



LUND UNIVERSITY

Quality of life and ethics-patients with ischemic heart disease

Westin, Lars

2005

[Link to publication](#)

Citation for published version (APA):

Westin, L. (2005). *Quality of life and ethics-patients with ischemic heart disease*. [Doctoral Thesis (compilation), Medical Ethics]. Department of Medical Ethics, Lund University.

Total number of authors:

1

General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

**Quality of life and ethics –
patients with ischemic heart disease**

Lars Westin

The department of Medical Ethics

Faculty of Medicine

Lund University, Sweden

2005

Original papers

The thesis is based on the following papers, which will be referred to in the text by their Roman numerals

I. Westin L, Carlsson R, Israelsson B, Willenheimer R, Cline C and McNeil TF.

Quality of life in patients with ischaemic heart disease: a prospective controlled study.

Journal of Internal Medicine.1997;242:239–247.

II. Westin L, Carlsson R, Erhardt L, Cantor-Graae E and McNeil T. Differences in quality of life in men and women with ischemic heart disease. A prospective controlled study. Scandinavian Cardiovascular Journal.1999; 33:160–165.

III. Westin L, Nilstun T, Carlsson R and Erhardt L. Patients with ischemic heart disease: Quality of life predicts long-term mortality. Scandinavian Cardiovascular Journal. 2005; 39:50–54.

IV. Westin L and Nilstun T. Principles help to analyse but often give no solution

– secondary prevention after a cardiac event.

Accepted for publication in Health Care Analysis.

...Första thesis blev nu den:
Om med moraliteten
Enligt är för Bacchi män
Att ändra om dieten.
Pro och pro,
contra, jo,
nej och ja nu skalla;
Movitz ropte posito,
Och posito skrek alla.

Andra thesis blev den här:
vad skillnad sig besticker
mellan öl pluraliter
och en person, som dricker.
Ratio? Jo,
dubito,
skrek en och orera.
Movitz ropte: Habeo,
Och kyparn slog i mera.

Tredje thesis skulle ges,
Men preses damp av stolen,
Och en opponent så hes
Damp med i kapriolen.
Fredman kom,
Filibom!
Med musik och flickor;
Och de lärde vände om
som åsnor och borickor.

C.M. Bellman (1740–1795) Fredmans sång N:o 28, Tre remmare.

Contents

Preface	5
Abbreviations	6
Scope	8
Introduction	9
Ischemic heart disease in the world	9
Ischemic heart disease in Sweden	10
Acute myocardial infarction	10
Coronary artery by-pass grafting	12
Percutaneous coronary intervention	13
Some aspects of ischemic heart disease	14
Emotional reactions and sexual dysfunction in relation to ischemic heart disease	15
Quality of life	18
Ethics	21
Ethics and quality of life	25
Questionnaires	25
Statistical methods used in papers I–II	30
Material	33
Method	37
Results	41
Paper I	42
Paper II	43
Paper III	44
Paper IV	45
Discussion	47
Conclusions	52
Summary in Swedish	53
Acknowledgements	55
References	57

Preface

I have been working as a cardiologist in a coronary care unit with myocardial infarction patients. In secondary prevention I have met patients after a coronary artery by-pass surgery or a balloon angioplasty as well as infarction patients. Some questions have always attracted my interest: How are these people getting on after they have left the hospital, how do they compare with other people? Do male and female patients differ in any relevant way? If you CAN get answers to these questions, do the answers matter in a down-to-earth way? For instance, does perceived quality of life at one time say anything about who is alive and who is dead after a couple of years? And finally, one important consequence of living with a cardiac disease is that doctors often try to change your way of life. Does the communication between the patient and the physician involve any ethical problems? If there are, how to solve them? These are a few of my favourite things ... and in these papers I have had a chance to discuss the topics. I have in mind at least two partners in this discussion, cardiologists and people in medical ethics (some are interested in both). The reason why you, dear reader, will certainly find some of the material a little below your intellectual level is because it is primarily meant for somebody else.

Abbreviations

AMI	Acute myocardial infarction
ANCOVA	Analysis of co-variance
APQLQ	Angina Pectoris Quality of Life Questionnaire
BMI	Body mass index
CABG	Coronary artery by-pass grafting
CASS	Coronary Artery Surgery Study
CI	Confidence interval
CKMB	Creatinkinase, isoenzyme MB (M=muscle, B=Brain)
COPD	Chronic obstructive pulmonary disease
CPRS	Comprehensive Psychopathological Rating Scale
CUA	Cost-utility analysis
ECC	Extracorporeal circulation
ECG	Electrocardiogram
ED	Erectile dysfunction
ENRICHD	Enhanced Recovery in Coronary Heart Disease
FRISC	Fast Revascularisation during Instability in Coronary artery disease
GUSTO	Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries
IHD	Ischemic heart disease
GP	General Practitioner
GP IIb-IIIa	Glycoprotein IIb-IIIa
HbA _{1c}	Glycosylated haemoglobin
HDL	High density lipoprotein
KKM	Kranskärlsmottagningen, Swedish for coronary outpatient unit
LAD	Anterior descending branch of the left coronary artery
LDL	Low density lipoprotein
MADRS	Montgomery Åsberg Depression Rating Scale
MAS	Malmö Allmänna Sjukhus, Swedish for Malmö General Hospital
MI	Myocardial infarction
MHIQ	McMaster Health Index Questionnaire
NHP	Nottingham Health Profile
NQMI	Non-Q wave myocardial infarction

NSTEMI	Non-ST segment elevation myocardial infarction
OR	Odds ratio
PCI	Percutaneous coronary intervention
PTCA	Percutaneous transluminal coronary angioplasty
QALY	Quality-adjusted life-years
QoL	Quality of life
QT	A part of the ECG recording
QwMI	Q-wave myocardial infarction
RITA	Randomized Intervention Trial of unstable Angina
SADHART	Sertraline Antidepressant Heart Attack Trial
SAQ	Seattle Angina Questionnaire
SF-36	Medical Outcome Study 36-Item Short-Form Health-Survey
SIP	Sickness Impact Profile
SPSS	Statistical Package for the Social Sciences
SSA-P	Subjective Symptoms Assessment Profile
SSRI	Selective Serotonin Reuptake Inhibitor
ST	A part of the ECG recording
STAI	State and Trait Anxiety Inventory
STEMI	ST-segment elevation myocardial infarction
STRESS	Stent Restenosis Study
TXA ₂	Tromboxan A ₂
UA	Unstable angina
UMAS	University hospital of Malmö (cf. MAS)
VA	Veterans Administration
VAS	Visual analogue scale
WHO	World Health Organization

Scope

As suggested in the preface, this thesis is about the *consequences* of a cardiac event for the persons involved. It is based on four papers, two dealing with different aspects of quality of life (QoL) after an acute myocardial infarction (AMI), a coronary artery by-pass grafting surgery (CABG) or a percutaneous coronary intervention (PCI), also called percutaneous transluminal coronary angioplasty, PTCA). The third paper discusses the possibility that perceived QoL may predict mortality some years after the index event. The fourth deals with ethical conflicts that may arise when the patient is recommended to change a way of life as a part of secondary intervention. Thus, *causes* of ischemic heart disease (IHD) are not discussed, and questions like if a patient is depressed because he or she has had an AMI or has had an AMI because of depression are not answered.

As the patients described suffer from IHD, I will begin with an outline of this disease, with epidemiology data from the World Health Organization (WHO) and the Swedish National Board of Health and Welfare. Diagnostic criteria for AMI have changed since paper I was published and this topic together with some old and some more recent data about CABG and PTCA/PCI will be discussed shortly. I turn then to some aspects, somatic and emotional, of IHD. QoL and ethics are main issues in this thesis and they will be discussed in the next sections. For anybody interested in QoL a central subject matter is the questionnaires that are used for its assessment, and some of the instruments used today are pointed out next. Then follows the “Material“ section, which gives a description of the patient sample and the story of the “Kranskärlsmottagning” (coronary out-patient unit) in Malmö, Sweden. “Method” includes a description of items used in papers I–III for QoL measurement; together with the background for the analysis of ethical conflicts in paper IV. What I consider the major results of papers I–IV are then presented before the Discussion in relation to the findings. A conclusion and a summary in Swedish end the thesis.

Introduction

IHD is one of the major disease entities worldwide (1, 2). Manifestations of IHD are the most frequent reasons for hospitalization in Sweden, a European country with 9 million inhabitants (3, 4).

As science makes progress, increasing numbers of patient survive an AMI. Many undergo procedures like CABG and PTCA/PCI. This also means that it becomes more important to study what the consequences are for the individual patient after a cardiac event. A crucial concept in this study is quality of life (QoL). The expression has been defined in many ways, as will be discussed below, but it suffices here to say that it turns the focus to the main person, the patient, the whole patient and nothing less.

The central question in the encounter between physician and patient is: “How are you”? Questionnaires in QoL research try, in a formalized way, to answer this question. The term “objective” is often used as in a positive way, but when it comes to QoL, subjectivity is the main thing, i.e. the task is to find out as unmodified as possible what the patient feels about his or her life.

Ischemic heart disease in the world

“The world health report” is WHO’s leading publication. The 2004 report gives mortality data for the year 2002 (5). Cardiovascular disease (including cerebrovascular disease, IHD and hypertensive heart disease) accounts for 29.3% of total world mortality, IHD alone is the cause of 7.2 million deaths equalling 12.6% (6). Male and female rates for IHD mortality are 12.7 and 12.5% respectively (3.8 million and 3.4 million). The total mortality attributable to all forms of neoplasms is 12.8%, if the neoplasm group is split up in different entities IHD emerges as the number one cause of death. Analysed by age groups, female deaths reach their peak after 80 years of age, while the corresponding male peak is in the 70–79 years of age-group. These statistics also make it very clear that the old conception of IHD as a predominantly “male” disease is indeed incorrect. While the total number of deaths from

cancer among men (4.04 million) is higher than IHD mortality, among women cancer death is totalling 3.22 million and is thus lower than mortality from IHD (7). Of course there are great geographical differences; e.g. in Africa, the total IHD mortality is 0.33 million, compared with deaths from HIV/AIDS: 2.09 million (7).

Ischemic heart disease in Sweden

In Sweden, IHD is the number one cause of death. 2002 (the total population was at that time 8.92 million inhabitants) 45.813 men and 49.258 women died. Of these 43.9% of the men and 45.2% of the women died from a disease of circulation organs. 10.697 men died of IHD, among them 6.250 from AMI. Corresponding figures for women were 9.090 (total IHD death) and 4.927 (AMI death) (8).

During the period 1987–2002 502.000 persons have suffered an AMI in Sweden. The total number of incident cases was 641.000. About 350.000 of this AMI population had died before the end of 2002, 255.000 from AMI. The number of AMI cases has declined at a rate of 1% per year, but as diagnostic criteria (see below) were modified in Sweden in 2001, the incidence has since then increased, and was in 2002 42.000 incident cases. Mortality from AMI has decreased over the years and the 28-day mortality was in 2002 for men 32% and for women 35%. In 1992 the corresponding figures were 42 and 46% (9, p 18–21).

Acute myocardial infarction

As stated in a cardiology handbook, “The classical World Health Organization (WHO) criteria for the diagnosis of AMI require that at least two of the following three elements be present: (1) a history of ischemic-type chest discomfort, (2) evolutionary changes on serially obtained ECG tracings, and (3) a rise and fall in serum cardiac markers” (10, pp 1114–1231).

Modern technology has made it possible to identify myocardial necrosis weighing <1.0 g. In an attempt to make a more precise definition of myocardial infarction, on the basis that any amount of such necrosis should be labelled as an infarct, a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction was issued in 2000 (11). An acute, evolving or recent MI is characterized by a typical rise and gradual fall (cardiac troponin) or more rapid rise and

fall (the MB fraction of creatin kinase =CK-MB) of biochemical markers of myocardial necrosis with at least one of

- (a) ischemic symptoms
- (b) development of pathological Q waves on the ECG
- (c) ECG changes indicative of ischemia (ST-segment elevation or depression) or
- (d) coronary artery intervention.

A finding of an acute MI at autopsy is also a possibility. An increased value for cardiac troponin should be defined as a measurement exceeding the 99th percentile of a reference control group (11). In the American College of Cardiology/American Heart Association guidelines for the management of patients with ST-elevation myocardial infarction the spectrum of acute coronary syndrome is illustrated (Figure 1).

Of patients with ST-segment elevation, most (large grey arrow) ultimately develop a Q-wave MI (QwMI), while a few (small grey arrow) develop a non-Q-wave MI (NQMI). Patients who present without ST-segment elevation are suffering from either unstable angina (UA) or a non-ST-segment elevation MI (NSTEMI), a distinction that is ultimately made on the presence or absence of a serum cardiac marker such as CK-MB or a cardiac troponin detected in the blood. Most patients presenting with NSTEMI ultimately develop a NQMI on the ECG; a few may develop a QwMI (12, p 7).

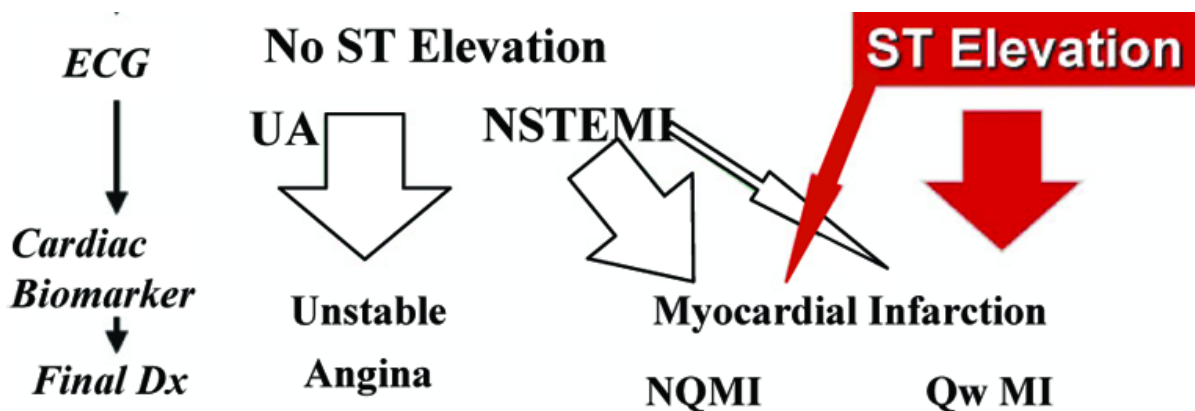


Figure 1: See text and (12)

Adopting new criteria for MI means that cases that should have been labelled as angina pectoris before the introduction of more refined biochemical markers now are identified as

MI. In Sweden acute MI accounted for 37.6% of patients hospitalized for MI or angina pectoris in 2000. Already in 2001 this quotient had risen to 42.2% (13, 14).

This also means that one cannot be sure that a population of MI patients assessed for e.g. dimensions of QoL or risk factors in 1990 corresponds to a MI population of 2005.

Coronary artery by-pass grafting

Survival after CABG compared with medical treatment was studied in three randomized major studies: the VA Study, the Coronary Artery Surgery Study (CASS), and the European Coronary Surgery Study (10, p 1313). The VA Study (686 patients, 11 yrs follow-up) showed benefit from surgical treatment in high-risk groups, but not in overall survival (15). In the Coronary Artery Surgery Study (780 patients) patients with ejection fraction 35-50% had improved survival with bypass surgery compared with medical treatment (16). The European Coronary Surgery Study (767 patients) showed a higher survival rate among surgically treated patients at 5-year follow-up, but the difference was attenuated after 12 years (17). Systematic overview of these investigations together with other smaller studies show the advantage for surgery to be greatest in patients with disease in the left main coronary artery (18). The great difference between various subgroups in these trials is obvious from the fact that 5-yr mortality in patients with left main disease was 36.5% in the medically treated group compared with 15.8% in the surgical group. If no LAD (anterior descending branch of the left coronary artery) was found, and the patient had a 1 or 2 vessel disease, no difference in 5-yr mortality was found (8.3% in both groups) (19). Many patients experience total relief from symptoms after CABG and in most cases an improvement is achieved. 5 years after CABG 78% freedom from angina is reported and after 10 years 52% in a study of patients using only venous grafts (20).

In 2003 6.627 CABG operations were performed in Sweden, 5.300 of them were by-pass surgery utilizing ECC (extracorporeal circulation), 442 were by-pass operations without the help of ECC, and 885 were operations combined with some other surgery, e.g. valvular operations. Operations without ECC have been performed since 1997 ("off pump") (21, p 10). Of CABG patients 78% were male, 42% were over 70 years of age. The average number of anastomosis was 3.07. The 30-day mortality was 1.9% (21, p 30). The number of CABG has been declining since the year 1994 when 6644 CABG were performed (21, p 13).

Percutaneous coronary intervention

The first PCI, or PTCA as it was called earlier, was performed in Zürich, Switzerland by Andreas Gruentzig (1939–1985), in September 1977. Obviously the inventor of the method did not foresee the future to come.” We estimate that only about 10 to 15 per cent of candidates for bypass surgery have lesions suitable for this procedure” (22). Since then constant improvements in both technology and pharmacology have resulted in progressively improved success rates after PCI. This development is reflected in the results in trials and registry studies. The National Heart, Lung, and Blood Institute registry reports results from PTCA 1977–1981, PTCA was successful (defined as “all attempted lesions reduced greater than or equal to 20%”) in 63.4% of patients. In-hospital events included CABG in 24% of patients (23). The use of coronary stents has dramatically decreased the frequency of restenosis, one of the first studies to show this was the Stent Restenosis Study (STRESS), comparing 207 patients randomized to stent placement and 203 to angioplasty. The primary endpoint of the study was restenosis, defined as at least 50% stenosis at a follow-up angiogram 6 months after the initial angioplasty or stent placement. The stent placement group proved to have a lower rate of restenosis (31.6% vs. 42.1%) (24).

An important feature in modern PCI is the combined use of platelet active drugs such as aspirin, blocking the formation of TXA₂, a mediator of platelet aggregation, clopidogrel, blocking the ADP-dependent pathway of platelet activation. GPIIb/IIIa antagonists block platelet aggregation (10, pp 2114–2117). Low-Molecular-Weight Heparin is used to inhibit both generation and action of thrombin (10, pp 1245, 2109–2110). The FRISC II study comparing invasive and non-invasive strategy in unstable coronary-artery disease recommends PCI in case of one or two target lesions and CABG if three vessels or main left coronary artery were affected (25).

During this century the trend in Sweden has been towards a steady increase in PCI utilization. In 2003, 13.656 PCI were performed at 25 centres in the country (26, p 9). 72% were men (26, p 12). The decision after coronary angiography was to perform a PCI in 42% of cases, the choice was CABG in 18% and “no intervention”, i.e. medical treatment, in 34% of cases (26, p 6). One or more stents were used in 87% of patients (26, p 23). Complications to PCI are rare, less than 0.1% of patients have to undergo acute CABG, mortality was for patients dilated during 2002 less than 4% after one year, and the group with highest mortality risk is patients with ST-elevation infarction. Internationally, there are large differences in how much

PCI is used, in France and Germany the number of PCI procedures/100.000 inhabitants are more than the double the corresponding figures for UK (26).

Some aspects of ischemic heart disease

In this and the next section (Emotional reactions and sexual dysfunction in relation to IHD) parts of the results published in papers I–III are referred to. See also the “Results” section and the individual papers.

In the Swedish population, about 1% suffer from angina pectoris, and 2.3% from heart failure (13). In follow-up studies after a cardiac event, these figures are of course much higher. The FRISC II study reports 21% angina in the invasive group and 44% in the non-invasive group at 3-month visit (27). At 6-month visit the numbers were 22% and 39% respectively. Reporting from a study comparing thrombolysis compared with PCI, Herlitz and co-workers found symptoms of angina in 27% of patients (thrombolysis group) vs. 14% in the PCI group after one year (28). The Danish DANAMI-2 study, also comparing outcome after thrombolysis and primary PCI, describes angina in 20% of PCI patients and 25–28% of thrombolysis patients after one month (29).

The questionnaire used in papers I–III differentiated controls from patients in the dimension thoracic pain both at one-month and one-year assessment (except for PTCA patients) (paper I), but thoracic pain was not significantly related to death until the time of census (paper III).

Heart failure during a hospitalization for a myocardial infarction is associated with a dramatic increase in mortality. 23% of patients had heart failure during the index admission of a worldwide fibrinolytic trial (30). This study reports 30-day mortality to be 18.9% for patients with heart failure and 3.1% for patients without. Breathlessness was significantly related to death until the time of census according to the analysis in paper III, and the differences between patients and controls were significant at one-month and one-year assessment (except for PTCA patients).

“Perceived arrhythmia” was also significantly related to death until census, and patients differ from controls at the two assessment occasions (papers I and III). The most important question (that unfortunately can not be answered here) in this matter is if the arrhythmia that the patient felt was a harbinger of a malignant ventricular arrhythmia. In Sweden, 2/3 of the 15.000 patients who die of heart disease, die outside the hospital, almost all because of

ventricular fibrillation (31, p 5). During the period 1990–2003 43.739 cases of heart arrest were reported, in 20% no attempt of resuscitation was performed. 62% of the cases took place at home. Among all patients, the first ECG recording showed ventricular fibrillation in 31% (31, p 9–11), probably because the mean time from heart arrest to first defibrillation was rather long in this material (mean delay 13 minutes) (31, p 24).

“Subjective general health” was likewise correlated to death in paper III. This may of course be due to co-morbidity.

Diabetes mellitus shares several risk factors with IHD, 20% of Swedish patients with MI or UA have manifest diabetes (32). As noted in paper III, patients who were non-survivors had significantly higher glucose levels than survivors. 80% of deaths in patients with diabetes are attributed to macrovascular complications, especially IHD, and the risk is increased for women (33). The macrovascular complications are the main reason for the decreased life expectancy in patients with diabetes mellitus type 2; a 40-year-old patient with newly diagnosed diabetes has 8 years shorter life expectancy. The risk of a cardiovascular complication in a patient with diabetes is similar to that of a patient without diabetes who has had an MI (34). In a study from Malmö, Sweden, Nilsson et al. found that hyperinsulinemia two hours after an oral glucose tolerance test in nondiabetic men was predictor of total mortality and cardiac events (35).

Chronic Obstructive Pulmonary Disease (COPD) shares a major risk factor (smoking) with IHD. Sidney et al. found that mortality from cardiovascular disease was significantly higher in COPD patients followed for about three years than in controls (36). The risk for hospitalization because of MI and other cardiovascular end-points was also higher than in controls. The authors point out that COPD is characterized by chronic pulmonary inflammation and that markers for systemic inflammation like levels of C-reactive protein are risk factors for cardiovascular events (36).

Emotional reactions and sexual dysfunction in relation to ischemic heart disease

Anxiety and depression are two emotional reactions to IHD that have attracted great interest. Anxiety is very common among patients with acute coronary syndrome, in a substudy of the GUSTO trial 86 MI patients were assessed, 26 of these had anxiety levels equivalent to those

seen in psychiatric in-patients. Complications to the MI were more common in patients with higher anxiety levels, odds ratio (OR) 4.9 (37). Anxiety is related to reduced vagal control of the heart (38). Anxiety also leads to adverse behavioural risk factors (smoking).

AMI patients differed from controls in levels of anxiety at one-month assessment (paper I), none of the patient categories differed from controls at one-year assessment, thus in the sample presented here, anxiety seems to be a sign of an acute crisis reaction.

The prevalence of major depression in patients with IHD ranges from 15–23% (39). Frasure-Smith et al. found in a study of 18-month mortality after MI that depression was significantly related to cardiac mortality, especially in combination with frequent premature ventricular beats. OR for patients depressed according to one of the measures used (The Beck Depression Inventory) was 7.8 (40). The same authors report that depression after MI is associated with three- to four-fold increase of cardiac mortality. There is also a depression-related increase in risk for cardiac events during a follow-up of one year in patients with unstable angina (41). In contrast, the Danish DANAMI-2 study only found 5.3–9.4% of patients to be depressed one month after infarction (29).

The adverse effects of depression are, at least in part, believed to be due to a lack of balance between adrenergic and parasympathetic activation. Decreased heart rate variability is an independent risk factor for mortality after MI, and is found in severely depressed patients. Stein et al. studied depressed and non-depressed patients with IHD and found markedly reduced heart rate variability among severely depressed patients compared to less depressed or non-depressed patients (42, 43). Depressed patients with risk factors for IHD have also been shown to have alterations in platelet function. It is discussed whether selective serotonin reuptake inhibitors (SSRI) may have a beneficial effect on platelet reactivity (44).

The Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) investigated safety and efficacy of Sertraline (Zoloft[®]) treatment in 369 patients with MI or unstable angina. Sertraline proved to be safe to use in a 24-week double-blind trial, but not very efficient in the total patient group, with a slight ($p=0.049$) superiority to placebo in one of the two used scales (39). The incidence of severe cardiac events was lower in the Sertraline group, but not statistically significant (39, 45).

The Enhancing Recovery In Coronary Heart Disease (ENRICHD) randomized trial enrolled 2481 patients with MI and depression and/or low perceived social support. Patients were randomized to “usual care” or cognitive behaviour therapy for depression. The intervention

for patients with low social support meant to strengthen network ties in counselling sessions. The therapy continued for six months, with a median of eleven sessions. At average follow-up of 29 months no differences were found between treatment arms in death or recurrent MI (46). It is of course important that depression and anxiety are recognized and properly treated in the period after a cardiac event, but the question of how the prognosis of IHD patients with depression shall be improved is not yet clarified.

At one-month assessment, AMI and CABG patients differed from controls in the dimension of depression (paper I). Depression was modestly ($p=0.04$) related to mortality in the analysis described in paper III.

Already in 1979, Cassem and Hackett wrote, describing the “Ego infarction”, that “of all the features of coronary artery disease, none is emotionally more significant than its potential to kill...The second major threat faced by the coronary patient is that to his self-esteem” (47). As a cure for anxiety and depression after an infarction the writers suggested progressive mobilization, at that time MI patients were recommended three weeks of bed rest!

Patients differed from controls in self-esteem at one-month assessment in paper I, and it was significantly related to death before census (paper III).

Many patients experience that a cardiac event has a negative impact on their sex life (48). A reason for the diminished or ceasing sexual relations may be that patients and their partners fear that they may trigger an infarction (49). Some studies, among them paper II, indicate that women experience a worse sex life than men after a cardiac event (at one-month, but not at one year assessment). Other studies have found that both men and women report decrease in and satisfaction with sexual activity after an AMI (48). The fear that coitus may trigger an infarction is exaggerated; the risk of an MI with sexual activity is extremely low, even in patients with known IHD (50). Most patients welcome that physicians discuss sexual functioning with their patients (51).

The Massachusetts Male Aging Study (52, 53) was a community-based observational study of middle-aged men (40–70 yrs of age). It showed that impotence was present in 52% of the population sampled. However, Erectile dysfunction (ED) was apparent in a higher degree among persons with hypertension, diabetes and heart disease. ED and IHD share the similar atherogenic risk factors and both are characterized by endothelial cell damage. ED is often the first manifestation of atherosclerosis (54). Thus, an evaluation of cardiovascular risk factors should be performed in patients presenting with ED. Inhibitors of the enzyme

phosphodiesteras 5 enhance erectile function; the most well known inhibitor is Sildenafil (Viagra[®]). ED is responsive to life-style changes, like weight loss and exercise, particularly in patients with concomitant cardiac disease (55). In low risk IHD patients, e.g. patients with MI 6 weeks ago, and post-CABG patients with no ischemia may safely engage in sexual activity or receive treatment for ED (55). Trials of the phosphodiesteras inhibitors have demonstrated no increase in ischemia in patients with IHD and thus they can be safely used, with the well-known absolute contraindication of organic nitrates used simultaneously with these agents (55). Psychosocial factors like depression have also a strong correlation with ED (53).

A decreased QoL with impaired experience of sex life (as in papers I–III) may mirror ED. This in turn may be an explanation why the dimension “experience of sex life” is significantly related to death in the Cox regression analysis in paper III. AMI and CABG patients differed from controls at one-month and one-year assessment in this dimension of QoL.



Figure 2: Arthur Cecil Pigou (1877–1959)

Quality of life

The expression “Quality of life” was first used by Cambridge economist A.C. Pigou, in his book “The Economics of Welfare” (1920), where he discussed governmental support for poor people. The term fell into oblivion and was not used until after World War II (56). The WHO definition of health: “Health is a state of complete physical, mental and social well-being and

not merely the absence of disease or infirmity” may have inspired the concept of QoL (57). It was used in American government documents, and American TV reporter Eric Sevarid used it to describe the politics of Adlai Stevenson in his campaign for the presidency in 1956 (58). (Stevenson lost in the election against Dwight D. Eisenhower). President Lyndon B. Johnson is also credited for making “Quality of life” a household word, in an attempt to describe values in life that are not possible to put a price-tag on (59, 60). The first mentioning of QoL in medicine was made by J.R. Elkington (an editorial in *Annals of Internal Medicine*) 1966. Between 1966 and 1974 there were 40 references in MEDLINE, between 1986 and 1994 over ten thousand (56).

Authors in the field agree that it is very difficult to define this term. In paper I QoL was defined as “A composite construct consisting of various aspects of somatic health, mental health, self-esteem, degree of optimism/pessimism, and the ability to perform and enjoy everyday activities associated with work, home and family life, sexual relationships and hobbies” (61). E.g. “somatic health” does not constitute QoL, but rather one could say that good somatic health constitutes a part of a good QoL.

The World Health Organization defines QoL thus: “An individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectation, standards and concerns. It is a broad ranging concept incorporating in a complex way the person’s physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of the environment” (62, p 3). Often, the term Health-related Quality of Life is used by medical researchers, to limit the span and exclude problems that may adversely affect health but are distant from medical concern (63). Although a precise definition is still lacking, also for this concept, many authors agree that the Health-related QoL takes into account levels of physical, mental, social and role functioning, and includes abilities, relationships, perceptions, life-satisfaction, and well-being (56). Even though the terms are often used as synonyms, “subjective health status”, and QoL or health-related QoL are not the same thing.

As the panorama of disease becomes more and more dominated by chronic illness and rehabilitative care instead of the sick/healthy dichotomy it is obvious that measures like mortality/survival are not enough. Cataract surgery e.g. is certainly a way of improving quality of life, but does not prolong life. Thus it is necessary to include notions of subjective well-being. In health policy and health economics both the prolongation of life AND increased QoL are wished for, at an acceptable price. The concept Quality-Adjusted Life-

Years (QALY), which is an attempt to bring these two dimensions together, is used in a cost-utility analysis (CUA) to put a price on those qualities that may be hard to price-tag. The cost per gained QALY admits comparisons between several interventions. In QALY calculations, one year of full health is given the value of one, and a year with diminished health is thus something between one and zero (being dead) (64, p 209). If a patient appreciates life with e.g. left ventricular failure as 0.5, ten years with that condition equals five QALYs. There are several ways to attach a value to a specified condition, e.g. the Rating Scaling method, where a respondent is asked to mark on a scale how bad or good a condition is (65, pp 145–147).

In 2002, the total cost for heart disease care was in Sweden 21.8 billion SEK, approx. 2.000.000.000 €. The cost for disability pensions caused by cardiac disease together with sick-leave, including the estimated loss of production due to absence accounted for 42% of this sum (66, p 35). The physician's decision about a sick-leave is to a major part guided by the perceived symptoms that patients report, and thus it becomes very important that QoL in the individual patient is correctly assessed.

The patient's own reactions, his or her subjective experiences and symptoms are, however, not the most studied aspect of IHD. A search on Pub Med (26 May 2005) on plain "Myocardial ischemia" yielded 234.407 articles. "Myocardial ischemia" AND "coronary artery bypass" returned 17833 papers, while "Myocardial ischemia " AND "quality of life" yielded exactly 10% of the scientific production used to describe by-pass surgery, i.e. 1783 studies.

Ethics

There are many theories in the field of ethics and moral. *Moral* refers to the practical actions of a human being; the concrete act may be moral or immoral (67). “*Ethics* is a generic term for various ways of understanding and examining the moral life” (my italics) (64, p 1) or otherwise phrased: Ethic is the theory of moral (68, p 14).

Utilitarianism (from latin, utilitas=utility) is a consequence-based theory. The act in itself has no interest, only the consequences. The theory holds that the right act is that which better than all other possible ways of acting in a given situation leads to maximization of utility, which for *hedonistic utilitarianism* means pleasure. Jeremy Bentham (1748–1832) and John Stuart Mill (1806–1873) are prominent writers in this tradition (69). *Act utilitarianism* stresses what the consequences of a particular act will be. *Rule utilitarianism* focuses the interest on what rule for the acting will lead to the maximal good, and so it becomes interesting what will happen if everybody will act in a certain way (68).

The obligation-based theory of Immanuel Kant (1724–1804) is quite different. According to this theory, the important thing is what characterizes an action, not just its consequences. Kant has formulated a categorical imperative: “I ought never to act except in such a way that I can also will that my maxim become a universal law (64, p 350)”. Another formulation: “One must act to treat every person as an end and never as a means only” (64, p 350–351).

Robert Nozick (1938–2002) was one of the most noted exponents for the libertarian political philosophy, perhaps most known for his book “Anarchy, State and Utopia” (1974). Nozick argues that everybody has a freedom to do what he or she likes with their lives and their property. Freedom should only be restricted if it interferes with the freedom of another individual.

John Rawls (1921–2002) published in 1971 “A theory of justice” with the famous device of postulating an “original position”, a hypothetical situation in which people decide to agree on principles of social cooperation, without knowing how anybody is placed in society. Everybody is placed behind the “veil of ignorance,” which ensures that nobody knows where he or she will be placed in the resulting society. They do not know their class, race, or sex. According to Rawls, economic and social inequalities are only justified if they benefit all of society, especially its most disadvantaged members. Furthermore, all economically and socially privileged positions must be open to all people equally (70).

Medical ethics may embrace elements from these and other traditions. One important and influential school of thought emanates from a rather recent work, “Principles of Biomedical Ethics” by Tom Beauchamp and James Childress. In this book, first published in 1979, now in its 5th edition (64), the ethical principles of *respect for autonomy*, with roots in libertarianism, *beneficence* and *non-maleficence*, with roots in utilitarianism, and *justice*, related to non-discrimination. The authors hold that they provide a solution for most, if not all, ethically complicated situations encountered in health care. The three principles are also defined in 1978 in the document called the Belmont report by the National Commission for the protection of human subjects of biomedical and behavioural research. The principles have achieved widespread recognition as *the* ethical principles, e.g. in a report from the Swedish Council on Technology Assessment in Health Care on routine ultrasound examination during pregnancy, in a chapter on ethical aspects the four principles are mentioned even without reference to Beauchamp and Childress, as if the principles were a part of an eternal canonical scripture (71).

”Principles of Biomedical Ethics” is probably the most read bioethics text in the world (72). Furthermore, in paper IV the principles approach was used to analyse ethical conflicts, and its limitations were discussed. It seems fair to let the authors themselves describe the principles:

Autonomy: To respect an autonomous agent is at minimum, to acknowledge that person’s right to hold views, to make choices and to take actions based on personal values (64, p 63). In Kant’s words violating a person’s autonomy is to treat him or her as a means, not as an end. Respect for autonomy also supports other specific moral rules such as: Tell the truth, protect confidential information, when asked, and help others make important decisions (64, p 64–65). Informed consent is an important part of autonomy, as physicians and investigators usually must obtain informed consent before any intervention. An action needs only a substantial degree of understanding and freedom to be autonomous, not a full understanding or complete absence of constraint (64, p 58–59).

Non-maleficence: This principle asserts an obligation not to inflict harm on others (64, p 113). It supports rules like: Do not kill, do not cause pain or suffering etc. (64, p 117). This principle also includes obligation of not imposing risks of harm. Under this heading conditions overriding the obligation to treat, e.g. if the treatment is futile or pointless, or if the burden of treatment outweigh benefits, are discussed by the authors. “Letting die” is acceptable in medicine under one of two justifying conditions: 1. Medical technology is

useless or 2. Patients (or their authorized surrogates) have validly refused a medical technology (64, p 141).

Beneficence: The principle refers to an action done to benefit others. This principle supports other moral rules like: Protect and defend the rights of others, help people with disabilities (64, p 167). While we can at all time act non-maleficently against all persons it is not possible to act beneficently against all (64, p 168). The conflict between autonomy and beneficence is referred to as possible paternalism. What principle should be overriding in medical practice cannot be solved by defending one principle against another, but beneficence provides the primary goal and rationale of medicine whereas respect for autonomy sets moral limits on the professional's pursuits of this goal (64, pp 176–177, 186). But determining which paternalistic actions are justifiable requires persons with good judgement in the handling of contingent conflicts (64, p 187).

Justice: According to the authors, the primary economic barrier to health care access, a problem discussed in the chapter dealing with the fourth principle, is the lack of adequate insurance. This is especially the case in USA, where 40 million inhabitants lack health insurance of any kind (64, p 240). Discussing the selection of recipients for certain treatments; medical utility, patients' needs and their prospects for successful treatment are relevant considerations. But sometimes the utility seems equal between patients, and in that case, the authors argue that both equality and fair opportunity justify the use of chance (i.e. a lottery) and queuing (64, p 267–269). Policies of just access to and financing of health care dwarf in social importance every other issue considered in this book (64, p 272), is the authors' conclusion.

I can only agree with Beauchamp and Childress in the case of justice. As I write this (August 2005), The New England Journal of Medicine reports that in an analysis of management of acute myocardial infarction between 1994 and 2002, black women had the highest adjusted mortality rate among all sex- and racial groups and the highest risk of not receiving reperfusion and angiography. The racial and sex differences were essentially unchanged during the period (73).

But what is the basis, the theory behind these principles? Two important ethical systems, Christianity and Islam, may serve as examples. For Christian thought, the Bible and the example that Jesus gives form the base that all rules stem from. If rules collide, going back to the Gospels may solve this conflict. For the Muslim world, the tradition, *sunna*, of

Muhammed and his followers together with the Quran can be used in all situations. Of course a principle such as beneficence is also found in Christian ethics, but here the principle is seen in the light of Jesus' acts, without this context it has no meaning (74).

For Beauchamp and Childress the ultimate source of moral norms is the "common morality". "We will refer to a set of norms that all morally serious persons share" (64, p 3), "there is ... a single, universal common morality" (64, p 403), "... all common-morality theories rely on ordinary, shared moral beliefs" (64, p 403). "We cannot reasonably expect that a contested moral theory will be better for practical decision-making and policy development than the morality that serves as our common heritage" (64, p 404). "In this 'theory', there is no single unifying principle or concept – a traditional goal of ethical theory that seems now to be fast fading" (64, p 405).

Tom Beauchamp has further discussed the nature of common morality in an article (75). "I define the 'common morality' as the set of norms shared by all persons committed to the objectives of morality. The objectives of morality, I will argue are those of promoting human flourishing by counteracting conditions that cause the quality of people's life to worsen" (75).

Examples of common morality are given: To keep promises, tell the truth etc. but "any given society's customary or consensus position may be a distorted outlook that functions to block awareness of common-morality requirements" (75). For Beauchamp and Childress the ethical principles develop from the common morality, but it seems to become obvious why there are problems in balancing them, they have no common denominator, or background.

K.D. Clouser writes that the principles of principlism are not action guides that stem from an underlying moral theory (76). Clouser and Gert argue that the "principles" are rather merely names for collection of superficially related matters for consideration when dealing with a moral problem (77). Søren Holm identifies "principlism" as an especially American model citing the authors' description of obligations of beneficence: "Person X has an obligation of beneficence toward person Y if X's action would not present significant risks, costs, or burdens to X" (64, p 171) (72). Holm also finds the rules for infringement totally uncontroversial and to very little help in the process of balancing. And compared to the propositions made by Jesus (love your enemies) (78), Beauchamp and Childress seem to be spokesmen of what could be called "beneficence-light"! But of course, many writers in medical ethics have been very enthusiastic about principlism, some even wanting to put up Beauchamp and Childress for the Nobel Peace Prize (79).

I recall John Donne's (1573–1631) words: “No man is an island” (80) when Edmund Pellegrino reflects about developments in medical ethics: “Autonomy is consistent with the individualistic temper of American life, which emphasizes privacy and self-determination” (81). A problem with applying the principles globally is that other cultures than the American where the principles originate may experience that e.g. autonomy has another meaning. In Asia family-determination may take the place of self-determination (82, 83). In old time China filial piety, *hiao*, was a very important feature and the regulated relations between father and son, husband and wife, older and younger were foundations of society (84). A modern version of the same thought seem to be found in the writings of Mao Tse-Tung: “The individual is subordinate to the organization ... the lower level is subordinate to the higher level, the entire membership is subordinate to the Central Committee” (85, p 255).

Discussing end-of-life questions from the Islamic view, A. Sachedina writes that the underlying rules in tradition should be consulted in ethical dilemmas and that in Islamic ethics, an individual's welfare is intimately linked with the family and community. The principle of autonomy is not invoked to determine a course of action, in some instances the matter is even referred to the religious leaders (86).

Ethics and quality of life

Medical ethics has helped to focus the perspective on the patient's autonomy, emphasizing e.g. the patient's decision-making capacity in accepting or rejecting an investigation or a treatment, even if it means refusing life-sustaining treatment. In essence, the concept of QoL is doing the same thing: Turning the attention to the patient, demanding respect for the patient's own assessment of health. If we are really interested in the patient's health, is it not best to ask the patient about it (87)?

Questionnaires

Self-assessment by the patient is usually performed with the help of a questionnaire. Questionnaires are primarily of two types, *disease-specific* and *generic*, i.e. not constructed specially for one type of disease. In the *Likert-type* of instrument (named after Rensis Likert, American psychologist), questions (items) are answered by choosing one of several alternatives which the patient feels best describes his or her situation best during a recall

period. Items with a visual analogue scale (VAS) are answered by placing a mark on a continuous scale, sometimes marked in the ends with words like “best” and “worst” to describe how the recall period has been.

There has been an exponential growth in reports relating to the development and evaluation of quality of life measures. By far, most of the instruments evaluated are disease-specific. Garratt et al. searched for reports concerning development and testing of patient assessed measures during the period 1990–1999. Having in mind the importance of IHD for mortality and morbidity, it is somewhat surprising that across specialities, cardiovascular diseases occupied the ninth (!) position (188 reports). Foremost among specialities were rheumatology and oncology (88).

Some questionnaires that have been frequently used in the study of QoL in IHD patients are:

EQ-5D (previously EuroQol) is a *generic* scale consisting of 5 *subscales*: *mobility*, *self-care*, *usual activities*, *pain/discomfort* and *anxiety/depression*. Each subscale is divided into three statements, describing increasing ill-health, e.g. I have no pain; I have moderate pain; I have extreme pain. Patients are asked to indicate which statement best describes their health *today*. The *EQ5D Feeling Thermometer* is a global health status measure. Patients indicate how good or bad their own health is on a 0–100 vertical VAS, where 0 is worst imaginable health state and 100 is best imaginable health state, also *today* (89, 90).

WHOQOL. WHO has developed two instruments for measuring quality of life, *WHOQOL-100* (100 items) and the *WHOQOL-BREF* (26 items in the UK version). The shorter version is composed of *Likert* type items, concerning life in *general terms*, *during the last two weeks* e.g. “Do you have enough energy for everyday life?”, “How much do you feel that pain prevents you from doing what you need to do?” Items about medical conditions are remarkably missing. The longer version is more detailed, focusing much on environmental and psycho-social conditions, e.g. “To what degree does the quality of your home meet your needs?”, “How much are you able to accept your bodily appearance?”, “How concerned are you with the noise in the area where you live?” (91, 92).

SF-36 (Medical Outcome Study 36-Item Short-form Health-Survey) is a *generic instrument* with 36 items. 35 of them are grouped into 8 scales: Physical functioning (limitations in physical activities, 10 items), role-physical (problems with activities as a result of health, 4 items), bodily pain (limitations due to pain, 2 items), and general health (5 items) these four may be considered together as *physical health*. Vitality (4 item), social functioning

(interferences with social activities due to physical and emotional problems, 2 items), role-emotional (problems with activities due to emotional problems, 3 items), and mental health (feelings of nervousness and depression, 5 items) make up *mental health* together. The remaining item concerns a comparison between the health now and a year ago. The recall period for symptoms reported is mostly *four weeks* (there is an acute version with the time frame of seven days). The “general health“ scale includes an “EVGFP rating” (In general would you say your health is: **Excellent**, **Very Good**, **Good**, **Fair**, **Poor**). Items are generally of Likert type, with a few Yes/No items. SF-36 is widely used, and the most evaluated questionnaire according to the study by Garratt et al mentioned above (88, 93, 94, 95).

Seattle Angina Questionnaire (SAQ) is a *disease specific* instrument for use in heart disease. It consists of 19 items, grouped into five domains: physical limitation, anginal stability, anginal frequency, treatment satisfaction and disease perception. The items for physical limitation are much related to those of the physical functioning scale in SF-36 (96, 97).

Nottingham Health Profile (NHP) is reported to be the most commonly used *generic* measure among patients with IHD (98). NHP consists of two parts: Part one consists of 38 yes/no items grouped into six scales: mobility (8 items), pain (8 items), energy (3 items), sleep (5 items), emotional reactions (9 items), and social isolation (5 items). Part two consists of seven more yes/no items asking about the effects of health on work, household chores, social life, family life, sex life, interests and hobbies, and holidays. The questions refer to the state *today* (99, 100).

MacNew Heart disease Health-Related QoL (MacNew) instrument is a *disease-specific* instrument consisting of 27 items, with three domains: physical limitation (13 items), emotional function (14 items), and social function (14 items). There is some overlap between domains. Only five items are directly symptom-oriented (angina, shortness of breath, fatigue, dizziness, and aching legs). The recall period is *two weeks* (101, 153).

Sickness Impact Profile (SIP) is a *generic* instrument consisting of 136 items, each describing a state of disease or ill-health (e.g. I have tried to commit suicide, I move clumsily, I can only get dressed if somebody helps me). Items are grouped into 12 scales: Ambulation, movement and mobility, body care, social interaction, communication, alertness, emotional behaviour, sleep, eating, work, household management, recreation. The respondent is asked to note which statements suit his/her situation *today*. Next to SF-36 it is the most evaluated questionnaire (102, 88).

Angina Pectoris Quality of life questionnaire (APQLQ) is a *disease-specific* instrument, made up of 22 items, grouped into four subscales: physical activity (6 items), somatic symptoms (6 items), emotional distress (5 items), and life satisfaction (5 items). The recall period is *the last week*. Items are of the *Likert* type with six-step response categories (e.g. “Did you have bouts of chest pain?” with alternatives of answer from “none of the time” to “all of the time”) (103, 104).

Minnesota Living with Heart failure questionnaire is a *disease-specific* instrument consisting of 21 items, grouped into three domains, physical with symptoms (11 items), psychological (7 items), and socio-economical (3 items). All questions are preceded by the words: “Did your heart failure prevent you from living as you wanted during the past month by–“. This phrase can be continued by e.g. “making your working to earn a living difficult?” or “making you tired, fatigued or low on energy?” (105, 106).

It is a well known problem that different instruments for quality of life measurements use different combinations of items for domains included, the time frame or recall periods differ and so do type of response scales (107). Even the classification of measures into generic or disease-specific questionnaires is arbitrary, as content in the questionnaires overlap. Comparing three much used generic instruments, NHP, SF-36 and SIP, they are found to differ in many aspects: Recall period is for SF-36 four weeks, for NHP and SIP “today”. The response format is for NHP yes/no, for SIP the patient is asked to note what statements fit his/her situation, and for SF-36 items are mostly answered in a *Likert* format. In SIP and NHP items all express a more or less “sick” state, (e.g. “I feel tired all the time”), while SF-36 items have a more “neutral” formulation: “Have you felt tired?” Wiklund writes that there is a disadvantage with NHP in that the 38 items in part one represent rather severe problems, which means that they are less responsive to detecting health-related problems in patients with slight disability. NHP may be perceived as a negative measure in that it measures the absence of health (100). There is a mobility section in NHP, where items are mainly centred around pain during motion, (“it hurts when I walk”) while SF-36 items in this field (seven items) are general in a way that maybe fits the cardiologic patient better (“Walk several blocks”, “walk one block”). In SIP there are about 25 items focusing on moving (I don’t walk at all, I am mostly bedridden”), seemingly directed to a patient category with pronounced general difficulties. This gives a hint of how widely the content of a dimension may differ between instruments. The span becomes even larger if the comparison is with EQ-5D, with only one item about mobility, making up a subscale. Wann-Hansson et al. compared NHP and

SF-36 in patients with chronic lower limb ischemia and found that the two instruments came to different results in subgroups (108).

Among disease-specific instruments for cardiac disease, items in SAQ are all about chest pain, in Minnesota Living with Heart failure all about heart failure. APQLQ and MacNew include domains about e.g. emotional distress. Similar emotional distress items are also featured in Minnesota Living with Heart Failure Questionnaire, but here distress seen as a consequence of heart failure is asked for. Janzon et al. used one disease-specific questionnaire (APQLQ) and one generic (SF-36) to assess QoL of patients in the FRISC II trial. After one year, invasively treated patients showed higher QoL than non-invasively treated patients as measured by SF-36 (7 of 8 scales), but in APQLQ only one out of four scales differed at that time. The only scale with items directly about chest pain (the somatic symptoms scales) did not differ between invasively and non-invasively treated patients. The authors conclude that a generic instrument should be combined with a more disease-specific one to capture the effects of the disease (104).

In oncology, core questionnaires have been developed including issues of concern to all patients with cancer. This example has maybe served as an inspiration for cardiologists. Oldridge and co-workers reported earlier this year (2005) that work is under way to create a single heart disease-specific health-related QoL questionnaire, the HeartQoL, based on the MacNew, SAQ and Minnesota Living with Heart Failure Questionnaire (109).

Statistical methods used in papers I–III

A combination of modesty and extreme caution is recommended when discussing statistical truths. Modesty because there are several potential methods to use in the analysis of a material, and caution because statistical truths simply are no truths.



Figure 3: William Sealey Gossett (1876-1937)

T-test

The t-test is also called Student's t-test, as it was introduced by W. S. Gossett under the pseudonym Student (110). It is used for normally distributed parameters.

Mann-Whitney test

The Mann-Whitney test, also known as the Wilcoxon rank-sum test, does not require a normal distribution. Such statistical procedures are termed distribution-free or non-parametric tests. The t-test is more powerful in detecting true differences between two populations than its non-parametric counterparts, and thus it should be used if the variable analysed is normally distributed. But if the data are non-normally distributed, the Mann-Whitney test is the method of choice (111). In this test values in two groups compared are ordered from lowest (rank number 1) to highest. Rank sums are then compared; the actual *values* are not used in the analysis (112).

The Kruskal-Wallis test is also a distribution-free method, used to compare *several* groups, where cases from the various groups are ranked. It is often referred to as an extension or generalization of the Mann-Whitney test (111, ch 20).

Spearman and Pearson correlation tests

To assess test-retest reliability, i.e. how well the answers to a set of questionnaire items corresponded with each other, when they were answered two times by the same person Spearman's correlation coefficient was used. It is usually recommended for use instead of Pearson's correlation coefficient for ordinal data or data that are not normally distributed (111, ch 10 and 16, 112). To calculate Spearman's correlation coefficient a ranking is made at both assessment occasions and the ranking forms the basis for a calculation by Pearson's correlation coefficient.

Logistic Regression

Logistic regression is used in paper II to analyse if perceived thoracic pain is correlated to other QoL dimensions for men and women analysed separately. The dependent variable has to be binary or dichotomy, in this case two groups of patients with and without thoracic pain. The odds ratio is often used in combination with logistic regression (113). There are several methods for the entry of covariates (predictor variables) into the model. We used the method where all variables are entered in one step.

Cox regression

There are several methods designed to assess the influence of predictor variables on survival, Cox regression is one that especially takes into consideration cases for which the event, e.g. death, has *not* occurred. Included in the method is a time factor, in our paper III this is defined as the period from cardiac event to death or the date that death/alive status was assessed (date of census). Together with the predictor variables i.e. QoL dimensions we entered age and sex, to make correction for these factors possible, but otherwise we have not tried to include other factors possibly influencing survival, such as cardiac function.

Cronbach α

To test internal consistency of a scale, i.e. that the included items measure the same thing, Cronbach α can be used. It is often referred to as a "reliability coefficient". Even if the average correlation between items is the same, α increases if the number of items is increased.

ANCOVA

Analysis of covariance is used in paper I for comparisons of patients vs. the control group and across patient groups for QoL dimensions. In an ANCOVA the effect of covariates, in our case age and sex, is removed from the analysis.

Fisher's exact test

Fisher's exact test is used to determine if there are non-random associations between two categorical variables, often illustrated in a two by two contingency table. It is an alternative to the χ^2 test, but returns exact one-tailed and two-tailed p -values for a given frequency table, while the χ^2 gives an approximation. It is recommended that Fisher's test be used if the expected number in one cell in a two by two table is less than five.



Figure 4: Sir Ronald Aylmer Fisher (1890–1962)

Statistical significance was accepted at two-tailed p -value ≤ 0.01 . SPSS versions 6–11 were used for statistical analyses (110).

Material

In 1989 secondary prevention programmes for follow-up after AMI, CABG and PTCA/PCI were somewhat uncommon in Sweden although pioneer work had been achieved, e.g. in Gothenburg and in Oskarshamn by Joep Perk (114). A study by Israelsson, Rüter and Solem showed that secondary prevention was unsatisfactory or totally lacking for many patients after CABG (115). Some clinically working cardiologists saw this as a room for improvement. To create a unit for follow-up of the three groups of patients together seemed to be worthwhile challenge. The physicians taking part in this work were Bo Israelsson, Roland Carlsson, Charles Cline, Ronnie Willenheimer and the present author. We were assisted by two dedicated nurses, specialized in cardiac care, Carin Alm and Elisabeth Hansson. It took place in Malmö, a town in southern Sweden (233.000 inhabitants). Strict adherence to agreed guidelines for risk factors such as smoking, blood glucose, lipids and blood pressure was essential (118). As we meant to include several types of patients with coronary heart disease the name Kranskärismottagningen, KKM (coronary outpatient unit) was chosen. Malmö has one hospital for coronary care (University Hospital of Malmö, UMAS, at that time known as Malmö General Hospital, MAS), and patients hospitalized there for AMI were included for follow-up. The nearest center for CABG and PTCA/PCI was the University Hospital of Lund, 20 km away, and all residents of Malmö were treated there. They were likewise invited to take part in this programme after the intervention. One aim of programme was to test whether patients profit if followed-up at a specialized centre compared to primary care. Several studies have been published describing findings in these and other fields deriving from the work at the KKM (116–119). Consecutively, most IHD patients, both men and women, within a specified age group (see below), were thus to be seen at the out-patient clinic. An excellent opportunity to perform an investigation in quality of life after a cardiac event was also at hand. The cohort investigated seems representative of the IHD population, at this time and place, within the given frame of age.

The inclusion date was for AMI patients the day of the acute myocardial infarction and for the other two patient categories the day of intervention. The diagnosis of AMI was based on the standard criteria in use at the time of the investigation, i.e. typical chest pain, ECG changes and elevation of cardio-specific enzymes. The inclusion was made at the coronary care unit after the patients had received information about the study and given their written consent to participate.

The first patient was included October 23, 1989 and the last on April 30, 1991. During the first year, all patients below 70 years of age were included, during the rest of KKM's existence patients between 50 and 70 years of age. These exclusions were due to the relative scarcity of staff. The only other exclusion criterion was that patients after the hospital stay had to be discharged to their home. A total of 413 patients were included and investigated. Papers I–III are based on data from these patients.

Number of patients according to sex and patient group is given in table I, mean age for all groups in table II.

Table I. Number of included patients according to sex and patient category

	AMI	CABG	PTCA/PCI	TOTAL
MEN	226	78	12	316
WOMEN	70	21	6	97
TOTAL	296	99	18	413

Mean age for male and female patients was 59.8 yrs and 61.5 yrs, respectively.

Four weeks after inclusion the patients were seen by one of the nurses at the KKM. At this visit a 24-h ECG recording and a symptom-limited exercise ECG were performed. The patients also received a self-administered questionnaire for QoL assessment, to be completed at home, and returned by mail or at the next visit, one week later. This time (five weeks after inclusion), the patients saw a physician. Now patients were randomized to follow-up either at the KKM or outside this unit (e.g. by a GP). Patients at elevated risk of heart failure or coronary ischemia in such a degree that they had to be followed by a cardiologist were not randomized, but followed at the KKM or by another specialist. The clinical picture, together with performed examinations, formed the platform for this decision (118). Patients below 50 yrs of age were not randomized, either.

The time of follow-up was one year. At that time, all patients were seen at the KKM for a concluding visit and the questionnaire was re-administered to everybody.

At inclusion, 175 patients (42%) described themselves as smokers. Some other relevant baseline characteristics of patient group at inclusion are shown in Table II.

Table II. Baseline characteristics of patient group

	Mean value	Standard deviation
Systolic blood pressure	129 mm Hg	21 mm Hg
Diastolic blood pressure	80 mm Hg	11 mm Hg
Total serum cholesterol	6.09 mmol/l	1.14 mmol/l
HDL-cholesterol	1.08 mmol/l	0.3 mmol/l
LDL-cholesterol	4.18 mmol/l	1.06 mmol/l
Serum triglycerides	1.7 mmol/l	0.87 mmol/l
Blood glucose	6.33 mmol/l	2.71 mmol/l
HbA _{1c}	5.66%	1.29%
Body Mass Index	25.9	3.7

HDL: High-density lipoprotein; LDL: low-density lipoprotein; HbA_{1c}: glycosylated haemoglobin

65% of female patients and 88% of male patients were married or living with a partner at inclusion.

At the time of inclusion, 34% of patients had a diagnosed hypertension, 31% had a recognized hyperlipidemia, and 10% were diabetics. 33% were treated with acetylsalicylic acid.

During the year of follow-up 39 patients included after AMI underwent CABG and nine were treated with PTCA/PCI. Even if such an intervention was performed, patient allocation to a category (AMI, CABG or PTCA/PCI) remained constant. Of the CABG patients, one was re-operated during the follow-up year and one underwent PTCA/PCI.

Attrition

30 AMI patients who met the formal inclusion criteria did not participate: eight had severe noncardiac disease (e.g. stroke, cancer with metastasis), three had severe abuse problems, and two were not Swedish-speaking. 11 did not want to participate because of ongoing contact with other physicians, and six refrained for unknown reasons. Among CABG patients nine had contact with other physicians and one was not Swedish-speaking. Mean age (60.4 years)

and sex ratio (74% males) among the non-participating patients were similar to the participating patients.

Control subjects

Letters of invitation were sent to 180 persons randomly selected from a population database. These control subjects were asked to report about their health. If they were considered “chronically ill” they were not used as controls. To decide if they were eligible, both their own information and, if available, hospital records were used. 34 persons were considered “chronically ill” and eight persons no longer resided in Malmö. 38 males and 12 females who were eligible as controls did not respond. 88 control persons finally participated in the study, 65 males and 23 females (74% males). Mean age among controls was 59.6 yrs. There were no statistically significant differences in age or sex distribution between controls, non-respondent controls and index patients. No information was available on perceived health status among non-respondent controls, and instead mortality rates in respondent and non-respondent controls were examined six years after the study onset. No significant difference was found in mortality rates. The geographical distribution of place of residence among non-respondent controls corresponded to that of the general population in Malmö.

Problems with the samples

As should be obvious from the paragraphs about AMI, CABG and PCI a patient sample in 2005 would look different. The proportions between CABG and PCI have changed considerably. Both diagnostic criteria and treatment for AMI have been altered since 1990, when levels of aminotransferases still were in common use for diagnosis. The AMI sample is not representative of a total AMI population, as many myocardial infarctions occur in the elderly population. However, reactions to a cardiac event in 2005 may very well resemble emotional responses to a life threatening disease in 1990. Positive aspects are that the material presented here is consecutive and not sex biased.

Method

Papers I, II, and III

According to our definition of QoL, it is a “composite construct” and thus the QoL questionnaire had to be composed of several parts, covering a wide range of perceived health aspects and emotions. Most of the items were thought to make up a “dimension”, although some items were just a single question. Slightly different headings for these dimensions are used in papers I–III, although they refer to the same entities. The alternative names for the dimensions are given within brackets. In papers I and II thoracic pain, breathlessness, and arrhythmia together are also called “*heart-related symptoms*”.

1. General health (perceived general health, subjective general health, physical health: *general*) 17 items
2. (Perceived) thoracic (chest) pain, 5 items
3. Feeling of arrhythmia (perceived arrhythmia) 4 items
4. Feeling of breathlessness (perceived breathlessness, shortness of breath, breathlessness) 2 items
5. Anxiety (experience of anxiety) 20 items
6. Depression (experience of depression) 8 items
7. Self-esteem (experience of self-esteem) 5 items
8. Experience of sex life 3 items
9. Experience of social life 20 items

Questionnaire items were of Likert type, on a scale from 1 to 4, with 1 representing absence of problematic state and 4 representing the greatest degree of abnormality. Patients were asked to choose the alternative that best described their situation during the past week. A mean score was derived for a dimension by adding the scores of the items and dividing this sum by the number of items answered by the patient. Thus, a higher score meant poorer QoL in that dimension.

Description of items

General health: Items covered symptoms of gastrointestinal, respiratory, neurological and muscular origin, together with some questions of more general nature: “Have you felt healthy?”, “Have you been able to hurry?”, “Have you been feeling tired?”, “Has your appetite been missing?” Scales with this content abound, two examples are the Subjective Symptom Assessment Profile (SSA-P) and the Memorial Symptom Assessment Scale (120, 121).

Perceived thoracic pain, feeling of arrhythmia, and feeling of breathlessness: Items assess heart related symptoms like:

Thoracic pain during rest, physical exertion, anxiety or worries.

Breathlessness during rest and exercise.

Feeling of arrhythmia during rest and exercise.

The items for these dimensions were found in The McMaster Health Index Questionnaire (MHIQ), and the Rose questionnaire according to Hagman (120, 122–125).

Anxiety: The “state“ part of the State-Trait Anxiety Inventory (STAI) (126).

Examples: “I feel upset”; “I feel nervous”.

Depression: Source for these items was the depressive symptom subscale of the Comprehensive Psychopathological Rating Scale (CPRS), also referred to as the Montgomery Åsberg Depression Rating Scale (MADRS) (127, 128).

Example: “I have felt low and gloomy”

Self-esteem: Items were taken from the McMaster Health Index Questionnaire. Similar items are found in the Rosenberg self-esteem scale (122, 123, 129, 130).

Exemples: “I feel that I am a failure”; “I feel satisfied with myself”.

Experience of sex life: 3 items: “Are you satisfied with your sex life?”; “Rate your interest for sex during the last week” and “Has your interest for sex changed due to your heart disease?” (The last item only for patients, not for controls) (91, 99, 120).

Experience of social life: items covering leisure activities and relations with family members, friends, and relatives, closely related to corresponding scale in the Sickness Impact Profile

(102), some items in common with the MacNew Heart disease health-related quality of life questionnaire (101).

Examples: “There is a lot of tension in the family”; “My family overprotects me”.

Background information about the sources of items:

The *SSA-P* was designed to quantify subjective symptoms during treatment with different classes of antihypertensives. It consists of 42 items, 25 of them grouped into six dimensions: Emotional distress, Gastrointestinal Symptoms, Peripheral Circulatory Symptoms, Cardiac Symptoms, Dizziness and Sex Life. The remaining 17 symptoms were represented as single items. Satisfactory reliability data and construct validity in relation to the NHP are reported (120). Both Likert scale and VAS have been used for response.

The *Memorial Symptom Assessment Scale* consists of 32 items, covering a diverse group of common symptoms. Answers describe how often a symptom occurs (four grades), how severe it was (four grades), and how bothering it was (four grades). The Memorial Symptom Assessment Scale is reported to be a reliable and valid instrument for the assessment of symptom prevalence, characteristics and distress (121).

The *McMaster Health Index Questionnaire* consists of 59 items that are grouped into three dimensions: Physical (24 items) covering physical activities, mobility, self-care activities, communication (sight and hearing) and global physical function. The 25 emotional function items cover feelings of self-esteem, feelings toward personal relationships, thoughts about the future, critical life events and global emotional function. The 25 social function items cover general wellbeing, work/social role performance/material welfare, family support/participation, friends support /participation and global social function. Some items overlap in social and emotional function. Answers are given in a Likert format. Acceptable data concerning reliability and validity are published (122, 123).

Hagman and coworkers studied the prevalence of angina pectoris and myocardial infarction in Gothenburg, Sweden, using a questionnaire consisting of 15 questions entirely about chest pain and one question about medication (125)

The *State-Trait Anxiety Inventory (STAI)* has been used extensively in clinical anxiety research since its development by Spielberger et al. in 1970. Spielberger defined state anxiety as a transitory emotional response to a stressful situation that involved unpleasant feelings of tension and apprehensive thoughts. In contrast, trait anxiety is an enduring personality characteristic that can predispose persons to state anxiety at times of stress. The STAI was

developed in 2 forms, one for the moment (state anxiety) and the other in general (trait anxiety). By 1989, more than 3000 studies using the STAI had been published (131). The State version of STAI was used. It consists of 20 items describing emotional states. Answers are given on a four grade Likert scale from “Not at all” to “Much”.

The *MADRS* is originally an interview-based depression rating scale that also has been used for self-assessment. It consists of ten items with Likert type answering alternatives. Satisfying reliability and validity data are reported (127, 128).

Apart from these dimensions the patients completed other parts of the questionnaire, of various natures. The outcome of some items (from both assessments) that has not been reported in papers I–III is given in the end of the “result” section. These items are:

How much is your life and your activity limited by your heart disease?

Has your life regained the quality it had before your heart infarction?

If you have had a by-pass operation or angioplasty, has your life regained the quality it had before your heart trouble (chest pain, breathlessness and tiredness) began?

Questionnaire item selection and dimension allocation was performed under guidance of Professor Tom McNeil, internationally acknowledged expert in psychiatric risk research (132).

Reliability and validity

Reliability and validity are mentioned above in the section about item selection. The term reliability means “repeatability” or “consistency”, an important element in this concept is “precision”. Depending on what kind of data is analysed reliability may take different forms:

Inter-rater or inter-observer reliability, an assessment of the degree to which different raters/observers give consistent estimates of the same phenomenon, e.g. if two raters interview a patient.

Test-retest reliability: Used to assess the consistency of a measure from one time to another.

Internal consistency: Used to assess the consistency of results across items within a test. The reliability of the instrument is judged by estimating how well the items that reflect the same construct yield similar results.

“Validity” also includes several concepts, with the common denominator “relevance of content”:

Face validity: The instrument seems to cover what it is supposed to cover. This is a subjective measure.

Content validity is concerned with a test's ability to include or represent all of the content of a particular construct. There is no easy way to determine content validity aside from expert opinion.

Convergent-discriminant validity means that the instrument yields similar (convergent) results as other instruments used to assess the same quality, and not similar (discriminant) results for measures of other qualities. Another term with this content is *construct validity*.

Criterion validity refers to how well a measurement device correlates with a "golden standard". A test for e.g. angina pectoris should be able to sort out "definite" angina patients from a group without angina (133).

Paper IV

In paper IV possible ethical conflicts that may arise in the encounter between patient and physician after a cardiac event, i.e. during secondary prevention, are discussed. The method used to elucidate the interactions is a matrix table with two dimensions: The ethical principles of autonomy, beneficence (including non-maleficence), and justice together with the persons affected (patient and spouse). The physician is of course also involved, but not affected by the process.

Results

Return rate

Fifteen patients were unable to respond to the first questionnaire: Seven patients died in the period between inclusion and the administration of the questionnaire, and eight were unable because of severe diseases like hemiparesis after CABG or severe infection. Of the remaining 398 patients, 376 (94%) participated by completing the questionnaire. Mean age among non-respondent patients was 58.5 years, 85% were males.

Due to death and serious diseases, 23 more patients were unable to complete the questionnaire at the one-year assessment. Of these 349 (93%) completed the one-year questionnaire.

The numbers of male and female AMI, CABG and PTCA/PCI patients who completed the questionnaire at the two assessment occasions are presented in Tables III and IV.

Table III. Study sample at the one-month assessment occasion

	AMI	CABG	PTCA/PCI	TOTAL
MEN	202	75	11	288
WOMEN	64	19	5	88
TOTAL	266	94	16	376

Table IV. Study sample at the one-year assessment occasion

	AMI	CABG	PTCA/PCI	TOTAL
MEN	185	73	11	267
WOMEN	59	16	5	82
TOTAL	244	89	16	349

Main results of papers I–IV. For complete results, see the individual paper.

Paper I: Westin L, Carlsson R, Israelsson B, Willenheimer R, Cline C, McNeil TF.

Quality of life in patients with ischaemic heart disease: a prospective controlled study.

J Intern Med. 1997;242:239–47.

1. At one month AMI patients had worse general health, more thoracic pain, more feeling of arrhythmia, more breathlessness, more anxiety, more depression, less self-esteem and worse experience of sex life than controls.

CABG patients had worse general health, more thoracic pain, more feeling of arrhythmia, more breathlessness, more depression, less self-esteem and worse experience of sex life than controls.

PTCA/PCI patients had more thoracic pain, more feeling of arrhythmia and less self-esteem than controls.

2. At one year after inclusion, AMI patients had worse general health, more thoracic pain, more feeling of arrhythmia, more breathlessness and worse experience of sex life than controls.

CABG patients had more thoracic pain, more feeling of arrhythmia, more breathlessness and worse experience of sex life than controls.

PTCA/PCI patients had only more feeling of arrhythmia than controls. Thus, in the three dimensions of anxiety, depression and self-esteem, the difference between controls and patients was no longer statistically significant.

3. At one month, AMI patients experienced more anxiety than CABG patients, CABG patients experienced worse sex life than AMI patients, and worse general health than PTCA/PCI patients. No statistically significant differences were found at the one-year assessment.

4. AMI patients who underwent an intervention (CABG or PTCA/PCI) during the year of follow-up had, at one month more thoracic pain, more breathlessness, lower self-esteem, more depression, and worse experience of sex life than the other AMI patients.

5. Patients who, during the year of follow-up, were treated at the emergency department of UMAS due to angina pectoris or cardiac incompensation had had at the one-month assessment more thoracic pain and breathlessness, respectively, than patients who did not seek such treatment. The diagnosis of “angina pectoris” or “cardiac incompensation” were made by the attending physician at the emergency department.

Paper II: Westin L, Carlsson R, Erhardt L, Cantor-Graae E, McNeil T. Differences in quality of life in men and women with ischemic heart disease. A prospective controlled study. *Scand Cardiovasc J.* 1999;33:160–65.

1. Comparisons across patient groups, within each gender for all QoL dimensions at both assessment occasions: the only significant result was that CABG patients had worse experience of sex life than AMI patients.

2. At one month female patients experienced worse general health, more arrhythmia, more anxiety, more depression, less self-esteem, and worse sex life than male patients.

3. At one year females continued to experience worse QoL in the dimensions of general health, anxiety and depression.

4. In male patients general health and arrhythmia were significant as predictors of thoracic pain at one-month assessment, while in female patients only general health. At one year arrhythmia was still significant for males together with shortness of breath, in females only shortness of breath.

Paper III: Westin L, Nilstun T, Carlsson R, Erhardt L. Patients with ischemic heart disease: Quality of life predicts long-term mortality. *Scand Cardiovasc J.* 2005;39:50–4.

Table V. Total patient group by type of event, sex and alive/dead status at census (2002)

Sex		Event			
		AMI	CABG	PCI	Total
Males	Dead	85	17	4	106
	Alive	141	61	8	210
Females	Dead	28	4	1	33
	Alive	42	17	5	64
Total		296	99	18	413

AMI, acute myocardial infarction; CABG, coronary artery by-pass grafting; PCI, percutaneous coronary intervention

1. From inclusion up to the census date (1 May 2002) 139 patients died. Subjective general health, perceived arrhythmia, experience of sex life, perceived breathlessness and experience of self-esteem were statistically significantly related to death (trend for experience of depression).
2. Of patients who died, 24% had been living without a partner, compared with 17% in the total patient sample. ($p < 0.01$, Fisher's exact test).
3. Survivors and non-survivors did not differ significantly on systolic and diastolic blood pressure, body mass index (BMI), serum cholesterol, serum triglycerides, high-density cholesterol (HDL) or low density cholesterol (LDL) at inclusion. Blood glucose was significantly higher among patients who died, 7.0 mmol/l vs. 5.98 mmol/l for survivors.
4. There were no differences in proportions of Q-wave/non-Q-wave infarction, proportions of patients receiving fibrinolysis or maximal levels of cardiospecific enzymes when survivors and non-survivors among AMI patients were compared. Cardiac decompensation during the initial hospital stay (when patients were included), however, was more common among non-survivors.
5. Comparing survivors and non-survivors, medication did not differ regarding beta-blocking agents, calcium channel antagonists, long-acting nitrates or lipid lowering drugs, at the first

visit after inclusion in the study. Non-surviving AMI patients were significantly more often using diuretics at that time, of 95 patients taking diuretics, 57 died.

Paper IV: Westin L, Nilstun T. Principles help to analyse but often give no solution—secondary prevention after a cardiac event. Accepted for publication in *Health Care Analysis*.

Paper IV has in common with the others that it deals with aspects of life that patients with IHD may encounter. Ethical problem involved in the encounter between patient and physician when the patient's lifestyle has to adjust due to the demands in secondary prevention are discussed. In medical ethics the principles of autonomy, beneficence and justice are well-known (64). These principles may serve as a guide in the physician's work. However, they are not always compatible with each other and a conflict could arise when they are balanced against each other.

1. Can the three (or four, if non-maleficence is counted as a separate principle) present a solution for the conflict that becomes obvious when a patient's autonomy is more or less overridden by the principle of beneficence? If the principle of autonomy is applied as the only one relevant, one can question if any of the usual recommended lifestyle changes would be compatible with the principle. On the other hand, if beneficence was applied as the only relevant principle, the conclusion seems to be that all guidelines should be followed.
2. In the case of the spouse, he or she is indirectly involved and beneficence to the spouse is made difficult by respect for autonomy of the patient. Moreover, the physicians are often unaware of how the spouse is affected by the doctor's actions. Is there a solution to this problem?

It seems that although Beauchamp and Childress (64) apply the four principles in almost all situations related to health care, no solution to these problems can readily be found. The situation of the spouse is often overshadowed by the needs of the patient, but nevertheless it constitutes a problem that deserves more efforts.

Furthermore, the claim by Beauchamp and Childress that the principles are based on “common morality... the set of norms that all morally serious persons share” (64, p 3) is not convincing. It is discussed further in the “Ethics” section above.

Some additional single items, i.e. not part of any dimension. Results in percentages for the response alternatives from the two assessment occasions are presented below in tables VI–VIII.

Table VI. How much is your life and your activity limited by your heart disease (%)?

	In very high degree	In rather high degree	In a certain degree	Not at all or in a low degree
One month	15.2	45.3	29.6	9.9
One year	41.2	40.1	13.8	4.9

Table VII. Has your life regained the quality it had before your heart infarction (%)?

	In very high degree	In rather high degree	In a certain degree	Not at all or in a low degree
One month	10.1	36.4	36.4	17.1
One year	19.4	42.4	28.5	9.7

Table VIII. If you have had a by-pass operation or angioplasty, has your life regained the quality it had before your heart trouble (chest pain, breathlessness and tiredness) began (%)?

	In very high degree	In rather high degree	In a certain degree	Not at all or in a low degree
One month	17.2	36.6	32.4	13.8
One year	30.6	41.5	20.8	7.1

Discussion

During recent years, a change in emphasis in health care is taking place. The patient's own assessment of his or her situation is increasingly being recognized as very important. Furthermore, the ethical conflicts that may arise in everyday medicine have led to growing interest in how to analyse and solve these conflicts. Both QoL aspects and medical ethics can help us to improve secondary prevention after a cardiac event. The following topics will be discussed, with focus on the results presented in papers I–IV, and comparisons with results of other researchers.

1. Impact on QoL and subjective health after a cardiac event.
2. It is important to recognize that some patient groups are at risk of a less fortunate outcome, and they should be given extra attention.
3. Careful monitoring of patients' symptoms is vital as they may predict future mortality.
4. To increase compliance with secondary prevention programmes, the patient must experience that the suggested changes in life-style are worthwhile. To identify and, if possible, solve ethical conflicts is important.

1. From paper I it is evident that compared to age-matched controls, at one-month assessment, QoL was affected in all dimensions except experience of social life. It is probable that QoL of patients improved during the year of follow-up. One year after the cardiac event, patients differed vs. controls only in somatic dimensions and experience of sex life. The questionnaire used was thus able to differentiate patients from population controls in most dimensions and the instrument was responsive enough to make evident the increased QoL in some dimensions. In certain dimensions e.g. thoracic pain and breathlessness, some patients still experienced a worse QoL than controls. The items for experience of social life focused on tensions within the family and might not have been relevant for this purpose, as patients and controls did not differ in this dimension and it was not predictive of mortality. This was unexpected, as a poor social network is associated with increase in mortality (134). However, in a study of QoL five years after MI, Wiklund et al. found social life and home life to be similar among patients and controls using the NHP, part II (135).

Researchers find that QoL is influenced by IHD in diverse ways. Brown and co-workers found that patients under the age of 65 had worse QoL than controls in all eight dimensions of SF-36, while patients over 65 years of age had QoL comparable to community norms four

years after a myocardial infarction (136). Brown et al. also showed that an inability to return to work caused a severe lowering of QoL scores and that all domains including role-emotional and mental health were highly significantly related to grade of dyspnea. Brown et al. conclude that SF-36 provides valuable information not identified in routine clinical evaluation. Bengtsson et al. also showed that younger patients (below 59 years of age) continued to experience worse QoL compared with community norms two years after an AMI (137). Psychological distress may be apparent for as long as 5 years after a first AMI (138). Brorsson et al. analysed PTCA and CABG patients together in a study of QoL four years after coronary revascularisation found that patients before revascularisation had QoL scores substantially below population norms, while four years later QoL had improved to the levels of controls, except for quality of sleep (139). Interesting findings in this study are that even four years after CABG/PTCA 55% of female patients and 36% of male patients still had angina. The relationship between frequency of angina and QoL was most significant in *all* dimensions of QoL. Wiklund et al. found in the study mentioned above that compared to a normal population, QoL was most impaired in energy, sleep and mobility, while emotionally patients had adjusted rather well. QoL was greatly influenced by angina pectoris (135). Kim et al., reporting from the RITA-3 trial, also found that benefits in QoL, appeared to be attributable to improvements in angina (141). In RITA-3 an early interventional and a conservative strategy for acute coronary syndrome were compared at four months and one year.

It is somewhat remarkable that the three patient-groups in our investigation were so much alike in the QoL measurements, although the “events” were different. A possible explanation, as discussed in paper I, is that from the patient’s point of view, AMI, CABG and PCI may have a lot more in common than the physician understands. It is noteworthy that in the three dimensions where a significant difference is seen at one-month assessment across patient groups, CABG patients were worse off than AMI and PCI patients in two (sex life and general health).

It is evident that the clinical picture of IHD is intricate, with somatic and emotional symptoms in a complex interplay. Its multi-dimensional impact on QoL is captured by the questionnaire used, which combines items covering cardiac symptoms, general health, and emotional problems. Puzzling problems in this area challenge our understanding, e.g. proved the feeling of loneliness prior to CABG as the only one out of NHP’s 38 items to be associated with both 30-day and 5-year mortality after CABG in a study by Herlitz et al. (134). Outright

contradictory findings exist, e.g. in the responses to the single items presented in the result section of this thesis. The item “How much is your life and your activity limited by your heart disease?” was at one month answered “In very high degree” by 15% of patients, at one year the same answer was given by 41%, while the general trend otherwise is that patients felt better at the end of the follow-up year. The interpretation of why patients differ from controls in some dimensions and not others, and the time frame for emotional and somatic rehabilitation after a cardiac event is still far from clear, and should be subject of more research. To elucidate the situation of the patient and how the *person* with IHD experiences his or her situation and in what degree this situation differs from that of the general population is quite naturally of fundamental interest to everybody interested in medical ethics, as the better we understand the patients, the better is the care we can offer. From this investigation we know e.g. that it is possible that patients with IHD will have some sexual problems in the period after a cardiac event. Many timid patients are reluctant to discuss this problem with the doctor, and they will certainly be thankful if *the doctor* asks about this important matter.

2. Several (five) dimensions of the questionnaire were shown to differentiate between AMI patients in need of CABG or PCI during the year of follow-up and the AMI patients who did not go through such interventions. AMI patients with earlier infarctions, who seem likely to have a lower QoL, differed from the rest of the AMI patients in four dimensions at one-month follow-up. Patients who were treated at the emergency department during the year of follow-up because of angina or heart failure had previously reported significantly higher levels of thoracic pain and breathlessness, respectively than the others. Female patients differ from males in six dimensions at one-month assessment and in three at one year.

It remains a daunting fact that “female sex” is found in many lists of predictors for inferior QoL in IHD patients. Gender differences in our sample are discussed in paper II. Recently, Norris and co-workers found that one year after a coronary angiography female patients experienced worse QoL in all five dimensions of the SAQ (which is originally evaluated in a patient sample with 95% men!) (142, 96). Herlitz et al. investigated determinants for an impaired QoL 10 years after CABG by means of three instruments, NPH, the psychological well-being index and the physical activity scale from the APQLQ. In the two latter instruments female sex proved to be a predictor of inferior QoL (143). Vaccarino et al. studied sex differences after CABG and found, using SF-36, that men improved much more in mental health and physical function (six months after CABG). Women also had more

frequent readmissions (144). However, some investigators find no gender differences in QoL during follow-up (145). It is well known that the clinical picture of IHD differs in men and women; angina pectoris is the predominant presentation in women, while MI or sudden coronary death is more common in men (146).

A questionnaire may help to identify patients in need of future therapy as well as draw attention to the special problems that female IHD patients face. For the busy clinician and for investigators alike, as well as people interested in medical ethics, it is of great importance that patients with possible special needs are recognized and sufficiently helped.

3. Five of the QoL dimensions at the one-year assessment proved to be predictive of death until the date of census. No analysis was made of mortality causes. It is becoming increasingly clear that there is a predictive potential in the patient's self-evaluation even when it comes to very important endpoints as total death. The questionnaire used in the present investigation is by no means perfect and immense progress has been made in the field of self-assessment instruments since the study began.

It has been shown before that also long-term mortality is related to perceived health (147). More recently, Spertus et al. investigated all-cause mortality and admissions for acute coronary syndrome in IHD patients using a *disease-specific* instrument (SAQ). Health status captured by SAQ was a strong predictor of both end-points (148).

A *generic* instrument, SF-36, was used by Rumsfield and co-workers in a study of 180-day mortality after CABG (149). The physical component score (but not the mental component score) was associated with the end-point. The authors argue that evaluating health-related QoL may be a tool for risk stratification before CABG surgery. Although mortality was not studied, Herlitz et al. showed in their studies of outcome 5 and 10 years after CABG that impaired pre-operative QoL is a determinant of impaired QoL also postoperatively (140, 143).

The results presented in paper III support the notion that both more disease-specific and generic instruments may predict mortality. High-risk patients might be identified, as suggested by Spertus et al. (148). In the discussion about medical ethics, a topic that attracts great interest is how we shall allocate resources. What patient group needs most help? An investigation such as this one is an attempt to participate in this immense work.

4. The cases listed in the end of "Principles of Biomedical Ethics" are rather dramatic (64, pp 415–431). In paper IV, a much more everyday situation in the encounter between patient and

physician is discussed. There is an ethical conflict, a value conflict, in that if the principles are applied, autonomy and beneficence will collide. We have used the principle approach to see how well it was suited to identify, analyse, and solve possible ethical conflicts. But no ready solution in the methodology of Beauchamp and Childress was found. If individualistic autonomy is the *only* origin for decision-making, the patient–doctor relationship is reduced to that of client and technician (150). Maybe this concern is reflected in the fifth edition of Ethics Manual by the Ethics and Human Rights Committee, American College of Physicians: “The Patient–Physician relationship entails special obligation for the physician to serve the patient’s interest because of the specialized knowledge that physicians possess” (151).

It is important that the clinician does not underestimate the difficult situation that the patient faces in secondary intervention. Even famous writers in ethics find it hard to change eating habits (79). EUROASPIRE II has reported a high prevalence of unhealthy lifestyles among coronary patients, one conclusion is that “patients’ attitude towards risk factor reduction will also determine whether lifestyle and risk factor goals are achieved” (152). As is pointed out in paper IV, it is of great importance that the patient is an acting agent in his or her own care, and that the change in habits is a result of the patient’s wish, not just the physician’s orders. Improved knowledge of risk factors for IHD correlates to compliance to some lifestyle changes, but not all needed changes (119). It is also of vital importance that the patient experiences that the treatment recommended is for him or her personally, as a unique entity, this will certainly improve compliance in secondary prevention. Patients may experience that medication is forced upon them, that medication is an intrusion on their daily life (153).

One aspect that maybe has been overlooked in bioethics is that we live in a multicultural, multifaith, pluralistic society, where several normative frameworks co-exist (154). Many IHD patients are immigrants and health-care has to acknowledge their problematic situation (155). Patient-centred care is one of the specific aims that the Institute of Medicine proposes to improve the quality of care in USA (quote in 156). The patient will certainly feel that respect for his or her autonomy is increased and the risk for paternalism is decreased the more the patient’s own health evaluation is taken seriously, and the use of a questionnaire to capture this appraisal seems logical. Physicians may significantly underestimate patient-reported symptoms (136). The physician’s intent to individualize treatment will be more obvious, thereby increasing beneficence. To satisfy the aspect of justice, all IHD patients should be given similar opportunities to express themselves. Thus, to include longitudinal health status

measurements by means of questionnaires as a part of the encounter between cardiac patient and physician would be a great improvement.

Conclusion

In Sweden today, the use of a QoL questionnaire for clinical follow-up of cardiac patients seems to be sparse (157). Skevington et al. approached a sample of GPs, to find out if they used QoL information in clinical practise. 97% of respondent GPs thought that QoL was fairly to very important for general practise, but only 8% had ever used formal standardised questionnaires. The most common reason for *not* using QoL information in daily practise was "Do not understand how QoL information would be used" (51%). Only 9% of GPs knew about the NHP (158, 159). Hopefully the resistance against using a new tool will vanish. Considering the evidence cited above, both IHD-patients and physicians would profit from the use of a combined generic and disease-specific instrument, to monitor symptom development of the individual patient. It is a well known fact for hospital-based doctors and GPs alike that a lot of important information is lost when the patient is referred from e.g. an out-patient clinic at the hospital to the GP's office. If the result of the patient's self-assessment is made part of the medical record, this will help to improve the communication. A clinical evaluation, made by e.g. a specialist in cardiology, may be difficult to convey, which makes the patient's self-evaluation more valuable.

Using a questionnaire to capture QoL is without risks and adverse effects, it is inexpensive and not time consuming. To complete the SF-36 takes approximately the same amount of time as an ECG recording takes, five minutes (160). The patient can better understand investigations and interventions, if the planned action has its origin in a documented decreased perceived health. For some QoL questionnaires there is expert consensus on what changes in scores constitute clinically important differences (161). To further elucidate what questionnaires or combined instruments are best suited to assess cardiac patients is a chief subject for further research.

From an ethical point of view there are good reasons to use questionnaires to measure QoL. Ethics is largely about choices: Who shall decide? (162). In this case the question is: What perspective is the most important? I have tried to show that the patient's viewpoint is most significant and that any decision about the patient must be taken together with the patient. The shift in paradigm that occurs as the patient is made a partner to the physician, participating in his or her own care, and not an object for medical curiosity is of supreme importance.

Thus, the whole investigation presented in this thesis is built around one concept: If physicians want to know how, or what, the patient feels, they should ask the patient.

Summary in Swedish

Sjukdomar som drabbar hjärtats kranskärl och ger upphov till bland annat hjärtinfarkt är den vanligaste dödsorsaken både i Sverige och i resten av världen. Avsikten med denna avhandling är att ge en bild av livskvaliteten hos hjärtpatienter samt att ta upp problem inom medicinsk etik, som berör dessa patienter. Män och kvinnor som vårdats för hjärtinfarkt vid Universitetssjukhuset Malmö Allmänna Sjukhus ingår i undersökningen, liksom patienter som behandlats med kirurgi för att förbättra blodflödet i hjärtmuskeln (by-passkirurgi) eller ballongvidgning av hjärtats kranskärl. Undersökningen ägde rum 1989–1991. En månad efter sjukhusvistelsen fick patienterna besvara ett frågeformulär som gällde olika områden viktiga för livskvaliteten. Frågorna gällde symtom på hjärtsjukdom, allmän hälsa, förhållanden inom familj och släkt, själsliga problem som självkänsla, nedstämdhet och ångest samt frågor om sexuallivet.

Undersökningen visade att patienterna hade sämre livskvalitet än ”vanliga” Malmöbor inom nästan alla områden. Skillnaderna var betydligt mindre när patienterna åter besvarade formuläret ett år senare. De infarktpatienter som under det första året behövde en operation eller ballongvidgning (sannolikt på grund av tilltagande hjärtsymtom) hade vid en månadsundersökningen sämre livskvalitet än de övriga. De patienter som sökte på akutmottagningen på grund av kärllkramp eller andfåddhet hade också sämre livskvalitet vid den första undersökningen. Ett frågeformulär som detta kan alltså ge en uppfattning om vilka patienter som kommer att må sämre än andra, och därför behöver större insatser från sjukvården. Det är känt att kvinnor med hjärtsjukdomar ofta har sämre livskvalitet än män och det visade även denna undersökning.

Ungefär 10 år senare undersökte vi vilka patienter som dött under den tid som gått, och om deras svar på frågeformuläret skiljde sig från dem som överlevt. Inom flera områden kunde man se skillnader mellan de som avlidit och de som överlevt.

I samband med att en person vårdas för en sjukdom i hjärtats kranskärl förväntas han eller hon att påtagligt ändra livsstil. Detta kan naturligtvis vara svårt och för många kan det kännas kränkande. Hur skall man lösa en sådan situation som läkare? Skall man till varje pris låta patienten utforma sitt liv på egen hand eller skall man försöka påverka i förvisningen om att man på så sätt gör det bästa för patienten? De här problemen har inte någon klar och enkel lösning, men riktar uppmärksamheten på patientens okränkbarhet. Sedan den här undersökningen gjordes har det skapats många nya, bra frågeformulär, en del för alla typer av patienter och andra som är avsedda för särskilda grupper av sjuka. Denna undersökning visar att man bör använda frågeformulär för att i högre grad belysa patientens uppfattning om sin hälsa. Resultaten talar för att patientens

värdering av sin egen hälsa har stor betydelse, och informationen kan användas för att förbättra patientens vård. Att fylla i ett kort frågeformulär kostar ingenting, har inga biverkningar och tar kort tid att utföra. Viktigast är att patienten kommer att vara medansvarig för sin egen vård.

Acknowledgements

Professor Thomas F McNeil, my first tutor and co-author, for excellent introduction to this exciting field of research.

Professor Leif Erhardt, my second tutor and co-author, for letting me profit from his great cardiological knowledge.

Professor Tore Nilstun, my mentor and final tutor, as well as co-author, without whom you would not be reading these words.

Roland Carlsson, PhD, MD, my friend and co-author, for companionship and financial advice.

To the co-authors, assistant professors Elizabeth Cantor-Graae, Ronnie Willenheimer, and Bo Israelsson, and Charles Cline MD, PhD I express my thanks.

Assistant professor Stig Persson for providing excellent research climate and all along generous support in my work.

Carin Alm RN and Elisabeth Hansson RN for their skill, cheerfulness and enormous help in our follow-up programme.

Jan-Åke Nilsson BS and Per-Erik Isberg BS for help with statistics.

Professor Lars Janzon, assistant professors Bo Hedblad and Peter M Nilsson, Dept of community medicine for valuable advice.

Professors Marianne Sullivan, Bengt Brorsson, and Ingela Wiklund for generous help regarding questionnaires.

All colleagues and nurses in Malmö and Landskrona for a good time some of the time and a great time the rest of the time.

Eddie Fremer, Birgitta Larsson, and Inger Olsson for their assistance in the library.

Antti Sivén for helpfulness and proofreading.

Elisabet Westin, my sister, for all the time shared.

The children, David, Eleonora, Johannes, Johannes, Karin, Klas, Viola, so many blessings.

My wife, Maria Westin; brain, beauty, beneficence, what more can you want?

Oh Mama can this really be the end

Bob Dylan: Stuck inside of Mobile with the Memphis blues again

References

- 1 Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet* 1997;349:1269–76.
- 2 Roeters van Lennep JE, Westerveld HT, Erkelens DW, van der Wall EE. Risk factors for coronary heart disease: implications of gender. *Cardiovasc Res.* 2002;53:538–49.
- 3 The National Board of Health and Welfare in Sweden. (Register of Information and Knowledge about Swedish Heart Intensive care Admissions). Web document http://www.socialstyrelsen.se/Amnesord/halso_sjuk_verk/Kvalitetsregister/kva026.htm
- 4 The Swedish Register of Information and Knowledge about Swedish Intensive Care Admissions. Report for 2003. Web document <http://www.socialstyrelsen.se/NR/rdonlyres/E4A160A6-ABA2-4E78-AB37-F02F4DF930CD/0/kva026r03.pdf>
- 5 World Health Organization. The world health report 2004. Geneva. Web document <http://www.who.int/whr/2004/en/index.html>
- 6 World Health Organization. The world health report 2004. Annex table 2. Death by cause, sex and mortality stratum in WHO regions, estimates for 2002. Geneva. Web document http://www.who.int/whr/2004/en/09_annexes_en.pdf
- 7 World Health Organization. Global burden of disease, Mortality 2002. Geneva. Web document http://www3.who.int/whosis/menu.cfm?path=evidence,burden,burden_estimates,burden_estimates_2002N,burden_estimates_2002N_2002Rev,burden_estimates_2002N_2002Rev_Region&language=english
- 8 The National Board of Health and Welfare, Centre for epidemiology. Official statistics of Sweden. Statistics–Health and Diseases Causes of death 2002. Web document <http://www.socialstyrelsen.se> or <http://www.socialstyrelsen.se/NR/rdonlyres/05714583-0572-4EDF-9E1C-96E5DC0DA947/2721/2004425reviderad.pdf> September 2004
- 9 The National Board of Health and Welfare, Centre for epidemiology. Official statistics of Sweden. Statistics–Health and Diseases Myocardial infarctions in Sweden 1987–2002. Web document <http://www.socialstyrelsen.se> or <http://www.socialstyrelsen.se/NR/rdonlyres/D6C986A4-957A-4BE3-9FAC-F672A5B5CD8A/3274/2005422.pdf>. April 2005

- 10 Braunwald E, Zipes DP, Libby P, editors. Heart disease 6th ed. Philadelphia: W.B. Saunders Company; 2001.
- 11 Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial Infarction redefined- A consensus document of The Joint European Society of Cardiology /American College of Cardiology Committee for the Redefinition of Myocardial Infarction. J Am Coll Cardiol. 2000;36:959–69.
- 12 Antman EM, Anbe DT, Armstrong PW, Bates ER, Green LA, Hand M, Hochman JS, Krumholz HM, Kushner FG, Lamas GA, Mullany CJ, Ornato JP, Pearle DL, Sloan MA, Smith SC Jr, Alpert JS, Anderson JL, Faxon DP, Fuster V, Gibbons RJ, Gregoratos G, Halperin JL, Hiratzka LF, Hunt SA, Jacobs AK, Ornato JP. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction; A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1999 Guidelines for the Management of patients with acute myocardial infarction). J Am Coll Cardiol. 2004;44:E1–E211.
- 13 The National Board of Health and Welfare. Nationella riktlinjer för kranskärlssjukvård 2001 (Swedish national guidelines for coronary care 2001). Socialstyrelsen Stockholm 2001. Web document www.sos.se or <http://www.sos.se/fulltext/9800062/9800-062.htm#instabilaanginpectoris>
- 14 The National Board of Health and Welfare, Centre for epidemiology. Web document 2003. www.sos.se (try the “search function” at www.sos.se with the search term “Snabbt genomslag för riktlinjer om kranskärlssjukvård”)
- 15 The Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. Eleven-year survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina. N Engl J Med 1984;311:1333–9.
- 16 Passamani E, Davis KB, Gillespie MJ, Killip T. A randomized trial of coronary artery bypass surgery. Survival of patients with a low ejection fraction. N Engl J Med. 1985;312:1665-71.
- 17 Varnauskas E. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. N Engl J Med. 1988;319: 332–37.

- 18 Yusuf S, Zucker D, Peduzzi P et al. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet* 1994;344:563–70.
- 19 Eagle KA, Guyton RA, Davidoff R, Ewy GA, Fonger J, Gardner TJ, Gott JP, Herrmann HC, Marlow RA, Nugent WC, O'Connor GT, Orszulak TA, Rieselbach RE, Winters WL, Yusuf S et al. ACC/AHA guidelines for coronary artery bypass graft surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1991 Guidelines for Coronary Artery Bypass Graft Surgery). *J Am Coll Cardiol* 1999;34:1262–1346.
- 20 van Brussel BL, Plokker HW, Ernst SM, Ernst NM, Knaepen PJ, Koomen EM, Tijssen JG, Vermeulen FE, Voors AA. Venous coronary artery bypass surgery. A 15-year follow-up study. *Circulation*. 1993;88:II87–92.
- 21 Svenska hjärtkirurgiregistret (Swedish coronary surgery registry). Web document <http://www.socialstyrelsen.se/NR/ronlyres/F2DD34DF-6576-4FE1-A04A-61730189B281/0/kva006r03.pdf>
- 22 Gruntzig AR, Senning A, Siegenthaler WE. Nonoperative dilatation of coronary-artery stenosis: percutaneous transluminal coronary angioplasty. *N Engl J Med*. 1979;301:61–8.
- 23 Bourassa MG, Wilson JW, Detre KM, Kelsey SF, Robertson T, Passamani ER. Long-term follow-up of coronary angioplasty: the 1977–1981 National Heart, Lung, and Blood Institute registry. *Eur Heart J*. 1989 Dec;10 Suppl G:36–41.
- 24 Fischman DL, Leon MB, Baim DS et al. A Randomized Comparison of Coronary-Stent Placement and Balloon Angioplasty in the Treatment of Coronary Artery Disease. Stent Restenosis Study Investigators. *New Engl J Med*. 1994;331:496–501.
- 25 Wallentin L, Lagerqvist B, Husted S, Kontny F, Stahle E, Swahn E. Outcome at 1 year after an invasive compared with a non-invasive strategy in unstable coronary-artery disease: the FRISC II invasive randomised trial. FRISC II Investigators. *Fast Revascularisation during Instability in Coronary artery disease*. *Lancet*. 2000;356:9–16.
- 26 Swedish Coronary and Angioplasty Registry (SCAAR) 2003. Web document http://www.socialstyrelsen.se/Amnesord/halso_sjuk_verk/Kvalitetsregister/ or <http://www.socialstyrelsen.se/NR/ronlyres/BD7009F0-930D-4A9D-9993-CF380BEC1D43/0/kva053r03.pdf>

- 27 Fragmin and Fast Revascularization during INSTability in Coronary artery disease (FRISC II) investigators. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. *Lancet*. 1999;354:708–15.
- 28 Herlitz J, Ekström L, Hartford M, Karlson BW, Karlsson T, Grip L. Characteristics and outcome of patients with ST-elevation infarction in relation to whether they received thrombolysis or underwent acute coronary angiography: are we selecting the right patients for coronary angiography? *Clin Cardiol*. 2003;26:78–84.
- 29 Mortensen OS, Bjorner JB, Oldenburg B, Newman B, Geoenvold M, Madsen JK, Andersen HR. Health-related quality of life one month after thrombolysis or primary PCI in patients with ST-elevation infarction. A DANAMI-2 sub-study. *Scand Cardiovasc J*. 2005;39:206–12.
- 30 Kashani A, Giugliano RP, Antman EM, Morrow DA, Gibson CM, Murphy SA, Braunwald E. Severity of heart failure, treatments, and outcomes after fibrinolysis in patients with ST-elevation myocardial infarction. *Eur Heart J*. 2004;25:1702–10.
- 31 Swedish National registry for heart arrest outside of hospital 2004. Web document <http://www.socialstyrelsen.se/NR/rdonlyres/86551F00-8217-4361-AE9F-A2242721A642/0/kva007r04.pdf>
- 32 Malmberg K, Norrhammar A, Rydén L. Diabetes och hjärtat. In Agardh C-D, Berne C, Östman J, editors. *Diabetes*. Stockholm: Liber; 2002,
- 33 Rosenberg DE, Jabbour SA, Goldstein BJ. Insulin resistance, diabetes and cardiovascular risk: approaches to treatment. *Diabetes, Obesity and Metabolism* 2005;7:642–53.
- 34 Dormandy JA, Charbonnel B, Eckland DJ, Erdman E et al on behalf of the PROactive investigators. Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive study (PROspective pioglitAzone Clinical Trial in macroVascular Events): a randomized controlled trial. *Lancet*. 2005;366:1279–89.
- 35 Nilsson P, Nilsson J-Å, Hedblad B, Eriksson K-F, Berglund G. Hyperinsulinaemia as long-term predictor of death and ischemic heart disease in nondiabetic men: The Malmö Preventive Project. *J Intern Med*. 2003;253:136–45.

- 36 Sidney S, Sorel M, Quensberry CP, De Luise C, Lanes S, Eisner MD. COPD and incident cardiovascular disease hospitalisation and mortality: Kaiser Permanente Medical Care Program. *Chest*. 2005;128:2068–75.
- 37 Moser DK, Dracup K. Is anxiety early after myocardial infarction associated with subsequent Ischemic and Arrhythmic Events? *Psychosom Med*. 1996;58:395–401.
- 38 Watkins LL, Grossman P, Krishnan K, Sherwood A. Anxiety and vagal control of the heart. *Psychosom Med*. 1998;60:498–502.
- 39 Glassman AH, O'Connor CM, Califf RM, Swedberg K, Schwartz P, Bigger JT Jr, Krishnan KR, van Zyl LT, Swenson JR, Finkel MS, Landau C, Shapiro PA, Pepine CJ, Mardekian J, Harrison WM, Barton D, McIvor M for the Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) group. Sertraline treatment of major depression in patients with acute MI or unstable angina. *JAMA* 2002;288:701–09.
- 40 Frasure-Smith N, Lespérance F, Talajic M. Depression and 18-month prognosis after myocardial infarction. *Circulation*. 1995;91:999–1005.
- 41 Lespérance F, Frasure-Smith N. Depression in patients with cardiac disease: a practical review. *J Psychosom Res*. 2000;48:379–91.
- 42 Stein PK, Carney RM, Freedland KE, Skala JA, Jaffe AS, Kleiger RE, Rottman JN. Severe depression is associated with markedly reduced heart rate variability in patients with stable coronary heart disease. *J Psychosom Res*. 2000;48:493–500.
- 43 Carney RM, Freedland KE, Veith RC. Depression, the autonomic nervous system, and coronary heart disease. *Psychosom Med*. 2005;67 Suppl 1:S29–S33.
- 44 Bruce EC, Musselman DL. Depression, alterations in platelet function, and ischemic heart disease. *Psychosom Med*. 2005;67 Suppl 1:S34–S36.
- 45 Joynt KE, O'Connor CM. Lessons from SADHART, ENRICHD, and other trials. *Psychosom Med*. 2005;67 Suppl 1:S63–S66.
- 46 Writing Committee for the ENRICHD Investigators. Effects of Treating Depression and Low Perceived social support on Clinical Events After Myocardial Infarction. *JAMA*. 2003;289:3106–16.
- 47 Cassem NH, Hackett TP. Caring for the cardiac patient. “Ego infarction” Psychological reactions to a heart attack. *J Pract Nurs*. 1979;29:17–20,39.

- 48 Drory Y, Kravetz S, Weingarten M, for the Israeli study group on first acute myocardial infarction. Comparison of sexual activity of women and men after a first acute myocardial infarction. *Am J Cardiol.* 2000;85:1283–87.
- 49 Muller JE: Triggering of cardiac events by sexual activity: findings from a case-crossover analysis. *Am J Cardiol.* 2000;86 (suppl 2A):14F–18F.
- 50 Cheitlin MD. Sexual activity and cardiovascular disease. *Am J Cardiol* 2003;92 (9, suppl 1):3M–8M.
- 51 Bedell SE, Duperval M, Goldberg R. Cardiologists' discussion about sexuality with patients with chronic coronary artery disease. *Am Heart J.* 2002;144:239–42.
- 52 Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol.* 1994;151:54–61.
- 53 Kloner RA. Introduction: Erectile dysfunction and cardiovascular risk factors. *Am J Cardiol.* 2003;92(9, suppl 1):1–2.
- 54 Brindis RG, Kloner RA. Sildenafil in patients with cardiovascular disease. *Am J Cardiol.* 2003;92 (9, suppl 1):26–36.
- 55 Kostis JB, Jackson G, Rosen R et al. Sexual dysfunction and cardiac risk (the second Princeton Consensus Conference). *Am J Cardiol.* 2005;96:313–21.
- 56 Wood-Dauphinee S. Assessing quality of life in clinical research: From where have we come and where are we going? *J Clin Epidemiol.* 1999;52:355–63.
- 57 Web document <http://www.who.int/about/definition/en/>
- 58 Korlén G. Livskvalitet. Om ett slagords historia. *Språkvård.* 1979;15(Nr 3):7–9.
- 59 President Lyndon B Johnson. State of the Union speech 1965. Web document <http://www.infoplease.com/t/hist/state-of-the-union/178.html>
- 60 Web document http://www.ceaa-acee.gc.ca/015/0002/0015/3_e.htm
- 61 Westin L, Carlsson R, Israelsson B, Willenheimer R, Cline C and McNeil TF. Quality of life in patients with ischaemic heart disease: a prospective controlled study. *J Intern Med.* 1997;242:239–47.
- 62 Web document http://www.who.int/mental_health/media/68.pdf

- 63 Guyatt GH, Feeny DH, Patrick DL. Measuring Health-related quality of life. *Ann Intern Med.* 1993;118:622–29.
- 64 Beauchamp T and Childress J. *Principles of Biomedical Ethics.* 5th ed. New York: Oxford University press; 2001.
- 65 Persson Å. Livskvalitetsmätningar i hälsoekonomiska utvärderingar. In: Richt B, editor. *Livskvalitet Teori, mätning och realitet. Studies on Health and Society 2.* Linköping: Linköping University; 1994.
- 66 The National Board of Health and Welfare. Socialstyrelsens riktlinjer för hjärtsjukvård 2004, beslutstöd för prioriteringar, Socialstyrelsen 2004. Web document <http://www.socialstyrelsen.se/NR/ronlyres/9E12CEDB-9459-4167-A3FC-57046AE68511/2562/20041023.pdf>
- 67 Fagerberg H, Bischofberger E, Jacobsson L, Lindmark G. *Medicinsk etik och människosyn.* 4th ed. Stockholm: Liber; 1997.
- 68 Arlebrink J. *Grundläggande vårdetik – teori och praktik.* Lund: Studentlitteratur; 1996.
- 69 Marc-Wogau K. *Filosofisk uppslagsbok.* 3rd ed. Klippan: Doxa; 1984.
- 70 Nilstun T. Paternalism and health behaviour. In Gochman DS, editor. *Handbook of Health Behaviour Research IV, Relevance for Professionals and Issues for the future.* New York: Plenum Press; 1997.
- 71 The Swedish Council on technology Assessment in Health Care (SBU) Rapport no 139, September 1998, Stockholm; 1998.
- 72 Holm S. Not just autonomy: The Principles of American Biomedical Ethics. In Harris J, editor. *Bioethics.* Oxford: Oxford University Press; 2001.
- 73 Vaccarino V, Rathore SS, Wenger NK, Frederick PD, Abramson JL, Barron HV, Manhapra A, Mallik S, Krumholz HM for the National Registry of Myocardial Infarction Investigators. Sex and Racial differences in the management of acute myocardial infarction, 1994 through 2002. *N Engl J Med.* 2005;353:671–82.
- 74 Catechism of the Catholic Church §§ 1950–1960, 2033. Web document http://www.vatican.va/archive/ENG0015/___P6T.HTM
- 75 Beauchamp T. A defence of the common morality. *Kennedy Inst Ethics J.* 2003;13:259–74.

- 76 Clouser KD. Common morality as an alternative to principlism. *Kennedy Inst Ethics J*. 1995;5:219–36.
- 77 Clouser KD, Gert B. A critique of principlism. *J Med Philos*. 1990;15:219–36.
- 78 New Testament: Matthew 5:43–47. Web document <http://etext.lib.virginia.edu/etcbin/toccer-new2?id=KjvMatt.sgm&images=images/modeng&data=/texts/english/modeng/parsed&tag=public&part=5&division=div1>
- 79 Gillon R. Ethics needs principles – four can encompass the rest– and respect for autonomy should be “first among equals” *J Med Ethics*. 2003;29:307–12.
- 80 Donne J. Devotions upon Emergent occasions. Meditation 17 (1624).
- 81 Pellegrino ED. The Metamorphosis of Medical Ethics. A 30-Year Retrospective. *JAMA* 1993;269:1158–62.
- 82 Fan R. Self-Determination vs. Family determination: Two Incommensurable Principles of Autonomy: A report from East Asia. *Bioethics* 1997;11:309–22.
- 83 Ruhnke GW, Wilson SR, Akamatsu T et al. Ethical decision making and patient autonomy: a comparison of physicians and patients in Japan and the United States. *Chest*. 2000;118:1172–82.
- 84 Karlgren B. Religion I Kina Antiken. Stockholm: Svenska bokförlaget/Bonniers; 1964.
- 85 Mao Tse-Tung. Quotations from Chairman Mao Tse-Tung. Peking: Foreign Languages Press; 1966.
- 86 Sachedina A. End-of-life: the Islamic view. *Lancet*. 2005;366:774–79.
- 87 Sullivan M. The new subjective medicine: taking the patient’s point of view on health care and health. *Soc Sci Med*. 2003;56:1595–1604.
- 88 Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R. Quality of life measurement: bibliographic study of patient assessed outcome measures. *BMJ*. 2002;324:1417–21.
- 89 The EuroQol Group. EuroQol — a new facility for the measurement of health-related quality of life. *Health Policy*. 1990;16:199–208.
- 90 EuroQol website. Web document <http://www.euroqol.org/web/>

- 91 Skevington SM. Measuring Quality of life in Britain: an introduction to the WHOQOL-100. *J Psychosom Res.* 1999;47:449–59.
- 92 WHO Field Centre for the study of quality of life website. Web document <http://www.bath.ac.uk/whoqol/>
- 93 Sullivan M, Karlsson J, Ware J. The Swedish SF-36 Health Survey–I. Evaluation of data quality, scaling assumptions, reliability and construct validity across general populations in Sweden. *Soc Sci Med.* 1995;41:1349–58.
- 94 Ware JE Jr., Sherbourne CD. The MOS 36 short-form health-survey (SF-36). I Conceptual framework and item selection. *Med Care* 1992;30:473–83.
- 95 SF-36 Community Website. Web document <http://www.sf-36.org/> or <http://www.sf-36.org/tools/sf36.shtml#CONSTRUCT>
- 96 Spertus JA, Winder JA, Dewhurst TA, Deyo RA, Prodzinski J, McDonell M, Fihn SD. Development and evaluation of the Seattle Angina Questionnaire. A new functional status measure for coronary disease. *J Am Coll Cardiol.* 1995;25:333–41.
- 97 Epimetrics website Web documents http://www.epimetrics.com/news/item.tcl?news_item_id=100067 or <http://www.cvoutcomes.org/questionnaires/>
- 98 Dempster M, Donnelly M. Measuring the health related quality of life of people with ischemic heart disease. *Heart* 2000;83:641–44.
- 99 Hunt SM, McKenna SP, Williams J. Reliability of a population survey tool for measuring perceived health problems: a study of patients with osteoarthritis. *J Epidemiol Community Health* 1981;35:297–300.
- 100 Wiklund I. The Nottingham Health Profile- A measure of health-related quality of life. *Scand J Prim Health Care Suppl.* 1990;1:15–18.
- 101 Höfer S, Lim L, Guyatt G, Oldridge N. The MacNew Heart Disease health-related quality of life instrument: A summary. *Health Qual Life Outcomes* 2004;2:3.
- 102 Bergner M, Bobbitt RA, Carter WB, Gilson BS. The sickness Impact Profile: development and final revision of a health status measure. *Med Care* 1981;19:787–805.
- 103 Wiklund I, Comerford MB, Dimenäs E. The relationship between exercise tolerance and quality of life in angina pectoris. *Clin Cardiol* 1991;14:204–8.

- 104 Janzon M, Levin LÅ, Swahn E. Invasive treatment in unstable coronary artery disease promotes health-related quality of life: Results from the FRISC II trial. *Am Heart J.* 2004;148:114–21.
- 105 Rector TS, Cohn JN with the Pimobendan Multicenter Research Group. Assessment of patient outcome with the Minnesota Living with Heart Failure Questionnaire; reliability and validity during a randomized, double-blind, placebo-controlled trial of pimobendan. *Am Heart J.* 1992;124:1017–25.
- 106 Minnesota Living with Heart Failure questionnaire website. Web document <http://www.mlhfq.org/default.htm>
- 107 Sadana R. Development of Standardized Health State Descriptions. Ch 7.1 in Summary Measures population Health, ed Murray Ch, Salomon J, Mathers C, LopezA., WHO, Geneva 2002
- 108 Wann-Hansson C, Hallberg IR, Risberg B, Klevsgård R. A comparison of Nottingham Health Profile and Short Form 36 Health Survey in patients with chronic lower limb ischemia in a longitudinal perspective. *Health Qual Life Outcomes.* 2004;2:9.
- 109 Oldridge N, Saner H, McGee HM for the HeartQoL Study Investigators. The Euro Cardio-QoL Projekt. An international study to develop a core heart disease health-related quality of life questionnaire, the Heart-QoL. *Eur J Cardiovasc Prev Rehabil* 2005;12:87–94.
- 110 Student. The probable error of a mean. *Biometrika.* 1908;6:1–25.
- 111 Norusis MJ. SPSS for Windows Base system User's Guide Release 6.0. Chicago, USA 1993.
- 112 Ejlertsson G. Statistik för hälsovetenskaperna. Lund: Studentlitteratur; 2003.
- 113 Bland JM, Altman DG. Statistics notes. The odds ratio. *BMJ.* 2000;320:1468.
- 114 Perk J. Cardiac Rehabilitation Medical and Socioeconomic Results of a Comprehensive Programme. [Dissertation] Linköping University; 1989.
- 115 Israelsson B, Rüter G, Solem JO. A deficient intervention against risk factors among patients with coronary vascular surgery. *Läkartidningen.* 1989;86:4121–4.

- 116 Carlsson R, Lindberg G, Westin L, Israelsson B. Serum lipids four weeks after acute myocardial infarction are a valid base for lipid lowering intervention in patients receiving thrombolysis. *Br Heart J.* 1995;74:18–20.
- 117 Carlsson R, Lindberg G, Westin L, Israelsson B. Influence of coronary nursing management follow up on lifestyle after acute myocardial infarction. *Heart* 1997;77:256–59.
- 118 Stagmo M, Westin L, Carlsson R, Israelsson B. Long-term effects on cholesterol levels and the utilization of lipid-lowering drugs of a hospital-based programme for secondary prevention of coronary artery disease. *J Cardiovasc Risk.* 2001;8:243–48.
- 119 Alm-Roijer C, Stagmo M, Uden G, Erhardt L. Better knowledge improves adherence to lifestyle changes and medication in patients with coronary heart disease. *Eur J Cardiovasc Nurs.* 2004;3:321–30.
- 120 Dimenäs E. Aspects of quality of life in hypertension: Methods for evaluation. [Dissertation] University of Göteborg; 1990.
- 121 Portenoy RK, Thaler HT, Kornblith AB, Lepore JM et al: The Memorial Symptom Assessment scale: an instrument for the evaluation of symptom prevalence, characteristics and distress. *Eur J Cancer.* 1994;30A:1326–36.
- 122 Chambers LW. The McMaster Health Index Questionnaire (MHIQ). Methodological documentation and report of second generation of investigation. Hamilton, Ontario: Department of Clinical Epidemiology and Biostatistics, McMaster University, 1982.
- 123 Chambers LW, Macdonald LA, Tugwell P, Buchanan WW, Kraag G. The McMaster Health Index Questionnaire as a measure of quality of life for patients with rheumatoid disease. *J Rheumatol.* 1982;9:780–84.
- 124 Rose GA. The diagnosis of ischemic heart pain and intermittent claudication in field surveys. *Bull World Health Organ.* 1962;27:645–58.
- 125 Hagman M, Jönsson D, Wilhelmsen L. Prevalence of angina pectoris and myocardial infarction in a general population sample of Swedish men. *Acta Med Scand.* 1977;201:571–77.
- 126 Spielberger CD, Gorsuch RL, Lushene RL. State-Trait Anxiety Inventory. Palo Alto: Consulting Psychologist Press; 1970.

- 127 Montgomery SA, Åsberg M. A new depression scale designed to be sensitive to change. *Br J Psychiatry*. 1979;134:382–89.
- 128 Svanborg P, Åsberg M. A comparison between the Beck depression inventory (BDI) and the self-rating version of the Montgomery Åsberg Depression Rating Scale (MADRS). *J Affect Disord*. 2001;64:203–16.
- 129 Web document http://www.bsos.umd.edu/socy/grad/socpsy_rosenberg.html
- 130 Web document <http://www.atkinson.yorku.ca/~psycytest/rosenbrg.pdf>
- 131 Kennedy BL, Schwab JJ, Morris RL, Beldia G. Assessment of state and trait anxiety in subjects with anxiety and depressive disorders. *Psychiatr Q*. 2001;72:263–76.
- 132 Web document http://www.hubin.org/about/staff/thomas_mcneil_se.html
- 133 Sullivan M. The art of reading an article on quality of life research—new checklist available to facilitate a critical evaluation. *Läkartidningen*. 2002;99: 2933–38.
- 134 Herlitz J, Wiklund I, Caidahl K, Hartford M, Haglid M, Karlson BW, Sjöland H and Karlsson T. The feeling of loneliness prior to coronary artery bypass grafting might be a predictor of short- and long-term postoperative mortality. *Eur J Vasc Endovasc Surg*. 1998;16:120–5.
- 135 Wiklund I, Herlitz J, Hjalmarson Å. Quality of life five years after myocardial infarction. *Eur Heart J*. 1989;10:464–72.
- 136 Brown N, Melville M, Gray D, Young T, Munro J, Skene AM, Hampton JR. Quality of life four years after acute myocardial infarction: short form 36 scores compared with a normal population. *Heart*. 1999;81:352–8.
- 137 Bengtsson I, Hagman M, Währborg P, Wedel H. Lasting impact on health-related quality of life after a first myocardial infarction. *Int J Cardiol*. 2004;97:509–16.
- 138 Drory Y, Kravetz S, Hirschberger G for the Israel Study Group on First Acute Myocardial Infarction. Long-Term Mental Health of men after a first acute myocardial infarction. *Arch Phys Med Rehabil*. 2002;83:352–59.
- 139 Brorsson B, Bernstein SJ, Brook RH, Werkö L for the SECOR/SBU Project Group. Quality of life of patients with chronic stable angina before and four years after coronary revascularisation compared with a normal population. *Heart*. 2002;87:140–45.

- 140 Herlitz J, Wiklund I, Caidahl K, Karlson BW, Sjöland H, Hartford M, Haglid M, Karlsson T. Determinants of an impaired quality of life five years after coronary artery bypass surgery. *Heart*. 1999;81:342–46.
- 141 Kim J, Henderson RA, Pocock SJ, Clayton T, Sculpher MJ, Fox KA for the RITA-3 Trial investigators. Health-related quality of life after interventional or conservative strategy in patients with unstable angina or non-ST-elevation myocardial infarction: one-year results of the third Randomized Intervention Trial of unstable Angina (RITA-3). *J Am Coll Cardiol*. 2005;45:221–28.
- 142 Norris CM, Ghali WA, Galbraith PD, Graham MM, Jensen LA, Knudtson ML and the APPROACH Investigators. Women with coronary artery disease report worse health-related quality of life compared to men. *Health Qual Life Outcomes* 2004;2:21.
- 143 Herlitz J, Brandrup-Wognsen G, Caidahl K, Hartford M, Haglid M, Karlson BW, Karlsson T, Sjöland H. Determinants for an impaired quality of life 10 years after coronary artery bypass surgery. *Int J Cardiol*. 2005;98:447–52.
- 144 Vaccarino V, Lin ZQ, Kasl SV, Mattera JA, Roumanis SA, Abramson JL, Krumholz HM. Sex differences in health status after coronary artery bypass surgery. *Circulation*. 2003;108:2642–47.
- 145 Kristofferzon M-L, Löfmark R, Carlsson M. Coping, social support and quality of life over time after myocardial infarction. *J Adv Nurs*. 2005;52:113–24.
- 146 Wenger NK. Clinical characteristics of coronary heart disease in women: emphasis on gender differences. *Cardiovasc Res*. 2002;53:558–67.
- 147 Svärdsudd K and Tibblin G. Is quality of life affecting survival? The study of men born in 1913. *Scand J Prim Health Care Suppl*. 1990 1:55–60.
- 148 Spertus JA, Jones P, McDonell M, Fan V, Fihn SD. Health status predicts long-term outcome in outpatients with coronary disease. *Circulation*. 2002;106:43–9.
- 149 Rumsfeld JS, MaWhinney S, McCarthy M Jr, Shroyer AL, VillaNueva CB, O'Brien M, Moritz TE, Henderson WG, Grover FL, Sethi GK, Hammerstein KE. Health-related quality of life as a predictor of mortality following coronary artery bypass graft surgery. Participants of the Department of Veterans Affairs Cooperative Study Group on Processes, Structures and Outcomes of Care in Cardiac Surgery. *JAMA*. 1999;281:1298–1303.

- 150 Stirrat GM, Gill R. Autonomy in medical ethics after O'Neill. *J Med Ethics*. 2005;31:127–30.
- 151 Snyder L, Leffler C for the Ethics and Human Rights Committee, American College of Physicians. Ethics Manual Fifth Edition. *Ann Intern Med*. 2005;142:560–82.
- 152 EUROASPIRE II Study Group. Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries; principal results from EUROASPIRE II Euro Heart Survey Programme. *Eur Heart J*. 2001;22:554–72.
- 153 Attebring MF, Herlitz J, Ekman I. Intrusion and confusion– the impact of medication and health professionals after acute myocardial infarction. *Eur J Cardiovasc Nurs*. 2005;4:153–9.
- 154 Turner L. Bioethics in pluralistic societies. *Med Health Care Philos*. 2004;7:201–8.
- 155 Dotevall A, Rosengren A, Lappas G, Wilhelmsen L. Does immigration contribute to decreasing CHD incidence? Coronary risk factors among immigrants in Göteborg, Sweden. *J Intern Med*. 2000;247:331–9.
- 156 Rumsfeld JS. Health status and clinical practice: When will they meet? *Circulation*. 2002;106:5–7.
- 157 Perk J. Personal communication.
- 158 Skevington SM, Day R, Chisholm A, Trueman P. How much do doctors use quality of life information in primary care? Testing the Trans-Theoretical Model of behaviour change. *Qual Life Res*. 2005;14:911–22.
- 159 Wiklund, I. NHP Manual. Svensk Version av Nottingham Health Profile – ett frågeformulär som mäter hälsorelaterad livskvalitet. Tryck OFTA, Göteborg 1992.
- 160 Web document <http://www.atsqol.org/sf36>.
- 161 Wyrwich KW, Spertus J, Kroenke K, Tierney WM, Babu AN, Wolinsky FD. Clinically important differences in health status for patients with heart disease: an expert consensus panel report. *Am Heart J*. 2004;147:615–22.
- 162 Hermerén G. 2003. Etik: innebörd, problem och metoder. Vårdalinstitutets tematiska rum: Etik. Web document <http://www.vardalinstitutet.net/documentarchive/1168/1575/1577/3368.pdf?objectId=6356>