Micro Level Priority Setting for Elderly Patients with Acute Cardiovascular Disease and Complex Needs

Practice What We Preach or Preach What We Practice?

Niklas Ekerstad

Department of Medical and Health Sciences
Faculty of Health Sciences
Linköping University, Sweden

Linköping University
FACULTY OF HEALTH SCIENCES

Linköping 2011

To Elin and Gustav

Si l'on pense à l'alternative**,**
vieillir n'est pas si mal

[Att åldras är inte så illa,
om man tänker på alternativet]

Maurice Chevalier (1888-1972)

CONTENTS

ABSTRACT

Demographic trends and other factors are expected to continue widening the gap between health care demands and available resources, especially in elder services. This growing imbalance signals a need for priority setting in health care. The literature has previously described problems in constructing useable means of priority setting, particularly when evidence is sparse, when patient groups are not satisfactorily defined, when interpretation of the term *patient need* is unclear, and when uncertainty prevails on how to weigh different ethical values. The chosen study object illustrates these problems. Moreover, the Swedish Government recently stated that care for elderly persons with complex health care needs remains underfunded. The general aim of this thesis is: to study microlevel priority setting for elderly heart patients with complex needs, as illustrated by those with non-ST-elevation myocardial infarction (NSTEMI); to relate the findings to evidence-based priority setting, e.g. guidelines for heart disease; and to analyse how complex needs could be appropriately categorised from a perspective of evidence-based priority setting.

Paper I presents a register study that uses data from the Patient Register to describe inpatient care utilization, costs, and characteristics of elderly patients with multiple diseases. Paper II presents a confidential survey study from a random sample of 400 Swedish cardiologists. Paper III presents a prospective, clinical, observational multicentre-study of elderly patients with myocardial infarction (NSTEMI). Paper IV presents a questionnaire study from a purposeful, stratified sample of Swedish cardiologists.

The results from Paper I show that elderly patients with multiple diseases have extensive and complex needs, frequently manifesting chronic and intermittently acute disease and consuming health care at various levels. A large majority have manifested cardiovascular disease. Results from Paper II indicate that although 81% of cardiologists reported extensive use of national guidelines in their clinical decision-making generally, the individual clinician's personal clinical experience and the patient's views were used to a greater extent than national guidelines, when making decisions about elderly multiple-diseased patients. Many elderly heart disease patients with complex needs manifest severe, acute or chronic, comorbid conditions that constitute exclusion criteria in evidence-generating studies, thereby limiting the generalisability of evidence and applicability of guidelines for these patients. This was indicated in papers I-IV. Paper III reports that frailty is a strong independent risk factor for adverse, short-term, clinical outcomes, e.g. one-month mortality for elderly NSTEMI patients. Particularly frail patients with a high comorbidity burden manifested a markedly increased risk.

In the future, prospective clinical studies and registries with few exclusion criteria should be conducted. Consensus-based judgments based on a framework for priority setting as regards elderly patients with complex needs may offer an alternative, estimating the benefit-risk ratio of an intervention and the time-frame of expected benefits in relation to expected life-time. Such a framework, which is tentatively outlined in this thesis, should take into account comorbidity, frailty, and disease-specific risk.

LIST OF PAPERS

I.   Ekerstad N, Edberg A, Carlsson P. Characteristics of multiple-diseased elderly in Swedish hospital care and clinical guidelines: Do they make evidence-based priority setting a "mission impossible"? *International Journal of Ageing and Later Life* 2009;3:71–95.

II.   Ekerstad N, Löfmark R, Carlsson P. Elderly with Multimorbidity and Acute Cardiac Disease: Doctors' Views on Decision-Making. *Scand J Public Health* 2010;3:325-331.

III.   Ekerstad N, Swahn E, Janzon M, Alfredsson J, Löfmark R, Lindenberger M, Carlsson P. Frailty as a Predictor of Short-Term Outcomes for Elderly Patients with non-ST-Elevation Myocardial Infarction (NSTEMI).
Submitted.

IV.   Ekerstad N, Löfmark R, Andersson D, Carlsson P. A Tentative Consensus-Based Model for Priority Setting – An Example from Elderly Patients with Myocardial Infarction and Multi-morbidity.
Accepted Scand J Public Health on the 4th of March 2011.

ABBREVIATIONS AND ACRONYMS

ACG	Adjusted clinical groups
AHA	American Heart Association
AMI	Acute myocardial infarction
CABG	Coronary artery bypass grafting
CAD	Coronary artery disease
CEA	Cost-effectiveness analysis
CFS	The Canadian Study of Health and Ageing Clinical Frailty Scale
CI	Confidence interval
CVD	Cardiovascular disease
CVR	Cardiovascular risk
DRG	Diagnosis-related groups
EBM	Evidence based medicine
ECG	Electrocardiogram
FRISC	FRagmin and Fast Revascularisation during InStability in Coronary artery disease Investigators
ICC test	Intra-class correlation test
ICF	International Classification of Functioning, Disability and Health (WHO)
IHD	Ischaemic heart disease
LARC	Linköping Academic Research Centre
LFN	The Pharmaceutical Benefits Board
MINAP	The Myocardial Ischaemia National Audit Project
NICE	National Institute for Health and Clinical Excellence
NIER	The National Institute of Economic Research
NSTE ACS	Non-ST-elevation acute coronary syndrome
NSTEMI	Non-ST-elevation myocardial infarction
OR	Odds ratio
PCI	Percutaneous coronary intervention
QALY	Quality-adjusted life-year
RCT	Randomised controlled trial
SALAR	Swedish Association of Local Authorities and Regions
SBU	Swedish Council of Health Technology Assessment
The Board	The National Board of Health and Welfare
The Model	The National Model for Transparent Vertical Priority Setting in Swedish Health Care
The Priority Setting Centre	The National Centre for Priority Setting in Health Care
TLV	The Dental and Pharmaceutical Benefits Agency

AIMS OF THE STUDY

General aim

The general aim of this thesis is: to study microlevel priority setting for elderly heart patients with complex needs, as illustrated by those with non-ST-elevation myocardial infarction (NSTEMI); to relate the findings to evidence-based priority setting, e.g. guidelines for heart disease; and to analyse how complex needs could be appropriately categorised from a perspective of evidence-based priority setting.

Specific aims

- To describe and quantify inpatient care utilisation, costs, and patient characteristics of multiple-diseased elderly patients, particularly concerning cardiovascular disease and co-morbidity; and to discuss the applicability of evidence-based guidelines for these patients in Swedish inpatient hospital care with regard to the reported characteristics. *(Paper I)*

- To evaluate the views of Swedish cardiologists on decision-making for elderly with multiple co-morbidities and non-ST-elevation acute coronary syndrome (NSTE-ACS); and to generate some hypotheses for testing. *(Paper II)*

- To describe patients aged 75 years or older with NSTEMI, especially regarding the following variables: cardiovascular risk, co-morbidity, and frailty; and to analyse how frailty predicts short-term outcomes for these patients and its implications for priority setting. *(Paper III)*

- To evaluate the interrater reliability of study experts' rankings regarding authentic, clinical, complex NSTEMI cases; to compare the experts' rankings with the guidelines; and to evaluate a tentative framework for priority setting regarding elderly with multimorbidity. *(Paper IV)*

BACKGROUND

Legal, demographic, and economic considerations

Since national legislation mainly defines the normative framework for priority setting in health care a natural approach would be to consider legal premises in a Swedish context. To some extent, however, such considerations may be generalisable to other countries' healthcare systems.

The Swedish healthcare system is based on a universal model, with basically full coverage, funded primarily through taxation. The parliament influences the structure and performance of health care by making laws, while the central government establishes goals concerning how to act and allocates various types of economic contributions to influence behaviour. The county councils (and two regions) are democratic bodies with their own right to levy taxes on the population. These governing bodies are responsible for financing and delivering health services, including primary care and hospital care. Similarly, Swedish municipalities are responsible for long-term care of the elderly [Anell 2005]. The National Board of Health and Welfare plays a crucial role, supervising medical quality and outcomes, and offering strategic support, e.g. in developing national guidelines for priority setting. Despite the central steering mechanisms mentioned above, considerable responsibility is placed on healthcare professionals to implement goals and apply resources in direct contact with citizens [The National Centre for Priority Setting in Health Care 2007; Waldau 2010].

Sweden and most other OECD countries anticipate a growing gap between healthcare demands and available resources. Three main causes for this gap have been proposed [Coulter and Ham 2000; Newdick 2005]. First, demographic and epidemiologic changes contribute to the gap. These changes stem from a growing population of elderly with major needs for care and a concurrent decline in the working-age proportion of the population contributing financially to the publicly funded health caresystem. A prognosis by the National Institute of Economic Research (NIER) indicates that increasingly fewer Swedish citizens are expected to work in the business sector in the future [The National Institute of Economic Research 2005]. The demographic prognosis for the Swedish population illustrates the scope of the problem. Today, approximately 500 000 people are aged 80 years or older; in 25 years this number is estimated to reach approximately 800 000 [Statistics Sweden 2009; Ministry of Health and Social Affairs 2010]. Although various theories exist concerning whether the period of frail years of elderly people will be extended or compressed in the future, reports of data on a few health indicators indicate that the status of the elderly in Sweden may have declined [Thorslund et al. 2004; Thorslund and Parker 2005]. Second, developments in health technology create possibilities to improve the quality of care, and also to treat new patient groups. Third, the healthcare system is constantly faced with higher public expectations. The report *Health Services Until 2030* predicts that by 2030 the resource needs of health services in Sweden will have increased by 50% [Swedish Association of Local Authorities and

Regions 2005]. Similarly, other reports on elder care predict increasing demands on elder services [The National Board of Health and Welfare 2007; Ministry of Health and Social Affairs 2010]. Most Western countries face similar challenges.

These pressures have induced policy-makers to look for more efficient and fairer ways to allocate public resources. Theoretically, various partly-interdependent actions can be taken to meet the predicted challenges, e.g. tax increases, redistribution of resources in the public sector, prioritisation within the health services sector, making resource utilisation in health services more efficient, rationing (including limitations in the content of publicly financed health services), and market solutions. Recently, it was reported that most Swedish citizens still maintain an overwhelmingly positive attitude towards the welfare state, including a willingness to pay higher taxes to finance the healthcare sector [Svallfors 2010]. However, the overall potential for solving financial problems through tax increases alone is considered to be limited, indicating a need for prioritisation.
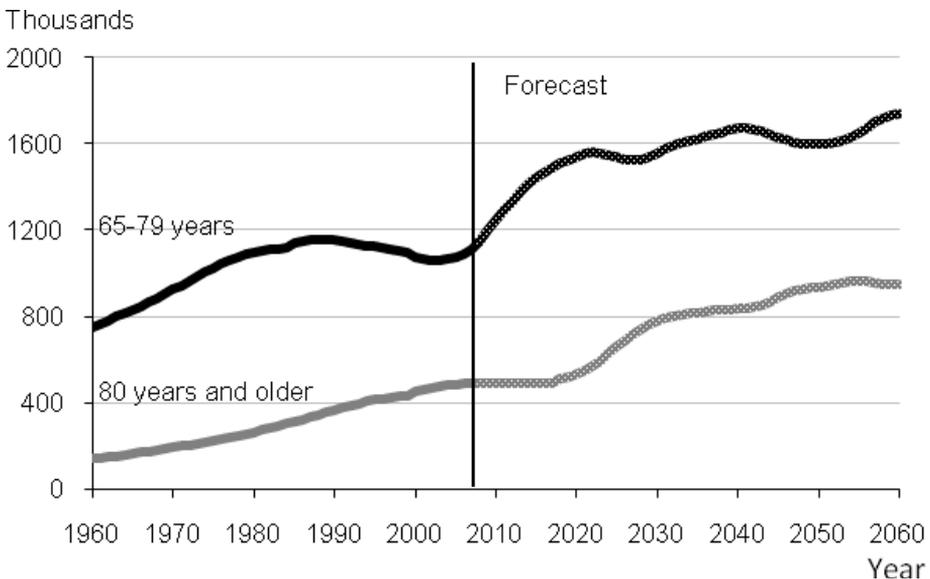
Figure 1. Demographic prognosis for Sweden (Statistics Sweden 2009).

The Swedish priority setting case

Priority setting can be described as a process to determine what is important and should be given special attention [Kenny and Joffres 2008]. In a healthcare context the following summary can be offered: "a more or less systematic approach to distributing the available resources among demands to fashion the best healthcare system possible, given the constraints." [Hauck et al. 2004].

Parliamentary decisions

In 1992, the Swedish Government launched a parliamentary commission to define the role of health services in a welfare society, focusing on the ethical principles that should guide the prioritisation of health resources [Ministry of Health and Social Affairs 1995]. The primary motive was the expected growing gap between healthcare demands and available societal resources. The primary outcome of the Priority Commission was formulated in the ethical platform, which contains basic ethical principles in hierarchical order and the same ethical principles should govern all priority setting levels [Ministry of Health and Social Affairs 1995]. A parliamentary decision in 1997 ratified the Commission's proposal and the Health and Medical Services Act was amended accordingly [The Swedish Parliament 1997].

Ethical platform. The basic ethical principles, in descending order, are:

- *The principle of human dignity*. All individuals have equal value and rights irrespective of personal characteristics and position in society.

- *The principles of need and solidarity*. Resources should be used in domains (or patients) where needs are considered to be greatest.

- *The principle of cost-effectiveness*. One should aim at a reasonable relation between cost and effect, i.e. resources should be used in the most effective way without neglecting fundamental tasks concerning improving health and quality of life.

The Commission pointed out that care for groups of patients with severe chronic disease, particularly at the end of life, and care for people with reduced autonomy are underfunded compared to care for less-severe acute and chronic disease. Consequently, both the Commission and the governmental proposition stated that it is important to emphasise severe chronic diseases [Ministry of Health and Social Affairs 1995; Ministry of Health and Social Affairs 1997]. On the other hand, according to the Committee on Health and Welfare, a determination of the need for care in each individual case must be based on conditions specific to the case [The Committee on Health and Welfare 1997].

The Commission pointed out unacceptable prioritisation principles, e.g. high chronological age per se should not be used as a basis for prioritisation. However, it also stated that chronological age determined by birth date should be distinguished from biological age involving medical judgment. Hence, although it is unacceptable to treat an individual solely on grounds of chronological age, the ability to benefit from treatment must be included in the decision, i.e. one does not need a treatment that one cannot potentially benefit from [Ministry of Health and Social Affairs 1997].

It has been argued that both the Parliament and the Commission emphasised an egalitarian value-base of priority setting, including a focus on distributive justice [Waldau 2010], e.g. with reference to John Rawls´ theory of justice [Rawls 1971]. Basically, I would agree, since the parliamentary decision clearly focuses on solidarity with groups and individuals perceived to be weak (e.g. elderly with severe chronic disease). This can be interpreted to mean that "…patients with more severe conditions should be able to receive treatment interventions that cost substantially more per health benefit compared to those with less severe disorders. In practise, this means that society is more willing to pay more per life-year gained or per quality-adjusted life-year gained for more severe conditions versus treatment for minor conditions" [Carlsson et al. 2007]. However, a few questions remain: When are the costs for the treatment of particular conditions considered to be too high to be acceptable? When is the probability for positive treatment effects in patients considered to be too low to be acceptable?

According to the parliamentary decision, the cost-effectiveness principle should be applied at the group level, not at the individual level. [The Swedish Parliament 1997; The National Centre for Priority Setting in Health Care 2007]. Furthermore, the Government stated that "…cost-effective delivery of services must never mean denying care or reducing the quality of care for the dying, severely and chronically ill, elderly, or people with dementia, developmental disabilities, severe functional impairment, or others in similar situations" [Ministry of Health and Social Affairs 1997]. On the other hand the Government stated that "… a cost-effectiveness principle that concerns choices between different interventions for the individual patient must be applied as proposed by the Commission, and is subordinate to the principles of human dignity and needs and solidarity. Nevertheless it is essential for health services to strive for high cost effectiveness as regards healthcare services in general and it is desirable that…the resources can benefit many"[Ministry of Health and Social Affairs 1997]. Moreover, the parliament's guidelines for the Pharmaceutical Benefits Board (LFN) state that the agency in its priority setting (drug subsidies) should determine whether the drug is cost-effective from a societal perspective, thus weighing cost effectiveness against the other principles in the ethical platform [Ministry of Health and Social Affairs 2002].

From an international perspective, the three ethical prioritisation principles described above are common in other countries [Melin 2007; The National Centre for Priority Setting in Health Care 2007; Kenny and Joffres 2008] and so are the three key criteria that have been derived from the principles, i.e. severity of the health condition, patient benefit-risk ratio, and the cost effectiveness of the intervention [Ministry of Health and Social Affairs 1995; Sabik and Lie 2008]. However, a report concluded that unlike Sweden, other countries do not strictly rank the ethical principles, and do not explicitly dismiss the benefit principle i.e. that interventions yielding the greatest collective benefit should be chosen [Melin 2007]. On the other hand, one could argue that since those countries address and often empasise the severity of the health condition, they do not advocate a strict use of the benefit principle either. Furthermore, in Sweden the assumption is that one does not need a treatment that one cannot potentially benefit from [Ministry of Health and Social Affairs 1997], and the patient benefit-risk ratio is considered crucial when operationalising priority setting.

Implementation of the parliamentary decisions

In addressing strategies to operationalise the contents of the parliamentary decision I will focus on the the National Board of Health and Welfare (the Board), the National Model for Transparent Vertical Prioritisation in Swedish Health Care (the Model), and evidence-based guidelines. The parliamentary decision on priority setting explicitly emphasised the role of the Board, which has taken important initiatives to interpret and implement the contents of the decision. The Board has aimed to facilitate knowledge management and contribute methodological support by developing quality indicators for appropriate care. Hence, care should be evidence based and effective, patient-focused and secure, offered on equal terms and timely [The National Board of Health and Welfare 2005].

In collaboration with organizations representing healthcare professionals, the Board and the National Centre for Priority Setting in Health Care developed a model to support vertical priority setting, e.g. drawing up guidelines. Although the Model primarily aims to guide policy decisions concerning groups of patients, it is assumed, indirectly, to provide support and guidance for decisions regarding individual patients, i.e. including microlevel priority setting [Carlsson et. al. 2007]. In drawing up guidelines by applying the Model several major steps can distinguished: First, the area for priority setting is defined. Then medical conditions and medical actions are paired, forming prioritisation objects. Experts review current scientific knowledge and information about the severity of the condition, patient benefit-risk and cost effectiveness. Finally, a consensus process is used to rank each prioritisation object on the basis of the following four aspects: valuation of the degree of severity of the medical condition (the needs of the patient group), the expected results of the action (patient benefit-risk), the cost effectiveness of the category, and the degree of evidence. In cases where information on cost effectiveness is inadequate, one can appraise only the severity level of the condition and patient benefit-risk ratio related to the action. The consequences of this ranking are not determined in advance, but it can serve as a basis for resource allocation or for rationing [Carlsson et al. 2007; The National Board of Health and Welfare 2008].

Health condition	Intervention	Severity of the condition	Effects of the intervention	Quality of facts	Costs/health gain	Quality of facts	Ranking	Comments

Figure 2. Work sheet for facts and ranking (The Model).

That which is ranked is referred to as the prioritisation object, which denotes a combination of a health condition and an intervention. Prioritisation objects should be formulated with regard to their clinical relevance. In determining a suitable level of detail for prioritization objects,

one has to balance precision and practical management. Categorisation is suggested to focus on typical cases, including common patients and interventions representing large volumes, as well as controversial issues including ethical dilemmas [Carlsson et al. 2007].

Evidence based medicine (EBM) is another key concept in the Swedish and international context of priority setting. EBM is usually defined as "a systematic approach to clinical problem solving which allows the integration of the best available research evidence with clinical expertise and patient values'' [Sackett et al. 2000]. Sweden's Health and Medical Services Act states that health care shall be given in accordance with science and clinical experience. EBM could be regarded as a refinement of this approach [Werkö et al. 2002; Balthussen and Niessen 2006]. In the 1990s, evidence-based guidelines became a common instrument in implementing EBM in many Western countries [Gabbay and LeMay 2011]. However, few countries have combined this strategy with transparent priority setting as in Sweden. Since 2000, the Board has been commissioned by the Government to draw up evidence-based guidelines to support priority setting in health care. The guidelines are expected to influence healthcare policy-making and clinical decision-making. The model for vertical priority setting, described above, functions as methodological support. The first guidelines on the care of heart disease were published in 2004, and a second generation of these guidelines was published in 2008. The guidelines have been compared with the American and European heart disease guidelines, focusing on a few differences, e.g. in the Swedish guidelines health economy is more explicitly addressed [Wallentin et al. 2008]. Other medical areas have undergone a similar process, e.g. cancer, cerebrovascular disease, and chronic obstructive pulmonary disease. To date, guidelines have been drawn up in 11 areas.

Moreover, other stakeholders and decisions on healthcare priority setting may have had a significant impact on the prioritisation process. Although a comprehensive description lies beyond the scope of this thesis, several stakeholders on the national level can be mentioned, e.g. the Dental and Pharmaceutical Benefits Agency (TLV) (earlier the Pharmaceutical Benefits Board (LFN)). Furthermore, the National Centre for Priority Setting in Health Care, formed in 2001, has focused on developing transparent prioritisation processes in health care and social services, while the Swedish Council on Technology Assessment in Health Care (SBU) has played an indirect but important role by systematically reviewing the scientific literature.

Obstacles for priority setting

Despite the aforementioned initiatives and other observed positive changes, crucial problems have been described regarding the implementation of priority setting in Sweden [e.g. The National Centre for Priority Setting in Health Care 2007]. Although some of these obstacles may relate primarily to a Swedish context, most of them are probably generalisable to other countries. The problems can be attributed to various domains, e.g. the political and legislative

framework including parliamentary decisions, implementation measures, and clinical matters at the micro level, i.e. including complex clinical practise. Those areas are seldom clearly distinguishable.

In 2006 the Board commissioned the National Centre for Priority Setting in Health Care to conduct a survey addressing the implementation of the Parliament's resolution. Its conclusions were largely similar to those drawn in earlier surveys by the Board (1999) and the Priorities Delegation (2001) respectively [The National Centre for Priority Setting in Health Care 2007; Waldau 2010], briefly summarised here in a slightly revised version. Strategies and consistent working methods to operationalise prioritisation are still lacking in county councils and municipalities. Generally, political decisions regarding priority setting are not transparent. Healthcare professionals at the micro level must assume the greatest responsibility. Healthcare staff still appear to be relatively unaware of the ethical principles intended to guide priority setting in care. Several of the most urgent areas for prioritisation, e.g. care of the elderly, affect both the county councils and the municipalities, but joint prioritisation efforts rarely take place between these governing bodies.

Problems in constructing useable priority setting in a Scandinavian context had been described earlier; particularly when evidence is sparse, when patient groups are not satisfactorily defined, when interpretation of the term *patient need* is unclear, and when uncertainty prevails on how to weigh different ethical values, especially concerning the aims of health care [Social- og Helsedepartementet 1997].

To some extent such problems could be attributed to an ambiguous message from the state, a matter described in a recent thesis [Tinghög 2011]. While the parliamentary priority setting decision has an egalitarian focus, including the hierarchical order of ethical principles, other political decisions at the macro level with priority setting implications may point in other directions, e.g. the parliamentary decision regarding the requirement for timely assessment of healthcare needs for all patients (later operationalised by the so-called "maximum waiting time guarantee"). This potentially reflects the view that the resources should benefit many, and the consequences of the decision were recently criticized by the medical profession as being unethical [Karlberg and Brinkmo 2009; Wedin 2011]. It has also been stated that there may be a need for clearer guidelines [Werntoft and Edberg 2009].

I would argue however that Sweden, by international comparison, is relatively well equipped with the prerequisites for healthcare priority setting. The Board, the National Centre for Priority Setting in Health Care, professional organizations, and a few county councils have taken important steps to assure implementation of the political intentions. By these steps, one can argue that processes beyond estimation of healthcare needs and EBM have been incorporated in practise, including construction of guidelines and evaluation of results, e.g. health economy and health technology assessment. In a sense, a sort of "multicriteria approach" is practiced [Balthussen and Niessen 2006].

On the other hand, obstacles continue to challenge the practical application of appropriate priority setting. I would suggest that such obstacles are, to a large extent, found at the micro level. Recently, several were comprehensively described, e.g. individual and organisational hindrances, lack of clinical applicability of evidence, inborn conflict between probabalistic science and the need to individualise treatment, and the tremendous complexity of clinical practise [Gabbay and Le May 2011]. Such obstacles are likely to remain even in a system of perfect meso- and macro-level priority-setting mechanisms.

THE STUDY OBJECT

The study object comprises priority setting for elderly patients with complex needs; study I in the context of acute cardiovascular disease, study II in the context of non-ST-elevation acute coronary syndrome (NSTE ACS) including non-ST-elevation myocardial infarction (NSTEMI) and unstable angina, and in studies III and IV in the context of NSTEMI.

Why study this object?

A matter of prior thinking and interest. As a clinician, I have practical experience in the medical and ethical challenges addressed in this thesis, i.e. microlevel priority setting for elderly patients with complex needs. To make the study manageable as a dissertation project I have focused on elderly NSTEMI patients. In this context, I consider my background as a cardiologist and internist to be an advantage, mindful that the task requires striking a balance between getting close enough to and remaining distant enough from the subject matter to maintain objectivity.

A matter of a typical case in terms of priority setting obstacles. The case may illustrate most of the priority setting problems described above, particularly at the micro level, i.e. when evidence is sparse, when patient groups are not satisfactorily defined, when interpretation of the term *patient need* is not clear, and when uncertainty prevails on how to weigh different ethical values.

A matter of volume and costs. Due to well-known epidemiological and demographic reasons, the group of elderly patients with complex needs is large. The parliamentary decision of 1997 acknowledged considerable deficits in the care of elderly with complex needs. Recently, the Swedish Government stated that the care for elderly with complex healthcare needs remains underfunded, though it should be highly prioritised and they announced a national investment of 3.75 billion Swedish kronor (SEK) for this group [Hägglund and Larsson 2011]. Cardiovascular disease is common among elderly patients.

A matter of a two-way, critical case. Cardiology is an area known to have a strong evidence base. The first national guidelines in Sweden addressed the care of heart disease. Hence, one could argue that if problems exist with microlevel priority setting of complex cases in this area, such problems are probably not less prevalent in other areas. Likewise, one could reasonably argue that reasonably the prerequisites for achieving solutions may be favourable in the area of cardiology. Hence, if we find it impossible to manage clinical microlevel priority setting for complex cardiology cases at the policy level, then we are likely to find this impossible in other areas as well. If so, microlevel priority setting for complex cases would in practise become a matter of individual decision-making.

Elderly patients with complex needs in a cardiovascular context

Cardiovascular disease (CVD) constitutes a common disease group affecting elderly patients and is the leading cause of death [Fitchett and Rockwood 2002; The National Board of Health and Welfare 2009]. Heart disease is known to have a greater impact on elderly patients than in a younger population, due in part to age-related cardiovascular changes, e.g. left ventricular diastolic dysfunction, increased cardiac afterload and decreased arterial compliance [American Heart Association 2007]. The consequences of cardiovascular disease in the elderly are influenced by reduced homeostatic reserves, increased comorbidity, polypharmacy, and social issues such as social deprivation [Fitchett and Rockwood 2002].

In a primary care study of elderly individuals in general (aged 65 years or older), 97% of males and 99% of females had two or more chronic conditions/diseases [Fortin et al. 2005]. The literature also reports on increasing morbidity among older people in general [Hughes et al. 2008]. In a study of community-dwelling elderly (aged 65 years or older) individuals with ischaemic heart disease (IHD), 90% were reported to have three or more chronic conditions, with a mean of five chronic conditions [Bierman 2004]. In health care, individuals with multiple coexisting diseases are the norm rather than the exception [Starfield 2006]. About 80% of Medicare spending involves the care of patients with four or more chronic conditions, and the costs increase exponentially as the numbers of chronic conditions increase [Wolf et al. 2002; Anderson 2007; Valderas et al. 2009].

One study group reported that 8.5% of acute myocardial infarction (AMI) patients had at least one acute life-threatening, non-cardiac, comorbid condition at admission, e.g. bleeding, stroke, or severe infection, and an additional 19.5% presented with at least one acute severe (though not life-threatening) non-cardiac, comorbid condition, e.g. delirium, acute renal failure, or metabolic derangements, and a later study reported similar results [Lichtman et al. 2006; Lichtman et al. 2007]. Additionally, many AMI patients have been reported to manifest a great burden of *chronic,* severe, non-cardiac and cardiac comorbid conditions [American Heart Association 2007; Singh et al. 2008]. Those conditions have been shown to be strong markers of risk, but neither guidelines nor textbooks comprehensively address this issue.

Acute cardiovascular disease including NSTEMI

Most CVDs have both chronic and acute manifestations, and they have common risk factors and aetiology. Among the most common acute manifestations of CVD are acute ischaemic heart disease, arrhythmias, and acute heart failure.

In Western countries, IHD remains a major cause of death, although mortality from myocardial infarction and other cardiovascular causes has declined in recent decades with the

identification of risk factors and development and introduction of new pharmacotherapies and coronary interventions [British Department of Health 2008; Hillis and Lange 2009].

The underlying cause of coronary artery disease (CAD) and its clinical manifestations is the development of cholesterol-rich plaque within the walls of coronary arteries (atherosclerosis). The myocardium is supplied with oxygen and nutriments by blood flowing through the coronary arteries. If the blood flow is markedly reduced, ischaemia can result in ischaemic chest pain, electrocardiogram (ECG) changes, and the release of biochemical markers detectable in peripheral blood [NICE 2010; Gray 2010]. Symptomatic IHD can be divided into various entities (Figure).
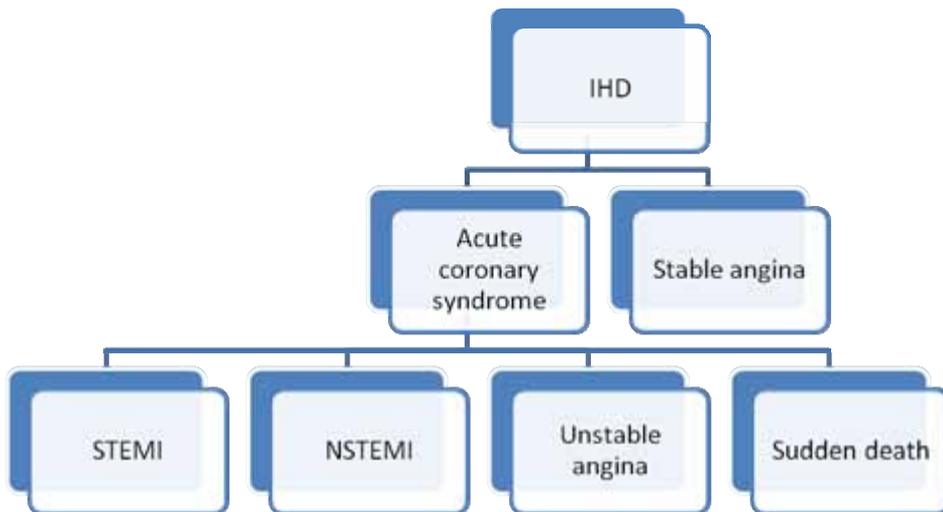

Figure 3. Classification of ischaemic heart disease. IHD=Ischaemic heart disease; STEMI=ST-elevation myocardial infarction; NSTEMI=non-ST-elevation myocardial infarction.

NSTEMI is caused by prolonged myocardial ischaemia and is differentiated from unstable angina by permanent myocardial damage and elevated levels of biochemical markers indicating myocardial necrosis. NSTEMI and its subclasses are defined according to consensus statements [Thygesen et al. 2007]. The term NSTE ACS denotes NSTEMI and unstable angina.

The diagnosis of NSTEMI relies primarily on the following: physical examination, ECG, biochemical markers and coronary angiography. Coronary angiography is the "gold standard" and provides information about the presence, site, and severity of CAD.

Basically, the treatment of NSTEMI patients aims to relieve symptoms, limit myocardial damage, and prevent future coronary events. Main components in drug treatment are anti-ischaemic agents, anti-thrombin therapy, coagulation inhibitors, and antiplatelet inhibition.

Furthermore, coronary revascularisation plays a crucial role in treating recurrent and ongoing myocardial ischaemia and avoiding progression to transmural myocardial infarction and death. Coronary revascularisation is performed either by percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Two treatment strategies have evolved; a medical, non-invasive strategy with revascularisation only in case of recurrent ischaemia (or ischaemia at predischarge stress test), or early coronary angiography followed by revascularisation, if appropriate. The early invasive strategy has been frequently advocated and used in recent years, based on well-known trials [e.g. FRISCII]. The clinical decision to perform or not perform coronary angiography for an NSTEMI patient can be regarded as crucial [Gray 2010; NICE 2010; Metha et al. 2009; Hillis and Lange 2009].

It is also evident that people with NSTEMI have quite varying outcomes. Considerable effort has gone into defining the clinical components that predict poor outcome, e.g. in-hospital mortality. In attempting to risk-stratify patients, several scoring systems [e.g. GRACE, PURSUIT, and FRISC] have been developed, and trials of drugs and other interventions such as coronary angiography and revascularisation have analysed the effect of an intervention by patient risk group [Gray 2010; NICE 2010]. On the other hand, what is regarded as an oversimplified use of risk scores in guidelines has been criticised [e.g. Glancy 2010; Roberts et al. 2010].

Clinical trials on NSTEMI patients have shown that as the underlying risk increases, the potential for an intervention to provide benefit, i.e. by avoiding adverse outcomes, also increases. However, the risk of major bleeding, which *per se* is an important predictor of poor outcome, and other complications, may similarly increase with underlying risk [American Heart Association 2007; Gray 2010; NICE 2010]. As the National Institute for Health and Clinical Excellence (NICE) puts it, this constitutes a dilemma: Should one offer a particular combination of drugs, each with individual evidence of benefit, to an individual patient, or will the potential for complications outweigh the combinations' benefit? This question probably highlights a general dilemma in treating elderly patients with complex needs.

A consensus document [American Heart Association 2007] concluded that elderly NSTEMI patients show a disproportionately lower use of cardiovascular interventions. Reasons included limited data from trials and uncertainty about risks and benefits in the elderly (aged 75-80 years or older). Regarding elderly NSTEMI patients, and probably other elderly patient groups, increased risk denotes potentially greater benefits of intervention, but also potentially greater risk for complications and side effects related to the intervention itself. Recently, publications have emphasised the importance of assessing the potential for treatment benefits and treatment-related complications - not merely from cardiovascular risk, but also from other conditions [American Heart Association 2007; Gray 2010]. This act of balancing is complex and often has to be performed in the absence of a distinct evidence base and through individualised clinical management [Gray 2010].

What characterises the needs that are relevant for priority setting as it relates to elderly patients with complex needs? Obviously we do not need to address all needs distinct from the

the needs connected with an index condition. However we should address complex needs that impact on the severity level of the health condition and the expected benefit-risk ratio of an intervention. Accordingly, the crucial research issue would be to categorise those complex needs in an appropriate and clinically relevant way, balancing precision and manageability.

CONCEPTUAL FRAMEWORK

This section aims to define terms that connote concepts perceived to be crucial in the context of this thesis. Basically, and slightly revised, it follows the model for concept analysis proposed by Walker and Avant, including the following key steps: choosing aim and objective related to the analysis; identifying defining attributes and alternative meanings of the concept; identifying related and opposite concepts distinct from that being studied; and defining consequences of and empirical references to the concept [Walker and Avant 2005].

Priority setting

The domains of law, philosophy, political science, medicine, and economics are all contributers to the field of priority setting [Martin and Singer 2000]. Furthermore, choosing between competing values makes priority setting an ethical issue [Singer and Mapa 1998; Sibbald et al. 2009]. The National Encyclopaedia's formulation "to give preference to" captures the core of the concept of priority setting. In a healthcare context the following summary can be offered: "a more or less systematic approach to distributing the available resources among demands to fashion the best healthcare system possible, given the constraints." [Hauck et al. 2004]. Related concepts are rationing and resource allocation. Rationing presupposes scarcity and concerns the controlled distribution of scarce resources by limiting the possibilities to fully meet the need, while resource allocation is more neutral towards the amount of available resources and involves a conscious decision to divide something and to distribute the shares to the recipients [Liss 2002; Sibbald et al. 2009; Martin and Singer 2003].

It has been stipulated that for a choice to be regarded as a priority it should involve an ordered ranking of the alternatives. Furthermore, the alternatives must be considered, and they must be relevant, i.e. viable options that could actually be considered [Liss 2002]. That which is ranked, i.e. one of the alternatives, can be referred to as a prioritisation object. In the Model the prioritisation object denotes a combination of a health condition and an intervention. The rank order could be used to determine the option of being allocated new resources or the option of being rationed. The concept can be limited to the act of putting something first or forward, and does not specify any consequences, as the case with like rationing or limiting [Liss 2002; Carlsson 2007 et al]. This seems to be a reasonable distinction.

Priority setting has been described as extremely complex, like "a series of unconnected experiments with no systematic mechanism for capturing the lessons..."[Martin and Singer 2000], and with a lack of consensus about which values should guide decisions [Holm 1998]. Accordingly, we find many discipline-specific approaches and priority-setting frameworks with various foci, e.g. evidence based medicine (EBM) (effectiveness), health economy (efficiency), equity analysis (equity), policy approaches (legitimacy), as well as interdisciplinary approaches, e.g. health technology assessment [Sibbald et al. 2009].

Furthermore, priority setting has been described as an ad hoc process, leading to suboptimal use of resources, while instead a comprehensive multi-criteria approach has been proposed. [Balthussen and Niessen 2006; Sibbald et al. 2009].

The concept of priority setting can be classified in various ways:

Degree of transparency. It can be explicit or implicit. Explicit prioritisation establishes clear priorities, basing the decisions on agreed-on priorities and making the basis for these priorities transparent. Implicit prioritisation lacks clarity regarding the priorities [Kenny and Joffres 2008]. Although implicit priority setting has been the historical norm, and advocated by a few authors [Ham 1997; Mechanic 1997], many authors in the field stress openness as a core value [Holm 1998; Balthussen and Niessen 2006; Coast et al. 1996; Daniels 2000].

Vertical or horizontal rankings. Priority setting can be considered as *vertical*, i.e. regarding patients within the same disease group or professional speciality area but with different levels of need, or *horizontal*, i.e. between patients in different disease areas. However, the distinction between the two types of priority setting remains unclear [Ham 1997; The National Centre for Priority Setting in Health Care 2007], e.g. due to the fact that many patients have comorbid conditions in various disease areas.

Stakeholders. Health care professionals, managers and politicians generally are considered be the main decision-making stakeholders in the priority setting process. However, actions taken and some research areas concerns how to involve patients and the public in the decision-making process [Waldau 2010; Ham 1993; Wiseman et al. 2003].

Organisational levels. Priority setting concerning health care occurs at all levels in society, but three levels are usually mentioned [Martin and Singer 2003; Kapiriri and Martin 2007; Kenny and Joffres 2008; Sibbald et al. 2009]. Decisions regarding how much to spend on individual patients could be labelled *microlevel priority setting*, which is primarily considered to be a clinical matter. Decisions concerning the distribution of resources between organizations, institutions, geographical areas, and services could be labelled *mesolevel priority setting* which is primarily a matter for health care managers. Decisions regarding the level of resources to be allocated to health services (e.g., versus education or military defence) could be labelled *macrolevel priority setting* which is primarily a concern of politicians.

Importantly, these three levels of priority setting are interrelated [Kenny and Joffres 2008], though there may be relatively little interaction between the decision makers at the different levels [Sibbald et al. 2009]. It should be emphasised that there is indeed a microlevel priority setting level [Sulmasy 1992; Ridderstolpe et al. 2003; Kapiriri and Martin 2007; Walton et al.2007; Arvidsson et al. 2010; Kenny and Joffres 2008]. Priority setting of health interventions is often ad-hoc [Balthussen and Niessen 2006]. It has been argued that a substantial amount of priority setting takes place on the micro level and often the evidence base provides relatively limited guidance for those decisions [Gabbay and LeMay 2011].

Ethical value base. Finally, priority setting could be classified in terms of its value base, e.g. the Swedish ethical platform, and the ethical dilemmas that are addressed. Although progress has been made in the last decade to develop theoretical frameworks to guide and evaluate priority setting, there is no international consensus concerning on the values that should guide priority setting decisions [Sibbald et al. 2010]. These dilemmas often include tradeoffs between equity and effectiveness [Daniels and Sabin 2002; Martin et al. 2002; Gibson et al. 2005]. In this context, equity refers to distributive justice of health or health care resources, while effectiveness often implies health maximization [Hauck et al. 2004].

Priority setting principles and criteria

The ranking of relevant and considered alternatives can be guided by specified priority setting principles and criteria. From an international perspective, the three ethical prioritisation principles (the ethical platform) described above, i.e. the principle of human dignity, the principle of need and solidarity, and the principle of cost-effectiveness, are common in other countries [Melin 2007; The National Centre for Priority Setting in Health Care 2007; Kenny and Joffres 2008], so are three key priority setting criteria that have been derived from these principles, i.e. the severity of the health condition, the patient benefit-risk ratio, and the cost-effectiveness of the intervention [The Ministry of Health and Social Affairs 1995; The National Centre for Priority Setting in Health Care 2007; Sabik and Lie 2008].

Severity of a health condition. Appraising the severity level of a health condition for a defined patient group involves weighing the current condition (including suffering, degree of functional impairment, and quality of life) and future risks (including prognosis regarding risk for premature death, disability, or continued suffering and impaired health-related quality of life).

Patient benefit-risk. The expected benefit is determined according to the effects of the intervention on the current health condition and future risks. Furthermore, the risk for side effects and complications from the intervention per se must be determined and weighed. This appraisal is usually based on the estimated average (not aggregated) expected benefit for a group of patients with a medical condition.

Cost-effectiveness. It is relevant to identify differences in costs and effects regarding two or more alternatives, and most cost-effectiveness analyses (CEA) use a ratio to describe the extra cost for achieving an extra health gain. Health economic data on cost-effectiveness is presented preferably as cost per quality-adjusted life-year gained (QALY).

Evidence based medicine

EBM is usually defined as "a systematic approach to clinical problem solving which allows the integration of the best available research evidence with clinical expertise and patient values" [Sackett et al. 2000]. Although the EBM concept took root in the 1990s [e.g. Sackett 2000; Gabbay and LeMay 2011], many authors have dated the development of EBM, recognised as a rational use of interventions with established effectiveness, much earlier - in fact, back to the beginning of the 20th century [Niessen et al. 2000; Claridge and Fabian 2005; Balthussen and Niessen 2006]. The Swedish Health and Medical Services Act states that health care shall be given in accord with science and clinical experience. EBM could be regarded as a practical refinement of this internationally long-established view [Levi 1998; Werkö et al. 2002; Balthussen and Niessen 2006]. EBM aims to assess the quality of evidence in relation to the risks and benefits of treatments [Sackett et al. 1996]. It emphasises deductive

reasoning, i.e. clinical decisions are properly made as one draws conclusions from the best available scientific base [Sackett et al. 2000]. The core values of EBM include the use of clinically relevant outcome measures, confidence intervals, appropriate randomisation and blinding procedures in studies, and a focus on absolute rather than relative risk reduction [e.g. Guyatt and Rennie 1993]. EBM can be contrasted with the term "eminence-based medicine", in which decisions rely primarily on expert opinions. However, EBM does not exclude using analogue reasoning, e.g. the intuitive recognition of similar cases or patterns, which in fact has been shown and reported to be crucial for experienced clinicians' decision making [Schmidt et al. 1990; Asplund 2001].
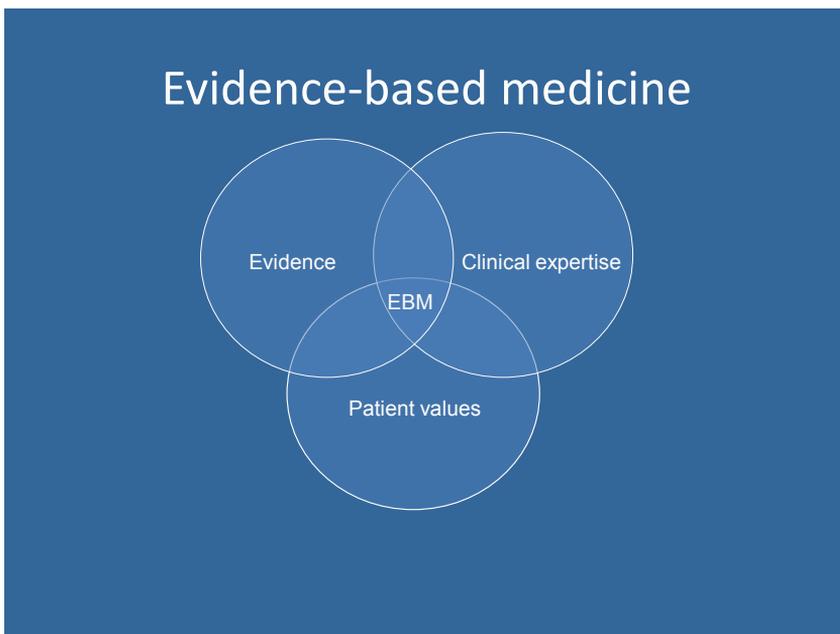

Figure 4. The components of evidence-based medicine (Sackett et al. 2000).

In the 1990s, evidence-based guidelines became a key instrument in implementing EBM in many Western countries [Gabbay and LeMay 2011] aiming to support clinicians in decision making [Guyatt et al. 2000]. By increasing provider compliance with evidence-based guidelines, the aim is to optimise benefits to patients with specific diseases. These benefits have been well documented [US National Committee for Quality Assurance 2003; Tinetti et al. 2004]. Randomised controlled trials (RCTs) and systematic reviews have been crucial in developing guidelines, providing the most reliable data. However, systematic reviews and RCTs primarily tend to focus primarily on internal validity [Altman et al. 2001; Anderson et al. 2004], while their external validity and generalisability, i.e. whether the results can be

applied to patients in a clinical setting in routine practise, have been questioned [Rothwell 2005; Green 2006; Tinetti et al. 2004, Toerien 2009; Ahmad et al. 2010].

Needs

Most stakeholders in health care would agree that assessing needs is crucial in priority setting. But how should the concept of need be interpreted in this context, and what components does it comprise? This issue has been thoroughly analysed by Liss, whose conclusions influence the following definitions. Health need can be defined as the gap between current health status and desired health status [e.g. Liss 1993]. In appraising the gap, i.e. the severity level of a health status for a defined patient group, one weighs the current condition (including suffering, degree of functional impairment, and quality of life) *and* future risks (including prognosis of risk for premature death, disability, or continued suffering and impaired health-related quality of life).

The concept of health *care* need has two prerequisites: the gap between current health state and desired health state (the health need), i.e. influenced by the severity level of the condition, *and* the potential for the intervention to reduce this gap, i.e. the potential to benefit. One does not need a treatment that one cannot potentially benefit from [Ministry of Health and Social Affairs 1997; The National Centre for Priority Setting in Health Care 2007]. Similarly, when no intervention exists that can potentially reduce the gap between the current health state and the desired health state, there is no health care need (although of course there is a health need).
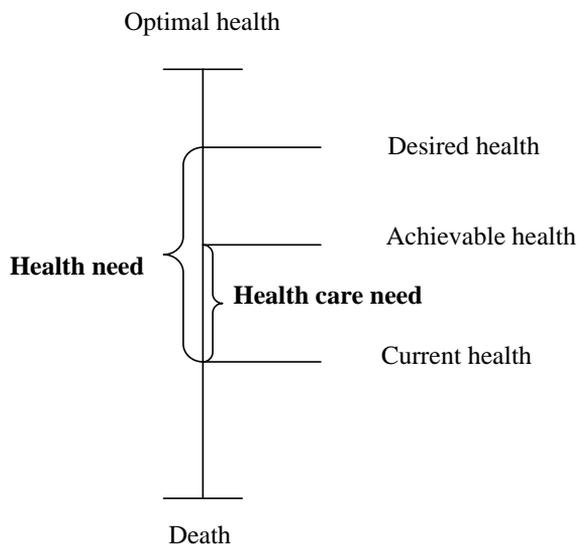

Figure 5. Description of the concept of health care need (Liss 2004).

However, in this context several questions seem justified: What would be a reasonable probability of benefit of an intervention for an individual or a group of patients justifying a health care need to arise by definition? How should the potential benefit of an intervention be weighed against its potential negative effects, i.e. side effects and complications? I would suggest that clinical practice often involves a substantial amount of uncertainty regarding such matters. One could argue that in a priority setting context we must deal with supposed average benefits for groups of patients. But what if large subgroups within a total group of patients with the specified index condition have strongly deviating (from the average) benefit-risk ratios?

# Complex needs with particular attention to comorbidity and frailty

How should complex needs (or complex health *care* needs) be defined and classified? What are the characteristics of individuals with complex needs? Statistically, there is an obvious association between higher age and more complexity and heterogeneity. But what is the potential relevance of this in priority setting?

Consensus is lacking on the definition and measurement of complex needs, comorbidity, and related constructs. Recently, Valderas et al. thoroughly discussed this issue, and their review influenced the following thoughts [Valderas et al. 2009]. Different diseases/conditions may be found in the one and same individual by three main ways: causal association, selection bias, or chance. Various constructs have been described and the value of a given construct is determined by its capacity to explain phenomena within various contexts including clinical care, epidemiology, and health services planning. The constructs, e.g. comorbidity, are associated with more complex clinical management, worse health outcomes, and increased healthcare costs [Fortin et al. 2007; Ritchie 2007].

Multimorbidity and comorbidity. Multimorbidity is often defined as "the co-occurrence of multiple chronic or acute diseases and medical conditions within one person" without any reference to an index condition [Bayliss et al. 2008]. Comorbidity is usually defined in the same way, although in relation to a specific index condition [Feinstein 1970; van den Akker et al.1998], e.g. NSTEMI. Both constructs can be used to describe the number of conditions and the character and severity of the conditions. Furthermore, various approaches have been taken to characterise the combined burden of diseases/conditions as a single measure on a scale, including the construction of different indices [de Groot et al. 2003]. Multimorbidity and comorbidity with their ability to inform patient management can be deemed appropriate in a clinical context including clinical research, i.e. microlevel priority setting, but also from an epidemiological perspective studying the genesis of concurrent diseases. However, the risk has been pointed out that the wider range of ways in which specific diseases may interact, e.g. with an intervention, may be concealed. Multimorbidity is often used in a primary care

context, while comorbidity, with its orientation towards an index disease, is considered useful in specialist care [Valderas et al. 2009].

Morbidity burden. Other measures classify patients into groups according to demographic and clinical characteristics, including age, sex, conditions, and diseases, explicitly addressing not only the presence but also the severity of different diseases, e.g. adjusted clinical groups (ACGs) [Starfield et al. 1991] and diagnosis-related groups (DRGs) [Fetter et al. 1980]. Those measures´ main purpose is to link (clusters of) diagnoses with their influence on consumption of healthcare resources. Consequently they have been considered as relevant to healthcare planning, i.e. concerning priority setting at the meso- and macro levels rather than at the micro level.
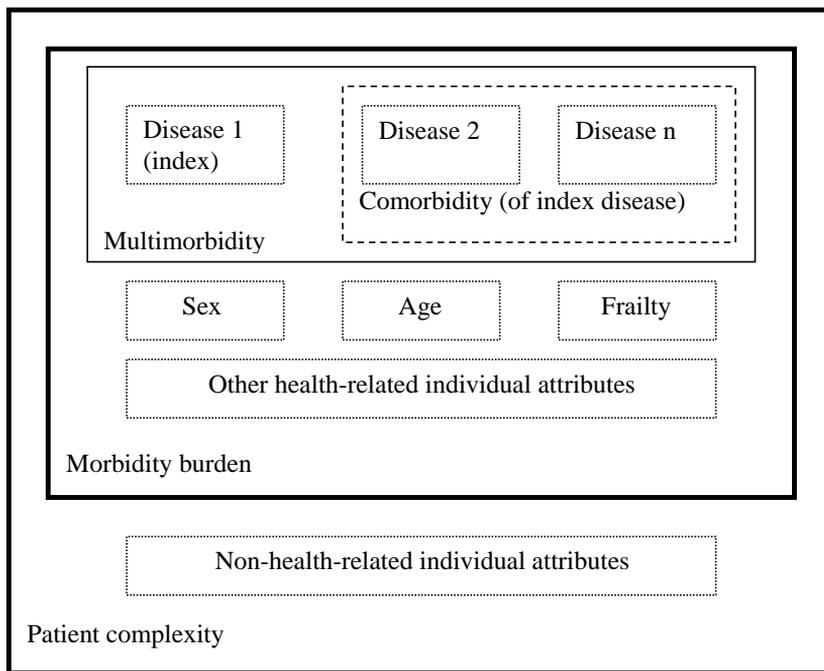
Comorbidity: presence of additional diseases in relation to an index disease in one individual.
Multimorbidity: presence of multiple diseases in one individual.
Morbidity burden: overall impact of the different diseases in an individual taking into account their severity.
Patient complexity: overall impact of the different diseases in an individual taking into account their severity and other individual attributes.

Figure 6. Constructs of complex needs (Valderas et al. 2009, slightly revised version).

Frailty. The term frailty denotes a multidimensional syndrome characterised by decreased physiologic reserves, including cognition, energy, physical ability and health, and increased vulnerability [Rockwood 1999; Fried et al. 2001; Singh et al. 2008]. In a geriatric context it has been shown that frailty stratification can predict a patient's risk of death and need for institutional care [Mitnitski et al. 2002; Rockwood et al. 2005; Lee et al. 2010] and is considered more appropriate than chronological age in determining the risk for adverse outcomes [Mitnitski et al 2002; Fitchett and Rockwood 2002]. Although the construct is well validated in a geriatric context, there is not a single, accepted, operational definition. A review identified three main types of operational definitions: rules-based, e.g. relying on whether a minimum number of predefined symptoms are present; the summing of the number of impairments; and classifications relying on clinical judgement. The Canadian Study of Health and Ageing Clinical Frailty Scale (CFS) is a 7-point scale relying on clinical judgment. It is a global clinical measure of biological age and it mixes comorbidity, disability, and cognitive impairment [Rockwood et al. 2005].

To date, frailty instruments have been used mainly in a geriatric context, but have been identified as potentially relevant for cardiac patients as well [Purser et al. 2006; American Heart Association 2007; Singh et al. 2008; Lee et al. 2010]. It has been estimated that 30% of octogenarians are frail [Fried et al. 2001; Singh et al. 2008]. Another study of elderly hospitalised patients with CAD reported that the prevalence of frailty ranged from 27% to 63%, depending on the classification scheme [Purser et al. 2006]. Despite some overlap between frailty and comorbidity, there is a clear distinction [Singh et al. 2008]. Frailty with its strong prognostic value can be deemed useful in a clinical context, but also at a healthcare policy level.

Patient complexity. Not only health-related characteristics, but also socio-economic, cultural, and environmental factors influence the morbidity burden, i.e. disease factors interact with economic and social factors, making clinical management more complicated [Nardi et al. 2007; Safford et al. 2007; Gabbay and LeMay 2011]. Patient complexity is a concept intended to address this issue, though measuring complexity remains a substantial challenge [Valderas et al. 2009]. Its main application would reasonably be at the health services level. The International Classification of Functioning, Disability, and Health (ICF) from the World Health Organisation (WHO), focuses on needs, function and activity, participation, and surrounding factors [Cieza et al. 2006]. ICF could be described as a relevant construct in this context, though it is not yet in common use or recognised in clinical practise.

Pragmatic definitions. Other definitions aim to address complex needs among elderly patients in what I would call a pragmatic way. In a Swedish context, the Centre of Epidemiology at the National Board of Health and Welfare has formulated the following definition of "multiple-diseased elderly patients": "Individuals 75 years old or older, who during the past 12 months have received inpatient hospital care three or more times and who have three or more diagnoses in three or more diagnostic groups according to the classification system ICD-10" (Gurner and Thorslund 2001; The Swedish National Board of Health and Welfare 2002).

This, and other similar definitions, could be relevant primarily at the health services planning level rather than in microlevel priority setting.

Biological age

Basically, two relevant ways are recognised in addressing age; *chronological age*, relating to birth date, and *biological age*, referring to biological status, e.g. life expectancy. The elderly population is a heterogeneous risk group reflecting a wide range of biological age for each chronological age range. In elderly people, the following have been described as main risk factors: comorbid conditions, cognitive impairment, degree of functional disability, and degree of social support [Fitchett and Rockwood 2002]. While chronological age is a reasonable indicator of the proportion of individuals in an age group who are relatively fit or frail, it is not a useful clinical tool in individual patients, due to low sensitivity and specificity [Fitchett and Rockwood 2002; Rockwood 2005]. In a geriatric context, biological age, e.g. measured by frailty, is known to be markedly more valuable than chronological age as a predictor of risk for adverse outcomes.

Thus chronological age provides information useful for population planning, while (measures of) biological age, e.g. conceptualised by frailty, may guide microlevel priority setting, including clinical guidelines and decision-making in the individual patient. In recent years various policy documents have stressed that it is crucial to assess risk by markers of biological age and comorbidities [e.g. American Heart Association 2007; NICE 2010; Gray 2010; The National Board of Health and Welfare 2008]. In a Swedish context, it has been stated that it is not acceptable to prioritise specifically on grounds of chronological age per se, but biological age and the ability to benefit from treatment should be considered in the decision, including the relation between the timeframe of an expected benefit and a patient's expected life-time. [Ministry of Health and Social Affairs 1997; The National Board of Health and Welfare 2008].

MATERIALS AND METHODS

This chapter describes the materials and methods of the four studies comprising this thesis.

Paper	Type of study	Study population	Analysis
I	Register study	57872 multiple-diseased elderly patients extracted from the National Patient Register	Frequencies
II	Survey study	Random sample of 400 Swedish cardiologists	Chi-square test Descriptive statistics Content analysis
III	Prospective clinical observational study	307 evaluable patients aged 75 years or older, with diagnosed NSTEMI, treated at three centres	Chi-square test Descriptive statistics Regression analysis Reliability test
IV	Questionnaire study	Purposeful, stratified sample of 60 Swedish cardiologists	Descriptive statistics Reliability test

Table 1. Overview of papers.

Paper I

To obtain an operational definition of multiple-diseased elderly, we conducted a literature review via various databases, e.g. MEDLINE. The following search words were used: *elderly, very elderly, frail elderly, frailty, multiple-diagnosed, multiple-diseased, multimorbidity, and comorbidity*. We chose the following definition of multiple-diseased elderly stipulated by the National Board of Health and Welfare: "Individuals 75 years old or older, who during the past 12 months have received inpatient hospital care three or more times and who have three or more diagnoses in three or more diagnostic groups according to the classification system ICD-10" (Gurner and Thorslund 2001; The Swedish National Board of Health and Welfare 2002). We argue that, in spite of its shortcomings at the clinical level, the definition's three

dimensions (age, number of diagnoses, and inpatient hospital care episodes) make it useful in quantifying and characterising patients at the hospital population level.

By the chosen definition we extracted a population, diagnosed in 2005, of elderly with multiple diseases. We focused on those patients with at least one documented episode of a cardiovascular disease. The population was characterised through the Patient Register, which is maintained by the National Board of Health and Welfare. The Patient Register is a comprehensive national register of the consumption of inpatient hospital care and is based on information from the patients' records. It contains information regarding patient characteristics, diagnoses, healthcare consumption, and major procedures for each patient and episode of care.

Furthermore, the costs of inpatient hospital care for the multiple-diseased elderly was estimated by using data from the national database on cost per patient (the KPP database) and two epidemiological reports (The National Board of Health and Welfare 2005; Swedish Association of Local Authorities and Regions 2005). Cost per patient is a method used to calculate the cost of each patient and episode of hospital care.

We based our estimation of the inpatient hospital care costs on three presumptions. First, we presumed that the age-related cost per day of inpatient hospital care for a multiple-diseased elderly patient would be similar to that of any individual aged 75 years or older. We used a template, derived from the KPP database and based on the age interval-related cost per day of inpatient hospital care. The cost per day in the age interval 75-84 years was 7 220 Swedish Kronor (SEK), and the cost per day in the interval 85 years or older was 5 895 SEK (1 Euro=9.40 SEK). Second, we presumed that the distribution of inpatient hospital care episodes in the two age intervals would be of the same proportion for the 83% of the multiple-diseased elderly patients who had manifested a cardiovascular disease (and for whom we had detailed information) as for the total number of multiple-diseased elderly patients. Third, we presumed that the distribution of inpatient hospital care episodes for the two age intervals (about which we had information) would be of the same proportion as the distribution of days of inpatient hospital care for the two age intervals.

Paper II

To assess the views of cardiologists on clinical decision-making for elderly with NSTE-ACS and multimorbidity, we conducted a confidential survey study. Before conducing the study we consulted statistical expertise to optimise the possibility of obtaining a proper sample size. The largest gain in precision was expected in the interval between 50 and 200 completed questionnaires. We projected a response rate between 50% and 60%, which we found to be a common response rate for doctors via a pilot search of earlier studies in this field. From a list of 641 cardiologists, obtained from the Swedish National Board of Health and Welfare and

the Swedish Health Care Address Register, all presumed to have dealt with multiple-diseased elderly patients with NSTE-ACS during the past year, 400 were randomly selected to receive a questionnaire via postal letter. Between September 2007 and January 2008 three distributions took place, approximately two months apart, and the questionnaires were sent with a cover letter describing the study. We conducted a nonresponder analysis via telephone.

We based the questionnaire (Appendix A) on a register study on multiple-diseased elderly patients (Paper I), a literature search, and discussions with a panel of cardiologists with experience in drawing up national guidelines. Multiple-diseased elderly were defined as follows: "Individuals 75 years of age or older, who have received inpatient hospital care three or more times during the past 12 months and who have three or more diagnoses in three or more diagnostic groups according to the ICD-10 classification system". The first part contained questions about the demographic and work-related characteristics of the physicians, and the second part consisted of nine questions regarding respondent views on evidence-based guidelines, care and priority setting for multiple-diseased elderly with NSTE-ACS, and areas of possible improvement. Throughout the questionnaire space was allocated for free comments. One hundred of the physicians received an extended version of the questionnaire with three additional open-ended questions, focusing on areas of possible improvement.

The data were quantitatively analysed using SPSS version 15. We analysed responses by using frequencies and descriptive statistics, and when appropriate, differences in proportions were assessed by chi-square tests. A content analysis was used to process the free comments and the answers to the open-ended questions.
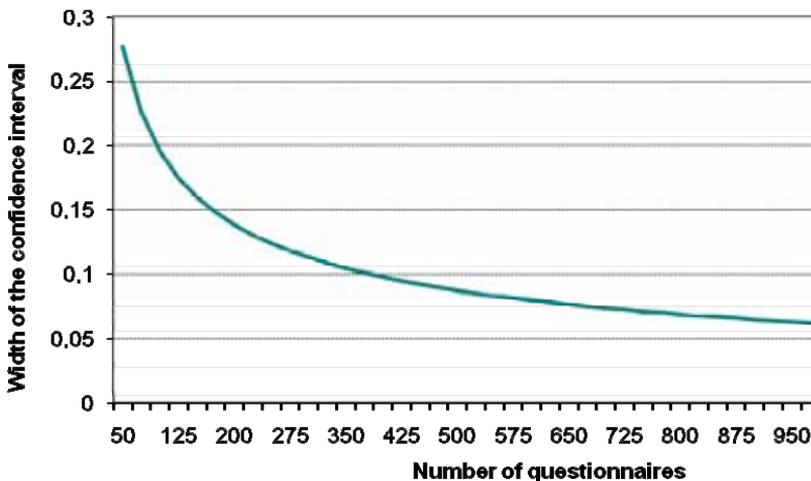

Figure 7. Precision (width 95% CI) regarding a proportion of 0,5 at different sample sizes. The largest gain of precision use to be by the interval between 50 and 200 answered questionnaires. (With permission from Marika Wenemark, statistician, Linköping University, Sweden)

Paper III

Between October 2009 and June 2010 we included 307 evaluable patients aged 75 years or older, with diagnosed NSTEMI, treated at three centres. We intended to describe a representative sample of NSTEMI patients. Frailty is an emerging concept in medicine denoting increased vulnerability and decreased physiologic reserves. The Canadian Study of Health and Aging (CSHA) Clinical Frailty Scale (CFS) is a 7-point scale with good predictive validity and prognostic power relying on clinical judgment (Appendices B and C). It can be characterised as a global clinical measure of biological age, combining comorbidity, disability, and cognitive impairment. Before launching the study, the study nurses were trained regarding frailty assessment, and then they individually assessed the frailty of 30 patients. An intra-class correlation (ICC) test indicated that the interrater reliability concerning the study nurses' judgment of frailty was very good at the individual level (ICC two-way random, consistency (30 cases, 4 raters): single measure: 0.97 (0.94-0.98, CI 95%).

There were only two exclusion criteria: if the patient was not willing to participate; or if the patient was not evaluable due to communication problems and insufficient clinical information to enable a judgment of frailty.

Potential confounders when testing the hypothesis, were the following: chronological age, sex, cardiovascular risk, myocardial infarction classification, ejection fraction, diabetes mellitus, previous myocardial infarction, and comorbidities. Cardiovascular risk (CVR) was assessed according to the FRISCII-score. The myocardial infarction was classified according to the Joint ESC/ACCF/AHA/WHF Task Force consensus statement. Echocardiography, electrocardiograms (ECGs), laboratory testing and registration of anthropometric data were performed according to routine practise. Those comorbidities with a supposed potential to change the benefit-risk ratio of intervention were registered. When one or more of the following conditions was present, the patient was considered to have severe comorbidity: severe degree of comorbidity according to consensus definitions, malignant disease, at least one complication of diabetes, an acute severe comorbid condition (i.e. bleeding, stroke, septic infection, pneumonia). Furthermore, the impact of the comorbid conditions on risk was quantified by the coronary artery disease (CAD)-specific index (Appendix D).

Follow-up was done one month after the time of inclusion via the patient files and the Causes of Death Register. The Linköping Academic Research Centre (LARC)-group at Linköping University Hospital performed study monitoring three times from study start until the first follow-up. We defined the primary outcome as the composite of death from any cause, myocardial re-infarction, revascularisation due to ischaemia, hospitalisation for any cause, major bleeding, stroke/TIA and need for dialysis up to one month after inclusion. The secondary outcome was the composite of major bleeding, stroke/TIA, and need for dialysis up to one month after inclusion.

We performed statistical analysis via SPSS version 19.0 and SAS version 9.1.3. Continuous data were compared using the Student's t-test, while categorical data were analysed by use of the chi-square test or Fisher's exact test. The association of frailty with the primary composite outcome was examined by multiple logistic regression models adjusted for relevant prognostic variables (age, sex, previous myocardial infarction, ejection fraction, cardiovascular risk, classification of myocardial infarction, and comorbidities, i.e. the score according to the CAD-index).

Paper IV

We based a tentative description (Appendix E) of the needs of elderly NSTEMI patients with multimorbidity on the following sources: a literature search; a register study on multiple-diseased elderly heart patients (Paper I); a questionnaire study on cardiologists´ decision-making for elderly with multimorbidity (Paper II); a pilot study; and discussions with a panel of cardiologists with experience in drawing up national guidelines. The description addresses the following components: disease-specific risk, comorbidity, and frailty. From this description of the needs of elderly NSTEMI patients we theoretically derived a model with eight categories. In a pilot study six expert cardiologists, who had participated in drawing up guidelines, considered 15 authentic NSTEMI cases to be realistic and the model's components to be relevant for clinical priority setting. From a theoretical standpoint and based on estimated benefit-risk ratios, a tentative relative ranking of these categories can be identified. The higher the potential benefit of the measure, with a supposed connection to the degree of cardiovascular risk, the higher the proposed ranking; the higher the intervention-related risk of complications/adverse effects, with a supposed connection to the degree of frailty and comorbidity, the lower the proposed ranking.

The study cardiologists were selected by a purposeful sampling procedure with stratification regarding sex, geographic area, and size of hospital. The six expert cardiologists in the pilot study recommended ten study cardiologists each, all deemed to be particularly competent concerning the ranking of elderly NSTEMI patients with multimorbidity. We conducted a confidential questionnaire study consisting of the 15 authentic and face-validated cases via postal letters; we added a few questions regarding the cases and the relevance of the model's components (Appendix G). Between December 2009 and April 2010 three distributions, approximately one month apart, took place. A nonresponder analysis was carried out by telephone.

We analysed the quantitative part of the data by using SPSS version 15. Responses were analysed with frequencies and descriptive statistics. An intra-class correlation test was used to estimate interrater reliability for the study experts' rankings of the cases. We used a content analysis to process the free comments and the answers to the open-ended questions.

RESULTS

Paper I

Of unique patients aged 75 years or older who consumed inpatient hospital care in 2005, 25 % were multiple-diseased elderly patients. Of all inpatient hospital care consumed by patients aged 75 years or older, these patients consumed 47 % of all days of care. Of the multiple-diseased elderly patients 81% consumed at least one care episode in internal medicine (the dominant speciality from a quantitative standpoint). Most of the multiple-diseased elderly patients were treated in county hospitals and smaller hospitals. The total annual cost of Swedish inpatient hospital care for the multiple-diseased elderly patients was estimated at SEK 11.5 billion, i.e. 19 % of the total cost of Swedish inpatient hospital care.

The multiple-diseased elderly patients had an average age of 83 years, and women dominated quantitatively in the very oldest age strata. Of the total group, 83 % manifested a cardiovascular disease. The most common non-cardiac comorbidities were as follows: cerebrovascular diseases, infections (urinary-, pulmonary-, septic- and influenza), diabetes, chronic diseases of the lower respiratory tract (chronic obstructive pulmonary disease and asthma), malignant diseases, anaemias, metabolic diseases (e.g. thyroid disorders), cognitive and mental diseases (e.g. dementia), renal insufficiency, injuries to the hip and thigh, gastric and intestinal diseases and injuries (e.g. liver insufficiency) and peripheral arterial diseases (Table).

Very elderly patients and patients with severe and/or multiple comorbid conditions are usually excluded from evidence-generating studies that form the foundation for clinical guidelines. We argue that the reported characteristics of multiple-diseased elderly patients are associated with potentially limited applicability of evidence-based guidelines, and that this can lead to both under- and overutilisation of medical interventions. We also argue in favour of future clinical studies, and for constructing an adapted model for priority setting for multiple-diseased elderly people, taking into account comorbidity and indicators of biological age, e.g. frailty.
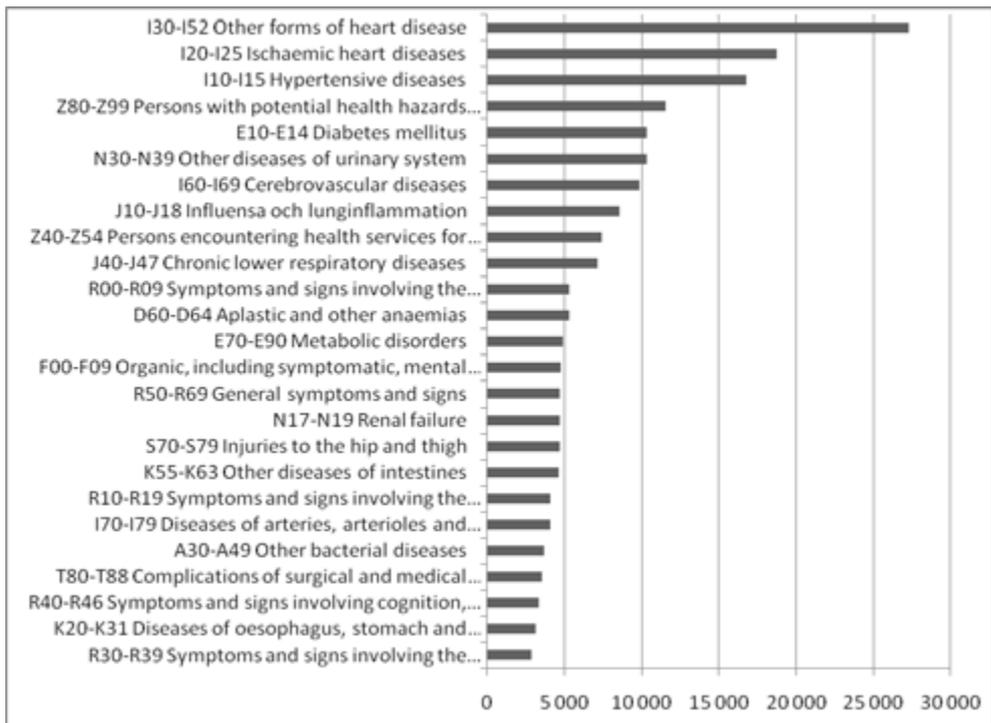
Table 2. The most common diagnostic sectors of the multiple-diseased elderly patients with cardiovascular disease (Paper I).

Paper II

Of the initial random sample of 400 cardiologists, 30 had not dealt with multiple-diseased elderly NSTE ACS patients in the past year. From the remaining 370 subjects we received 255 completed questionnaires, i.e. a total response rate of 69%. For the nonresponder analysis, we reached 21 non-responding cardiologists (of 25 randomly chosen physicians) via telephone; no one objected to the contact. This analysis did not indicate any evidently different views among the non-responding cardiologists. Approximately 50% of the respondents estimated that they treated multiple-diseased elderly patients with NSTE-ACS every day. We argue that given that 39% of all Swedish myocardial infarction patients have been reported to be over 80 years of age [Stenestrand 2008; RIKS-HIA 2008], the cardiologists' estimates concerning numbers of elderly with comorbid conditions seem realistic. Of the respondents, 81% reported extensive use of national guidelines for the treatment of NSTE-ACS patients in general (Table). However, regarding treatment of multiple-diseased elderly patients, the most frequently used sources in clinical decision-making were patient views and the individual cardiologist's own clinical experience. Several

comments and answers to open-ended questions focused on limitations in the applicability of guidelines in this clinical context (see referenced example). This could be related to the fact that the median age of patients in NSTE-ACS clinical trials is 65 years [Metha et al. 2005]. Moreover, many studies exclude elderly patients with severe comorbid conditions.

> "We do somewhat more than is reasonable with these patients. A cardiologist may tend to focus on the coronary vessels, overestimating the coronary disease and underestimating cognitive functions and comorbidity, which can limit length of life and quality of life to a greater extent."
> (53-year-old male cardiologist at a small hospital)

Questions	Very small	Rather small	Rather large	Very large
To what extent do you use the following sources when making clinical decisions for multiple-diseased elderly with NSTE ACS?				
National guidelines for heart care	4 (11)	28 (71)	60 (152)	8 (20)
Your own clinical experience		3 (7)	55 (141)	42 (106)
Patient views		5 (12)	57 (146)	38 (96)
Relative views	6 (15)	44 (111)	44 (111)	6 (16)
To what extent do you think that the following measures would improve clinical decision-making for multiple-diseased elderly with NSTE ACS?				
Improved adherence to *National guidelines for heart care*	6 (15)	44 (109)	43 (105)	7 (16)
Specific evidence-based national guidelines for multiple-diseased elderly	1 (3)	10 (25)	48 (121)	40 (101)
Local guidelines for care for multiple-diseased elderly	4 (10)	21 (53)	57 (142)	18 (45)
More treatment studies including multiple-diseased elderly	1 (3)	8 (20)	39 (97)	52 (130)

Table 3. Clinical decision-making for multiple-diseased elderly with NSTE-ACS. % (n) (Paper II).

Preferred reported measures to improve decision-making for these patients were: a) conducting treatment studies with few exclusion criteria and including elderly patients with multiple comorbidities; b) preparing specific national guidelines for multiple-diseased elderly patients. In both cases, it would be important to assess patients' biological age, cognitive status, preferences, and comorbidities, thus considering the total risk (not only the cardiovascular risk). We argue that future national guidelines for heart disease should be adapted to become more applicable for elderly patients with multiple comorbidities.

| *Theme: enhancing clinical prioritization* |
| What would be the most important measure in order to enhance clinical priority setting (decision-making) for elderly multiple-diseased NSTE ACS patients? How could clinical decision-making regarding elderly multiple-diseased NSTE ACS patients be enhanced, when choosing between life prolonging treatment and good nursing and alleviation of symptoms? |

Category: treatment studies Carrying out prospective treatment studies including multiple-diseased elderly patients.	*Category: specific guidelines* Working out specific guidelines for multiple-diseased elderly patients.	*Category: communication* Enhancing communication related to decision-making in multiple-diseased elderly patients
-Few exclusion criteria -Evaluating the role of comorbidity, cognitive impairment and frailty in the benefit-risk ratio -End-points focusing on quality of life	-Considering the total risk, not only the cardiovascular risk -Assessing the biological age/frailty of patient groups -Considering the most relevant comorbidities	-Communicating risk-benefit ratios properly to patients and relatives -Determining patients' attitudes and preferences -Better communication between cardiologists, internists and general practitioners
'Treatment studies including multiple-diseased elderly are needed. Most studies on ACS preferably include mainly patients approximately 60-65 years old.' (47-year-old male at a university hospital) 'Solid studies, with few exclusion criteria, including multiple-diseased patients over 75 years of age.' (47-year-old female at a small hospital)	'Distinct guidelines are needed for patients with NSTE ACS and some of the following (co-morbidities): advanced renal insufficiency, advanced liver insufficiency, advanced malignant disease, gastrointestinal bleeding, age over 90 years, and ongoing treatment with warfarin.' (42-year-old male at a university hospital) 'The problem complex should be considered in national guidelines.' (48-year-old male at a mid-sized hospital)	'Honesty in the communication with patients. Information about procedure-related risks should be given properly – no false expectations.' (43-year-old female at a university hospital) 'Computerized medical records are necessary, with doctor access to records of other clinics and primary care.' (56-year-old male at a university hospital)

Figure 8. Content analysis of the first two open-ended questions in the questionnaire, consisting of one theme and three categories, i.e. the main proposals from the responders, each proposal consisting of three sub-categories, and two representative quotations (Paper II).

Paper III

Our study demonstrates frailty as an independent risk factor for adverse short-term clinical outcomes for elderly NSTEMI patients. Of the patients in this study, 48.5% were frail, and 24.1% were moderately or severely frail. Frail patients presented with a greater burden of comorbidity and were slightly older. Severe comorbidity (one or more) was manifested by 78.5% of the frail patients and 43.0% of the non-frail patients.

Variable, n (%)	Nonfrail (n=158)	Frail (n=149)	P
Primary composite outcome	43(27.2)	68(45.6)	0.001
Mortality, one month	5 (3.2)	23(15.4)	0.0001
Mortality, in-hospital	3 (1.9)	15(10.1)	0.003
Major bleeding, stroke/TIA or need for dialysis, in-hospital	6 (3.8)	14(9.4)	0.063
Number of bed days	7.5	13.4	0.0001
	Nonfrail (n=155)	Frail (n=134)	
Re-hospitalization, one month	34(21.9)	40(29.9)	0.138
Re-infarction, one-month	8 (5.2)	10(7.5)	0.470
Major bleeding, stroke/TIA or need for dialysis, one month	5 (3.2)	2 (1.5)	0.456

* Primary composite outcome denotes the composite of death from any cause, myocardial re-infarction, revascularisation due to ischemia, hospitalisation for any cause, major bleeding, stroke/TIA and need for dialysis up to one month after inclusion.

Table 4. Short-term outcomes of elderly NSTEMI patients (Paper III).

By multiple logistic regression, frailty was identified to be a strong independent risk factor for in-hospital mortality, one-month mortality (OR 3.8, 95% CI 1.3 to 10.8), and the primary composite outcome (OR 2.2, 95% CI 1.3 to 3.7). Particularly frail patients with a high comorbidity burden, i.e. medium or high CAD-index score, manifested a markedly increased risk for the primary composite outcome. No other interaction with any independent variable, including age, was found. A sensitivity analysis showed that the predicitive strength of frailty was similar when the patients were stratified into one group including moderately or severely frail, but not mildly frail, patients. By multiple linear regression, frailty was found to be a strong independent predictor for prolonged hospital care (frail 13.4 bed days, nonfrail 7.5 bed days; P<0.0001).

	OR (95% CI)	P
Age		0.34
75-79	REF	
80-84	1.19 (0.62 - 2.30)	0.60
85+	0.76 (0.39 - 1.49)	0.43
Gender		0.48
Male	REF	
Female	0.82 (0.47 - 1.41)	0.48
Ejection fraction		0.58
Higher then 40%	REF	
Lower then 40%	1.11 (0.58 - 2.14)	0.75
Not recorded	1.37 (0.76 - 2.44)	0.30
Cardiovascular risk		0.26
1	REF	
2	1.74 (0.64 - 4.72)	0.28
3	2.49 (0.81 - 7.63)	0.12
Frailty		
Non-frail	REF	
Frail	2.17 (1.28 - 3.67)	0.0041
CAD index		0.049
Low	REF	
Moderate	0.57 (0.29 - 1.13)	0.11
Severe	1.36 (0.76 - 2.45)	0.31

Table 5. Risk-adjusted impact of frailty on the primary composite outcome (Paper III). REF=reference value.

Frail patients were less likely to be treated in intensive cardiac care units and to undergo coronary angiography than were nonfrail patients. Frailty and severe comorbidity, but not cardiovascular risk-score or CAD-index score, were negative predictors for performance of coronary angiography. Further, the proportion of frail patients who underwent coronary angiography differed markedly between the three centres. We argue that the combined use of frailty and comorbidity may constitute an ultimate risk prediction concept regarding cardiovascular patients with complex needs.

	OR (95% CI)	P
Age		0.10
75-79	REF	
80-84	0.90 (0.23 - 3.57)	0.89
85+	2.58 (0.79 - 8.46)	0.12
Gender		
Male	REF	
Female	0.71 (0.28 - 1.80)	0.47
Ejection fraction		0.14
Higher then 40%	REF	
Lower then 40%	2.60 (0.80 - 8.52)	0.12
Not recorded	2.88 (0.98 - 8.47)	0.056
Cardiovascular risk		0.61
1	REF	
2	3.04 (0.34 - 26.81)	0.32
3	2.80 (0.27 - 28.70)	0.39
Frailty		
Non-frail	REF	
Frail	3.79 (1.33 - 10.81)	0.013
CAD index		0.035
Low	REF	
Moderate	0.63 (0.15 - 2.57)	0.52
Severe	2.77 (1.02 - 7.49)	0.046

Table 6. Risk-adjusted impact of frailty on one-month mortality (Paper III).
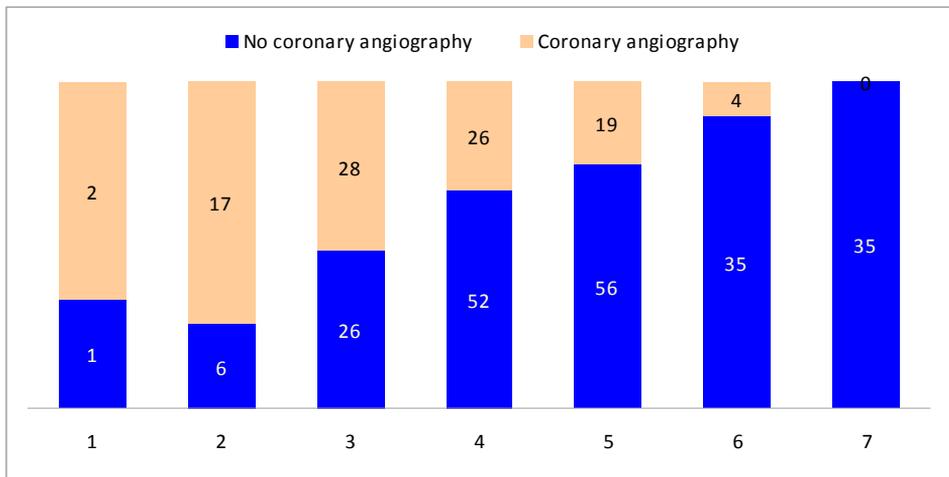
Figure 9. The proportion of patients in each frailty stage (1-7) undergoing coronary angiography.

Paper IV

Our aim was to validate the relevance of authentic clinical NSTEMI cases of elderly patients with multimorbidity. Further, we evaluated the inter-rater reliability of the study experts' rankings of the cases (Appendix G), and compared the Swedish national guidelines' rankings with the study experts´ rankings. Of the initial sample of 60 purposefully selected cardiologists, two had not dealt with NSTEMI patients within the past six months. From the remaining 58 subjects we received 41 questionnaires (response rate 71%). The responders answered 93% to 100% of the items, and the response rate for the open-ended question was 56%. In addition, 37 free comments were given. The nonresponder analysis did not reveal any evident deviations in the views of nonresponders.

Concerning the question "Do you consider the cases to be realistic?" 28 of 40 responders (70%) answered "Yes", 12 (30%) answered "Yes, partly"; no one answered "No". Nearly all of the respondents considered the cases to be representative for a hospital care population of NSTEMI patients. A typical comment was:

> "Very realistic cases! Daily problems!"
> (A male cardiologist at a small hospital in the north region of Sweden)

The inter-rater reliability regarding the group of cardiologists' individual rankings of each case was very good (ICC consistency, average measure 0.98 [95% CI 0.96 to 0.99]). The estimated relevance of the model's three components was reported by the responders: (i) 39 of 40 respondents (97.5%) reported high or very high relevance of comorbidity, while one (2.5%) reported moderate or low relevance; (ii) 34 respondents (85%) reported high or very high relevance of frailty, while 6 (15%) reported moderate or low relevance; and (iii) 27 respondents (67.5%) reported high or very high relevance of cardiovascular risk, while 13 (32.5%) reported moderate or low relevance.

Regarding the need for coronary angiography for the different categories of NSTEMI patients, the cardiologists' rankings differed from the proposed rankings of the national guidelines for heart disease (see Table). In general, the cardiologists' rankings were lower than those of the guidelines, particularly regarding patients with high cardiovascular risk. Cardiovascular risk influenced the study experts' rankings to a lesser extent than did comorbidity and frailty.

The gradient of the relative rankings of the experts was similar to the gradient of the tentative relative rankings of the model. In this study we argue that a model taking cardiovascular risk, comorbidity, and frailty into account could constitute a framework for consensus-based guidelines for frail elderly heart patients.

High cardiovascular risk			Low cardiovascular risk		
Category	Guidelines' rankings	Experts' rankings	Category	Guidelines' rankings	Experts' rankings
IV	2	4.2 [3.7-4.8]	VIII	7	3.2 [2.4-3.9]
III	2	7.4 [6.7-8.2]	VII	7	8.0 [7.3-8.6]
II	2	7.8 [7.4-8.2]	VI	7	9.4 [8.6-10.1]
I	2	9.6 [9.0-10.3]	V	7	10.1[9.5-10.7]

Table 7. The rankings of the model's NSTEMI categories based on the following: the categories of the model, guidelines and experts (means [95% CI]). 1 denotes the highest possible rank (Paper IV).

DISCUSSION

The general aim of this thesis is to study microlevel priority setting for elderly patients with acute cardiovascular disease, e.g. NSTEMI, and complex needs, and to relate the findings to evidence based priority setting, e.g. guidelines for heart disease. Furthermore, it aims to analyse whether or not complex needs can be categorized in an appropriate way in an evidence based priority setting perspective.

In Paper I a primary aim was to describe and quantify inpatient care utilisation and costs, and patient characteristics, regarding multiple-diseased elderly patients, particularly concerning cardiovascular disease and comorbidity. By using a definition [Gurner and Thorslund 2001; The National Board of Health and Welfare 2002] deemed appropriate for quantifying patients in the hospital population, we found that of unique patients aged 75 years or older who consumed hospital care in 2005, 25% were multiple-diseased elderly patients. Of all inpatient hospital care consumed by patients aged 75 years or older, these patients consumed 47% of all inpatient days. The estimated number of these patients, generally constituting 7% of individuals aged 75 years or older in society, is in line with earlier and later estimates [e.g. The National Board of Health and Welfare 2002; Akner 2010]. These patients have extensive and complex needs, resulting in high utilisation of inpatient hospital care. The majority, i.e. 83%, have manifested cardiovascular disease and multiple comorbidities, which is in line with a recent estimate [SALAR 2011]. For perspective, the average age of patients in Swedish medical departments has been estimated at 75 years, and at 80 years in geriatric departments [The Swedish Council on Technology Assessment in Health Care 2003].

Elderly patients with complex needs were not only of high chronological age and had a large *number* of medical conditions per individual patient, which follows from the aforementioned definition, but to a great extent they also had *specified comorbid conditions*, e.g. malignant disease and dementia, which constituted exclusion criteria in relevant evidence-generating studies. Patients aged 80 year or older and patients with severe and/or multiple comorbid conditions are usually excluded from the evidence-generating studies that constitute a basis for clinical guidelines [e.g. The Swedish Council on Technology Assessment in Health Care 2003; Rothwell 2005; American Heart Association Council 2007; Boyd 2005]. Hence, we suggested that a relationship exists between reported characteristics, i.e. very high age and severe comorbidity, and potentially limited applicability of evidence-based guidelines. This can lead to underutilisation and overutilisation of medical interventions, possibly resulting in unfair and arbitrary care with large variations between both clinics and individual physicians. The view that there may be limited applicability of guidelines for elderly with complex needs is supported by the findings in papers II, III and IV, including patient characteristics, reported views of cardiologists and their actual decision making, and by the views of other authors found in a complementary literature search [e.g. Tinetti 2004; Rockwood 2005; Lichtman 2007; May 2010; Gray 2010].

The term ageism, or age discrimination, was minted in the late 1960s and use to denote discrimination against and stereotyping of individuals and groups because of their chronological age [Butler 1969; Tornstam 2006]. Prejudical attitudes, discriminatory practice and institutional policies can contribute to and constitute ageism [Butler 1969]. Stereotypical views on age have been pointed out or implied to cause discrimination against elderly persons within health care [Bowling 1999; Bowling et al. 2006; Harries et al. 2007; Judge 2010]. Both attitudes of health care professionals and limited generalisability of evidence due to a lack of scientific studies including elderly with complex needs, may contribute to this phenomenon. Furthermore, in practise models for priority setting have been based on the ranking of *one* medical action for *one* medical condition, which does not seem to be adapted for the use for elderly patients with complex needs. Nevertheless, in the clinical setting decisions are made daily regarding these patients. If possible ageism in clinical research and policy-making could be tackled, then possible ageism in clinical practise would be easier to disclose and control. This could facilitate fair and appropriate microlevel priority setting for elderly patients with complex needs.

Our primary aim in Paper II was to evaluate the views of Swedish cardiologists on decision-making for elderly with multiple comorbidities and NSTE-ACS. We found that 81% of the cardiologists reported extensive use of national guidelines in treating heart disease in their clinical decision-making generally. This constitutes crucial knowledge from a priority setting perspective, since in Sweden and other Western countries evidence-based guidelines are intended to play an important role in healthcare decision-making. However, when making decisions for multiple-diseased elderly patients, the individual physician's personal clinical experience and the patient's views on treatment choice were evidently used to greater extent than national guidelines. Several comments and answers to open-ended questions focused on limitations in the applicability of guidelines in this clinical context. Although this finding does not violate the concept of EBM itself [Sackett et al. 2000], it is consistent with the results in papers I, III, and IV and other sources that debate the applicability of evidence-based guidelines for elderly with severe comorbidities [Tinetti 2004; Rockwood 2005; Lichtman 2007; May 2010]. The median age of patients in NSTE-ACS clinical trials is 65 years [Metha et al. 2005]; and more importantly, many studies exclude elderly patients with significant comorbid conditions [e.g. AHA 2007]. Many respondents emphasised the need for clearer guidelines, which viewpoint has been reported in other publications [Ridderstolpe et al. 2003; Werntoft 2009].

The mean of the responders' estimates of the proportion of patients with NSTE-ACS who are multiple-diseased elderly, according to the stipulated definition, was 37%. This figure can be compared to the results in Paper III and other studies [e.g. Lichtman et al. 2006; Lichtman et al. 2007; AHA 2007] indicating similar or higher percentages of severe and/or multiple comorbidities among the elderly. Moreover, a recent estimate indicated a "lack of firm evidence" for 40% to 50% of the patients with NSTEMI included in the Myocardial Ischaemia National Audit Project (MINAP) in Great Britain [Gray 2010]. To our knowledge, the views of cardiologists of decision-making for multiple-diseased elderly patients with NSTE-ACS have not been evaluated before. Since cardiology is a field with a recognised

tradition of performing good-quality RCTs [Strippoli 2004], it is reasonable to assume that microlevel priority setting in other fields is no less dependent on individual clinical judgment. This could imply that a large part of healthcare priority setting takes place implicitly at the clinical level. To our knowledge, most registers do not analyse outcomes for patients aged 80 or older. Hence, we know relatively little about the consequences for this category, which constitutes approximately 40% of all Swedish myocardial infarction patients [Stenestrand 2008; RIKS-HIA 2008].

Considering the present volume of this patient population and the demographic prognosis in industrialised countries, limited applicability of guidelines may constitute a growing decision-making and quality problem in health care. One possible expression of this problem would be polypharmacy, when many guidelines are concomitantly adhered to in a stereotypical way. The cardiologists' preferred measures for improving decision-making were to conduct treatment studies with few exclusion criteria (i.e. to include elderly patients with multiple comorbidities) and to prepare specific national guidelines for multiple-diseased elderly patients. In the future, however, we argue that such studies could be rare due to methodology-related factors (aiming at good internal validity), ethics (informed consent), and costs (lack of financing incentives).

In Paper III we described patients aged 75 years or older with NSTEMI, especially regarding cardiovascular risk, comorbidity, and frailty, and we analysed how frailty predicts short-term outcomes for these patients. In our study, frailty was shown to be an independent risk factor for adverse short-term clinical outcomes in elderly NSTEMI patients. Of the patients, 48.5% were frail, and 24.1% were moderately or severely frail. Frailty was a strong independent predictor of in-hospital mortality, one-month mortality, prolonged hospital care, and primary composite outcome. In particular, frail patients with a high burden of comorbidity manifested a markedly increased risk for the primary composite outcome. A sensitivity analysis showed that the predictive strength of frailty was similar when the patients were stratified into one group including moderately or severely frail, but not mildly frail, patients. Frail patients were less likely to be treated in intensive cardiac care units and to undergo coronary angiography than were nonfrail patients.

Given our aim to describe a representative sample of elderly NSTEMI patients treated in clinical practise (including patients not being treated in coronary care units and patients with secondary coronary ischaemia) the study design seems appropriate and included few exclusion criteria. To our knowledge, this is the first study to demonstrate frailty as a risk factor for adverse short-term clinical outcomes in elderly NSTEMI patients. We did this using an easily applied clinical measure of frailty, which was evaluated prior to the outset of the study and was shown to have very good interrater reliability. We chose to use the CSHA Clinical Frailty Scale, since it is based on clinical judgement and is relatively easily applied in a clinical context.

Most frailty studies have addressed a geriatric patient cohort rather than acute heart disease patients. These studies have demonstrated that frailty predicts long-term mortality,

hospitalisation and institutionalisation of geriatric patients [Fried 2001; Rockwood 2005]. Our study indicated that frailty predicts short-term outcomes for elderly NSTEMI patients.
As many as 60.3% of our study patients manifested one or more severe comorbid conditions, e.g. severe renal insufficiency, malignant disease or severe dementia. Such conditions constitute exclusion criteria in most evidence-generating studies, which raises questions about the generalisability of those studies' results in a clinical context involving elderly patients with severe comorbidities or severe frailty. This information can be related to the findings in papers I, II, and IV and aforementioned publications on the same theme [e.g. Lichtman et al. 2006; Lichtman et al. 2007; AHA 2007].

Frail patients were less likely to be treated in intensive cardiac care units than nonfrail patients, and they were less likely to undergo coronary angiography. Frailty and severe comorbidity were strong negative predictors for performing coronary angiography, while the degree of cardiovascular risk did not influence the use of this measure. Clinical decision-making for elderly NSTEMI patients appears to be based on factors other than the estimation of cardiovascular risk, i.e. frailty and comorbidity, which harmonises with findings in Paper IV regarding study experts' views on ranking complex cases. This observation could be compared with recommendations in Swedish, European, and American heart disease guidelines. To our knowledge, these guidelines rely on disease-specific (cardiovascular) risk, which is the case with most guidelines regarding other disease areas [Tinetti et al. 2004]. Despite the relatively conservative treatment strategies chosen for frail patients, they accounted for a remarkably high number of hospital bed days. Further, the proportion of patients who underwent coronary angiography differed markedly among the three centres, despite their similar patient characteristics regarding age, sex and comorbidity burden (Figure). This emphasises the findings in Paper II, i.e. in complex cases the individual physician uses personal clinical experience to a greater extent than national guidelines, and raises the apprehensions from papers I and II about potentially arbitrary care in predominantly implicit priority setting at the micro level. The discrepancy between biological and chronological age has been identified as a major obstacle in applying evidence-based treatments [Singh et al. 2008]. For the large and growing population of elderly patients with cardiovascular disease it is important to identify clinically relevant measures of biological age and their contribution to risk, which was also a common view among the respondents in Paper II. The combined use of frailty and comorbidity may constitute an ultimate risk prediction concept regarding cardiovascular patients with complex needs. This is relevant, since risk prediction is a crucial component when assessing benefit-risk ratios in priority setting guidelines [e.g. NICE 2010].

In Paper IV the main aim was to evaluate a tentative framework for priority setting regarding elderly patients with multimorbidity. For this purpose we aimed to evaluate the interrater reliability of study experts' rankings regarding authentic, clinical, complex, NSTEMI cases, and to compare the experts' rankings with the guidelines. The framework is based on Papers I, II, and III, a pilot study in 2009 including six experienced cardiologists who had participated in drawing up guidelines, and a complementary literature search that was undertaken in order

to provide input regarding the components of the framework, e.g. defining severe comorbidity (Appendix E).

The cardiologists in the study considered the clinical cases (Appendix G), to be realistic and representative for a hospital care population of NSTEMI patients, which harmonises with the results of patient characteristics in Papers I, II, and III. The interrater reliability (consistency, average measure) of the group of cardiologists' individual rankings of each complex case was very good, which may indicate the presence of collectively reinforced tacit experience-based knowledge [Gabbay and LeMay 2011]. The respondents considered comorbidity to be the most relevant of the framework's components; frailty the second most relevant; followed by cardiovascular risk. These results are in accordance with the experts' actual rankings of the cases. Concerning complex NSTEMI cases, severe comorbidities and frailty seem to outweigh the degree of cardiovascular (disease-specific) risk, as a basis for clinical priority setting. Accordingly, the study experts even gave low rankings to high-cardiovascular-risk elderly multiple-diseased NSTEMI patients. One probable explanation for this expert view is that they considered the expected benefit-risk ratio to be altered in a negative direction due to severe comorbidities and frailty. Hence, the cardiologists' rankings of cases, each case representing one of the model's eight categories, differed strikingly from the rankings of the national guidelines. In general, the cardiologists' rankings were lower than those of the guidelines, particularly regarding high-cardiovascular-risk patients, which harmonises with the observed decision-making discussed in Paper III.

In contrast to the guidelines, the tentative framework addresses all three of the aforementioned components, and its gradient of rankings (Appendix E) coincided with the gradient of rankings by the study experts. The results of study II-IV indicate that clinicians use comorbidity and biological age (frailty) rather than cardiovascular risk in prioritising NSTEMI patients with complex needs. Regarding the justified distinction between "current behaviour" and "preferred behaviour", it should be noted that the purposefully selected cardiologists in study IV were deemed to be exceptionally competent in this decision area. Moreover, because the generalisability of the evidence is limited, one can argue that solid evidence *pro* or *contra* intervention for these patients is unavailable.

We suggest that a model for priority setting of frail elderly patients should include information about comorbidity and frailty in addition to information connected with the index-disease, e.g. myocardial infarction. In a guideline context it is difficult to determine a suitable level of detail, thus requiring one to balance precision and practical management. However, it seems reasonable and manageable to deal with categories, based on comorbidity, frailty and disease-specific risk, since the precision of using disease-specific risk alone is considered to be far too low in the complex cases, that account for large volumes of patients.
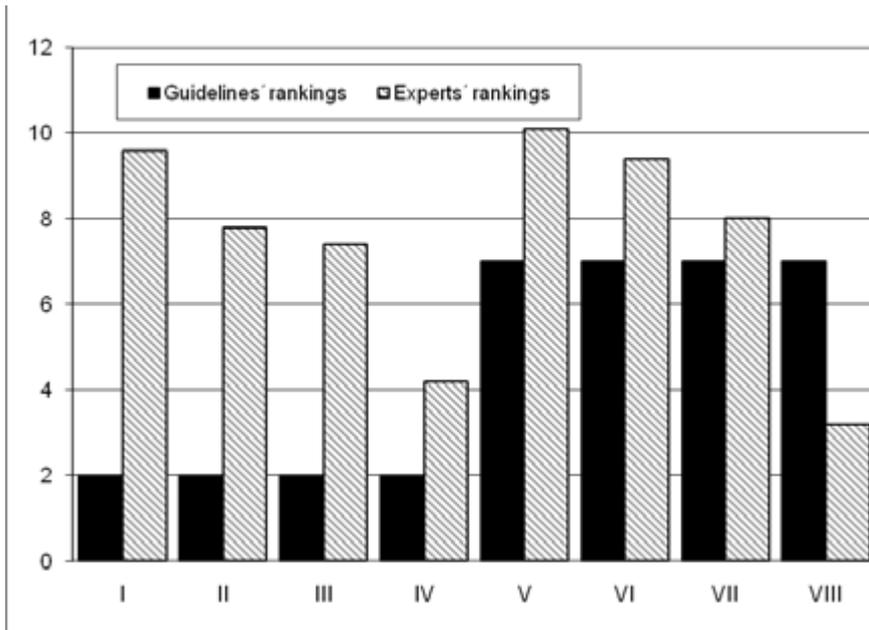
Figure 10. The rankings of cases belonging to the framework's eight NSTEMI categories (Appendix E) based on the following: the categories of the model, guidelines and study experts (means [95% CI]). 1 denotes the highest possible rank. Category I-IV denotes high cardiovascular risk; category V-VIII denotes low cardiovascular risk (Paper IV).
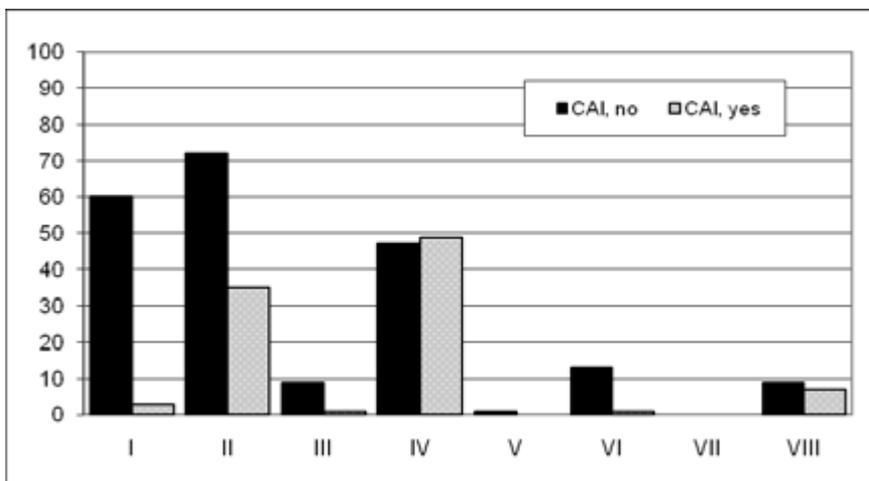

Figure 11. The distribution of NSTEMI patients from the FINE study (Paper III) on the framework´s eight categories, and the decision regarding performing or not of coronary angiography (cai). Category I-IV denotes high cardiovascular risk; category V-VIII denotes low cardiovascular risk (Paper IV).

Unit	Coronary angiography (%)
Hospital A (n=54)	63,0
Hospital B (n=161)	21,7
Hospital C(n=92)	29,3
Total (n=307)	31,3

Table 8. The proportion of NSTEMI patients, aged 75 years or older, that underwent coronary angiography at each site in the FINE study (Paper III). Proportion of patients with severe comorbidity at each site (%): A 63; B 60; C 61. Proportion of frail patients at each site (%): A 45; B 53; C 43.

Demographic trends and other factors are expected to continue widening the gap between healthcare demands and available resources, especially in elder services. This growing imbalance signals a need for priority setting in health care. From an international perspective I argue that Sweden is well equipped with the prerequisites for priority setting in general. Apart from a certain amount of inherent ambiguity in the legal framework, the ethical platform constitutes a needs-based value-base for health care, emphasising distributive justice with a focus on solidarity with groups and individuals perceived as being weak, e.g. elderly with severe chronic disease. Furthermore, the practical philosophy of EBM, including evidence, clinical expertise, and patient values is well established in practise and through the Health and Medical Services Act ("science and clinical experience"). Moreover, important steps have been taken to implement the political intentions, e.g. incorporating health economics and health technology assessment, thus applying a multicriteria approach in priority setting.

However, problems in constructing useable priority setting have been described; particularly when evidence is sparse, when patient groups are not satisfactorily defined, when interpretation of the term *patient need* is unclear, and when uncertainty prevails on how to weigh different ethical values. Despite the strategic and normative control mechanisms introduced by the central governing bodies (e.g. national guidelines), in practise considerable responsibility is placed on healthcare professionals to implement goals in direct contact with citizens. This thesis suggests that, in fact, a substantial number of the priority setting decisions are implicit and are made at the micro (clinical) level. This is due, in part, to limited applicability of evidence-based guidelines for large groups of patients with complex needs, i.e. the priority setting is left to the clinician's clinical experience and the view of the patient. Although to some extent this may be unavoidable and in fact desirable, it can potentially lead

to arbitrary and ineffective care with wide variations between hospitals and professionals. I suggest that some of the main obstacles for evidence based priority setting are to be found at the micro level including clinical practise and guidelines. Several were recently described by Gabbay and Le May, e.g. individual and organisational hindrances, lack of clinical applicability of evidence, an inborn conflict between probabalistic science and the need for individualised treatment in practise, and the tremendous complexity in clinical practise.

The chosen study object, i.e. elderly patients with acute cardiovascular disease and complex needs, illustrates most of the problems described above. Epidemiological and demographic data show this group of patients to be large and growing and thereby relevant from medical, ethical, and socioeconomic perspectives. These patients constitute a heterogeneous, hard-to-define, population encompassing a wide spectrum of chronological and biological ages, types and severity of medical conditions/diseases, and socio-economic and cultural issues and needs. They often consume health care in various contexts and at various levels: primary care, municipal public health services, and specialized hospital care. Most of their healthcare consumption is probably connected with specialised care in hospitals as a result of acute conditions. By definition, this group carries a heavy burden of chronic illness, but episodes of acute disease are common. When afflicted by acute disease these patients often have severe and potentially life-threatening illness. Due to their complex needs, e.g. including multiple and/or severe comorbidities involving different disease areas, one could argue that these patients are often subject to both horizontal and vertical priority setting. Many have one or more characteristics (elderly, severe chronic disease, end of life stage, reduced autonomy) that place them at risk of being neglected and underfunded, according to the Priority Commission and government. At the microlevel, in an evidence-based, priority-setting context that includes the clinical level and, indirectly, guidelines and the model for vertical priority setting, I propose the following as main issues:

- Due to the *complexity* of many patient cases, e.g. due to interactions between many concomitant conditions, frailty, and polypharmacy, it is difficult to formulate proper type cases (*prioritisation objects*) in guidelines. It is a challenge to balance exactness and practical management in describing the health condition and its subsequent health care needs within the Model (or similar frameworks) of vertical priority setting.

- The alternatives in microlevel priority setting must be *relevant*, i.e. viable options that could actually be considered. What constitutes a relevant alternative under the concept of EBM (or "science and clinical knowledge") and the crucial assumption that one does not need a treatment that one cannot potentially benefit from? A practical conceptualisation of EBM that relies on RCTs with extensive exclusion criteria and very good internal validity but questionable generalisability, raises questions about the *applicability* of guidelines to specific patient groups with complex needs (including probabilities of large deviations in patient benefit-risk ratios). Regarding elderly NSTEMI patients, and probably other elderly patient groups, higher risk suggests not

only potentially greater benefits from intervention, but also potentially greater risks for complications and side effects related to the intervention itself.

- Health care legislation renders it unacceptable to prioritise solely on grounds of chronological age, and states that the *biological age* and the ability to benefit from treatment should be considered in decision-making. This includes considering how the time-frame of an expected benefit relates to a patient's expected life-time. However, how should biological age be estimated?

In health care, individuals with multiple coexisting diseases are the norm rather than the exception [Starfield 2006]. Hence, I would argue that the challenge of priority setting for elderly patients with complex needs is relevant for a substantial volume of patients receiving hospital care [e.g. Lichtman et al. 2006; Lichtman et al. 2007; AHA 2007; Gray 2010; papers I-IV in this thesis]. EBM can be considered a practical philosophy that is necessary, though not sufficient, in guiding a clinician's priority setting. According to experts, estimating the benefit-risk for patients with complex needs is crucial in microlevel priority setting. In calculating this estimate, the concepts of severe frailty (biological age) and severe comorbidity are regarded as crucial; in fact, tentatively more important than the disease-specific risk of the index condition.

In microlevel priority setting for these patients, there is no single way to overcome obstacles and reduce the risk for potentially irrational, ineffective, and unfair care. There is, however, a need for improvements and actions related to individual clinical judgment, organisational and structural matters, evidence-generating studies and registers. Furthermore, we suggest the using of a tentative framework for microlevel priority setting for elderly patients with complex needs, taking into account comorbidity, frailty, and disease-specific risk. The aim is to facilitate adaptation of the priority setting model and clinical guidelines to make them more applicable to this large group of patients striving to avoid unfair, arbitrary, and inefficient care.

Ethical considerations

I have attempted to keep methods on a solid ethical foundation throughout this thesis. Many of the patients studied have one or more characteristics (elderly, severe chronic disease, end of life stage, reduced autonomy) that place them at risk of being neglected and underfunded according to the Priority Commission.

There are possible medical and ethical implications of lack of generalisable evidence and applicable guidelines for elderly patients with complex needs. It could lead to overutilisation of treatments, e.g. polypharmacy potentially causing adverse effects, and underutilisation of interventions that could potentially benefit the elderly patients. Both of them may have deleterious consequences for the elderly. Moreover, a possible implication would be large

variations between clinics and individual physicians, implying risk of arbitrary and unfair care [Ridderstolpe et al. 2003]. In summary, the bioethical principles of beneficence, non-maleficence and justice [Beauchamp and Childress 1994] could be violated. Whether the lack of applicable evidence and guidelines for these patients, in fact, is due to ageistic attitudes at the clinical level or institutional policies or other factors, e.g. methodology issues or lack of financial incentives, is difficult to say.

However, since this lack may constitute a main obstacle and risk factor of unfair care, the studying of elderly patients with complex needs can be justified not least from an ethical viewpoint. More and appropriate clinical research and policy-making regarding elderly with complex needs could make possible ageism in clinical practise easier to disclose and control. These measures are proposed in this thesis and they could facilitate fair and appropriate microlevel priority setting for elderly patients with complex needs, reducing variations between clinics. This viewpoint would harmonise with the main function of the principle of human dignity, i.e. constraining decision-makers from setting priorities based on the patient´s personal characteristics [Collste 1999]. This would also harmonise with paragraph 5 in the Declaration of Helsinki in the 2008 version:
"Medical progress is based on research that ultimately must include studies involving human subjects. Populations that are underrepresented in medical research should be provided appropriate access to participation in research." [World Medical Association 2008]

Study III addressed elderly patients, many of whom had complex needs and potentially reduced autonomy. It was a clinical, prospective, observational study and the participating patients received the same treatment they would have received as nonparticipants. The study was undertaken after the Independent Ethics Committee (IEC) gave full approval to the protocol and its appendices. The risk that a patient would experience any violation of his/her integrity was considered to be minimal, and there was no interdependence between the investigators and the patients. Furthermore, we made a concerted effort to avoid and prevent any violation of patient integrity. After the patient had given informed consent and the inclusion criteria were fulfilled, the patient's degree of frailty was evaluated based on bedside judgment of frailty and other clinical information, e.g. records in the patient's file. If a patient was unable to give informed consent, but there was sufficient clinical information (including records in the patient's file), an evaluation of the patient's frailty was based solely on this information, i.e. without bedside judgment. A few patients who fulfilled the inclusion criteria, while evidently not fulfilling any of the exclusion criteria, were not evaluated during the hospital care episode. In these cases the evaluation of frailty was based on records in the patient's file and/or information obtained via a telephone call to the patient after the patient had provided written consent via a letter. After receiving permission from the hospital board, we intermittently conducted a computer-based screening of the hospital's diagnosis register to identify potentially eligible, but already discharged, NSTEMI patients. We considered the potential benefits for the group of patients being studied to outweigh the potential risks for the patients included.

Limitations

This thesis has focused on priority setting for elderly patients with complex needs; study I in the context of acute cardiovascular disease, study II regarding NSTE-ACS patients, and studies III and IV in the context of NSTEMI. It is difficult to assess generalisability to disease areas other than cardiovascular disease and to other countries. Although the generalisability of the results in study IV to medical conditions and measures other than NSTEMI and coronary angiography can be questioned, it seems plausible that comorbidity and frailty (which were considered relevant to priority setting in this specific context) are also crucial for other decision-making situations involving elderly patients with acute disease and complex needs. Our aim was not to identify a general model for priority setting of complex cases that could be standardised and applied to all index conditions, but to suggest a framework for prioritisation of complex cases. The contents of this framework should be revised and adjusted to be applicable in various contexts, i.e. for various index conditions and regarding symptom-relieving and prognosis-improving indications. We also recommend that the framework be further tested concerning its validity and reliability. In addition, I would argue that due to demographic and epidemiological causes, frailty and comorbidity have become concepts that are, or will be, relevant in most countries worldwide, independent of development level or healthcare system.

This thesis does not attempt to explicitly describe quality-of-life measures and preferences concerning elderly patients with complex needs, although I consider these issues to be relevant. Apart from the ethical issues involved in studying patients with reduced autonomy, e.g. difficulties in getting informed consent, our primary aim was to identify categories perceived as relevant from a clinical priority setting perspective. Those categories, comprised of combinations of disease-specific risk, comorbidity, and frailty, may be used in future studies that address quality-of-life outcomes. Furthermore, the primary composite outcome in study III includes re-hospitalisation for any cause within one month of inclusion. To some extent, this reflects the burden of symptoms and quality of life, albeit indirectly and roughly.

In this thesis I have not aimed to analyse the various theories of health, e.g. the health theories of Boorse [Boorse 1977] and Nordenfelt [Nordenfelt 1991], nor have I addressed the distinction between illness and disease. Although it is beyond the scope of this thesis to choose a single health theory, one could argue that the thesis concerns actual premises in present healthcare practise, preferably implying a biostatistical, "objective" view. On the other hand, I would argue that the concept frailty (including focus on function and activity) come close to a more holistic view towards health.

For similar reasons, the thesis has not focused on health economic estimations. Since the evidence base for medical benefit-risk ratio is generally weak or very weak for elderly patients with complex needs, it is reasonable to assume that the evidence base for cost-effectiveness would be even weaker. Nevertheless, it should be noted that most respondents in

study IV were able to offer rough estimates of presumed cost-effectiveness for the authentic, complex, clinical cases.

Our study of elderly patients with complex needs did not analyse their healthcare consumption in primary care, which is a limitation. On the other hand, this was beyond the stated scope of the thesis, which instead focused on these patients in an acute disease context. Recent estimates suggest that 70% to 80% of healthcare consumption by multiple-diseased elderly people is associated with hospital care [Swedish Association of Local Authorities and Regions 2011].

CONCLUSIONS

- Multiple-diseased elderly individuals constitute 7% of Swedish individuals aged 75 years or older in society, and we found that they consumed 47% of all days of inpatient hospital care in this age stratum. They have large and complex needs, frequently manifesting chronic and intermittently acute disease and consuming health care at various levels. A large majority have manifested cardiovascular disease.

- We found that a majority of patients aged 75 years or older with NSTEMI manifested one or more severe comorbid conditions. Many elderly patients with heart disease and complex needs manifest acute or chronic severe and/or multiple comorbid conditions that constituted exclusion criteria in evidence-generating studies, which limits the generalisability of evidence and applicability of guidelines for these patients.

- Although 81% of cardiologists reported extensive use of national guidelines in their clinical decision-making generally, the individual clinician's personal clinical experience and the patient's views were used to an evidently greater extent than national guidelines when making decisions about multiple-diseased elderly patients. This indicates that the actual priority setting for these patients takes place, to a large extent, at the clinical micro level.

- We found that frailty is a strong, independent, risk factor for adverse short-term clinical outcomes, including one-month mortality, in elderly NSTEMI patients. Particularly frail patients with a high comorbidity burden manifested a markedly increased risk. Cardiologists and selected study experts, in practice, base their clinical priority setting for elderly NSTEMI patients on comorbidity and frailty rather than on disease-specific (cardiovascular) risk.

- Prospective clinical studies and registries with few exclusion criteria should be performed. Another option could be consensus-based judgments, founded on a framework of priority setting for elderly patients with complex needs, and aimed at estimating the benefit-risk ratio of an intervention and the time-frame of expected benefits in relation to life expectancy. Such a conceptual framework should take into account comorbidity, frailty, and disease-specific risk.

THE FUTURE CHALLENGE OF ELDERLY WITH COMPLEX NEEDS

Using evidence-based guidelines or "mindlines" in priority setting

EBM has had a strong impact on priority setting at all levels in the health care system, and today few would dispute the advantages of the basic principles of EBM. However, those (including myself) who are proponents of EBM may also address some of its limitations, e.g. regarding the application of scientific knowledge in complex clinical practise. One could argue that some of the concept's partly intrinsic limitations are highlighted in the context of elderly patients with complex needs, as our studies have also indicated. Potential obstacles, in some cases interrelated, against the use of evidence-based guidelines in day-to-day practise have been outlined recently [Gabbay and LeMay 2011], and are summarized below:

1. Individual clinicians' ignorance of evidence or reluctance to use the guidelines. More protocol-driven systems of care can induce tensions between professionals' individual clinical autonomy and rationalist bureaucracy.
2. Organisational and structural barriers, including inadequate resources and inappropriate systems, e.g. leading to lack of time.
3. Limited applicability of the evidence, i.e. the research is often restricted to selected minorities of patients, who differ from the majority that are treated in practise.
4. Limited feasibility of evidence. Even if applicable evidence is available, many confounding factors might make it infeasible for a clinician to use a proper scientific approach in selecting the best treatment option.
5. An intrinsic conflict between probabilistic scientific generality relying on statistical odds and the care of particular individuals, i.e. "marrying the generalities of science with the specifics of individual care."
6. Complexity of specific clinical situations. The clinical reality involves "a web of causes" of conflicting goals, balancing values and processes e.g. cultural, political, economic, commercial, organisational, social, and religious.

In reference to point 3, many RCTs exclude elderly patients with severe or multiple chronic comorbid conditions [The Swedish Council on Technology Assessment in Health Care 2003; Fortin et al. 2006; American Heart Association 2007; Van Spall 2007] or patients with acute comorbidities [Lichtman et al. 2006; Lichtman et al. 2007]. The same is true for most registries, cohort studies, and administrative data sets [Lichtman et al. 2007; American Heart Association 2007; Gray 2010]. Extrapolating from studies on younger populations without significant multimorbidity might be appropriate at the clinical level, but could be problematic due to limited generalisability connected with an uncertain benefit-risk ratio, since comorbid conditions and frailty may modify risks and benefits in elderly patients [Tinetti et al. 2004;

AHA 2007; Boyd et al. 2005; Lichtman et al. 2007; Braithwaite et al. 2007; Lee et al. 2010; Gray 2010]. Adhering to guidelines in caring for elderly patients with several comorbid conditions may have undesirable or unclear effects [Tinetti 2004; Boyd 2005; May 2010].

Although, in principle, the guidelines' recommendations should be rooted in data that apply to routine clinical practise (effectiveness) rather than data generated under optimal circumstances (efficacy) [The National Board of Health and Welfare 2008], one could argue that the widespread problem of exclusion criteria makes this goal difficult to achieve. Usually, guidelines fail to comprehensively address the effects of complexity and severe comorbidity [Lichtman et al. 2007; May 2006]. Although guidelines may address comorbidities, if they increase the risks associated with the target disease (index condition), they are rarely rated in priority terms, e.g. drug recommendations for elderly with multiple conditions [Tinetti 2004]. The phenomenon of excluding elderly patients from studies may have various causes, e.g. methodological (aiming at good internal validity), ethical (difficulties in obtaining informed consent), or lack of financial incentives.
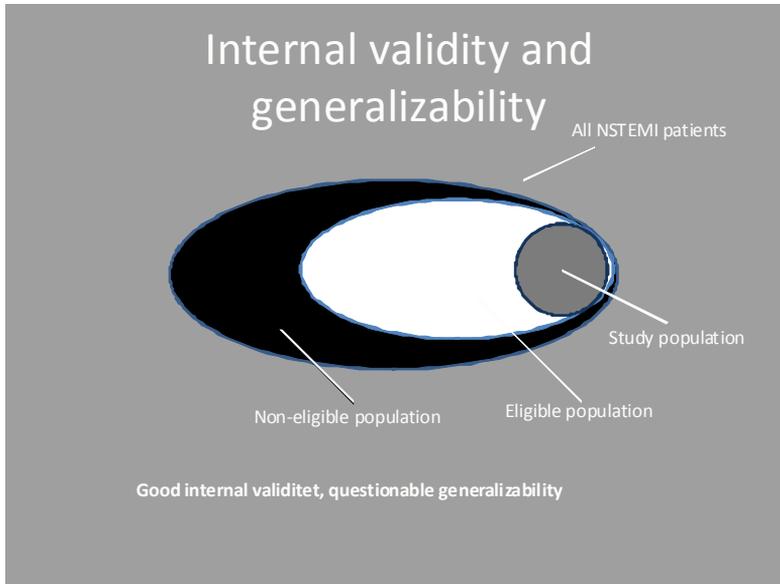
Figure 12. Most scientific studies exclude elderly patients with severe comorbidity or severe frailty. Good internal validity implies applicability of evidence for patients with characteristics resembling those of the eligible population, while the generalisability of evidence for patients with the non-eligible population's characteristics should be questioned.

One could counter-argue that even though the obstacles (1-6) outlined above are factual, none actually violate the concept of EBM. Some of the points could be addressed within the framework of EBM, e.g. clarifying the applicability of guidelines by conducting studies with few exclusion criteria and with a focus on the generalisability of results from RCTs.

Moreover, it would not be realistic to dismiss EBM for not solving or addressing all practical problems related to complexity.

On the other hand, Gabbay and Le May make the point that there may be a "…persistent mismatch between the rational, linear, scientistic approach that the EBP (evidence based practice) movement demands and the pragmatic, workable approach demanded by the messy world of practice". In other words, they emphasise complexity (point 6 above) in practise, including the notion that "…guidelines do not even come close to dealing with all the considerations that a clinician needs to weigh up…as an *inherent* part of dealing with clinical problems" [Gabbay and LeMay 2011]. Hence, due to complex and often incompatible goals and values, complexity is the rule rather than the exception.

Here, again, one could counter-argue that the evidence base is quite solid for many types of interventions, at least interventions in specialised care. For instance, some studies have dismissed the widely suggested, though unsubstantiated, proposition that only 10% to 20% of medical actions have a research base [e.g. Nordin-Johansson and Asplund 2000]. On the other hand, in cardiology, known for its tradition of performing good-quality RCTs [Strippoli 2004], a "lack of firm evidence" was recently reported for an estimated 40% to 50% of the patients with NSTEMI included in the Myocardial Ischaemia National Audit Project (MINAP) in Great Britain [Gray 2010]. One could add that the information that a large part of the *interventions* actually performed for a specified index condition are supported by solid evidence, does not guarantee evidence-based *decisions* (e.g. regarding performance or non-performance of interventions or how to prioritise among various regimens) for the large subgroup of patients with the specified index condition *and* complex needs, e.g. severe comorbidity.

Hence, since EBM is regarded as necessary, but not sufficient, as a basis for decision making, what instead, if anything, should guide the individual decision making of clinicians? Gabbay and Le May refer to the concept "science of intuition" [Greenhalgh 2002], but they emphasise that "intuition" is in fact a word for tacit (in the sense of unspoken or difficult-to-express) or implicit knowledge that clinicians can instantly access without being able to explain it. They argue that clinicians in practise rely on "mindlines", i.e. "…internalized, collectively reinforced and often tacit guidelines" instead of science-based guidelines. Furthermore, they propose that mindlines, being inherently flexible, adaptable, and based on analogue thinking, e.g. pattern recognition, are more adapted to the complex clinical context ("swampy lowlands") than science-based guidelines grounded in deductive reasoning, implying that clinical practise is a series of decisions [Schön 1991; Gabbay and LeMay 2011]. Mindlines are transformed and developed by social processes including collective sense-making, by which analogue reasoning and interaction with trusted colleagues are crucial. A key question is, whether the contents of mindlines could be made more explicit.

Choosing pathways

In the context of this thesis, i.e. elderly with complex needs, the mindlines concept seems potentially highly relevant. However, apart from the intriguing advocacy by Gabbay and LeMay, the relevance of mindlines, i.e. internalised, collectively reinforced, tacit guidelines, is not quite clear. What about the reliability of mindlines? Are mindlines distinct from "clinical expertise", a long-standing component of EBM, or do these terms actually relate to a similar phenomenon? Further, *eminence-based medicine* is not a good alternative to EBM, and relying on experts' intuition does not assure better answers; anecdotal evidence can be misleading. Moreover, besides the well-known advantages of the basic principles of EBM, one can argue that most of the aforementioned obstacles (1-6) could be tackled within the EBM framework. To conclude, I think that the many relevant points drawn by Gabbay and Le May do not violate a positive view of the EBM concept. EBM is a practical philosophy with recognised advantages and is necessary, though not sufficient, in guiding priority setting by clinicians.

Concerning priority setting for elderly patients with complex needs, where the applicability of existing evidence is limited, the clinician has to strike a balance to avoid the two extremes that I would call *evidence fundamentalism*, i.e. unreasonable demands on the level of evidence or guidance from guidelines not allowing reasonable extrapolations, and *extrapolation fundamentalism*, i.e. unrealistic and counterintuitive extrapolating from evidence applying to other populations with markedly deviating probable benefit-risk ratios.

One can agree with Gabbay and LeMay on many of the points addressing how decisions are actually made in practise, and that probably much of the decision burden is rooted in tacit knowledge. It would be narrow-minded to dismiss mindlines when discussing microlevel priority setting for complex cases, particularly if it would be possible to enable tacit (implicit) knowledge to become more explicit - hopefully reducing unacceptable variations and arbitrary care.

I would argue that the challenges of priority setting for elderly patients with complex needs is relevant to a substantial volume of patients receiving hospital care. Moreover, there is no single way to overcome the obstacles (points 1-6) that stand in the way of reducing the risk for potentially irrational, ineffective, and unfair care. A comprehensive discussion of relevant structural and organisational matters, e.g. concerning number of geriatricians and hospital beds, lies beyond the scope of this thesis; likewise the issue of coordinating the actions of various care-givers, e.g. primary care and specialist care. This issue has been justifiably addressed as "Director's missing!" [Gurner and Thorslund 2003]. However, the mere presence of a director will not be sufficient in the absence of notes to guide the directing. I would stress the following points regarding microlevel priority setting for elderly heart disease patients with complex needs:

Evidence-generating studies. Prospective clinical trials including RCTs and observational studies, with few exclusion criteria, that assess comorbidities and frailty would be desirable, as would registries and preference studies designed to include even frail patients and patients with multiple and/or severe comorbidities. However, such studies may be rare in the future due to methodological and ethical factors and a lack of financial incentives.

Individual judgment. When evidence-based guidelines are perceived to be inapplicable, a high degree of adapting of the treatment to the individual patient is advisable, taking into account organ-specific risk, functional status, comorbidities, frailty, patients' preferences**,** and drawing on discussions with trusted colleagues. It may be appropriate to extrapolate from studies on younger populations without complex needs, but then it is particularly important to evaluate and analyse the treatment results. Further, to merely rely on individual judgment may lead to unacceptable variations between health-care stakeholders.

A tentative framework for priority setting of complex needs. Substantial evidence *pro* or *contra* interventions, e.g. coronary angiography, is unavailable regarding many elderly patients with complex needs, e.g. severe comorbidity. Moreover, for reasons mentioned above, high-quality studies are unlikely to take place. In this situation, consensus-based priority setting may be justified. In study IV, the interrater reliability was very good in the study experts' individual rankings of each complex case. This may indicate the presence of tacit, experience-based, collectively reinforced, knowledge that could constitute a base for decision-making regarding complex cases. However, a conceptual framework and a legitimate procedure may be needed to transform this knowledge into explicit consensus-based guidelines.

The aim of using a tentative framework for microlevel priority setting for elderly patients with complex needs, would be to facilitate adaptation of the vertical priority setting model and clinical guidelines to make them more applicable to this large group of patients striving to avoid unfair, arbitrary, and inefficient care. From ethical and legal standpoints the framework should be compatible with the ethical platform and the Swedish Health and Medical Services Act. Basically, it addresses the components and terms described in the national working model for priority setting.

Typical cases (pairs of medical condition-action, prioritisation objects, relevant alternatives) should be formulated with regard to their clinical relevance. In determining a suitable level of detail for prioritisation objects, one has to balance precision and practical management. Since practically all patients with complex health needs have a high severity level of a condition, the focus lies on determining the expected benefit-risk of an action. Theoretically, one or more new typical cases that explicitly address complex needs should be derived from a typical case comprising a total group of patients with an index condition x, if two prerequisites are present: (a) With a substantial degree of probability, the characterisable complex health needs (distinct from the index condition x) of a subgroup of patients with the index condition x cause the benefit-risk ratio of an intervention to deviate substantially from the average benefit-risk ratio of the total group of patients with the index condition x; (b) A substantial

number of patients have similar and characterisable complex health needs in this subgroup with the index condition x.

Regarding the estimation of benefit-risk ratio connected to the index condition (disease-specific risk) and an intervention, we suggest using an established concept such as the FRISC score. Appropriate measures of complex health needs should be relevant to the expected benefit-risk ratio of the intervention. This includes potential positive effects of the intervention on the current health condition and future risks, and the risk for side effects and complications from the intervention per se. Besides, the complex needs' implication regarding the relation between the time-frame for an expected benefit (pay-off-time) and the relation between this time-frame and a patient's expected life-time should be taken into account [Tinetti et al. 2004; Berry 1997; Elwyn 2003; Braithwaite 2007].

We suggest that severe comorbidity and severe frailty are used to categorise complex needs. Comorbidity, with its ability to inform patient management and its orientation towards an index disease, can be deemed appropriate in a clinical context, particularly in specialist care. Likewise frailty, with its strong prognostic value, can be considered useful in a clinical context. Although frailty and comorbidity overlap, there is a clear distinction between them, i.e. they constitute mutually complementary measures of complex needs. Furthermore, frailty and comorbidity are well-established concepts, that clinical experts recognise as relevant.

SAMMANFATTNING PÅ SVENSKA

I framtiden förväntas ett ökande gap mellan vårdbehov och tillgängliga resurser, i synnerhet beträffande äldrevård, på grund av förutsedd demografisk utveckling. Detta kommer att skärpa kraven på medicinska prioriteringar. Det har visat sig vara särskilt svårt att skapa en grund för prioriteringar vid följande förhållanden: då patientgrupper är oklart definierade, vid brist på relevanta vetenskapliga undersökningar, då patienternas behov är svåra att kategorisera, samt vid oklarhet om hur olika etiska värden ska sammanvägas. Äldre patienter med akut hjärtsjukdom (NSTEMI) och komplexa behov illustrerar dessa problem. Dessutom framhöll nyligen den svenska regeringen att vården av äldre svårt sjuka individer är eftersatt i Sverige.

Det övergripande målet med denna avhandling är att studera hur prioriteringar av äldre hjärtpatienter med komplexa behov sker, illustrerat med äldre NSTEMI patienter, samt att relatera gjorda fynd till nuvarande stöd för evidensbaserade prioriteringar, särskilt nationella riktlinjer för hjärtsjukdom. Vidare att analysera hur komplexa behov skulle kunna kategoriseras för att skapa en grund för evidensbaserade prioriteringar av dessa fall. I studie I beskrivs multisjuka äldre patienters slutenvårdkonsumtion och karaktäristika med hjälp av slutenvårdsregistret och KPP-databasen. Studie II är en konfidentiell enkätstudie av ett slumpmässigt urval av 400 kardiologer. Studie III är en klinisk, prospektiv, multicenter observationsstudie beträffande äldre patienter med NSTEMI. Studie IV är en enkätstudie av svenska kardiologer via ändamålsenligt, stratifierat urval.

Resultaten från den första studien visar, givet vald definition, att multisjuka äldre har stora och komplexa vårdbehov, flera kroniska sjukdomar, blir återkommande akut sjuka och konsumerar olika slags sjukvård samt att de flesta är hjärtkärlsjuka. Den andra studien talar för att en stor majoritet av kardiologerna använder nationella riktlinjer i stor skala vid kliniskt beslutsfattande i allmänhet. Vid kliniskt beslutsfattande beträffande multisjuka äldre patienter används dock den enskilde klinikerns egen erfarenhet och patientens uppfattningar i betydligt högre grad. Många äldre hjärtsjuka patienter med komplexa behov uppvisar minst ett allvarligt, akut eller kroniskt, komorbitt tillstånd, vilket utgjorde exklusionskriterium i tidigare utförda evidensgenererande studier. Därigenom begränsas evidensens generaliserbarhet och riktlinjernas applicerbarhet på dessa patienter. I studie III fann vi att frailty (skörhet) är en stark oberoende riskfaktor för kliniskt utfall på kort sikt, inklusive en-månadsmortalitet, hos äldre patienter med NSTEMI. I synnerhet sköra patienter med hög grad av komorbiditet uppvisade en markant ökad risk för negativt kliniskt utfall.

Framöver bör prospektiva kliniska studier och registerstudier med få exklusionskriterier utföras. Ett alternativ skulle kunna vara konsensus-baserade bedömningar, baserade på ett ramverk för prioritering av äldre patienter med komplexa behov. Dessa bedömningar skulle syfta till att skatta nytta-risk relationen för en intervention samt tidsramen för förväntad nytta i relation till förväntad återstående livstid. I avhandlingen presenteras ett tentativt begreppsligt ramverk baserat på komorbiditet, frailty (skörhet) och sjukdomsspecifik risk.

ACKNOWLEDGEMENTS

After working in clinical practise for almost 15 years it has been a pleasure to focus on this field. I would like to express my gratitude to everyone who has contributed to the accomplishment of this thesis, particularly the following persons:

Per Carlsson, my supervisor, for your enthusiasm, great wisdom, generous attitude, and for your friendship. It has been a privilege to be a PhD candidate.

Rurik Löfmark, my co-supervisor, for your practical, highly effective, clever and encouraging support.

Katrin Lindroth, Karin Bäckman, Ann-Charlotte Nedlund, and Peter Garpenby for very interesting and intriguing priority setting discussions during long-lasting coffee breaks.

Magnus Husberg, for invaluable help in solving complicated computer and societal problems.

Lena Hector, for all your effective help in the dark jungle of administrative issues!

David Andersson, statistician and freedom fighter, for sharing your statistical expertise.

Mikael Rahmqvist, register expert of CMT, for fruitful and constructive discussions.

All **other colleagues** at the CMT and the Priority setting centre for interesting and encouraging discussions.

Magnus Janzon, Eva Swahn, Joakim Alfredsson, and Marcus Lindenberger for being my partners and tutors in the FINE75+ study. It has been a true privilege to benefit from your outstanding research scholarship!

Elisabeth Logander, outstanding research nurse, for your invaluable contribution to the FINE75+ study and for teaching me the tricks of the trade.

Erling Karlsson, retired cardiologist and former member of the Priority setting centre, whose wisdom and experience from clinical and scientific areas were a source of inspiration in planning studies I and II.

Stella Cizinsky, Carl-Johan Höijer, Peter Eriksson, Martin Stagmo, and Maria Hårdstedt in the Working Group for Ethics and Health Economy of the Swedish Society of Cardiology for very valuable discussions and active contributions in two pilot studies. (Magnus Janzon and Rurik Löfmark have already been mentioned)

APPENDICES

Appendix A

**Enkät till kardiologer –
Multisjuka äldre patienter med instabil kranskärlssjukdom**

Din bakgrund

Antal år verksam inom kardiologi	0-5☐	6-10☐	11-20☐	21-☐

Kön   Man ☐   Kvinna ☐

Är du även specialist i
allmän internmedicin?   Ja ☐   Nej ☐

Din nuvarande arbetsplats

Typ av sjukhus   Länsdels- ☐   Läns- ☐   Region- ☐   Annat ☐

Klinik   Kardiologisk ☐   Medicinsk ☐   Annan ☐

Antal år på samma klinik   _____

Utförs PCI på indikationen instabil
kranskärlssjukdom på ditt sjukhus?   Ja ☐   Nej ☐

Har du deltagit i formellt
prioriteringsarbete i landstinget/
regionen (policynivå)?   Ja ☐   Nej ☐

Användning av dokumentet *Nationella riktlinjer för hjärtsjukvård (SoS)*

1. **I vilken utsträckning är du förtrogen med innehållet i *Nationella riktlinjer för hjärtsjukvård?***

   Mycket liten   *Ganska liten*   *Ganska stor*   *Mycket stor*
   ☐   ☐   ☐   ☐

2a. **I vilken utsträckning används idag *Nationella riktlinjer för hjärtsjukvård* för att skapa lokala handläggningsriktlinjer inom kardiologi på ditt sjukhus?**

   Mycket liten   *Ganska liten*   *Ganska stor*   *Mycket stor*
   ☐   ☐   ☐   ☐

2b. **I vilken utsträckning anser du att *Nationella riktlinjer för hjärtsjukvård* är användbart för att skapa lokala handläggningsriktlinjer inom kardiologi på ditt sjukhus?**

   Mycket liten   *Ganska liten*   *Ganska stor*   *Mycket stor*
   ☐   ☐   ☐   ☐

3a. **I vilken utsträckning använder du idag, direkt eller indirekt, innehållet i *Nationella riktlinjer för hjärtsjukvård* i ditt kliniska beslutsfattande?**

   Mycket liten   *Ganska liten*   *Ganska stor*   *Mycket stor*
   ☐   ☐   ☐   ☐

3b. **I vilken utsträckning anser du att *Nationella riktlinjer för hjärtsjukvård* borde vara användbart i ditt kliniska beslutsfattande?**

   Mycket liten   *Ganska liten*   *Ganska stor*   *Mycket stor*
   ☐   ☐   ☐   ☐

Kommentar:

Vård av multisjuka äldre med instabil kranskärlssjukdom på ditt sjukhus

Definition av multisjuka äldre: Personer 75 år och äldre som under de senaste 12 månaderna har varit inneliggande minst tre gånger inom slutenvården och med tre eller flera diagnoser i tre eller flera skilda diagnosgrupper enligt klassifikationssystemet ICD 10. (Socialstyrelsen 2002).

4. Hur stor andel av alla patienter med instabil kranskärlssjukdom på ditt sjukhus uppskattar du utgörs av multisjuka äldre patienter?

_____%

5. Uppskatta andelen av de multisjuka äldre med instabil kranskärlssjukdom på ditt sjukhus som får vård på följande typ av vårdenhet

HIA/IVA _____%

Annan kardiologisk vårdenhet _____%

Internmedicin/MAVA _____%

Annan vårdenhet _____%

Summa **100 %**

6. Hur ofta handlägger du multisjuka äldre patienter med instabil kranskärlssjukdom?

☐ **dagligen**

☐ **någon eller några gånger per vecka**

☐ **någon eller några gånger per månad**

☐ **mer sällan/aldrig**

Kommentar:

Prioritering av multisjuka äldre med instabil kranskärlssjukdom på ditt sjukhus

7. **Hur stor vikt lägger du vid följande då du handlägger individuella multisjuka äldre patienter med instabil kranskärlssjukdom?**

	Mycket liten	*Ganska liten*	*Ganska stor*	*Mycket stor*
Nationella riktlinjer för hjärtsjukvård	☐	☐	☐	☐
Egen klinisk erfarenhet	☐	☐	☐	☐
Patientens åsikter	☐	☐	☐	☐
Anhörigas åsikter	☐	☐	☐	☐

8. **Hur prioriteras multisjuka äldre med instabil kranskärlssjukdom i förhållande till andra patienter med samma tillstånd på ditt sjukhus?**

Avseende	*Alltför högt*	*Rättmätigt högt*	*Rättmätigt lågt*	*Alltför lågt*
koronarangiografi	☐	☐	☐	☐
läkemedel	☐	☐	☐	☐
PCI/CABG	☐	☐	☐	☐
val av vårdnivå	☐	☐	☐	☐

Kommentar:

9. **I vilken utsträckning anser du att det följande skulle förbättra prioriteringen av multisjuka äldre med instabil kranskärlssjukdom på klinisk nivå?**

	Mycket Liten	*Ganska liten*	*Ganska stor*	*Mycket stor*
Ökad följsamhet mot *Nationella riktlinjer för hjärtsjukvård*	☐	☐	☐	☐
Specifika evidensbaserade nationella riktlinjer för multisjuka äldre	☐	☐	☐	☐
Lokala handläggnings-riktlinjer för multisjuka äldre	☐	☐	☐	☐
Fler behandlingsstudier inkluderande multi-sjuka äldre	☐	☐	☐	☐

10. **Vilken åtgärd (av de ovan nämnda eller någon annan åtgärd) anser du vara viktigast för att underlätta prioriteringen av multisjuka äldre med instabil kranskärlssjukdom på klinisk nivå? Konkretisera!**

v.g.v.

11. **Hur kan kliniskt beslutsfattande rörande multisjuka äldre med instabil kranskärlssjukdom underlättas när valet står mellan alternativen livsförlängande behandling (exempelvis i form av PCI) och enbart god omvårdnad/symtomlindring?**

12. **Finns det några hinder mot att tillämpa detta arbetssätt (enligt svaret på fråga 11) idag och i så fall vilka?**

TACK FÖR DIN MEDVERKAN!

ENKÄTEN SKICKAS ÅTER I BIFOGAT SVARSKUVERT

Appendix B

The Canadian Study of Health and Aging (CSHA) Clinical Frailty Scale (CFS)

1 Very fit – robust, active, energetic, well motivated and fit; these people commonly exercise regularly and are in the most fit group for their age

2 Well – without active disease, but less fit than people in category 1.

3 Well, with treated comorbid disease – disease symptoms are well controlled compared with those in category 4

4 Apparently vulnerable – although not frankly dependent, these people commonly complain of being "slowed up" or have disease symptoms.

5 Mildly frail – with limited dependence on others for instrumental activities of daily living

6 Moderately frail – help is needed with both instrumental and non-instrumental activities of daily living

7 Severely frail – completely dependent on others for the activities of daily living, or terminally ill.

(Rockwood, K. et al. (2005). A global clinical measure of fitness and frailty in elderly people. *CMAJ* 173(5): 489-95.)

Appendix C

CSHA-skalan för klinisk skörhet

Översättning av The Canadian Study of Health and Aging Clinical Frailty Scale (Rockwood et al. 2005) enligt Linköpingsversionen (Ekerstad et al. 090917)

1   Mycket vital – är stark, aktiv, energisk, motiverad och i gott skick; dessa individer tränar ofta regelbundet och tillhör den grupp som är i bäst skick för sin ålder.

2   Vital – har ingen aktiv sjukdom, men är i sämre skick än individer i kategori 1.

3   Vital, med behandlad komorbid sjukdom – bättre kontroll över sjukdomssymtomen jämfört med kategori 4.

4   Uppenbart sårbar – är inte direkt beroende av andra, men klagar ofta över att de begränsas ("saktas ned") på grund av sitt tillstånd eller över sjukdomssymtom.

5   Lindrigt skör – är till viss grad beroende av andra för att klara av instrumentella aktiviteter i det dagliga livet.

6   Måttligt skör – behöver hjälp med såväl instrumentella som icke-instrumentella (personliga) aktiviteter i det dagliga livet.

7   Allvarligt skör – är fullständigt beroende av andra för att klara av aktiviteter i det dagliga livet, eller är terminalt sjuk.

Appendix D

The CAD-specific index (Sachdev 2004).

Risk factor	Integer coefficient
Current smoker	1
Hypertension	1
History of CVA/TIA	1
DM	2
DM with sequelae	3
COPD	2
PVD	2
Tumour/lymphoma/leukemia	2
Moderate to severe renal disease*	7
Metastatic cancer	5

*Defined as creatinine > 3 mg/dl (29)

Appendix E

Tentative framework for the categorization (I-VIII) of the needs of elderly NSTEMI patients with multi-morbidity and a tentative relative ranking of the categories regarding coronary angiography from a theoretical standpoint.

Abbreviations and definitions:

NSTEMI: Non ST Elevation Myocardial Infarction

CVR+: High or medium cardiovascular risk according to FRISC score
CVR-: Low cardiovascular risk

FRISC score: an internationally accepted scoring system assessing cardiovascular risk, taking into account the following parameters denoting high risk: chronological age>70 years, male sex, diabetes, former myocardial infarction, inflammatory activation, positive biochemical markers (troponins), and electrocardiographic signs of myocardial ischemia. The presence of three or more of the mentioned parameters implies medium or high cardiovascular risk

CM+: The presence of at least one severe co-morbid condition, to a degree defined as severe and/or potentially affecting the one-year prognosis; constituting exclusion criteria in the largest evidence-generating studies on NSTEMI, e.g. severe renal insufficiency, severe dementia, severe anemia, active severe bleeding or non-curable malignant tumor
CM-: The absence of any severe co-morbid condition according to the above-mentioned definition
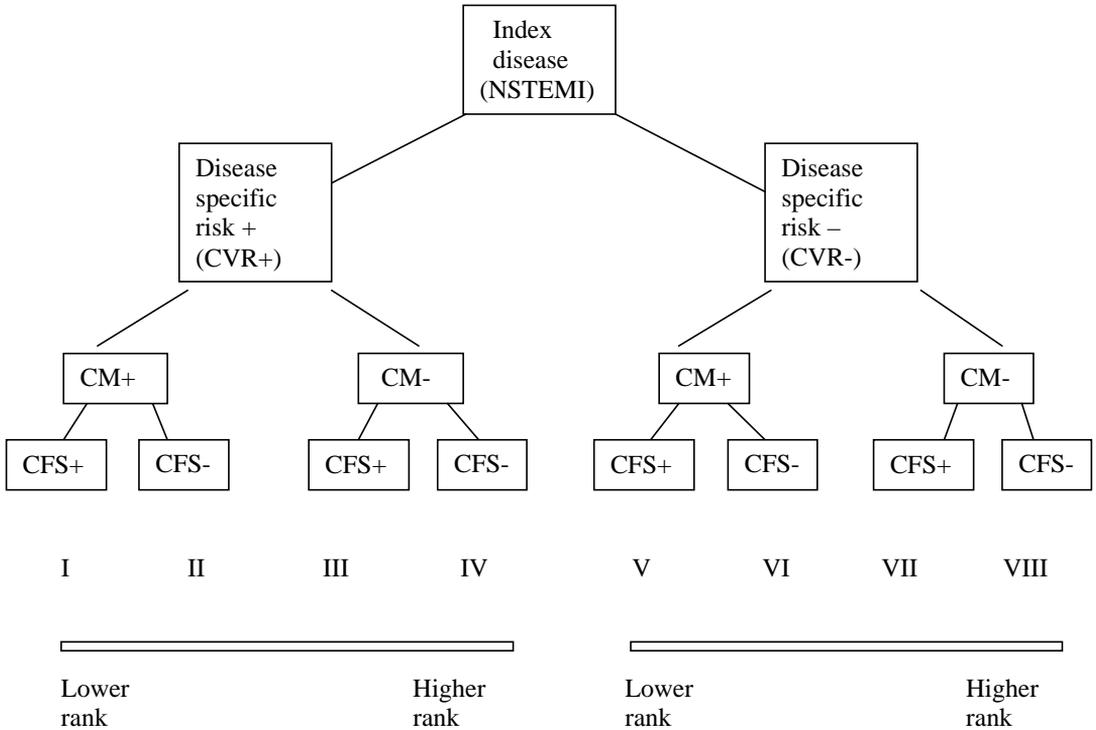
CFS+: Moderate or severe degree of frailty, i.e. 6-7 on the 7-point Clinical Frailty Scale
CFS-: The absence of moderate or severe frailty, i.e. 1-5 on the 7-point Clinical Frailty Scale
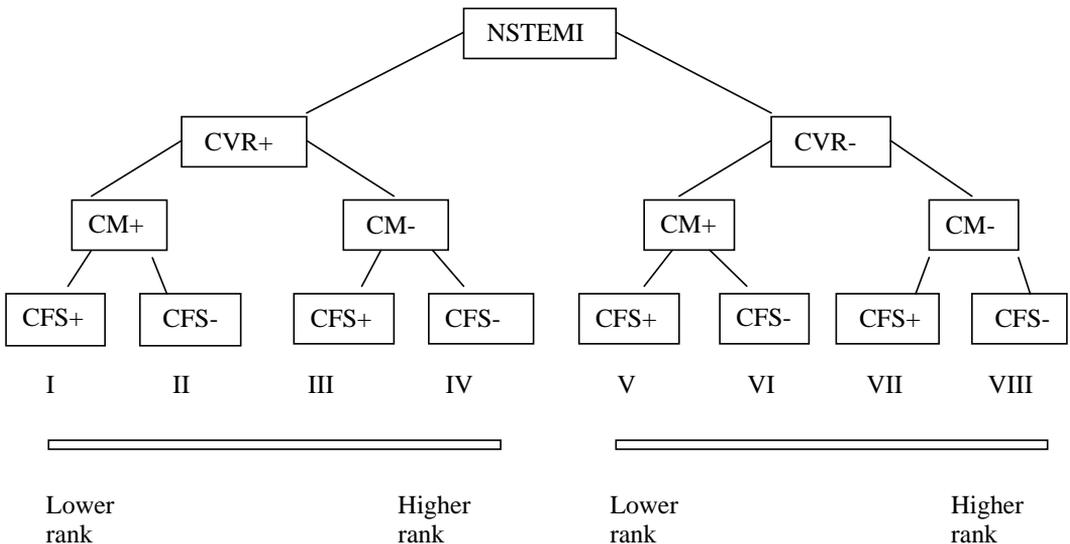
Appendix F

Tentative framework for categorization of elderly patients with complex needs (revised)

```
                              Index
                             disease
                            (NSTEMI)

        Disease                                    Disease
        specific                                   specific
        risk +                                     risk –
        (CVR+)                                     (CVR-)

      CM+         CM-                           CM+         CM-

  CFS+   CFS-   CFS+   CFS-               CFS+   CFS-   CFS+   CFS-

   I      II     III    IV                 V      VI    VII    VIII


Lower              Higher          Lower              Higher
rank               rank            rank               rank
```

Proposed typical cases in micro level priority setting, i.e. prioritization objects, (I-VIII) of the health care needs of elderly patients with complex needs and the same index condition, e.g. NSTEMI, and a tentative relative ranking of the typical cases regarding an intervention, e.g. coronary angiography.

Abbreviations and definitions:

NSTEMI: Non ST Elevation Myocardial Infarction

CVR+: High or medium cardiovascular risk according to FRISC score [Lagerqvist 2005; National Board of Health and Welfare 2008]

CVR-: Low cardiovascular risk

FRISC score: an internationally accepted scoring system assessing cardiovascular risk, taking into account the following parameters denoting high risk: chronological age>70 years, male sex, diabetes, former myocardial infarction, inflammatory activation, positive biochemical markers (troponins) , and electrocardiographic signs of myocardial ischemia. The presence of three or more of the mentioned parameters implies medium or high cardiovascular risk

CM+: The presence of one or more severe co-morbid condition: acute severe comorbid condition [Lichtman 2007], e.g. stroke, active bleeding, severe infection; severe degree of comorbidity according to consensus definitions, e.g. severe renal insufficiency, severe COPD, severe dementia, severe anemia [Levey et al. 2005; The Swedish National Board of Health and Welfare 2004; The Swedish Dementia Centre 2008; Nilsson-Ehle et al. 2000]; non-curable malignant tumor; or any other condition constituting exclusion criteria in the largest evidence-generating studies on NSTEMI [Metha et al. 2005], including conditions with impact on the one-year prognosis.

CM-: The absence of any severe co-morbid condition according to the above-mentioned definition

CFS+: Moderate or severe degree of frailty, i.e. 6-7 on the 7-point Clinical Frailty Scale [Rockwood 2005]

CFS-: The absence of moderate or severe frailty, i.e. 1-5 on the 7-point Clinical Frailty Scale

Appendix G

Niklas Ekerstad
Per Carlsson
Rurik Löfmark

Prioritering av sköra äldre patienter med NSTEMI

Bakgrund

Nationella riktlinjer för prioritering inom hjärtsjukvård är i allmänhet accepterade och uppskattade bland kardiologer, men de har visat sig ha vissa begränsningar bland annat avseende klinisk relevans vid komplexa patientfall. Dagens riktlinjer för prioriteringar berör nästan enbart renodlade tillstånd, där hjärtproblematiken är helt dominerande för beslutsfattande och prioritering. I själva verket utgörs en betydande del av hjärtsjukvården av patienter med flera samexisterande tillstånd och komplexa behov.

I metodbilagan till Nationella riktlinjer för hjärtsjukvård 2008 framhålls att "Det är den totala bedömningen av patientens behov och hur patienten kan tillgodogöra sig vården som ska avgöra insatsen". Vidare poängteras att det inte är patientens kronologiska ålder, den tid som förflutit sedan personen föddes, som ska ha betydelse ur prioriteringssynvinkel. I stället understryks betydelsen av att värdera patientens biologiska status och förväntade livslängd. Såväl förväntad nytta av en åtgärd som risken för komplikationer av åtgärden kan påverkas av den biologiska åldern inklusive förekomst av samsjuklighet (komorbiditet). Ovanstående måste vägas in i beslutsprocessen för att undvika såväl under- som överbehandling.

I den tillämpning av Nationella modellen för öppna vertikala prioriteringar inom svensk hälso- och sjukvård som de nationella riktlinjerna representerar, beskrivs ingående nytta-riskrelationen för olika åtgärder vid olika tillstånd ur kardiovaskulär synvinkel. Emellertid ges begränsad vägledning avseende hur patientens biologiska ålder kan uppskattas, hur olika (företrädesvis icke-kardiovaskulära) samsjukliga tillstånd påverkar nytta-riskrelationen samt hur patientens totala behov kan uppskattas. Med tanke på att omkring 40 % av hjärtinfarkterna drabbar individer äldre än 80 år gamla (genomsnittsåldern i de största hjärtstudierna är 63 år) kan detta utgöra ett problem. Dessutom uppvisar många äldre en betydande och växande samsjuklighet. Bristen på vägledning riskerar att leda till godtyckliga beslut.

Syfte

Vi tror att riktlinjerna för prioriteringar inom hjärtsjukvård skulle behöva kompletteras med stöd för prioritering avseende komplexa sjukdomstillstånd. Då förutsätts att mer information beaktas vid den sammanvägda prioriteringen samt att erfarenhetsbaserad kunskap om patientnytta och kostnadseffektivitet kan systematiseras och användas som grund för prioriteringar när vetenskapliga underlag delvis saknas.

Tentativt, och applicerat på NSTEMI, arbetar vi med utgångspunkten att följande aspekter kan påverka rangordningen av prioriteringsobjekt:
1) den stratifiering avseende kardiovaskulär risk som idag vägs in i bedömningen i riktlinjerna (hög/måttlig versus låg risk enligt FRISCII-score);
2) information om de vanligaste och mest relevanta komorbida tillstånden; samt
3) information om patientens skörhet (frailty, se nedan).

För att undersöka dessa tre variablers kliniska relevans och därmed relevans för prioriteringar studerar vi deras förmåga att diskriminera mellan 15 autentiska (men förenklade) patientfall med NSTEMI. Vi vill undersöka i vilken utsträckning information om sjukdomsspecifik (kardiovaskulär) risk, samsjuklighet samt skörhet påverkar det kliniska beslutet.

Du ombeds ta ställning till de 15 fallbeskrivningarna och ange ditt beslut. På slutet ställer vi några frågor.

Premisser
Kliniskt relevant bröstsmärta förutsätts föreligga i samtliga fall.
Patienter/anhöriga har inga bestämda uttalade preferenser avseende handläggning.
I inget fall uppvisas refraktär ischemi, kardiogen chock eller ST-höjning.

Följande information återges: kön, kronologisk ålder, kardiovaskulära riskfaktorer, tidigare hjärtinfarkt, aktuell infarktdiagnosrelaterad information (ekg, hjärtenzymer), bedömd vänsterkammarfunktion (företrädesvis via ekokardiografi), hemoglobin, kreatinin, GFR, känd samsjuklighet, nedsatt förmåga till att ge informerat samtycke samt skörhet (frailty).

Skörhet (frailty) är ett validerat globalt mått på biologisk ålder med prognostisk innebörd (The Canadian Study of Health and Ageing Clinical Frailty Scale)[1]. Ju högre grad av skörhet desto sämre prognos.

The CSHA Clinical Frailty Scale (CFS)
1 Very fit – robust, active, energetic, well motivated and fit; these people commonly exercise regularly and are in the most fit group for their age
2 Well – without active disease, but less fit than people in category 1.
3 Well, with treated comorbid disease – disease symptoms are well controlled compared with those in category
4 Apparently vulnerable – although not frankly dependent, these people commonly complain of being "slowed up" or have disease symptoms
5 Mildly frail – with limited dependence on others for instrumental activities of daily living
6 Moderately frail – help is needed with both instrumental and non-instrumental activities of daily living
7 Severely frail – completely dependent on others for the activities of daily living, or terminally ill.

Nomenklaturen i *Nationella modellen för öppna vertikala prioriteringar inom svensk hälso- och sjukvård* eftersträvas vid bedömningen om än i förenklad form. För varje patientfall betraktas "Hälsotillstånd" som summan av följande: det kardiovaskulära tillståndet (NSTEMI), aktuell samsjuklighet samt aktuell skörhet (enligt CFS). Följande åtgärd bedöms: *coronarangiografi med möjlighet till invasiv åtgärd vid samma vårdtillfälle.*

För varje fall ber vi dig bedöma följande:
- **hälsotillståndets svårighetsgrad**
- **patientnytta**
- **kostnad per hälsovinst.**

- **Under "Rangordning" ange siffra (1-10; högsta rangordning: 1) eller icke-göra.**

1. Rockwood, K., Song, X., MacKnight, C., Bergman, H., Hogan, D.B., McDowell, I., Mitnitski, A. (2005). A global clinical measure of fitness and frailty in elderly people. *CMAJ* 173(5): 489-95.

Fall 1

Man. 62 år. Hyperkolesterolemi, diabetes mellitus. Ekg: ischemiska ST-sänkningar V3-V6. TroponinT 0.35-0.87. Normal VK-funktion. Hb 130. Krea 105; GFR 85. Clinical Frailty Scale: grad 1 (se nyckel under Premisser ovan).

Hälsotillstånd/ Åtgärd	Hälso- tillståndets svårighetsgrad ☐ Mycket hög ☐ Hög ☐ Måttlig ☐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang- ordning (1-10 eller icke- göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		☐ Mycket stor ☐ Stor ☐ Måttlig ☐ Liten	☐ Hög ☐ Måttlig ☐ Låg ☐ Ej bedömbar	

Fall 2

Kvinna. 67 år. Rökare. Lindrig övervikt; BMI 26. Ekg: diskret formförändring avseende STT-sträckan V1-V4. TroponinT 0.05-0.16. VK-funktion i nedre normalintervallet. Hb 123. Krea 95; GFR 81. Clinical Frailty Scale: grad 2.

Hälsotillstånd/ Åtgärd	Hälso- tillståndets svårighetsgrad ☐ Mycket hög ☐ Hög ☐ Måttlig ☐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang- ordning (1-10 eller icke- göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		☐ Mycket stor ☐ Stor ☐ Måttlig ☐ Liten	☐ Hög ☐ Måttlig ☐ Låg ☐ Ej bedömbar	

Fall 3

Kvinna. 89 år. Hypertoni. Känd ischemisk hjärtsjukdom, tidigare NSTEMI 2005. Tidigare UVIx2. Bilat. höftopererad (artros). Levaxinsubstituerad hypotyreos. Ekg: formförändrad STT-sträcka V2-V6, ST-sänkning V4-V6. TroponinT 0.11-0.35. Inga kliniska svikttecken. Hb 115. Krea 76; GFR 61. Clinical Frailty Scale: grad 2-3.

Hälsotillstånd/ Åtgärd	Hälso- tillståndets svårighetsgrad ☐ Mycket hög ☐ Hög ☐ Måttlig ☐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang- ordning (1-10 eller icke- göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		☐ Mycket stor ☐ Stor ☐ Måttlig ☐ Liten	☐ Hög ☐ Måttlig ☐ Låg ☐ Ej bedömbar	

35

Fall 4

Kvinna. 81 år. F.d. rökare. Hypertoni. Hyperkolesterolemi. Diabetes mellitus. Tidigare NSTEMI 2004, PCI med stent mot culprit lesion (RCA), 3-kärlssjuk. Hjärtsvikt; måttligt nedsatt VK-funktion. Biologisk aortaklaffprotes. Kroniskt förmaksflimmer. Lindrig KOL. Kronisk njursvikt. Ekg: ST-sänkningar II, aVF och III samt V3-V6. TroponinT 0.09-2.1-0.13. Hb 122. Krea 345; GFR 13. Clinical Frailty Scale: grad 7.

Hälsotillstånd/ *Åtgärd*	Hälso-tillståndets svårighetsgrad ❐ Mycket hög ❐ Hög ❐ Måttlig ❐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		❐ Mycket stor ❐ Stor ❐ Måttlig ❐ Liten	❐ Hög ❐ Måttlig ❐ Låg ❐ Ej bedömbar	

Fall 5

Man. 83 år. Hypertoni. Benign prostatahyperplasi. Inkontinens. Nedsatt hörsel och syn bilat. Lindrig-måttlig osteoporos. Tidigare op pga pertrochantär höftfraktur. Obstipationsbesvär. Lindrig kognitiv nedsättning. Ekg: vänstergrenblock. TroponinT 0.06-0.11. Lindrigt nedsatt VK-funktion. Hb 137. Krea 98: GFR 47. Clinical Frailty Scale: grad 6.

Hälsotillstånd/ *Åtgärd*	Hälso-tillståndets svårighetsgrad ❐ Mycket hög ❐ Hög ❐ Måttlig ❐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		❐ Mycket stor ❐ Stor ❐ Måttlig ❐ Liten	❐ Hög ❐ Måttlig ❐ Låg ❐ Ej bedömbar	

Fall 6

Kvinna. 81 år. Lindrig osteoporos. Tidigare pneumonix2. Bilat hörselnedsättning. RA. Måttlig Mb Parkinson. Lindrig kognitiv nedsättning. Ekg ua. TroponinT 0.09-0.17. VK-funktion i nedre normalintervallet. Hb 120. Krea 92; GFR 51. Clinical Frailty Scale: grad 6-7.

Hälsotillstånd/ *Åtgärd*	Hälso-tillståndets svårighetsgrad ❐ Mycket hög ❐ Hög ❐ Måttlig ❐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		❐ Mycket stor ❐ Stor ❐ Måttlig ❐ Liten	❐ Hög ❐ Måttlig ❐ Låg ❐ Ej bedömbar	

Fall 7

Kvinna. 74 år. F.d. rökare. Metastaserande, icke-kurabel pancreascancer; smärtproblematik. Kronisk anemi. Ekg: ST-sänkningar V4-V6 och inferiort. TroponinT 0.04-0.05. Inga kliniska sviktsymtom, lungröntgen ua. Hb 105. Krea 110; GFR 48. Clinical Frailty Scale: grad 6-7.

Hälsotillstånd/ *Åtgärd*	Hälso-tillståndets svårighetsgrad ❒ Mycket hög ❒ Hög ❒ Måttlig ❒ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		❒ Mycket stor ❒ Stor ❒ Måttlig ❒ Liten	❒ Hög ❒ Måttlig ❒ Låg ❒ Ej bedömbar	

Fall 8

Man. 69 år. Rökare. Hyperkolesterolemi. Lindrig kognitiv nedsättning. In pga bröstsmärta och högersidig hemipares, central facialispares samt dysfasi. Ekg ua. Troponin T 0.11-0.07. CT skall: färsk, vänstersidig utbredd cerebral infarkt. Normal VK-funktion. Clinical Frailty Scale: grad 3-4 (innan aktuell episod).

Hälsotillstånd/ *Åtgärd*	Hälso-tillståndets svårighetsgrad ❒ Mycket hög ❒ Hög ❒ Måttlig ❒ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		❒ Mycket stor ❒ Stor ❒ Måttlig ❒ Liten	❒ Hög ❒ Måttlig ❒ Låg ❒ Ej bedömbar	

Fall 9

Man. 84 år. Hypertoni. Diabetes mellitus. Konstaterat ulcus ventriculi för två månader sedan. Mörk avföring igår kväll och idag. Ekg: bifascikulärt block (RBBB+LAH). TroponinT 0.04-0.13. Lindrigt nedsatt VK-funktion. Hb 93 (118 för en månad sedan). Krea 135; GFR 49. Clinical Frailty Scale: grad 3.

Hälsotillstånd/ *Åtgärd*	Hälso-tillståndets svårighetsgrad ❒ Mycket hög ❒ Hög ❒ Måttlig ❒ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		❒ Mycket stor ❒ Stor ❒ Måttlig ❒ Liten	❒ Hög ❒ Måttlig ❒ Låg ❒ Ej bedömbar	

Fall 10

Man. 79 år. F.d. rökare. Hyperkolesterolemi. Prostatahyperplasi. Senaste dygnen sveda vid miktion. In pga bröstsmärta och högfebrilitet. Ekg: sinustakykardi, utbredda ST-sänkningar V3-V6. TroponinT 0.10-0.23. Hb 121. Krea 119; GFR 51. Clinical Frailty Scale: grad 2-3.

Hälsotillstånd/ Åtgärd	Hälso-tillståndets svårighetsgrad ☐ Mycket hög ☐ Hög ☐ Måttlig ☐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		☐ Mycket stor ☐ Stor ☐ Måttlig ☐ Liten	☐ Hög ☐ Måttlig ☐ Låg ☐ Ej bedömbar	

Fall 11

Kvinna. 76 år. Hypertoni. Hyperkolesterolemi. Tidigare NSTEMI, PCI med stent mot culprit lesion (LAD). Uttalad demens, troligen på cerebralt vaskulär bas. Oförmögen att lämna informerat samtycke avseende handläggning. Ekg: formförändring avseende STT-sträckan inferiort. TroponinT 0.13-0.05. Lindrigt nedsatt VK-funktion. Hb 119. Krea 99; GFR 61. Clinical Frailty Scale: grad 5.

Hälsotillstånd/ Åtgärd	Hälso-tillståndets svårighetsgrad ☐ Mycket hög ☐ Hög ☐ Måttlig ☐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		☐ Mycket stor ☐ Stor ☐ Måttlig ☐ Liten	☐ Hög ☐ Måttlig ☐ Låg ☐ Ej bedömbar	

Fall 12

Kvinna. 79 år. F.d. rökare. Diabetes mellitus. Hyperkolesterolemi. Hypertoni. Tidigare NSTEMI, konservativt behandlad. Kronisk njursvikt (diabetesnefropati). TroponinT ej taget. Ekg: ST-sänkningar V2-V5. Hb 112. Krea 240; GFR 17. Clinical Frailty Scale: grad 3-4.

Hälsotillstånd/ Åtgärd	Hälso-tillståndets svårighetsgrad ☐ Mycket hög ☐ Hög ☐ Måttlig ☐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		☐ Mycket stor ☐ Stor ☐ Måttlig ☐ Liten	☐ Hög ☐ Måttlig ☐ Låg ☐ Ej bedömbar	

Fall 13

Man. 80 år. Rökare. Tidigare STEMI, behandlad med primär PCI. Kronisk hjärtsvikt; senaste ekokardiografin visade uttalat nedsatt VK-funktion med skattad EF 10-20%. In i bilden av manifest hjärtinkompensation (pre-lungödem). Ekg: vänstergrenblock. TroponinT 0.13-0.57. Aktuell VK-funktion som tidigare. Hb 110. Krea 135; GFR 45. Clinical Frailty Scale: grad 4-5.

Hälsotillstånd/ *Åtgärd*	Hälso-tillståndets svårighetsgrad ❐ Mycket hög ❐ Hög ❐ Måttlig ❐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		❐ Mycket stor ❐ Stor ❐ Måttlig ❐ Liten	❐ Hög ❐ Måttlig ❐ Låg ❐ Ej bedömbar	

Fall 14

Man. 81 år. Diabetes mellitus. Hypertoni. Måttlig övervikt. Kronisk ischemisk hjärtsjukdom och hjärtsvikt. Tidigare NSTEMI x 2. PCI med stent vid första infarkten, CABG vid andra infarkten för ett år sedan (trekärlssjuka). Kroniskt förmaksflimmer, Waranbehandlad. Senaste månaden accelererande angina. Ekg: FF, 105/min, vänstergrenblock. TroponinT 0.11-0.23. Lindrigt nedsatt VK-funktion. Hb 127. Krea 124; GFR 53. Clinical Frailty Scale: grad 3-4.

Hälsotillstånd/ *Åtgärd*	Hälso-tillståndets svårighetsgrad ❐ Mycket hög ❐ Hög ❐ Måttlig ❐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		❐ Mycket stor ❐ Stor ❐ Måttlig ❐ Liten	❐ Hög ❐ Måttlig ❐ Låg ❐ Ej bedömbar	

Fall 15

Man. 77 år. Leverinsufficiens på basen av etylorsakad levercirros. Ekg: uttalade ST-sänkningar V1-V6. TroponinT 0.23-0.68. Lindrigt till måttligt nedsatt VK-funktion. Hb 114. Krea 123; GFR 55. ASAT 2.44, ALAT 2.11, PK 1.7 INR. Clinical Frailty Scale: grad 4-5.

Hälsotillstånd/ *Åtgärd*	Hälso-tillståndets svårighetsgrad ❐ Mycket hög ❐ Hög ❐ Måttlig ❐ Låg	Effekt av åtgärd/ Patientnytta (beakta möjlig nytta och komplikationsrisk)	Kostnad/ hälsovinst (t.ex. kvalitetsjusterade levnadsår)	Rang-ordning (1-10 eller icke-göra)
Coronarangiografi med möjlighet till invasiv åtgärd under vårdtiden		❐ Mycket stor ❐ Stor ❐ Måttlig ❐ Liten	❐ Hög ❐ Måttlig ❐ Låg ❐ Ej bedömbar	

Vid prioritering avseende sköra äldre med NSTEMI, hur stor är relevansen av

Kardiovaskulär risk	❒ Mycket stor	❒ Stor	❒ Måttlig	❒ Liten
Samsjuklighet	❒ Mycket stor	❒ Stor	❒ Måttlig	❒ Liten
Skörhet (CFS)	❒ Mycket stor	❒ Stor	❒ Måttlig	❒ Liten

Är annan information relevant för prioriteringen; i så fall vilken?

Hur uppfattade du uppgiften?

❒ Mycket svår
❒ Svår
❒ Ganska enkel
❒ Enkel

Uppfattade du fallen som realistiska?

❒ Ja
❒ Ja, delvis
❒ Nej

Kommentarer:

Uppfattade du fallen som representativa för en patientpopulation <u>på</u> HIA?

❒ Ja
❒ Ja, delvis
❒ Nej

Uppfattade du fallen som representativa för en patientpopulation <u>utanför</u> HIA?

❒ Ja
❒ Ja, delvis
❒ Nej

Kommentarer:

REFERENCES

Ahmad N, Boutron I, Dechartres A, Durieux P, Ravaud P. Applicability and generalisability of the results of systematic reviews to public health practice and policy: a systematic review. Trials 2010;11:20. doi:10.1186/1745-6215-11-20.

Akner G. Bräckligt åldrande och multisjuklighet drabbar allt fler. Läkartidningen 2010;107: 2707-2711. (In Swedish).

Alderson P, Green S, Higgins JPT (Eds). Cochrane Reviewers'Handbook 4.2.1 [updated December 2003]. In: The Cochrane Library, Issue. Chichester: John Wiley and Sons Ltd, 2004.

Altman DG, Schulz KF, Moher D. For the Consort Group. The revised CONSORT statement for reporting randomised trials: explanation and elaboration. Ann Intern Med 2001;134: 663–694.

American Heart Association Council. Acute Coronary Care in the Elderly, Part 1. Circulation 2007;115:2549-2569.

Anderson G. Chronic conditions: making the case for ongoing care. Baltimore: Johns Hopkins University, 2007. (Accessed February 20, 2011, at http://www.fightchronicdisease.com/news/pfcd/documents/ChronicCareChartbook_FINAL.pdf.)

Anell A. Swedish healthcare under pressure. Health Econ 2005;14:237-254.

Arvidsson E, André M, Borgquist L, Carlsson P. Priority setting in primary health care - dilemmas and opportunities: a focus group study. Fam Pract 2010;11:71. doi:10.1186/1471-2296-11-71.

Asplund K. Den evidensbaserade medicinen är nödvändig men inte tillräcklig. Läkartidningen 2001;98:3898-3901. (In Swedish).

Baltussen R, Niessen LW. Priority setting of health interventions: the need for multi-criteria decision analysis. Cost Effectiveness and Resource Allocation 2006;4:14. doi:10.1186/1478-7547-4-14.

Bayliss EA, Edwards AE, Steiner JF, Main DS. Processes of care desired by elderly patients with multimorbidities. Fam Pract 2008;25:287-293.

Beauchamp TL, Childress JF. Principles of biomedical ethics, 4th ed. New York: Oxford University Press, 1994.

Berry DC, Michas IC, Gillie T, Forster M. What do patients want to know about their medicines and what do doctors want to tell them? A comparative study. Psychol Health 1997;12:467-480.

Bierman AS. Coexisting Illness and Heart Disease Among Elderly Medicare: Managed Care Enrollees. Health Care Financing Rev 2004;25:105-117.

Boorse C. Health as a theoretical concept. Philosophy of Science 1977;4:542-573.

Boyd CM, Darer J, Boult C, Fried LP, Boult L, Wu AW. Clinical Practice Guidelines and Quality of Care for Older Patients With Multiple Comorbid Diseases: Implications for Pay for Performance. JAMA 2005;294:716-724.

Bowling A. Ageism in Cardiology. BMJ 1999;319;1353-1355.

Bowling A, Harries C, Forrest D, Harvey N. Variations in cardiac interventions: doctors practices and views. Fam Pract 2006;23:427-436.

Braithwaite RS, Concato J, Chang CC, Roberts MS, Justice AC. A Framework for Tailoring Clinical Guidelines at the Point of Care. Arch Intern Med 2007;167:2361-2365.

British Department of Health. The Coronary Heart Disease National Service Framework: Buildning on excellence, maintaining progress – Progress report for 2008. London, UK.

Butler RN. Ageism: Another form of bigotry. The Gerontologist 1969;9:243-246.

Carlsson P, Kärvinge C, Broqvist M, Eklund K, Hallin B, Jacobsson C, Jacobsson, Ekman G, Källgren Peterson C, Lindh M, Nordlander B, Rosén P, Sjöblom U, Sohlberg A. The National Model for Transparent Vertical Prioritisation in Swedish Health Care, Report 2007;1. Linköping: National Centre for Priority Setting in Health Care, 2007.

Carlsson P. Priority setting in health care: Swedish efforts and experiences. Scand J Public Health 2010; 38:561-564.

Cieza A, Geyh S, Chatterji S, Kostanjsek N, Üstün B, Stucki G. Identification of candidate categories of the International Classification of Functioning Disability and Health (ICF) for a Generic Core Set based on regression modelling. BMC Medical Research Methodology 2006; 6:36. doi:10.1186/1471-2288-6-36.

Claridge JA, Fabian TC. History and development of evidence-based medicine. World J Surg 2005;29:547-553.

Coast J, Donovan J, Frankel S. Priority setting: The health care debate. New York: John Wiley and Sons, 1996.

Collste G. Should Every Human Being Get Health Care? Priorities in Health Care and the Principle of Human Dignity. Ethical Perspectives 1999;6:115-125.

Coulter A, Ham C. The global challenge of health care rationing. Buckingham: Open University Press, 2000.

Daniels N, Sabin J. The ethics of accountability in managed care reform. Health Affairs 1998;17:50–56.

Daniels N. Accountability for reasonableness. BMJ 2000;321:1300–1302.

Daniels N, Sabin J. Setting limits fairly: Can we learn to share scarce resources? Oxford: Oxford University Press, 2002.

de Groot V, Beckerman H, Lankhorst GJ, Bouter LM. How to measure comorbidity. A critical review of available methods. J Clin Epidemiol 2003;56:221-229.

Elwyn G, Edwards A, Britten N. What information do patients need about medicines? "Doing prescribing": how doctors can be more effective. BMJ 2003;327:864-867.

Feinstein AR. Pre-therapeutic classification of co-morbidity in chronic disease. J Chronic Dis 1970;23:455-468.

Fetter RB, Shin Y, Freeman JL, Averill RF, Thompson JD. Case mix definition by diagnosis-related groups. Med Care 1980;18:1-53.

Fitchett D, Rockwood K. Introduction: Heart Disease in an Elderly Population. Canadian Cardiovascular Society Consensus Conference. Toronto. 2002.

Fortin M, Bravo G, Hudon C, Vanasse A, Lapointe L. Prevalence of multimorbidity among adults seen in family practice. Ann Fam Med 2005;3:223-228.

Fortin M, Soubhi H, Hudon C, Bayliss EA, van den Akker M. Multimorbidity's many challenges. BMJ 2007;334:1016-1017.

FRagmin and Fast Revascularisation during In Stability in Coronary artery disease (FRISC) Investigators. Invasive compared with non-invasive treatment in unstable coronary-artery disease: FRISC II prospective randomised multicentre study. Lancet 1999;354:708–715.

Fried LP, Tangen CM, Walston J. Cardiovascular Health Study Collaborative Research Group Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56:146-156.

Gabbay J, Le May A. Practice-based Evidence for Healthcare: Clinical Mindlines. London: Routledge, 2011.

Gibson JL, Martin DK, Singer PA. Priority setting in hospitals: Fairness, inclusiveness, and the problem of institutional power differences. Social Science and Medicine 2005; 61:2355-2362.

Glancy JM. Dangers of implementation of NICE guideline in acute coronary syndrome. BMJ 2010;340:c2395.

Glenngård AH, Hjalte F, Svensson M, Anell A, Bankauskaite V. Health Systems in Transition: Sweden. Copenhagen: WHO Regional Office for Europe on behalf of the European Observatory on Health Systems and Policies, 2005.

Gray HH, Henderson RA, de Belder MA, Underwood SR, Camm AJ. Early management of unstable angina and non-ST-segment elevation myocardial infarction: summary of NICE guidance. Heart 2010;96:1662-1668.

Green LW, Glasgow RE. Evaluating the relevance, generalization, and applicability of research. Issues in external validation and translation methodology. Evaluation and Health Professions 2006;29:126-153.

Greenhalgh T. Intuition and evidence - uneasy bedfellows? British J of Gen Pract 2002;52:395-400.

Gurner U, Thorslund M. Helhetssyn behövs i vården av multisviktande äldre. Förslag till förändring av vård- och omsorgsstrukturen i Stockholms län. [Overall Vision is Needed in the Care for Multiple-diseased Elderly]. Läkartidningen 2001;98;2596-2602.

Gurner U, Thorslund M. Dirigent saknas i vård och omsorg för äldre. Om nödvändigheten av samordning. Stockholm: Natur och kultur, 2003. (In Swedish).

Guyatt GH, Rennie D. Users' guides to the medical literature [editorial]. JAMA 1993;270:2096-2097.

Guyatt GH, Haynes RB, Jaeschke RZ. Users' Guides to the Medical Literature: XXV. Evidence-based medicine: principles for applying the Users' Guides to patient care. Evidence-Based Medicine Working Group. JAMA 2000;284:1290-1296.

Ham C. Rationing in action. Priority setting in the NHS: reports from six districts. BMJ 1993;307:435-438.

Ham C. Priority setting in health care: learning from international experience. Health Policy 1997;42:49-66.

Harries C, Forrest D, Harvey N, McClelland A, Bowling A. Which doctors are influenced by a patient's age? A multi-method study of angina treatment in general practice, cardiology and gerontology. Qual Saf Health Care 2007;16:23-27.

Hauck K, Smith PC, Goddard M. The Economics of Priority Setting for Health care: A Literature review. HNP Discussion Paper. The World Bank, 2004.

Hillis LD, Lange RA. Optimal Management of Acute Coronary Syndromes. NEJM 2009; 360:2237-2240.

Holm S. Goodbye to the Simple Solutions: the Second Phase of Priority Setting in Health Care. BMJ 1998;317:1000–1007.

Hughes H, Jordan KP, Rajaratnam G, Fawcett S, Croft P. Age Ageing 2008;37:572-575.

Hägglund G, Larsson M. Vi satsar 3,75 miljarder på de allra mest sjuka äldre. The Dagens Nyheter 20110121. (In Swedish).

Judge A, Welton NJ, Sandhu J, Ben-Shlomo Y. Equity in access to total joint replacement of the hip and knee in England: cross sectional study. BMJ 2010:341:c4092.

Kapiriri L, Martin DK. Bedside rationing by health practitioners: A case study in a Ugandan hospital. Medical Decision Making 2007;27:44–52

Karlberg HI, Brinkmo BM: The unethical focus on access: a study of medical ethics and the waiting-time guarantee. Scand J Public Health 2009;37:117-121.

Kenny N, Joffres C. An Ethical Analysis of International Health Priority-Setting. Health Care Anal 2008;16:145–160.

Lee DH, Buth KJ, Martin B-J, Yip AM, Hirsch GM. Frail Patients Are at Increased Risk for Mortality and Prolonged Institutional Care After Cardiac Care. Circulation 2010;121;973-978.

Levi R. Evidensbaserad sjukvård. Vård på säkrare grund. Lund: Studentlitteratur, 1998. (In Swedish).

Lichtman JH, Fathi A, Radford MJ, Lin Z, Loeser CS, Krumholz HM. Acute, severe noncardiac conditions in patients with acute myocardial infarction. Am J Med 2006;119: 843–850.

Lichtman JH, Spertus JA, Reid KJ, Radford MJ, Rumsfeld JS, Allen NB, Masoudi FA, Weintraub WS, Krumholz H. Acute noncardiac conditions and in-hospital mortality in patients with acute myocardial infarction. Circulation 2007;116:1925-1930.

Lindholm L, Henriksson R, Rosén M, Bergenheim T, Salander P. Modified cost-effectiveness analysis takes equity into consideration; malignant glioma treatment more costeffective than hip replacement. Läkartidningen 1999;96:2749-2754.

Liss P-E. Health care need: meaning and measurement. Aldershot: Avebury, 1993.

Liss P-E. Allocation, priority setting and rationing of health care – A concept analysis, Report 2002:4. Linköping: The National Centre for Priority Setting, 2002.

Martin DK, Singer P. Priority Setting and Health Technology Assessment: Beyond Evidence Based Medicine and Cost-Effectiveness Analysis. In Coulter A, Ham C. (Eds.) The Global Challenge of Health Care Rationing. Buckingham: Open University Press, 2000.

Martin DK, Giacomini M, Singer PA. Fairness, accountability for reasonableness and the views of priority setting decision-makers. Health Policy 2002;6:279–290.

Martin DK, Singer P. A strategy to improve priority setting in health care institutions. Health Care Anal 2003;1:59-68.

May C, Rapley T, Moreira T, Finch T, Heaven B. Technogovernance: evidence, subjectivity, and the clinical encounter in primary care medicine. Social Science and Medicine 2006;62: 1022–1030.

May C, Montori VM, Mair FS. We need minimally disruptive medicine. BMJ 2009; 339:b2803.

Mechanic D. Muddling Through Elegantly: Finding the Proper Balance in Rationing. Health Aff 1997;16:83–92.

Melin A. Etiska riktlinjer och principer för prioriteringar inom hälso- och sjukvård – en internationell översikt. Rapport 2007:3. Linköping: The National Centre for Priority Setting in Health Care, 2007. (In Swedish).

Metha SR, Cannon CP, Fox KA, Wallentin L, Braunwald E, Yusuf S. Routine vs Selective Invasive Strategies in Patients With Acute Coronary Syndromes. JAMA 2005;293:2908-2917.

Mehta SR, Granger CB, Boden WE, Steg PG, Bassand J-P, Faxon DP. Early versus delayed invasive intervention in acute coronary syndromes. N Engl J Med 2009;360:2165-2175.

Ministry of Health and Social Affairs 1982. Health and Medical Services Act. SFS 1982:763. Stockholm.

Ministry of Health and Social Affairs. The Swedish Parliamentary Priorities Commission. Priorities in health care: Ethics, economy, implementation. Health Care´s Difficult Choices SOU 1995:5. Stockholm, 1995.

Ministry of Health and Social Affairs. Government bill 1996/97:60. "Priority Setting in Health Care". Stockholm, 1997.

Ministry of Health and Social Affairs. Act on Pharmaceutical Benefits. SFS 2002:160. Stockholm, 2002.

Ministry of Health and Social Affairs. The Future Need for Care, Results from the LEV Project. Reports S2010.021. Stockholm, 2010.

Mitnitski A, Graham JJ, Mogilner AE, Rockwood K. Frailty, fitness and late-life mortality in relation to chronological and biological age. BMC Geriatr 2002;2:1.

Nardi R, Scanelli G, Corrao S, Iori I, Mathieu G, Cataldi Amatrian R. Co-morbidity does not reflect complexity in internal medicine patients. Eur J Intern Med 2007;18:359-368.

National Committee for Quality Assurance. The state of health care quality: 2003. Washington, D.C., 2003.

National Institute for Health and Clinical Excellence. Unstable angina and NSTEMI: the early management of unstable angina and non-ST-segment-elevation myocardial infarction [CG94]. London: NICE, 2010.

Newdick C. Who should we treat?: rights, rationing, and the resources in the NHS. 2nd ed. New York: Oxford University Press, 2005.

Niessen LW, Gijssels EW, Rutten FF. The evidence-based approach in health policy and health interventions delivery. Soc Sci Med 2000;51:859-869.

Nordenfelt L. Health and value: studies in the theory and ethics of health care. Stockholm: Thales, 1991. (In Swedish).

Nordin-Johansson A, Asplund K. Randomised controlled trials and consensus as a basis for interventions in internal medicine. J Intern Med 2000;247:94–104.

Purser JL, Kuchibhatla MN, Fillenbaum GG, Harding TH, Peterson ED, Alexander KP. Identifying Frailty in Hospitalized Older Adults with Significant Coronary Artery Disease. JAGS 2006;54:1674-1681.

Rawls J. A theory of justice. Cambridge: Harvard University Press, 1971.

Ridderstolpe L, Collste G, Rutberg H, Åhlfeldt H. Priority setting in cardiac surgery: a survey of decision making and ethical issues. Journal of Medical Ethics 2003;29:353-358.

Ritchie C. Health care quality and multimorbidity: the jury is still out. Med Care 2007;45:477-479.

Roberts E. GRACE risk recommendations in NICE GC94 are not appropriate. Heart 2010; doi:10.1136/hrt.2010.20451.

Rockwood K. A Brief Clinical Instrument to Classify Frailty in Elderly People. The Lancet 1999;353:205–206.

Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

Rockwood K. An unsuitable old age: the paradoxes of elder care. CMAJ 2005;173:1500-1501.

Rothwell PM. External validity of randomised controlled trials: "to whom do the results of this trial apply?" Lancet 2005;365:82–93.

Sabik LM, Lie RK. Priority setting in health care: Lessons from the experiences of eight countries. Int J Equity Health 2008;7:4. doi:10.1186/1475-9276-7-4.

Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: What it is and what it is not. BMJ 1996;312:71–72.

Sackett DL, Strauss SE, Richardson WS. Evidence-based medicine: how to practice and teach EBM. London: Churchill-Livingstone, 2000.

Safford MM, Allison JJ, Kiefe CI. Patient complexity: more than comorbidity. The vector model of complexity. J Gen Intern Med 2007;22:382-390.

Schmidt HG, Norman GR, Boshuizen HP. A cognitive perspective on medical expertise: theory and implications. Acad Med 1990;65:611-621.

Schön, Donald A. The Reflective Practitioner: How professionals think in action. Aldershot: Arena, 1991.

Sibbald SL, Singer PA, Upshur R, Martin DK. Priority setting: what constitutes success? A conceptual framework for successful priority setting. BMC Health Serv Res 2009;9:43. doi: 10.1186/1472-6963-9-43.

Sibbald SL, Gibson JL, Singer PA, Upshur R, Martin DK. Evaluating priority setting success in healthcare: a pilot study BMC Health Services Research 2010; 10:131. doi:10.1186/1472-6963-10-131.

Singer PA, Mapa J. Ethics of resource allocation: dimensions for healthcare executives. Hosp Q 1998;1:29–31.

Singh M, Rihal CS, Roger VL, Lennon RJ, Spertus J, Jahangir A, Holmes DR. Comorbid conditions and outcomes after percutaneous coronary intervention. Heart 2008;94:1424–1428.

Singh M, Alexander K, Roger VL. Frailty and Its Potential Relevance to Cardiovascular Care. Mayo Clinical Proc 2008;83:1146-1153.

Social- og Helsedepartementet [Ministry of Health and Social Affairs]. Nya prioriteringar. [New priorities] NOU 1997:18. Oslo.

Starfield B, Weiner J, Mumford L, Steinwachs D. Ambulatory care groups: a categorization of diagnoses for research and management. Health Serv Res 1991;26:53-74.

Starfield B. Threads and yarns: weaving the tapestry of comorbidity. Ann Fam Med 2006;4:101-103.

Statistics Sweden, Demographic reports 2009:1. The future population of Sweden 2009–2060. Stockholm: Statistics Sweden, 2009.

Stenestrand U. Än styr åldern val av behandling. Dagens Medicin 20080423. (In Swedish).

Strippoli GF, Craig JC, Schena FP. The number, quality, and coverage of randomized controlled trials in nephrology. J Am Soc Nephrol 2004;15:411–419.

Sulmasy DP. Physicians, cost control, and ethics. Ann Intern Med 1992;116:920-926.

Svallfors S. A bedrock of support? Trends in welfare state attitudes in Sweden, 1981-2010. Manuscript submitted in January 2011.

Swedish Association of Local Authorities and Regions (SALAR). Health Services Until 2030. Report. Stockholm, 2005.

Swedish Association of Local Authorities and Regions (SALAR). Statistics of Healthcare and Regional Development. Report. Stockholm, 2005.

Swedish Association of Local Authorities and Regions (SALAR). Multisjuka äldre. Hur fungerar vården och vad kostar den? Conference Stockholm, 2011. (In Swedish).

The Committee on Health and Welfare;1996/97:SOU14 Priority Setting in Health Care. Ministry of Health and Social Affairs Report. Stockholm 1997.

The National Board of Health and Welfare. Prioritisation in Health Care. Decision and Implementation. Report. Stockholm, 1999. (In Swedish).

The National Board of Health and Welfare. Care and Nursing for Elderly. Report. Stockholm, 2002. (In Swedish).

The National Board of Health and Welfare and the Swedish Association of Local Authorities and Regions (SALAR). Patienter i slutenvård 2005. Report. Stockholm, 2005. (In Swedish).

The National Board of Health and Welfare. Directives on management systems for quality and patient security in health care. SOSFS 2005:12. Stockholm, 2005. (In Swedish).

The National Board of Health and Welfare. The Elderly Care and Nursing. Report. Stockholm, 2007. (In Swedish).

The National Board of Health and Welfare. Patienter i specialiserad vård 2007. Report. Stockholm, 2009. (In Swedish).

The National Board of Health and Welfare. National guidelines for heart disease 2008. Stockholm, 2008. (In Swedish).

The National Centre for Priority Setting in Health Care. Resolving Health Care's Difficult Choices, Report 2007:2. Linköping, 2007.

The National Institute of Economic Research. Productivity and Wages Through 2015. Special Study No. 6. Stockholm, 2005.

The Register of Information and Knowledge about Swedish Heart Intensive care Admissions (RIKS-HIA) 2008. http://www.ucr.uu.se/rikshia/.

The Swedish Council on Technology Assessment in Health Care (SBU). Geriatric Care and Treatment. A systematic compilation of existing scientific literature. Stockholm, 2003.

The Swedish National Audit Office. Guidelines for priority setting in health care. SNAO Report 2004:9. (In Swedish).

The Swedish Parliament 1997. The Swedish Parliament's decision on priority setting in the health care. Regeringsbeslut om prioriteringar i sjukvården (1996/97:SoU14, rskr. 1996/97:186.). Stockholm, 1997.

Thorslund M, Lennartsson C, Parker, MG, Lundberg O. De allra äldstas hälsa har blivit sämre. Könsskillnaderna är stora – kvinnorna mår sämre än männen visar nya data. Läkartidningen 2004;101:1494-1499. (In Swedish).

Thorslund, M, Parker MG. Hur mår egentligen de äldre? Läkartidningen 2005;102:3119-3124. (In Swedish).

Thygesen K, Alpert JS, White HD. Universal definition of myocardial infarction. Eur Heart Journal 2007;28:2525-2538.

Tinetti ME, Bogardus ST Jr, Agostini JV. Potential pitfalls of disease-specific guidelines for patients with multiple conditions. NEJM 2004;351:2870-2874.

Tinghög G. The Art of Saying No - The Economics and Ethics of Healthcare Rationing. Linköping University Medical Dissertations No. 1215. 2011. Linköping, 2011.

Toerien M, Brookes ST, Metcalfe C, De Salis I, Tomlin Z, Peters TJ, Sterne J, Donovan JL. A review of reporting of participant recruitment and retention in RCTs in six major journals. Trials 2009;1:52. doi:10.1186/1745-6215-10-52.

Tornstam L. The Complexity of Ageism. A Proposed Topology. International Journal of Ageing and Later Life 2006;1:43-68.

Valderas JM, Starfield B, Sibbald B, Salisbury C, Roland M. Defining comorbidity: implications for understanding health and health services. Ann Fam Med 2009;7:357-363.

Van den Akker M, Buntinx F, Metsemakers JF, Roos S, Knottnerus JA. Multimorbidity in general practice: prevalence, incidence, and determinants of co-occurring chronic and recurrent diseases. J Clin Epidemiol 1998;51:367-375.

Van Spall HG, Toren A, Kiss A, Fowler RA. Eligibility criteria of randomized controlled trials published in high-impact general medical journals: a systematic sampling review. JAMA 2007;297:1233-1240.

Waldau S. Creating organisational capacity for priority setting in health care: using a bottom-up approach to implement a top-down policy decision. Umeå University medical dissertations No. 1368. 2010. Umeå, 2010.

Walker LO, Avant KC. Strategies for Theory Construction in Nursing (Fourth ed.). Upper Saddle River, NJ: Pearson Prentice Hall, 2005.

Wallentin L, Lindahl B, Karvinge C, Eklund K, Levin LÅ, Grip L. Svenskt arbete med nationella riktlinjer kan bli internationellt föredöme. Med perspektiv från riktlinjerna vid hjärtsjukdom. Läkartidningen 2008;105:1194-1198.

Walton NA, Martin DK, Peter EH, Pringle DM, Singer PA. Priority setting and cardiac surgery: a qualitative case study. Health Policy 2007;80:444–458.

Wedin M. Stimulera rätt saker i sjukvården. Läkartidningen 2011;108:315. (In Swedish).

Werkö L, Asplund K, Aspelin P, Britton M, Eliasson M, af Geijerstam JL. Två år med EBM i Läkartidningen. Klinisk forskning och rutinsjukvård har närmat sig varandra. Läkartidningen 2002;99:3478-3482. (In Swedish).

Werntoft E, Edberg A-K. The views of physicians and politicians concerning age-related prioritisation in healthcare. Journal of Health Organization and Management 2009;23:38-52.

Wiseman V, Mooney G, Berry G, Tang KC. Involving the general public in priority setting: experiences from Australia. Soc Sci Med. 2003;56:1001-1012.

Wolff JL, Starfield B, Anderson G. Prevalence, expenditures, and complications of multiple chronic conditions in the elderly. Arch Intern Med 2002;162:2269-2276.

World Medical Association Declaration of Helsinki, Ethical Principles for Medical Research involving human subjects. Available from: http://www.wma.net/e/policy/b3.htm. Accessed on the 31st of March 2011.