Living with genetic risk of coronary heart disease:

A qualitative interview study of patients with familial hypercholesterolemia

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"Except for monozygotic twins, each person's genome is unique. All physicians will soon need to understand the concept of genetic variability, its interactions with the environment, and its implications for patient care ... the practice of medicine has now entered an area in which the individual patient's genome will help determine the optimal approach to care, whether it is preventive, diagnostic, or therapeutic."

– Alan E. Guttmacher & Francis S. Collins, *N Engl J Med*, 2003

"We live in a time of deep interest in – of not obsession with – the problems of health and disease ... For those who are media vigilant, questions about the consumption of cholesterol (good or bad) ... and a host of other specified "risk factors" are daily fare. Increasingly, we are told that new knowledge gives us new opportunities to take control of our health. With this new knowledge, however, come new responsibilities and a new set of moral expectations about health and disease."

– Alan M. Brandt & Paul Rozin, *Morality and health*, 1997

ABSTRACT

Heterozygous familial hypercholesterolemia (FH) is a genetic condition associated with increased risk of coronary heart disease (CHD). The overall aim of the thesis is to explore how individuals with FH perceive and manage their condition.

We did a qualitative interview study, based on semi-structured interviews with 40 women and men diagnosed with FH. Participants were recruited from the Lipid Clinic, Medical Department, Rikshospitalet-Radiumhospitalet HF, in Oslo, Norway, which is an outpatient clinic for metabolic lipid disorders.

The majority of participants convey images of individuals they considered to be likely victims of CHD, and portray the coronary candidate as someone who was different from themselves. The typical image was an unfit, middle-aged man, often a business man or a taxi driver. Women reports barriers in the health service related to diagnosis and treatment. Participants negotiate a personal and dynamic sense of their vulnerability to CHD, grounded in notions of their genetic and inherited risk. Participants' perceived vulnerability could shift dynamically, due to changes in situational factors such as cardiac events in the family, illness experiences, or becoming a parent. Participants do not report guilt or shame for having FH, but they experience guilt and shame related to how well they manage their condition. Health professionals may cause feelings of guilt and shame in patients with FH.

Health professionals should recognize that patients may have moral and psychological reasons for distancing themselves from the "coronary candidate". The stereotype of CHD as a men's disease may result in barriers to diagnosis and treatment for women. In order to individualize clinical management of patients with FH doctors should elicit patients' understanding of their family history of CHD and their perceived vulnerability to CHD. Health professionals should recognize patients' preferences and use communicative strategies that diminish such experiences in their patients.

SAMMENDRAG [abstract in Norwegian]

Arvelig høyt kolesterol, familiær hyperkolesterolemi (FH), er en genetisk tilstand som er forbundet med øket risiko for hjertesykdom. Målsettingen i denne avhandlingen er å utforske hvordan personer med FH opplever og håndterer sin tilstand.

Vi har gjort en kvalitativ intervjustudie, basert på individuelle semistrukturerte intervjuer med 40 kvinner og menn diagnostisert med FH. Deltakerne er rekruttert via Lipidklinikken, Medisinsk avdeling, Rikshospitalet-Radiumhospitalet HF, som er en poliklinikk for metabolske lipidforstyrrelser.

De fleste deltakerne formidler bilder av individer de mener har økt risiko for koronar hjertesykdom, og de fremstiller den koronare kandidaten som en som er ulik dem selv. Det typiske bildet er en usunn, middelaldrende mann som gjerne var foretningsmann eller drosjesjåfør. Kvinner rapporterer at de møter hindringer i helsetjenesten relatert til diagnose og behandling. Deltakerne etablerer en dynamisk forståelse av egen sårbarhet for koronar hjertesykdom som er forankret i forståelse egen genetisk og arvelig risiko. Deltakernes oppfatning av egen risiko kunne endres over tid på grunn av endringer i faktorer som hjertekarsykdom i familien, sykdomserfaringer, eller ved at man ble foreldre. Deltakerne rapporterer ingen skyld- eller skamfølelse for at de har FH, men opplever skyld og skam knyttet til hvor godt de håndterer tilstanden. Helsepersonell kan vekke følelser av skyld og skam hos pasienter med FH.

Helsepersonell bør anerkjenne at pasienter kan ha moralske og psykologiske grunner for å distansere seg fra det typiske bildet av en person med økt risiko for koronar hjertesykdom. Det stereotype bildet av koronar hjertesykdom som en tilstand som rammer menn kan føre til at kvinner opplever diagnostiske og behandlingsmessige hindringer. For å kunne skreddersy den kliniske håndteringen av pasienter med FH bør leger ha innsikt i hvordan pasienten forstår belastningen for hjertesykdom i egen slekt og hvordan de forstår sin egen sårbarhet for hjertesykdom. Helsepersonell bør anerkjenne pasientens preferanser og anvende samtalestrategier som reduserer erfaringer av skyld og skam hos pasienter.

CONTENTS

PREFACE

One night, when I was 20 years old, my father was struck by nausea and a severe, squeezing pain in the stomach and chest. He phoned the casualty clinic. He did not have pain radiating down the left arm, and his case was regarded as an acute abdominal condition. He passed away while waiting for the doctor, 62 years old, from what was later diagnosed as an inferior myocardial infarction.

This incident occurred in 1991 when I was in the middle of the first year of my medical studies. The death of my father made me reflect on my own possible hereditary susceptibility to heart disease, and it also made me reflect on how health professionals depend on diagnostic categories and stereotypes to interpret symptoms and to organize medical knowledge and clinical work. This experience was an important reason for my interest in the concept of risk and how people reflect on and manage uncertainties and risks of future suffering. I therefore dedicate this thesis to the memory of my father Alf.

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The good working facilities and atmosphere at the Institute have been a great support for me. I have been affiliated with the Section of Medical Anthropology and Social Medicine and it has offered me a stimulating and critical interdisciplinary milieu. I have also received important input from being a member of the cross disciplinary network "Vulnerability as strength". Many colleagues have commented on my work and have shared reflections and been supportive in rough times. I thank you all for everything you have contributed during these years.

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LIST OF PAPERS

Paper I-IV

I.   Frich JC, Malterud K, Fugelli P. How do patients at risk portray candidates for coronary heart disease? A qualitative interview study. Scand J Prim Health Care 2007; (in press).

II.   Frich JC, Malterud K, Fugelli P. Women at risk of coronary heart disease experience barriers to diagnosis and treatment: a qualitative interview study. Scand J Prim Health Care 2006; 24: 38-43.

III.   Frich JC, Ose L, Malterud K, Fugelli P. Perceived vulnerability to heart disease in patients with familial hypercholesterolemia: a qualitative interview study. Ann Fam Med 2006, 4; 198-204.

IV.   Frich JC, Malterud K, Fugelli P. Experiences of guilt and shame in patients with familial hypercholesterolemia: a qualitative interview study. Submitted.

I refer to the papers by their Roman numerals.

LIST OF ABBREVIATIONS

ApoB100   Apolipoprotein B-100

CHD   Coronary heart disease

FDB   Familial defective ApoB100

FH   Familial hypercholesterolemia

HBM   Health belief model

LDL   Low-density lipoprotein

LDLR   Low-density lipoprotein receptor

NNT   Numbers-needed-to-treat

WHO   World Health Organization

1. INTRODUCTION

"When you hear hoofbeats behind you, don't expect to see a zebra" is an aphorism that warns doctors against the danger of thinking about rare conditions at the expense of the most common and obvious causes of symptoms or clinical findings (1). With respect to coronary heart disease (CHD), the condition known as familial hypercholesterolemia (FH) is likely to be classified as a zebra.

April 14st, 2003, The International Human Genome Sequencing Consortium announced that the Human Genome Project had been completed. An article in New England Journal of Medicine declared that we have entered a new area of "genomic medicine" in which molecular biology will transform clinical practice (2). Genomics refers to the study of not only single genes, but of the functions and interactions of various genes. This "molecularization of medicine", a phrase used by Rheinberger (3), has led to new insight about genetic aspects of atherosclerosis and CHD (4), and there appears to be an ongoing "geneticisation" of CHD in clinical practice (5). Some authors claim that we are entering an area "in which FH might very well constitute a unique example of what "the zebra can tell us about the horse"" (6).

This thesis will look at what the zebra can tell about the horse. Its overall aim is to explore how individuals with FH perceive, understand and manage their condition. I will explore what the experiences of individuals with FH can tell about what it means to be diagnosed with a cardiovascular risk in the genomic area. These experiences will need to be situated within the history and management of CHD in general, and therefore I will also address what the horse can tell about the zebra.

I will not be able to cover all aspects of living with a genetic risk of CHD. I have chosen to focus particularly on how patients with FH perceive and manage their own risk, and therefore I will not explore issues such as family planning among patients with FH, parental responsibilities, genetic testing of family members, and issues concerning life insurance.

1.1 Coronary heart disease

CHD is caused by atherosclerosis in the coronary arteries and is the cause of seven million deaths annually and is one of the leading causes of lost life years worldwide

(7). In Norway, CHD accounts for 18% of deaths in men and 15% of deaths in women (8). Atherosclerosis is a mulitfactorial disease, and about 300 risk factors have been reported in the literature (9). Risk factors are typically classified as either modifiable, such as elevated serum lipids, smoking habits, high blood pressure, obesity, and diabetes, or nonmodifiable, such as age, gender, genetic susceptibility, and possibly also birth weight. Risk factors tend to cluster in individuals. Blood lipid disorders have a principal role in the pathogenesis of CHD and have been characterized as "the pivotal CHD risk factor" (9). There are several lipid disorders, including FH (10, 11). As this thesis explores CHD from the perspective of patients with FH, I will provide a brief overview of disorders in the cholesterol metabolism.

1.2 Cholesterol as cardiovascular risk factor

Hypercholesterolemia refers to a condition characterised by elevated levels of serum cholesterol. Cholesterol is a sterol (a combination of steroid and alcohol). The name originates from the Greek "chole" (bile) and "stereos" (solid), and the chemical suffix "-ol" for an alcohol. Cholesterol was isolated in solid form from gallstones in 1784, but Chevreul, a French chemist, is credited with the initial discovery of cholesterol (or "cholesterine") in 1815 (12, 13). In 1913, the Russian pathologist Anitschkow found that rabbits fed with cholesterol developed atherosclerosis and he claimed that there was a correlation between hypercholesterolemia and atherosclerosis (14). In the 1940s, Keys conducted an epidemiological worldwide survey in populations whose diets varied in fat content (15). He found a correlation between high dietary intake of fat and increased cholesterol levels in the populations he had studied. Keys also suggested a causal relationship between the percentages of fat in the diet and the rate of CHD. Keys' findings caught the media's interest, but there were scientists who questioned his findings and made efforts to pull cholesterol back into the research laboratories (15). Until the early 1950s many researchers and clinicians perceived CHD as a chronic, degenerative disease that could not be prevented.

Results from The Framingham Heart Study, an ongoing follow-up study of the population in the city of Framingham in Massachusetts which was initiated in 1948, suggested in 1961 that high cholesterol levels preceded the development of CHD and increased the risk of CHD (16). However, as these results were generated

in an observational study, controversies surrounding cholesterol went on for decades until intervention trials, such as The Multiple Risk Factor Intervention Trial (MRFIT), suggested in the 1980s that a cholesterol-lowering diet could reduce the risk of CHD (10). In 1988 the National Cholesterol Education Programme in USA launched the "Know your Number" campaign and recommended that all adults should have their cholesterol tested. By the end of 1980s the campaign had spread to other countries in the Western world, including Norway. Cholesterol still remained a controversial issue in the early 1990s because researchers were uncertain about the effect of cholesterol-lowering therapy on overall mortality (10). In 1994, it was showed that the overall mortality was reduced in the group who received cholesterol-lowering medication and that this was achieved without any increase in mortality of other causes (17). It is now documented that lowering serum cholesterol by means of diets or medication reduces morbidity and mortality of CHD without an increase in mortality from other causes (11), although cut-off points for intervention are vividly discussed.

1.3 Cholesterol and its metabolism

Cholesterol is a major building block in cell membranes and it is also precursor of steroid hormones and of bile acids (10). Cholesterol in its pure form is insoluble in blood, but lipoproteins make it soluble in the form of a lipid droplet in which the insoluble part is turned inwards into the core of the particle. Different types of lipoproteins serve to transport absorbed dietary fat, endogenously synthesized cholesterol and fatty acids (triglycerides). Cholesterol and triglyceride (TG) synthesized in the liver are secreted into the circulation in very low-density lipoprotein (VLDL) particles. The TG component is hydrolysed by the enzyme lipoprotein lipase in peripheral tissues and is released from the particle. The VLDL remnant is either removed from the circulation by the liver or metabolized to low-density lipoprotein (LDL) by the enzyme hepatic lipase. LDL is a cholesterol-rich lipoprotein that transports cholesterol to peripheral cells. A high intake of fat, and especially saturated fat, increases the amount of VLDL particles and hence also the amount of LDL particles in the blood. Large numbers of LDL particles are correlated with atherosclerosis and CHD, and LDL-cholesterol is thus commonly referred to as "bad cholesterol". High-density lipoprotein (HDL) particles transport

cholesterol back to the liver for excretion. A large number of HDL particles are correlated with better health outcomes, and HDL-cholesterol is thus often referred to as "good cholesterol".

A LDL-receptor (sometimes abbreviated "LDLR") on the cell surface recognizes a protein (apoprotein B-100) in LDL particles and this recognition is necessary for transport of LDL into the cell. Approximately 70% of LDL is removed from the circulation by the liver. The presence of LDL-receptor in the liver thus has a major influence on clearance of LDL from the circulation and thereby the amount of circulating LDL. A mutation in the gene that codes for the LDL-receptor may result in a failure to produce receptor or a reduction of receptor activity, which leads to accumulation of LDL-cholesterol in the blood. An individual with this condition has a specific genetic form of hypercholesterolemia, referred to as FH.

1.4 Familial hypercholesterolemia

FH is an inherited autosomal dominant disorder of lipoprotein metabolism and was described for the first time in 1873 (18). Harbitz published his first observations of a group of patients with this condition in 1925, but it was a Norwegian colleague Müller who noticed a correlation between hypercholesterolemia and early onset of CHD (19). The condition was previously known as "Müller-Harbitz' disease", but the correct term at present is familial hypercholesterolemia (FH). It was poorly understood until Brown & Goldstein in the early 1970s discovered that elevated LDL-cholesterol was the hallmark of FH (12). They discovered that the elevated LDL-cholesterol in this disease could be explained by reduced or absent activity of the LDL-receptor. The gene that codes for the receptor was later located to the short arm of chromosome 19.

Heterozygous FH occurs with a frequency of 1 in 500 and the homozygous form occurs in 1 per million in most populations (20). In heterozygous individuals LDL-receptor activity is substantially reduced and in homozygous individuals receptor activity is virtually absent. In Norway, the diagnosis can be based on clinical and laboratory findings or be based on DNA-testing. More than 700 mutations have been reported in the gene that codes for the LDL-receptor, but mutations are only detected in 30-50% of patients with a clinical diagnosis of FH (21, 22). A mutation in the gene for apolipoprotein B-100 (ApoB100), the molecule

that serves to bind LDL to the LDL-receptor, leads to the same phenotype as FH, but may be referred to as familial defective ApoB-100 (FDB). There are two sets of diagnostic criteria that are commonly used (appendix A) (20, 23).

Studies of mortality and morbidity of untreated men and women with FH are based on register-data and probably overestimate the risk of CHD (24). A recent cumulative risk estimate suggests that, left untreated, 50% of men aged 50 years and 30% of women aged 60 years with the condition develop symptoms of CHD (20). Although FH is a monogenic condition (caused by a mutation in one gene only), there is a wide variety in the onset and severity of symptoms of CHD. The clinical severity has been found to vary considerable between families, with less variation within the same family (25). The literature suggests that the clinical severity is determined by environmental risk factors (24), other genetic factors, and by the type of mutation in the gene for the LDL-receptor (25-28). Mutations are classified into five or six categories, and while some mutations result in failure to produce any LDL-receptor protein, other mutations lead to impairments in binding capacity or other disturbances (26). Patients with so-called "null-alleles" where there is no production of LDL- receptor appear to have a higher risk of CHD (29).

LDL-cholesterol in untreated adults with FH is typically in the range of 5-10 mmol/l and there is hence an overlap of cholesterol levels in individuals with FH and individuals in the general population. A healthy lifestyle is an important aspect of treatment and comprises ideal body weight, no smoking, moderate physical activity, and a healthy diet with a low amount of saturated fat and a cholesterol intake of less than 200 mg per day (30). A LDL-cholesterol level < 2.6 mmol/l is considered optimal, but such a goal is not obtainable for all patients due to limited efficacy of current LDL-cholesterol-lowering drugs and their side effects. There are three major groups of LDL-cholesterol-lowering drugs available. HMG CoA reductase inhibitors ("statins") inhibit production of cholesterol in the liver, and it is the drug of first choice. Bile acid sequestrants ("resins") bind bile acids and prevent bile acids containing cholesterol from being reabsorbed in the gastrointestinal tract. Ezetimibe is a lipid-lowering drug that inhibits absorption of cholesterol from dietary and biliary sources.

An international panel on management of FH has listed eight major risk factors for cardiovascular disease in patients with FH (30):

- Age (men $\geq$ 30 years, and women $\geq$ 45 years or postmenopausal

- Cigarette smoking: active smokers

- Family history of premature CHD (CHD in male first degree relative < 55 years or in female first-degree relative < 65 years)

- High blood pressure (> 140/90 mmHg)

- Diabetes mellitus

- Very high LDL-cholesterol (> 8.5 mmol/l)

- Low HDL-cholesterol < 1.0 mmol/l

- Lipoprotein (a) > 60 mg/dl

Patients can be categorized into three groups regarding ten-year risk of cardiovascular events. With no major risk factors the risk is low, with one major risk factor the risk is moderate, and with two or more major risk factors, or if the patient has non-symptomatic atherosclerosis or clinical cardiovascular disease, the risk is high. Individuals with FH do not score lower on quality of life compared with controls who do not have hypercholesterolemia (31, 32).

1.5 Professional and lay epidemiology of heart disease

The Framingham Heart Study was launched in 1948 with the aim of understanding more about causes of CHD. While scientists had previously searched exclusively in the laboratory for cues about causes, the Framingham study was a population based study. The investigators coined the term "risk factor" (16) which proved to be an essential conceptual achievement in what has been referred to as the "risk factor approach" in epidemiology (33).

A landmark paper from The Framingham Heart Study in 1961 declared: "from a study of the characteristics of persons who develop coronary heart disease under observation in comparison with those who remain free of disease it is possible to determine the characteristics of susceptible individuals" (16). The Framingham investigators found that young women had a lower rate of CHD compared with young men and that gender was greater than any other risk factor (16). Additionally, numerous epidemiological studies of cardiovascular risk factors provided evidence

that biological traits such as elevated serum cholesterol, blood pressure, obesity and diabetes were associated with increased risk of CHD (10).

In 1959, Friedman and Rosenman claimed that a certain behavioural pattern, called "type A behaviour pattern" or "coronary prone personality", was associated with increased risk of CHD (34). A series of publications during the following decades indicated an increased risk of CHD in individuals with a behaviour characterised by excessive drive, competition, meeting deadlines, a desire for recognition and advancement. Within this model, CHD was seen as a psychosocial disease and as a consequence of people's worries and strains in modern society (33, 34). A bestselling book entitled "Type A behaviour and your heart" was published in 1974 (35). During the late 1970s, however, negative studies that investigated the type A hypothesis appeared more often than positive ones, and the interest in the type A behaviour as risk factor of CHD declined (33, 36).

How was epidemiological knowledge about CHD received by the lay public? How did lay people make sense of cardiovascular risk? How did lay people explain coronary events? Questions such as these were the starting point for Davison et al who did fieldwork and qualitative interviews with 180 lay informants in three communities in different areas of the South of Wales during 1988 and 1989 (37, 38). The study team coined the term "lay epidemiology" for lay theories about "heart trouble" (38), and they found that the notion of "candidacy" or "coronary candidate" was essential in lay explanations of CHD.

A "candidate" was "a person who (for a variety of possible reasons) is seen as being at particular risk from the misfortune of heart disease" (38). Among some of the characteristics associated with the "candidate" are fat people, people who don't take exercise and are unfit, red faced people, people with a grey pallor, smokers, people with a heart trouble in the family, heavy drinkers, people who eat excessive amounts of rich, fatty food, worriers (by nature), and bad tempered, pessimistic or negative people (37). The hereditary disposition to heart disease was a key characteristic of the candidate. Davison and colleagues found that lay individuals used their notion of the candidate as a tool to explain one's own illness or other people's illness and death from CHD and to predict one's own or other people's risk of being hit by CHD. Lay epidemiology explained unwarranted survivals and anomalous deaths through reference to "luck" or "unluck".

Davison and colleagues' work on lay epidemiology has been criticised for ignoring gender. Emslie and colleagues conducted a qualitative study in 1997 and 1998 with 61 informants among participants in a cross-sectional survey about cardiovascular and respiratory diseases in the West of Scotland (39). They found that accounts of coronary candidacy were structured by gender: "Whenever respondents talked about specific coronary candidates, they were invariably talking about men" (39). Later research on the lay epidemiology of CHD has explored the issue of gender and how individuals without increased risk of CHD reason about their medical family history (40, 41).

Research suggests that CHD has been perceived and represented in the public as a disease that affects men (34, 36, 39, 42, 43). We know little about how individuals at risk of CHD portray the coronary candidate and how they relate to their notion of the candidate. A better understanding of how patients at risk of CHD conceive and reflect on their notion of the coronary candidate may foster an improved clinical management.

1.6   Gender and coronary heart disease

Gender influences health and patients' management of disease (44). Mortality rates for all leading causes of death in the Western world are generally lower for women compared with men for all ages, and women also use health care more frequently (45). Gender needs to be considered in clinical settings as well as in public health (45, 46). On the other hand, clinicians and researchers may essentialize gender and thus overlook that differences within groups may be more striking than between groups (46).

Women's risks of CHD increases with age (47), and on average women develop symptoms of CHD one decade later than men. In Norway, 3557 men and 3212 women died from CHD (ICD codes I20-I25) in 2004 (8). There has been a decline in mortality rates of CHD in Norway the last decades, and the decline has been higher for men than for women (8). The demography of CHD is changing in Western countries. A recent study indicates that more women than men are affected and that CHD has shifted from a disease of middle-aged men to a chronic condition of elderly women (48).

Although women tend to use health care more often than men (45), the literature suggests that women are diagnosed later and seek health care later than men for symptoms of CHD (49). Research also suggests that women are less likely to receive lipid-lowering medication and to have a coronary revascularization procedure when diagnosed with CHD (50-54). Some studies find no gender differences (55, 56), and it has been argued that gender differences may be a result of unadjusted age-effects and poor study design (57). A recent study that adjusts for age and previous risk factors found a significant gender bias in clinical management in disfavour of women (58). The impact of gender on clinical management of CHD and cardiovascular risk factors varies with the patient's age (59). The overall picture appears to be multifaceted.

A gender difference in the management of CHD and risk of CHD may be explained along three axes: biological differences between women and men, lack of knowledge in women or reluctance to perceive oneself as someone at risk, and the existence of gender-specific barriers in the health service.

There is evidence that that men and women differ in the clinical presentation of cardiovascular symptoms and that CHD may be more difficult to diagnose in women (47, 60, 61). Research suggests that most women do not see CHD a substantial health concern and that they have little knowledge about their risk (62, 63). A qualitative study suggests that women's delay to seek care and their treatment decisions are linked to broader social and structural constraints and obligations (63). Research indicates that the candidate for CHD is often portrayed as a man and that women with symptoms of CHD adopt risk assessment strategies that enable them to conceptually distance themselves from risk of CHD by attributing risky lifestyle behaviour to men (64).

A study that investigated barriers to uptake of services for CHD in UK identified barriers such as patients' fear of hospitals, patients' denial of symptoms, and diagnostic confusion in the health service (65). No barriers in this study were specifically related to gender. An interview study with young women diagnosed with CHD found that women had experienced that their symptoms of CHD were not recognized in the health service (66).

Biological differences, patients' distancing from risk of CHD, and barriers in the health service may all be important explanations for gender differences in the

clinical management of CHD. Little is known about how women at risk of CHD experience the health service, and what barriers they may experience to diagnosis and treatment.

1.7   Perceived vulnerability

There are various approaches to the study of how people perceive risk. Psychological research on risk perception originated in empirical studies of probability assessment and has been referred to as "the psychometric paradigm" (67, 68). This approach uses psychophysical scaling and multivariate analysis techniques to produce quantitative representations of how people perceive risk. There is also a considerable literature that studies how people perceive risk using qualitative methodology (69-71). "Perceived vulnerability" is a notion that has been used to denote patients' perceived risk (72). Perceived vulnerability corresponds with "perceived susceptibility" which is a component of the health belief model (HBM) that was developed in the 1950s and has been used to explain health related behaviour (73, 74). Perceived vulnerability can be studied in quantitative terms or in qualitative terms. According to HBM, behaviour change requires that people must feel threatened by their behaviour or condition and believe that a change will result in a valued outcome at acceptable cost. The model contains various components which are used to explain and predict health-related behaviour: perceived susceptibility, perceived severity, perceived benefits, perceived barriers, cues to action, and variables such as sociodemographic characteristics. Research suggests that perceived vulnerability is a strong predictor of preventive health behaviour (72, 74). Several studies suggest that individuals make sense of their vulnerability to CHD in ways that differ from quantitative and numerical risk measures (37, 38, 71, 75, 76). Heredity and notions about the coronary candidate appears to be important.

A study in Scotland found that people who say they have a family history of CHD are more likely to see themselves "at risk" of CHD and are less likely to smoke (77). A study in the Netherlands of risk perception among individuals who had been screened on FH found that a high actual risk was correlated with an increased perceived vulnerability to myocardial infarction and that a greater portion of these individuals used lipid-lowering medication (78). The perception of the risk of getting a myocardial infarction was affected by age, education, cholesterol level

and cardiovascular disease in the family. A qualitative interview study of 50 individuals diagnosed with FH suggests that patients use their own general knowledge, clinical observations, and knowledge of personal family medical histories to make sense of risk (79).

More knowledge is needed about how individuals with FH resolve their vulnerability to CHD and how perceived vulnerability to CHD may change over time. There is significant variation in the severity of FH between families, and a better understanding of how patients with FH understand and resolve their vulnerability to CHD may foster an individualized and improved clinical management.

1.8   Risk, guilt and shame

Until the twentieth century the concept of risk had a limited use in sea navigation, gambling, mathematics and insurance (80). Beck has argued that the modern world is best understood as a "risk society" because the scientific and technological development, and modernity itself, has lead to numerous hazards that are difficult to calculate in terms of probabilities (81). The risk society affects individuals in two distinct ways. First, it increases the individual's awareness of risks outside individual control, leading to uncertainty and unease. Second, a focus on individual risk leads to greater emphasis on individual agency. In modernity self-identity is more and more "reflexively organised", and an individual's biography, education, career, health, etc, is perceived as results of individual agency (82, 83). Awareness and knowledge of risk, dangers and hazards plays a vital role for individual decisions regarding the future and the modern self.

Identifying and classifying risk or risk factors has been central in epidemiology, and this "risk factor approach" has led to a "risk epidemic" in medical journals with an increasing production of knowledge about health risks from the 1960s and onwards (84). The body has become a primal site for discourses on health risks in the Western health culture (85). Health and fitness have become important values that are pursued in order to express self-control and are used as social tools to convey symbolic resources (86, 87). Health messages such as to stop smoking, to eat a healthy diet, to drink only moderate amounts of alcohol and to take regular exercise are daily fare in the media. An occupation with risk and preventive

health measures pervades modern medicine and raises a series of ethical dilemmas and questions concerning when and what to test for, and if or how health risks should be managed, treated or prevented (88).

Douglas has argued that the language of risk has become a substitute for the language of danger, and she sees a new blaming system emerge under the banner of risk reduction (89). The notion that the individual is responsible for their own health is wide-spread in western societies (90, 91), and to take a risk may involve transgressing a moral border and threatening social structure (92). Marantz has put it like this: "Have we reached such a point in our "health conscious" society that every individual who suffers an illness classified as "preventable" must bear the burden of responsibility for that illness? Why isn't it possible to just get sick without it also being your fault?" (93).

A negative effect of health promotion is that people may feel anxiety, fear, guilt and shame (94, 95). Research shows that feelings of guilt and shame may influence patients' health-seeking behaviours and the patients' relationship with health professionals (96, 97). Guilt and shame may have positive effects such as to motivate patients to health-related behaviours, but may also have a negative effect by causing anger, self-blame or depression (98, 99). Guilt and shame are connected, but are usually distinguished as two separate emotions. Guilt is a self-directed anger over a violation of a norm, whereas shame is linked with anticipated or actual disapproval from others (98). One may say that guilt is caused by something one has done, while shame is related to something one is. Research indicates that patients may experience guilt or shame if they have been diagnosed with a potentially discrediting condition such as CHD (97).

Research suggests that patients diagnosed with FH may feel guilt if they fail to comply with treatment recommendations (100). An understanding of the psychological, moral and social aspects of living with such a genetic risk in the context of late modern health culture may improve management and reduce health professionals' risk of inadvertently causing experiences of blame and shame in patients.

2. AIMS OF THE STUDY

The overall objective of the study is to explore how individuals with familial hypercholesterolemia (FH) perceive, understand and manage their condition. This thesis has four specific aims:

- Explore how patient at risk of coronary heart disease (CHD) portray candidates for CHD
- Explore barriers in the health service to diagnosis and treatment experienced by women at increased risk of CHD
- Explore how patients diagnosed with heterozygous FH understand and perceive their vulnerability to CHD
- Explore patients' experiences of guilt and shame with regard to how they manage FH

3. MATERIAL AND METHODS

3.1 Participants

The empirical data in this study were generated in semi-structured interviews with a sample of participants diagnosed with familial hypercholesterolemia (FH) according to the *Simon Brome Register Group definition of FH* (appendix A) (20, 23). Participants were recruited from Lipid Clinic, Medical Department, Rikshospitalet-Radiumhospitalet HF, which is a specialist clinic for metabolic lipid disorders in Oslo, Norway. The clinic has a scheme for diagnosing and treating patients with FH. Patients were referred to the clinic for diagnosis and evaluation based on their elevated lipid values and their family history of hypercholesterolemia and coronary heart disease (CHD). The Norwegian health service is predominantly publicly financed and equal access according to need is a pivotal principle.

We used a purposeful sampling strategy and aimed for a sample of relatively young participants with a diversity regarding social background, family history of CHD, and time since diagnosis. We anticipated that having symptoms of CHD might influence how participants perceived and managed their condition and for this reason we recruited some participants who had experienced a myocardial infarction or had been diagnosed with angina pectoris.

Participants were approached through an invitation letter distributed to patients by health professionals at the clinic. The sample size of forty participants (20 men and 20 women) was a result of saturation in the data as consecutive interviews yielded diminishing returns in regard to new information. The mean age for participants was 31 years. Seven participants had developed symptoms of CHD. Further characteristics of the sample are shown in appendix B.

3.2 Interviews

The interviews were conducted in the period June 2000 until March 2002, lasted from 45 to 90 minutes, and were tape-recorded. Of the 40 participants, 30 were interviewed in the interviewers' office, eight in the interviewee's home, two in the interviewee's work office, according to their own wish.

My interview approach was inspired by Kvale's principles for qualitative research interviewing (101). I used various strategies and questions to structure the dialogue, such as introducing questions, direct and indirect questions, specifying questions, silence and interpreting questions. My point of departure was an interview guide that was developed based on eight weeks of fieldwork in the Lipid Clinic where I engaged in informal conversations with patients and observed consultations between health professionals and patients. The interview schedule covered issues about health and disease, and addressed how participants perceived and managed their risk of heart disease (appendix C). I did not follow the interview guide strictly, but aimed at creating an atmosphere where interviewees were encouraged to talk freely about their experiences, views, and feelings. I used the interview guide to check that topics were covered. In addition I explored themes and hypotheses that emerged in subsequent interviews.

According to Rabinow, qualitative data do not represent "rocks, picked up and put into cartons and shipped home to be analyzed in the laboratory" (102). I use the phrase "data collection" with an understanding that data from research interviews are not collected like physical objects, but are generated in the dialogue between interviewer and interviewee. Still, qualitative data are not necessarily biased or without any truth value. In order to assess their validity, one needs to account for the circumstances under which the data were collected and one also needs to reflect on how the interviewer and the research context may have influenced the data (103).

3.3   Interviewer's role, background and perspectives

In the interview setting I was particularly aware that participants should be encouraged to speak freely about their views and experiences. I presented myself as a "researcher with an interest in how it is to live with a genetic risk of heart disease". I explained the aim of the study, and emphasized that I had no other role in the clinic than being a researcher. I also said that accounts of experiences with health professionals could be helpful in improving the health service and that the information they gave me would be treated with confidentiality.

My professional background is being a medical doctor with an academic degree in medical anthropology. During interviews some participants asked my

about my background, and in such cases I answered that I was a medical doctor who had also studied social science. I deliberately tried to avoid being perceived as a medical expert on their condition, and emphasized that my knowledge about CHD and FH was limited. Sometimes participants asked me to comment on medical questions, and in such cases I encouraged them to contact their doctor if they were concerned about their medication or had other worries concerning their condition. I chose this strategy in order to convey to participants that I was interested in their own views spoken out in their own words.

Some participants asked me why I was interested in doing research on patients' experiences with FH. I never told participants about my own personal experiences, briefly described in the preface, because I feared that it would disturb the necessary distance between interviewee and interviewer and shift the attention towards me. The first interviewee asked me if I had checked my own cholesterol, and he was angry to hear that I had not taken a cholesterol test. Earlier, during the interview, he had used the expression "ticking bombs" about people who were unaware of their hypercholesterolemia. He convinced me to take a cholesterol test when he said: "You can't fool people like me that you are seriously interested in people with FH if you don't bother to take your health seriously and check up your own cholesterol!" A few weeks later I received the results from the test and was relieved to learn that my total cholesterol was well bellow 5 mmol/l. My first participant taught me a lesson that was important also from a methodological point of view – it was a good thing to have taken that test. It made it easier for me to listen to participants' stories about premature cardiac deaths in their families, and their concerns and fears, without worrying about my own cholesterol level.

Malinowski claims that "foreshadowed problems" and theoretic perspectives are important resources in qualitative research: "[T]he more problems he brings with him into the field, the more he is in the habit of moulding his theories according to facts, and of seeing facts in their bearing upon theory... foreshadowed problems are the main endowment of a scientific thinker, and these problems are first revealed to the observer by his theoretical studies (104). I brought with me some "foreshadowed problems", preconceptions, perspectives, and motivations into this project. Based on anthropological readings on health beliefs and the doctor-patient relationship, I expected to find that patients' understanding of FH and CHD could differ from the

way these conditions were understood among doctors (105, 106). I thought that patients' notions about risk would be somewhat different from epidemiological concepts of risk, and I expected to find variation among individuals in how they understood and related to their condition. I assumed that women and men could perceive and manage their condition somewhat differently. I was familiar with insights from Davison and colleagues' work on lay epidemiology and I had a particular interest in exploring how patients with a genetic risk perceived their vulnerability to CHD (38).

I embarked on this research project with an interest in understanding more about patients' experiences of living with risk of CHD, because I assumed that such knowledge could facilitate a better and individualized clinical management. I have been inspired by works within patient-centered and biopsychosocial medicine, in which it is key task for health professionals to recognize patients' agendas and get insight into patients' own appraisal of their health-related risks and resources (107-111).

3.4 Analysis

I transcribed the tape-recorded interviews in verbatim, and these transcripts were analyzed qualitatively. I and a coauthor read ten transcripts independently and developed a coding frame for the analysis (appendix D). I coded all transcripts and used the qualitative research software N6 during the coding process (112). All collaborating researchers (coauthors) independently read the material (excerpts from interviews) organized under the code(s) that provided material for each study (paper I-IV). They then contributed in negotiating the final categories and their contents. The procedure for analysis we used was "systematic text condensation", according to the principles of Giorgi's phenomenological analysis (113), modified by Malterud (103, 114). The analysis followed four steps: (i) reading all the material to obtain an overall impression and bracketing previous preconceptions; (ii) identifying units of meaning, representing different aspects of the theme and coding for these; (iii) condensing and summarizing the contents of each of the coded groups; and (iv), to generalize descriptions and concepts about the specific theme for each study. Figure 1 gives an overview of the data collection and analysis.

Figure 1. An overview of data collection and analysis.

```
40 tape-recorded        ┌ "Memo" for each ┐      Analysis: Summary of
semi-structured   ──►   ┆   participant   ┆ --►  categories and findings
interviews              └────────────────┘       in an "analysis
    │                                             document", which were
    ▼                                             commented by all
Transcription                "Reports" for each code        authors
    │                        (excerpts of text)          ╱
    ▼                                         ▲       ╱
40 transcripts      ╲                         │
    │                 ╲   Coding of transcripts         English translation
    ▼                                         ▲          of illustrating quotes
┌ Independent reading ┐    ┌────────────┐     │              │
┆ of 10 transcripts   ┆ ─► ┆ Codes      ┆ ────┘              ▼
└────────────────────┘    ┆ (appendix D)┆          Writing and revision of
                          └────────────┘           manuscript/paper
```

The findings and analysis were summed up in an "analysis document" that was used as a basis for writing and revision of each manuscript (paper I-IV). Quotes from the interviews were translated from Norwegian to English by me in the process of writing the papers. I had written a note ("memo") with demographic information for each participant, observations from the interview setting, and a characteristic of main issues that emerged in each interview. I used these memos during all stages of the analysis and they proved to be very helpful tools that informed the analysis, and I consulted them if I needed any contextual information about ext excerpts or illustrating quotes.

3.5 Ethical considerations

Ethical approval for the study was obtained from The Regional Committee for Medical Research Ethics (Health Region East), Norway (reference: S-99053). Norwegian Data Inspectorate granted us permission to make a temporary register of participants in the study (reference: 9900510 LT/BHB, 9900510 LT/RH). All participants were informed about the purpose of the study, and that they could stop the interview at any time without giving a reason. Written informed consent and an

agreement that quotes from the interviews could be used anonymously were obtained from all participants. An interviewer who interview individuals at risk of a potentially fatal disease may impose risk awareness or increase the participant's sense of vulnerability. I paid attention to interviewees' emotional responses during our dialogue, and in a few of the interviews we came to a point where I chose to shift topic due to the interviewee's response. The data were anonymized and health professionals at the clinic could not identify the interviewees when being presented with parts of the material.

4. SUMMARY OF RESULTS

4.1 Paper I

Frich JC, Malterud K, Fugelli P.

How do patients at risk portray candidates for coronary heart disease? A qualitative interview study.

The aim of this paper was to explore how patients at risk of coronary heart disease (CHD) portray candidates for CHD.

We found that some participants believed that CHD could happen to anyone, while the majority conveyed detailed notions of persons they considered to be likely victims of CHD. Participants often portrayed the coronary candidate as someone who was different from themselves; the typical image was an unfit, middle-aged man, often a business man or a taxi driver. Some women said that they had to reconcile themselves to being at risk of CHD, since they at first had conceived CHD as a men's disease. While some participants considered their notions to be valid for assessing people's risk of CHD, others questioned how valid their notions were.

We conclude that doctors should recognize that distancing is a way patients cope with risk and that such a strategy may have psychological and moral reasons, and that when communicating about risk, doctors should take into account that patients' notion of risk may differ from medical notions of risk.

4.2 Paper II

Women at risk of coronary heart disease experience barriers to diagnosis and treatment: a qualitative interview study.

The aim of this paper was to explore barriers in the health service to diagnosis and treatment experienced by women at increased risk of coronary heart disease (CHD).

The paper is based on an analysis of twenty women's accounts of their experiences with the health service.

We found that women reported three specific barriers related to diagnosis and treatment of CHD. They had to struggle to take a cholesterol test; they experienced that their risk was being downplayed by doctors; and, that their symptoms of CHD were misinterpreted when they consulted doctors for evaluation and treatment.

We conclude that stereotyping CHD as a men's disease may result in be barriers to diagnosis and treatment for women, and that doctors should ask the patient about the family history of CHD if a concern about heart disease is on the patient's agenda.

4.3 Paper III

Perceived vulnerability to heart disease in patients with familial hypercholesterolemia: a qualitative interview study.

The aim of this paper was to explore how patients diagnosed with heterozygous familial hypercholesterolemia (FH) understand and perceive their vulnerability to CHD.

We found that participants negotiated a personal and dynamic sense of vulnerability to coronary heart disease, grounded in notions of their genetic and inherited risk. Participants developed a sense of their vulnerability in a two-step process. First, they consulted their family history to assess their genetic and inherited risk, and for many a certain age designated when one could expect to develop symptoms of CHD. Second, they negotiated a personal sense of vulnerability through comparisons between themselves and family members. In these comparisons they accounted for individual factors such as gender, cholesterol levels, use of lipid-lowering medication, and lifestyle. Participants' personal sense of vulnerability to CHD could shift dynamically, due to changes in situational factors, such as cardiac events in the family, illness experiences, or becoming a parent.

We conclude that doctors should elicit patients' understanding of their family history and their personal vulnerability, in order to individualize clinical management.

4.4 Paper IV

Frich JC, Malterud K, Fugelli P.

Experiences of guilt and shame in patients with familial hypercholesterolemia: a qualitative interview study.

Submitted.

The aim of this paper was to explore patients' experiences of guilt and shame related to management of familial hypercholesterolemia (FH).

We found that participants did not feel guilt or shame for having the condition, but they usually made efforts to convey to others that their raised cholesterol was inherited and was not caused by an unhealthy lifestyle. Participants reported guilt if they had violated their standards for dietary management. They could feel guilt and shame if the result of a cholesterol test was not favorable. Though some participants had experienced health professionals as too persistent and eager, most were satisfied with how they had been met. One group, however, reported experiences of frustration, humiliation and shame in consultations.

We claim that recognition of patients' preferences and readiness for lifestyle counseling may reduce the health professionals' risk of unintentionally inducing guilt and shame in patients, and that health professionals need to be aware of patients' vulnerability to experience guilt and shame and should use communicative strategies that diminish such experiences in their patients.

5. DISCUSSION

5.1 Methodological considerations

Reflexivity

We approached the material as medical doctors with an interest in exploring how patients diagnosed with familial hypercholesterolemia (FH) perceive and manage their condition. We chose to focus on four specific themes (paper I-IV).

My preconceived ideas about lay epidemiology of coronary heart disease (CHD) was confirmed, but I was somewhat surprised that participants' notion of the coronary candidate appeared to be similar to that of the general public. When I planned the project, I did not expect that gender would become such an important theme. During the first interviews issues related to gender, and particularly women's experiences of being at risk of CHD, was a theme that spontaneously emerged in participants' accounts. By focusing on women (paper II) I may have overlooked issues regarding men's experiences with the health service. When analyzing the data I found hardly any talk about barriers to diagnosis and treatment among men. Being a man, I may have influenced how both women and men talked about their views, experiences, health and risk-status. Perhaps women were more willing to talk openly about their frustrations and experiences of barriers in the health service? The literature indicates a gender difference in disfavor of women and for this reason we investigated women's experiences (paper II), based on data from the interviews with women only.

I was theoretically influenced by the health belief model (HBM) and the notion of "perceived vulnerability". I was interested in exploring the way in which participants' reasoned about their vulnerability and the factors that could influence their perceived vulnerability over time (paper III). The participants in our sample have different socioeconomic backgrounds and educational levels, and the analysis may have overlooked the possible impact of such factors on participants' perceived vulnerability. Paper III suggests that the risk of CHD may be given lower priority in competition with psychosocial constraints or other more urgent obligations and risk. The same may be true for people who experience socioeconomic deprivation.

Internal validity

Participants in this study were recruited from a specialist clinic and were all diagnosed with FH. We have no indications that there is a selection of worriers or patients with multiple risk factors in our sample, but there has probably been a selection towards individuals who were in favor of medical treatment. Individuals who were not motivated for medical treatment of their lipid disorder would not have enrolled as patients, and this may explain why we found few participants in our sample who conveyed a fatalist attitude to their condition.
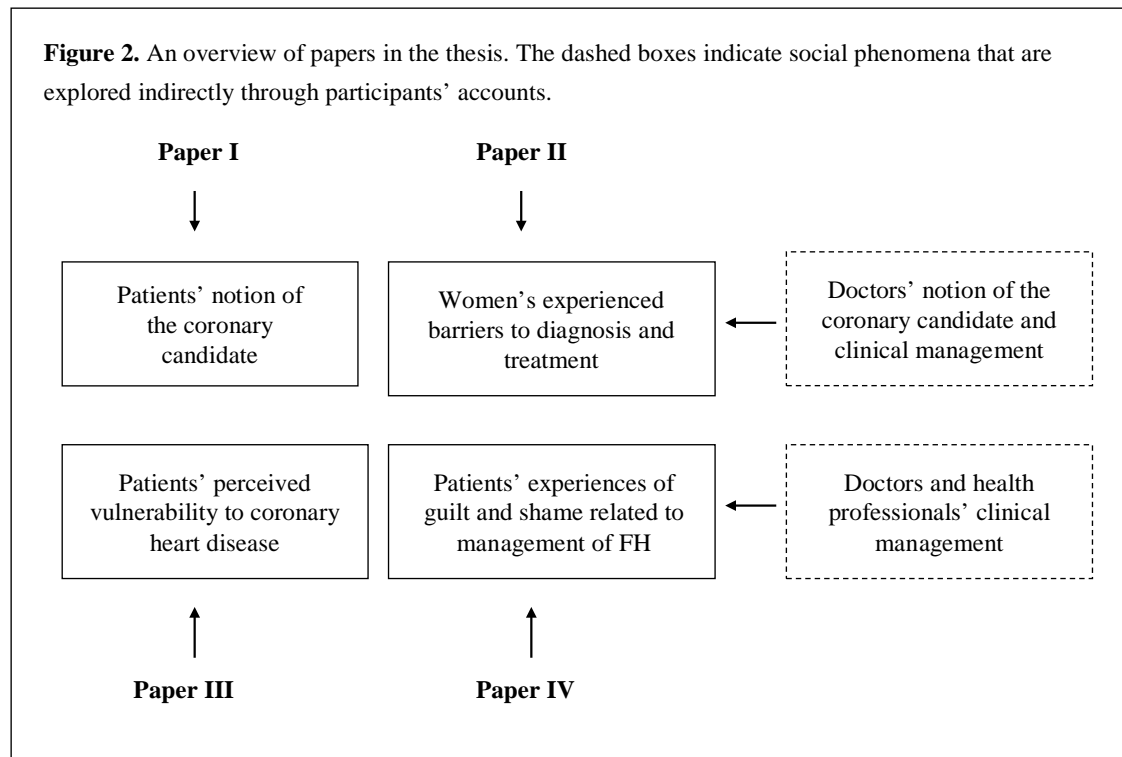
Referral and regular monitoring in a specialist clinic may have modified patients' understanding of their condition and they may have become more aware of the importance of heredity and their family histories of CHD.

A majority of participants in our sample were young and asymptomatic (appendix B). Older participants in the study provided valuable insights about how growing older and experiencing symptoms of CHD could influence perceived vulnerability to CHD.

Paper I and III addresses participants' own notion of the coronary candidate and factors that influence perceived vulnerability to CHD. Individual semi-structured interview is a suitable and valid tool for exploring such phenomena. Paper II and paper IV explore patients' experiences with the health service. In these two papers, participants' accounts are used as an indirect source of social reality, which is mirrored through patient's experiences and felt disagreements with health professionals (figure 2). We have no data on what actually took place in the medical encounters that our participants refer to. One may thus speculate whether there has been a selection to the clinic of patients with negative experiences with the health service, but the reverse may also be true (paper II). One may also question the validity of participants' accounts. The patterns we identified are consistent in the material and there is nothing in the data suggesting that we should distrust their accounts. Further, data about how participants experience the health service are valid in their own terms, as the patient's experience is an important clinical outcome measure (115).

Issues concerning guilt and shame emerged as themes in the interviews (paper IV). It was not an easy theme to address explicitly, because people seldom display their perceived failures. One has to expect that individuals will try to present

themselves in the best possible way to an interviewer. Further, admitting experiences of guilt or shame may actually induce feelings of shame in people, because such emotions are often experienced as shameful (96). People may express guilt and shame in other terms. We have interpreted participants' frustrating experiences as indication of an experience of shame in the clinical encounter even though they seldom talked about shame explicitly (paper IV).

Figure 2. An overview of papers in the thesis. The dashed boxes indicate social phenomena that are explored indirectly through participants' accounts.

Paper I	Paper II	
↓	↓	
Patients' notion of the coronary candidate	Women's experienced barriers to diagnosis and treatment	← Doctors' notion of the coronary candidate and clinical management
Patients' perceived vulnerability to coronary heart disease	Patients' experiences of guilt and shame related to management of FH	← Doctors and health professionals' clinical management
↑	↑	
Paper III	Paper IV	

External validity

I stated that this thesis aims at exploring what the zebra could tell about the horse, and at the same time address what the horse can tell about the zebra. Some findings are valid only for "zebras" – patients diagnosed with FH who are treated in a specialist clinic. Our study suggests that patients with FH in some respects are perceived and managed as horses in general practice and in the health service in general, and that in particular women may experience barriers to diagnosis and treatment (paper II). We also found that individuals with FH resolve their vulnerability to CHD by drawing partly on the notions of risk in lay epidemiology (paper I) and on their family history of CHD (paper III). Some findings may be valid for "horses" – patients at risk of CHD in general – though we should be cautious

about stating that they are transferable to other clinical settings without further consideration. Our findings about coronary candidacy among patients with FH (paper I and II) may be transferable to patients at risk of CHD in general. Barriers to diagnosis and treatment are likely to be experienced also by women who do not have a specific genetic risk of CHD (paper II). Our findings about the role of family history in patients' understanding of their vulnerability to CHD (paper III) may be relevant for people who do not have a specific genetic risk of CHD such as FH. Previous research suggests that people use their family histories to assess their risk for common diseases such as CHD and cancer (71). Our findings concerning patients' experiences of guilt and shame (paper IV) may be transferable to clinical settings in which health professionals manage patients with chronic conditions that require self-management and where communication about lifestyle and diets is part of the treatment.

5.2   Does coronary candidacy matter?

Our study shows that patients diagnosed with a genetic risk of CHD convey notions of the coronary candidate (paper I). There are striking similarities between the image of the coronary candidate among individuals at risk and individuals without a known risk of CHD (38, 39). Public imagery of the candidate appears to be important for how individuals at risk perceive CHD. We found that both men and women distanced themselves from their notiom of the candidate, and we found that some women at risk experience that they have to reconcile themselves to being at risk of CHD, because they at first considered CHD to be a man's disease (paper I). Distancing oneself from the coronary candidate may be a way of coping that relieves the sense of vulnerability and anxiety related to being diagnosed with increased risk. Such a strategy may be a moral statement that signifies that one takes the risk seriously, and it may also be a consequence of an insight that an individual with FH is different from other individuals who they think have a self-inflicted hypercholesterolemia (paper I, paper IV).

Research suggests that the quality of health care regarding diagnosis, referral and treatment of CHD is lower for women compared with men (51, 52, 54, 58). Our study of women's experiences with the health service (paper II) suggests that a portion of doctors perceive CHD primarily as a men's disease, and that this

influences doctors' management of risk factors and symptoms of CHD in women. Women's experienced barriers to diagnosis and treatment may be explained by a mismatch between women who are concerned about their risk and doctors' stereotypes of the candidate. Previous research has found that doctors assess equal cardiovascular risks differently in women and man, and that there is gender bias disfavouring women (116).

Research suggests that women wait longer than men before they contact the health service with symptoms of CHD (49, 117). Furthermore, women may contribute to lower quality of care by distancing themselves from cardiovascular risk (63, 64). An understanding of gender inequalities of health care need to consider both women's distancing to risk (paper I) and experienced barriers (paper II). Coronary candidacy seems to be a common denominator for an understanding of both lay and professional management of CHD.

Coronary candidacy matter in clinical settings because such beliefs most likely have an influence on how cardiovascular risks and symptoms are being interpreted and managed. Mongomery claim that medical knowledge in clinical practice is structured around narratives and analogical reasoning (1). Diagnostic stereotypes are helpful tools that organize clinical reality, but they may also influence doctors' capability to recognize a pattern that does not fit a stereotype. I think doctors may manage patients better if they are conscious about how coronary candidacy may influence professional judgment and lay people's health-related behaviors. Sounds clinical judgment is to be able to recognize the sound of hoofbeats, but to know when to think about zebras and to reassess your initial diagnostic judgment when think you hear a horse behind you. Sound clinical judgment involves the skill to recognize that not all horses are alike.

Future research should explore how doctors reason about cardiovascular risk, and particularly investigate how notions of coronary candidates may influence clinical management. Coronary candidacy matter in public health because lay epidemiology partly echoes how professional epidemiology portrays the coronary candidate. As the demographics of CHD are changing and more women are affected (48), there is a need for health promotion and information campaigns addressing cardiovascular risk in women. Future research should monitor and explore how coronary candidates are portrayed in the public.

European Society of Cardiology has recently launched the campaign "Women at heart" which is an initiative with the aim of "highlighting to medical professionals the growing burden and under-appreciation of women's heart disease and promote improved handling of women at risk of cardiovascular disease in clinical practice" (118, 119). An increased focus on women and women's experiences does not leave out that there may be specific issues and challenges related to how men perceive and manage cardiovascular risks or symptoms. A gender-sensitive approach to management of patients with cardiovascular risk of disease is needed, both for women and men (120).

5.3   How to deal with family histories?

A family history of premature coronary heart disease is one of the most important determinants of early and severe cardiac events in individuals with FH (26). The clinical severity of FH varies considerably between families, and information from the family history is usually more relevant than average risk estimates when assessing an individual patient's risk. In paper III we explore how patients diagnosed with FH understand their vulnerability to CHD. Previous research suggests that people consult their family histories to assess risk by counting affected relatives, and use similarities in looks, personality or mannerism to assess whether they have inherited a certain constitution or disposition (40, 121-124). In our study we found that participants seldom made reference to physical or mental similarities (paper III). "Family statistics", the age-pattern for onset of CHD in a family, appeared to be an important predictive device for many participants. Our study adds to previous knowledge by demonstrating how patients diagnosed with FH develop a dynamic and personal sense of vulnerability to CHD, grounded in notions of their inherited risk. Paper II demonstrates that a patient's family history can offer doctors clues to why an "untypical" patient seeks health care.

Previous research suggests that people in the general public emphasize heredity when reasoning about their risk of CHD (40, 121). Patients' assessment of cardiovascular risks and their family histories of CHD may deviate from doctors' assessment of risk (40, 76, 125, 126). A hereditary disposition to CHD is a risk factor also for individuals without FH. Doctors should therefore ask patients about their medical family histories and explore how patients understand their own

hereditary dispositions. There is need for more research on how information for patients' family histories are recorded, interpreted, and managed in clinical practice, and there is also a need for research that investigate how individuals recount and perceive their family histories of common diseases (127).

At present there are genetic tests for over 1000 different diseases and conditions (128). Family history will nevertheless remain the first "screening test" before individuals are referred to genetic assessment and is a key to an individualized assessment of risk (129). In USA, the U.S. Surgeon General's Family History Initiative was recently launched to increase the awareness of family history in relation to disease (130).

An increasing awareness about hereditary dispositions to disease in the population will probably pose a challenge for the health care system, and particularly for general practitioners. In Norway, patients are likely to consult their general practitioner first for an evaluation and assessment of their genetic vulnerability to disease. Are general practitioners prepared for this task? Rich and colleagues claim that there are substantial barriers to application of new genetic knowledge in general practice, and that it may be difficult to find time to obtain, organize, visualize, and analyze the patient's family medical history (132). Wattendorf & Hadley argue that general practitioners ought to practice "family medicine" and that this involves constructing a three-generation pedigree for each patient (132).
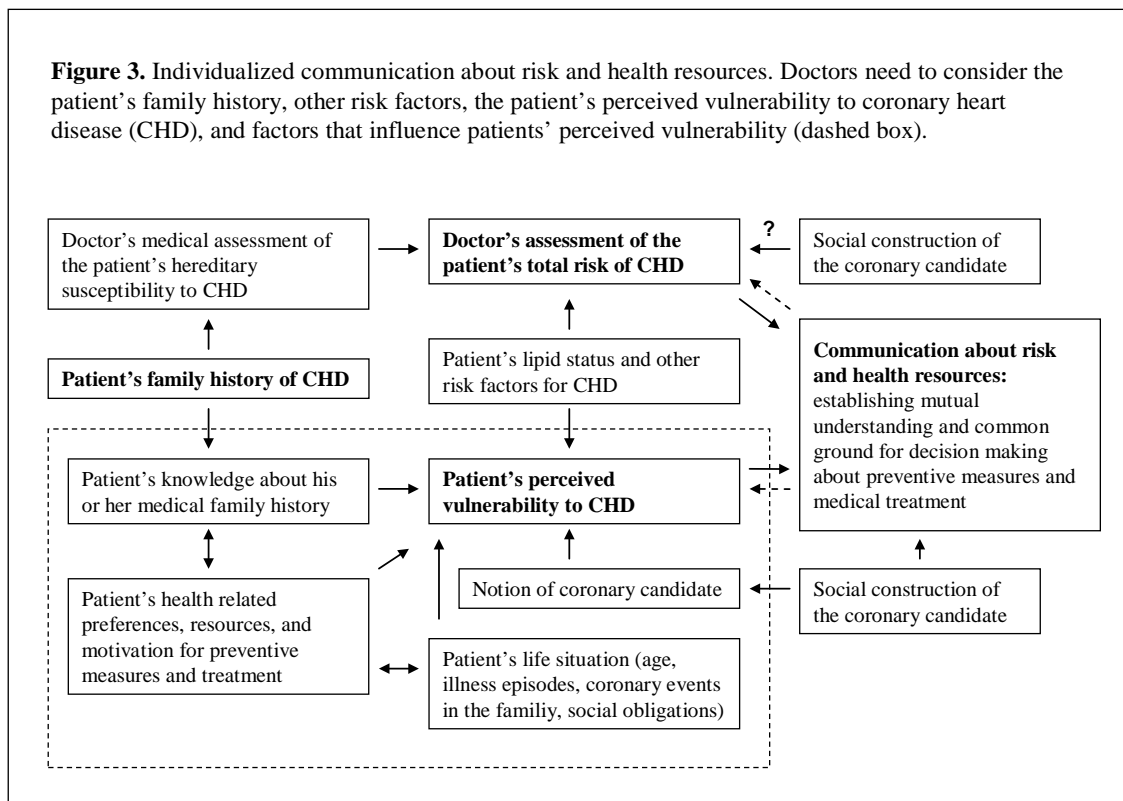
An increased awareness about family history raises some dilemmas and ethical issues. An increased awareness of health risks may have psychological and social negative effects (88, 97, 100). Further, a portion of families are not biologically related and there may also be conflicts or lack of contact between family members. Doctors should be sensitive to such issues and need to recognize that it may not be possible or desirable to construct a three-generation pedigree for all patients. An increased emphasis on patients' family histories may help doctors to detect and manage patients who are at high risk, but may lead to a "medicalization" of family relations. In clinical practice, doctors need to find a balance between possible benefits and costs for the patient and his or her family.

5.4 Communicating about risk

There are several reasons why communication about risk is a challenge for doctors. First, it may not be clear what the actual risk is, and the doctor's task is to communicate about uncertainty rather than a quantifiable risk. Second, patients' understanding of risk may be different from medical and quantitative risk estimates (paper III, 69, 76, 133, 134). Third, the way risk is presented influence decision-making in both doctors and patients (135-137).

A solution to some of these challenges has been a suggestion that the language of risk should be clarified and standardized (139). Numbers-needed-to-treat (NNT) is a format that has been promoted as a standardized tool for communicating quantitative risk and effect of medical treatment. Empirical studies indicate that both lay people and doctors misunderstand NNT (140). Though a standardized language of risk in terms of NNT or other formats may prevent misunderstandings and be helpful for communication between health professionals, such a language may not be helpful when communicating with patients. Steiner puts it like this: "As physicians, we need to become bilingual – that is, we must speak the language of populations as well as the language of individual patients." (141). Doctors think the best strategy is to combine different formats (quantitative, qualitative, and visual) and accommodate to the varying needs, preferences and abilities of patients (142).

Our findings suggest that communication about cardiovascular risk in patients with FH should be individualized and be a two-way process that involves a dialogue that should aim at establishing mutual understanding and a common ground for decision-making about preventive measures and medical treatment. It is a major task is to establish a dialogue and ask questions that mobilize the patient's personal health-related resources (110). On the basis of paper I and paper III, I have constructed a figure that illustrates the factors involved in communication about risk with patients diagnosed with FH (figure 3). The figure illustrates essential components of the patient-centered clinical method which aims at exploring both the disease and the disease experience, understanding the whole person, finding common ground for mutual understanding (111).

Figure 3. Individualized communication about risk and health resources. Doctors need to consider the patient's family history, other risk factors, the patient's perceived vulnerability to coronary heart disease (CHD), and factors that influence patients' perceived vulnerability (dashed box).

Patients' motivation for preventive health behaviours increases if they are given personally relevant information rather than information about average risks (136). Doctors need to be sensitive to the individual patients' preferences. An acquaintance with a patients' psychosocial context, in addition to knowledge about how the patient understands his or her family history, can give important clues about a patient's readiness for preventive behavior (paper III).

Future research should develop and evaluate methods and tools for recording and assessing family history information in clinical practice, and explore how doctors communicate about cardiovascular risk. There is also a need for need for research on methods and tools for dialogic and patient-centred communication about risk.

5.5. Guilt and shame in the clinical encounter

Communication about risk often involves discussing preventive health measures that concerns the patient's agency, identity, and preferences, and there is a potential of blaming or shaming patients in the clinical encounter (paper IV). According to

Davidoff, shame is "something so big and disturbing that we don't even see it, despite the fact that we keep bumping into it." (143). Berger coined the notion of "iatrogenic guilt" (144). Doctors and health professionals need to recognize patients' vulnerability to experience guilt and shame, and use communicative strategies that are likely to diminish such experiences in patients (96, 98, 111). Enhancing the patient-doctor relationship and being realistic are two components of the patient-centered clinical method (111). The following rules of thumb are based on such a patient-centered approach and on literature about shame and guilt in the clinical encounter (96, 98, 144, 145, paper IV):

- Doctors and health professionals should elicit patients' readiness for counseling and health education and respect the patients' health-related preferences.
- One may diminish a patient's guilt by emphasizing the uncertainties with self-management, and tell the patient that there may be a rise in cholesterol or a worsening of other risk factors even with the best efforts of the patient.
- One should encourage the patients' responsibility up to a certain point and be realistic about treatment goals.
- If the patient expresses guilt or shame, either verbally and non-verbally, one should not confirm the emotion by telling the patient that you understand that the patient feels ashamed. Such a strategy may only enhance the feeling of shame because it may convey to the patient that he or she ought to feel ashamed. One may use one's authority to normalize such emotions by telling the patient that you know that it can be difficult sometimes and that in your experiences other patients have felt the same.

Patient education and counseling should be based on recognition of the patient as the authority on his or her own life (145). Nevertheless, doctors may experience ethical dilemma when patients make very unfortunate choices and there is a conflict between autonomy and the principle of benevolence. Patients who are competent have the right to make unfortunate decisions concerning their own health, but it is legitimate for the doctor to give information and check that the patient has understood the possible consequences of a decision.

As patients have different values and preferences, information about a patient's health-related preferences may be included in the patient's medical records. Personal continuous health care is linked with increased patient satisfaction (146, 147), and systems which promote continuity of care will probably foster mutual understanding and common ground for decision-making in management of cardiovascular risk.

5.6. Variation and medical evidence in a genomic age

An individualized approach communication and management of cardiovascular risk does not necessarily conflict with an evidence-based approach in health care (148), but I think our research indicates the need for a wide concept of evidence in clinical practice. Narrative evidence from the patient's family history needs to be considered together with statistical group evidence about risk factors, effect of treatment and prognosis. There is, nevertheless, a potential tension between an individualized approach and current ideologies that emphasize evidence from randomized controlled trials, standardization of health care, guidelines for clinical practice, and clinical governance (149-150). FH calls for an individualized risk assessment and management, and is perhaps an extreme case – a true zebra. Perhaps the zebra can teach us something about management of horses? Guttmacher & Collins claim that all physicians need to understand the concept of genetic variability, and that the practice of medicine has entered an area in which the individual patient's genome will help determine the optimal approach to care (1). Cassell claims that there exists a tension in contemporary medicine between different notions of clinical evidence: "Withdrawal from the patient is rewarded with certainty and punished with sterile inadequate knowledge; movement towards the patient is rewarded with knowledge and punished with uncertainties. The fact remains, however, that to disengage from the patient is to lose the ultimate source of knowledge in medicine." (151). Will genomic medicine bring us into a situation where the movement towards the individual patient is rewarded with both adequate knowledge and certainty?

Genomic medicine is in its wake, and I do not know if it will fulfill all its promises. So far, patients' family history, though it is far from a perfect tool, is one of strongest and most easy accessible tools clinicians may use to get hints about a patients hereditary disposition to disease (127, 129, 152). Variation, whether it is

due to a patient's genome, life situation, values or preferences, calls for a multifaceted concept of evidence in clinical medicine. McWhinney's statement that medicine is "a science of particulars" seems to hold true also in tomorrow's medicine (108).

6. CONCLUSION

In conclusion, this thesis suggests:

- When doctors and health professionals communicate about cardiovascular risk, they should take into account that patients' notion of risk may differ from medical notions of risk and recognize that patients may have moral and psychological reasons for distancing themselves from the typical image of the "coronary candidate".

- The stereotype of CHD as a men's disease may result in barriers to diagnosis and treatment for women, and the issue of gender in relation to CHD should warrant more attention in clinical practice and public health.

- Doctors need to be sensitive to the patient's family history of CHD and examine the patient about CHD in the family if a concern about cardiovascular risk is on the patient's agenda.

- In order to individualize clinical management, doctors should communicate with patients in ways that elicit patients' understanding of risk and the factors that influence their perceived personal vulnerability to CHD.

- Recognition of patients' preferences and readiness for lifestyle counseling may reduce doctors and health professionals' risk of unintentionally inducing guilt and shame in patients, and health professionals should use communicative strategies that diminish such feelings in their patients.

7. FUTURE RESEARCH

Our study suggests that there is need for research that:

- Explore how doctors reason about cardiovascular risk, and how doctors' notions of coronary candidates may influence clinical management.

- Investigate how coronary candidates are portrayed in the public.

- Investigates how individuals recount and perceive their family histories of common diseases.

- Explore how information from patients' family histories are recorded, interpreted, and managed in clinical practice.

- Develop and evaluate methods and tools for recording and interpreting family history information in clinical practice.

- Explore how doctors communicate about cardiovascular risk, and what strategies and forms of evidence they use to individualize clinical management.

- Develop and evaluate methods and tools for dialogic and patient-centred communication about risk and patient counselling.

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APPENDIX A – DIAGNOSTIC CRITERIA

The Simon Brome Register Group definition of FH

Criteria

A.   Total cholesterol > 7.5 mmol/l (adults) or a total cholesterol level > 6.7 mmol/l (children < 16) or LDL-cholesterol level > 4.9 mmol/l (adults) or a > 4.0 mmol/l (children < 16 years)

B.   Tendon xanthomas in patient or any of the patients' first or second degree relatives

C.   DNA-based evidence of an LDL-receptor mutation or familial defective apo B-100

D.   Family history of myocardial infarction before the age of 50 years in grandparent, aunt, uncle or before the age 60 years in parent, sibling or child

E.   Family history of raised total cholesterol in parent sibling or child, or level above 7.5 mmol/l in grandparent, aunt, uncle

Diagnosis:	Criteria required
Definite FH	A + B or C
Probable FH	A + D or A + E

Adopted from ref. 20 and 23

Dutch Lipid Network clinical criteria for diagnosis of FH

	Points
1. *Family history*: A first-degree relative (a parent or offspring or sibling of the patient) with known:	
A) Premature coronary and vascular disease (< 55 yrs men; < 60 yrs women)	1
B) LDL-cholesterol concentration > 95th percentile for age and gender	
i) In adult relative	1
ii) In a relative < 18 years of age	2
C) Tendon xanthomata or arcus cornealis	2
2. *Clinical history*: Patient has a premature (< 55 years men; < 60 years women)	
A) Coronary event	2
B) Cerebral or peripheral disease	1
3. *Physical examination* of the patient	
A) Tendon xanthomata	6
B) Arcus cornealis in patient < 45 years of age	4
4. *LDL-cholesterol levels* in patients' blood (mmol/L)	
A) ≥ 8.5	8
B) 6.5-8.4	5
C) 5.0-6.4	3
D) 4.0-4.9	1
5. *DNA analysis* showing functional mutation in the LDL- receptor gene	8

Diagnosis	Total points
Definite FH	> 8
Probable FH	6-8
Possible FH	3-5

Adopted from ref. 20 and 23

APPENDIX B – PARTICIPANTS

Characteristics of participants (N = 40)

Characteristic	No.	(%)
Age, years		
10-19	9	(22,5)
20-29	10	(25)
30-39	9	(22,5)
40-49	8	(20)
50 +	4	(10)
Gender		
Male	20	(50)
Female	20	(50)
	35	(88)
Use of lipid-lowering medication		
	7	(18)
Symptoms of coronary heart disease		
Children		
No	21	(52,5)
Yes	19	(47,5)
Occupation		
Professional or higher managerial	7	(17,5)
Other non-manual	7	(17,5)
Skilled manual	4	(10)
Manual	7	(17,5)
Student / secondary education	14	(23)
Disablement benefit	1	(0)

APPENDIX C – INTERVIEW GUIDE

Sociodemographic questions

Age

Civil status

Education and work experience

Family

Previous illness experiences?

Previous experiences with the health service and health professionals?

Membership in patients' organizations?

Understanding of health and disease

What does the word health mean to you?

How do people stay healthy?

Why do some people have better health than others?

Are people able to have control with their own health?

What does fate mean to you?

Do you have a religious perspective on issues related to health and disease?

The condition

How did you get this and how were you diagnosed?

Do you have any symptoms, ailments, pains, of anything that limits your daily activities?

What influences how your condition will develop?

How will this condition influence your own future health?

To what extent are you able to influence how it develops?

Understanding of risk/own vulnerability to disease

What are the risks/uncertainties connected with your condition?

How do you estimate your own vulnerability of developing coronary heart disease?

Have the way you think about your own vulnerability to heart disease changed?

What does the risk mean for you personally?

What can you do to influence your risks?

Do you make any efforts at reducing your risk?

Experiences with the health service

How has your contact with the health service been?

How can health professionals help you managing your condition?

What do you think about the information you have been given?

Can health professional influence how you perceive your risk?

The psychosocial context

Has the condition influenced your quality of life?

Have you talked with people outside your family about your condition?

Can you give any examples of issues you would talk about?

How does your family and friends manage your condition?

How do you think other people perceive your condition? (health professionals, friends, family, people in general)

Sources of knowledge / media

What do you think about how your condition is portrayed in the media?

How does information in the media influence how you understand your condition?

Do you seek knowledge through other sources?

APPENDIX D – LIST OF CODES

Religion/destiny/control

Death

Time

Body

Luck/bad luck

Perception of health

Cholesterol

Risk

Views concerning causes of heart disease

Family history

Coronary candidates

Gender

Medical knowledge

Definition of FH

Beliefs about own influence on health

Motivation for preventive health behaviour

Social relations (support or conflicts)

Distancing and resistance

Management of lifestyle factors

Medication (effects/side-effects)

Relatives

Children

Stigma

Guilt

Psychological reactions

Genetic and clinical testing Experiences

with health professionals

Uncertainty

The health service

Complementary treatment

PAPERS I-IV (web-links)