MANAGING DRUG USE IN THE ELDERLY. General practitioners' adherence to guidelines and patients' conceptions of medication

Modig, Sara

2012

Citation for published version (APA):
Modig, S. (2012). *MANAGING DRUG USE IN THE ELDERLY. General practitioners' adherence to guidelines and patients' conceptions of medication*. [Doctoral Thesis (compilation), Family Medicine and Community Medicine]. Generel Practive/Family Medicine, Clinical Sciences in Malmö.

Total number of authors:
1

MANAGING DRUG USE IN THE ELDERLY

General practitioners' adherence to guidelines and patients' conceptions of medication

Sara Modig

LUND
UNIVERSITY

Managing drug use in the elderly

*General practitioners' adherence to guidelines
and patients' conceptions of medication*

LUND
UNIVERSITY

by

Sara Modig

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen

vid medicinska fakulteten, Lunds universitet,

kommer att offentligen försvaras i aulan, Clinical Research Centre, Malmö

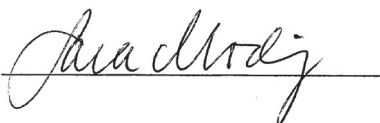fredagen den 16 november 2012, kl. 9.00.

FAKULTETSOPPONENT:

Prof. Peter Engfeldt, Örebro Universitet

Organization LUND UNIVERSITY Department of Clinical Sciences in Malmö, General Practice/Family medicine	Document name DOCTORAL DISSERTATION
	Date of issue 2012-10-23
Author(s) Sara Modig	Sponsoring organization

Title and subtitle
Managing drug use in the elderly.
General practitioners' adherence to guidelines and patients' perpectives of medication.

Abstract

Introduction: Older patients' knowledge about their medicines is generally poor. Patients are entitled to be informed on an individual and adequate level.

Evidence-based guidelines should, in most cases, be followed also in the treatment of elderly to avoid suboptimal treatment, for example for cardiovascular conditions, or risky prescriptions in the case of renal impairment.

Objectives: 1. To describe frail elderly patients' knowledge about and attitudes towards their medicines and to explore their experiences of receiving information about their medications. 2. To describe how well general practitioners (GPs) adhere to guidelines when using renal risk drugs in frail elderly patients and when treating elderly with cardiovascular disease and to evaluate local education of GPs as a tool for improvement.

Methods: (Paper I, IV) For each prescribed medicine, the patients were asked about the indication and possible adverse effects. Attitudes were investigated with the Beliefs about Medicines Questionnaire. Semi-structured interviews covering questions on information about medication were analysed qualitatively. (Paper II) Medications for elderly patients in nursing homes were registered and the use of renal risk drugs was compared to renal function, estimated from s-creatinine and s-cystatin C. (Paper III) Data about GPs adherence to guidelines was collected from the medical records of patients aged ≥ 65 with a cardiovascular diagnosis. Local education was organized, followed by repeated measurements.

Results: The knowledge about indication was satisfying but the knowledge about possible adverse effects was poor. The patients believed strongly in the benefits of their medication. The elderly felt comfortable with information when they trusted their physician or their medication, when they received enough information from the prescriber or when they knew how to find out sufficient information by themselves. They felt insecure if they were anxious, if the availability of medical care was poor or if they did not receive enough information. Reduced renal function was common (53%) in nursing home patients but s-creatinine was often normal. Renal risk drugs were rarely prescribed. The adherence to guidelines about cardiovascular diseases was low among GPs, but educational efforts appeared to increase the adherence.

Conclusions: To receive an adequate drug therapy in the elderly, GPs should pay attention to patients' need for suitable information on their medication and follow evidence-based guidelines about when to initiate and when to avoid certain drugs.

Key words
Elderly, drug therapy, medication knowledge, beliefs about medicines, adherence, guidelines, renal function, renal risk drugs, cardiovascular disease, GP, primary care

Classification system and/or index terms (if any)

Supplementary bibliographical information	Language English

ISSN and key title 1652-8220	ISBN 978-91-87189-24-1
Recipient´s notes	Number of pages 100	Price
	Security classification	

Distribution by (name and address): Sara Modig, sara.modig@med.lu.se

I, the undersigned, being the copyright owner of the abstract of the above-mentioned dissertation, hereby grant to all reference sources permission to publish and disseminate the abstract of the above-mentioned dissertation.

Signature _____   Date 2012-10-02_____

Cast me not off in the time of old age;
forsake me not when my strength faileth.

Book of Psalms 71:9

CONTENTS

ABSTRACT

Introduction: Older patients' knowledge about their medicines is generally poor. Patients are entitled to be informed on an individual and adequate level.

Evidence-based guidelines should, in most cases, be followed also in the treatment of elderly to avoid suboptimal treatment, for example for cardiovascular conditions, or risky prescriptions in the case of renal impairment.

Objectives: 1. To describe frail elderly patients' knowledge about and attitudes towards their medicines and to explore their experiences of receiving information about their medications. 2. To describe how well general practitioners (GPs) adhere to guidelines when using renal risk drugs in frail elderly patients and when treating elderly with cardiovascular disease and to evaluate local education of GPs as a tool for improvement.

Methods: (Paper I, IV) For each prescribed medicine, the patient was asked about the indication and possible adverse effects. Attitudes were investigated with the Beliefs about Medicines Questionnaire. Semi-structured interviews covering questions on information about medication were analysed qualitatively. (Paper II) Medications for elderly patients in nursing homes were registered and the use of renal risk drugs was compared to renal function, estimated from s-creatinine and s-cystatin C. (Paper III) Data about GPs adherence to guidelines was collected from the medical records of patients aged $\geq$ 65 with a cardiovascular diagnosis. Local education was organized, followed by repeated measurements.

Results: The knowledge about indication was satisfying but the knowledge about possible adverse effects was poor. The patients believed strongly in the benefits of their medication. The elderly felt comfortable with information when they trusted their physician or their medication, when they received enough information from the prescriber or when they knew how to find out sufficient information by themselves. They felt insecure if they were anxious, if the availability of medical care was poor or if they did not receive enough information. Reduced renal function was common (53%) in nursing home patients but s-creatinine was often normal. Renal risk drugs were rarely prescribed. The adherence to guidelines about cardiovascular diseases was low among GPs, but educational efforts appeared to increase the adherence.

Conclusions: To receive an adequate drug therapy in the elderly, GPs should pay attention to patients' need for suitable information on their medication and follow evidence-based guidelines about when to initiate and when to avoid certain drugs.

ABBREVIATIONS

ACEI	Angiotensin Converting Enzyme Inhibitor
ARB	Angiotensin Receptor Blocker
BP	Blood Bressure
CAF	Chronic Atrial Fibrillation
C-G	Cockcroft-Gault's formula
CHADS$_2$	Stroke risk scheme, based on the risk conditions **c**ongestive heart failure (1p), **h**ypertension (1p), **a**ge ≥75 (1p), **d**iabetes (1p) and previous **s**troke (2p)
GFR	Glomerular Filtration Rate
GP	General Practitioner
HF	Heart Failure
MDD	Multi-dose Drug Dispensing System
MDRD	Modification of Diet in Renal Disease
NSAID	Non-Steroidal Anti-Inflammatory Drug
RN	Registered Nurse
SBP	Systolic Blood Pressure

ORIGINAL PAPERS

This thesis is based on the following papers referred to in the text by their Roman numerals:

I   Modig S, Ekwall A, Kristensson J, Rahm Hallberg I, Midlöv P. Frail elderly patients in primary care—their medication knowledge and beliefs about prescribed medicines. *Eur J Clin Pharmacol* **65**, 151-5 (2009)

II   Modig S, Lannering C, Mölstad S, Östgren CJ, Midlöv P. The assessment of renal function in relation to the use of drugs in elderly in nursing homes; a cohort study. *BMC Geriatr* **11**:1 (2011)

III Modig S, Höglund P, Troein M, Midlöv P. GP's adherence to guidelines for cardiovascular disease among elderly. A quality development study. *TSWJ* **2012**:767892, doi:10.1100/2012/767892

IV   Modig S, Kristensson J, Troein M, Brorsson A, Midlöv P. Frail elderly patients'experiences of information on medication. A qualitative study. *BMC Geriatr* **12**:46 (2012)

INTRODUCTION

Multi-drug use is common in elderly patients. The consumption tends to be highest among those who, due to age and disease, are the most vulnerable to drugs. Elderly in nursing homes, as well as older persons with multiple diseases in ordinary housing, currently use an average of ten medications per person, continuously or as needed [1, 2]. Basically, drug treatment is positive for the patient and contributes to improved health and quality of life far into old age. Effective therapy should not be withheld only because of old age. However, the risk of unwanted side effects increases with age and the number of drugs. Therefore, a continuous evaluation of treatment quality is essential. The purpose of pharmacotherapy must be regularly reviewed and adjusted.

Adequate drug treatment primarily leads to less suffering for the patient due to higher efficacy as well as fewer adverse effects. Furthermore, it leads to fewer emergency visits to health care centres and hospital clinics and a decreased number of hospital care days. Drug-related problems are a common cause of hospitalization in the elderly, causing up to thirty per cent of admissions [3-6]. Adequately treated patients also facilitate the municipal home care and the care at nursing homes, where the general practitioner (GP) most often is the main professional care provider and optimally has a coordinating responsibility for the medication. Hence, improvements of drug treatment are best carried out in concordance with GPs.

BACKGROUND

Pharmacotherapy in primary care

Physicians in primary care prescribe the majority of drugs in southern Sweden [7]. The patients treated in primary care rarely have only one disease, but often have significant co-morbidities to consider when selecting a proper drug therapy. Thorough medical investigation and a precise diagnostics in fragile older patients with several concurrent diseases are required to avoid various drug-related problems. A holistic approach and a plan for an active follow-up are essential. The more appropriate the medication, the better the patients' quality of life [8], so there is every reason to continuously evaluate treatment. However, in more than one third of Swedish health care centres consultation time is the same irrespective of the age (and consequent disease burden) of the patient [9].

There is sometimes a perceived lack of communication between GPs and hospital specialists concerning their patients' medication, and this might reduce treatment quality [10]. Since many physicians seem reluctant to finish other physicians' prescriptions, a result may be further polypharmacy (more than 5 drugs).

Changes in medication performed during hospital stay are often poorly documented and communicated to patients and other care providers, which result in errors in the drug lists at admission. In order to solve this problem, a model to improve quality has been developed in Lund in southern Sweden: the Lund Integrated Medicines Management (LIMM) model [11, 12]. A clinical pharmacist prepares an accurate medication list for the physician at admission and the discharging physician prepares a

medication report of the changes made. This structured medication report provides the patient and the general practitioner with information regarding changes in drug therapy during hospital stay and a structured updated list of current medications at discharge. The model significantly reduces the number of unscheduled drug-related hospital revisits among elderly [11].

The Swedish National Board of Health and Welfare has recently investigated the role of GPs in relation to drug use in elderly, and possibilities for quality improvements [9]:

- All elderly patients need a physician with a coordinating responsibility for medication. Medication lists must be complete and up-to-date.
- Consultation time must be adapted to the older patient´s needs.
- Better practice and support is needed for documentation in the medical records on prescription indications and follow-ups.
- Procedures need to be developed for the follow-up of new prescriptions. At present, an admission to hospital often leads to one or more new prescriptions which are administered without proper planning for how the treatment should be continued and evaluated. Information must reach the responsible GP quickly.
- Guidelines and recommendations should include specific sections on the treatment of elderly patients with multiple diseases.

Primary care and community care

"The Elderly Reform" took place in Sweden 1992 and implied that the main responsibility for the care of elderly was transferred from the county council to the municipality [13]. The idea behind the reform was to demedicalize the care of elderly and to enhance and encourage social environmental factors. However, with an ageing population the morbidity has increased due to a higher disease burden and hence also the need of medical support. Registered nurses (RNs), employed by the municipality, have the central role in the care of elderly and as leaders for the nursing staff. The GPs are employed by the county council and work mainly at health care centres. They are responsible for the medical care, prescriptions and evaluations. The RNs have regular rounds with the physicians and also contact them when needed. There is a written agreement between the municipality and the health care centres about the obligations for the GPs to participate in the care of the elderly, especially at the nursing homes.

Frailty and medication

Among frail elderly living at home, the average number of medications is almost 10 and drug-related problems (DRPs) are common, about five per patient. The DRPs are highly related to adverse reactions. These patients frequently see many different physicians during hospitalization, at emergency clinics, at outdoor clinics and at health care centres (on average 15 per 18 months), all potential drug prescribers. More than half of these patients think that their medications cause problems [14].

In nursing homes inappropriate treatment of elderly is common [15] and over 70% of nursing home residents with MDD (see below) have one or more potentially inappropriate prescriptions. Here, the average number of prescribing physicians per resident is also high, almost four. Increasing numbers of prescribers per resident are

associated with a higher number of drugs prescribed and a lower quality of drug therapy [16, 17]. Fortunately enough, educational interventions in nursing homes in Sweden have been shown to give a reduction in the number of drugs used per patient. Evaluation of the effects of medications was also more frequent after education [18]. A systematic review of randomized clinical trials revealed that interventions using educational outreach, on-site education given alone or as part of an intervention package and pharmacist medication review may under certain circumstances reduce inappropriate drug use, but the evidence is still limited [19].

Multi-dose drug dispensing system (MDD)

The Swedish multi-dose drug dispensing system is commonly used for elderly with multiple illnesses, in their own houses as well as in nursing homes. This means that the patients get their drugs machine dispensed into one unit for each dose occasion, a service offered by the National Corporation of Pharmacies. The system has advantages for the prescriber with an improved comprehensive view, for the nursing personnel with easier drug management in the nursing homes and for the patient with increased security. There are, however, obvious risks with MDD and among these is the inertia to finish a regular treatment. One can easily renew the prescription list digitally for another year. However, the physician should remember to reconsider the need of every drug, which unfortunately is often less prioritized because of the lack of time. It is also important to remember to check renal function, since drugs which were previously indicated, might no longer be suitable because of the risk using them in renally impaired patients. Renewal of multi-dose dispensed drugs should be accompanied by the same blood tests as other drug prescriptions.

It has been shown that patients with MDD have poorer quality of drug treatment than patients with ordinary prescriptions [20]. This finding is true for all established quality indicators (≥ 10 drugs, long-acting benzodiazepines, drugs with anticholinergic action, ≥ 3 psychotropics, and drugs combinations that should be avoided [21]) and cannot be explained by differences in age, sex, burden of disease, or residence.

One advantage with the MDD-system is the possibility for all physicians who are in contact with the patient to see all prescriptions on one list, which enhance security. MDD patients often have multiple chronic diseases and hence visit different clinics.

Polypharmacy

The term *polypharmacy* is often used when a patient takes more than five drugs regularly. However, there is no clear definition. GPs in a Swedish focus group study gave the spontaneous definition of polypharmacy as 'the administration of more medicines than are clinically indicated' [10]. The risk of adverse reactions and interactions between drugs increases with the number of drugs. There are several reasons why elderly are often subjected to polypharmacy. Firstly, elderly people suffer from more diseases and should therefore with adequate treatment also receive more medication. Medications are basically something good. However, if the treatment is not regularly evaluated, there is a risk of routine prescriptions and a growing medication list. Many elderly are under treatment long after the need for treatment is over. The higher the number of prescribers for a patient, the higher the risk of polypharmacy [17]. Optimally, every elderly patient should have a physician with a

coordinating responsibility for the medication, i. e. a GP. Unfortunately, adverse reactions are often judged as symptoms of new diseases and hence treated with further medication.

Sometimes medications are prescribed due to wishes from staff at nursing homes. There might be wishes for sedatives if the patient does not sleep the whole night or anxiolytica if the patient seems to be anxious or restless and the personnel are short of time for care. However, a careful judgment must always precede prescription and prescriptions by telephone should preferably be avoided.

The last decade, structured medication reviews conducted by clinical pharmacists in cooperation with the physician, the nurse and the nursing personnel, have been a way of improving the quality of drug treatment for elderly with multiple diseases in Sweden. The aim of medication reviews is to evaluate the medication for separate individuals, to achieve consistency between prescribed and used medicines and hereby attain as adequate medication as possible and to avoid incorrect or unnecessary drug treatment [22].

Causes of polypharmacy
Elderly patients are multiply ill and need several treatments
The need for drug treatment is not evaluated
Many prescribers
Adverse reactions treated with further medications
Wishes from nursing personnel

Risks with polypharmacy:
Higher number of adverse reactions
More interactions – less therapeutic effects

Pharmacology in the elderly

Normal aging means a continuous reduction of physiological functions. Elderly are therefore more susceptible to adverse reactions of drugs that do not appear in healthy younger adults.

Absorption and distribution of drugs

The absorption of most oral drugs is not diminished with age whereas the transdermal, subcutaneous and intramuscular administrations may be affected due to reduced tissue perfusion [23]. A reduction in total body water and an increase in the proportion of body fat result in the fact that drugs depending on lipid solubility may accumulate in the body and cause prolonged effects. Medium- and long-acting benzodiazepines are examples of drugs which may be harmful due to this mechanism.

Elimination of drugs and decreasing renal function

Renal function normally decreases with age. Hence, drug elimination through the kidneys is impaired in the elderly, both due to reduced renal blood flow and perturbations in glomerular filtration rate (GFR) [24]. In addition, elderly patients

often have other diseases, such as hypertension, diabetes, and atherosclerotic disease, which contribute to a reduced renal function. This is the most important pharmacokinetic alteration in elderly patients. Most drugs and their active metabolites are eliminated through the kidneys. Therefore, dosage adjustment according to renal function is indicated for many drugs in order to avoid accumulation of the drugs or their metabolites, adverse reactions and/or aggravation of renal impairment [25]. However, it has been shown that such adjustments are often inadequately performed by clinicians [26, 27].

There is no ideal way to assess renal function in the elderly. Serum creatinine level alone is often misleading since muscle mass is reduced and creatinine production thus is decreased. Many geriatric patients with a "normal" serum creatinine level actually have a moderate renal impairment when GFR is estimated [27-29]. The use of GFR estimation equations, such as the Modification of Diet in Renal Disease (MDRD) [30] or the Cockcroft and Gault formula (CG), should increase the awareness about the accuracy of renal function among physicians [31]. However, there is a variation in creatinine metabolism in these comorbid patients [32]. The use of cystatin C for estimating GFR may be a better alternative, since it is not affected by muscle volume [33]. There are, however, studies showing that cystatin C is not independent of body composition [34]. S-cystatin C seems to be a useful and reliable marker for estimating GFR in the elderly, comparable to the creatinine formulas, including the newer CKD-EPI formula [35, 36].

There are many common pharmaceuticals that may be harmful to patients with renal impairment if dosage is not adjusted according to the GFR, for example metformin, non steroidal anti-inflammatory drugs (NSAID), digoxin, angiotensin converting enzyme inhibitors (ACEI), opioids and many antibiotics [37].

Pharmacodynamical alterations in old age

Since many organ systems are more vulnerable in the elderly, they are also more sensitive to side effects. Pharmacodynamic changes occur, for example in the brain. The sensitivity to sedative hypnotics such as benzodiazepines and to opioids is higher in the elderly, leading to a higher risk of sedation and cognitive impairments. The old brain is also more susceptible to drugs with anticholinergic effects, which can cause cognitive dysfunction and, in severe cases, confusion. Examples of drugs with anticholinergic properties are medication used for urinary incontinence and many anti-psychotic drugs. Anticholinergic effects also include urinary retention, constipation and xerostomia.

Another important pharmacodynamic change is related to blood pressure regulation. Orthostasis, with symptoms such as dizziness, unsteadiness or even cognitive dysfunctions, is common. There is also an increased sensitivity to drugs with anti-hypertensive effects, which include not only antihypertensives but also a number of other cardiovascular medications, drugs for Parkinson´s disease and antipsychotics. People with dementia sometimes already show a low blood pressure, which can increase the sensitivity to drugs with antihypertensive effects even further.

Potentially inappropriate medications for elderly

Since elderly are more susceptible to adverse drug reactions due to the pharmacokinetic and pharmacodynamic changes, international criteria for medications that are inappropriate for elderly are developed and established. These are the so called Beer's criteria [38]. Many of the listed drugs in Beer's criteria are, however, unavailable in Sweden. Therefore, criteria corresponding to Swedish drug formularies have been developed by the Swedish National Board for Health and Welfare [21]. The quality indicators include avoidance of ≥ 10 drugs, long-acting benzodiazepines, drugs with anticholinergic action, ≥ 3 psychotropics, and drugs combinations that should be avoided.

Adherence

Adherence to prescribed medication is important for effective medical therapy. Not taking ones medicines as prescribed can lead to a decreased effect or overdose related problems. That in turn might result in more medication, unnecessary investigations or hospitalization. Elderly patients are more sensitive to an incompliant behaviour since their illnesses more often require a multiple and long-term therapy. They are also more vulnerable as a consequence of the diminished plasticity due to their old age. Many elderly do not take their medicines as prescribed [39]. A common reason for lower adherence is forgetfulness, but it can also be due to misunderstandings or intentional avoidance because of adverse reactions or fear of long-term consequences of the treatment [40].

A more modern and pleasant way of discussing adherence (or compliance) is to use the term "concordance", implying prescribing *with* rather than *for* the patient [41, 42]. The role of the patient in the consultation must be emphasised, notably through the adoption of 'patient-centred' strategies. Models that promote the active involvement of patients in the decision-making process about treatment should be stressed. However, physicians are not fully responsive to the preferences of elderly, multiply ill patients regarding either the degree of communication or the patients' participation in decision making when hospitalized [43]. Furthermore, medicine intake is a complex task and a large proportion of the elderly population has cognitive, visual or physical limitations that may affect their ability to take medicines accurately [44]. Awareness of these limitations is essential to concordance.

Adherence is significantly related to attitudes towards medication and to medication knowledge [39, 45-50].

Attitudes towards medication

In order to receive good adherence, motivation for taking prescribed medicines is necessary. The patient must realize that he or she is susceptible to the illness, that he or she actually suffers from the illness and that the medication can temper its consequences [48, 49]. Motivation is supposed to be high if the patients consider that the prescribed medication is necessary for maintaining health [49]. By using the "Beliefs about Medicines Questionnaire" (a questionnaire assessing attitudes toward medication), it has been shown that higher necessity scores correlate with higher

reported adherence and higher concerns correlate with lower reported adherence [47]. It has been shown that attitudes to medication is a more reliable predictor of adherence than clinical and sociodemografic factors.

Medication knowledge

The patient's knowledge of medications is of utmost importance for secure administration of drugs. A level of knowledge admitting the ability to differentiate between symptoms caused by the illness and adverse effects caused by the medication is valuable for all patients. Elderly patients' knowledge of their medication is generally poor [39, 45, 51, 52].

Knowledge also affects healthcare consumption. The care seeking pattern of frail elderly with less knowledge differs from that of those with more knowledge. The former group shows more acute inpatient care and more and longer acute hospital stays [53].

Knowledge is influenced by the way information is given. It has been shown that many elderly patients experience insufficient information from their physician and have unanswered questions. They do not know the indications of their medicines and have worries about possible adverse effects. However, they often do not raise these concerns with the physician [54, 55]. The reason for this behaviour must be further investigated in order to facilitate optimized information. This issue is further pursued in paper IV.

Individually adjusted information

If the patients' knowledge about medications is poor, it is more difficult to involve them in decisions about the treatment, to which they are legally entitled [56]. Furthermore, according to Patient Safety Act [57], every patient has the right to receive individually adjusted information about his condition and available treatments. The physician who is responsible for the medical care of a patient also has the obligation to supply this information.

Patients at all health literacy levels gain from plain language explanations. Health literacy is the ability to obtain, understand and use health information. Information adjusted to the literacy level will improve medical knowledge of the condition, treatment and self care [58, 59]. Strategies for this can be to limit the information content at one visit, to encourage the patient to ask questions and to use "the teach back method" – assess comprehension by asking the patient to recall the information [60]. The "Newest Vital Sign" test, consisting of a nutrition label and six related questions, can be used as a quick screening test for limited literacy in primary health care settings [61]. It has been found that elderly with lower health literacy are more likely to use the emergency department even for routine visits and incur higher emergency care costs, suggesting that inadequate health literacy may be associated with an inefficient use of health care resources among elderly [62].

GP's adherence to guidelines

Elderly are commonly treated with many medicines, which contribute to higher risks for interactions and adverse effects. There are, however, also risks associated with the underuse of recommended treatment. For several diseases it has been shown that it is

more common for elderly than for younger patients to receive suboptimal treatment with the recommended drugs [63-68]. An example of this is the use of diuretics instead of angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) for elderly patients with heart failure. Evidence based guidelines should in most cases be followed also in the diagnosis and treatment of elderly [69]. They are meant to ensure that patients receive the most efficient therapy. Old age should not discriminate patients from certain medications. However, to precisely follow every guideline and recommendation strongly contributes to polypharmacy, according to many GPs [9]. The clinical practice guidelines might be thought of as 'medicine generators', having an ambiguous effect on the GPs, who both trust them and find them difficult to apply [10]. Reported barriers to adherence to guidelines also include patient related factors, suggesting that current guidelines do not always adequately incorporate patient preferences, needs and abilities [70].

In a Swedish study of back pain more than half of the physicians agreed that the guidelines were useful in clinical praxis and the majority indicated that they followed the key points in the guidelines [71]. However, many physicians were unfamiliar with the contents of the guidelines. Such a lack of knowledge has also been shown concerning guidelines for appropriate prescribing for elderly [72] as well as for cardiovascular risk factors, where GPs tended to make experience-based decisions regarding prevention while internists and cardiologists tended to use the guidelines [73].

Guidelines can also contain information on when to avoid certain drugs, for example Beer's criteria or lists of drugs that are harmful to patients with renal impairment. If adherence to these guidelines is low, the barriers presumably are not related to the risk of polypharmacy, but rather to lack of knowledge or forgetfulness. This kind of adherence was investigated in paper II. Automatic reporting of estimated GFR (eGFR) whenever serum creatinine or serum cystatin C is measured might increase adherence to recommended avoidance of renal risk drugs [74, 75], but the clinician should be aware of the limitations of the estimates used [76].

Many studies confirm physicians' low adherence to guidelines, but there are few studies on how educational efforts can affect the adherence. There is not much evidence showing positive results of educational interventions [77, 78] but the results are diverging [79]. However, an intervention in Swedish nursing homes trying to improve the quality of drug treatment, showed a significant reduction in the number of drugs used per patient at the intervention homes, where physicians focused on patients' health status as a baseline for continued medication [18]. Methods on how to improve GPs' adherence to guidelines still have to be developed and this forms the basis of paper III.

AIMS

The general aim of this thesis was to describe drug use in the elderly, both regarding physicians' prescriptions and patients' understanding of their treatment, in order to improve the quality of the drug use.

The specific objectives were:

- To describe fragile elderly patients' knowledge of and attitudes towards their medication. (Paper I)

- To explore the renal function in elderly patients in nursing homes by using different GFR estimates and to investigate the association between these estimates. (Paper II)

- To assess the use of pharmaceuticals that may be harmful to patients with renal impairment. (Paper II)

- To describe how well general practitioners adhere to current guidelines in the treatment of elderly with cardiovascular disease and to evaluate local education as a tool for improvement. (Paper III)

- To explore frail elderly patients' experiences of receiving information about their medications and their views on how information optimally would be given. (Paper IV)

MATERIALS AND METHODS

Design

Different methods have been used in the different studies. Complete and detailed descriptions are provided in each publication.

Paper I and paper II were quantitative studies with a descriptive design. Paper III was an intervention study, which also could be seen as a local quality improvement project. Paper IV was qualitative in design. The divergence in methods used, contributed to make the doctoral studies as comprehensive as possible. Qualitative research contributes to our understanding of important clinical issues, such as patients' reasons for compliance/noncompliance or patients' and care-givers needs and wishes [80].

Data collection

Study participants

Two of the studies in this thesis (paper I and paper IV) were carried out as parts of a larger project, designed to evaluate the use of case managers for multiply ill patients living at home [81]. This was a randomized controlled study, which took place in a town in southern Sweden with 30 000 inhabitants, including both rural and urban areas. Those included were aged 65 and above, needed help with at least two activities of daily living, such as cooking, washing or personal hygiene, had been admitted to hospital at least twice, or had at least four contacts in outpatient or primary care, during the last twelve months. They were able to communicate verbally and had no cognitive impairments. The respondents were collected from primary care, from the emergency department at the hospital or announced their interest in the study spontaneously. Many patients who were eligible in paper I dropped out due to the extent of the larger main project. However, all those invited to participation in an interview (paper IV) agreed to do so.

The study that assessed renal function (paper II) was also carried out as part of a larger project, SHADES (Study on Health And Drugs in Elderly in nursing homes in Sweden) [82], a cohort study which describes and analyzes mortality, morbidity and the use of pharmaceuticals in people living in nursing homes in three municipalities in southern Sweden: Jönköping, Linköping and Eslöv. The aim of SHADES is to use the results for interventions resulting in better health, less adverse drug reactions and a reduced number of unplanned hospital admissions. All participants in paper II were elderly with multiple comorbidities, living in nursing homes and aged 65 years or over. All subjects living in the 11 participating nursing homes were invited to participate in the study. Exclusion criteria were severe illness/palliative care or language problems. The assessments were performed when 243 of the total 315 subjects in SHADES had been included and the drop-out was negligible.

Paper III was a quality improvement project, examining the behaviour of the physicians. Hence the patients were not participants in the study. All nine GPs from one health care centre participated.

Procedure

Paper I

Patients' knowledge about their medicines was assessed with a questionnaire developed for the study (Appendix 1). For each drug, knowledge about indication and possible adverse effects or risks was assessed. Knowledge about indication was graded in "good knowledge", "knowledge with written information" and "no knowledge". Patients who use written lists know where to find the information in daily life. Since there is generally no information about adverse effects in written information, knowledge about possible adverse effects was graded in "yes" or "no".

Patients' beliefs about their medicines were assessed using the Beliefs about Medicines Questionnaire (BMQ) [49, 83], a scale which has been translated and is validated for use in Swedish [84]. The BMQ comprises two five-item scales assessing patients' beliefs about the *necessity* of prescribed medication for controlling their illnesses and their *concerns* about the potential adverse consequences of taking it. For each individual statement the patient indicate his degree of agreement on a five-point scale, ranging from strongly disagree (1) to strongly agree (5). Scores from each scale are summed and the difference between *necessity score* and *concern score* indicates if the patient considers that the benefits of the medication (*necessity beliefs*) outweigh the costs (*concerns*). (Appendix 2)

The assessments of attitudes and knowledge were made in the patient's home by researchers in the main project (Case Manager). Other variables were also assessed, making it possible to evaluate prospective correlations to medication knowledge and beliefs about medicines.

Paper II

S-creatinine and s-cystatin C were analysed in the elderly patients living in nursing homes. Renal function was estimated using the Cockgroft-Gault formula, the MDRD [30] and cystatin C-estimated GFR [85]. Concomitant medication was registered for each patient and four groups of renal risk drugs were identified: metformin, NSAID, ACEI/ARB and digoxin.

Paper III

Data was collected from the medical records of patients aged $\geq$ 65, who visited Tåbelund health care centre in 2006 and had one or more of the following diagnoses: hypertension, ischemic heart disease (IHD), heart failure (HF), chronic atrial fibrillation (CAF) or prior stroke. The variables which were investigated were (in harmonization with the recommendations in the regional guidelines of 2006):

For hypertension:
- Target blood pressure reached (130/80 for diabetes and 140/90 for others)?
- If not, number of antihypertensive drugs?
- ECG during the last 2 years?
- Blood lipids tested during the last 5 years?

For ischemic heart disease:
- Diagnosis based on: cardiac stress test / myocardial scintigraphy / prior verified acute myocardial infarction?
- Treated with betablocker?
- Treated with aspirin (or clopidogrel/warfarin)?
- Blood lipids tested during the last 5 years?
- Target level for cholesterol reached (LDL ≤ 2.5 mmol/L and total cholesterol ≤ 4.5 mmol/L)?

For heart failure:
- Diagnostics performed: Echocardiography ever performed? NT-proBNP tested ever? Pulmonary x-ray performed initially?
- Treated with ACEI or, if intolerant, ARB?
- Target dose used for ACEI/ARB?
- Treated with betablocker with indication for HF?
- Treated with NSAID regularly?

For chronic atrial fibrillation:
- Treated with warfarin? If no, treated with aspirin 320 mg?
- Which CHADS$_2$-score does the patient reach?

For stroke:
- Target blood pressure 140/90 reached?
- If ischemic stroke: Treated with recommended anticoagulation (aspirin 160 mg, warfarin or clopidogrel)?

Local education was organized and included feed-back to the responsible GP and discussion about regional guidelines. Repeated measurements were performed in 2008.

Paper IV
Semi-structured interviews were carried out in the participants' homes by the first author, who was not involved in the medical care of the participants. The interviews followed a thematic interview-guide (Appendix C), which comprised questions concerning pharmaceutical treatment in general and specific questions about how the patients experienced receiving information about their prescribed medications. The interviews were tape-recorded and transcribed verbatim.

Quantitative analysis (I-III)

Statistical analyses in paper I and II were performed using SPSS statistical package 14.0 and 18.0 and in paper III computer software R version 2.6.0 was used (R Foundation for Statistical Computing, Vienna, Austria).

For correlation analyses in paper I the exact Pearson chi-square test was used.

In paper II we set cut-off points for GFR in the analyses at 60 ml/min and 30 ml/min respectively, in order to harmonize with the National Kidney Foundation staging of chronic kidney disease (CKD): GFR > 60 ml/min stage 1+2 (normal renal function and mild reduction), GFR 59-30 ml/min stage 3 (moderate reduction) and GFR <30 ml/min stage 4+5 (severe reduction and renal failure) [86]. Kappa-value was calculated to describe concordance between the different methods of estimating GFR (method given by Fleiss [87]).

Power calculations for changes in proportions of adherence to guidelines were performed before the study of paper III started. For each diagnosis, one variable was considered as the main variable, presented in table 1.The proportion of the main variable was analysed in a smaller sample. The power calculation was performed on clinically reasonable improvements in the variables. For example the proportion who reached target blood pressure in the sample was 35% and a clinically relevant proportion in the hypertension population should be 60%. The observation period was set up in order to get the sufficient number of patients. It was enough to investigate a random sample of every fifth patient with hypertension aged 65-84. For IHD, HF and CAF, adequate numbers of patients were available during the observation period. Enough stroke patients were not found at the centre to expect significant changes. The number of patients in each group is presented in table 1. Observed proportions of adherence and their exact confidence limits were calculated. The proportions from the studied periods were compared using Two-sample test for Equality of Proportions.

Table 1. Number of patients from each diagnosis investigated and main variables in paper III.

Diagnosis	Main variable	N 2006	N 2008
Hypertension (65-84/≥85)	Reached target BP?	39/24	54/41
Ischemic heart disease	Treated with betablocker?	113	105
Heart failure	Treated with ACEI/ARB?	75	94
Chronic atrial fibrillation	Treated with warfarin?	77	73
Stroke	Reached target BP?	50	59

Qualitative analysis (IV)

A qualitative content analysis was performed in paper IV. According to Berg, content analysis may cover latent and manifest levels and a combination of the two. The manifest level concerns the surface of the text focusing on the more visible and obvious parts. The latent level comprises an interpretation in which deeper aspects of meaning are sought in the text [88]. The text was analysed in five steps, inspired by Graneheim and Lundman [89]. In the first step the interviews were read through and listened to several times to gain a sense of the whole and to become familiar with the individual interviews. In the second step meaning units related to the aim were identified. In the third step the meaning units were condensed and labelled and finally coded on the basis of their content. Based on the codes, sub-categories and categories

were developed in the fourth step. There was an ongoing dialogue between the authors throughout all steps and in the fifth step the categories were carefully discussed until two main categories could be identified. (Table 2)

Table 2. Example of the analytical process

Meaning unit	Code	Subcategory	Category	Main category
I trust the doctor, that these are the right medicines for me	Confidence in the doctor, despite lack of information about side effects	Confidence in the medications and in the physician	Trust/ confidence	Comfortable with information
The ordination you get from a doctor, I think you should stick to it and if it doesn´t help, you should call the doctor to get the green light. You shouldn´t medicate yourself.	You should adhere to the doctor´s ordination and not change it yourself	Compliance		
I am very satisfied, since I don´t miss any information, about anything, what kind of pill it is or why I get it and if she changes the dose she tells me why.	Very satisfied with the complete information from the doctor. Receives information when changes are performed and why.	Satisfactory information	Satisfaction with information	
..such as when I am called for an appointment with my doctor, then he isn´t at the ward but in the consulting room where we sit in peace and quiet and talk.	Information in peace and quiet during the next visit is appreciated	Timing of information		

After 12 interviews, there was consensus that saturation had been reached as no new categories reflecting the study aim could be developed from the data. The last two interviews were analysed without producing any additional change in the structure.

ETHICAL CONSIDERATIONS

The Regional Ethical Review Board, Lund approved study I and IV. The Regional Ethical Board, Linköping approved study II. Study III did not need an ethical approval, according to the Regional Ethical Review Board, Lund.

Participation in study I, II and IV was voluntary and a written informed consent was obtained from all participants or from their relatives, in case of inability due to dementia or stroke.

In case of obvious faults in the medication lists in study I, the responsible physician was contacted.

The researcher was not involved in the medical care of the participants who were interviewed in study IV.

In study III, data was collected from the medical records and there were no risk of harm for the patients. Instead, the study was a local quality improvement project, which only could benefit the patients.

FINDINGS

Knowledge of and attitudes towards medication (Paper I)

Thirty-four frail elderly in ordinary housing were included, 14 men and 20 women. Median number of medicines was 8. Six patients had multi-dose drug distribution. The number who answered a particular question ranged from 27 to 34.

The indication of at least 75% of their medicines was known to 22 (71%) of the patients. Patients with MDD had significantly less knowledge than patients with ordinary prescription and patients with polypharmacy (>five medicines) had significantly less knowledge than those with less medication.

Twenty-six patients (84%) did not have any knowledge about possible adverse effects for any of their prescribed medicines.

For the vast majority of the sample, 26 (93%), the difference between BMQ necessity score and concern score was positive, indicating strong beliefs in the benefits of the medication which outweighed the costs. Strongest agreement was found for the statements "My medicines protect me from becoming worse" and "My health, at present, depends on my medicines". However, more than a third felt that "My medicines are a mystery to me".

No differences in BMQ score were found in relation to gender, educational level or polypharmacy. Neither were there any differences between patients with or without MDD.

The sample was too small to show any possible relation between beliefs about medicines and medication knowledge.

The assessment of renal function in relation to the use of drugs (Paper II)

Cystatin C-estimated GFR was 58.5 ml/min/1.73 m^2 on average. One hundred and twenty-nine subjects (53%) had a cystatin C-estimated GFR of less than 60 ml/min/1.73 m^2 and of those, 53 (41%) had a normal serum creatinine level, indicating that the assessment of renal function must not be based only on the levels of serum creatinine. Of 30 subjects with GFR of less than 30 ml/min, 4 patients had normal serum creatinine levels.

Different estimates gave varying GFR. With weighted kappa as measure, the concordance was moderate to good between MDRD and cystatin C and it was moderate between the C-G and cystatin C and between C-G and MDRD.

Metformin was prescribed to four patients. Of those, all had a GFR of more than 60 ml/min if GFR was estimated from cystatin C or with the MDRD formula.

Prescription of digoxin, NSAID and ACE inhibitors/ARBs respectively for patients in different stages of renal function is shown in table 3. In total digoxin was prescribed to 19 patients. Four of those had normal serum creatinine levels but a reduced GFR. NSAID was prescribed for regular use to 4 patients. ACEI/ARB was prescribed to 40 patients and the most common drug was enalapril with a median daily dose of 10 mg.

Table 3. The number of patients in different GFR stages that were prescribed digoxin, NSAID and ACEI/ARB, respectively.

	eGFR/CRcl (ml/min/1.73m^2)		
	>60	59-30	<30
Digoxin n = 19			
Cystatin C-estimated	10	8	1
Cockcroft-Gault	6	13	0
MDRD	13	6	0
NSAID n =4			
Cystatin C-estimated[a]	1	2	1
Cockcroft-Gault[a]	1	2	1
MDRD[a]	2	2	0
ACEI/ARB n =40			
Cystatin C-estimated[a]	14	20	6
Cockcroft-Gault[a]	11	23	6
MDRD[a]	22	14	4

GP´s adherence to guidelines for cardiovascular disease among elderly (Paper III)

The adherence to guidelines was low in general, but educational interventions appeared to increase the adherence.

Only approximately one third of the hypertension patients reached target blood pressure (BP) and this fraction was not influenced by the intervention. Many had mono-therapy although they did not reach target BP but the intervention appeared to increase the number of antihypertensives in these patients. The assessment of blood lipids increased significantly between 2006 and 2008 for the oldest with hypertension.

For the patients with IHD the treatment with beta blocker and especially aspirin was stable and high.

In the treatment of heart failure, the use of beta blocker and the assessment of NT-proBNP increased significantly. Regularly treatment with NSAID was avoided. Of those treated with ACEI/ARB approximately one third was treated up to target dose.

There were too few stroke patients at the centre to expect significant changes. Approximately two third of the stroke patients reached target BP[1]. About half of the CAF patients were treated with warfarin and this was not influenced by the intervention. Patients with lower CHADS$_2$-score were more frequently treated with warfarin.

---

[1] Errata: In the publication (paper III) this fraction was stated as one third, which is wrong.

Frail elderly patients' experiences of information on medication (Paper IV)

The findings from the interviews revealed that the experiences which the elderly participants had regarding the receiving of medical information fell into two main categories: "Comfortable with information" or "Insecure with information". The elderly felt comfortable when they trusted their physician or their medication, when they received enough information from the prescriber or when they knew how to find out sufficient information by themselves. They felt insecure if they were anxious, if the availability of medical care was poor or if they did not receive enough information (Figure 1).
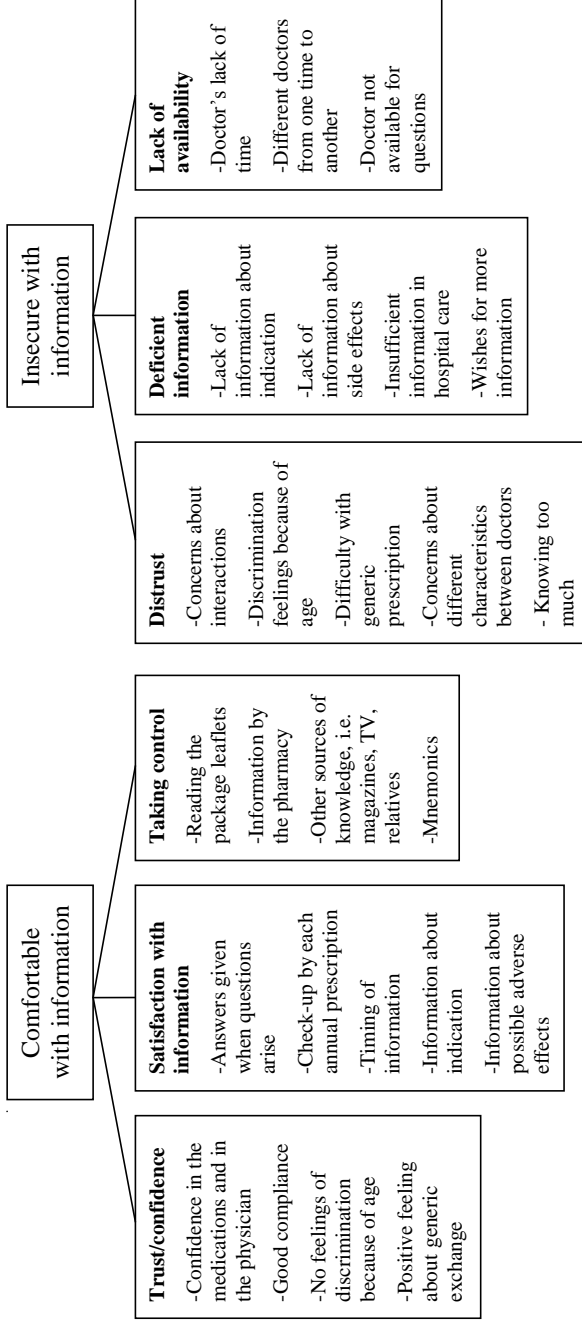
Comfortable with information

Trust/confidence

-Confidence in the medications and in the physician

-Good compliance

-No feelings of discrimination because of age

-Positive feeling about generic exchange

Satisfaction with information

-Answers given when questions arise

-Check-up by each annual prescription

-Timing of information

-Information about indication

-Information about possible adverse effects

Taking control

-Reading the package leaflets

-Information by the pharmacy

-Other sources of knowledge, i.e. magazines, TV, relatives

-Mnemonics

Insecure with information

Distrust

-Concerns about interactions

-Discrimination feelings because of age

-Difficulty with generic prescription

-Concerns about different characteristics between doctors

- Knowing too much

Deficient information

-Lack of information about indication

-Lack of information about side effects

-Insufficient information in hospital care

-Wishes for more information

Lack of availability

-Doctor's lack of time

-Different doctors from one time to another

-Doctor not available for questions

Figure 1

DISCUSSION

The aim of this thesis was, as previously stated, to describe drug use in the elderly, both regarding the physicians' prescriptions and regarding the patients' understanding of their treatment, in order to improve the quality of the drug use. The studies are carried out in primary care.

Many elderly use several medications daily although their aged bodies are vulnerable and easily can be affected by drug related problems (DRPs). The physician should deal with drug treatment as the potent force it is – to reach therapeutic effect for symptoms and diseases of the elderly patient and to avoid adverse effects. The old patient should not be undertreated due to age, but the physician should also keep in mind which medications that could be harmful to the aged patient and that require dose adjustment or even avoidance, especially in the case of renal impairment.

Awareness of renal function

In order to pay attention to the risk of certain drugs to a certain patient, the physician must be aware of the renal function (GFR) of the patient. S-creatinine is still the most frequently used marker to judge renal function in Sweden [90]. However, in paper II we could confirm the findings from previous studies that older patients frequently have impaired renal function despite normal serum creatinine levels (concealed renal insufficiency) and are exposed to an increased risk of DRPs [91]. Hence, the importance of estimating GFR is evident. Particularly patients in primary care commonly have co-morbidities such as diabetes, atherosclerosis or hypertension that may further reduce renal function.

There is not yet any consensus whether assessing s-creatinine or s-cystatin C is the most appropriate way to estimate GFR. A scientific task group with members from various pertinent medical specialties has now been formed under The Swedish Council on Health Technology Assessment (SBU) and given the task to assess which method and formula that can best be used to assess GFR [92]. The report is planned to be presented in the nearest future. In paper II we found varying GFR when using different estimates. The important thing in primary care, however, is not the choice of a particular estimate, but to use GFR at all instead of trusting s-creatinine level only. Automatic electronic reporting of estimated GFR based on creatinine has been implemented in some regions in Sweden and if cystatin C is analyzed, estimated GFR is almost always part of the laboratory answer. This can be useful, since GPs rarely prioritize the time needed to perform the estimation themselves.

Adherence to guidelines

Existing clinical guidelines are not developed explicitly for elderly. Instead, they are based on clinical trials where elderly often are excluded. Nevertheless, we still have to lean on these guidelines in our efforts to work evidence-based and the older patient should not be discriminated from effective therapy. Low adherence to guidelines, as in paper III, has been previously found in primary care [93-95]. The question is how GPs can be motivated to change this behaviour and improve adherence. GPs' can

sometimes experience quality work, such as efforts to follow guidelines, as a control function and a top-down obligation. It may be perceived as a time-consuming process, not infrequently borrowed from some other sphere than primary care [96]. This might influence GPs' adherence. If the methods for follow-up instead are designed according to the needs that doctors themselves feel that they have, one can suppose that it is easier to improve treatment patterns.

GPs attitudes towards guidelines are yet another factor to deal with. A Swedish study about attitudes revealed that the degree of reliance on research data varied among GPs. Some were convinced of an actual and predictable risk for the individual; others strongly doubted it. Some were relying firmly on protection from disease by pharmaceutical treatment; others were strongly questioning its effectiveness in individual cases[97]. Since guidelines are constantly renewed and changed, some GPs might adapt their behavior according to the current guidelines more slowly. The European guidelines on cardiovascular prevention, which were prevailing at the time for paper III, have been updated 2012 [98]. The current Swedish guidelines from The National Board of Health and Welfare are dated 2008, with a complementary addition from 2011 [99].

GPs might be more motivated to follow guidelines if they are developed and adjusted for the treatment of elderly. A Swedish study found that old age of the patient seemed to be an important barrier among GPs when considering pharmacological treatment for the management of hypertension [93]. There are indications that an optimal systolic blood pressure (SBP) for the oldest could be above the recommended 140 mmHg [100] and a lower SBP seems to be associated with greater mortality in patients aged 85 or more, irrespective of health status. The question arises whether many GPs already consider this BP level ideal for this elderly group and therefore are not so eager to follow existing guidelines.

Patients' understanding of their treatment

A level of knowledge admitting the ability to differentiate between the symptoms of illness and adverse effects of the medication is valuable to all patients. In paper I we found a satisfying knowledge about indication, but the knowledge about possible adverse effects of the medication was generally alarmingly poor. Perhaps this is not a surprising result, since the patients who were interviewed in paper IV commonly reported deficient information about possible side effects. Patients with multi-dose drug dispensing (MDD) have less medication knowledge than patients without. This might indicate that the right group of patients receives MDD. Without distribution their medication adherence probably would have been lower. On the other hand one might suggest that patients who receive MDD lose their knowledge when the demands of daily medicine administration of their own are reduced. This might be one of the risks associated with MDD apart from the ones previously stated: a higher number of inappropriate drugs and the risk of persistent polypharmacy [20].

As a prescriber, it is important to remember that there is no "ideal" patient. One patient has not the same wishes and needs for information as another. However, all patients are legally entitled to individually adjusted information and benefit from a knowledge that admits secure administration of their medication. The patients are not gained by a patient–physician communication that is insufficient or characterized by misunder-

standings. Individual feedback to the GP and training sessions can improve medication counselling and increase patients' satisfaction with medicines information received [101]. Another way of improving GPs' listening to patients' views and concerns is to notice and spread the results of paper IV.

Our study (paper I) reveals strong beliefs in the benefits of the medication, which for the vast majority outweighed the concerns. This has been shown to be associated with higher adherence [102, 103]. The attitudes towards medication were confirmed in paper IV, where many respondents had great confidence in their medication and their physician. Some, however, reported feelings of distrust towards the health system and concerns about the amount of drugs and if all the drugs were necessary, which must not be ignored.

Methodological considerations

The studies in this thesis (paper I, II, IV) did not observe elderly patients in general, but did study patients with special needs, who are weaker and also have more medicines than the average. The results can therefore not be generalized to the entire population of elderly. On the other hand, the clinical relevance of the studies is high, since these frail patients are more sensitive to adverse reactions and, hence, secure administration of drugs is even more important. In a qualitative study the findings cannot be generalized anyway (extern validity is not the purpose) and the reader must judge transferability; whether the findings are useful in a specific population [80]. These frail, multimorbid patients are common in a primary care population and the average GP might find the transferability obvious to a great amount of his/her patients.

The thesis has some limitations. We showed in paper I that 71% of the included elderly patients could account for the indication of at least 75% of their medicines. In the paper we argued that this was higher than previously seen in a Danish study [45], where only 60% of the subjects knew the purpose of their medication, although the patients in our study were both older and frailer. However, since our study was descriptive and no separate power calculation was made, this comparison is doubtful. In addition, the number of patients in paper I was small. This made it difficult to judge the findings of lack of correlation between medical knowledge and attitudes. It might also have been of interest to examine the correlation between the use of some drugs, i.e. psychotropic drugs, and knowledge. However, the study was too small to find such a correlation.

When calculating GFR in paper II, we used different estimate formulas and did not have any true values of GFR to compare with, i.e. iohexol clearance. Furthermore the study was cross-sectional and therefore it was not possible to state if s-creatinine was a stable value.

In paper III we did not have a control group that was not exposed to the intervention. This means that we cannot eliminate other influences on the results. However, the project is not first and foremost an intervention study, but a description of how it is possible to work with quality improvement in the clinics and on small units.

Paper IV was qualitative in design and should be assessed accordingly. Some strengths are to be pointed out. All the authors participated in the analysis process and this triangulation increases credibility. In addition the analytical process was made

transparent in a table and by the use of quotations from the interviews. The use of a semi-structured interview guide strengthened trustworthiness and ensured that the participants were asked questions about the same areas. The detailed and rich data were well covered in the main categories and categories, securing credibility. According to Kuper, credibility is the term used to describe to which extent the findings are believable to others. In quantitative research, this is often referred to as intern validity [80].

Another strength of the thesis is the diversity of analyse methods used. It strengthens the education value of the doctoral studies, but also illustrates the subject from different angles of approach and they complement each other. Furthermore there are various study designs: study I and II are cohort studies, study III an intervention study and study IV is an interview study.

CONCLUSIONS AND CLINICAL IMPLICATIONS

- Elderly patients with multi-dose drug dispensing had less medication knowledge than patients without. This might indicate that the right group of patients receives multi-dose drug dispensing. Their adherence might have been lower with ordinary prescription. Patients with polypharmacy had less knowledge than patients with fewer medicines. This can be seen as one further reason to limit polypharmacy.

  The knowledge about possible adverse effects of or risks with the medication was generally poor. This was seen although potent drugs, as for example warfarin, were prescribed. This should be seen as a problem, since it is more difficult to report relevant adverse effects to the prescriber if you do not know which you should pay attention to.

  Attitudes towards medication were mostly positive. Possibly our elderly group is less demanding than younger patients, giving different BMQ-differences. However, many considered their medicines "a mystery", indicating that more weight should be given to information when medicines are prescribed.

- The elderly felt comfortable with information when they trusted their physician or their medication, when they received enough information from the prescriber or when they had the tools to find out enough information by themselves. They felt insecure if they were anxious, if the availability of medical care was poor or if they did not get enough information. Since patients who feel secure and comfortable with both information and their medications are considered to show greater adherence, it is desirable that such feelings should be engendered. Patients are also entitled to be informed at an individually optimal level.

- Reduced renal function is common among frail elderly subjects living in nursing homes, although nearly half of those with renal impairment have a normal creatinine level. Physicians have to be cautious when prescribing medications which may be harmful to elderly patients with renal impairment and this decision should not be based solely on serum creatinine levels. GFR has to be estimated before prescribing renal risk drugs, but using different estimates may give different results.

- Adherence to guidelines about the treatment of cardiovascular disease is low in primary care. Educational efforts appear to increase the adherence and should therefore be encouraged.

Further research

In existing clinical trials elderly patients are often excluded, although they account for the largest drug usage. Since the elderly are more severely affected by incorrect use of medicines, it is of great importance with further research to optimize older people's drug use, focusing on both patient factors and physician factors. Development of

evidence-based guide-lines for the treatment of elderly is essential and could possibly increase adherence among physicians. The importance of more research is especially evident in primary care, where the majority of the prescriptions are made.

SUMMARY IN SWEDISH

Svensk sammanfattning

Bakgrund

Med stigande ålder ökar antalet kroniska sjukdomar hos patienten och därmed även mängden läkemedel. I grunden är läkemedel bra produkter som lindrar, botar eller förebygger sjukdomar och lidande. Dock är äldre (>65 år) mer utsatta för potentiellt negativa effekter av läkemedel. Äldre personer använder många läkemedel, i synnerhet gäller det de äldre som bor på särskilda boenden. Ju fler läkemedel en patient intar desto större är risken för negativa bieffekter som interaktioner och biverkningar. Behandlingarna måste därför anpassas och alltid utvärderas. Med ökad ålder sker ett antal förändringar som successivt försämrar funktionen i olika organsystem. Detta innebär att äldre patienter har mindre marginaler och därmed ökad risk för negativa effekter av läkemedel.

Den viktigaste förändringen är äldres minskade njurfunktion. Det är därför nödvändigt att inför läkemedelsförskrivning skatta njurfunktionen för att rätt dosera och kanske utesluta vissa läkemedel, för att undvika biverkningar och/eller ytterligare försämring av njurfunktionen. Det finns många sätt att uppskatta njurfunktion, men ingen är optimal. Vanligt är att mäta ett blodprov – kreatinin. Att enbart bedöma njurfunktion med kreatininvärdet är dock inte tillförlitligt, speciellt inte hos äldre. Bättre är att uppskatta den sanna njurfunktionen med olika formler, baserade på blodprov.

Det finns också risker med underbehandling och vid flera tillstånd har man sett att äldre i lägre omfattning behandlas fullt ut med rekommenderade läkemedel. En högre ålder får inte betyda att en effektiv behandling undanhålls patienten. Tillgängliga vårdprogram som bygger på vetenskapligt beprövade data bör i normalfallet följas även vid behandling av äldre, även om ett individanpassat behandlingssätt är viktigt speciellt vid multisjuklighet.

Det är av största vikt att följsamheten till ordinerad behandling blir så god som möjligt. Vanligaste orsaken till dålig följsamhet (compliance) är glömska, men den kan också bero på missförstånd eller att patienten avsiktligt låter bli att ta sin medicin till exempel på grund av biverkningar eller rädsla för långsiktiga följder av behandlingen. God följsamhet är av vikt för god behandlingseffekt och minskad risk för läkemedelsrelaterade problem. Följsamheten är bl. a. relaterad till kunskap om och attityder till sina läkemedel. Kunskapen påverkas av att informationsöverföringen sker på ett så optimalt sätt som möjligt. Man har tidigare sett att många patienter upplever otillräcklig information från förskrivande läkare och har obesvarade frågor. Många är också rädda för biverkningar, men har fått bristande information om dessa.

Antalet äldre ökar ständigt i vårt samhälle och i vårdapparaten. I befintliga studier avseende läkemedelsbehandling är ofta äldre patienter exkluderade, trots att de står för den största läkemedelsanvändningen. Eftersom äldre drabbas hårdare vid felaktig läkemedelsanvändning, är det av stor vikt med ytterligare forskning för att optimera äldres läkemedelsanvändning, med inriktning både på patientfaktorer och på läkarfaktorer. Detta gäller speciellt i primärvården där den största delen av läkemedels-förskrivningen sker.

Syftet med avhandlingen var att belysa olika aspekter av kvaliteten i läkemedels-behandling av äldre i primärvården.

Resultat

I studie I mättes kunskap om och attityd till sin medicinering hos sköra äldre patienter i eget boende. Kunskapen om anledningen till behandling var relativt tillfredsställande, men kunskapen om sidoeffekter var svag. Patienter med fem eller fler läkemedel samt patienter med ApoDos (separat förpackade påsar med medicin för varje dos) hade signifikant lägre kunskap. Patienterna hade stark tro på nyttan av sina mediciner. Eftersom kunskapen delvis kan förmodas vara beroende av den information som getts om läkemedlen, följdes denna studie upp av studie IV, som var en intervjustudie som utforskade patienters erfarenheter av information om förskrivna läkemedel. Det framkom att det finns faktorer som gör att patienter känner sig nöjda och trygga, t ex när de har stort förtroende för sin doktor eller litar på sin medicinering och även när de vet själva var och hur de skaffar sig tillräcklig kunskap om sina mediciner. Det finns också faktorer som skapar otrygghet eller rent av missnöje, t ex när det är svårt att nå sin doktor eller när informationen är för sparsam.

Studie II undersökte njurfunktion och användning av riskläkemedel vid sänkt njurfunktion hos sjukhemspatienter i tre olika kommuner. Minskad njurfunktion sågs hos drygt hälften av patienterna, men normalt kreatininvärde sågs i 41 % av patienterna med minskad njurfunktion. Riskläkemedel förskrevs ganska sällan. Det verkar alltså finnas en god medvetenhet bland allmänläkare om vikten att njurfunktionsanpassa läkemedelsförskrivningen. Läkaren måste vara observant på njurfunktion innan läkemedel förskrivs till en äldre patient och bör inte bara lita på kreatininvärdet. Njurfunktion bör beräknas innan riskläkemedel förskrivs, men olika sätt att uppskatta kan ge skilda resultat.

Studie III var en journalstudie och ett lokalt kvalitetsförbättringsprojekt som mätte hur väl allmänläkare följer regionala vårdprogram vid behandling av äldre patienter med hjärt-kärlsjukdom. Studien undersökte också om utbildningsprogram kan förbättra följsamheten till rekommendationer. Man kunde se att följsamheten till rekommendationer i många fall var låg, men att den kunde förbättras genom upprepade informationsmöten och feedback till patientansvarig läkare.

ACKNOWLEDGEMENTS

REFERENCES

1. The Swedish Council on Health Technology Assessment *[How Can Drug Consumption among the Elderly be Improved?]*. Stockholm; 2009

2. Kragh, A. (2004) [Two out of three persons living in nursing homes for the elderly are treated with at least ten different drugs. A survey of drug prescriptions in the northeastern part of Skane]. *Lakartidningen* **101**, 994-996, 999.

3. Fryckstedt, J. and Asker-Hagelberg, C. (2008) [Drug-related problems common in the emergency department of internal medicine. The cause of admission in almost every third patient according to quality follow-up]. *Lakartidningen* **105**, 894-898.

4. von Euler, M., Eliasson, E., Ohlen, G. and Bergman, U. (2006) Adverse drug reactions causing hospitalization can be monitored from computerized medical records and thereby indicate the quality of drug utilization. *Pharmacoepidemiol Drug Saf* **15**, 179-184.

5. Mjorndal, T., Boman, M. D., Hagg, S., Backstrom, M., Wiholm, B. E., Wahlin, A. and Dahlqvist, R. (2002) Adverse drug reactions as a cause for admissions to a department of internal medicine. *Pharmacoepidemiol Drug Saf* **11**, 65-72.

6. Paul, E., End-Rodrigues, T., Thylen, P. and Bergman, U. (2008) [Adverse drug reactions a common cause of hospitalization of the elderly. A clinical retrospective study]. *Lakartidningen* **105**, 2338-2342.

7. Apoteket: **Drug Statistic 2011**. In.; 2012.

8. Olsson, I. N., Runnamo, R. and Engfeldt, P. (2011) Medication quality and quality of life in the elderly, a cohort study. *Health Qual Life Outcomes* **9**, 95.

9. The National Board of Health and Welfare: *[Quality of drug treatment of the elderly. The role of the physician]* Stockholm; 2011

10. Moen, J., Norrgard, S., Antonov, K., Nilsson, J. L. and Ring, L. (2010) GPs' perceptions of multiple-medicine use in older patients. *J Eval Clin Pract* **16**, 69-75.

11. Hellstrom, L. M., Bondesson, A., Hoglund, P., Midlov, P., Holmdahl, L., Rickhag, E. and Eriksson, T. (2011) Impact of the Lund Integrated Medicines Management (LIMM) model on medication appropriateness and drug-related hospital revisits. *Eur J Clin Pharmacol* **67**, 741-752.

12. Midlov, P., Holmdahl, L., Eriksson, T., Bergkvist, A., Ljungberg, B., Widner, H., Nerbrand, C. and Hoglund, P. (2008) Medication report reduces number of medication errors when elderly patients are discharged from hospital. *Pharm World Sci* **30**, 92-98.

13. Andersson, G. and Karlberg, I. (2000) Integrated care for the elderly: the background and effects of the reform of Swedish care of the elderly. *Int J Integr Care* **1**, e01.

14. Swedish Association of Local Authorities and Regions: *[Outside the hospital - Investigation of elderly with multiple diseases in ordinary housing]*. Stockholm; 2011

15. National Board of Health and Welfare: *[Open comparisons of quality and efficiency in the health care system. Care of elderly.]* Stockholm; 2011

16. Olsson, J., Bergman, A., Carlsten, A., Oke, T., Bernsten, C., Schmidt, I. K. and Fastbom, J. (2010) Quality of drug prescribing in elderly people in nursing homes and special care units for dementia: a cross-sectional computerized pharmacy register analysis. *Clin Drug Investig* **30**, 289-300.

17. Bergman, A., Olsson, J., Carlsten, A., Waern, M. and Fastbom, J. (2007) Evaluation of the quality of drug therapy among elderly patients in nursing homes. *Scand J Prim Health Care* **25**, 9-14.

18. Olsson, I. N., Curman, B. and Engfeldt, P. (2010) Patient focused drug surveillance of elderly patients in nursing homes. *Pharmacoepidemiol Drug Saf* **19**, 150-157.

19. Forsetlund, L., Eike, M. C., Gjerberg, E. and Vist, G. E. (2011) Effect of interventions to reduce potentially inappropriate use of drugs in nursing homes: a systematic review of randomised controlled trials. *BMC Geriatr* **11**, 16.

20. Sjoberg, C., Edward, C., Fastbom, J., Johnell, K., Landahl, S., Narbro, K. and Wallerstedt, S. M. (2011) Association between multi-dose drug dispensing and quality of drug treatment--a register-based study. *PLoS One* **6**, e26574.

21. The National Board of Health and Welfare: *[Indicators for evaluation of the quality of drug use by elderly]*. Stockholm; 2003

22. Kragh, A. and Rekman, E. (2005) [Remote drug-review for better use of pharmaceuticals among the elderly]. *Lakartidningen* **102**, 1143, 1145-1146, 1149.

23. Turnheim, K. (2003) When drug therapy gets old: pharmacokinetics and pharmacodynamics in the elderly. *Exp Gerontol* **38**, 843-853.

24. Turnheim, K. (2004) Drug therapy in the elderly. *Experimental gerontology* **39**, 1731-1738.

25. Muhlberg, W. and Platt, D. (1999) Age-dependent changes of the kidneys: pharmacological implications. *Gerontology* **45**, 243-253.

26. Salomon, L., Deray, G., Jaudon, M. C., Chebassier, C., Bossi, P., Launay-Vacher, V., Diquet, B., Ceza, J. M., Levu, S., Brucker, G. and Ravaud, P. (2003) Medication misuse in hospitalized patients with renal impairment. *Int J Qual Health Care* **15**, 331-335.

27. Wong, N. A. and Jones, H. W. (1998) An analysis of discharge drug prescribing amongst elderly patients with renal impairment. *Postgraduate medical journal* **74**, 420-422.

28. Kurtal, H., Schwenger, V., Azzaro, M., Abdollahnia, N., Steinhagen-Thiessen, E., Nieczaj, R. and Schulz, R. J. (2009) Clinical value of automatic reporting of estimated glomerular filtration rate in geriatrics. *Gerontology* **55**, 288-295.

29. Fehrman-Ekholm, I. and Skeppholm, L. (2004) Renal function in the elderly (>70 years old) measured by means of iohexol clearance, serum creatinine, serum urea and estimated clearance. *Scandinavian journal of urology and nephrology* **38**, 73-77.

30. Levey, A. S., Coresh, J., Greene, T., Marsh, J., Stevens, L. A., Kusek, J. W. and Van Lente, F. (2007) Expressing the Modification of Diet in Renal Disease Study equation for estimating glomerular filtration rate with standardized serum creatinine values. *Clin Chem* **53**, 766-772.

31. Mayer, G. (2009) Renal function in the elderly and drug dosing. *Gerontology* **55**, 417-421; discussion 422-416.

32. Wasen, E., Isoaho, R., Mattila, K., Vahlberg, T., Kivela, S. L. and Irjala, K. (2004) Estimation of glomerular filtration rate in the elderly: a comparison of creatinine-based formulae with serum cystatin C. *Journal of internal medicine* **256**, 70-78.

33. Grubb, A. O. (2000) Cystatin C--properties and use as diagnostic marker. *Advances in clinical chemistry* **35**, 63-99.

34. Macdonald, J., Marcora, S., Jibani, M., Roberts, G., Kumwenda, M., Glover, R., Barron, J. and Lemmey, A. (2006) GFR estimation using cystatin C is not independent of body composition. *Am J Kidney Dis* **48**, 712-719.

35. Fehrman-Ekholm, I., Seeberger, A., Bjork, J. and Sterner, G. (2009) Serum cystatin C: a useful marker of kidney function in very old people. *Scandinavian journal of clinical and laboratory investigation* **69**, 606-611.

36. Bevc, S., Hojs, R., Ekart, R., Gorenjak, M. and Puklavec, L. (2011) Simple cystatin C formula compared to sophisticated CKD-EPI formulas for estimation of glomerular filtration rate in the elderly. *Ther Apher Dial* **15**, 261-268.

37. Modig, S., Lannering, C., Ostgren, C. J., Molstad, S. and Midlov, P. (2011) The assessment of renal function in relation to the use of drugs in elderly in nursing homes; a cohort study. *BMC Geriatr* **11**, 1.

38. Panel, T. A. G. S. B. C. U. E. (2012) American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* **60**, 616-631.

39. Okuno, J., Yanagi, H., Tomura, S., Oka, M., Hara, S., Hirano, C. and Tsuchiya, S. (1999) Compliance and medication knowledge among elderly Japanese home-care recipients. *Eur J Clin Pharmacol* **55**, 145-149.

40. Vlasnik, J. J., Aliotta, S. L. and DeLor, B. (2005) Medication adherence: factors influencing compliance with prescribed medication plans. *Case Manager* **16**, 47-51.

41. Kiesler, D. J. and Auerbach, S. M. (2006) Optimal matches of patient preferences for information, decision-making and interpersonal behavior: evidence, models and interventions. *Patient Educ Couns* **61**, 319-341.

42. Vermeire, E., Hearnshaw, H., Van Royen, P. and Denekens, J. (2001) Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther* **26**, 331-342.

43. Ekdahl, A. W., Andersson, L. and Friedrichsen, M. (2010) "They do what they think is the best for me." Frail elderly patients' preferences for participation in their care during hospitalization. *Patient Educ Couns* **80**, 233-240.

44. Beckman, A. G., Parker, M. G. and Thorslund, M. (2005) Can elderly people take their medicine? *Patient Educ Couns* **59**, 186-191.

45. Barat, I., Andreasen, F. and Damsgaard, E. M. (2001) Drug therapy in the elderly: what doctors believe and patients actually do. *Br J Clin Pharmacol* **51**, 615-622.

46. Burge, S., White, D., Bajorek, E., Bazaldua, O., Trevino, J., Albright, T., Wright, F. and Cigarroa, L. (2005) Correlates of medication knowledge and adherence: findings from the residency research network of South Texas. *Fam. Med.* **37**, 712-718.

47. Clifford, S., Barber, N. and Horne, R. (2008) Understanding different beliefs held by adherers, unintentional nonadherers, and intentional nonadherers: Application of the Necessity-Concerns Framework. *J. Psychosom. Res.* **64**, 41-46.

48. Griffith, S. (1990) A review of the factors associated with patient compliance and the taking of prescribed medicines. *Br. J. Gen. Pract.* **40**, 114-116.

49. Horne, R. and Weinmann, J. (1999) Patients' beliefs about prescribed medicines and their role in adherence in cronic physical illness. *Journal of Psychosomatic Research* **47**, 555-567.

50. Menckeberg, T. T., Bouvy, M. L., Bracke, M., Kaptein, A. A., Leufkens, H. G., Raaijmakers, J. A. and Horne, R. (2008) Beliefs about medicines predict refill adherence to inhaled corticosteroids. *J. Psychosom. Res.* **64**, 47-54.

51. Granas, A. G. and Bates, I. (2005) Patients' understanding and management of their illnesses and prescribed medicines--a descriptive study. *Pharm World Sci* **27**, 321-328.

52. Jaye, C., Hope, J. and Martin, I. R. (2002) What do general practice patients know about their prescription medications? *N Z Med J* **115**, U183.

53. Kristensson, J., Modig, S., Midlov, P., Hallberg, I. R. and Jakobsson, U. (2010) Healthcare utilisation and knowledge concerning prescribed drugs among older people. *Eur J Clin Pharmacol* **66**, 1047-1054.

54. Gordon, K., Smith, F. and Dhillon, S. (2007) Effective chronic disease management: patients' perspectives on medication-related problems. *Patient Educ Couns* **65**, 407-415.

55. Moen, J., Bohm, A., Tillenius, T., Antonov, K., Nilsson, J. L. and Ring, L. (2009) "I don't know how many of these [medicines] are necessary.." - a focus group study among elderly users of multiple medicines. *Patient Educ Couns* **74**, 135-141.

56. **Health and Medical Services Act**. In: *SFS 1982:763*. 1982/2011.

57. **Patient Safety Act**. In: *SLS 2010:659 Ch 6, §6.* Government Offices of Sweden; 2010.

58. Colledge, A., Car, J., Donnelly, A. and Majeed, A. (2008) Health information for patients: time to look beyond patient information leaflets. *J R Soc Med* **101**, 447-453.

59. Coulter, A. and Ellins, J. (2007) Effectiveness of strategies for informing, educating, and involving patients. *BMJ* **335**, 24-27.

60. Roett, M. A. and Wessel, L. (2012) Help your patient "get" what you just said: a health literacy guide. *J Fam Pract* **61**, 190-196.

61. Weiss, B. D., Mays, M. Z., Martz, W., Castro, K. M., DeWalt, D. A., Pignone, M. P., Mockbee, J. and Hale, F. A. (2005) Quick assessment of literacy in primary care: the newest vital sign. *Ann Fam Med* **3**, 514-522.

62. Herndon, J. B., Chaney, M. and Carden, D. (2011) Health literacy and emergency department outcomes: a systematic review. *Ann Emerg Med* **57**, 334-345.

63. Ramsay, S. E., Whincup, P. H., Lawlor, D. A., Papacosta, O., Lennon, L. T., Thomas, M. C., Ebrahim, S. and Morris, R. W. (2006) Secondary prevention of coronary heart disease in older patients after the national service framework: population based study. *BMJ* **332**, 144-145.

64. Litaker, J. R. and Chou, J. Y. (2003) Patterns of pharmacologic treatment of congestive heart failure in elderly nursing home residents and related issues: a review of the literature. *Clin. Ther.* **25**, 1918-1935.

65. Klarin, I., Fastbom, J. and Wimo, A. (2003) A population-based study of drug use in the very old living in a rural district of Sweden, with focus on cardiovascular drug consumption: comparison with an urban cohort. *Pharmacoepidemiol. Drug Saf.* **12**, 669-678.

66. Boyles, P. J., Peterson, G. M., Bleasel, M. D. and Vial, J. H. (2004) Undertreatment of congestive heart failure in an Australian setting. *J Clin Pharm Ther* **29**, 15-22.

67. Gaw, A. (2004) The care gap: underuse of statin therapy in the elderly. *Int J Clin Pract* **58**, 777-785.

68. Sloane, P. D., Gruber-Baldini, A. L., Zimmerman, S., Roth, M., Watson, L., Boustani, M., Magaziner, J. and Hebel, J. R. (2004) Medication undertreatment in assisted living settings. *Arch Intern Med* **164**, 2031-2037.

69. Castilla-Guerra, L., Fernandez-Moreno Mdel, C. and Alvarez-Suero, J. (2009) Secondary stroke prevention in the elderly: new evidence in hypertension and hyperlipidemia. *Eur J Intern Med* **20**, 586-590.

70. Lugtenberg, M., Burgers, J. S., Besters, C. F., Han, D. and Westert, G. P. (2011) Perceived barriers to guideline adherence: a survey among general practitioners. *BMC Fam Pract* **12**, 98.

71. Overmeer, T., Linton, S. J., Holmquist, L., Eriksson, M. and Engfeldt, P. (2005) Do evidence-based guidelines have an impact in primary care? A cross-sectional study of Swedish physicians and physiotherapists. *Spine (Phila Pa 1976)* **30**, 146-151.

72. Maio, V., Jutkowitz, E., Herrera, K., Abouzaid, S., Negri, G. and Del Canale, S. (2011) Appropriate medication prescribing in elderly patients: how knowledgeable are primary care physicians? A survey study in Parma, Italy. *J Clin Pharm Ther* **36**, 468-480.

73. Reiner, Z., Sonicki, Z. and Tedeschi-Reiner, E. (2010) Physicians' perception, knowledge and awareness of cardiovascular risk factors and adherence to prevention guidelines: the PERCRO-DOC survey. *Atherosclerosis* **213**, 598-603.

74. Levey, A. S., Stevens, L. A. and Hostetter, T. (2006) Automatic reporting of estimated glomerular filtration rate--just what the doctor ordered. *Clin Chem* **52**, 2188-2193.

75. Nyman, U., Grubb, A., Sterner, G. and Bjork, J. (2009) Different equations to combine creatinine and cystatin C to predict GFR. Arithmetic mean of existing equations performs as well as complex combinations. *Scand J Clin Lab Invest* **69**, 619-627.

76. Botev, R., Mallie, J. P., Wetzels, J. F., Couchoud, C. and Schuck, O. (2011) The clinician and estimation of glomerular filtration rate by creatinine-based formulas: current limitations and quo vadis. *Clin J Am Soc Nephrol* **6**, 937-950.

77. Kasje, W. N., Denig, P., Stewart, R. E., de Graeff, P. A. and Haaijer-Ruskamp, F. M. (2006) An educational programme for peer review groups to improve treatment of chronic heart failure and diabetes mellitus type 2 in general practice. *J Eval Clin Pract* **12**, 613-621.

78. Midlov, P., Bondesson, A., Eriksson, T., Petersson, J., Minthon, L. and Hoglund, P. (2002) Descriptive study and pharmacotherapeutic intervention in patients with epilepsy or Parkinson's disease at nursing homes in southern Sweden. *Eur J Clin Pharmacol* **57**, 903-910.

79. Midlov, P., Bondesson, A., Eriksson, T., Nerbrand, C. and Hoglund, P. (2006) Effects of educational outreach visits on prescribing of benzodiazepines and antipsychotic drugs to elderly patients in primary health care in southern Sweden. *Fam Pract* **23**, 60-64.

80. Kuper, A., Reeves, S. and Levinson, W. (2008) An introduction to reading and appraising qualitative research. *BMJ* **337**, a288.

81. Kristensson, J., Ekwall, A. K., Jakobsson, U., Midlov, P. and Hallberg, I. R. (2010) Case managers for frail older people: a randomised controlled pilot study. *Scand J Caring Sci* **24**, 755-763.

82. Ernsth Bravell, M., Westerlind, B., Midlov, P., Ostgren, C. J., Borgquist, L., Lannering, C. and Molstad, S. (2011) How to assess frailty and the need for care? Report from the Study of Health and Drugs in the Elderly (SHADES) in community dwellings in Sweden. *Arch Gerontol Geriatr* **53**, 40-45.

83. Horne, R., Weinmann, J. and Hankins, M. (1998) The Beliefs about Medicines Questionaire (BMQ): the development and evaluation of a new method for assessing the cognitive representation of medication. *Psychol Health* **14**, 1-24.

84. Jorgensen, T. M., Andersson, K. A. and Mardby, A. C. (2006) Beliefs about medicines among Swedish pharmacy employees. *Pharm. World Sci.* **28**, 233-238.

85. Grubb, A., Bjork, J., Lindstrom, V., Sterner, G., Bondesson, P. and Nyman, U. (2005) A cystatin C-based formula without anthropometric variables estimates glomerular filtration rate better than creatinine clearance using the Cockcroft-Gault formula. *Scand J Clin Lab Invest* **65**, 153-162.

86. **"K/DOQI clinical practice guidelines for chronic kidney disease"**. In.: National Kidney Foundation; 2002.

87. Fleiss, J.: **Statistical Methods for Rates and Proportions.**, 2nd edn. New York: Wiley; 1981.

88. Berg, B. L.: **Qualitative research methods for the social sciences.**, Fifth edn. Boston: Allyn and Bacon; 2004.

89. Graneheim, U. H. and Lundman, B. (2004) Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today* **24**, 105-112.

90. Allander, S. V., Larsson, A., Marke, L. A., Svensson, M. K., Bjorn, W. and Elinder, C. G. (2012) [Creatinine is still the most common kidney function assay: Examination of the practice in Sweden]. *Lakartidningen* **109**, 960-962.

91. Corsonello, A., Pedone, C., Corica, F., Mussi, C., Carbonin, P. and Antonelli Incalzi, R. (2005) Concealed renal insufficiency and adverse drug reactions in elderly hospitalized patients. *Arch Intern Med* **165**, 790-795.

92. Elinder, C. G., Allander, S. V. and Farrokhnia, N. (2010) [Assessment of renal function--unclear which method is best. Background to SBU investigation of endogenous markers]. *Lakartidningen* **107**, 3138-3140.

93. Midlov, P., Ekesbo, R., Johansson, L., Gerward, S., Persson, K., Nerbrand, C. and Hedblad, B. (2008) Barriers to adherence to hypertension guidelines among GPs in southern Sweden: a survey. *Scandinavian Journal of Primary Health Care* **26**, 154-159.

94. Vashitz, G., Meyer, J., Parmet, Y., Henkin, Y., Peleg, R. and Gilutz, H. (2011) Physician adherence to the dyslipidemia guidelines is as challenging an issue as patient adherence. *Fam Pract* **28**, 524-531.

95. Nieburg, I. and Kahan, T. (2010) Cardiovascular risk factors are not treated to target in hypertensive patients in primary care. *Blood Press* **19**, 176-181.

96. Strandberg, E. L., Ovhed, I., Hakansson, A. and Troein, M. (2006) The meaning of quality work from the general practitioner's perspective: an interview study. *BMC Fam Pract* **7**, 60.

97. Silwer, L., Wahlstrom, R. and Lundborg, C. S. (2010) Views on primary prevention of cardiovascular disease--an interview study with Swedish GPs. *BMC Fam. Pract.* **11**, 44.

98. Perk, J., De Backer, G., Gohlke, H., Graham, I., Reiner, Z., Verschuren, M., Albus, C., Benlian, P., Boysen, G., Cifkova, R., Deaton, C., Ebrahim, S., Fisher, M., Germano, G., Hobbs, R., Hoes, A., Karadeniz, S., Mezzani, A., Prescott, E., Ryden, L., Scherer, M., Syvanne, M., Scholte op Reimer, W. J., Vrints, C., Wood, D., Zamorano, J. L. and Zannad, F. (2012) European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J* **33**, 1635-1701.

99. National Board of Health and Welfare: *[National Guidelines for Cardiac Care].* Stockholm; 2008

100. Molander, L., Lovheim, H., Norman, T., Nordstrom, P. and Gustafson, Y. (2008) Lower systolic blood pressure is associated with greater mortality in people aged 85 and older. *J. Am. Geriatr. Soc.* **56**, 1853-1859.

101. Mahler, C., Hermann, K., Jank, S., Haefeli, W. E. and Szecsenyi, J. (2012) Can a feedback report and training session on medication counseling for general practitioners improve patient satisfaction with information on medicines? *Patient Prefer Adherence* **6**, 179-186.

102. Mahler, C., Hermann, K., Horne, R., Jank, S., Haefeli, W. E. and Szecsenyi, J. (2012) Patients' beliefs about medicines in a primary care setting in Germany. *J Eval Clin Pract* **18**, 409-413.

103. Schuz, B., Marx, C., Wurm, S., Warner, L. M., Ziegelmann, J. P., Schwarzer, R. and Tesch-Romer, C. (2011) Medication beliefs predict medication adherence in older adults with multiple illnesses. *J Psychosom Res* **70**, 179-187.

APPENDICES

Appendix A

<u>LÄKEMEDELSANAMNES/KUNSKAP</u>

Läkemedel	Dosering	Kunskap om ordinerat läkemedel	Kunskap om orsak till behandling*			Kunskap om biv/risker**	
			1	2	3	1	2

***Kunskapsnivå indikation:** 1. Har ingen kunskap alls 2. Har kunskap med hjälp av lista 3. Har kunskap
****Kunskapsnivå biv/risker:** 1. Har ingen kunskap 2. Har kunskap

<u>Apodos:</u> ☐ Nej ☐ Ja
<u>Hjälp med medicindelning:</u> ☐ Nej ☐ Ja, av anhörig ☐ Ja, av sjukvården

Appendix B

BMQ- Specifik

DINA UPPFATTNINGAR OM LÄKEMEDEL SOM FÖRSKRIVITS FÖR DIG

**Inga svar är mer rätt eller fel än andra.
Vi är intresserade av Dina personliga
uppfattningar.**

Uppfattningar om **läkemedel som förskrivits för Dig**	Stämmer mycket bra	Stämmer bra	Osäker	Stämmer dåligt	Stämmer inte alls
Min nuvarande hälsa är beroende av mina läkemedel					
Det oroar mig att jag måste ta läkemedel					
Mitt liv skulle vara omöjligt utan mina läkemedel					
Ibland oroar jag mig för mina läkemedels långsiktiga effekter					
Utan mina läkemedel skulle jag vara mycket sjuk					
Mina läkemedel är en gåta för mig					
Min framtida hälsa kommer att bero på mina läkemedel					
Mina läkemedel stör mitt liv					
Ibland oroar jag mig över att bli alltför beroende av mina läkemedel					
Mina läkemedel skyddar mig från att bli sämre					

Appendix C
Semistrukturerad intervjuguide

Vilka mediciner har du för hjärtat?

Vad vet du om hur de fungerar?

Vad har du fått veta om eventuella biverkningar?

Vilken medicin tycker du är den viktigaste?

Vad har du fått veta om dessa mediciner? Av vem? När? Berätta om…

Vad fick du veta första gången medicinen skrevs ut?

Känner du dig tillfreds med den infon du fått? Varför? Varför inte?

Skulle du ha velat bli informerad på annorlunda sätt? Eller utökat?

Hur skulle du vilja få info?

Vad brukar du få för information om medicinerna av din dr när recept förnyas?

Hämtar du din medicin själv eller får du hjälp? (på apoteket ges info)

Läser du bipacksedeln? Söker du själv information om dina läkemedel på annat sätt, tex Internet, patient-FASS etc?

Använder du dosett? Vem laddar den i så fall – du själv, anhörig, hemsjukvård?

Eller tar du direkt ut förpackningen?

Många hoppar över någon tablett ibland. Händer det dig? Hur kommer det sig? Hur tänker du då?

Hur upplever du att få preparat på apoteket som inte heter samma som dem du fått info om?