compared between cohorts, applying Bonferroni correction to reduce risk of false positive findings due to multiple testing. A significance level of 0.0025 was required for this. Post hoc comparisons were performed for items with significant differences between the cohorts.

Principal component analysis (PCA) with Varimax rotation was used to extract clusters of highly interrelated variables and performed in both the three cohorts and the combined cohort with similar results. Components identified with eigenvalues ≥ 1 were reported and factor loadings ≥ 0.35 was used to identify correlated sets of statements in each component. After identification of the dimension of the scale, the amount of variance within the variables was calculated. After having identified the underlying dimensions of the scale, communalities representing the amount of variance each variable shares with the other variables were calculated. Assessment of internal consistency was tested using Chronbach's α.

Studies II-III

Descriptive statistics were used to summarize the characteristics of the participants as well as the scores on both the Lynch syndrome self-concept scale and the SOC scale. Continuous data was presented as mean values and standard deviations and discrete data were presented as counts and percentages. Missing values and answers labelled as "non applicable" on the self-concept scale were considered missing. For both the self-concept scale and the SOC scale, responders with more than three missing values were excluded from the analysis. Three or less missing

values were imputed using the average mean of the informant. Univariate analysis included sex, formal education (dichotomized into "primary school" and "continued"), time since testing, cancer status (currently or previously affected or non-affected) and experiences from cancer in close relatives.

In study II, non-responder analysis was performed in order to identify whether they differed from the responders in relation to age, sex, time since test and cancer status. Univariate analysis, using Wilcoxon two-sample test, was used to analyze dichotomized variables and Kendals Tau-b correlation to analyze continuous data. The Wilcoxon's signed rank test was used to analyze individual scores in relation to sex and education. Finally, logistic regression analysis was applied using the upper quartile as the outcome variable.

Phenomenological analysis

The interviews in *study IV* were analysed using Giorgi's phenomenological method based on four steps where each step is a prerequisite for the next (Giorgi A, 2009; Giorgi A, 2011). In the first step, the texts were read and re-read in order to grasp a sense of the whole experience while trying to assume naïve openness to the phenomena and a willingness to wonder about what is said by the participants (Giorgi A, 2009). At this step, one must try to keep an open mind: bracketing one's pre-understanding and being conscious to pre-assumptions. Thereafter, the text was divided into different text blocks of self-containing meaning units, while keeping an open mind on the phenomenon of interest. Nvivo® 9 software was used to name the meaning units with a short codename and sort them into clusters and sub-clusters. During this step the first ideas of the structure of the phenomenon started to appear. In the following step, the meaning units were condensed; firstly through rewriting the meaning units using third-person language to describe the contents. Secondly, careful descriptions related to how these "present them selves to the consciousness of the researcher", were made in intuitive sentences. In the final step, the transformed meaning units formed the basis for the structure, in which the most invariant constitutions and an expression of the essential constitution were formed (Giorgi A, 2009). All steps were performed in collaboration between HVP and CC and the final structure of the phenomenon was presented and discussed with all co-authors.

Table 3. Examples of condensed meaning units

Meaning unit and the corresponding code name	Re-writing	How it present it self
Focus on living *"One should not be so focused on the risk that you forget to live. I want to live while I can." KF*	***K do not focus on the risk but live while she can.***	Living in the present and not thinking about what may happen.
Living in the present *"You' got to learn to live in the present. Not ruining your life by thinking about what might happen. You don't know if it happens." MF*	***Learning to live in the present is important to M. She will not allow her life to be ruined by thinking about what may happen.***	

Ethical considerations

The studies in this thesis were carried out in accordance with the ethical principles in the Helsinki declaration. According to the Danish *Act on Research Ethics Review of Health Research Projects*, ethical approval for the four studies was not needed in Denmark. For *study I* ethical approval in Sweden was obtained from the Lund University Ethical committee and in Canada from the Toronto Mount Sinai Hospital Research Ethics Board and the Memorial University Ethics Review Board.

Precautions were taken to secure confidentiality and voluntarieness. The letters of invitation stated that non-participation would not influence usual care and participants were informed about voluntariness as well as possibility to withdraw from the study. For *studies I-III* consent was obtained when the questionnaires were returned. In *study IV*, the informants either returned a signed consent form or contacted HVP directly by post or phone for inclusion.

Prior to the studies, ethical considerations were made regarding potential harm from participation. Receiving a letter from the HNPCC-register and filling out the self-concept questionnaire with statements related to negative thoughts and emotions could evoke worry and anxiety. Considerations in relation to not disturbing people made us refrain from sending out multiple questionnaires in May 2008. The high response rate (80%) suggested an interest in participation, which encouraged us to include the SOC questionnaire in January 2009. Ethical considerations were similarly made in relation to *study IV*. The informants had been invited because of their mutation status, which potentially could create feelings of pressure, or obligation to participate for the sake of other mutation carriers or obligation to make a contribution to science. On the other hand, the interviews could be perceived as an opportunity for the mutation carriers to talk about their situation and to provide health professionals with information they considered important. The in-depth interviews aimed to encourage reflection on issues related to heredity, which might evoke negative as well as positive emotions.

Findings

Validity of the self-concept scale

As a first assessment of the external validity of the Lynch syndrome self-concept scale, pooled data from Denmark, Sweden and Canada were used to perform a PCA. This analysis identified similar sets of linked statements as those reported in the original scale development (Esplen *et al.* 2009b). Initially, the PCA identified three components; the first including 12 statements related to feeling labeled, isolated, different and cursed due to the test result as well as statement 8 (*I feel guilt that I might pass on cancer risk to my children*), which was considered part of the anxiety subscale in the initial scale development. The second component identified 5 statements, 4 of which related to worries about bowel changes and one, statement 11 (*I think about my test result a lot*), originally considered belonging to the stigma and vulnerability subscale. The third component represented the two positive and future oriented statements. Communalities that express the degree of uniqueness/overlap were calculated (table 3, *study I*). As an example, statement 20 (*I feel embarrassed when I go for my bowel screening*) showed low variance (0.15) suggestive of uniqueness. In contrast, high variance for statement 15 (0.74) suggests that other statements also capture its impact.

The total mean score was 54.4 without significant differences between the three cohorts for the total score and the subscale scores (table 2, *study I*). When differences in individual statements were analysed, significant differences were related to four statements (figure 2). Differences remained significant for statements 8 (*I feel guilty that I might have passed on cancer risk to my children*), 10 (*I feel I have lost my sense of privacy*) and 13 (*I am worried that cancer will be found when I go for screening*) after Bonferroni correction. For items related to guilt, no differences were found between the Danish and the Swedish cohorts, whereas significantly higher scores were reported in the Canadian cohort ($p<0.001$). When these data were stratified for sex and previous cancer, women across the cohorts reported higher scores than men ($p<0.01$). Individuals with cancer reported higher scores (0.001), with the highest impact reported in the Canadian cohort (interaction, ($p<0.001$). Danish carriers reported significantly lower scores than the Canadians related to feelings of loosing one's privacy

(p<0.0001). No interaction was found for sex and previous cancer history for statements 10 and 13.

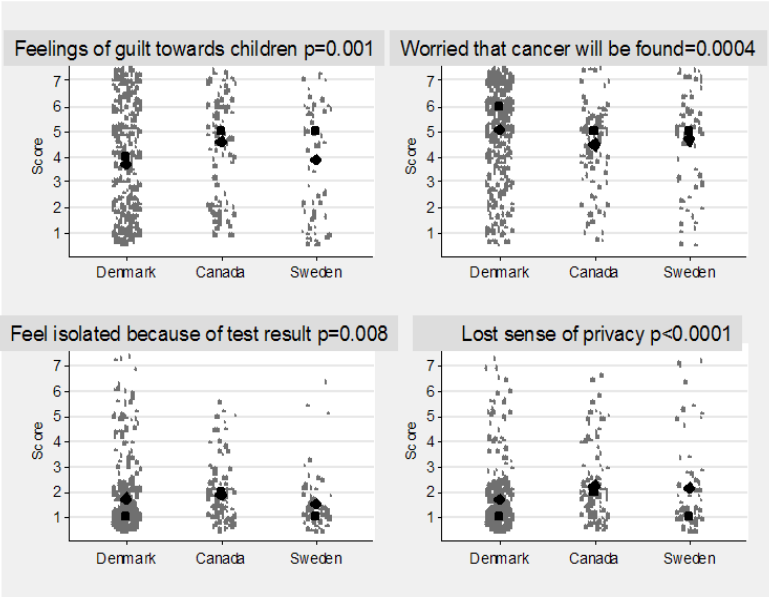

Figure 2. Scores for statements where significant differences were found between the cohorts. Random noise has been added to each score to visualize the number of identical scores. Filled diamonds and squares represent the mean and median scores respectively.

Self-concept in the Danish Lynch syndrome cohort

Study II evaluated the impact on self-concept in the entire Danish Lynch syndrome cohort. A total of 568 carriers were included in the combined cohort. A wide range of scores (range 20-132) were obtained with the majority unimodal skewed in a positive direction (figure 3). Results from the combined cohorts (*study III*) were similar to results from *study II* where a mean sum score of 54.8 was found. In the combined cohort the mean sum score was 55.2 (SD 22.6), which when divided with the number of statements corresponded to a mean score of 2.8 (SD 1.13). For

the stigma and vulnerability subscale and the bowel symptom-related subscales the mean scores were 35.4 (SD 17.1) and 19.9 (SD 7.6) respectively.

In the multivariate regression analysis predictors for highest impact on self-concept were identified. Female sex and lower education correlated with an increased OR for scores in the upper quartiles. Women reported more impact on self-concept both on the total scale (OR 1.84 (CI 1.14 –2.99)) and for the individual subscales (OR 1.7 and 1.8 respectively). Individuals with lower education reported higher impact on the stigma and vulnerability subscale (OR 1.8 (CI 1.06-3.03)).

In table 4 the distribution of self-concept scores for each statement in the Danish Lynch syndrome cohort and combined data from *studies I-III* are presented.

Table 4. Response distribution for each self-concept statement (%)

Statement	Strongly disagree	Disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Agree	Strongly agree	Non applicable	Total (n)
I am hopeful about myself in the future	1	2	4	4	10	30	49	1	566
I am able to deal with my test result	1	0	4	3	12	39	38	3	565
I am worried about bowel symptoms (like bleeding) when going to the bathroom	19	23	8	9	13	16	9	3	564
I feel my body has betrayed me	42	29	4	10	5	4	3	3	564
I feel like a walking time bomb	43	24	5	7	10	5	5	2	564
I feel different from others my age	37	28	5	6	9	9	5	1	564
I feel cursed because of my test result	39	27	6	9	8	5	4	1	566
I feel guilty that I might pass on a cancer risk to my children	20	18	6	10	13	10	15	7	552
I feel isolated because of my test result	58	28	3	4	4	1	1	1	565
I feel I have lost my sense of privacy	58	28	3	4	3	2	1	1	565
I think about my test result a lot	20	23	12	8	16	11	9	1	564
I'm afraid of having bowel pain	24	25	11	9	11	11	8	1	564
I am worried that cancer will be found when I go for screening	6	8	9	7	18	24	27	1	564
I feel labelled	49	27	3	6	6	3	4	1	565
I worry about chances in my bowels	13	14	11	11	15	18	16	1	565
I feel burdened with this information	28	30	6	8	11	9	5	2	565
I distrust my body	36	30	6	10	6	5	4	3	562
My test result get in the way of who I really am	47	32	6	3	4	3	3	2	567
I have become more secretive	49	32	2	5	4	3	3	1	564
I feel embarrassed when I go for my bowel screening	30	23	8	9	11	9	9	1	565

Statements for bowel-symptom related anxiety are in green

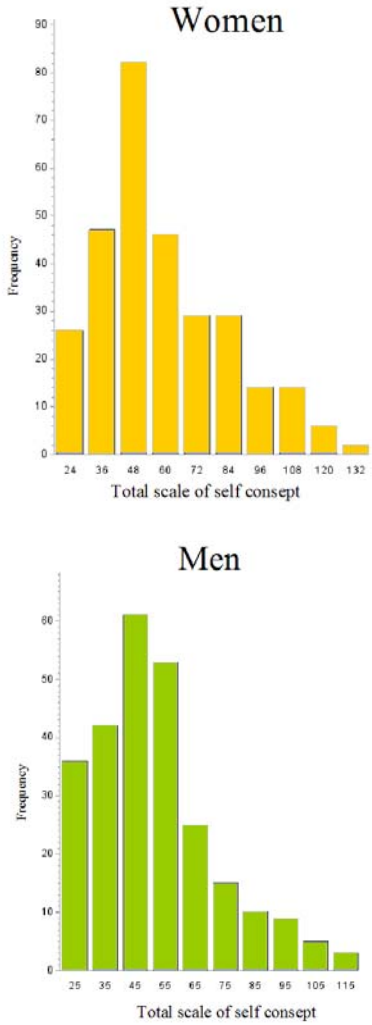

Figure 3. Self-concept score distribution for women and men.

SOC and self-concept

In *study III*, we assessed SOC in Lynch syndrome mutation carriers and correlated the data to self-concept and to SOC in a general Danish population. The mean self-concept score was 55 (SD 22.5) ranging from 20-132. In the Lynch syndrome

subset the mean SOC was 70, which was significantly higher than scores reported in the general population (mean 65, $p<0.0001$). We used the cut-off values defined in the general population and found that 16% of the mutation carriers reported low scores, 21% under average, 22% over average and 40% high scores. No differences in SOC were found in relation to sex ($p = 0.41$). Carriers affected with cancer had somewhat higher scores than non-affected (mean 71 *versus* 68) ($p=0.047$), but the findings were not significant after adjusting for sex and cancer in multivariate analysis. The distribution of SOC scores was similar to that of the general population except for the older age groups, in which carriers reported significantly higher scores. SOC increases with age in both cohorts, but the increase was more pronounced in the Lynch syndrome cohort.

Correlation between SOC and specific statements on the self-concept scale revealed that all but one statement showed significantly higher impact on self-concept with decreasing SOC scores (data not shown). Some statements presented a larger span in SOC scores than others, e.g. in those who strongly agreed in "feeling like a walking time bomb" we found a mean of 52 on the SOC scale compared to those who strongly disagreed scoring 74. Statement three related to worries for bowel symptoms on a daily basis did not show significantly differences, indicating that this statement is not related to SOC. Assessment of the correlation between self-concept and SOC adds to a further evaluation of the criterion validity of the self-concept scale. A favourable agreement between SOC and self-concept was found (Pearson correlation coefficient – 0.51) ($p<0.0001$). When correlating SOC scores to the self-concept subscales the correlation became weaker for gastrointestinal anxiety whereas it remained the same for the stigma and vulnerability subscale. Scatter plots demonstrating the for weak/strong SOC and high and low impact on self-concept have been applied, correlation between SOC and self-concept are shown below (figure 4). Cut off values resulting in 4 groups with different combinations of SOC and self-concept scores: A: weak SOC/high impact in self-concept, B: strong SOC/high impact on self-concept, C: weak SOC and low impact on self-concept and D: Strong SOC and low impact on self-concept.

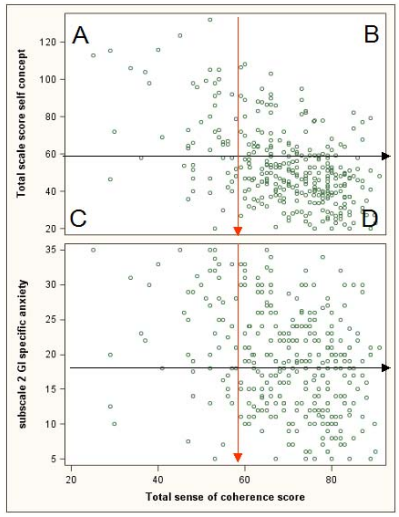

Figure 4. Scatter plot demonstrating the correlation between SOC and total self-concept (top) and SOC and bowel symptom-related anxiety (bottom).

Lived experiences

In *study IV*, the lived experiences from being at risk were explored. Four major themes or constitutions were identified: Relational context, interpretation and transformation, approach to risk and balancing life at risk. A key feature related to life with Lynch syndrome is the relational context in which life is led and understood. Family history, communication within the family, support from family members and caring for other members of the family are other factors that influence how risk is perceived and handled.

Interpretation of knowledge and personal as well as familial experiences, influences risk perception. Different reactions, from shock and panic to relief and confirmation, are described after learning about hereditary cancer. Heredity provides an explanation of many cancer deaths in the family and while it initially may be perceived as a death sentence, most informants consider it an opportunity to change the family history. Lack of knowledge contributed to feelings of loosing control. Factual knowledge provided an overview of the situation in some

mutation carriers, whereas it in others created anxiety and feelings of being different. The notion that cancer was preventable, meant that in most individuals, fear of cancer was not dominating daily life. However, experiences from previous colonoscopies created different levels of anxiety. Though some individuals struggled to accept the situation, most informants considered themselves healthy with normal lives.

Approaches and strategies to handle life at risk differ. Choosing the right time for disclosure of risk to children was important to many informants. In some families communication was open, knowledge was shared among family members and children were informed about heredity from an early age. In other families children were protected from the information, which was considered potentially harmful for them, sometimes to an extent that negatively influenced family communication and interaction. The impact from heredity on family planning varied. For some individuals this knowledge did not influence decisions related to family planning, whereas others considered pre-implantatory or prenatal diagnostics. Several informants referred to consciously choosing a positive approach to life, e.g. by positive thinking. Even if cancer was considered unavoidable, they were reassured that it would be discovered at an early stage. The informants referred to two major issues related to cancer prevention, i.e. following the surveillance program and considering lifestyle changes. Though some informants had considered not attending the colonoscopies because of discomfort and pain, all eventually chose to participate. Personal experiences had formed the informants approach to the colonoscopies and it was important for them to be able to manage the situation. Informants expressed doubts that lifestyle would influence their cancer risk but some still chose to lead a healthy lifestyle including diet and physical activity. Such decisions also influenced children who were taught to maintain a healthy diet and to be physically active.

The interaction between interpretation and approach to risk constitutes a balance (or un-balance) in the informants' lives. Life at increased risk is associated with ambivalent feelings and emotions. A conscious choice of positive thinking, being able to do something and feelings of control and security helps in balancing the negative emotions like fear, anxiety and worries related to risk. Living with risk is a learning process in which experiences and approach to risk helps the informants to balance life. In this perspective, the mutation carriers compare their situation to earlier generations who did not have any opportunity for preventive measures.

Table 5. Examples of meaning units for each constitution

Constitution	Meaning unit
Relational context	*"We (EM and her mother) have a special bond….[…]. It probably has to do with all of us (the family) having experienced loosing someone" EM* *"Suddenly my mother and my cousin started getting ill. And you just think: When will it be me?" AF*
Approach to risk	*"Not even my mother knows that of her three children it is me carrying the gene. She loves talking about that disease and I just don't want to talk about it. SF* *"I am convinced that children are exposed to so many big things when they are growing up […] It would be too much (to tell them about risk)." CF*
Interpretation and transformation	*"Through your knowledge you are able to process, you can give yourself an overview. With the overview comes the energy to handle it (the risk) emotionally. PM* *"I feel extremely lucky compared to others from my family…. MM*
Balancing life at risk	*"…trying to make it a natural part of your life […] I decided from the beginning that this is just a part of who I am." CF* *"Well, it is a load of shit (the mutation), to tell you the truth. That is the way it is, but, well… there is nothing we can do about it, so we must take it from there." PM*

Mutation carriers' perspectives

Studies II and *IV* describe mutation carriers' perspectives of living with Lynch syndrome. In total, 79% of the mutation carriers reported feeling hopeful about the future and 78% reported being able to deal with their test result. The overall scores related to the future are reflected in findings from *study IV,* where the informants described how initial shock and disbelief after learning about a mutation was gradually replaced by more optimistic feelings and thoughts linked to prevention. Thoughts about cancer in previous generations evoked feelings of security and optimism. Only a few individuals strongly disagreed to an optimistic perspective on the future. As an example, a female informant was struggling a lot with knowledge about the increased risk of cancer and expressed fear of cancer. She did not have an optimistic perspective with a score of 5 on the statement related to the future and in general reported a high impact on self-concept with an overall sum score of 111. In the interview she said: " *because… you don't know how long you'll be here"*.

The model in *study IV* describes the structure of the lived experiences of Lynch syndrome mutation carriers and illustrates how information and experiences create thoughts and feelings related to risk in a relational context. In *study IV,* we found that some carriers experienced worries and anxiety to a degree, where they felt it influenced their lives negatively. Others, although being attentive to symptoms, did not worry on a daily basis. Anxiety and worries related to symptoms were strongly influenced by previous experiences of cancer. Though the informants had not been diagnosed with cancer, some had had adenomas removed during colonoscopies, which contributed to the perception risk, but also to feelings of security and control. One participant from *study II* wrote in a note on the questionnaire that her worries related to symptoms were not caused by the test result, but by the fact that she had previously been diagnosed with cancer. In total, 235 individuals had been diagnosed with cancer and of those 26% agreed or strongly agreed in worrying about bowel symptoms compared to 24% among non-affected carriers. Attending colonoscopies meant confronting the risk and sometimes also anxiety and worry. In other carriers, thoughts about risk did not create any negative feelings; however the colonoscopy procedure itself could create feelings of anxiety and worries. The large variety to which knowledge about Lynch syndrome create feelings of anxiety and worry are reflected in a less skewed distribution of answers related to worries Among the informants 43% of the carriers disagree to the statement that they think about the test result a lot, while 20% agreed. Worries about bowel changes were reported by 34%, whereas 27% reported not being worried.

Guilt towards children was reported to some degree by 38% of the carriers, including 67% of the women and 33% of the men. Feelings of guilt were not specifically articulated by the informants (*study IV*) but the scores related to guilt may reflect concern for children, particularly in relation to different aspects of heredity. Different approaches to children's risk, e.g. disclosure of risk and striving to influence children's lifestyle, as well as thoughts and feelings related to passing on a disease predisposing mutation to children may be expressed in the statement related to guilt.

Only 10% of the carriers stated that their test result "gets in the way of whom they are". In *study IV* we found that mutation carriers strive to balance life at risk. Some of the aspects related to this balance were acceptance of the situation and integration of risk knowledge into their perception of themselves. This can be exemplified by the quote *"it is just a part of who I am"*(table 5).

Discussion and perspectives

The discussion has been divided into two major sections related to self-concept/SOC and lived experiences in Lynch syndrome. Here, methodological considerations and major findings are discussed, followed by strengths and weaknesses.

Methodological considerations related to studies I-III

Our studies are the first to apply the Lynch syndrome self-concept scale in a setting outside of North America. We have thereby generated data on scale validity and reliability. The internal validity is supported by the high response rates (78–80%) without differences in key factors such as sex, age, previous cancer and time since genetic testing in responders and non-responders. The Swedish and Canadian cohorts are restricted in size and the latter cohort had also been used for the construction of the scale. The participants included in *studies I-III* represent selected groups in regard to external validity since all participants had a verified disease-predisposing mutation. Data on the number of individuals at risk of Lynch syndrome who fail to undergo genetic testing in Denmark are lacking. However, clinical experience suggests a high up-take rate, which is supported by data from Finland where 75% of the individuals at risk undergo genetic testing (Aktan-Collan *et al.* 2000). Whether the findings from this study apply to other groups at risk needs further investigation. Studies I-III inlude a relatively large number of individuals. The two scales used for *study III* have been validated and tested in both Danish and Swedish populations, which are similar in relation to culture and health care system. The comparison to a general population is valuable, though the cohorts are not matched as regards age cohorts. Moreover, the population data were generated 18 years age. Another limitation of the study is the use of cut-off points. Division into high or low impact on both the self-concept scale and the SOC scale has been made using lower and upper quartiles respectively. The cut-off points are arbitrary and optimal cut-offs needs further investigation.

The concept of self in Lynch syndrome

A test is valid only if it measures an attribute that actually exists and if the attribute affects the outcome of the measure (Borsboom *et al* 2004). Self-concept scales for different types of hereditary cancer have been developed since global measures may not reflect issues specifically related to hereditary cancer (Esplen *et al.* 2009a; 2009b; 2011). Whether a distinct self-concept domain related to Lynch syndrome indeed exists and whether knowledge about high risk has an impact on the specific self can be questioned. The Lynch syndrome self-concept scale is based on a scale developed for hereditary breast cancer (BRCA) (Esplen *et al.* 2009b). However, aspects related to self-concept, e.g. sexuality, body image and femininity, may differ between hereditary breast cancer and colorectal cancer (Curbow *et al.* 1990). Women with breast cancer have described altered self-perceptions (Esplen *et al.* 2004). In patients with colorectal cancer, impaired body image has been reported among patients with stomas (Gosselink *et al.* 2006; Mrak *et al.* 2011). Anxiety and depression have been found to increase one to 5 years after genetic testing for breast and ovarian cancer, but the impact may be confounded by the impact from prophylactic surgery (van Oostrom *et al.* 2003). In hereditary colorectal cancer the results are more clear-cut in that carriers experince no long-term increase in distress, which may relate to the proven effect from colorectal cancer surveillance (Meiser, 2005). Whether this is relevant and to what extent Lynch syndrome mutation carriers' interpretations and experiences can be inferred from hereditary breast and ovarian cancer needs further support. The self-concept scale showed a positive skew towards the favourable end, with the majority of the participants' responses clustered around the positive answers. This produced a floor effect, which means that the scale may be limited in capturing improvements and to distinguish between various grades of low impact.

Information about a disease-predisposition may impact one's self (Stein, 1995). A genetic self has been described in relation to genetic counselling and hereditary cancer (Read *et al.* 2005). In *study II*, 7% of the participants reported feeling betrayed by their body and 9% stated that they distrusted their body. This suggests that body image may be of relevance in Lynch syndrome. Findings from study IV show that thoughts and feelings related to risk were internalized in the carriers as an "actual self" (Markus H and Wurf E, 1987), e.g. "*I am healthy"*, "*I am lucky"* and "*this is just a part of who I am*", that might also be expressed in the second statement (*I am able to deal with the test result)*. The "future self " (Markus and Wurf, 1987) integrates former experiences from other difficult situations. In *study IV*, one carrier described the test result as a death sentence, implying a "future self" of being dead. Another informant had experienced a brother having a colostomy and consequently imagined himself as a stoma patient. Several informants described that they tried to prepare themselves for becoming cancer

patients. Still, it can be discussed whether statements related to worries about cancer can be interpreted as an expression of a future self in a hereditary context.

Impact on self-concept

The studies included in this thesis comprised a large number of participants with long experience from living with Lynch syndrome. This provides a broad picture of how carriers of Lynch syndrome perceive themselves. These results are supported by the findings from study IV, where the complexity in life at risk is described. Though we did not link our data to any evaluation of depression or general anxiety, the high frequency of positive answers in the self-concept scale suggests that most mutation carriers adapt well to the situation. This is also supported by findings from other investigations (table 1), (Bleiker *et al*. 2007; Esplen *et al*. 2003; Landsbergen *et al*. 2009; Meiser, 2005; Shiloh *et al*. 2008).

Subgroups who report a higher impact on their self-concept were identified. Adverse scores on the stigma and vulnerability subscale were overrepresented among individuals with lower education. This is supported by evidence that women report higher levels of distress and anxiety disorders than men and individuals with low education and income have the highest levels of psychological distress and mental disorders (Thoits, 2010). Female mutation carriers also report a larger impact on their self-concept. This may relate to responsibilities for spread of information and coordinating surveillance in the family (Bartuma *et al*. 2012). Differences in how men and women perceive their roles in the family and their responsibility for other family members could also influence how they regard their situation (d'Agincourt-Canning and Baird, 2006). Another aspect may be that women are also at risk of gynaecological cancers and undergo surveillance and/or prophylactic procedures (Hadley et al. 2008). A recent study showed that in younger individuals reporting high levels of anxiety prior to genetic testing, men were less likely to experience decreased anxiety levels shortly after genetic testing than women (Hasenbring *et al*. 2011). However, the study was based on a small sample size and the importance of gender in Lynch syndrome needs further investigation.

SOC and self-concept

The concepts of SOC and self-concept are theoretically related in that SOC expresses a person's perceived ability to handle difficult situations, whereas self-concept reflects the impact specific situations or circumstances may have on a person's self. Assessment of the correlation between these two scales adds information related to the self-concept scale's convergent validity. The concept of SOC is considered a health resource that influences quality of life. However, SOC may also be mediated by good perceived health (Eriksson and Lindstrom, 2007). The correlation between SOC and self-concept was expected, but also raises questions about face validity and internal consistency, i.e. whether self-concept indeed captures issues *specifically related to* Lynch syndrome (Esplen *et al.* 2011). SOC has been found to predict anxiety and depression in hereditary cancer, but may not constitute an as a strong predictor for anxiety (Eriksson and Lindstrom, 2006; Lindstrom and Eriksson, 2005; Siglen *et al.* 2007). When SOC was correlated to the self-concept subscales, the correlation between SOC and self-concept weakened for the anxiety subscale. This result supports the content validity in that the scale captures anxiety related to Lynch syndrome that SOC couldn't predict. Whether the statements related to bowel symptom-related anxiety are of relevance to self-concept needs further exploration.

In *study III*, 76% of the SOC and self-concept scores were in accordance. The majority of the mutation carriers (66%) reported strong SOC and low impact on self-concept, which supports the notion that the majority of individuals at increased risk are able to handle the situation well. Weak SOC and high impact on self-concept were reported by 10%. In women with verified or suspected breast cancer, SOC is a main predictor of distress levels and women diagnosed with breast cancer reporting strong SOC experienced fewer stressful events and reported better health status (Gilbar, 2003; Kenne *et al.* 2011). In colorectal cancer, SOC has been shown to correlate to psychological distress and represents an independent predictor of health-related quality of life (Hyphantis *et al.* 2011). However, previous history of depression has also been shown as to be a strong predictor of depression in cancer patients (Nordin *et al.* 2001). The subgroup reporting weak SOC and high impact on self-concept may include individuals who, in general, are vulnerable and in need of specialized support to be able to handle the different aspect of hereditary cancer.

The 14% that reported weak SOC and low impact on self-concept may represent individuals who, despite reporting having difficulties in handling difficult situations in general, do not experience a large impact on self-concept from the knowledge about hereditary cancer. This subgroup may include mutation carriers who have chosen a blunting coping style, where they avoided or distracted

themselves from information deemed as threatening (Hickman, Jr. *et al.* 2010; Miller, 1987). In line with that, weak SOC has been found to predict anxiety and depression in hereditary cancer with the strongest correlation for depression (Siglen *et al.* 2007). Although a blunting coping style may be important to some mutation carriers' psychological wellbeing, it is necessary to evaluate the impact this may have on adherence to surveillance.

High SOC and high impact on self-concept were reported by 9% of the individuals. These individuals represent a subgroup that despite reporting feeling able to deal with difficult situations in general, experience high impact on their self-concept. The relatively weak correlation between SOC and the subscale for bowel related anxiety suggests that the impact is primarily related to anxiety. SOC has not been found to be a strong predictor of anxiety in carriers of Lynch syndrome, which adds to the impression that anxiety is a complex structure in hereditary cancer (Siglen *et al.* 2007; Sivell *et al.* 2008). A high monitoring coping style means to process the situation emotionally, actively engage with information, active problem solving and taking precaution. These are issues that relates to a strong SOC. Monitoring coping style influences distress in mutation carriers with high monitors being generally more distressed than low monitors 6 -12 month after testing (Shiloh *et al.* 2008). It can be discussed whether anxiety reported by individuals with a strong SOC is an expression of awareness and high levels of information, rather than a condition that requires intervention (Peters *et al.* 2006).

When assessing the psychological impact from a specific situation, comparison to general population is relevant. Lynch syndrome mutation carriers reported SOC scores similar to a general population, which suggests that despite a high risk of cancer, most individuals find themselves capable of handling difficult situations to the same extent as a reference group. In breast and ovarian cancer, no differences in depression were found between women attending genetic counselling and a reference group (Mikkelsen *et al.* 2009).

Methodological considerations related to study IV

Phenomenological philosophy provides an essential element for lifeworld research. The phenomenological idea of going "to the things themselves" means to do justice to the everyday experience and approach the world as it is experienced, in all its variety (Dahlberg K *et al.* 2010).

By perceiving the lived experiences as one, we revealed an essence of these (illustrated in the model presented in *study IV)*. The essence was found across informants (representing both sexes, different ages and variable times since genetic testing), which increases the applicability of the data transferability of the

findings. However, the informants represent a select group of healthy mutation carriers, which implies that the findings may not e.g. apply for individuals who declined participation in genetic counselling and testing. To increase the credibility, we used an interview technique with open-ended questions. Efforts were made to make the informants feel confident and to encourage talking about what they found important. Application of the phenomenological research method requires that the researcher puts his/her knowledge about the phenomenon aside (Giorgi A, 2011; Giorgi, 2005). The interviews were performed over a span of two years, during which the investigator's knowledge increased, which may have influenced the interviews. The investigator and co-analyzer were, however, aware of this and used self-reflection during the data analysis process and interpretation (Dahlberg K *et al.* 2010).

Lived experiences

Study IV revealed 4 constitutions related to mutation carriers' lived experiences; *Interpretation and transformation, Approach to risk, Balancing life* and *Relational context*, all of which may influence each other. By interrelation of the constitutions, the essence of the phenomenon "living with Lynch syndrome" became: *Balancing life at risk in a relational context through interpretation and transformation of experiences and knowledge, and approach to risk.*

It is the perception of an event rather than the event itself that determines the emotional, cognitive and behavioural consequences (Rao, 2009). Our findings illustrate how experiences and knowledge related to risk were interpreted and transformed into thoughts and feelings, which influenced the way the healthy mutation carriers approached their increased risk. The informants interpreted knowledge and experiences related to heredity and risk differently, which was reflected in the variety in descriptions of reactions to learning about cancer, but also in assimilation and acceptance. Perception of risk was influenced by both familial beliefs about risk, personal experiences and communication within the family, which is in line with findings from other studies (Codori *et al.* 2005; Palmquist *et al.* 2010). In the majority of mutation carriers of Lynch syndrome, increased levels of anxiety related to a positive test result return to normal levels after six to 12 months (Aktan-Collan *et al.* 2001; Bjorvatn *et al.* 2008; Broadstock *et al.* 2000; Meiser, 2005). Initial shock and disbelief was gradually replaced by more positive emotions, and anxiety seems to be variable and very much influenced by the specific time and specially situation. This is supported by results from *study II* where 69% of the participants reported worrying about cancer when they went for screening but much less (36%) were thinking a lot about their test result.

Our findings indicate that mutation carriers do indeed use an active coping style in an attempt to gain a sense of control over their situation and reduce their emotional distress (Buckmaster and Gallagher, 2010). Mutation carriers, not having a colonoscopy 6 months following genetic testing, are 6 times more likely to report depressive symptoms (Hadley *et al.* 2011). Adherence to surveillance is an active and conscious coping style and it is important to note that informants with a long-term experience described the surveillance programs as the main reason for feeling secure and in control.

Balancing life at risk implies balancing perceptions of being healthy even though in need of health care. Informants described how they aimed for influence and control over their situation and thereby led normal lives. The notion of a shared family history, but different destinies and possibilities contributed to balance in individuals at high risk. The wish to continue with life as normal is common (Steinvall *et al.* 2011) and reflected in expressions such as "learning to live with" and "coming to terms with"(McAllister, 2003). Interventions and support may therefore consider support related to personal balance, e.g. between anxiety and worries *versus* security and control, and in the context of relations.

Relational contexts were identified as a key feature related to how risk was perceived and handled (McAllister, 2003; Palmquist *et al.* 2010; Underhill *et al.* 2012). Experience from cancer in family members and the notion of not being the only one affected provides a reference frame within which life at increased risk is understood and lived. Heredity is not only understood in a tangible manner, but also in relation to family structure, which creates a sense of responsibility and care for others (Bartuma *et al.* 2012; Palmquist *et al.* 2010). Support from family members was described to be the main support mechanism though it is likely to be sensitive to communication. Whereas open communication can create feelings of support and balance, restricted communication may infer uncertainty and anxiety (Barthuma K *et al.* 2011; Bleiker *et al.* 2007; McCann *et al.* 2009).

Table 6. Strengths and weaknesses of the studies

Strengths	*Studies I-III* The self-concept scale was validated in Lynch syndrome populations from different countries and showed stable performance. PCA verified the basic scale structure and also recognized the two subscales. Self-concept was assessed in a large Danish cohort with minor selection bias. Possibilities to compare self-concept with SOC. Comparison between SOC in the Lynch syndrome cohort and in the general population. *Study IV* Included mutation carriers with long-term experiences ranging from 3-14 years. Men and women of different ages were included. Open ended interview technique and co-analysers were used. Focus were on the mutation carrier' own perspectives.
Weaknesses	*Studies I-III* Limited-size cohorts from Sweden and Canada used for scale validation. Generalizability in non-western populations has not been demonstrated. About 20% non-responders. Different age cohorts used for comparison between SOC in Lynch syndrome and in the general population. Uncertain relevant cut-off levels; quartile values used. The degree to which self-concept is relevant in Lynch syndrome and to which it corresponds to a need for additional psychosocial support is unknown. *Study IV* The findings are limited to the perspectives of healthy mutation carriers. The interviewers own pre-assumptions may have influenced the interviews and the analysis process.

Conclusions and future perspectives

Our results validate the self-concept scale, which is found to be psychometrically sound as regards aspects related to external and internal validity and reliability. Its use is supported in Western Lynch syndrome populations, though its performance in other population needs to be confirmed. The scale seems to measure aspects relevant for mutation carriers, including issues related to the genetic self. The relevance of statements related to gastrointestinal-related anxiety can be questioned. Though our overall results support its application, its impact, as compared to other psychological measures, is not fully known. Correlation to additional measures may therefore be relevant. Overall, it can also be questioned, whether self-concept as a phenomenon is equally important in Lynch syndrome as in other hereditary diseases, particularly against the background of a successful surveillance program with a significantly reduced risk of cancer.

The self-concept scale may also be applied to identify specific issues of relevance for individuals with Lynch syndrome. In such applications it is central to keep in mind that the "self" represents one issue among others related to living with risk. For the individual, other areas may be of greater importance in order to create a balance in life. The development of genetic counselling and the inclusion of high-risk individuals into surveillance programs will likely change the family patterns and diminish experiences from cancer in Lynch syndrome families.

Self-concept correlated to SOC scores in the majority of the individuals, but the identification of subsets with divergent results is interesting. We suggest that these subgroups may reflect individuals who find different aspects of heredity difficult, which may suggest need for different types of support. The possibility to apply self-concept and SOC in order to identify subgroups with different needs should be further explored. Such data could be generated through correlations between self-concept data and registry data on, e.g. health care consumption, and through further prospective evaluation of self-concept and other measures in conjunction with genetic counselling and testing.

.

Though it has been argued that the focus in genetic counselling should be on health (Siglen *et al.* 2007), a large proportion of mutation carriers of Lynch syndrome are cancer survivors. We did not detect differences related to previous cancer, but our studies have not considered survivorship perspectives (Chubak *et al.* 2012). Aspects relevant in cancer survivorship may also be of importance for healthy individuals at increased risk. Cancer rehabilitation represents another area where current knowledge suggests that support should be initiated early in the course of the disease (Anonymous, 2010; Chubak *et al.* 2012). In hereditary cancer this could potentially imply after learning about a predisposition, but before a diagnosis of cancer. In most individuals, simple rehabilitation methods are sufficient, whereas a smaller number of individuals need highly qualified support. Whether the principles and need for cancer rehabilitation also applies to hereditary cancer and to individuals at increased risk remains to be demonstrated, but would be of interest to define (Mitchell *et al.* 2012).

Our results demonstrate that most mutation carriers do well and indicate that a monitoring coping style with adherence to surveillance and focus on lifestyle is commonly used. The model presented in *study IV* suggests dynamics between the different constitutions. Several issues related to these constitutions are already used as outcome variables to assess the psychological impact from genetic testing and life at risk, e.g. risk perception, anxiety, coping strategies, social support and family history. Thus, this model may be useful to increase the understanding of different areas and issues important to mutation carriers of Lynch syndrome. The model also suggests that changes in one area may influence the others and this focus may guide the development of targeted interventions. Whereas some mutation carriers may need additional information to decrease anxiety and handle specific situations, others may rather need specific psychological intervention to handle intrusive and irrational thoughts. Studies that contribute to the identification of such subgroups would be valuable for individualized management of Lynch syndrome from a psychological point of view.

Summary in Swedish

Lynch syndrom är den vanligaste typen av ärftlig cancer i tjock- och ändtarm och beräknas utgöra 2-4% av all tarmcancer. Syndromet medför förutom den ökade risken för tarmcancer (på 60-80% livstidsrisk) också ökade risker för livmodercancer (endometriecancer, ca 40-60% risk) och äggstockscancer (ovarialcancer, ca 10-15% risk). I mitten av 1990-talet upptäcktes de genetiska förändringar som ligger bakom Lynch syndrom, vilket möjliggjorde genetisk diagnostik i familjer med misstänkt ärftlig tarmcancer. Ett ökande antal individer lever därmed med kunskap om en ökad cancerrisk.

Flera undersökningar har visat att individer med Lynch syndrom upplever ökad ångest, oro och har en ökad risk för depression efter att ha genomgått genetisk diagnostik och befunnits bära sjukdomsorsakande mutationer. Hos de flesta individer sjunker oron och mätningar ger normala resultat efter 6-12 månader. Hos en mindre grupp kvarstår oro och ångest, vilket kan antyda att dessa individer är behov av psykosocialt stöd. De flesta studier inom området har använt sig av generella mått på t.ex. ångest och oro. Det finns anledning att ifrågasätta om dessa i tillräcklig omfattning fångar de särskilda problem och den oro som orsakas av ärftlig cancer.

Nyligen har en s.k. självuppfattningsskala utvecklats för Lynch syndrom. Denna mäter genom 20 påståenden hur en person uppfattar att risken påverkar avseende sårbarhet och oro (särskilt kopplat till symptom från mag-tarmkanalen). I *studie I* testades skalans giltighet (validitet). Dessutom utvärderades den i tre populationer av individer med Lynch syndrom från Sverige, Danmark och Kanada. Studien visade att skalans struktur var robust och att endast små skillnader fanns mellan de tre patientgrupperna.

I *studie II* undersöktes självuppfattning med användande av skalan ovan bland alla danska mutationsbärare med Lynch syndrom. Det danska HNPCC registret användes för att identifiera 550 mutationsbärare som per brev inbjöds att delta och med svar från 80% av de tillfrågade. Av dessa uttryckte 80% hoppfulhet över framtiden och uppfattade att de var i stånd att hantera sitt testresultat. Endast en mindre grupp rapporterade höga poäng, vilket indikerar en större påverkan på självuppfattningen.

Känsla av sammanhang (SOC) anger hur stressande en person uppfattar en viss situation. I *studie III* mättes SOC hos 345 individer med Lynch syndrom och korrelerades till känsla av sammanhang. SOC skiljde sig inte mellan individer med ärftlig cancer och danskar i allmänhet. SOC och korrelerade väl med känsla av sammanhang. 10% av individerna rapporterade att de var påverkade av kunskapen med utfall på båda skalorna, vilket antydera att dessa individer behöver stöd i kunskapen om ärftlig cancer. Två grupper med skilda resultat mellan skalorna påvisades En grupp visade hög påverkan på självuppfattningen trots normal SOC, vilket sannolikt betyder att dessa individer, även om de normalt hanterar svåra situationer väl, tycker att kunskapen om ärftlig cancer är särskilt svår att hantera. En annan grupp hade låg SOC men mindre påverkad självuppfattning. Dessa individer tycks alltså, trots att de generellt har svårare att klara påfrestande situationer, hantera kunskapen om ärftlig cancer väl.

I *studie IV* undersöktes hur 12 friska individer med ökad risk uppfattade sin situation. Individer med påvisat Lynch syndrom, men som inte utvecklat cancer intervjuades och materialet analyserades med fenomenologisk metod. Fynden visar att den ökade cancerrisken tolkas och hanteras i relation till erfarenheter i familjen. Individerna beskriver en balans mellan medvetenhet om hög risk och känsla av trygghet och kontroll genom deltagande i kontrollprogram. Resultaten indikerar att redskap som kan hjälpa individer med ökad risk att behålla denna balans kan vara av värde för att hantera kunskapen om en ökad cancerrisk vid Lynch syndrom.

Acknowledgements

The work of this thesis was conducted in collaboration between the Department of Oncology, Lund University and the HNPCC register and the Clinical Research Center, Hvidovre University Hospital. Financial support was granted from the Danish Cancer Society and Hvidovre University Hospital. Many people have contributed and generously shared their experiences and knowledge. Firstly, sincere thanks to all the people who took their time to complete the questionnaires and tell me what life at high risk of hereditary cancer implies.

I would especially like also to thank:

My supervisors, *Mef Nilbert* and *Christina Carlsson* for introducing me to this field of research, and for challenging me and patiently teaching me the ways of academic science and writing. *Mef,* you have been an excellent mentor and taught me never to compromise. There is always room for improvement! *Christina*, thank you for teaching me the skills of qualitative research and for being such a great companion on our trips around the world.

All the collegues at the Clinical Research Center for help and support. Especially *Steen Ladelund*, head of the statistical section for helping me with the analysis in *studies II* and *III* and for many great discussions, and *Yoshio Suzuki* for help with the datamanagement. *Christina* and *Anja* for help and support and teaching me about all "the little things". Thank you *Ove Andersen*, Head of Clinical Research Center and *Linda Andresen* for believing in me and for giving me the opportunity to pursue a new career.

My co- workers at the department of oncology in Lund for a fruitful collaboration, in particular *Katarina* and *Pia* from the FOPP seminar group. Thank you, for making me feel welcome, for trying to understand my "Swedish" and for including me in the Swedish group on our many trips. A special thanks to *Pär-Ola Bendahl* for help with the statistics in *study I*.

My co-workers and collegues at the HNPCC register and Department of gastroenterology, in particular Head of the HNPCC register, *Inge Bernstein*, *Elza Ahmedovska* and *Jeanet Kruse Rasmussen* for all your help with the data collection. *Zoreh* and *Line* for inspiring discussions and great company.

Lone Sunde, Aarhus for help with data collection.

Mary Jane Esplen, and *Jiahui Wong*, de Souza Institute, Toronto, Canada for inspiring discussions and good collaboration.

My ph.d. network, *Nete Hornnes* for introducing me to research, and "Spiregruppen" in particular the "adults" *Tove Lindhardt*, *Hanne Kjærgaard*, *Bente Appel Esbensen and Ingrid Poulsen* for being a great source of support and inspiration.

All my fellow students from VIA University College in Aarhus.

Anne-Marie Gerdes for introducing me to genetic counselling.

My family, especially *Jan*, *Katrine* and *Andreas* for all your love and support and for reminding me of what is important in life. Also thanks to *Emma* for help with the languish revision.

All my friends, *Gitte* for keeping my social life going and my *MPH* group for being a pillar of support.

References

Anonymous (2008). International Agency for Research on cancer. Globocan 2002. http://www.iarc.fr/

Anonymous (2010). Priorities for Research on Cancer Survivorship. http://www.ncsi.org.uk/wp-content/uploads/NCSI-Research-Priorities-Report.pdf

Aktan-Collan, K., Haukkala, A., Mecklin, J. P., Uutela, A. & Kaariainen, H. (2001). Psychological consequences of predictive genetic testing for hereditary non-polyposis colorectal cancer (HNPCC): a prospective follow-up study. *Int. J Cancer* 93, 608-611.

Aktan-Collan, K., Mecklin, J. P., Jarvinen, H., Nystrom-Lahti, M., Peltomaki, P., Soderling, I., Uutela, A., de la, C. A. & Kaariainen, H. (2000). Predictive genetic testing for hereditary non-polyposis colorectal cancer: uptake and long-term satisfaction. *Int. J. Cancer* 89, 44-50.

Antonovsky A (1987). *Unravelling the mystery of health. How people manage stress and stay well.* Jossey-Bass: San Francisco.

Antonovsky, A. (1993). The structure and properties of the sense of coherence scale. *Soc. Sci. Med.* 36, 725-733.

Bartuma, K., Nilbert, M. & Carlsson, C. (2012). Family perspectives in lynch syndrome becoming a family at risk, patterns of communication and influence on relations. *Hered. Cancer Clin. Pract.* 10, 6.

Bjorvatn, C., Eide, G. E., Hanestad, B. R. & Havik, O. E. (2008). Anxiety and depression among subjects attending genetic counseling for hereditary cancer. *Patient Education and Counseling* 71, 234-243.

Bjorvatn, C., Eide, G. E., Hanestad, B. R., Øyen, N., Havik, O. E., Carlsson, A. & Berglund, G. (2007). Risk Perception, Worry and Satisfaction Related to Genetic Counseling for Hereditary Cancer. *Journal of Genetic Counseling* 16, 211-222.

Bleiker, E. M., Menko, F. H., Kluijt, I., Taal, B. G., Gerritsma, M. A., Wever, L. D. & Aaronson, N. K. (2007). Colorectal cancer in the family: psychosocial distress and social issues in the years following genetic counselling. *Hered. Cancer Clin. Pract.* 5, 59-66.

Bojesen, S., Bernstein, I., Gerdes, A. & Hartlev, M. (2007). Hereditary nonpolyposis colorectal cancer in Denmark - a health technology assessment. In (Anonymous).

Bonomi, A. E., Cella, D. F., Hahn, E. A., Bjordal, K., Sperner-Unterweger, B., Gangeri, L., Bergman, B., Willems-Groot, J., Hanquet, P. & Zittoun, R. (1996). Multilingual translation of the Functional Assessment of Cancer Therapy (FACT) quality of life measurement system. *Qual. Life Res.* 5, 309-320.

Borsboom, D., Mellenbergh, G. J. & van, H. J. (2004). The concept of validity. *Psychol. Rev.* 111, 1061-1071.

Botkin, J. R., Croyle, R. T., Smith, K. R., Baty, B. J., Lerman, C., Goldgar, D. E., Ward, J. M., Flick, B. J. & Nash, J. E. (1996). A model protocol for evaluating the behavioral and psychosocial effects of BRCA1 testing. *J. Natl. Cancer Inst.* 88, 872-882.

Braithwaite, D., Emery, J., Walter, F., Prevost, A. T. & Sutton, S. (2006). Psychological impact of genetic counseling for familial cancer: a systematic review and meta-analysis. *Fam. Cancer* 5, 61-75.

Broadstock, M., Michie, S. & Marteau, T. (2000). Psychological consequences of predictive genetic testing: a systematic review. *Eur. J Hum. Genet.* 8, 731-738.

Bronner, C. E., Baker, S. M., Morrison, P. T., Warren, G., Smith, L. G., Lescoe, M. K., Kane, M., Earabino, C., Lipford, J., Lindblom, A. & . (1994). Mutation in the DNA mismatch repair gene homologue hMLH1 is associated with hereditary non-polyposis colon cancer. *Nature* 368, 258-261.

Buckmaster, A. M. & Gallagher, P. (2010). Experiences of and perspectives on genetic testing for breast/ovarian cancer in and outside of the customary clinical setting. *Psychol. Health* 25, 1041-1059.

Butow, P. N. & Lobb, E. A. (2004). Analyzing the process and content of genetic counseling in familial breast cancer consultations. *J. Genet. Couns.* 13, 403-424.

Chubak, J., Tuzzio, L., Hsu, C., Alfano, C. M., Rabin, B. A., Hornbrook, M. C., Spegman, A., Von, W. A., Williams, A. & Nekhlyudov, L. (2012). Providing care for cancer survivors in integrated health care delivery systems: practices, challenges, and research opportunities. *J. Oncol. Pract.* 8, 184-189.

Codori, A. M., Waldeck, T., Petersen, G. M., Miglioretti, D., Trimbath, J. D. & Tillery, M. A. (2005). Genetic counseling outcomes: perceived risk and distress after counseling for hereditary colorectal cancer. *J. Genet. Couns.* 14, 119-132.

Conkie-Rosell, A., Spiridigliozzi, G. A., Sullivan, J. A., Dawson, D. V. & Lachiewicz, A. M. (2000). Carrier testing in fragile X syndrome: effect on self-concept. *Am. J. Med. Genet.* 92, 336-342.

Curbow, B., Somerfield, M., Legro, M. & Sonnega, J. (1990). Self-concept and cancer in adults: theoretical and methodological issues. *Soc. Sci. Med.* 31, 115-128.

d'Agincourt-Canning, L. & Baird, P. (2006). Genetic testing for hereditary cancers: the impact of gender on interest, uptake and ethical considerations. *Crit Rev. Oncol. Hematol.* 58, 114-123.

Dahlberg K, Dahlberg H & Nystrom M (2010). *Reflective Lifeworld Research.* Studentlitteratur AB, Sweden.

de la Chapelle A. (2005). The incidence of Lynch syndrome. *Fam. Cancer* 4, 233-237.

Due, E. P. & Holstein, B. E. (1998). ["Sense of coherence", social class and health in a Danish population study]. *Ugeskr. Laeger* 160, 7424-7429.

Ellington, L., Roter, D., Dudley, W. N., Baty, B. J., Upchurch, R., Larson, S., Wylie, J. E., Smith, K. R. & Botkin, J. R. (2005). Communication analysis of BRCA1 genetic counseling. *J. Genet. Couns.* 14, 377-386.

Eriksson, M. & Lindstrom, B. (2005). Validity of Antonovsky's sense of coherence scale: a systematic review. *J Epidemiol. Community Health* 59, 460-466.

Eriksson, M. & Lindstrom, B. (2006). Antonovsky's sense of coherence scale and the relation with health: a systematic review. *J Epidemiol. Community Health* 60, 376-381.

Eriksson, M. & Lindstrom, B. (2007). Antonovsky's sense of coherence scale and its relation with quality of life: a systematic review. *J Epidemiol. Community Health* 61, 938-944.

Esplen, M. J., Hunter, J., Leszcz, M., Warner, E., Narod, S., Metcalfe, K., Glendon, G., Butler, K., Liede, A., Young, M. A., Kieffer, S., DiProspero, L., Irwin, E. & Wong, J. (2004). A multicenter study of supportive-expressive group therapy for women with BRCA1/BRCA2 mutations. *Cancer* 101, 2327-2340.

Esplen, M. J., Madlensky, L., Aronson, M., Rothenmund, H., Gallinger, S., Butler, K., Toner, B., Wong, J., Manno, M. & McLaughlin, J. (2007). Colorectal cancer survivors undergoing genetic testing for hereditary non-polyposis colorectal cancer: motivational factors and psychosocial functioning. *Clin. Genet.* 72, 394-401.

Esplen, M. J., Stuckless, N., Berk, T., Butler, K. & Gallinger, S. (2009a). The FAP self-concept scale (adult form). *Fam. Cancer* 8, 39-50.

Esplen, M. J., Stuckless, N., Hunter, J., Liede, A., Metcalfe, K., Glendon, G., Narod, S., Butler, K., Scott, J. & Irwin, E. (2009b). The BRCA Self-Concept Scale: a new instrument to measure self-concept in BRCA1/2 mutation carriers. *Psychooncology.* 18, 1216-1229.

Esplen, M. J., Stuckless, N., Wong, J., Gallinger, S., Aronson, M., Rothenmund, H., Semotiuk, K., Stokes, J., Way, C., Green, J., Butler, K. & Petersen, H. V. (2011). Development and Validation of an Instrument to Measure the Impact of Genetic Testing on Self-Concept in Lynch Syndrome (LS). *Clin. Genet.*

Esplen, M. J., Urquhart, C., Butler, K., Gallinger, S., Aronson, M. & Wong, J. (2003). The experience of loss and anticipation of distress in colorectal cancer patients undergoing genetic testing. *J. Psychosom. Res.* 55, 427-435.

Evans, D. G., Gaarenstroom, K. N., Stirling, D., Shenton, A., Maehle, L., Dorum, A., Steel, M., Lalloo, F., Apold, J., Porteous, M. E., Vasen, H. F., van Asperen, C. J. & Moller, P. (2009). Screening for familial ovarian cancer: poor survival of BRCA1/2 related cancers. *J. Med. Genet.* 46, 593-597.

Feldt, T., Lintula, H., Suominen, S., Koskenvuo, M., Vahtera, J. & Kivimaki, M. (2007). Structural validity and temporal stability of the 13-item sense of coherence scale: prospective evidence from the population-based HeSSup study. *Qual. Life Res.* 16, 483-493.

Fishel, R., Lescoe, M. K., Rao, M. R., Copeland, N. G., Jenkins, N. A., Garber, J., Kane, M. & Kolodner, R. (1993). The human mutator gene homolog MSH2 and its association with hereditary nonpolyposis colon cancer. *Cell* 75, 1027-1038.

Gilbar, O. (2003). Do attitude toward cancer, sense of coherence and family high risk predict more psychological distress in women referred for a breast cancer examination? *Women Health* 38, 35-46.

Gili, M., Roca, M., Ferrer, V., Obrador, A. & Cabeza, E. (2006). Psychosocial factors associated with the adherence to a colorectal cancer screening program. *Cancer Detect. Prev.* 30, 354-360.

Giorgi A (2009). *The Descriptive Phenomenological Method in Psychology: a modified Husserlian approach.* Dusquesne University Press, Pittsburg, Pensylvania; USA.

Giorgi A (2011). An application of Phenomenological Method in Psychology. In *Duqesne studies in Phenomenological Psychology*, (Anonymous).

Giorgi, A. (1975). Phenomenology and the foundations of psychology. *Nebr. Symp. Motiv.* 23, 281-348.

Giorgi, A. (2005). The phenomenological movement and research in the human sciences. *Nurs. Sci. Q.* 18, 75-82.

Gosselink, M. P., Busschbach, J. J., Dijkhuis, C. M., Stassen, L. P., Hop, W. C. & Schouten, W. R. (2006). Quality of life after total mesorectal excision for rectal cancer. *Colorectal Dis.* 8, 15-22.

Gritz, E. R., Peterson, S. K., Vernon, S. W., Marani, S. K., Baile, W. F., Watts, B. G., Amos, C. I., Frazier, M. L. & Lynch, P. M. (2005). Psychological impact of genetic testing for hereditary nonpolyposis colorectal cancer. *J Clin Oncol.* 23, 1902-1910.

Hadley, D. W., Ashida, S., Jenkins, J. F., Calzone, K. A., Kirsch, I. R. & Koehly, L. M. (2011). Colonoscopy use following mutation detection in Lynch syndrome: exploring a role for cancer screening in adaptation. *Clin. Genet.* 79, 321-328.

Hadley, D. W., Jenkins, J. F., Steinberg, S. M., Liewehr, D., Moller, S., Martin, J. C., Calzone, K. A., Soballe, P. W. & Kirsch, I. R. (2008). Perceptions of cancer risks and predictors of colon and endometrial cancer screening in women undergoing genetic testing for Lynch syndrome. *J. Clin. Oncol.* 26, 948-954.

Hasenbring, M. I., Kreddig, N., Deges, G., Epplen, J. T., Kunstmann, E., Stemmler, S., Schulmann, K., Willert, J. & Schmiegel, W. (2011). Psychological impact of genetic counseling for hereditary nonpolyposis colorectal cancer: the role of cancer history, gender, age, and psychological distress. *Genet. Test. Mol. Biomarkers* 15, 219-225.

Hickman, R. L., Jr., Daly, B. J., Douglas, S. L. & Clochesy, J. M. (2010). Informational coping style and depressive symptoms in family decision makers. *Am. J. Crit Care* 19, 410-420.

Higgins, E. T. (1987). Self-discrepancy: a theory relating self and affect. *Psychol. Rev.* 94, 319-340.

Horowitz, M., Wilner, N. & Alvarez, W. (1979). Impact of Event Scale: a measure of subjective stress. *Psychosom. Med.* 41, 209-218.

Hyphantis, T., Paika, V., Almyroudi, A., Kampletsas, E. O. & Pavlidis, N. (2011). Personality variables as predictors of early non-metastatic colorectal cancer patients' psychological distress and health-related quality of life: a one-year prospective study. *J. Psychosom. Res.* 70, 411-421.

Idler, E. L. & Benyamini, Y. (1997). Self-rated health and mortality: a review of twenty-seven community studies. *J. Health Soc. Behav.* 38, 21-37.

Jakobsson, L., Loven, L. & Hallberg, I. R. (2004). Micturition problems in relation to quality of life in men with prostate cancer or benign prostatic hyperplasia: comparison with men from the general population. *Cancer Nurs.* 27, 218-229.

Jarvinen, H. J., Aarnio, M., Mustonen, H., ktan-Collan, K., Aaltonen, L. A., Peltomaki, P., de la, C. A. & Mecklin, J. P. (2000). Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. *Gastroenterology* 118, 829-834.

Keller, M., Jost, R., Haunstetter, C. M., Kienle, P., Knaebel, H. P., Gebert, J., Sutter, C., Knebel-Doeberitz, M., Cremer, F. & Mazitschek, U. (2002). Comprehensive genetic counseling for families at risk for HNPCC: impact on distress and perceptions. *Genet. Test.* 6, 291-302.

Kenne, S. E., Browall, M., Persson, L. O., Fall-Dickson, J. & Gaston-Johansson, F. (2011). Relationship of sense of coherence to stressful events, coping strategies, health status, and quality of life in women with breast cancer. *Psychooncology*.

Koornstra, J. J., Mourits, M. J., Sijmons, R. H., Leliveld, A. M., Hollema, H. & Kleibeuker, J. H. (2009). Management of extracolonic tumours in patients with Lynch syndrome. *Lancet Oncol.* 10, 400-408.

Landsbergen, K. M., Prins, J. B., Brunner, H. G., Kraaimaat, F. W. & Hoogerbrugge, N. (2009). Genetic testing for Lynch syndrome in the first year of colorectal cancer: a review of the psychological impact. *Fam. Cancer* 8, 325-337.

Langius-Eklof, A., Lidman, K. & Wredling, R. (2009). Health-related quality of life in relation to sense of coherence in a Swedish group of HIV-infected patients over a two-year follow-up. *AIDS Patient. Care STDS.* 23, 59-64.

Lim, J., Macluran, M., Price, M., Bennett, B. & Butow, P. (2004). Short- and long-term impact of receiving genetic mutation results in women at increased risk for hereditary breast cancer. *J. Genet. Couns.* 13, 115-133.

Lindblom, A., Tannergard, P., Werelius, B. & Nordenskjold, M. (1993). Genetic mapping of a second locus predisposing to hereditary non-polyposis colon cancer. *Nat. Genet.* 5, 279-282.

Lindmark, U., Stenstrom, U., Gerdin, E. W. & Hugoson, A. (2009). The distribution of 'sense of coherence' among Swedish adults: A quantitative cross-sectional population study. *Scand. J Public Health* .

Lindor, N. M., Petersen, G. M., Hadley, D. W., Kinney, A. Y., Miesfeldt, S., Lu, K. H., Lynch, P., Burke, W. & Press, N. (2006). Recommendations for the care of individuals with an inherited predisposition to Lynch syndrome: a systematic review. *JAMA* 296, 1507-1517.

Lindstrom, B. & Eriksson, M. (2005). Salutogenesis. *J. Epidemiol. Community Health* 59, 440-442.

Lynch, H. T. & Krush, A. J. (1971a). Cancer family "G" revisited: 1895-1970. *Cancer* 27, 1505-1511.

Lynch, H. T. & Krush, A. J. (1971b). The cancer family syndrome and cancer control. *Surg. Gynecol. Obstet.* 132, 247-250.

Lynch, H. T. & Lynch, J. F. (2002). Hereditary cancer: family history, diagnosis, molecular genetics, ecogenetics, and management strategies. *Biochimie* 84, 3-17.

Lynch, H. T., Lynch, P. M., Lanspa, S. J., Snyder, C. L., Lynch, J. F. & Boland, C. R. (2009). Review of the Lynch syndrome: history, molecular genetics, screening, differential diagnosis, and medicolegal ramifications. *Clin Genet.* 76, 1-18.

Lynch, H. T., Smyrk, T. & Lynch, J. F. (1996). Overview of natural history, pathology, molecular genetics and management of HNPCC (Lynch Syndrome). *Int. J. Cancer* 69, 38-43.

Markus H & Wurf E (1987). The dynamic self-concept: a social psychological perspective. In *Annual rewiew of psychologi*, (ed. Rosenweig MR), pp. 299-337.

McAllister, M. (2003). Personal theories of inheritance, coping strategies, risk perception and engagement in hereditary non-polyposis colon cancer families offered genetic testing. *Clin. Genet.* 64, 179-189.

McCann, S., Macauley, D., Barnett, Y., Bunting, B., Bradley, A., Jeffers, L. & Morrison, P. J. (2009). Family communication, genetic testing and colonoscopy screening in hereditary non-polyposis colon cancer: a qualitative study. *Psychooncology.*

Meiser, B. (2005). Psychological impact of genetic testing for cancer susceptibility: an update of the literature. *Psychooncology.* 14, 1060-1074.

Meiser, B., Collins, V., Warren, R., Gaff, C., St John, D. J., Young, M. A., Harrop, K., Brown, J. & Halliday, J. (2004). Psychological impact of genetic testing for hereditary non-polyposis colorectal cancer. *Clin Genet.* 66, 502-511.

Mikkelsen, E. M., Sunde, L., Johansen, C. & Johnsen, S. P. (2009). Psychosocial consequences of genetic counseling: a population-based follow-up study. *Breast J.* 15, 61-68.

Miller, S. M. (1987). Monitoring and blunting: validation of a questionnaire to assess styles of information seeking under threat. *J. Pers. Soc. Psychol.* 52, 345-353.

Mitchell, A. J., Meader, N., Davies, E., Clover, K., Carter, G. L., Loscalzo, M. J., Linden, W., Grassi, L., Johansen, C., Carlson, L. E. & Zabora, J. (2012). Meta-analysis of screening and case finding tools for depression in cancer: evidence based recommendations for clinical practice on behalf of the Depression in Cancer Care consensus group. *J. Affect. Disord.* 140, 149-160.

Miyaki, M., Konishi, M., Tanaka, K., Kikuchi-Yanoshita, R., Muraoka, M., Yasuno, M., Igari, T., Koike, M., Chiba, M. & Mori, T. (1997). Germline mutation of MSH6 as the cause of hereditary nonpolyposis colorectal cancer. *Nat. Genet.* 17, 271-272.

Mrak, K., Jagoditsch, M., Eberl, T., Klingler, A. & Tschmelitsch, J. (2011). Long-term quality of life in pouch patients compared with stoma patients following rectal cancer surgery. *Colorectal Dis.* 13, e403-e410.

Murakami, Y., Okamura, H., Sugano, K., Yoshida, T., Kazuma, K., Akechi, T. & Uchitomi, Y. (2004). Psychologic distress after disclosure of genetic test results regarding hereditary nonpolyposis colorectal carcinoma. *Cancer* 101, 395-403.

Nicolaides, N. C., Papadopoulos, N., Liu, B., Wei, Y. F., Carter, K. C., Ruben, S. M., Rosen, C. A., Haseltine, W. A., Fleischmann, R. D., Fraser, C. M. & . (1994). Mutations of two PMS homologues in hereditary nonpolyposis colon cancer. *Nature* 371, 75-80.

Nordin, K., Berglund, G., Glimelius, B. & Sjoden, P. O. (2001). Predicting anxiety and depression among cancer patients: a clinical model. *Eur. J. Cancer* 37, 376-384.

Nordin, K., Liden, A., Hansson, M., Rosenquist, R. & Berglund, G. (2002). Coping style, psychological distress, risk perception, and satisfaction in subjects attending genetic counselling for hereditary cancer. *J Med. Genet.* 39, 689-694.

Palmquist, A. E., Koehly, L. M., Peterson, S. K., Shegog, M., Vernon, S. W. & Gritz, E. R. (2010). "The cancer bond": exploring the formation of cancer risk perception in families with Lynch syndrome. *J. Genet. Couns.* 19, 473-486.

Patel, S. G. & Ahnen, D. J. (2012). Familial Colon Cancer Syndromes: an Update of a Rapidly Evolving Field. *Curr. Gastroenterol. Rep.*

Peltomaki, P. & Vasen, H. (2004). Mutations associated with HNPCC predisposition -- Update of ICG-HNPCC/INSiGHT mutation database. *Dis. Markers* 20, 269-276.

Peters, E., Slovic, P., Hibbard, J. H. & Tusler, M. (2006). Why worry? Worry, risk perceptions, and willingness to act to reduce medical errors. *Health Psychol* 25, 144-152.

Quehenberger, F., Vasen, H. F. & van Houwelingen, H. C. (2005). Risk of colorectal and endometrial cancer for carriers of mutations of the hMLH1 and hMSH2 gene: correction for ascertainment. *J. Med. Genet.* 42, 491-496.

Rao, K. (2009). Recent research in stress, coping and women's health. *Curr. Opin. Psychiatry* 22, 188-193.

Read, C. Y., Perry, D. J. & Duffy, M. E. (2005). Design and psychometric evaluation of the Psychological Adaptation to Genetic Information Scale. *J. Nurs. Scholarsh.* 37, 203-208.

Resta, R., Biesecker, B. B., Bennett, R. L., Blum, S., Hahn, S. E., Strecker, M. N. & Williams, J. L. (2006). A new definition of Genetic Counseling: National Society of Genetic Counselors' Task Force report. *J. Genet. Couns.* 15, 77-83.

Shiloh, S., Koehly, L., Jenkins, J., Martin, J. & Hadley, D. (2008). Monitoring coping style moderates emotional reactions to genetic testing for hereditary nonpolyposis colorectal cancer: a longitudinal study. *Psychooncology.* 17, 746-755.

Siglen, E., Bjorvatn, C., Engebretsen, L. F., Berglund, G. & Natvig, G. K. (2007). The influence of cancer-related distress and sense of coherence on anxiety and depression in patients with hereditary cancer: a study of patients' sense of coherence 6 months after genetic counseling. *J Genet. Couns.* 16, 607-615.

Sivell, S., Elwyn, G., Gaff, C. L., Clarke, A. J., Iredale, R., Shaw, C., Dundon, J., Thornton, H. & Edwards, A. (2008). How risk is perceived, constructed and interpreted by clients in clinical genetics, and the effects on decision making: systematic review. *J. Genet. Couns.* 17, 30-63.

Soderhamn, O. & Holmgren, L. (2004). Testing Antonovsky's sense of coherence (SOC) scale among Swedish physically active older people. *Scand. J. Psychol.* 45, 215-221.

Sousa, V. D. & Rojjanasrirat, W. (2011). Translation, adaptation and validation of instruments or scales for use in cross-cultural health care research: a clear and user-friendly guideline. *J. Eval. Clin. Pract.* 17, 268-274.

Stankunas, M., Kalediene, R. & Starkuviene, S. (2009). Sense of coherence and its associations with psychosocial health: results of survey of the unemployed in Kaunas. *Medicina (Kaunas.)* 45, 807-813.

Stein, K. F. (1995). Schema model of the self-concept. *Image J. Nurs. Sch* 27, 187-193.

Steinvall, K., Johansson, H. & Bertero, C. (2011). Balancing a changed life situation: the lived experience from next of kin to persons with inoperable lung cancer. *Am. J. Hosp. Palliat. Care* 28, 82-89.

Stuckless, S., Green, J., Dawson, L., Barrett, B., Woods, M., Dicks, E. & Parfrey, P. (2012). Impact of gynecological screening in Lynch syndrome carriers with an MSH2 mutation. *Clin. Genet.*

Thoits, P. A. (2010). Stress and health: major findings and policy implications. *J. Health Soc. Behav.* 51 Suppl, S41-S53.

Trimbath, J. D. & Giardiello, F. M. (2002). Review article: genetic testing and counselling for hereditary colorectal cancer. *Aliment. Pharmacol. Ther.* 16, 1843-1857.

Underhill, M. L., Lally, R. M., Kiviniemi, M. T., Murekeyisoni, C. & Dickerson, S. S. (2012). Living My Family's Story: Identifying the Lived Experience in Healthy Women at Risk for Hereditary Breast Cancer. *Cancer Nurs.*

Vadaparampil, S. T., Ropka, M. & Stefanek, M. E. (2005). Measurement of psychological factors associated with genetic testing for hereditary breast, ovarian and colon cancers. *Familial Cancer* 4, 195-206.

van Oostrom, I., Meijers-Heijboer, H., Lodder, L. N., Duivenvoorden, H. J., van Gool, A. R., Seynaeve, C., van der Meer, C. A., Klijn, J. G., van Geel, B. N., Burger, C. W., Wladimiroff, J. W. & Tibben, A. (2003). Long-term psychological impact of carrying a BRCA1/2 mutation and prophylactic surgery: a 5-year follow-up study. *J. Clin. Oncol.* 21, 3867-3874.

Van Zuuren, F. J. (1988). The fear questionnaire. Some data on validity, reliability and layout. *Br. J. Psychiatry* 153, 659-662.

Vasen, H. F., Abdirahman, M., Brohet, R., Langers, A. M., Kleibeuker, J. H., van, K. M., Koornstra, J. J., Boot, H., Cats, A., Dekker, E., Sanduleanu, S., Poley, J. W., Hardwick, J. C., de Vos Tot Nederveen Cappel WH, van der Meulen-de Jong AE, Tan, T. G., Jacobs, M. A., Mohamed, F. L., de Boer, S. Y., van de Meeberg, P. C., Verhulst, M. L., Salemans, J. M., van, B. N., Westerveld, B. D., Vecht, J. & Nagengast, F. M. (2010). One to 2-year surveillance intervals reduce risk of colorectal cancer in families with Lynch syndrome. *Gastroenterology* 138, 2300-2306.

Vasen, H. F., Mecklin, J. P., Khan, P. M. & Lynch, H. T. (1991). The International Collaborative Group on Hereditary Non-Polyposis Colorectal Cancer (ICG-HNPCC). *Dis. Colon Rectum* 34, 424-425.

Vasen, H. F., Moslein, G., Alonso, A., Bernstein, I., Bertario, L., Blanco, I., Burn, J., Capella, G., Engel, C., Frayling, I., Friedl, W., Hes, F. J., Hodgson, S., Mecklin, J. P., Moller, P., Nagengast, F., Parc, Y., Renkonen-Sinisalo, L., Sampson, J. R., Stormorken, A. & Wijnen, J. (2007). Guidelines for the clinical management of Lynch syndrome (hereditary non-polyposis cancer). *J Med. Genet.* 44, 353-362.

Vasen, H. F., Watson, P., Mecklin, J. P. & Lynch, H. T. (1999). New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. *Gastroenterology* 116, 1453-1456.

Warthin A (1985). Classics in oncology. Heredity with reference to carcinoma as shown by the study of the cases examined in the pathological laboratory of the University of Michigan, 1895-1913. By Aldred Scott Warthin. 1913. *CA Cancer J. Clin.* 35, 348-359.

Weissman, S. M., Bellcross, C., Bittner, C. C., Freivogel, M. E., Haidle, J. L., Kaurah, P., Leininger, A., Palaniappan, S., Steenblock, K., Vu, T. M. & Daniels, M. S. (2011). Genetic counseling considerations in the evaluation of families for Lynch syndrome-a review. *J. Genet. Couns.* 20, 5-19.

Appendix

Hvidovre Hospital

└_┴_┴_┴_┴_┘ – └_┴_┴_┘

Spørgeskema
Risiko for arvelig kræft - selvopfattelse og viden

Spørgeskemaet består af 3 dele:

DEL1: Grundlæggende oplysninger om køn, alder, uddannelse og sygdomserfaring.

DEL 2: Selvopfattelse *Her bedes du angive, hvor enig du er i 20 udsagn.*

DEL 3: Viden *Her bedes du at svare "sandt" eller "falsk" på 11 udsagn.*

Det besvarede spørgeskema bedes returneret i den vedlagte frankerede svarkuvert inden 2 uger.

Med venlig hilsen

Overlæge Inge Bernstein og forskningssygeplejerske Helle Vendel Petersen

HNPCC registret

Klinisk Forskningscenter

Hvidovre Hospital

Kettegård Allé 30

2650 Hvidovre

Dato: └_┴_┘ – └_┴_┘ – └_┴_┴_┴_┘
dag måned år

DEL 1: Grundlæggende oplysninger

1. Køn ☐ Mand ☐ Kvinde

2. Alder ⌊__⌋ år

3. Min højeste uddannelse er:
☐ Folkeskole
☐ Gymnasium
☐ Universitetet
☐ Andet

4. Jeg har eller har haft kræft ☐ Ja ☐ Nej

5. Jeg føler, jeg har været tæt involveret i nærtstående familiemedlems kræftsygdom
☐ Ja ☐ Nej

6. Synes du selv, du har tilstrækkelig viden til at håndtere livet med risiko for arvelig kræft?
☐ Ja ☐ Nej

Hvis nej, hvad vil du gerne vide mere om?: ……

……

……

7. Oplever du selv, at du har brug for hjælp til at håndtere, at leve risiko for arvelig kræft?
☐ Ja, i høj grad
☐ Ja, af og til
☐ Nej, slet ikke

DEL 2: Selvopfattelse

Følgende 20 udsagn afspejler reaktioner hos personer, som har fået resultatet af genetisk undersøgelse for arvelig tyktarmskræft.
Vi er interesseret i at vide, i hvilken grad du er enig eller uenig i disse udsagn. Angiv venligst dine svar ved at sætte **X** *i boksene, der passer bedst med din opfattelse. Brug din første indskydelse.*

	Helt uenig	Uenig	Delvis uenig	Hverken enig eller uenig	Delvis enig	Enig	Helt enig	Ved ikke
1. Jeg ser positivt på min fremtid	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
2. Jeg er i stand til at håndtere mine testresultater	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
3. Jeg er bekymret for tarmsymptomer (f.x. blødning), når jeg går på toilettet	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
4. Jeg føler, at min krop har forrådt mig	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
5. Jeg føler mig som en tidsindstillet bombe	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
6. Jeg føler mig anderledes end andre i min alder	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
7. Jeg føler, at testresultatet er en forbandelse, der har ramt mig	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
8. Jeg føler skyld over muligvis at have påført mine børn risiko for kræft	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
9. Jeg føler mig isoleret på grund af mit testresultat	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
10. Jeg føler, at jeg har mistet mit privatliv	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
11. Jeg tænker meget på mit testresultat.	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
12. Jeg er bange for at få mavesmerter	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
13. Jeg er bekymret for, at der vil blive fundet kræft ved tarmundersøgelserne	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
14. Jeg føler mig stemplet	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
15. Jeg er bekymret for ændringer i min tarmfumktion	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
16. Jeg føler mig tynget af denne information	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
17. Jeg stoler ikke på min krop	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
18. Testresultatet hæmmer min mulighed for at være den, jeg er	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
19. Jeg er blevet mere indelukket	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐
20. Jeg føler mig pinligt berørt, når jeg skal have foretaget tarmundersøgelserne	1☐	2☐	3☐	4☐	5☐	6☐	7☐	8☐

DEL 3: Viden

Nedenfor kommer 11 udsagn. Angiv venligst om du mener de er sande eller falske ved at sætte et **X** *i en af boksene. Brug din første indskydelse.*

	Sandt	Falsk
1. Tyktarmskræft rammer cirka 5% af alle individer i Danmark	☐	☐
2. En person, der bærer en HNPCC-genfejl, vil helt sikkert udvikle kræft	☐	☐
3. En person, der ikke bærer en HNPCC-genfejl, kan aldrig få tyktarmskræft	☐	☐
4. Kvinder med HNPCC har en forhøjet risiko for livmoderkræft (endometriecancer)	☐	☐
5. Kvinder med HNPCC har en forhøjet risiko for æggestokskræft	☐	☐
6. Coloskopi (tarmundersøgelse) er af værdi for individer med tarmsymptomer	☐	☐
7. En person, som bærer en HNPCC-genfejl, skal tilbydes regelmæssige tarmunderøgelser	☐	☐
8. En person med HNPCC vil videregive arveanlægget til 25% af sine børn	☐	☐
9. I forbindelse med udredning for HNPCC vil man i enkelte tilfælde undersøge prøver fra pårørende, som har haft kræft	☐	☐
10. Genetisk diagnostik af HNPCC kan udføres på blodprøve fra en enkelt person	☐	☐
11. Sygdommen HNPCC nedarves oftest gennem familiens mandlige medlemmer	☐	☐

Tak for din medvirken!

DEL 4: Oplevelse af sammenhæng

Følgende 13 spørgsmål har ikke direkte relation til risiko for arvelig tarmkræft, men berører forskellige sider af livet. Hvert spørgsmål har syv svarmuligheder. Marker venligst hvor på skalaen mellem yderpunkterne 1 og 7, du selv føler du hører til. Sæt ***O*** *omkring tallet.*

	Meget sjældent/ aldrig						Ofte
1. Oplever du, at du er ligeglad med det, der sker omkring dig?	1	2	3	4	5	6	7

	Der er aldrig sket						Det er sket mange gange
2. Er det sket for dig, at du er blevet overrasket over opførslen hos personer, du kendte godt?	1	2	3	4	5	6	7

	Der er aldrig sket						Det er sket mange gange
3. Er det sket, at mennesker, du stolede på, har skuffet dig?	1	2	3	4	5	6	7

	Helt savnet mål og mening						Haft både mål og mening
4. Indtil nu har dit liv:	1	2	3	4	5	6	7

	Meget ofte						Meget sjældent/ aldrig
5. Føler du dig uretfærdigt behandlet?	1	2	3	4	5	6	7

	Meget ofte						Meget sjældent/ aldrig
6. Oplever du, at du er i en uvant situation og ikke ved, hvad du skal gøre?	1	2	3	4	5	6	7

		Glæde og dyb tilfredsstillelse						Smerte og kedsomhed
7.	Er din dagligdag en kilde til…	1	2	3	4	5	6	7

		Meget ofte						Meget sjældent/ aldrig
8.	Har du meget modstridende tanker og følelser?	1	2	3	4	5	6	7

		Meget ofte						Meget sjældent/ aldrig
9.	Sker det, at du har følelser, du helst ikke vil føle?	1	2	3	4	5	6	7

		Aldrig						Meget ofte
10.	Selv mennesker med en stærk personlighed føler sig indimellem som tabere. Hvor ofte har du følt dig sådan?	1	2	3	4	5	6	7

		Over- eller undervur-derer betydningen af det, der sker?						Ser sagen i dens rette forhold
11.	Når noget er sket, oplever du, at du generelt	1	2	3	4	5	6	7

		Meget ofte						Meget sjældent/ aldrig
12.	Hvor ofte føler du, at de ting du foretager dig i din hverdag er uden mening?	1	2	3	4	5	6	7

		Meget ofte						Meget sjældent/ aldrig
13.	Hvor ofte har du følelser, du ikke er sikker på, du kan kontrollere?	1	2	3	4	5	6	7

Paper I

J Genet Counsel
DOI 10.1007/s10897-011-9349-x

ORIGINAL RESEARCH

Validation of a Self-Concept Scale for Lynch Syndrome in Different Nationalities

Helle Vendel Petersen · Katarina Domanska · Pär-Ola Bendahl · Jiahui Wong · Christina Carlsson · Inge Bernstein · Mary Jane Esplen · Mef Nilbert

Received: 23 August 2010 / Accepted: 6 January 2011

Abstract Learning about hereditary cancer may influence an individual's self-concept, which otherwise represents a complex but stable cognitive structure. Recently, a 20-statement self-concept scale, with subscales related to stigma-vulnerability and bowel symptom-related anxiety, was developed for Lynch syndrome. We compared the performance of this scale in 591 mutation carriers from Denmark, Sweden and Canada. Principal component analysis identified two sets of linked statements—the first related to feeling different, isolated and labeled, and the second to concern and worry about bowel changes. The scale performed consistently in the three countries. Minor differences were identified, with guilt about passing on a defective gene and feelings of losing one's privacy being more pronounced among Canadians, whereas Danes more often expressed worries about cancer. Validation of the Lynch syndrome self-concept scale supports its basic structure, identifies dependence between the statements in the subscales and demonstrates its applicability in different Western populations.

Keywords HNPCC · Hereditary nonpolyposis colorectal cancer · Psychological impact · Reliability · Questionnaire · Validity

H. V. Petersen · M. Nilbert
Clinical Research Centre, Hvidovre University Hospital,
Copenhagen University,
Hvidovre, Denmark

H. V. Petersen · K. Domanska · P.-O. Bendahl · C. Carlsson · M. Nilbert
Department of Oncology, Institute of Clinical Sciences,
Lund University,
Lund, Sweden

J. Wong · M. J. Esplen
Department of Psychiatry, Faculty of Medicine, University of Toronto, Behavorial Sciences and Health Research Division,
University Health Network,
Toronto, Canada

I. Bernstein
HNPCC-register, Hvidovre University Hospital,
Copenhagen University,
Hvidovre, Denmark

H. V. Petersen (✉)
Clinical Research Centre 136, Hvidovre Hospital,
Kettegård allé 30,
2650, Hvidovre, Denmark
e-mail: helle.vendel.petersen@hvh.regionh.dk

Introduction

Lynch syndrome is a hereditary multi-cancer syndrome characterized by early onset (mean 45 years) and particularly high lifetime risks for colorectal cancer (50–80%) and gynecological cancer (40–60% risk for endometrial cancer, and 10–15% risk for ovarian cancer). Germ-line mutations in the mismatch repair genes *MLH1, MSH2, MSH6* and *PMS2* were identified as the genetic causes of hereditary non-polyposis colorectal cancer, HNPCC, in the early 1990's (Lynch and de la Chapelle 2003; Lynch et al. 2008, 2009). Today, mutation positive families are referred to as having Lynch syndrome and genetic counseling and testing are well established in clinical routine. Early identification of individuals at increased risk of colorectal cancer is important since colonoscopic surveillance reduces morbidity and mortality by up to 60% (Jarvinen et al. 2000; Lindor et al. 2006; Renkonen-Sinisalo et al. 2000; Stupart et al. 2009).

An increasing number of individuals live with knowledge of a high risk of cancer, which may have psychosocial effects and evoke feelings of being different, alluded to in

Published online: 26 January 2011

expressions such as "altered, abnormal and mutated" (Bleiker et al. 2003; Lynch 2008; Vadaparampil et al. 2005; Esplen et al. 2009b). Increased anxiety and depression have been demonstrated 6–12 months after genetic testing (Aktan-Collan et al. 2001; Collins et al. 2007; Meiser 2005) and subgroups such as young individuals and females, seem to be more vulnerable to test-related distress (Gritz et al. 2005; Keller et al. 2002, 2008; Meiser 2005). To date, most studies of psychological function have, however, applied global measures, which have limited ability to identify specific psychosocial issues associated with hereditary cancer (Bleiker et al. 2003; Esplen et al. 2010; Vadaparampil et al. 2005).

Self-concept is a complex cognitive structure that influences how individuals think about and evaluate themselves in relation to identity, social roles, values and interests. Several factors, including knowledge, experience, sex and internalized cultural values form a person's self-concept and individuals with a positive perception of the self are more capable of handling challenges (Esplen et al. 2009b; Markus 1977; Markus and Wurf 1987). Though self-concept remains relatively stable throughout life, it may change during difficult periods or due to crises that evoke feelings or alter perceptions about one's identity. Recently, self-concept scales for hereditary cancer have been developed and applied to cohorts affected by hereditary breast and ovarian cancer, familial adenomatous polyposis and most recently Lynch syndrome (Esplen et al. 2009a, b, 2010). The Lynch syndrome self-concept scale contains general items related to self-concept (e.g., feelings of guilt and isolation, vulnerability, and sense of being labeled) as well as specific items (e.g., worry about bowel symptoms and anxiety at cancer surveillance) (Table 1). The self-concept scales reflect psychosocial aspects of being at high risk of cancer and may potentially be used to identify individuals in need of extended psychosocial support. The aim of our study was to validate the structure of the Lynch syndrome self-concept scale and evaluate its performance in populations from different Western countries.

Methods

Instrumentation

Individual interviews and focus group interviews with patients and genetic counselors formed the basis for identification of items in the construction of the Lynch syndrome self-concept scale and after item selection, reliability and construct validity were assessed in an independent cohort (Esplen et al. 2010). The Lynch syndrome self-concept scale contains 20 statements (Table 1) divided into two subscales related to stigma and vulnerability (15 statements) and to bowel symptom-related anxiety (5 statements). Responders are asked to indicate their degree of agreement with each statement on a 7-point, Likert scale ranging from "strongly disagree" to "strongly agree." By adding the scores and dividing by number of statements in each subscale, we

Table 1 Individual statements in the Lynch syndrome self-concept scale

1 [a]	I am hopeful about myself in the future[c]
2 [a]	I am able to deal with my test result[c]
3 [b]	I am worried about bowel symptoms (like bleeding) when I go to the bathroom
4 [a]	I feel my body has betrayed me
5 [a]	I feel like a walking time bomb
6 [a]	I feel different from others my age
7 [a]	I feel cursed because of my test result
8[b]	I feel guilty that I might have passed on a cancer risk to my children
9 [a]	I feel isolated because of my test result
10 [a]	I feel I have lost my sense of privacy
11 [a]	I think about my test result a lot
12 [b]	I am afraid of having bowel pains
13 [b]	I am worried that cancer will be found when I go for screening
14 [a]	I feel labelled
15 [b]	I worry about changes in my bowels
16 [a]	I feel burdened with this information
17 [a]	I distrust my body
18 [a]	My test result gets in the way of who I am
19 [a]	I have become more secretive
20 [a]	I feel embarrassed when I go for my bowel screening

Statements are rated on a 7-point scale where 1=strongly disagree and 7=strongly agree

[a] Statements on the Bowel-Symptom Related Anxiety subscale

[b] Statements on the Stigma and Vulnerability subscale

[c] Statements for which scores should be reversed in the analysis

get a summed score with the same range, 1–7, as the individual statements. The first 2 statements are positive (and consequently reverse scored), whereas the remaining 18 statements are negative. Higher scores indicate a stronger negative impact on an individual's self-concept. The self-concept scale was translated from English into Danish and Swedish (translations available from the authors upon request) according to recommended guidelines, including back-translation into English (Cha et al. 2007).

Sample and Procedures

The study sample of 591 individuals was recruited from Denmark (n=415), Sweden (n=68), and Canada (n=108). The Danish data were collected from a national study on self-concept that included all identified carriers of Lynch syndrome predisposing germ-line mutations in Denmark (Vendel Petersen, unpublished data). The Swedish data were collected for the present study and have not previously been published. The Canadian sample consisted of secondary data from carriers of Lynch Syndrome included in the development of the self-concept scale (Esplen et al. 2010). Data on age, sex and previous cancer were available for all three cohorts. The response rate was 79% in Denmark, 76% in Sweden, and 72% in Canada. Fifteen questionnaires contained missing data for 4 or more statements and thus were excluded, leaving 576 individuals for the final analysis (Table 2).

In all three countries, genetic counseling took place prior to genetic testing. The test results were communicated at a second counseling session in Sweden and Canada, whereas the Danish individuals had a choice between a second session or receiving information about the result by mail. All participants were offered surveillance programs, including biannual colonoscopies. Ethical approval for the study was, according to the Danish ethical regulation, not needed. Ethical approval was obtained in Sweden obtained from the Lund University Ethics committee and in Canada from the Toronto Mount Sinai Hospital Research Ethics Board and the Memorial University Ethics Review board.

Data Analysis

Demographic differences between the cohorts were evaluated using analysis of variance (ANOVA) for age and chi square tests for sex and previous Lynch syndrome-associated cancer. Analysis of variance was also used to test for differences in self-concept scale scores as a function of cohort, sex and cancer history. All tests were two-tailed and the significance level was set to 0.05. For items where significant differences were found, paired comparisons were performed. Bonferroni correction was used to reduce the risk of false positive findings due to multiple testing. Since differences in the distribution of the 20 items were evaluated, a p-value$<0.05/20=0.0025$ was required for significance.

Principal component analysis (PCA) with Varimax rotation was used to explain score variability. In this analysis, missing values, on average 1.6%, were imputed with the group median score for each item. The principal components were normed to the associated eigenvalues and Varimax rotation was applied. Components with eigenvalues ≥1 were reported, and a cut off value of 0.35 for factor loadings was used to identify correlated sets of statements representative of each factor. After having identified the underlying dimensions of the scale, communalities, representing the amount of variance each variable in the analysis shares with other variables, were calculated. To assess the internal consistency of the scale Cronbach's alpha was used. Stata 11.0 (StataCorp LP, College Station, TX, USA, 2010) and PASW Statistics 18 were used for the statistical analyses.

Results

The average inter-item correlation between the 20 items in the scale was 0.4 and Cronbach's alpha, used for testing for internal consistency, was 0.93 indicating that the statements in the self-concept scale are measuring a uni-dimensional construct.

Principal component analysis identified three components (Table 3), of which the first component defined 12

Table 2 Summary of self-concept data in the different cohorts

	Total Sample	Denmark	Canada	Sweden	p value
Number of informants	576	404	107	65	
Mean age	48	48	50	49	0.37
Sex, male/female (%)	47/53	48/52	45/55	43/57	0.77
Previous Lynch syndrome-associated cancer (%)	48	43	63	52	0.001
Mean (SD) total self-concept score	2.72 (1.14)	2.74 (1.16)	2.68 (1.00)	2.64 (1.20)	0.78
Mean (SD) stigma and vulnerability	2.31 (1.12)	2.33 (1.14)	2.25 (0.98)	2.30 (1.18)	0.81
Mean (SD) GI anxiety	3.91 (1.49)	3.93 (1.51)	3.97 (1.41)	3.64 (1.50)	0.30

Table 3 Factor loadings from principal component analysis (n=576)

Statement	Component			Communalities
	1	2	3	
1	0.28	0.08	*0.74*	0.64
2	0.20	0.20	*0.81*	0.73
3	0.17	*0.76*	0.07	0.61
4	*0.70*	0.30	0.06	0.57
5	*0.63*	0.33	0.31	0.61
6	*0.71*	0.20	0.10	0.56
7	*0.71*	0.27	0.16	0.60
8	*0.43*	0.33	−0.23	0.35
9	*0.77*	0.12	0.17	0.63
10	*0.75*	0.13	0.15	0.60
11	0.34	*0.63*	0.28	0.59
12	0.30	*0.73*	0.15	0.65
13	0.14	*0.78*	0.12	0.65
14	*0.71*	0.26	0.22	0.62
15	0.24	*0.82*	0.08	0.74
16	*0.55*	0.39	0.36	0.58
17	*0.66*	0.34	0.25	0.61
18	*0.73*	0.19	0.27	0.64
19	*0.66*	0.14	0.27	0.53
20	0.28	0.15	0.23	0.15

Predominant factor loadings are in italics

statements related to feeling labeled, isolated, different and cursed due to the test result. The second component identified 5 statements, 4 of which related to concern and worry about bowel changes and belonged to the bowel symptom-related anxiety subscale. The third component filtered out statements 1 and 2, which represent positive and future-directed statements. These three components respectively explained 44%, 9% and 5% of the total variance. The PCA in the individual cohorts revealed the same overall picture (data not shown). Calculations of communalities (Table 3) showed a variable degree of overlap/uniqueness, which can be exemplified by a high variance for statement 15 (0.74) suggesting that other statements also capture its impact, whereas statement 20 (0.15) showed low variance suggestive of uniqueness.

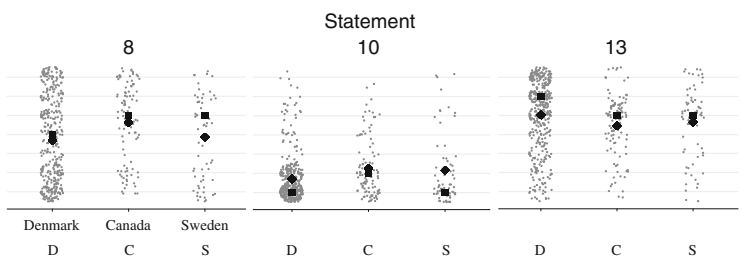

Fig. 1 Scores for statements 8, 10, and 13, which showed significant differences between the cohorts. To visualize the number of identical integer scores, random noise on a unit circle has been added to each score. The mean and the median scores are represented by filled diamonds and squares, respectively

The total mean score for the whole sample was 2.72, and there were no significant differences between the three cohorts (Table 2). When individual items were analyzed, significant differences (p<0.05) were identified for 4 of the 20 statements, 3 of which remained after the Bonferroni correction (Fig. 1). These items related to guilt about passing on a mutated gene to children (statement 8), feelings of losing one's privacy (statement 10), and worries about cancer found at surveillance (statement 13).

For statement 8 *(I feel guilty that I might pass on cancer risk to my children*) no significant differences were found between the Danish and Swedish cohorts, whereas higher scores were reported in the Canadian cohort (p<0.001). When these data were stratified for sex and previous cancer, women across all three cohorts reported higher scores (p<0.01) than men. Individuals affected by cancer reported higher scores (p<0.001) and the impact hereof was highest in the Canadian cohort (interaction, p<0.001), whereas individuals without previous cancer showed similar scores (p=0.5). For statement 10 (*I feel I have lost my sense of privacy*) Danes had significantly (p<0.0001) lower scores than Canadians. There were no significant effects or interactions for sex and previous cancer history. For statement 13 (*I am worried that cancer will be found when I go for screening*) significantly higher scores were observed in the Danish cohort compared to the Canadian cohort (p=0.0001). Consistent with the results for statement 10, there were no significant main effects or interactions for sex and previous cancer history.

Discussion

International guidelines for genetic testing and surveillance have been established for Lynch syndrome (Bleiker et al. 2003; Lindor et al. 2006; Vasen et al. 2007, 2010), but recommendations regarding optimal psychological management and support are lacking. Though the majority of individuals adapt to a genetic test result, a subset experience an adverse outcome, expressed as increased anxiety and depression (Bjorvatn et al. 2008, 2009; Hamilton et al. 2009; Keller et al. 2008; Murakami et al.

2004). Changes in overall psychological functioning following genetic testing have been documented. Knowledge is, however, lacking about how specific psychological factors, such as self-concept, contribute to how individuals adapt to living with a high risk of cancer and whether self-concept may influence participation in surveillance programs. Tools that measure variables such as self-concept would allow for individualized psychosocial follow-up. As self-concept is a psychological structure that incorporates past, present and future sense of self and is influenced by internalized cultural values and norms (Markus and Wurf 1987), it may be used to identify individuals in need of psychosocial intervention.

In the present study, using the Lynch syndrome self-concept scale, we applied the same statistical methods as Esplen et al. (2010) and obtained similar results regarding scale reliability and inter-item correlation, which supports internal consistency of the scale. In order to assess the basic structure of the scale, PCA with Varimax rotation was used (Table 3). The first component identified 12 statements related to the "stigma and vulnerability" subscale. All but one of these statements (no. 11, *I think about my test result a lot*) related to intrusive thoughts about the genetic test result, are consistent between this study and the original study, suggesting little differences in self-concept between the cohorts. The second component identified 5 statements (nos. 3, 11, 12, 13 and 15), 4 of which are represented in the bowel symptom-related anxiety subscale proposed by Esplen et al. (2010). Statement 8 (*I feel guilty that I might pass on a cancer risk on to my children*) did not load well on either factor in the current combined sample. Our data thus support the use of both subscales, but suggests that statements 8 and 11 are more complex and warrant further examination, (e.g., related to the sex by cohort interaction observed for statement 8). The third component identified the two positive future orientated statements in the scale (*I am hopeful about myself in the future* and *I am able to deal with my test result*), which were part of the stigma and vulnerability subscales and represent positive appraisals of the impact of a genetic test result. Though the two statements were the weakest in the PCA analysis, we believe they are relevant since they represent future-directed aspects of a person's "self" (Esplen et al. 2009b; Markus and Wurf 1987). Minor modifications of the subscale may be relevant, but the similar structures in the cohorts provide strong evidence that the Lynch syndrome self-concept scale is valid and support extended use of the scale in different settings.

When the Danish, Swedish and Canadian cohorts were compared, their total mean scores were not significantly different, suggesting that the impact on self-concept, as measured by the Lynch syndrome self-concept scale is similar in these countries. Significant differences were identified for three of the 20 statements (Fig. 1). The Canadian cohort reported higher scores for guilt about passing on cancer risk to children (statement 8) than either the Danish or Swedish cohorts. When stratified for sex and previous cancer, the difference was explained by higher values reported by women and by individuals with previous cancer. These findings are consistent with data suggesting that women in Western societies traditionally take responsibility for family health (d'Agincourt-Canning 2001) and may therefore more often experience guilt towards children. Parents affected by cancer are struggling with feelings of guilt about the possible transmission of a cancer gene and feel responsible for their children's' health. Pressures to engage in "good parenting" or a strong sense of responsibility to be an "ideal parent" may be culturally linked and may thus vary across countries (Semple and McCance 2010). However, the differences in reported guilt identified between the cohorts are subtle and might also reflect differences in sample sizes, genetic counseling services, information and follow-up recommendations. Compared to the Canadian cohort, Danish mutation carriers reported lower scores related to feelings of losing one's privacy (statement 10), but higher scores for worry about cancer being found at surveillance (statement 13). The differences in statements 10 and 13 were, in contrast to statement 8, independent of sex and previous cancer. The smaller impact on privacy could perhaps be linked to Danes having a long tradition of national registries based on unique civic registration numbers. The causes of the higher degree of worry about cancer reported by Danes remain unknown, but might reflect a need for additional information and psychological support in Denmark, where the HNPCC register mainly focuses on genetic counseling and information about test results and surveillance.

In conclusion, the present data are the first to assess the psychosocial impact of genetic testing for Lynch syndrome across populations and constitute the first validation of this scale outside of North America. The minor differences identified between the cohorts, related to feeling guilt about passing on a defective gene, losing privacy and worries about cancer found at surveillance, could possibly be explained by cultural factors and differences in genetic counseling. Limitations of the present study include the validity of the constructs measured, which is not demonstrated herein. This was, however, taken into account in the original development of the Lynch syndrome self-concept scale with comparison to 4 other scales related to distress, self-esteem, social desirability and fear. Furthermore, the cohorts had different sample sizes and data from the Canadian cohort had previously been used for scale construction (Esplen et al. 2010). Use of data from three populations with similar cultures and health care systems limit the generalizability of the findings to Western

populations, and its applicability in populations with different health care systems, cultures and religions needs further investigation. Further validation could include e.g. confirmatory factor analysis and Rasch analysis. Moreover, correlations between self-concept and educational level, prior loss of family members to cancer, surveillance attitudes, and long-term mutation carrier perspectives could be investigated with the aim to identify specific groups in higher need of psychosocial intervention after genetic testing for Lynch syndrome.

Acknowledgments The Danish Cancer Fund and the Hvidovre University Hospital financially supported the study.

References

Aktan-Collan, K., Haukkala, A., Mecklin, J. P., Uutela, A., & Kaariainen, H. (2001). Psychological consequences of predictive genetic testing for hereditary non-polyposis colorectal cancer (HNPCC): a prospective follow-up study. *International Journal of Cancer, 93*, 608–611.

Bjorvatn, C., Eide, G. E., Hanestad, B. R., & Havik, O. E. (2008). Anxiety and depression among subjects attending genetic counseling for hereditary cancer. *Patient Education and Counseling, 71*, 234–243.

Bjorvatn, C., Eide, G. E., Hanestad, B. R., Hamang, A., & Havik, O. E. (2009). Intrusion and avoidance in subjects undergoing genetic investigation and counseling for hereditary cancer. *Supportive Care in Cancer, 17*, 1371–1381.

Bleiker, E. M., Hahn, D. E., & Aaronson, N. K. (2003). Psychosocial issues in cancer genetics—current status and future directions. *Acta Oncológica, 42*, 276–286.

Cha, E. S., Kim, K. H., & Erlen, J. A. (2007). Translation of scales in cross-cultural research: issues and techniques. *Journal of Advanced Nursing, 58*, 386–395.

Collins, V. R., Meiser, B., Ukoumunne, O. C., Gaff, C., St John, D. J., & Halliday, J. L. (2007). The impact of predictive genetic testing for hereditary nonpolyposis colorectal cancer: three years after testing. *Genetics in Medicine, 9*, 290–297.

d'Agincourt-Canning, L. (2001). Experiences of genetic risk: disclosure and the gendering of responsibility. *Bioethics, 15*, 231–247.

Esplen, M. J., Stuckless, N., Berk, T., Butler, K., & Gallinger, S. (2009a). The FAP self-concept scale (adult form). *Familial Cancer, 8*, 39–50.

Esplen, M. J., Stuckless, N., Hunter, J., Liede, A., Metcalfe, K., Glendon, G., et al. (2009b). The BRCA Self-Concept Scale: a new instrument to measure self-concept in BRCA1/2 mutation carriers. *Psychooncology, 18*(11), 1216–1229.

Esplen, M. J., Stuckless, N., Wong, J., Gallinger, S., Aronson, M., Rothenmund, H., et al. (2010). Development and validation of an instrument to measure the impact of genetic testing on self-concept in hereditary non-polypos colorectal cancer (HNPCC). In J. C. Holland & M. Watson (Eds.), *IPOS 12th World Congress of Psycho-Oncology 25–29 May 2010; QC, Canada* (pp. 161). Wiley-Blackwell.

Gritz, E. R., Peterson, S. K., Vernon, S. W., Marani, S. K., Baile, W. F., Watts, B. G., et al. (2005). Psychological impact of genetic testing for hereditary nonpolyposis colorectal cancer. *Journal of Clinical Oncology, 23*, 1902–1910.

Hamilton, J. G., Lobel, M., & Moyer, A. (2009). Emotional distress following genetic testing for hereditary breast and ovarian cancer: a meta-analytic review. *Health Psychology, 28*, 510–518.

Jarvinen, H. J., Aarnio, M., Mustonen, H., Ktan-Collan, K., Aaltonen, L. A., Peltomaki, P., et al. (2000). Controlled 15-year trial on screening for colorectal cancer in families with hereditary nonpolyposis colorectal cancer. *Gastroenterology, 118*, 829–834.

Keller, M., Jost, R., Haunstetter, C. M., Kienle, P., Knaebel, H. P., Gebert, J., et al. (2002). Comprehensive genetic counseling for families at risk for HNPCC: impact on distress and perceptions. *Genetic Testing, 6*, 291–302.

Keller, M., Jost, R., Haunstetter, C. M., Sattel, H., Schroeter, C., Bertsch, U., et al. (2008). Psychosocial outcome following genetic risk counselling for familial colorectal cancer. A comparison of affected patients and family members. *Clinical Genetics, 74*, 414–424.

Lindor, N. M., Petersen, G. M., Hadley, D. W., Kinney, A. Y., Miesfeldt, S., Lu, K. H., et al. (2006). Recommendations for the care of individuals with an inherited predisposition to Lynch syndrome: a systematic review. *JAMA, 296*, 1507–1517.

Lynch, P. M. (2008). Standards of care in diagnosis and testing for hereditary colon cancer. *Familial Cancer, 7*, 65–72.

Lynch, H. T., & de la Chapelle, A. (2003). Hereditary colorectal cancer. *The New England Journal of Medicine, 348*, 919–932.

Lynch, H. T., Lynch, J. F., Lynch, P. M., & Attard, T. (2008). Hereditary colorectal cancer syndromes: molecular genetics, genetic counseling, diagnosis and management. *Familial Cancer, 7*, 27–39.

Lynch, H. T., Lynch, P. M., Lanspa, S. J., Snyder, C. L., Lynch, J. F., & Boland, C. R. (2009). Review of the Lynch syndrome: history, molecular genetics, screening, differential diagnosis, and medicolegal ramifications. *Clinical Genetics, 76*, 1–18.

Markus, H. (1977). Self-schemas and processing information about the self. *Journal of Personality and Social Psychology, 35*, 63–78.

Markus, H., & Wurf, E. (1987). The dynamic self-concept: A social psychological perspective. In M. R. Rosenweig (Ed.), *Annual review of psychology* (pp. 299–337).

Meiser, B. (2005). Psychological impact of genetic testing for cancer susceptibility: an update of the literature. *Psychooncology, 14*, 1060–1074.

Murakami, Y., Okamura, H., Sugano, K., Yoshida, T., Kazuma, K., Akechi, T., et al. (2004). Psychologic distress after disclosure of genetic test results regarding hereditary nonpolyposis colorectal carcinoma. *Cancer, 101*, 395–403.

Renkonen-Sinisalo, L., Aarnio, M., Mecklin, J. P., & Jarvinen, H. J. (2000). Surveillance improves survival of colorectal cancer in patients with hereditary nonpolyposis colorectal cancer. *Cancer Detection and Prevention, 24*, 137–142.

Semple, C. J. P. B. R., & McCance, T. D. M. B. H. (2010). Parents' experience of cancer who have young children: a literature review. [Article]. *Cancer Nursing, 33*, 110–118.

Stupart, D. A., Goldberg, P. A., Algar, U., & Ramesar, R. (2009). Surveillance colonoscopy improves survival in a cohort of subjects with a single mismatch repair gene mutation. *Colorectal Disease, 11*, 126–130.

Vadaparampil, S. T., Ropka, M., & Stefanek, M. E. (2005). Measurement of psychological factors associated with genetic testing for hereditary breast, ovarian and colon cancers. *Familial Cancer, 4*, 195–206.

Vasen, H. F., Moslein, G., Alonso, A., Bernstein, I., Bertario, L., Blanco, I., et al. (2007). Guidelines for the clinical management of Lynch syndrome (hereditary non-polyposis cancer). *Journal of Medical Genetics, 44*, 353–362.

Vasen, H. F., Moslein, G., Alonso, A., Aretz, S., Bernstein, I., Bertario, L., et al. (2010). Recommendations to improve identification of hereditary and familial colorectal cancer in Europe. *Familial Cancer, 9*, 109–115.

Paper II

Familial Cancer (2011) 10:633–639
DOI 10.1007/s10689-011-9459-5

Limited impact on self-concept in individuals with Lynch syndrome; results from a national cohort study

Helle Vendel Petersen · Mary Jane Esplen · Steen Ladelund · Inge Bernstein · Lone Sunde · Christina Carlsson · Mef Nilbert

Published online: 21 June 2011

Abstract An increasing number of individuals seek genetic counseling and hereby learn about hereditary cancer in the family. Lynch syndrome is associated with an inherited high risk for colorectal and gynecological cancer, but knowledge about how family members at risk perceive their situation is limited. We used the national Danish HNPCC register to collect data on self-concept from 413 individuals with Lynch syndrome. The recently developed Lynch syndrome self-concept scale contains 20 items within two subscales related to stigma-vulnerability and bowel symptom-related anxiety. Significantly higher total scores, indicating a greater impact on self-concept, were reported by females and by individuals with experience from cancer in close relatives, whereas individuals with less formal education scored significantly higher on the stigma and vulnerability subscale. Scores in the upper quartile were more often reported by women (odds ratio 1.8) and by individuals with less education (OR 1.8). This study provides the first extended use of the Lynch syndrome self-concept scale and suggests that the majority of the Danish mutation carriers adapt well to the situation, though knowledge about the increased risk of cancer seem to have a greater impact in females, individuals with less education and those with experience of cancer in close relatives.

Keywords Anxiety · Hereditary cancer · Hereditary nonpolyposis colorectal cancer · Psychosocial · Vulnerability

H. V. Petersen (✉) · S. Ladelund · M. Nilbert
Clinical Research Centre, Hvidovre University Hospital, Copenhagen University, Copenhagen, Denmark
e-mail: helle.vendel.petersen@hvh.regionh.dk

M. J. Esplen
Division of Behavioral Science and Health, Toronto General Research Institute, University Health Network, Toronto, Canada

I. Bernstein
HNPCC-register, Hvidovre University Hospital, Copenhagen University, Copenhagen, Denmark

L. Sunde
Department of Clinical Genetics, Aalborg University Hospital, Aalborg University, Aalborg, Denmark

C. Carlsson · M. Nilbert
Department of Oncology, Institute of Clinical Sciences, Skane University Hospital, Lund University, Lund, Sweden

Introduction

Genetic counseling services have been expanding during the last decade, following the identification of causative genes for e.g. breast cancer, ovarian cancer, and colorectal cancer [1–3]. An increasing number of individuals live with knowledge about hereditary cancer in the family. Lynch syndrome (formerly referred to as hereditary non-polyposis colorectal cancer, HNPCC) is one of the most common hereditary cancer syndromes identified and accounts for 2–4% of colorectal cancer. Tumors typically develop at an early age (mean 44 years) and mutation carriers are at 60–90% lifetime risk of colorectal cancer, 40–60% risk of endometrial cancer, and are at increased risks also for ovarian cancer, gastric cancer, urothelial cancer, brain tumors and skin tumors [1, 4, 5]. Mutations in DNA mismatch repair genes have been identified as the underlying cause [5]. Identification and optimal management of these families is important since surveillance programmes for colorectal cancer have proven effective in reducing morbidity and mortality from colorectal cancer

[6, 7]. The possibility to prevent colorectal cancer has been identified as a major motivating factor for at-risk individuals' participation in surveillance programmes and also evokes hope for the future [8].

Most patients with colorectal cancer express positive attitudes toward genetic testing with colorectal cancer in close relatives as being a major motivating factor [9, 10]. Though the vast majority of counselees are satisfied with their decision, emotional issues are among those where expectations are not always fulfilled [11]. Worry and distress have been reported by one-third of individuals with suspected Lynch syndrome prior to genetic counseling with figures decreasing to 13–25% shortly afterwards [12]. The increased levels of distress, anxiety and depression observed in mutation carriers after genetic testing seem to be temporary with little undue psychological distress reported one and 3 years post testing for the majority of individuals [13–16]. Disclosure of an increased risk of cancer may not only influence psychological functioning, but may also evoke feelings of being different, alluded to as in such self expressions as "abnormal, mutated and altered", used by mutation carriers [17, 18]. Global measures, such as those to assess depressive symptomatologi used in most studies of psychological function may fail to capture the specific psychological issues linked with being at high risk of cancer and the long-term perspectives of living with an increased risk of colorectal cancer is at present largely unknown [16, 19–22].

Self-concept is a complex cognitive structure related to perception about one's self and refers to how we think about and evaluate ourselves in relation to the surrounding society. Social roles, physical appearance, experiences, values and interests are among the factors that influence our self-concept, [23, 24]. In hereditary cancer, self-concept may influence how mutation carriers adopt to the situation and whether individuals at risk participate in surveillance programmes. Self-concept scales have been developed for hereditary breast and ovarian cancer (BRCA1/2) [25], familial adenomatous polyposis (FAP) [26] and most recently for Lynch syndrome [18, 27]. The self-concept scales differ from the more global depression and anxiety scales in taking specific psychological issues related to the specific type of hereditary cancer into account and may thereby contribute to the identification of individuals in need of extended support. We have demonstrated favorable performance of the Lynch syndrome self-concept scale after validation in different western populations [27]. In order to contribute to knowledge about self-concept in individuals with hereditary colorectal cancer, we evaluated self-concept in the entire national Danish Lynch syndrome cohort with over 500 individuals at high risk of colorectal cancer.

Material and method

Sample

In Denmark, more than 1,000 families (excluding familial adenomatous polyposis) with suspected or verified risk of hereditary colorectal cancer, are registered in the national HNPCC register, which was established in 1991. Clinical geneticists, pathologists, surgeons and gynecologists report data on a national basis. At the time of the study, Lynch syndrome had been identified in 180 families in which 522 adult (>18 years of age) mutation carriers were eligible.

The Lynch syndrome self-concept scale was distributed by ordinary mail at two time points (May 2008 in eastern Denmark and January 2009 in western Denmark). A reminder was sent after 3–4 weeks. The two data sets were pooled for further analysis. Demographic data on gender, age, education, previous/current cancer and experience from cancer in close relatives were collected from the participants. The total response rate was 79% (N = 413) and the 109 non-responders did not differ significantly from the responders regarding the demographic variables available, i.e. sex, age, previous cancer, and time since genetic testing (data not shown).

The Lynch syndrome self-concept scale

The self-concept scale is a two-factor scale containing 20 statements intended to reflect issues specific for Lynch syndrome mutation carriers. Responders are asked to indicate their degree of agreement on a seven-grade Likert scale (range: 1–7) [18, 19]. Sum scores may range from 20 to 140, with higher scores linked to a greater impact on the individual's self-concept. The scale contains two subscales, which reflect stigma-vulnerability (15 items) and bowel symptom-related anxiety (5 items). Statements 1 and 2 are positive, and consequently reversed in the analyses, whereas the remaining 18 statements are negative. The scale was translated into Danish according to recommended guidelines, including re-back-translation and the use of a bilingual panel to ensure preservation of the conceptual meaning [28–30].

Statistical analysis

Missing data and answers labeled "non applicable" were coded as "missing" and responders with more than 3 missing values were not included in the final analysis, whereas responders with 1–3 missing values were re-coded using the average mean of the informant. Univariate analysis included sex, formal education (dichotomized into "primary school", which equals maximum 9 years, and "continued"), time since genetic testing, current or previous cancer, and self-reported experience with cancer in close relatives.

Descriptive analysis of the total score and the subscales included mean values and standard deviations. The total sum score as well as the mean score were calculated. Wilcoxon two-sample test was used to analyze dichotomized variables and Kendals Tau–b correlation was used to analyze the continuous data (age and time since genetic testing). Wilcoxon signed rank test was used to analyze individual scores in relation to sex and education. Logistic regression analysis was used to assess explanatory variables in individuals using scores in the upper quartile (sum score >66) as the outcome variable. Significance was set at $P = 0.05$. The statistical analyses were performed using SAS version 9.1.

Results

In total, 419 individuals, including 218 women, with a mean age of 48 (18–85) years contributed with data. Time since genetic testing was mean 5.2 (range 0.7–14.8) years, 182 individuals (44%) had been affected by cancer, and the majority (87%) reported experience from cancer in close relatives. Non-responders did not differ from responders regarding gender, time since genetic testing, cancer status and age (data not shown). After excluding responders with incomplete data, 398 (75%) individuals were included in the final analysis.

The distribution of the scores for the 20 items is presented in Table 1 with the majority unimodal right-skewed towards positive self-concept. A wide range (20–132) of self-concept scores was obtained with 75% reporting scores less than 3.4 out of 7 possible (Table 2). The results can be exemplified by item 1 (*feeling hopeful about my future*) to which 78% agreed or strongly agreed and item 2 (*able to deal with the test result*) to which 78% agreed or strongly agreed. Less than 4% reported *not having hope for the future* and the same number reported feeling *unable to deal*

Table 1 Response distribution for each self-concept statement (%)

Statement	Strongly disagree	Disagree	Some-what disagree	Neither agree nor disagree	Somewhat agree	Agree	Strongly agree	Not applicable	Total(n)
I am hopeful about myself in the future[a]	2	2	4	3	11	28	50	1	417
I am able to deal with my test result[a]	1	0	3	3	12	37	41	3	417
I am worried about bowel symptoms (like bleeding) when going to the bathroom[b]	19	2	7	9	13	15	8	4	415
I feel my body has betrayed me[a]	41	34	4	10	4	4	2	4	415
I feel like a walking time bomb[b]	44	24	5	6	9	5	4	2	415
I feel different from others my age[a]	39	28	4	6	8	9	4	1	415
I feel cursed because of my test result[a]	34	30	5	8	7	6	3	2	417
I feel guilty that I might pass on a cancer risk to my children[b]	22	17	7	9	12	11	16	7	408
I feel isolated because of my test result[a]	59	26	3	3	5	2	1	2	417
I feel I have lost my sense of privacy[a]	59	28	3	4	3	2	1	1	417
I think about my test result a lot[a]	21	23	11	9	15	11	9	1	416
I'm afraid of having bowel pain[b]	25	25	11	8	11	10	8	1	416
I am worried that cancer will be found when I go for screening[b]	6	7	9	8	18	23	27	1	415
I feel labeled[a]	50	26	3	6	5	4	5	1	417
I worry about chances in my bowels[b]	15	13	11	9	16	18	17	1	417
I feel burdened with this information[a]	31	30	5	8	10	8	6	2	416
I distrust my body[a]	37	29	6	9	6	5	5	2	413
My test result get in the way of who I really am[a]	47	30	6	3	5	3	4	2	418
I have become more secretive[a]	48	32	2	5	5	3	4	1	415
I feel embarrassed when I go for my bowel screening[a]	31	26	7	10	9	8	9	1	417

[a] Stigma-vulnerability

[b] Gastrointestinal anxiety

Table 2 Mean self-concept scores stratified for demographic variables and correlated to age and time since testing

	Total score		Subscale scores			
			Stigma vulnerability		Gastrointestinal-related anxiety	
	Mean (SD)	*P*-value[a]	mean (SD)	*P*-value[a]	Mean (SD)	*P*-value[a]
Total cohort (n = 398)	2.74 (1.14)	–	2.34 (1.15)	–	3.94 (1.50)	–
Gender						
Male (n = 192)	2.55 (1.03)		2.16 (1.04)		3.71 (1.47)	
Female (n = 206)	2.91 (1.21)	**0.003**	2.50 (1.23)	**0.004**	4.1 (1.56)	**0.008**
Education						
Primary school (n = 111)	2.93 (1.78)	**0.02**	2.55 (1.18)	**0.007**	4.07 (1.51)	0.31
Continued (n = 287)	2.66 (0.89)		2.26 (1.50)		3.88 (1.54)	
Previous cancer)						
Yes (n = 180)	2.82 (1.14)	0.12	2.41 (1.17)	0.17	4.05 (1.51)	0.13
No (n = 226)	2.67 (1.15)		2.29 (1.14)		3.84 (1.55)	
Experience from cancer in close relatives						
Yes (n = 344)	2.8 (1.16)	**0.018**	2.39 (1.72)	**0.03**	4.02 (1,55)	**0.013**
No (n = 54)	2.37 (0.95)		2.03 (0.97)		3.4 (1.33)	
Correlation with self-concept scores						
	Tau-b [95% CI]	*P*-value[b]	Tau-b [95% CI]	*P*-value[b]	Tau-b [95% CI]	*P*-value[b]
Age	0.0003 [−0.66–0.07]	0.99	0.014 [−0.08–0.05]	0.68	0.012 [−0.06–0.08]	0.72
Time since genetic testing	0.0083 [−0.08–0.06]	0.81	0.019 [−0.09–0.08]	0.59	0.015 [−0.08–0.05]	0.67

Bolded figures refer to significant findings

SD standard deviation

[a] Wilcoxon rank test

[b] Kendals Tau-b two-sided Z

Table 3 Adjusted odds ratios for self-concept scores within the upper quartile in relation to demographic variables

	Total score	Subscale score	
		Stigma vulnerability	Gastrointestinal-related anxiety
	OR (95% CI)		
Gender			
Female: male	**1.84 (1.14–2.99)**	**1.66 (1.04–2.66)**	**1.77 (1.1–2.86)**
Education			
Primary school: continued	1.41 (0.82–2.43)	**1.8 (1.06–3.03)**	1.38 (0.81–2.37)
Previous cancer			
Yes: no	1.62 (0.94–2.81)	1.05 (0.61–1.8)	1.42 (0.82–2.44)
Experience from cancer in close relatives			
Yes: no	1.58 (0.77–3.27)	1.46 (0.71–3.03)	1.8 (0.83–4.0)
Age			
continuous	0.98 (0.96–1.0)	0.99 (0.97–1.01)	1.0 (0.98–1.02)
Time since genetic testing			
continuous	0.99 (0.93–1.06)	1.0 (0.94–1.07)	0.97 (0.91–1.04)

Bolded figures refer to significant findings

with the test result. Among the negative statements, feelings of guilt for having passed on a defective gene to children were reported as agree/strongly agree by 27% and worries that cancer would be found when going to screening was agreed upon by 50% of the responders.

The mean sum score was 54.8, which when divided by the number of statements corresponded to a mean score of 2.74. The mean subscale scores were 35.1 (2.34 per statement) for the stigma and vulnerability subscale and 19.7 (3.94) for the bowel symptom-related anxiety

subscale. Females, individuals with less formal education and individuals with experience from cancer in close relatives reported significantly higher scores on the total scale (Table 2). When the subscales were analyzed, women and individuals with experience from cancer reported higher scores on both subscales, whereas individuals with less education had higher scores on the stigma and vulnerability subscale. Previous cancer, age and time since genetic testing did not correlate with the self-concept scores.

Multivariate regression analysis was used to identify subsets with the highest impact on self-concept. Herein, female sex and lower education correlated with an increased OR for scores in the upper quartile (Table 3). Females had higher scores on the total scales (OR 1.8) as well as on both subscales (OR 1.7 and 1.8, respectively) and individuals with lower education showed an increased risk (OR 1.8) for high scores on the stigma and vulnerability subscale (Table 3). Further investigation demonstrated that the higher scores in females derived from 12 statements, which were equally distributed on both subscales. In individuals with less formal education, the higher scores derived from 7 of the 15 statements on the stigma-vulnerability subscale, which indicates that several issues, rather than specific statements, account for the differences in scores related to sex and education.

Discussion

We investigated self-concept in the entire Danish Lynch syndrome population with more than 400 responders in order to obtain a broad picture of how these individuals perceive themselves and to identify subsets with a higher impact on self-concept. The individuals had undergone genetic testing mean 5 years prior to the study, which implies that the results reflect self-concept in a cohort with relatively long experience from being at increased risk of cancer. The majority of the Danish mutation carriers reported minor impact on self-concept, which suggests that they, in general, adapt well to the situation. Though we did not evaluate depression, the high frequency of positive answers in the self-concept scale suggests that psychological distress is not a predominant problem in Danish mutation carriers. This is in line with results from studies that have evaluated anxiety and depression among Lynch syndrome mutation carriers and concluded that most individuals seem to be able to handle the genetic test result [14]. Higher scores were, however, reported by women, individuals with less formal education, and those with experience from cancer in close relatives. These subsets are among those previously identified as vulnerable in studies of anxiety and psychological distress in hereditary cancer [31–34]. In this regard, it is interesting to note that neither young individuals nor individuals affected by cancer in our cohort reported higher self-concept scores, which supports the underlying concept that the Lynch syndrome self-concept scale measures issues different from global anxiety and depression measures. The lack of correlation to time since genetic testing also suggests that factors other than time influences self-concept in mutation carriers.

Multivariate analysis revealed increased risks of high self-concept scores in women and individuals with less formal education (Table 3). Women had an OR of 1.8 for scoring in the upper quartile on both subscales, which may reflect differences in how men and women perceive themselves in relation to cancer risk. In this regard, it is the perception of an event rather than the event itself that determine the emotional, cognitive and behavioral responses [35]. Women have in previous studies been suggested to take on responsibility for the well-being of family members and for coordinating surveillance and spreading information in the family [36]. This could reflect differences in how women and men perceive their roles and could imply that the women's feelings of responsibility for other family members may influence how they regard their own situation. Another explanation for the higher impact on self-concept in women may be that whereas men are recommended colonoscopic surveillance only, women are also at risk of endometrial and ovarian cancer and undergo surveillance and/or prophylactic procedures for these cancer types.

Differences in coping styles could also represent an explanation with women preferentially using problem-focused coping, distraction methods and seeking social support [35, 37–39]. Psychological coping mechanisms are among the factors that influence the emotional outcome of genetic testing [40]. Passive or escape-avoidant coping style and pessimistic perception of the reaction to the test result or the disease itself has been shown to increase post distress counseling in hereditary colorectal cancer as well as in hereditary breast-ovarian cancer [39, 41]. Several items in the self-concept scale relate to coping mechanisms, e.g. being able to deal with the test results and feeling hopeful about the future. Detailed understanding of how coping mechanisms relate to self-concept, however, needs further investigation and a major research challenge related to psychosocial aspects of Lynch syndrome lies in the identification of relevant causes since the genetic testing procedure, the surveillance programs, and the increased risk of cancer may all represent stressful events.

Individuals with less formal education showed an increased risk (OR 1.8) for scores in the upper quartile on the stigma and vulnerability subscale, whereas no increased risk was identified for high scores on the gastrointestinal-related anxiety subscale. Hence, worry or anxiety about bowel symptoms seems unrelated to educational level,

whereas stigmatization seems to be particularly pronounced in individuals with a lower educational level. Socioeconomic status and educational level have previously been identified as important determinants of health [42]. We did not collect information on socioeconomic status, but this factor may be relevant to consider in the development of psychosocial support and intervention programs for mutation carriers.

The present study represents the first extended use of the Lynch syndrome self-concept scale and reveals a relatively low impact on self-concept in Danish mutation carriers. Women, individuals with less former education and experience from cancer in close relatives reported higher impact on self-concept, which needs further investigation. Self-concept also needs further investigated in relation to e.g. anxiety, depression, coping-style, and participation in surveillance programs in order to assess its potential as an indicator of target groups for extended psychosocial support.

Acknowledgments The study was supported by Hvidovre University Hospital and the Danish Cancer Fund.

References

1. Lynch HT, Lynch JF, Lynch PM, Attard T (2008) Hereditary colorectal cancer syndromes: molecular genetics, genetic counseling, diagnosis and management. Fam Cancer 7:27–39
2. Lynch PM (2007) New issues in genetic counseling of hereditary colon cancer. Clin Cancer Res 13:6857s–6861s
3. Marshall M, Solomon S (2007) Hereditary breast-ovarian cancer: clinical findings and medical management. Plast Surg Nurs 27:124–127
4. Aarnio M, Sankila R, Pukkala E, Salovaara R, Aaltonen LA, de la CA, Peltomaki P, Mecklin JP, Jarvinen HJ (1999) Cancer risk in mutation carriers of DNA-mismatch-repair genes. Int J Cancer 81:214–218
5. Lynch HT, Lynch PM, Lanspa SJ, Snyder CL, Lynch JF, Boland CR (2009) Review of the Lynch syndrome: history, molecular genetics, screening, differential diagnosis, and medicolegal ramifications. Clin Genet 76:1–18
6. Jarvinen HJ, Renkonen-Sinisalo L, Aktan-Collan K, Peltomaki P, Aaltonen LA, Mecklin JP (2009) Ten years after mutation testing for lynch syndrome: cancer incidence and outcome in mutation-positive and mutation-negative family members. J Clin Oncol 27:4793–4797
7. Renkonen-Sinisalo L, Aarnio M, Mecklin JP, Jarvinen HJ (2000) Surveillance improves survival of colorectal cancer in patients with hereditary nonpolyposis colorectal cancer. Cancer Detect Prev 24:137–142
8. Mack LA, Cook LS, Temple WJ, Carlson LE, Hilsden RJ, Paolucci EO (2009) Colorectal cancer screening among first-degree relatives of colorectal cancer patients: benefits and barriers. Ann Surg Oncol 16:2092–2100
9. Keller M, Jost R, Kadmon M, Wullenweber HP, Haunstetter CM, Willeke F, Jung C, Gebert J, Sutter C, Herfarth C, Buchler MW (2004) Acceptance of and attitude toward genetic testing for hereditary nonpolyposis colorectal cancer: a comparison of participants and nonparticipants in genetic counseling. Dis Colon Rectum 47:153–162
10. Kinney AY, Choi YA, DeVellis B, Kobetz E, Millikan RC, Sandler RS (2000) Interest in genetic testing among first-degree relatives of colorectal cancer patients. Am J Prev Med 18: 249–252
11. Pieterse AH, Ausems MG, Van Dulmen AM, Beemer FA, Bensing JM (2005) Initial cancer genetic counseling consultation: change in counselees' cognitions and anxiety, and association with addressing their needs and preferences. Am J Med Genet A 137:27–35
12. Keller M, Jost R, Haunstetter CM, Kienle P, Knaebel HP, Gebert J, Sutter C, Knebel-Doeberitz M, Cremer F, Mazitschek U (2002) Comprehensive genetic counseling for families at risk for HNPCC: impact on distress and perceptions. Genet Test 6:291–302
13. Aktan-Collan K, Haukkala A, Mecklin JP, Uutela A, Kaariainen H (2001) Psychological consequences of predictive genetic testing for hereditary non-polyposis colorectal cancer (HNPCC): a prospective follow-up study. Int J Cancer 93:608–611
14. Collins VR, Meiser B, Ukoumunne OC, Gaff C, St John DJ, Halliday JL (2007) The impact of predictive genetic testing for hereditary nonpolyposis colorectal cancer: three years after testing. Genet Med 9:290–297
15. Meiser B, Collins V, Warren R, Gaff C, St John DJ, Young MA, Harrop K, Brown J, Halliday J (2004) Psychological impact of genetic testing for hereditary non-polyposis colorectal cancer. Clin Genet 66:502–511
16. Meiser B (2005) Psychological impact of genetic testing for cancer susceptibility: an update of the literature. Psychooncology 14:1060–1074
17. Esplen MJ, Stuckless N, Hunter J, Liede A, Metcalfe K, Glendon G, Narod S, Butler K, Scott J, Irwin E (2009) The BRCA Self-Concept Scale: a new instrument to measure self-concept in BRCA1/2 mutation carriers. Psychooncology 18:1216–1229
18. Esplen MJ, Stuckless N, Wong J, Gallinger S, Aronson M, Rothenmund H, Semotiuk K, Stokes J, Way C, Green J, Butler K (2011) Development and validation of an instrument to measure the impact on self-concept in Lynch syndrome. Unpublished
19. Bleiker EM, Hahn DE, Aaronson NK (2003) Psychosocial issues in cancer genetics–current status and future directions. Acta Oncol 42:276–286
20. Esplen MJ, Stuckless N, Hunter J, Liede A, Metcalfe K, Glendon G, Narod S, Butler K, Scott J, Irwin E (2009) The BRCA self-concept scale: a new instrument to measure self-concept in BRCA1/2 mutation carriers. Psychooncology 18:1216–1229
21. Landsbergen KM, Prins JB, Brunner HG, Kraaimaat FW, Hoogerbrugge N (2009) Genetic testing for Lynch syndrome in the first year of colorectal cancer: a review of the psychological impact. Fam Cancer 8:325–337
22. Vadaparampil ST, Ropka M, Stefanek ME (2005) Measurement of psychological factors associated with genetic testing for hereditary breast, ovarian and colon cancers. Fam Cancer 4: 195–206
23. Corte C, Zucker RA (2008) Self-concept disturbances: cognitive vulnerability for early drinking and early drunkenness in adolescents at high risk for alcohol problems. Addict Behav 33: 1282–1290
24. Markus H, Wurf E (1987) The dynamic self-concept: a social psychological perspective. Ann Rev Psychol 38:299–337
25. Esplen MJ, Stuckless N, Hunter J, Liede A, Metcalfe K, Glendon G, Narod S, Butler K, Scott J, Irwin E (2009) The BRCA self-concept scale: a new instrument to measure self-concept in BRCA1/2 mutation carriers. Psychooncology 18:1216–1229
26. Esplen MJ, Stuckless N, Berk T, Butler K, Gallinger S (2009) The FAP self-concept scale (adult form). Fam Cancer 8:39–50

27. Petersen HV, Domanska K, Bendahl PO, Wong J, Carlsson C, Bernstein I, Esplen MJ, Nilbert M (2011) Validation of a self-concept scale for Lynch syndrome in different nationalities. J Genet Couns 20:308–313
28. Bonomi AE, Cella DF, Hahn EA, Bjordal K, Sperner-Unterweger B, Gangeri L, Bergman B, Willems-Groot J, Hanquet P, Zittoun R (1996) Multilingual translation of the functional assessment of cancer therapy (FACT) quality of life measurement system. Qual Life Res 5:309–320
29. Hunt SM, Alonso J, Bucquet D, Niero M, Wiklund I, McKenna S (1991) Cross-cultural adaptation of health measures. European group for health management and quality of life assessment. Health Policy 19:33–44
30. Sousa VD, Rojjanasrirat W (2010) Translation, adaptation and validation of instruments or scales for use in cross-cultural health care research: a clear and user-friendly guideline. J Eval Clin Pract 17:268–274
31. Esplen MJ, Urquhart C, Butler K, Gallinger S, Aronson M, Wong J (2003) The experience of loss and anticipation of distress in colorectal cancer patients undergoing genetic testing. J Psychosom Res 55:427–435
32. Murakami Y, Gondo N, Okamura H, Akechi T, Uchitomi Y (2001) Guilt from negative genetic test findings. Am J Psychiat 158:1929
33. Murakami Y, Okamura H, Sugano K, Yoshida T, Kazuma K, Akechi T, Uchitomi Y (2004) Psychologic distress after disclosure of genetic test results regarding hereditary nonpolyposis colorectal carcinoma. Cancer 101:395–403
34. Vernon SW, Gritz ER, Peterson SK, Amos CI, Perz CA, Baile WF, Lynch PM (1997) Correlates of psychologic distress in colorectal cancer patients undergoing genetic testing for hereditary colon cancer. Health Psychol 16:73–86
35. Rao K (2009) Recent research in stress, coping and women's health. Curr Opin Psychiatry 22:188–193
36. Barthuma K, Nilbert M, Carlsson C (2011) Family perspectives in Lynch syndrome; transition to a risk family, communications and relations. Unpublished
37. Schmaus BJ, Laubmeier KK, Boquiren VM, Herzer M, Zakowski SG (2008) Gender and stress: differential psychophysiological reactivity to stress reexposure in the laboratory. Int J Psychophysiol 69:101–106
38. Wang J, Korczykowski M, Rao H, Fan Y, Pluta J, Gur RC, McEwen BS, Detre JA (2007) Gender difference in neural response to psychological stress. Soc Cogn Affect Neurosci 2:227–239
39. Bennett P, Wilkinson C, Turner J, Edwards RT, France B, Griffin G, Gray J (2009) Factors associated with intrusive cancer-related worries in women undergoing cancer genetic risk assessment. Fam Cancer 8:159–165
40. Broadstock M, Michie S, Marteau T (2000) Psychological consequences of predictive genetic testing: a systematic review. Eur J Hum Genet 8:731–738
41. van OI, Meijers-Heijboer H, Duivenvoorden HJ, Brocker-Vriends AH, van Asperen CJ, Sijmons RH, Seynaeve C, van Gool AR, Klijn JG, Tibben A (2007) Prognostic factors for hereditary cancer distress six months after BRCA1/2 or HNPCC genetic susceptibility testing. Eur J Cancer 43:71–77 43
42. Thoits PA (2010) Stress and health: major findings and policy implications. J Health Soc Behav 51(Suppl):S41–S53

Paper III

Paper IV