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QUALITY OF CARE AND QUALITY OF LIFE IN CORONARY ARTERY DISEASE

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Stockholm 2005

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Printed by Repro Print AB, Stockholm, Sweden

ISBN 91-7140-205-5

Back cover *"Hägerökarten"* (1981) by Hans Kiessling (1926-2003)

Curiosity is one of the permanent and certain characteristics of a vigourous mind

- Samuel Johnson (1709-1784)

ABSTRACT

The aim was to study the efficacy in primary care of Case method learning (CML) in secondary prevention of patients with coronary artery disease (CAD). A further aim was to explore the structure of health related quality of life (HRQL) in these patients and its relations to chest pain and ill health. 54 general practitioners and 255 consecutive patients with CAD participated in a randomised controlled educational trial with the intention to improve the quality of care in secondary prevention of CAD. Practice guidelines were initially distributed and presented at a lecture. General practitioners – whose Primary health care centre (PHCC) – was randomised to the intervention group participated in recurrent interactive Case method learning dialogues at their own PHCC during the two years of the study. Statistical analysis was performed according to intention-to-treat based on group affiliation at baseline.

CML resulted in a lipid lowering in patients in primary care – whose general practitioners participated in recurrent interactive CML dialogues – comparable to what was concurrently achieved at a specialist clinic. Presentation of practice guidelines had no effect per se. Low-density lipoprotein cholesterol concentration decreased 9.3% from 4.2 (CI 4.0-4.5) to 3.7 (CI 3.4-4.0) mmol/l in the intervention group – and was 0.5 (CI 0.1-0.9) mmol/l lower (effect size 0.56) in the intervention group as compared to the control group ($p < 0.05$) after two years. We found no change in the control group. The cost of the education represented only 2% of the cost of lipid lowering drugs. The resulting discounted cost per gained QALY was equal to US$ 24 300. This indicates that CML supported lipid lowering is a cost-effective strategy.

HRQL was assessed by the Cardiac Health Profile (CHP), EuroQol-VAS and EuroQol-5D questionnaires. Chest pain was ranked according to the Canadian Cardiovascular Society (CCS) classification. Principal component analysis of HRQL – as assessed by CHP – identified four principal components (independent sub domains) representing perceived cognitive function, physical function/general health, and social respectively emotional functions. All components correlated to EuroQoL-VAS. Perceived cognitive function – reflecting the ability to concentrate, activity drive, memory and problem solving – had a major impact on HRQL. Physical function/general health ($p = 0.000000$) and emotional domains ($p<0.04$) related to CCS but perceived cognitive function and social function did not. Furthermore, both perceived cognitive function ($p=0.0006$) and physical function/general health predicted unemployment at baseline and at two years in patients at a working age. CCS decreased during the two years ($p<0.00022$). By contrast, HRQL did not change as assessed by any of the instruments or sub domains.

To conclude, CML for general practitioners resulted in lipid lowering in their CAD patients due changed clinical practice. Furthermore, CML is cost-effective. The low cost in addition to its positive effects should probably warrant its use in the improvement of the quality of care of other major diseases. Perceived cognitive function is a major determinant of HRQL in CAD patients and predicts ill health as assessed by prevalence of unemployment. Perceived cognitive function was not related to prevalence and grade of chest pain. Furthermore, the major part of the HRQL in these unselected patients was insensitive to change in chest pain symptoms during a two-year period.

Keywords: Coronary artery disease, secondary prevention, health related quality of life, quality of care, case method learning, cost-effectiveness, chest pain, perceived cognitive function.

LIST OF ORIGINAL PAPERS

This thesis is based on the following papers

I. Kiessling A, Henriksson P. Efficacy of case method learning in general practice for secondary prevention in patients with coronary artery disease: randomised controlled study. *BMJ* 2002;325(7369):877-80.

II. Kiessling A, Zethraeus N, Henriksson P. The cost of lipid lowering in patients with coronary artery disease by Case Method Learning. *Int J Technol Assess Health Care* 2005; In press.

III. Kiessling A, Henriksson P. Perceived cognitive function is a major determinant of health related quality of life in a non-selected population of patients with coronary artery disease – a principal components analysis. *Qual Life Res* 2004;13(10):1621-31.

IV. Kiessling A, Henriksson P. Perceived cognitive function in coronary artery disease, an unrecognised predictor of unemployment. *Qual Life Res* 2005; In press.

V. Kiessling A, Henriksson P. Time trends of chest pain symptoms and health related quality of life in non-selected patients with coronary artery disease. Submitted

ABBREVIATIONS

4S	Scandinavian Simvastatin Survival Study
CABG	Coronary Artery Bypass Graft surgery
CAD	Coronary Artery Disease
CHP	Cardiac Health Profile
CI	Confidence Interval
CCS	Canadian Cardiovascular Society classification grading of angina pectoris symptoms
DALY	Disability Adjusted Life Year
DDD	Defined Daily Doses
ECG	Electro Cardio Gram
EQ-5D	EuroQol-5 Dimensional Classification
EQ-VAS	EuroQol single item Visual Analogue Scale (also called Rating Scale)
FRISC	Fragmin and/or early Revascularization during InStability in Coronary artery disease
GISSI	Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico
GP	General Practitioner
HRQL	Health Related Quality of Life
ICD	International Classification of Diseases
INTERHEART	A global study of risk factors in acute myocardial infarction http://www.phri.ca/interheart/
LDL	Low Density Lipoprotein
OR	Odds Ratio
PC	Principal Component
PCI	Percutaneous Coronary Intervention
PHCC	Primary Health Care Centre
QALY	Quality Adjusted Life Year
SBU	The Swedish Council on Technology Assessment in Health Care
SEK	Swedish Crowns
WHO	World Health Organization

CONTENTS

1 INTRODUCTION

1.1 Health

The unifying aim of all medical research, medical education and health care development is the improvement of health. However, the meaning of the concept health has been open to debate. The ancient Nordic word for health *hælsa* is built from *hæl ,hel* meaning happiness or whole [1]. However, WHO defined health in 1946 [2] as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity". No general agreement on the definition of the concept health seems to exist. The content of the concept health differs depending on the perspective, knowledge, values and beliefs of the person or group of persons defining health. The physician's perspective is on assessment of organ function and on signs of disease. The patient's perspective of health is on life and its quality. That implies to feel well, to be satisfied, to have sufficient abilities and to have a sense of coherence [3]. The individual is the one who defines his or hers health related quality of life (HRQL) [4 5]. We as health care workers and researchers need to understand this construct and its relation to objectively measured signs of disease. The health economist perspective of health is focused on resources (costs) and its relation to utilities and effects on health. Common measures are Disability Adjusted Life Years (DALY) [6 7]and Quality Adjusted Life Years (QALY) [8 9]. A societal perspective of health could be general well-being and working capacity. Examples from these four perspectives on health are presented in figure 1.

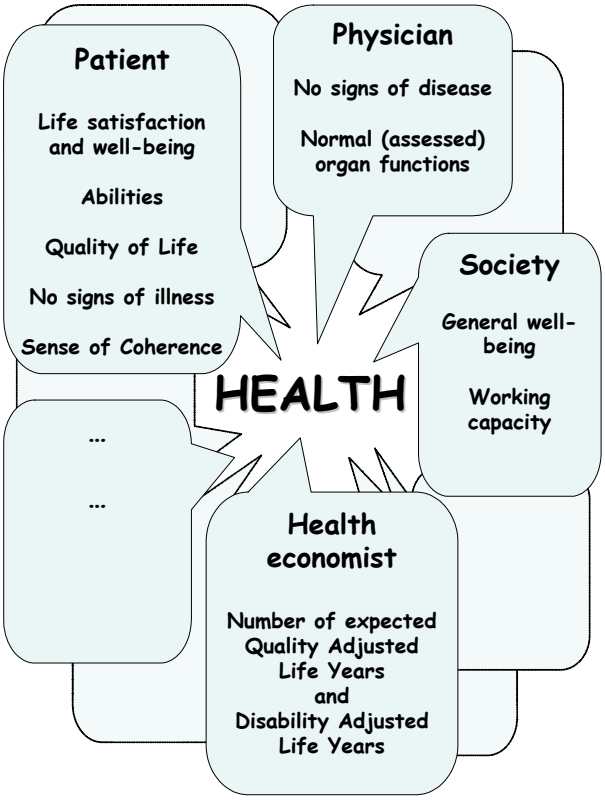

Figure 1. Examples of aspects of health, from the perspectives of the patients; physicians; society and health economist.

Berg [10] pointed out some – from a patient's perspective – neglected but import aspects of health in 1976; "ability to use one's mental abilities; to see; to think clearly; to love and be loved in return and to make decisions for oneself".

1.2 Quality of Care – General knowledge translation and application

Quality of care is also a complex multidimensional construct. The Institute of Medicine defined quality of care as "the degree to which health services for individuals and populations increase the likelihood of successful health outcomes and are consistent with current professional knowledge." [11 12].

One way to improve quality of care could be by participation of health care professionals in knowledge generation (research), knowledge translation (education) and knowledge application (development) in clinically relevant areas. The word participation stands for ''the action or state of taking part with others in an activity'' [13]. To participate is an opportunity to learn from and together with others [14]. There are different ways of participation that could be used in the improvement of the quality of care. This could be exemplified by e.g. participation in collaborative research, in organisational development or in interactive education [14-20] . A schematic illustration of participatory learning [21] is presented in figure 2.

The fundamental basis of all participatory learning methods is that ''learners'' are active participants instead of passive listeners or readers. However, this is actually seldom the case in continuous medical education (CME). The most common CME activities - aimed to improve professional practice - are still at least in Sweden: lectures, meetings, and printed educational materials.

Figure 2. Knowledge building and behavioural change by participation in research, organisational development processes and interactive education (Kiessling A, Heart 2004).

All professional health care decisions should be founded on scientific evidence and on reliable experience. Physicians have increasing difficulties to meet this challenge. The pace of the presentation of new scientific results has increased. Concurrently the complexities increase in both the medical and psychosocial dimensions of the clinical decision processes. This is especially true regarding decisions concerning diagnosis and therapies of the unselected patients present in primary care. The aim of CME is to facilitate the translation and application of new evidence based on scientific studies into relevant contexts of routine clinical care. Practice guidelines have been proposed as tools in the translation process [22]. However, their effect have been limited [23].

Research including assessment of the outcome of knowledge translation strategies and traditional education is a challenge. Kirkpatrick have described four outcome levels in the evaluation of training [24]. The outcome levels are reactions (satisfaction or happiness); learning (knowledge or skills); behaviour (learning transfer to workplace) and results (learning transfer or impact on society). The difficulties in evaluating and researching the effectiveness of educational interventions are also described and discussed by Hutchinson [25].

Evaluation of CME is a relatively new research field. Intervention studies comparing different educational strategies in health care are rare. The most common assessed outcome level in CME is on reaction level (e.g. satisfaction). Several investigators have failed to show an effectiveness of lectures or distribution of written information, at the behaviour level [23 26-29]. Educational intervention studies with patient related endpoints (result level) are scarce. Consequently, studies measuring cost-effectiveness of CME methods and implementation are even more scant [30 31]. Figure 3 shows Kirkpatrick's hierarchy of levels of education applied in a CME context.

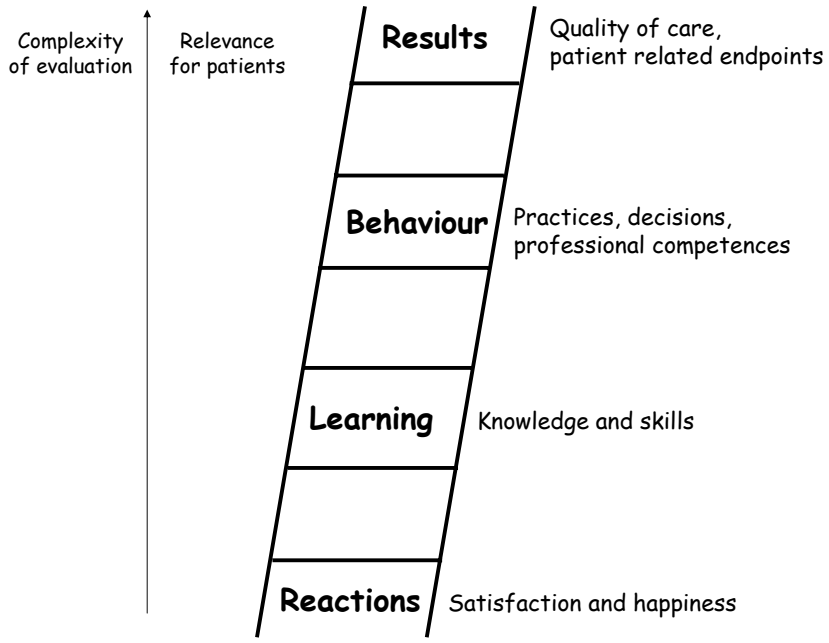

Figure 3. Evaluation of the outcome of Continuous Medical Education (CME) at four levels. The relevance for the patients and the complexity of the evaluation increases by the level on the ladder. Adopted from Kirkpatrick [24], 1967.

1.3 Quality of Care in coronary artery disease

Several randomised controlled trials [15-17 32-35] have shown convincing results in reducing cardiovascular mortality and morbidity in patients with coronary artery disease (CAD) during the last part of the previous millennium. Treatment with statins has been shown to be cost-effective [32] with a reduction in the need of hospital services [36 37]. The higher the CAD event risk is, the stronger is the evidence that lipid-lowering therapy is cost-effective [38].
In addition, the overall risk for death and all-cause mortality have declined in patients with coronary artery disease (CAD) during the last decades [39]. However, CAD is still – at least in Sweden – a common cause of sickness absence and disability pension despite all improvements in the quality of care [40]. Return to work after coronary events have been shown to be predicted by age, place of residence and education but only to a limited degree by severity of disease [41 42]. Furthermore, patients' beliefs about their illness and affective reactions have been found to influence return to work [43 44].

The recent report from The Swedish Council on Technology Assessment in Health Care (SBU) [40] states, "Disorders of the circulatory system are the third most common cause for disability pension. There is limited evidence that most people of working age return to work following stroke, myocardial infarction, or heart surgery (Evidence Grade 3). However, no evidence identifies interventions that can shorten the length of a sick-leave spell. The reasons for the relatively long periods of sick leave that are common in Sweden, e.g. after myocardial infarction, are not known".

Numerous recommendations and practice guidelines have been produced throughout Europe on the subject secondary prevention of coronary artery disease. Congresses, educational meetings, and lectures have been held with the purpose to facilitate implementation of evidence-based clinical practice. Despite all these efforts, the gap is still wide between what is achieved in clinical practice, and what should be achieved according to scientific evidence-based goals for secondary prevention in patients with coronary artery disease [45-50]. The reason is probably that there are several barriers and complexities between the guidelines and an actual behavioural change in routine clinical practice [51 52]. The way to close the gap is probably the choice of educational method, rather than production of more scientific evidence. Wood [53] states that; "The real task facing cardiovascular medicine is implementation of these recommendations into clinical practice". Majumdar [54] discussed the problem of translating knowledge into practice in chronic cardiovascular disease; "We need to accept that changing physician practice has less to do with detailed knowledge of the evidence and more to do with being convinced that a particular patient may benefit by applying the evidence when the opportunity arises in our clinics".

The context and content of a consultation in daily clinical practice is unstructured, unlike the strictly structured situation when a patient is enrolled in a clinical trial [55]. The frames of clinical practice decisions will thus vary from patient to patient. Framing has been recognised to have a great impact on the psychology of choice [56].

It has – in a qualitative study on hyperlipidemia in primary care – been suggested that experiences from the practice in itself generates new information, which is added to or counteracts the acquisition of new behaviour in primary care [57]. The information transfer – of new scientific evidence – was improved by ongoing dialogues between staff members [57]. The knowledge transfer seemed also to be influenced by participating person's professions, professional roles and gender.

Sackett et al [58] have tried to define evidence-based medicine as the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of the evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.

Clearly something more has to be done than just writing and distributing practice guidelines to improve the implementation of relevant new scientific evidence in routine care. A learning method suited to improve and support the complex clinical decision making process is needed [59 60]. Case method learning seemed to us to be an attractive activating learning method, well suited to be tested in CME in primary care [61-64]. The method is interactive and focuses on the decision process in a defined context and with a defined decision maker.

1.4 Health Related Quality of Life in coronary artery disease

Measurement of Health Related Quality of Life (HRQL) is aimed to tap the patient's own experience of health and illness in a broad perspective. A person's perception of health and satisfaction with life is greatly affected by his or hers expectations regarding health and their ability to cope with limitations and disability [4 65]. Most investigators in cardiology uses generic scales or disease specific scales with a dominance of items regarding physical and emotional aspects [66-68]. Development of disease specific HRQL instruments with a broad perspective on quality of life in cardiovascular disease [69] is not as yet on par with other chronic diseases concerning quality.

Health and health related quality of life in coronary artery disease is from the patient's perspective more than just to live without objectively measurable function deficits and physical symptoms. To many CAD patients the ability to function in daily life, both physically and mentally is probably important. Well-being and ability to participate in social life is also of importance.

CAD is a chronic disease. Patients often have long periods with few symptoms interrupted by episodes of acute chest pain and recurrent health care contacts. These contacts are often difficult to predict. HRQL may for these individuals be influenced by their sense of coherence [3 70]. Important determinants of sense of coherence are their apprehension of the present situation as meaningful, comprehensive and manageable. We have in an earlier study evaluated patient satisfaction with care in an unselected cohort of patients with acute chest pain [71]. We found that perceived participation in care respectively perceived compliance of the physician and nurses' were important determinants for patient satisfaction.

It has been increasingly common to include assessment of HRQL in randomised controlled trials in CAD. Several randomised controlled studies in selected groups of patients have

reported on the correlation between objectively measured morbidity and different aspects of HRQL in CAD [72 73]. Objective – e.g. patency – and subjective – e.g. HRQL – results are often in conflict. Some studies report improved perceived function and well-being after an intervention resulting in similar levels of HRQL as in normative populations [74 75]. By contrast, a patient group examined one respectively four years after an acute myocardial infarction still showed a decreased HRQL as compared to healthy controls [76 77]. Similar discrepancies between subjective and objective measures of health have been shown in other diseases as well [78 79]. Questions have been raised if present HRQL can predict future risk for coronary events. Recently the INTERHEART study was presented [80]. The investigators state that presence of psychosocial stressors is associated with an increased risk of acute myocardial infarction [80].

A problem – in real world application – of randomised controlled trials is that they are often performed on highly selected patient groups[81]. This selection decreases the ability to extrapolate the effect of an intervention – on e.g. HRQL – to the unselected populations in routine clinical care.

Patients with CAD have at present often well-treated physical symptoms and cardiovascular drugs help to reduce their risk of a new coronary event. By contrast, the perception of the disease – the illness perspective – by patients treated in general practice is at large unexplored. Descriptive studies of HRQL in unselected populations of patients with CAD receiving routine clinical care are few. Consequently, studies examining time trends in such populations are scarce. One way to increase knowledge of health and perceived illness in unselected patients with CAD is the study of HRQL and its components.

2 AIMS

The aims of the present studies are:

- To assess the efficacy of case method learning for quality of care in patients with coronary artery disease.
- To assess the cost of lipid lowering by case method learning in patients with coronary artery disease.
- To increase the understanding of health related quality of life and its independent components in patients with coronary artery disease.
- To assess whether health related quality of life and in particular perceived cognitive function influences employment in patients with coronary artery disease.
- To assess time trends of chest pain symptoms and health related quality of life in an unselected cohort of patients with coronary artery disease.

3 ETHICAL CONSIDERATIONS

It is a complex situation to evaluate an educational intervention in real practice. One of the main aims of the research design is to minimize the influence – at result level – of other factors than just the intervention. It is impossible to conduct a randomized controlled educational intervention trial with informed consent in advance and achieve such an aim. It should have been a potential risk for biases, confounding and unwanted effects if we had informed the general practitioners in advance. A knowledge of the nature and the period of the study could by the expectancy effect influence the general practitioners´ performance [82]. In addition, even the awareness of "something extraordinary going on" could act as a trigger for change in behaviour according to the so called attention or Hawthorne effect [83]. Thus, the general practitioners in the present study had no knowledge that they were participating in a study.

In addition, other ethical aspects have to be considered. Is it justifiable to withhold the information content of the case seminars in the intervention from the control group? We did not consider this as a problem since the guidelines had in fact already been presented at a lecture and had been distributed to all general practitioners.

Finally, how is the anonymity and confidentiality preserved? The anonymity and confidentiality was preserved by separate researchers meeting the physicians respectively the patients, and by coding all data. We did not break the code until all databases were completed and the statistical analysis had been performed. The research nurse did not have any contact with the general practitioners during the study. Further, she had no knowledge regarding randomisation of patients and PHCCs. The analysis was further performed as intention-to-treat at group level - the intervention and the control groups - and not at individual physician or patient level.

On the contrary, if we had informed the general practitioners in advance, the main ethical research question should have been how to interpret the results and validate the conclusions. All participating patients gave written informed consent. All studies in this thesis are based on ethical approval. The studies comply with the Declaration of Helsinki and were approved by the ethics committee of Karolinska Institutet at Huddinge University Hospital.

4 METHODS

4.1 Patients

Södertälje Primary Health Care and the department of medicine at Södertälje Hospital provide health care to approximately 95 000 inhabitants in the southernmost part of Stockholm County, Sweden. No registry exists that allows direct identification of all these patients. However, the patient registry of Stockholm County Council allows identification of all inpatients and outpatients visiting the department of medicine at Södertälje Hospital. We could thus identify all patients in the population who had visited Södertälje Hospital as inpatients or outpatients during the preceding year with a diagnosis of coronary artery disease (ICD-9 code 410-414); we identified 429 patients aged 70 years and younger with such a diagnosis and scrutinised their medical records. Criteria for a confirmed diagnosis of coronary artery disease in the patient record were as follows.
1: A diagnosis of angina pectoris, either by objective criteria based on coronary angiography, or a pathologic exercise- or stress-test, or a clinical assessment based on typical angina symptoms at exercise with or without ECG-evidence of possible or definite ischemia.
2: A diagnosis of myocardial infarction based either on WHO-criteria [84] or on unequivocal ECG-findings.

We excluded 106 patients—mainly as a result of miscoding and in a few cases because of other life threatening diseases or because the patients had moved out of the catchment area. Three hundred and twenty three patients fulfilled the inclusion criteria. We had thus identified all the patients in the population with a recent need for specialist care. We invited all of these patients to participate in the study (January 1995); 68 patients refused to participate, leaving 255 patients to be included in the study, table 1.

Table 1. Baseline characteristics of included patients. Values are numbers (percentages) unless stated otherwise

Characteristics	Total (n=255)
Mean (SD) age (years)	60.1 (7.5)
Females	57 (22)
Family history of coronary artery disease	97 (38)
Diabetes	37 (15)
Hypertension	67 (26)
History of stroke	3 (1)
History of peripheral artery disease	5 (2)
History of other comorbidity	71 (28)
Smoking status:	
Never smoked	107 (42)
Ex-smoker	85 (33)
Current smoker	61 (24)
Mean (SD) body mass index (kg/m^2)	28 (4.2)
Mean (SD) waist:hip ratio	0.95 (0.1)
Mean (SD) systolic blood pressure (mm Hg)	139 (20)
Mean (SD) diastolic blood pressure (mm Hg)	84 (9)
Mean (SD) duration of coronary artery disease (years)	6.0 (5.6)
History of myocardial infarction	167 (65)
History of coronary artery bypass graft surgery	95 (37)
History of percutaneous coronary intervention	29 (11)
Current angina (n=250):	
CCS 0	100 (39)
CCS 1	47 (18)
CCS 2	75 (29)
CCS 3	17 (7)
CCS 4	11 (4)
Use of cardiovascular drugs:	
Acetyl salicylic acid	205 (80)
βblockers	166 (65)
Lipid lowering drugs	49 (19)
Mean (SD) lipid concentrations (mmol/l):	
Total cholesterol	6.4 (1.1)
Triglycerides	2.1 (1.1)
High density lipoprotein cholesterol	1.2 (0.3)
Low density lipoprotein cholesterol	4.2 (1.0)

CCS=Canadian Cardiovascular Society classification system of current angina pectoris symptoms.

A research nurse drew blood samples from all patients—in the morning after an overnight fast—at baseline and at two years from the start of the study. We measured concentrations of total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides. A questionnaire including quality of life, questions regarding life style, family history and own prior disease history, direct and indirect costs were handed out once a year during the study. The research nurse handled all questionnaires and performed the interviews and physical examinations at the department (the same nurse performed all interviews). The patients themselves presented all data on present medication, occupation and sick leave etc.

253 of the patients were able to answer at least one of the HRQL instruments at baseline. During the study five patients died (all due to cardiovascular disease), three had to be excluded owing to other serious disease, eight moved out of the district, and 19 refused to participate. This resulted in 220 (86%) patients completing the two-year study period (April 1997).

In paper I-II, the 255 included patients were studied in three groups. We assigned patients who indicated a specialist physician (specialist in cardiology or internal medicine at the hospital or in private practice) to the specialist (S) group (n=167) for study purposes. The remaining patients (n=88) were studied in intervention (I) and control (C) groups according to which group their responsible general practitioner's primary healthcare centre was subsequently randomised into. The effect on change in lipid levels was analysed in the 220 patients who completed the two-year study.

The results in paper III are based on the 250 patients answering the Cardiac Health Profile (CHP) questionnaire at baseline.

Paper IV is based on the 169 patients less than 65 years of age, the regular age of retirement due to Swedish legislation. 22 patients achieved the age of retirement during the study and 20 patients did not complete the study of other reasons. The follow-up analysis after two years is based on the remaining 127 patients.

The time trends in paper V are calculated on the 202 patients answering the CHP, EuroQoL-5 Dimensons classification(EQ-5D), EuroQoL-Visual Analogue Scale (EQ-VAS) and Canadian Cardiovascular Society (CCS) classification at all 3 assessment points.

4.2 Primary care physician groups

Södertälje Primary Health Care consists of 14 primary health care centres. We divided these centres into two matched and balanced pairs, taking into account geographic location, physician numbers, physician relationships, patient volume, and the socioeconomic status of the patient populations as presented in table 2. The two groups contained 26 respectively 28 general practitioners, with an equal sex and age distribution. Descriptive and socioeconomic

data regarding the inhabitants, PHCCs and the general practitioners were taken from different registers in Stockholm County Council and municipals.

We did also distribute a postal questionnaire about perceived knowledge and attitudes regarding risk factors and secondary prevention of coronary artery disease to all the employed general practitioners at baseline. We distributed a new questionnaire to all general practitioners in exactly the same way at the end of the study. The questionnaire did also include questions regarding knowledge and relevance of scientific evidence and practice guidelines and satisfaction with the collaboration with the local hospital. The questionnaires to the general practitioners were answered anonymously but single-blinded to group code (different colours).
All data were kept in coded electronic registers.

Table 2. Baseline characteristics of primary health care centres and general practitioners in intervention and control groups

Characteristic	Intervention	Control
No of general practitioners	26	28
Mean (SD) age (years)	47.0 (6.3)	46.4 (4.8)
No (%) women	9 (35)	9 (32)
No (%) specialised in general medicine	26 (100)	28 (100)
No of physicians with known relation to a physician in other group	0	0
No of included patients	43	45
No of included patients per physician (median (range))	1 (0-4)	1 (0-5)
No of primary health care centres	7	7
No of primary health care centres with:		
1-3 physicians	3	3
4-5 physicians	3	2
>5 physicians	1	2
<5000 inhabitants	2	2
5000-9999 inhabitants	2	3
>10 000 inhabitants	3	2
Mean population income†:		
<150 kSEK	1	1
150-199 kSEK	5	4
>199 kSEK	1	2
Urban population	5	5
Mixed urban and rural population	2	2

†Part of population aged >16 years (kSEK=1000 Swedish Crowns).

4.3 Setting and general background

The health care district of Södertälje is located in the southwest part of Stockholm County, Sweden, see figure 3. It consists of Södertälje, Salem, Nykvarn and parts of Botkyrka

municipalities. An average of 95 000 people live in this area of roughly 800 km^2. The city of Södertälje is dominated by a great truck producer and a large drug company in the industrial centre and is surrounded by mixed urban and rural districts. Over 30 % of the inhabitants have an immigrant background. Södertälje Primary Health Care consisted of 14 primary health care centres (PHCC) during the study period. The PHCCs together with Södertälje Hospital provide acute and elective health care to the inhabitants in this part of Stockholm County Council. The characteristics of the PHCCs and the general practitioners participating in the study are shown in table 2.

We planned these studies in the autumn of 1994. At that time, the scientific evidence of the importance of lipid lowering in coronary artery disease was still open to debate. The landmark study of 4S was just to be presented [32]. It was a period when many national and local guidelines in different areas of medicine were written and distributed in purpose to improve the implementation of evidence-based medicine in both primary and secondary care.

Figure 4. Target catchment area of Södertälje Primary Health Care in Stockholm County Council, Sweden. The municipalities of Södertälje, Salem, Nykvarn and the southwest part of Botkyrka.

4.4 The educational intervention study (paper I-II)

At first, we completed the baseline inclusion procedure of the patients. The second step was to develop the first local practice guidelines on secondary prevention of coronary artery disease in this part of Stockholm County. We did this immediately after the presentation of the results of the landmark Scandinavian Simvastatin Survival Study (4S) [32]. The guidelines were presented and distributed at a local lecture (February 1995) to all general practitioners and specialists in the catchment area. The practice guidelines were distributed together with a personal letter after the meeting to all relevant physicians in this area. We randomised the two primary healthcare centre clusters into control and intervention groups, after checking for balance between both patients and physicians in the clusters. We offered the general practitioners in the intervention group Case method learning seminars at their own primary healthcare centre. All the general practitioners accepted the invitation. We held three to four seminars at each primary healthcare centre during the two years study period. Four to seven general practitioners and one facilitator participated on each occasion (attendance rate > 82%). Each seminar lasted one hour.

4.4.1 The participatory learning technique - Case method learning

We wanted to use a learning method suited to support and improve the complex clinical decision making process present in primary health care. We chose to base the participatory learning seminars on a slightly modified Case method learning technique [61-64]. The seminars began with the presentation of a Case. Look at page 23 for a short summary of a Case and some examples of aspects to discuss. A case is a description of a defined critical situation related to the real context of a general practitioner and involving a decision. It could be about an authentic patient or a defined critical situation concerning aspects of secondary prevention in daily clinical practice and involving a decision. A case in Case method learning includes analytical, conceptual, and presentation dimensions [62]. These dimensions could be divided into three levels of difficulties. Cases in clinical practice are all complex in the analytical and conceptual dimensions. There is no given obvious decision, and the sessions require that the participants have an extensive amount of knowledge and skills not supplied in the case. We kept the cases short (and well organised in the presentation dimension) because most general practitioners do not have time to prepare a case in a more traditional sense. This permitted concentration on the complex conceptual and analytical dimensions.

A locally well-known cardiologist together with 4-7 general practitioners participated at each seminar. The interactive dialogue starts with the evidence followed by a discussion on the context e g working conditions, family situation, life style, economical constraints, and social and cultural settings of both the patient and the physician. However, the most important components of the decision process are believed to be of abstract nature and include values, attitudes, beliefs, emotions, motivation, knowledge, ethical aspects and communicative capability of both the patient and the physician. Important components affecting the decision, and the final treatment result, are also the physician's sense of professional coherence, and the patient's sense of coherence as a patient [3 70 85]. Subsequently, urgency and timing – i.e.

WHEN – and practical aspects – i.e. HOW – are discussed and analysed. The discussion will end in a decision. Figure 5 shows the schematic cause effect diagram illustrating the concrete and abstract parts of the clinical decision process.

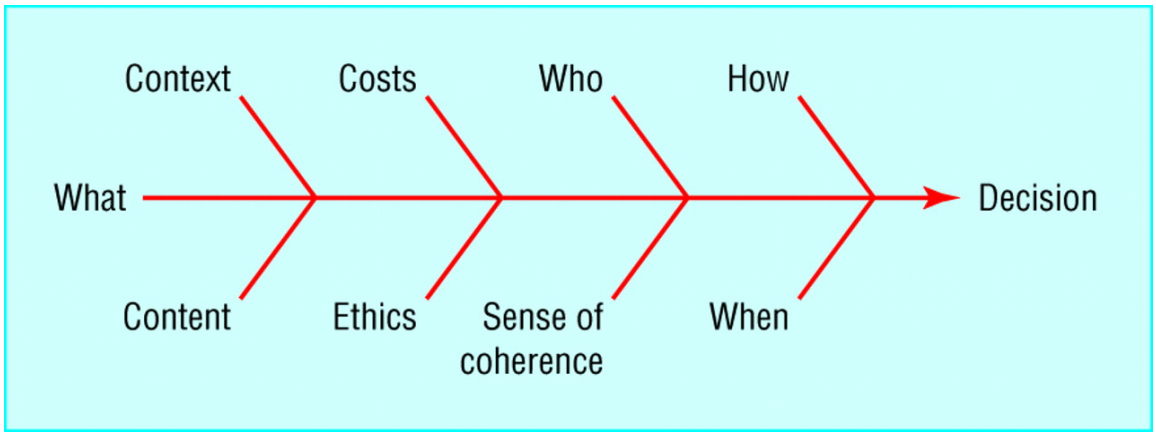

Figure 5. Cause effect diagram illustrating the clinical decision-making process integrating scientific evidence (what) with the concrete and abstract components of clinical practice © *Kiessling A, Henriksson P.*

4.4.2 Cost and effectiveness of Case method learning

The primary research question in paper II was to evaluate if the educational intervention was cost-effective from a population perspective. We had the cost-effectiveness of the 4S-trial [36] [86]. Outcome variables were change in LDL-cholesterol (mmol), lipid-lowering drugs assessed both as Defined Daily Doses (DDD) and as present costs, and estimated QALYs [8] [9]. In the QALY analysis by group, the EQ-5D Index was calculated both at baseline and after two years.

We assumed in the cost analysis, that the general practitioners treated all their CAD patients in the same way. The intervention cost per patient was thus distributed to all their CAD patients. Data on consumption of health care resources (in- and outpatient visits) was retrieved from the patient registry of Stockholm County Council. Mean salaries of GPs and hospital-based consultants in Stockholm County Council were used in the cost analysis. Pay roll taxes were included. All cost were calculated based on Swedish prices in 2002 and converted to US $ at the 2002 exchange rate (1 US $ = 9.5 SEK [Swedish Crowns]).

Short summary of a Case: the what, how, and when of a decision

Dr Fredrik Anderson, a general practitioner at Lunda Primary Health Care Centre, has as usual a fully booked day. His last patient for the day is Oscar Berg, who is scheduled for a regular check of his diabetes and hypertension. Just before preparing to leave, Oscar Berg mentions that two months ago he had an episode of chest pain during heavy exercise.

Background—Lunda Primary Health Care Centre is located in a district with many immigrants, high rates of unemployment, and a high need for social services. Four general practitioners work at the centre; one position has been vacant for a couple of months. Also based at the primary health care centre are eight busy but highly competent district nurses, an efficient secretarial service, and a small local laboratory. Cooperation with the local hospital is rare, apart from referrals and telephone calls about specific patients. Two half days a month are scheduled for continuing medical education activities together with surrounding primary health care centres.

New scientific evidence on the effects of lipid lowering has been presented in international medical journals. Eight months ago, local guidelines on secondary prevention in patients with coronary artery disease were distributed to all general practitioners. During the past year five other guidelines about different medical conditions have also been distributed to the general practitioners.

Dr Fredrik Anderson is 45 years old, married, with three children. He is a smoker and no longer has any time for exercise. He has been working at Lunda Primary Health Care Centre for nine years. In the past year he has also been the head of the centre. As a result of the vacant general practitioner position and various reorganisations, he has been working too much in recent months. He has not had any time for reading and reflection either. He has never met Oscar Berg before. Oscar's previous general practitioner has left, and his new one has not yet begun working at the primary health care centre.

Oscar Berg is a 62 year old divorced taxi driver. He smokes, and he eats a lot of fast food. He has a medical history that includes well controlled hypertension for five years, and he was diagnosed as having diabetes two years ago. Three years ago he had strong chest pains during a visit abroad, but he did not consult a doctor and has never told his general practitioner about it. His available medical and laboratory records give a blood pressure of 180/90 mm Hg, total cholesterol of 6.2 mmol/l, LDL-cholesterol of 4.2 mmol/l, haemoglobin $A1_c$ of 8.5%, and body mass index of 30 kg/m^2.

Specific problem—This is formulated at the seminar in terms of "What decision would you make if you stood in the position of Dr Anderson".

Some examples of aspects to discuss during the seminar

What—The local practice guidelines; scientific evidence (the 4S study and so on).

Context—Social and cultural setting of Lunda Primary Health Care Centre and the surrounding health care organisation; Dr Anderson's workload; Oscar Berg's current lifestyle and medical history.

Content—Dr Anderson's and Oscar Berg's knowledge, attitudes, behaviour, ability to communicate, motivation, and so on.

Costs—Dr Anderson's responsibility for a balanced budget for the primary health care centre; his own increased time commitment if he starts to motivate and further investigate Oscar Berg; financial and time commitments for Oscar Berg.

Ethics—The priority of this problem compared with Dr Anderson's other urgent issues.

Who—Does Dr Anderson have a responsibility to make a decision? Are the guidelines applicable to Oscar Berg?

Sense of coherence—Dr Anderson's sense of professional coherence and Oscar Berg's sense of coherence as a patient.

How—Can Dr Anderson use the help of someone else at the primary health care centre (for example, a district nurse) in the motivational work with Oscar Berg?

When—Urgency, importance, and timing in the life of Oscar Berg and in the schedule of Dr Anderson.

Dr Anderson's task—To advise against or to recommend and schedule an investigational, treatment, or motivational plan for Oscar Berg; to preserve or change the local organisation of Lunda Primary Health Care Centre.

4.5 Assessments of health related quality of life and chest pain (paper III-V)

HRQL is not a well-defined concept. The definition used in this thesis is that 'quality of life' in clinical medicine represents the functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient [87]. The instruments chosen for these studies are the disease specific Cardiac Health Profile (CHP) questionnaire [88], and the generic instruments EuroQol-VAS (EQ-VAS) and EuroQol 5 Dimension questionnaire (EQ-5D Index) [89]. We used the Swedish versions of the instruments.

4.5.1 The Cardiac Health Profile (CHP)

CHP is a disease-specific HRQL questionnaire. It is developed, tested and found to be reliable, valid and sensitive in a Swedish population of patients with CAD [88]. CHP consists of three parts. Part 1 consists of a single question about chest pain symptoms, where the patient ranks existence and degree of current angina according to the Canadian Cardiovascular Society (CCS) classification 0-4 [90-92]. The second part assesses HRQL in a broad perspective. The 16 items were selected from a great pool of items as especially important by coronary patients. The selection procedure has been reported [88]. The questionnaire includes questions about physical function/general health, emotional, social and cognitive function. The 16 items in the CHP questionnaire (English version) are shown in table 3. The last part consists of two items covering "the psychosocial cost-benefit" of patient's who had passed an intervention, e.g. coronary artery bypass graft surgery (CABG) or percutaneous coronary intervention (PCI). This part was not used in this thesis.

Part 2 is answered on a visual analogous scale (VAS) [93]. The respondent is asked to indicate his or hers present situation by placing an X on the scale, a 100-mm long line with verbal "anchors" expressing extremes. The score for each item is obtained by measuring the millimetres from the left anchor to the X mark. The total CHP score is obtained by adding the scores of all items in part 2. The number of answered items in this part then divides the sum. The CHP yields an estimate of HRQL between 0 and 100 were 0 is equal to full health and 100 is equal to worst imaginable state. For further details of content, development, validity, reliability and sensitivity in Swedish populations of patients with CAD see previous publications [88 94]. In this thesis, the results from parts I and II are presented. The CHP results were analysed per item, as a total score and in the four identified independent domains.

Table 3. Domains and items in the Cardiac Health Profile questionnaire (CHP)

Domains	Items
Perceived Cognitive function	1. How do you cope with tasks that require concentration and reflection?
	2. Are you an active person, full of initiative or passive and listless?
	3. Do you easily forget things in the immediate past or where, for example, you have placed things?
	4. Do you easily understand and solve problems, make decisions adapt to new situations?
Emotional function	5. Do you feel depressed or have difficulty finding pleasure in things you used to find pleasant?
	6. Do you easily become irritated, sad, worried, or anxious?
	7. Do you often experience fear, uneasiness or anxiety?
	8. Do you easily lose control over your feelings?
Social function	9. Are you satisfied with your sleep (quality of sleep, ability to fall asleep, etc.)?
	10. Do you have a good relationship to those connected to you (family and friends)?
	11. Are you satisfied with your daily life (at work, as a pensioner, as a housewife, as a student, etc.)?
	12. Do you experience your leisure time as meaningful and enriching?
Physical function/General health	13. How is your sexual life?
	14. Are you satisfied with your physical capacity to accomplish things you wish to do?
	15. How do you experience your general health status?
	16. Are you troubled by various kinds of pain other than your known anginal chest pain?

The answers are marked on a 100 mm VAS-scale with verbal anchors. High scores indicate a worse Health Related Quality of Life.

4.5.2 The EuroQol 5D Index and the EuroQol-VAS scale

The generic HRQL questionnaires EuroQol-5 Dimensions (EQ-5D) self-classifier and EuroQol-VAS (EQ-VAS) were used for evaluation of the disease specific CHP questionnaire. In the EQ-5D self classifier the respondents classified their own health status in five aspects – mobility, self-care, usual activities, pain/discomfort and anxiety/depression into one of three levels – no problems, moderate problems and severe problems [89 95]. The English version of the questionnaire is presented in table 4. Each obtained individual health state was then given an index value (0-1) based on a method described by Dolan [96]. Since there is no Swedish tariff for EQ-5D-index, the UK EQ-5D index tariff was used to calculate the EQ-5D-index values,

were 0 is equal to death and 1 is equal to full health [96]. Health states worse than death were given a score of 0 since the scaling of negative health states are controversial [97 98].

Table 4. The EuroQol 5D self-classifier

Mobility	
I have no problems in walking about	□
I have some problems in walking about	□
I am confined to bed	□
Self-Care	
I have no problems with self-care	□
I have some problems washing and dressing myself	□
I am unable to wash or dress myself	□
Usual activities (e.g. work, study, housework, family or leisure activities)	
I have no problems with performing my usual activities	□
I have some problems with performing my usual activities	□
I am unable to performing my usual activities	□
Pain/Discomfort	
I have no pain or discomfort	□
I have moderate pain or discomfort	□
I have extreme pain or discomfort	□
Anxiety/Depression	
I am not anxious or depressed	□
I am moderately anxious or depressed	□
I am extremely anxious or depressed	□

Instructions: By placing a tick in one box in each group, please indicate which statements best describe your own health state today.

In the EQ-VAS method the respondent marks present HRQL on a 20 cm vertical measurement scale with labelled anchors 'worst imaginable health state' (death; 0) and 'best imaginable health state' (full health; 100), see figure 6. 100 divided the individual numbers marked on the scale in order to obtain EQ-VAS scores between 0 and 1. Both EuroQol methods are easy and rapid generic instruments, well validated and found to be reliable in different cultures and in different disease including a new validation study in patients after myocardial infarction [99 100].

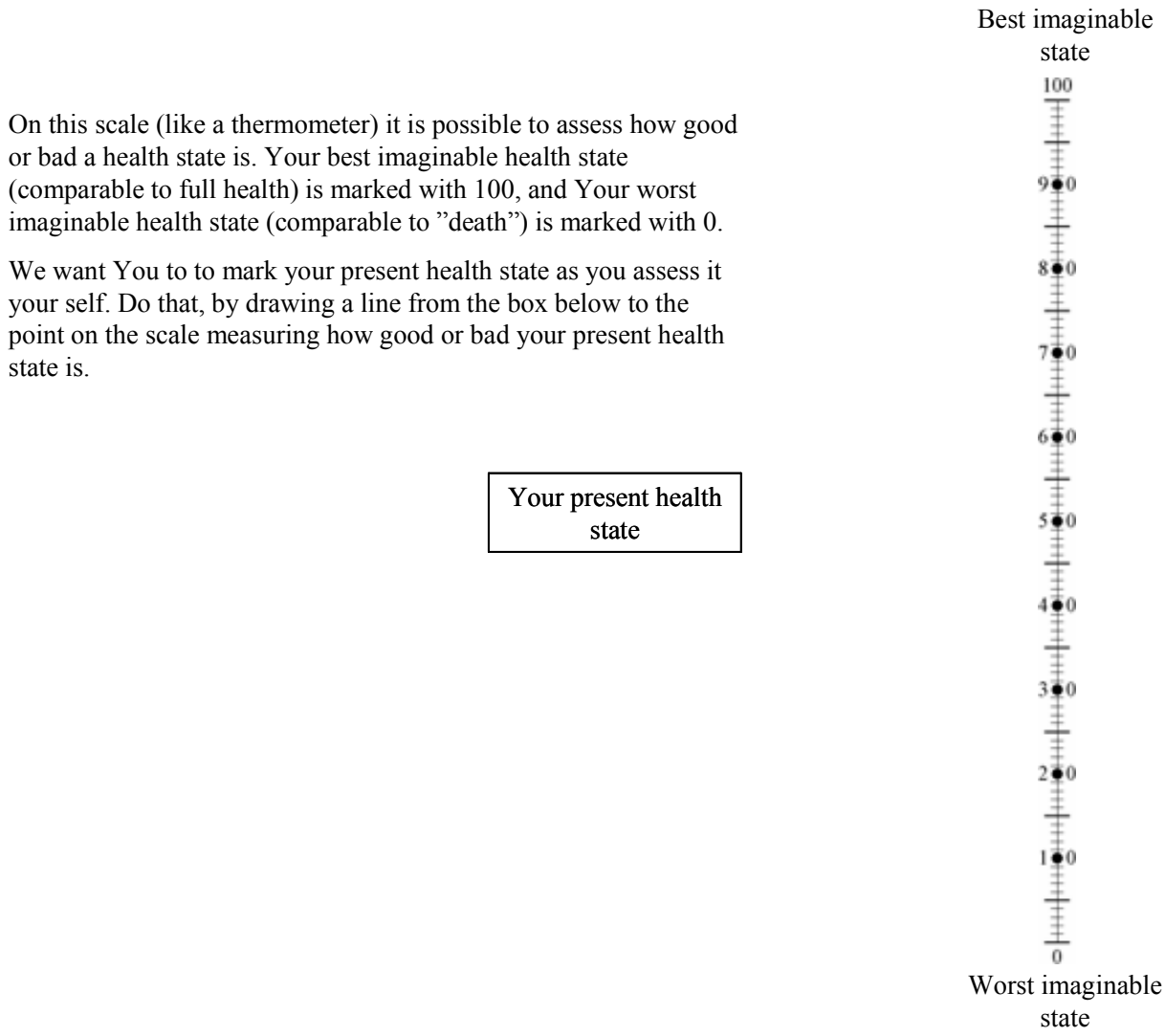

Figure 6. The EuroQol-VAS scale (0-100) including instruction to the respondent.

4.5.3 Chest pain symptoms

The patients assessed their chest pain symptoms in part I of the CHP instrument. All patients ranked present chest pain symptoms according to the Canadian Cardiovascular Society classification of angina pectoris [90-92] (CCS) 0-4, table 5. The EuroQol 5 dimension questionnaire also includes one question about present pain/discomfort were the respondent classifies present situation into one of three levels – no problems, moderate problems and severe problems, table 4.

Table 5. Canadian Cardiovascular Society (CCS) classification of angina pectoris (0–4).
The following question concerns your chest pain (i.e. angina pectoris) and physical capacity. Place an X in the square that best fits your present situation.

	Description
□	No chest pain.
□	Ordinary physical activity, such as walking and climbing stairs, does not cause angina. Strenuous, rapid, or prolonged exertion at work or recreation causes angina.
□	Slight limitation of ordinary activity. Walking or climbing stairs rapidly, walking uphill, walking or stair climbing after meals, in cold weather, in wind, or when under emotional stress, or only during the few hours after awaking causes angina.
□	Marked limitation in ordinary physical activity due to angina. Walking one or two blocks on the level and climbing more than one flight of stairs under normal conditions causes' angina.
□	Unable to perform any physical activity without discomfort – angina may be present at rest.

4.6 Statistical considerations

The primary effect variable in paper I was change in low-density lipoprotein cholesterol concentration in the intervention group as compared to the control group. We analysed the data according to intention-to-treat, depending on which group of primary healthcare centres the physician responsible for patient care belonged to at the initiation of the study, irrespective of any change during the study. To check for robustness of results in this experimental study we used analysis of variance, analysis of covariance, and nested design. We used the non-parametric Mann-Whitney U test for the ordinal data of the questionnaires. We present the results as means and 95% confidence intervals or medians and quartiles.

The aim of the analysis in paper III was to assess the validity and reliability of the CHP questionnaire and to explore the underlying structure of HRQL. We used two different multivariate techniques. The first one, principal component analysis, was used as the major explorative technique to reduce the 16 item variables into principal components, i.e. to get rid of the influence of multicollinearities and to find orthogonal (independent) factors explaining the variance in the sample [101 102]. Varimax rotation was used. The Kaiser criterion was used to demarcate the total number of factors (principal components) to retain. Only factors with Eigenvalues greater than 1 were retained; i.e. unless a factor extracts at least as much as the equivalent of one original variable, it is dropped. To further explore the robustness of the components the alternate multivariate technique, explorative factor analysis with maximum likelihood and varimax raw rotation, was used. This analysis divides the variance of each item into one part that is explained by the factor model (communality) and a specific residual of each item.

Criterion validity of the CHP-instrument was evaluated against EQ-VAS and CCS-class. Reliability as concerns internal consistency, split-half; Cronbach's alpha and inter-rater reliability were also assessed.

In paper IV, we performed three logistic regression analyses with loss function maximum likelihood and Quasi-Newton estimations, with dependent variables representing slightly different aspects of employment. The dependent variables were unemployment, early retirement or sick leave due to coronary artery disease respectively return to work after an index event. The reason why we performed three analyses was to test the homogeneity of the results. Independent variables were the four domains – principal components – of HRQL, age and CCS grade. The analyses were performed at baseline and after two years. Odds Ratios (OR), 95% confidence intervals (CI) and p-values were calculated. Adjusted ORs were calculated after addition of covariates such as risk factors for coronary artery disease (diabetes mellitus, hyperlipidemia, hypertension and smoking) and previous coronary events (myocardial infarction and coronary interventions). To compare the working and nonworking groups, t-tests for continuous variables, Pearson Chi^2 -test for ordinal variables and Fishers exact test for dichotomous variables were used.

The main outcome variable in paper V was HRQL and CCS change over time. HRQL change was analysed by ANOVA and change in chest pain symptoms was analysed by Friedman non-parametric ANOVA. The HRQL was analysed both at global level (CHP, EQ-5D and EQ-VAS) and in sub domains. The factor coefficients of the four extracted PCs at baseline were used to calculate the principal components (domains) at one respectively two years. The calculated principal components were then used in the time trend analysis.

The individual CHP mean scores in paper IV-V were transformed to a 0-1 scale were 0 is equal to death and 1 is equal to full health in order to facilitate a comparison to EuroQol values.

We used Statistica 6.0 (StatSoft, Tulsa, OK, USA) [103] for all statistical analyses.

5 RESULTS

5.1 Baseline characteristics of included patients

257 patients underwent blood tests including serum lipids. 255 of these completed the inclusion procedure for the quality of care studies (paper I-II). Of these, 253 were able to answer at least one of the quality of life instruments and were therefore included in the quality of life studies (paper III-V). Baseline characteristics of included patients are presented in table 1.

5.2 Studies on quality of care - effects of Case Method Learning (paper I-II)

5.2.1 Effects on physicians attitudes and perceived knowledge (paper I)

General practitioners in the intervention and control groups did not differ in perceived knowledge and attitudes about secondary prevention at baseline. The general practitioners in the intervention group rated a higher perceived knowledge (p=0.007) and relevance (p=0.045) of scientific evidence and practice guidelines than controls after two years. Furthermore, we noted a higher satisfaction with the cooperation with the local hospital (p=0.004) concerning practice guidelines and policies in the intervention group.

5.2.2 Effects at patient level (paper I)

LDL cholesterol level decreased from 4.2 (95% confidence interval 4.0 to 4.5) mmol/l to 3.7 (3.4 to 4.0) mmol/l in the intervention group – a 9.3% (2.9% to 15.8%) change. We found no change in the control group. In the specialist group LDL cholesterol concentration decreased from 4.3 (4.1 to 4.4) mmol/l to 3.6 (3.4 to 3.8) mmol/l – a 12.6% (9.1% to 16.1%) change. LDL cholesterol level after two years was 0.5 (0.1 to 0.9) mmol/l lower (effect size 0.56) in the intervention group than in the control group ($p < 0.05$; figure 7). There were similar results of change in total cholesterol (paper I).

5.2.3 Cost-effectiveness of Case Method Learning (paper II)

Defined Daily Doses (DDD) of lipid lowering drugs increased by 0.2 (CI 0.04 – 0.3) in the primary care intervention group and by 0.3 (CI 0.2-0.5) in the specialist group ($p<0.03$; figure 8). No change in DDD in the primary care control group occurred during the two years period 0.0 [CI (-0.1) - 0.1].

The cost of the educational intervention represented only 2% of the drug cost. The cost of lipid lowering in the intervention group including the cost of the educational intervention was actually lower than that of patients treated at the specialist clinic. 106 US $ per mmol decrease in LDL cholesterol in the intervention group; and 153 US $ per mmol decrease in LDL cholesterol in the specialist group. Assuming the same gain in life expectancy per mmol decrease in LDL cholesterol as in the 4S-study gives a cost per gained quality adjusted life year (QALY) of US$ 24 000. Earlier studies in secondary prevention shows that lipid-lowering is cost-effective [36 86]. Only adding a small investment cost for the educational program should not change this conclusion.

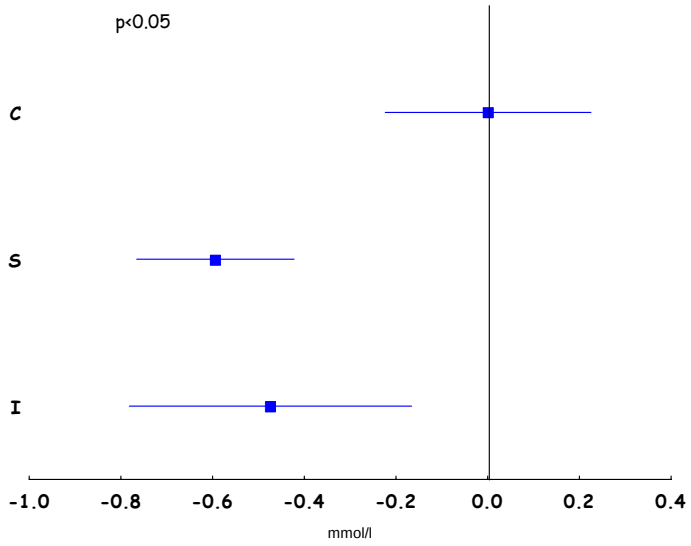

Figure 7. Decrease in LDL cholesterol (mmol/l) at two years as compared to baseline in the intervention (I), control (C) and specialist (S) groups. Means and 95% confidence intervals.

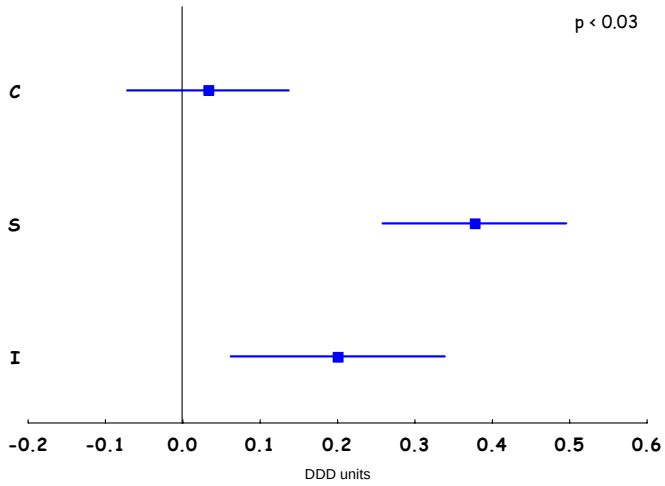

Figure 8. Increase in defined daily doses (DDD) of statins at two years as compared to baseline in the intervention (I), control (C) and specialist (S) groups. Means and 95% confidence intervals.

5.3 Studies on quality of life in coronary artery disease (paper III-V)

5.3.1 Validity and reliability of the Cardiac Health Profile questionnaire (paper III)

The reliability of the instrument was good with a high internal consistency. The Cronbach α-coefficient for total CHP was 0.91. The Cronbach α-coefficient per item in part 2 varied between 0.90 and 0.91. The split-half reliability was 0.82. The inter-rater reliability showed a good correlation to the results from comparable cohorts with CAD. A high sensitivity to discriminate between CAD patients and healthy controls was found. Table 6 shows how total CHP scores obtained in this study compares to scores from healthy controls and scores from three other cohorts of patients with different severity of CAD [88 94 104]. The subgroup of patients (n=100) without chest pain symptoms (CCS 0) in the present study estimated their HRQL significantly worse as compared to healthy controls. Total CHP-scores were 28.5 (25.3–31.7), respectively 22.5 (16.3–28.7; p=0.019). Gender or age did not explain this difference. Total CHP-scores showed good criterion validity when correlated to HRQL as measured by EQ-VAS [r=(-0.59); p=0.0000(6.2E-25)] and as mentioned before to CCS-class.

Table 6. Total Cardiac Health Profile (CHP) scores in relevant subgroups, total study cohort, other CAD populations and in healthy controls

	Subgroup	Number (%)	Mean CHP	95% CI	p-value*	p-value†
Gender	Men	195 (78)	33.7	(31.2-36.2)	0.083	
	Women	55 (22)	38.3	(34.0-42.5)		
Prior MI	Yes	164 (66)	34.5	(31.8-37.1)	0.78	
	No	86 (34)	35.1	(31.4-38.9)		
Prior coronary intervention	Yes	113 (45)	35.4	(32.1-38.6)	0.58	
	No	137 (55)	34.2	(31.2-37.1)		
Current angina (CCS)	CCS 0	100 (40)	28.5	(25.3-31.7)	0.000005	0.019
(n=247)	CCS 1	46 (19)	34.2	(29.8-38.7)		0.0000(3.5E-5)
	CCS 2	75 (30)	37.9	(34.0-41.8)		0.0000(7.9E-9)
	CCS 3	15 (6)	47.7	(37.8-57.6)		0.0000(2.4E-6)
	CCS 4	11 (4)	47.6	(40.1-55.1)		0.0000(6.3E-9)
Total study cohort		**250 (100)**	**34.7**	**(32.5-36.9)**		**0.0000(4.7E-10)**
Pts 3-month post MI §		47	29.5	(24.4-34.5)		0.0193
CAD pts prior to cor ai‡		76	35.7	(31.9-39.5)		0.0000(4.4E-7)
Pts with extended sick leave after cardiac event**		12	53	(42.2-63.8)		0.0000(1.3E-6)
Healthy controls‡		51	22.5	(16.3-28.7)		

CCS Canadian Cardiovascular Society Classification of angina pectoris symptoms; MI Myocardial Infarction; cor ai Coronary Angiography

* The p-value denotes a comparison between the two subgroups

† The p-value denotes a comparison to healthy controls

§Publication 2001 [94]

‡ Publication 1996 [88]

**Publication 1997 [104]

5.3.2 Multivariate principal component and factor analysis (paper III)

Four independent principal components (PC) were identified. These four PC's explained 66% of the variation in answers in this cohort. The first PC – explaining 43% of the total variation – mainly reflects questions regarding cognitive function – ability to concentrate, drive to purposive activity, memory and problem solving. This first PC showed the highest loading (most influence) for item 1 (How do you cope with tasks that require concentration and reflection?). The second PC comprised questions reflecting physical function/general health with item 14 (Are you satisfied with your physical capacity to accomplish things you wish to do?) showing the highest loading. The third PC reflecting social function showed the highest loading for item 11 (Are you satisfied with your daily life?). The last and fourth PC concerning emotional functioning had the highest loading in item 6 (Do you easily become irritated, sad, worried or anxious?). A reliability analysis of the four PCs showed a high to moderate internal consistency. The Cronbach α-coefficient per PC varied between 0.88 and 0.74. Explorative factor analysis (maximum likelihood, varimax raw rotation) did also identify four factors with the 16 items loading together in the same groups of understandable domains of HRQL as by the principal component analysis.

Perceived cognitive and social function was not significantly related to CCS class. By contrast, physical function/general health showed a highly significant relation to CCS class. Figure 9 shows the relation between physical function/general health respectively the perceived cognitive function domain and CCS grade.

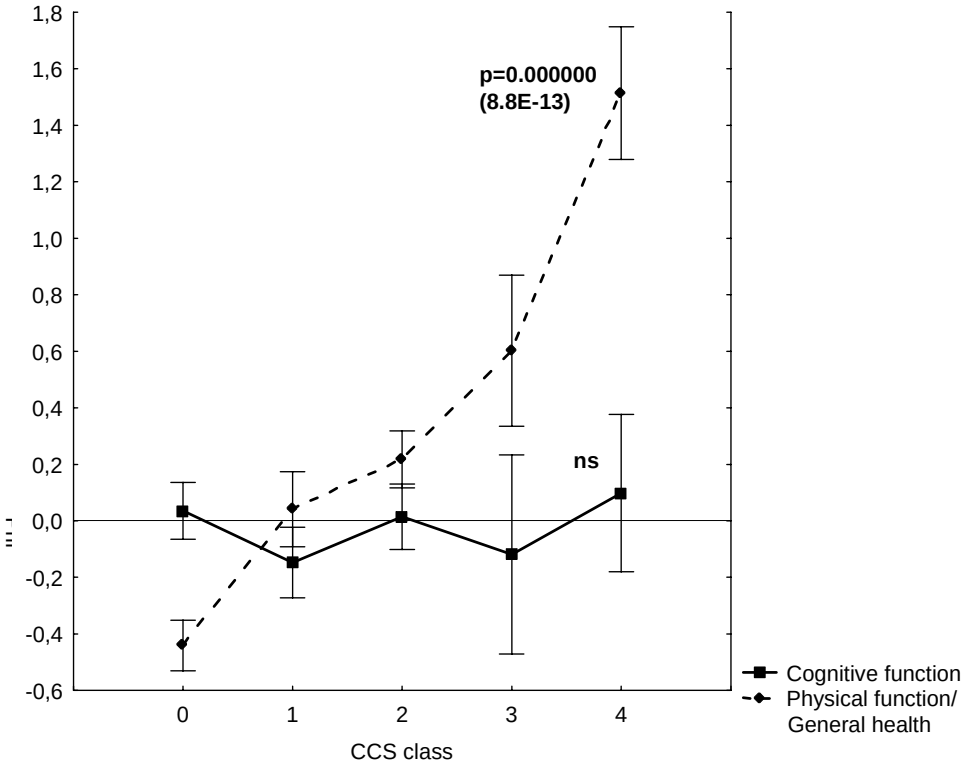

Figure 9. Relations between the principal components Cognitive function, respectively, Physical function/General health [p=0.0000(8.8E-13)] and Canadian Cardiovascular Society (CCS) class (0-4). Values are given as means with an indication of the standard error. (ns denotes no significant).

5.3.3 Health related quality of life and unemployment (paper IV)

We aimed to assess whether perceived cognitive function – or the other domains of HRQL – influenced employment. The unemployed patients were slightly older but had no significant difference in chest pain grade as compared the employed patients. The unemployed patients rated their global HRQL significantly worse than the gainfully employed (p=0.00005).

Perceived cognitive function predicted both prevalence of unemployment [OR 2.06 (95% CI 1.36-3.13) (p=0.0006)], and early retirement or sick leave due to coronary artery disease [OR 1.59 (95% CI 1.12-2.25)] at baseline and at two years. Furthermore, perceived cognitive function predicted return to work after an acute coronary event [OR 2.28 (95% CI 1.08-4.84)]. Covariates such as age, sex, prevalence and degree of angina (CCS grade), cardiovascular risk factors and events did not change the predictive power. The results from the logistic regression analysis of prediction of unemployment are presented in figure 10.

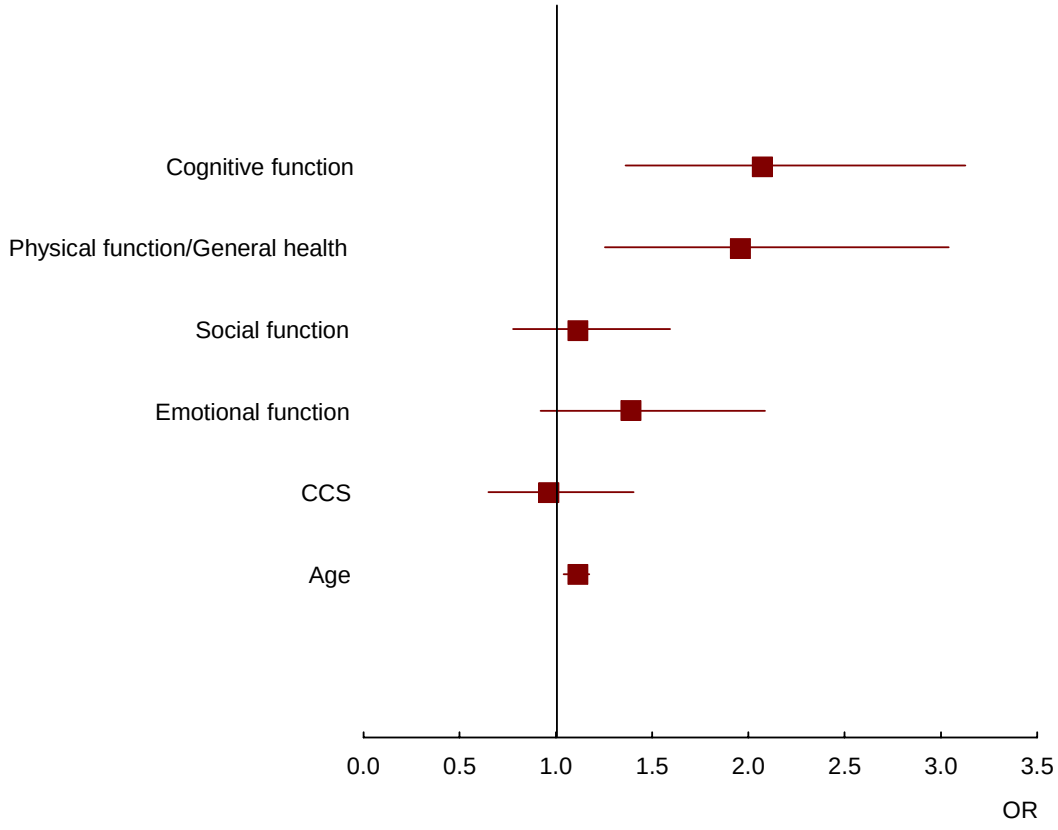

Figure 10. Influence of perceived cognitive function, physical function/general health, emotional function, social function, age and current angina (CCS) on unemployment in patients with coronary artery disease. *Values are Odds ratios (OR) and 95% confidence limits. CCS denotes Canadian Cardiovascular Society Classification of angina pectoris symptoms*

5.3.4 Time trends of health related quality of life and chest pain (paper V)

The prevalence and severity of chest pain symptoms decreased during two years of follow-up as assessed by CCS grade ($p<0.00022$). However, no change in global HRQL as assessed by three different HRQL instruments (CHP, EQ-5D and EQ-VAS) was found, despite this symptom reduction. This indicates that an important part of HRQL in such patients is not sensitive to change in the existence or degree of chest pain.

An analysis of the relations between chest pain symptoms and HRQL showed significant correlations between CCS and all three global assessments of HRQL at all three time points; table 5 ($p=0.000000$). A similar analysis of the four independent domains – principal components – showed a correlation between chest pain symptoms and the physical/ general health domain at all three time points ($p=0.000000$). A slight but significant correlation was also present at all time points between CCS and the emotional domain ($p<0.04$). By contrast, no relation between cognitive function respectively social function and chest pain symptoms was found at any time point.

6 DISCUSSION

6.1 Quality of care in coronary artery disease

6.1.1 Case method learning in continuous medical education – effects on quality of care

We have shown that Case method learning for general practitioners resulted in a decrease in their patients' low-density lipoprotein cholesterol concentrations to a degree that, according to current knowledge, should decrease mortality and morbidity in coronary artery disease [32]. We have also shown positive effects of CML as regards attitudes and perceived knowledge at physician level.

We would propose that crucial components of our case method seminars were the focus on the physicians' own clinical practice, the small groups, the location of the seminars at their own practice, the recurrence of the seminars, and that the opinion leader was just a leader of the dialogues and not a lecturer. A Cochrane Collaboration evaluation states, “Didactic sessions alone are unlikely to change professional practice. By contrast interactive workshops have at least in some cases been shown to alter practice” [28]. One reason for the lack of impact on clinical practice of attending lectures and of reading printed materials could be the absence of active participation and interaction. It has been shown that participation, interaction, recurrence, and facilitators, rather than lecturers are important ingredients in effective educational technologies [26-29 105].

The study is an intention to educate study, and not primarily an intention to treat study. A inherent weakness in all evaluations of educational interventions [24 25], and in our study as well, is the difficulty to separate the effect of the educational method to that of the tutor. However, a tutor/facilitator is an essential part of most learning techniques and the tutor has to

be trained and fit for the role. Another factor influencing the learning effect is the learners' level of commitment. This level depends both on the learner´s ability and motivation to active participation, and on the educational method used [106]. Student activating learning methods [107] such as problem-based learning [108 109] and Case method learning [62 63] have been increasingly used in especially undergraduate university teaching. A review of the use of problem based learning in CME, which was published in 2002, did only find limited evidence of an effect [110]. However, Case based learning has been shown to have effects at the postgraduate level [111].

The use of the Case method learning technique in the present study improved the quality of care of the patients at only a marginal additional cost of 2% of the drug cost. LDL cholesterol in the present study was reduced at a fraction of 0.29 (0.5/1.7) as compared to the 4S study [32 36]. However, the clinical relevance of the lipid lowering in the present study is strengthened by several arguments. 4S was a randomized controlled trial with the intention to give all patients in the active group statin treatment. In the present study, the intention was to give all physicians in the active group education in purpose to increase the intensity of secondary prevention by e.g. increased use of statins in the treatment of their CAD patients. We calculated the mean lipid lowering in the whole group of patients and not only in the subgroup that actually got treatment. The proportion of patients treated with statin increased by 20% in the intervention group. This means that the patients – who actually had statin treatment instituted during the study – had at least the same lipid lowering as shown to be of clinical significance in the 4S study. Furthermore, it is known that the clinical benefit from statin treatment is more clearly shown to be related to baseline risk than to actual lipid levels [112]. The patients had a high baseline risk in the present study. The waste majority of them had in addition too their CAD, risk factors shown to be of importance in e. g. the INTERHEART study [113].

It should be pointed out that the assessed use of DDD of lipid lowering drugs was calculated from the patients´ own reports of actual present drug use. This means that we assessed use of DDD of lipid lowering drugs at patient level and not at prescription or "physicians´ reported intention-to-treat" level.

6.1.2 Application in primary care – guidelines and then

The main aim of our educational intervention was to translate the content of the first local practice guidelines on secondary prevention of CAD into clinical practice in primary care and to evaluate the efficacy. The fact that patients treated by general practitioners in the control group (only receiving practice guidelines) had no decrease of their lipid levels despite publication of firm scientific evidence and presentation of local practice guidelines is disconcerting. Several explanations have been offered for the inefficiency of practice guidelines as such [23 60 114-117]. One is that practice guidelines are not written for practising physicians but focus on scientific knowledge [118]. Another explanation is the risk of negative attitudes among general practitioners to guidelines written by experts [119-121]. Several reports have discussed different barriers and facilitators for application of evidence in clinical care [54 122].

The knowledge translation has been slow concerning the efficacy of lipid lowering and the consequent application in primary care. The attitudes and willingness to put LDL cholesterol lowering into practice have become more positive by time, but practice is still not optimal [123].

One explanation could be that patients with coronary artery disease represent only a minority of all patients treated at a generalist practice as opposed to a majority at a specialist clinic. Moreover, not all physicians at a generalist practice may be aware of the scientific evidence supporting the use of these drugs [124]. Finally, the actual nature of outpatient practice may interfere with guideline adherence, as patients and physicians may prioritise acute care at expense of preventive issues [51 124].

The context and content of the consultation of the patient at his or her physician differ a lot in the primary care setting as compared to that at a specialist clinic. This implies quite different HOWs and WHENs in the clinical decision processes (figure 5). The results in the control group should be viewed against this fact.

The interplay between learning methods and the learning styles of learners are important to the outcome [125]. Physicians working in different contexts have been shown to prefer different learning methods [119]. Specialists at hospitals were shown to be more influenced by medical journals and scientific conferences in one report; whereas general practitioners were more influenced by general medical newspapers and postgraduate meetings. The efficacy of methods aimed to change physicians' practices have been reviewed [29 115 121 126]. In-depth interviews indicate that personal experience or the advice and recommendations of colleagues are the most important factors determining attitudes and behaviour [127].

Generalists are faced with a difficult task to ensure that they are updated on scientific evidence relating to all the different diseases of their patients [118]. However, a positive finding in our study is that a mere of three to four hours spent during a two year period seems to improve the quality of care of a particular patient group to a level similar to that achieved at a specialist clinic. A high grade of time efficiency has to be a prerequisite, because of the broad spectrum and number of diseases in primary care. This prerequisite seems to be fulfilled by the Case method learning technique.

6.2 Quality of life and chest pain symptoms in coronary artery disease

A strength of the present studies was that HRQL assessments were performed by three different global instruments and further analysed by its principal components. This should increase the robustness of the conclusions. The global estimate of EQ-5D seems to give a roughly better HRQL by 0.1 than CHP and EQ-VAS. An explanation to this might be the more narrow scope of EQ-5D tapping mainly physical and emotional function aspects of HRQL.

The CHP instrument was found to be highly reliable and valid in this unselected cohort of patients with CAD. A decreased HRQL assessed by CHP as compared to healthy controls was found even in patients without current angina. This is in contrast to some other studies [74 75].

The CHP items were analysed by multivariate explorative factor analysis. Four principal components – independent domains – of HRQL representing perceived cognitive function, physical function/general health, social and emotional functions could be identified. Perceived cognitive function is a major determinant – explaining 43 % of the variation in CHP ratings – in this unselected cohort of patients with CAD. Perceived cognitive function was not related to existence or severity of chest pain. By contrast, it predicted unemployment, sick leave and early retirement both at baseline and after two years.

Cognition is defined as the process of knowing. Perceived cognitive function can be addressed by questions concerning the ability to select relevant information, and to understand, retain, express and apply knowledge in specific contexts of life [128].

Cognitive function has been shown to be decreased in elderly patients with cardiovascular risk factors – hypertension and diabetes mellitus – and in elderly patients with sub clinical arteriosclerosis [129-132]. Furthermore, a decreased objectively measured cognitive function has been recognized to be a major although probably partly reversible sequel after e.g. coronary artery bypass grafting (CABG) [133 134]. The results might, however, not be identical if subjective – perceived – cognitive function is assessed. Several reports have been presented showing a discrepancy between objectively measured and subjectively perceived cognitive function [135 136]. The reason for the discrepancy between objective and subjective measurements might be that objective neuropsychological tests are too insensitive to measure small but to the individual very significant cognitive declines [134]. Another explanation could be that the poor perceived cognitive function seen after CABG is related to presence of anxiety and depression [137]. However, in our study perceived function was not related to the emotional function domain of the CHP questionnaire. This domain includes questions regarding anxiety and depression; see table 3. Further evidence for an importance of cognitive impairment in patients with CAD, are two reports showing an influence on the effectiveness of cardiac rehabilitation and on the prognosis after PCI [138 139]. These two reports are of particular interest indicating a tentative importance of this aspect of mental function in CAD patients that might be unrelated to structural changes. Such changes have been hypothesised to explain the previously mentioned incidence and prevalence of cognitive dysfunction after open-heart surgery.

The finding in the present study that physical function influences employment was expected. However, that perceived cognitive function predicts unemployment is hitherto unrecognised. However, cognitive function is vital in modern working life. Studies of, for example, patients with acquired brain damage have shown that perceived cognitive function and life satisfaction are closely related to the ability to perform the usual activities of daily living, including return to work [128 140 141]. Recently a study of predictors of employment in men with HIV showed that

impaired cognitive function, rather than severity of HIV disease, was a barrier to return to work [142].

An individual's capabilities and own perception of health seem only to a limited degree to be explained by severity of disease and objectively measured functional status and grading of symptoms [79 143 144]. Perceived cognitive function is the patient's experience of cognitive ability reflecting a complex synthesis of objective function and an individual's psychological and sociological content.

The influence of perceived cognitive function on unemployment in CAD is hitherto unrecognised. The reason is probably that most instruments – used for assessment of HRQL in CAD – do not contain questions aimed to assess perceived cognitive function. The frequently used questionnaires such as Nottingham Health Profile (NHP) [67], Seattle Angina Questionnaire [145], EuroQol-5D [99] and the MOS 36-item Short-form Health Survey (SF-36) [146] have a dominance of questions relating to physical function and the emotional component of mental function but no questions at all reflecting perceived cognitive function.

A potential limitation of our study is that the data are drawn from the Swedish health care system. The Swedish social insurance legislation system may be more liberal concerning long-term disability than that of other countries. Furthermore, we chose the cutoff for the employment study at the age 65 years in view of the Swedish retirement system. Those facts could hamper international comparisons. Our results should, however, initiate research of the impact of perceived cognitive function on ability to work in other countries.

40% of included patients did not have present chest pain symptoms. It may sound a high figure but it is actually lower than in the recently published follow-up report from the Third Randomized Intervention Trial of Unstable Angina; the RITA-III trial [129] were 54% to 67% of the patients assessed CCS class 0, four months respectively one year after an episode of unstable angina.

Total CHP score was significantly correlated to functional status as assessed by severity of chest pain symptoms according to CCS. However, the relation between severity of chest pain and the independents sub domains of HRQL were not homogenous. CCS grade and physical function/general health had a highly significant relation but CCS grade and emotional function was only moderately related. No relations at all were found between CCS grade and social respectively perceived cognitive functions. Those different patterns of relations between chest pain symptoms and the four domains of HRQL were constant over time. In the FRISC II cohort a similar significant relation between grade of angina and HRQL was found both at three and six months after an episode of unstable angina [147]. The relation was highly apparent for physical score as compared to a more moderate relation for the mental component score. However, the SF-36 instrument [146] , used in the FRISC II study, mostly includes questions regarding emotional aspects of mental function but no questions at all regarding the cognitive aspects.

7 CONCLUSIONS

- Case method learning for general practitioners resulted in a beneficial change in clinical practice.

- Case method learning supported lipid lowering strategy is cost-effective. The low cost in addition to its positive effects should probably warrant its use in the improvement of the quality of care in other major diseases.

- Perceived cognitive function seems to be a major determinant of health related quality of life in patients with coronary artery disease.

- Perceived cognitive function predicted ill health assessed as unemployment, sick leave and delayed return to work. However, this component of quality of life was not related to severity of chest pain symptoms.

- HRQL did not increase despite a reduction in the severity of chest pain during two years in this non-selected population of patients with CAD. This implies that a major part of the HRQL in these patients is not sensitive to change in chest pain symptoms. Our findings add a new perspective on quality of life and gainful employment, which might have significance both to individual care and to society.

8 FUTURE PERSPECTIVES

Some ways in which health could be understood and improved are outlined in figures 1 and 11. The research fields in the present thesis are shown in figure 12. Quality of care is by many synonymous with a focus on management, health economy, costs and QALYS. A central role of education could be a surprise. However, our results showing a significant effect on the quality of care by applying a modern – in undergraduate teaching – but not new – in management as such – interactive learning technique in primary care could be an initiator of future research. Evidence based medicine has been in focus but evidence based care is still to come. We would like to propose that modern teaching such as CML should be tried also in other areas of care. A combination of interactive learning and other techniques such as e.g. feedback of care results should probably be tried. An interesting area could also be care performed in interprofessional teams.

The findings of discrepancies between subjectively perceived illness and objectively measurable disease and ill health should stimulate further research. Our findings of an importance of perceived cognitive function in CAD is interesting and new. The relations between perceived cognitive function, depression and objectively measured cognitive function and severity of disease should be further explored also in other cohorts of patients.

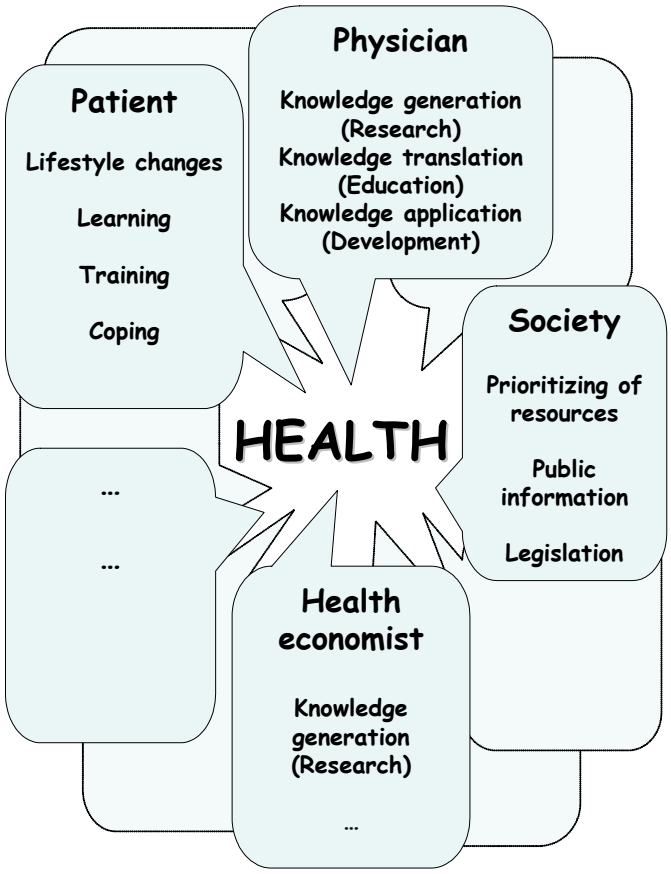

Figure 11. Examples of ways to improve health from the perspective of the patient, physician, society and health economist.

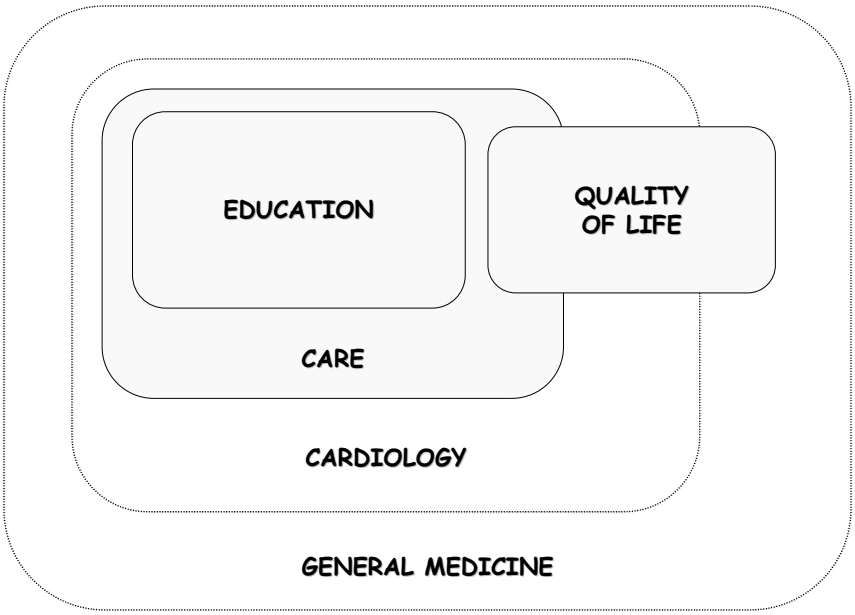

Figure 12. Research fields of this thesis.

9 ACKNOWLEDGEMENTS

I wish to express my sincere thanks to all patients and general practitioners who participated in this study. I also want to express my deepest gratitude to all persons who in different ways and at different times during my research made my work both enjoyable and possible.

I would in particular mention:

Professor *Peter Henriksson* my principal tutor. First, for his curiosity and courage to try to make a scientist out of me. Second, for that he believed me when I told him that I had time to do it! Third, for his unyielding never-ending belief in that this will work. Finally, I want to thank him for all fruitful discussions regarding apparently unsolvable statistical, intellectual and presentational problems, which all suddenly found their solutions.

Professor *Christer Sylvén,* for being the first to speak to me as a prospective scientist. For his creation of an encouraging climate for research at the department of Cardiology at Huddinge University Hospital and for his calm and friendly manner during the years, both as a colleague and as I believe a supporter. Thank you for your advice on how to improve my oral presentation of the principal components statistics, so that the audience have at least a chance to grasp the main points.

Katarina Patzelt-Brandt for excellent nursing and skilful handling of all patient data. I could not have managed this without your help. I think I found no errors in the variables during all years of calculating and working with the databases. I also want to thank you for all our faithful chats during the years at Södertälje Hospital.

Bengt Jönsson for creating an excellent climate for research and positive collaborative attitude at the Centre for Health Economics, Stockholm School of Economics, University of Stockholm. *Magnus Johannesson* for constructive criticism and encouragement especially in the design of the health economy part of this thesis. *Niklas Zethraeus* my co-author for valuable guidance and collaboration through all health economic calculations.

Peter Währborg for creating the Cardiac Health Profile questionnaire, for letting us use it and for sharing his valuable experiences with us.

The former head of the Department of Medicine at Södertälje Hospital *Alf Nyberg* together with *Sven-Gunnar Eklund* and *Lars-Gunnar Hjerne* for being excellent mentors and tutors during my years as assistant physician, for being patient with my curiosity on the complexities of internal medicine and cardiology.
The staff and colleagues at the Department of Medicine at Södertälje Hospital for their support during the study. Especially *Torsten Molin* for careful handling of our resources, *Peter Knutsson* for energizing critical discussions, *Kjell Haglund* for believing in my ideas, *Torbjörn Kullenberg* for being a perfect room mate, *Marianne Erlandsson*, *Ida Löfman, Anita Conrad, Ann-Marie Strand, Åsa Hed, Anita Eriksson* and all others for their support.

Later on during the study the staff at the Department of Cardiology at Huddinge University Hospital for valuable criticism and support, especially the former heads of the department *Olof Nyqvist, Inger Hagerman* and *Eva Stråât* and among my former colleagues, *Hans Berglund, Anna Freyschuss, Aida Hot-Bjelak, Monica Fogelberg, Björn E Eriksson, Thomas Flodin, Amon Gabriel, Eva Mattson* and *Arne Martinsson.*
During the last part of the research, the former head of Karolinska Institutet at Danderyd University Hospital, Professor *Claes Frostell* for support and encouragement.
Associate professor Carl-Göran Ericsson, Professor Ulf Adamson and professor Per-Eric Lins for creation of an excellent and supportive climate for research at the Department of Internal Medicine at Karolinska Institutet Danderyds University Hospital.
Magnus Edner, Thomas Kahan, Håkan Wallén and all other colleagues at Cardiovascular medicine for valuable criticism and support.

Carola Lemne and *Jörgen Striem* for encouragement, support and the opportunity to finish this thesis.

All my colleagues and co-workers at Danderyd University Hospital and in different research and educational groups at Karolinska Institutet for interest and encouragement and for patiently tolerating several moments of absence during the last months. *Rolf Wahlström, Stellan Arvidsson, Ester Mogensen, ViviAnne Sundqvist* and several others, I will thank you all.

Margareta Hemström, my mentor and friend for all encouragement and support, and for learning me to start to prioritize and to say no and "I do not have time for this at the moment".

During these years, I have learned a lot in collaboration with many enthusiastic and knowledgeable general practitioners. I want to thank you all, especially *Christer Norman, Mikael Ohrling, Thomas Jacobsson, Raymond Netzell, Kerstin Adamson, Per Guterstam* and *Henrik Hallberg.*

Most of all, I had wanted to thank my late parents *Ingegerd* and *Hans* for everything.

My love to *Jenny, Anton* and *Julia* for involving me in at least some of your dreams and your worries, and for being the three suns in my life.

Peter, for your love and for sharing both your deepest feelings and your curiosity with me.

I also want to acknowledge Stockholm County Council. This study was supported mainly by grants from the Stockholm County Council (PICKUP), but also from the Swedish Heart and Lung Foundation and Karolinska Institutet.

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