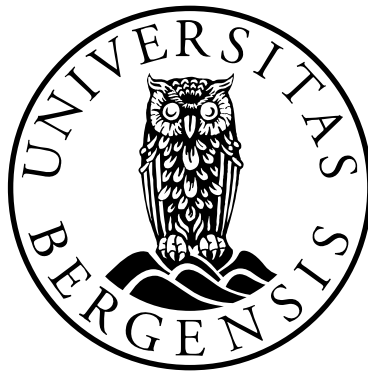# Drug prescribing quality
for older patients

Explicit indicators and multidisciplinary medication reviews

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SCIENTIFIC ENVIRONMENT

This work has been performed at the Research Group for General Practice, Department of Public Health and Primary Health Care, University of Bergen. Paper II was accomplished in collaboration with the Department of Pharmacotherapeutics, University of Oslo.

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CONTENTS

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LIST OF PUBLICATIONS

Paper I Halvorsen KH, Granas AG, Engeland A, Ruths S.

Prescribing quality for older people in Norwegian nursing homes and home care services using multi-dose dispensed drugs.

Pharmacoepidemiology and Drug Safety. 2011 (E-pub).

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Paper II Halvorsen KH, Ruths S, Granas AG, Viktil KK.

Multidisciplinary intervention to identify and resolve drug-related problems in Norwegian nursing homes.

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Paper III Halvorsen KH, Stensland P, Granas AG.

Physicians and nurses experiences of multidisciplinary collaboration with pharmacists at case conferences - A qualitative study.

International Journal of Pharmacy Practice. 2011; 19: 350-57.

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ABBREVIATIONS

ACE	Angiotensin converting enzyme
ADE	Adverse drug event
ADR	Adverse drug reaction
ASA	Acetylsalicylic acid
ATC	Anatomical Therapeutic Chemical
CI	Confidence interval
DDI	Drug-drug interaction
DRP	Drug-related problem
DRUID	Drug Information Database
HNS	Home nursing service
MDD	Multi-dose dispensed drug
NH	Nursing home
NORGEP	Norwegian General Practice (criteria)
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
PASW	Predictive Analytics Software
PIM	Potential inappropriate medication
PQI	Prescribing quality indicator
p.r.n.	*pro re nata* = "as needed" or "as required" medication
GP	General Practitioner
SPSS	Statistical Package for Social Sciences
START	Screening Tool to Alert doctors to the Right Treatment
STOPP	Screening Tool of Older persons' Potentially inappropriate Prescriptions
vs.	Versus
WHO	World Health Organisation

SUMMARY

This thesis is based on three published papers that illuminate different aspects of prescribing quality and drug use in older patients who receive home nursing services or live in nursing homes.

Persons older than 65 years account for about 15% of the Norwegian population, but use almost half of all prescribed drugs. Age-related and physiological changes affect drugs' pharmacokinetics (absorption, distribution, metabolism and elimination). For example, a reduction of muscle mass and an increase in fat percentage will allow an accumulation of fat-soluble drugs, while reduce renal function will influence the pharmacological response and the elimination of drugs. Pharmacodynamic changes include up or down-regulation of receptors and altered receptor sensitivity. Along with reduced homeostasis, these factors puts older patients at risk of adverse drug events, possibly resulting in reduced quality of life, hospitalization and in worst case death. It is therefore important to identify and prevent inappropriate prescribing and drug-related problems.

An explicit method for assessing prescribing quality is to compare patients' medication lists with a predefined list of drugs considered to be inappropriate for use in older patients. Such lists are eligible for screening of large populations, but they rarely take the patients' clinical conditions into consideration. Another method is to consider drug-related problems by conducting a systematic review of patients' overall drug use, taking their clinical conditions into consideration. Although systematic medication reviews are suitable for multidisciplinary collaboration between physicians, nurses and pharmacists, little knowledge exists about how this collaboration works and how it is perceived.

The purpose of *Paper I* was to examine the quality of drug prescribing in older patients in nursing homes and home nursing services receiving multidose dispensed drugs, by means of explicit quality indicators. We studied 11 254 patients, of whom 2 986 were living in nursing homes, and 8 268 received home nursing services. On average, both patient groups were prescribed 5.7 regular multidose dispensed drugs. While relatively more patients in nursing homes used psychotropic drugs, those in

home nursing service used cardiovascular drugs more frequently. Inappropriate drug use was found in 31% of patients in nursing homes and in 25% of home nursing service patients. Concomitant use of three or more psychotropic drugs and/or opioid drugs caused most problems. Potentially serious drug-drug interactions were found in ~ 10% of patients.

The aim of *Paper II* was to test a multidisciplinary model to identify and resolve drug-related problems in nursing homes. Three pharmacists conducted systematic medication reviews in 142 patients. A total of 719 potential problems was presented to and discussed with the patients' physician and primary nurse at case conferences, of which 504 drug-related problems were acknowledged by the multidisciplinary team. Most problems were associated with unnecessary drug use (n = 194) and the need for monitoring (n=68). Paracetamol, lactulose and zopiclone caused most drug-related problems. 94% of the problems were resolved within the next three weeks. The intervention resulted in an average reduction of 1.5 prescribed drugs per patient.

In *Paper III*, we explored how physicians and nurses working in nursing homes and hospitals experienced multidisciplinary collaboration with pharmacists to optimize drug therapy in older patients. By interviewing physicians and nurses, we found that these two professions had different expectations in relation to pharmacist contributions. While physicians felt that the pharmacists questioned their drug therapy choices, nurses experienced that focus changed away from their tasks, and towards drug-related issues. Both professions expressed, however, that the presence of pharmacists resulted in a positive focus on prescribing quality and quality improvement. However, before implementing this service in NHs, there is a need to make an organisational frame for this collaboration to support the professional role of the pharmacist.

This thesis shows that the quality of drug treatment in the studied patient groups is sub-optimal. Many older patients in nursing homes and those receiving home nursing services are exposed to potentially inappropriate medications. Multi-disciplinary cooperation between physicians, nurses and pharmacists can be developed in order to identify inappropriate drug use, and to resolve drug-related problems.

SUMMARY IN NORWEGIAN (sammendrag)

Avhandlingen er basert på tre publiserte artikler som belyser ulike aspekter ved forskrivningskvalitet og legemiddelbruk hos eldre pasienter som mottar hjemmesykepleie eller som bor på sykehjem.

Eldre over 65 år utgjør i dag ca 15 % av den norske befolkning, men står for bruken av nesten halvparten av alle forskrevne legemidler. Aldersrelaterte fysiologiske forandringer kan påvirke legemidlenes farmakokinetikk (absorpsjon, distribusjon, metabolisme og eliminasjon). Eksempelvis vil redusert muskelmasse og økt fettprosent medføre en opphopning av fettløselige legemidler, og redusert nyrefunksjon kan påvirke farmakologisk respons og utskillelse av legemidler. Farmakodynamiske endringer inkluderer blant annet opp- eller nedregulering av reseptorer og endret reseptorsensitivitet. Samtidig som homeostasen reduseres medfører disse faktorene en økt risiko hos eldre for uhensiktsmessige legemiddeleffekter som kan resultere i redusert livskvalitet, sykehusinnleggelser og i verste fall død. Det er derfor viktig å identifisere og forebygge uhensiktsmessig forskrivning og legemiddelrelaterte problemer.

En eksplisitt metode for å vurdere forskrivningskvalitet er å sammenlikne pasientens legemiddelliste mot en forhåndsdefinert liste over legemidler som er ansett uhensiktsmessige for bruk hos eldre. Slike lister er egnet for å screene store populasjoner, men tar imidlertid sjeldent høyde for pasientens kliniske tilstand. En annen metode er en systematisk gjennomgang av pasientens samlede legemiddelbruk hvor man benytter eksplisitte kategorier for legemiddelrelaterte problemer (indikasjon, legemiddelvalg, dosering, bivirkning, interaksjon, bruk), og hvor pasientens kliniske tilstand tas med i vurderingen. Denne metoden egner seg for tverrfaglig samarbeid mellom leger, sykepleiere og farmasøyter. Vi vet derimot lite om hvilke erfaringer og oppfatninger helsepersonell har, samt hvordan et slikt samarbeid fungerer.

Formålet med *artikkel 1* var å undersøke legemiddelbruk og kvalitet på legemiddelforskrivning hos eldre personer i sykehjem og i åpen omsorg som mottar multidosepakkede legemidler, basert på eksplisitte kvalitetsindikatorer. Vi screenet legemiddellistene hos 11 254 pasienter, hvorav 2 986 var innlagt i sykehjem og 8 268

mottok hjemmesykepleie. I gjennomsnitt brukte begge pasientgruppene 5.7 multidose-pakkede legemidler på fast, daglig basis. Mens psykofarmaka ble hyppigere forskrevet til sykehjemspasienter, fikk flere pasienter i åpen omsorg legemidler for kardio-vaskulære lidelser. Uhensiktsmessige legemidler ble brukt av 31 % av sykehjems-pasientene og 25 % av pasientene som mottok hjemmesykepleie. Samtidig bruk av tre eller flere psykofarmaka og/eller opioide legemidler forårsaket flest problemer. Potensielt alvorlige legemiddelinteraksjoner ble funnet hos ca 10 % av pasientene.

Hensikten med *artikkel 2* var å utprøve en tverrfaglig modell for å identifisere og løse legemiddelrelaterte problemer i norske sykehjem. Tre farmasøyter foretok systematiske legemiddelgjennomganger hos 142 pasienter. I alt 719 potensielle problem ble presentert for og diskutert med pasientens lege og primærsykepleier på previsitten, hvorav 504 legemiddelrelaterte problem ble anerkjent av det tverrfaglige teamet. Flest problemer var knyttet til unødvendig legemiddelbruk (n=194), og behov for monitorering (n=68). Paracetamol, laktulose og zopiclone var oftest innblandet i legemiddelrelaterte problemer. 94 % av problemene ble løst i løpet av de påfølgende tre ukene. Intervensjonen resulterte i en gjennomsnittlig reduksjon av 1,5 forskrevne legemidler per pasient.

I *artikkel 3* utforsket vi hvordan leger og sykepleiere erfarte tverrfaglig samarbeid med farmasøyter. Gjennom intervju fant vi at disse to yrkesgruppene hadde ulike forventinger til hva farmasøyten skulle bidra med. Mens legene erfarte at farmasøytene utfordret dem på spørsmål angående legemiddelterapi, erfarte syke-pleierne at fokus ble endret bort fra deres oppgaver, og mot farmakoterapeutiske problemstillinger. Begge yrkesgruppene uttrykte at farmasøytens nærvær satte fokus på og hevet forskrivningskvalitet. Likevel, før en slik tjeneste kan implementeres i sykehjem, bør det utvikles en organisatorisk ramme som ivaretar farmasøytenes profesjonelle rolle i dette samarbeidet.

Denne avhandlingen viser at kvaliteten på legemiddelbehandling hos eldre pasienter ikke er optimal. Mange eldre i sykehjem og åpen omsorg bruker potensielt uhensiktsmessige legemidler. Tverrfaglig samarbeid mellom leger, sykepleiere og farmasøyter har potensial for å videreutvikles med tanke på å avdekke uhensiktsmessig legemiddelbruk, samt løse legemiddelrelaterte problemer.

INTRODUCTION

Older patients receiving home nursing services (HNS) or living in nursing homes (NH) commonly suffer from complex health problems and often use multiple medications concomitantly. Age-related changes affecting pharmacodynamic and pharmacokinetic properties, and co-morbidity, are great challenges for optimal drug therapy and put frail and vulnerable patients at increased risk of adverse drug events (ADE) [1], hospitalization [2] and death [3]. The lack of evidence-based treatment recommendations for older people, and the fact that most drugs are tested (pre-marketing studies) in younger individuals, makes the situation even more difficult. Nevertheless, medications are the most commonly used treatment modality for older patients; emphasising the need to assess and improve the quality of drug therapy. During the last years, patient-centered clinical pharmacist services have gradually been implemented in Norwegian hospitals. In contrast, similar services have not been put into practice in primary health care.

This thesis aims to assess the quality of drug utilization among older people in two primary care settings, i.e. HNS and NHs. In the introduction, HNS and NHs in Norwegian primary health care system are outlined. Then, a short description of drug utilization and quality of drug prescribing in older patients is provided. Finally, clinical pharmacist services and pharmacists' involvement in multidisciplinary teams are briefly described. Two comprehensive quantitative studies and one supplementary qualitative study have been performed. The first study examines drug use by means of explicit prescribing quality indicators. The second study investigates drug-related problems in NH patients based on systematic multidisciplinary medication reviews. The third study explores physicians' and nurses' experiences of collaborating with pharmacists.

The health care system for older patients

Figure 1. Population projection for Norway [4]
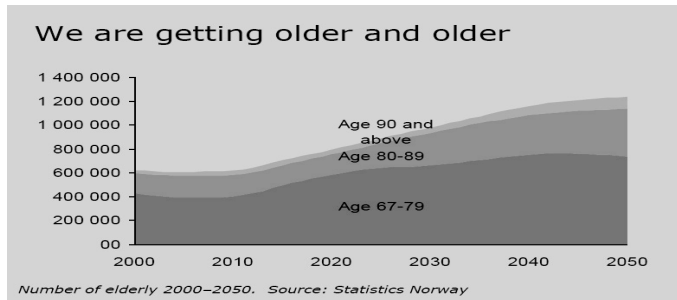
(Reprinted with permission)

Increased life expectancy combined with large birth cohorts following World War II until 1975, is leading to increasing numbers and proportions of older people in high income countries in years to come, Figure 1. Life expectancy has increased continuously for the last two hundred years. Today's newborn girls and boys have an average life expectancy of 83 and 79 years, respectively [4]. Population projections for the year 2060 estimate about 1.5 million people ≥67 years old compared to 625 000 in 2010 [4]. In addition, the proportion of elderly ≥80 years increases as well (Figure 1). The aging population represents a major challenge to our country's health care system. In the present work older people are defined as those ≥65 years.

Ageing is accompanied by age-related changes and health problems. Functional decline increases older peoples' need for health care services. Both somatic diseases such as cardiovascular and musculoskeletal morbidity and cancer, as well as mental disorders such as dementia, depressions and anxiety are prevalent [4-6]; illustrating a range of complex illnesses among older patients.

The municipalities in Norway are obliged by law to provide health care services to their inhabitants with essential needs. The services comprise two levels; HNS is provided to people living in their own home or in residential care facilities; institutionalized services comprise people living in NHs and homes for the aged. From 1996 to 2010, the capacity in homes for the aged has been reduced from 9 500 to 1 600 places [4]. A politically intended strengthening of HNS and reduction of the capacity

in homes for the aged, has been leading to that older people reside at home longer than before. An application for HNS or NH placement is put forward to the local health authorities, usually by patients' relatives. The municipalities decide on allocation of HNS, and on temporary or permanent placement in an institution. Definite inclusion criteria do not exist. The HNS and NH settings are devoted attention in this thesis.

Home nursing service

HNS provide professional health care to patients with widely varying needs. The majority of users are ≥65 years, with a range of somatic and mental disorders and symptoms. The number of older persons receiving HNS approximated 130 000 in 2010 [4]. During the last two decades the demand for this service has increased, in particular among individuals younger than 65 years [7]. The annually net increase during the last years has been estimated to 8-9% [6].

HNS are organized and financed by the municipalities, and carried out by licensed nurses, auxiliary nurses and care-workers. In addition, unskilled personnel account for a significant proportion of the staff, ranging from 21% during weekdays to 34% at weekends [8]. HNS comprise tasks such as medication management including collecting prescriptions at local pharmacies, filling of one-week drug dispensers, measuring blood glucose, injection of insulin, pain management (i.e. pain pump), and wound care. Some municipalities also offer physical therapy or occupational therapy, for instance during rehabilitation after stroke or surgery.

Approximately 99% of the Norwegian population is contracted to a specific physician through the Regular General Practitioners (GP) Scheme that was implemented in 2001. GPs are responsible for older patients' medical assessment and treatment, including drug therapy and referral to specialist health care. Prescriptions are usually dispensed for 3-months supply from local pharmacies and/or delivered as multi-dose dispensed drugs (MDD). Although the municipalities are required to facilitate multidisciplinary collaboration between GPs and HNS, it is rarely put into the system.

Nursing homes

In Norway, eligible patients for NH placements are those with severe functional impairment and/or in need of more continuous health care services than offered by the HNS, i.e. 24-hour nursing care. NHs are intended to constitute both a home and a health care institution at the same time. The mean age of NH patients is on average 84 years, and more than 70% are women [9]. Mean life expectancy on NH admittance is shorter than 2 years, and approximately 40% of all deaths occur in this setting [10], similar to all-cause mortality in hospitals [4].

In 2010, the almost 900 NHs had a total capacity of 41 000 beds [4], of which 80% were long-term care beds in regular wards or in special care units for patients with dementia. The remaining 20% comprised respite care, rehabilitation or palliative care. About 220 000 people were 80 years or older; NH coverage for this population in Norway was about 19% [4], exceeding proportions in Sweden (16%), Denmark (13%) and The Netherlands (9%). The Norwegian Government aims to increase the capacity by establishing 12 000 new places by 2015 [11].

NHs in Norway are heterogeneous with regard to size, ward types and services provided. These differences exist as the municipalities vary in terms of size (Oslo has 600 000 inhabitants, Røst in Lofoten about 605), population demographics and health care needs [4]. However, most patients entering the NHs have severe physical and/or mental impairment, and are in need of care around the clock over a shorter or longer period of time.

Known predictors for institutionalization are dementia in persons living alone, behavioural and psychological symptoms of dementia, and patient carers with mental problems [12]. About 80% of NH patients suffer from moderate to severe dementia, and 72% have clinically significant neuropsychiatric symptoms [9]. Another challenge for NHs is that the number of patients with special care needs such as dementia care or palliative care outweighs the present capacity of specialized health care services. Nursing care is normally provided by licensed nurses (20% of nursing staff), auxiliary nurses, care workers and unskilled personnel. Other health care professions such as physiotherapists and occupational therapists are scarce in NHs [10].

Medical care is most commonly provided by part-time contracted GPs who are working in a NH one or two days weekly. Larger institutions in bigger cities may employ physicians full-time. The physicians are responsible of diagnostics and treatment including drug therapy, while nursing staff is setting the agenda. Normally, initiation and adjustment of drug therapy is discussed between physicians and nurses at regular patient-centred case conferences. Electronic patient record systems with good functionality are not yet implemented in Norwegian NHs. Drugs are requisitioned and received directly from pharmaceutical wholesalers or pharmacies, either in separate packages or as MDD. Only licensed nurses are allowed to conduct drug dispensing, usually into one-week pill dispenser, while auxiliary nurses and care workers may administer drugs to the patients. Pharmacists have until now not been directly involved in drug therapy in the NH multidisciplinary team [10, 13].

Drug use in older patients

Older persons constitute about 15% of the total Norwegian population, and are responsible for almost 50% of the total prescribed drug consumption [14]. Drug therapy is a cornerstone of medical care for older patients with complex health problems and severe functional and/or mental impairment.

A multicenter study in eight European countries including older patients receiving home care services reported that more than half of the patients used six or more drugs [15]. Another study comprising 786 older patients receiving HNS identified a mean of eight drugs per patient, while 40% of the patients used nine or more drugs concomitantly [16]. Comparable drug utilization studies from Norwegian HNS are sparse.

Table 1. Average regular drug use among older patients in nursing homes

Author	Year	Country	N	Average number of regular drugs used
Ruths [17]	2003	Norway	1 354	5.0
Snowdon [18]	2006	Australia	3 054	5.4
Bergman [19]	2007	Sweden	7 904	9.0
Rytter [20]	2007	Norway	1 053	7.0
Hosia-Randell [21]	2008	Finland	1 987	7.9
Olsson [22]	2010	Sweden	2 938	8.5

The five most frequently used drug groups in Norwegian NHs, classified according to the Anatomical Therapeutic Chemical (ATC) system [23], were laxatives (60% of the patients), diuretics (34%), antidepressants (31%), analgesics (28%) and acetylsalicylic acid (23%) [24]. Drug utilization studies of older patients in NHs during the last ten years suggest an increase in number of regular drugs prescribed, Table 1 [17-22, 25, 26]. Not included in these numbers are *pro re nata* (p.r.n.) medication, also referred to 'as required' or 'as needed' medications, i.e. drugs prescribed on each patient's drug list, or drugs given according to NHs' individual guidelines for use of p.r.n. medications. Two Scandinavian studies report a mean of 2.1-2.5 p.r.n. medications prescribed per patient [20, 22]. According to a Norwegian study the most frequently prescribed p.r.n. medications were: paracetamol, metoclopramide, zopiclone, glyceryl trinitrate and diazepam [27]. NHs' individual p.r.n. guidelines, issued by the NH physician to nursing staff recommend drugs for treatment of minor already diagnosed medical problems such as pain, nausea, sleeping disorders, angina or constipation, when the physician is not available. Concerns regarding the quality of p.r.n. administration guidelines have been put forward. Guidelines of low quality impede the nurses' decision process whether to give drugs or not, and may subsequently jeopardize patient safety [27].

Polypharmacy addresses the use of multiple drugs by one patient, normally suffering from more than one illness. The term is often associated with drug use in older persons [28]. Several definitions exist: i] concomitant use of five or more drugs [29], although some NH studies have set a cut off of nine drugs [30, 31], ii] unnecessary drug use, i.e. use of more medications than clinically indicated [32, 33],

or iii] the use of at least one inappropriate drug [34]. To avoid confusion, the neutral term 'multiple drug use' is applied throughout this thesis.

Challenges for drug treatment

There are many challenges at the patient level regarding the quality of drug prescribing and drug use [35]. Age-related changes, inadequate prescribing and incorrect use are all considered to reduce overall quality of drug treatment. Physiological alterations lead to pharmacological change and in particular affect drugs' pharmacokinetic properties. While age seldom influences drug absorption, the distribution, metabolism and elimination are often affected and require dose alterations [36]. In addition, changed body composition, e.g. increased fat:water ratio, potentially results in accumulation of lipid-soluble drugs. The annually 1% decline in renal function from young adult age reduces the elimination of water-soluble drugs, underlining the importance of monitoring renal function. Simultaneously, pharmacodynamic alterations, such as up or down regulation of receptors, modified receptor-sensitivity and reduced homeostatic mechanisms affect older patients. In consequence, enhanced drug effects pose older patients at increased risk of ADR such as constipation, falls, fatigue and confusion [37, 38].

At the organization level, challenges include discrepancies between drug lists kept by patients' regular GP and HNS [39], and sub-optimal flow of information between hospitals and primary health care [40, 41], due to sub-optimal communication and collaboration between different health care levels [42]. In addition, problems with self-medication by either using over-the-counter medications [43], or non- compliance of various reasons [44], are prevalent. Non-compliance may lead to reduced therapeutic outcome or adverse drug effects, which are reported to cause 10% of hospital admissions. However, it should be noted that old age is not necessarily associated with poor compliance [45].

Drug-drug interactions

Multiple drug use is associated with increased risk of drug-drug interactions (DDIs) [46-48]. A DDI can be defined as; "*The action of a drug that may affect the activity, metabolism, or toxicity of another drug*" [49]. DDIs can be divided into pharmacodynamic interactions; two drugs competing for the same target receptor, or pharmacokinetic interactions; one drug altering the metabolism of another [50], thus lowering or increasing drug effects. However, the clinical consequences of DDIs are often difficult to predict.

Studies report 25% prevalence of DDIs in older NH patients [31] and 46% in geriatric outpatients [51]. Comparable statistics for HNS could not be identified. Drugs commonly involved in DDIs include diuretics, NSAIDs, ACE-inhibitors, oral anti-diabetics, calcium-channel blockers, anticoagulants and beta-blockers [52]. Multiple drug use combined with age-related physiological changes put older patients at increased risk of DDIs. The probability of experiencing DDIs was more than five times higher in patients receiving five or more regular drugs, compared to those using less than three drugs concurrently [53]. Therefore, older persons who use multiple drugs should be carefully monitored [52].

There has been progress in terms of identifying DDIs from patients' drug records. Moving from using works of reference, like the book 'Stockley's Drug Interactions' [50], to online web-based tools [50, 54, 55], or works of references implemented in the computer software at GPs' offices or pharmacies considerably ease the task. This development allows a systematic approach to avoid preventable DDIs. In Norway, GPs are responsible for the total overview of their patients' drug use; most GPs and all pharmacies have implemented a DDI-checker into their electronic patient medical record system. Patients can freely choose which pharmacy they want to dispense their prescription drugs, however transfer of patient or drug information between pharmacies is not allowed. For patients to gain full benefit of the systematic DDI-checker, they must be regular customers. In most NHs, however, electronic patient record systems with integrated tools to check for DDIs are not available. Although the functionalities of such databases differ, they are usually convenient in use. Still, it is important to be aware of the limitations of DDI-checkers. For instance,

in the Norwegian 'Drug information database' (DRUID) [54], in general only previously documented interactions appear; meaning that suspected interactions based on similarities such as metabolism are not included [56]. Neither will the co-prescribing of two generic drugs such as Furix® and Diural® (furosemide), nor two chemically related substances such as Furix® and Burinex® (bumetanide). Therefore, basic pharmacological knowledge and skills are important to maintain, both for physicians and pharmacists. A strategy to prevent DDIs is to perform a DDI-check whenever new drugs are prescribed or released, however, independent critical thinking is also necessary [56].

Multi-dose dispensed drugs

In 2002 the Norwegian Board of Health Supervision reported problems in the medication management in NHs and HNS and depicted that about 12% of the errors was related to the dispensing phase and 38% to the administering phase [57]. In attempt to increase the quality of drug dispensing and administering, multidose dispensing drug (MDD) systems were implemented. In 2009, approximately 35 000 people in Norway received their drugs as MDD [58], mostly older persons receiving HNS or living in NHs. The MDD system is an automated system, dispensing only per oral solid drug formulations (tablets and capsules) by and large prescribed for regular use. Consequently, other drug formulations and p.r.n. medications are not dispensed as MDD; a second dispensing system is needed for managing p.r.n. medications, injectables, inhalators, ointments and mixtures, as well as drugs that needs close monitoring such as antibiotics and warfarin.

The implementation of MDD was intended to increase overall quality of the drug administration process; hereby reducing nurses' workload for drug dispensing and liberating time for patient care, reducing discharge of drugs from stocks, and maybe most importantly preventing dispensing errors [59]. On the other hand, questions regarding how MDD affects overall prescribing quality, the impact of excluding nurses from drug dispensing, and dispensing quality for drugs not comprised by the MDD system. One study suggests that MDD users are more prone to receive

inappropriate drugs [60]. In addition, discrepancies have been found between GPs' and HNS' MDD lists [61].

Quality concerns regarding drug treatment in HNS and NHs are similar. Compared to HNS, coordination of services is probably better in NHs due to the organizational framework. In 2008-2010 the Norwegian Board of Health Supervision performed a system audit of drug treatment in NHs, and concluded that patient safety may be threatened. Deviations were found in 51 of the 67 inspected NHs. The identified problems included physician time constraints regarding follow up of patients' drug treatment, lack of time and competence among nursing personnel to observe and report drug effects and ADRs, and NHs management lacking overview of risk factors related to drug treatment [62]. Provided the impending increase in institutional capacity [11], it is important to implement quality systems to support health professionals responsible of drug treatment in NHs.

Drug prescribing quality for older patients

Pharmacoepidemiology consist of the words pharmacology and epidemiology and deals with '*the use and effects of drugs in a large number of persons*' [63]. Pharmacoepidemiological methods are suitable to measure the quantity of drug use in populations and how this quantity compares between populations [64]. Drug databases are often sources for such studies, like for instance the Norwegian prescription database [65]. Different study designs can be used to assess drug utilization and to improve the quality of drug prescribing in older persons.

Descriptive studies are conducted to map drug use in populations according to number and proportion of users, and distribution regarding age, gender, geography, and other determinants. Such studies are often performed at a particular point of time (cross-sectional) or longitudinal (prospective or retrospective). For instance, the design can be used to describe the prevalence of potentially inappropriate medications (PIMs) [66].

Analytical studies assess how drug utilization is associated with factors like demography, geography, disease or other drugs. Analytical studies can either be observational (e.g. case-control or cohorts) or interventional (e.g. randomised control trials). For instance, interventional studies are conducted to investigate the effect of certain drugs on a certain disease, or the consequences of educational programmes on prescribing quality. Studies may be conducted with control groups, or with before-after design. The latter design has previously been used to evaluate the effects of systematic medication reviews [67].

Qualitative methods based on interviews explore aspects that are difficult, or even impossible to obtain quantitatively. In particular, the method is useful to explore beliefs, experiences and feelings [68]. Morgan emphasizes the importance of combining quantitative and qualitative research as it follows the principle of complementarity. However, one needs to decide in what sequence the methods should be applied [69]. To improve quality of drug treatment in older patients, qualitative methods like focus group interviews or individual interviews may help to explore interactions between e.g. health professions [70]. The method may also be applied on patients and their relatives to explore their thoughts and experiences regarding drug treatment and high compliance.

Prescribing quality indicators

What constitutes good prescribing? According to Barber, at least four different domains need to be judged [71]. First, one has to respect the patients' autonomy and choice. Second, one should seek to maximize effectiveness of drug therapy. Third, the risk of treatment must be minimized, and fourth, total costs should be kept low, both for patients and society.

Prescribing quality indicators (PQI) may be defined as follows; "*A measurable element of prescribing for which there is evidence or consensus that it can be used to assess the quality, and hence change in the quality, of treatment provided*" [72]. It is normal to refer to indicators as implicit; which are judgement based, or explicit; which are rigid standard indicators. The choice of indicator depends on the purpose. For

instance, when evaluating specific medicines or group of medicines, explicit criteria can be useful [24].

Prescribing is a complicated task. When dealing with PQI the terms "appropriate" and "inappropriate" are often used to describe the quality of prescribing. There exists no rationale behind choosing one over the other, but some prefer "appropriate" because the term implies achievable quality in practice [73]. Inappropriate prescribing, on the other hand, may potentially be easier to detect, because violating only one of the four domains may trigger a result.

Different indicators to assess the quality of drug therapy have been elaborated; a selection is presented in Table 2. Most indicators' main purpose is to examine the prevalence of PIMs used by older patients. However, the Screening Tool to Alert doctors to the Right Treatment (START) is intended to systematically identify omitted drugs in clinical practice [74], while the Australian Prescribing Indicators Tool is more comprehensive in terms of medications considered inappropriate, recommendations for treatment of certain diseases, drugs requiring monitoring or those causing DDIs [75]. When selecting tools to assess the quality of drug prescribing, one should consider availability of clinical information, convenience of use, as well as clinical relevance for the studied population [76].

Explicit criteria can be used to identify PIMs. An advantage of such criteria is that they are easy to apply on large datasets, like the Norwegian prescription database [65]. However, a major drawback is that they seldom take into account clinical information such as diseases [73]. Another disadvantage is that they cannot automatically be transferred to other countries, as indicators' applicability relies on drug therapy traditions and correspondence with national drug formularies. This is also the main reason for developing national indicators [75, 77]. In later years, however, it may look like that national and international guidelines are merging [77-80]. Furthermore, explicit criteria are usually developed from expert opinions, using the modified Delphi method [81], and hence not evidence based. Last, maintenance of the criteria must be performed regularly to avoid conflicts with current treatment guidelines [82].

The Beers list is the most frequently used criteria set to assess PIMs worldwide, but for reasons stated above, national indicators have been developed in several countries during the last decade, Table 2. Studies encountering PIMs based on Beers criteria report prevalence among older patient to range from 18 to 50% in NH [19, 21, 22, 24, 81, 83-87], and from 20 to 34% in HNS [15, 16, 88-91]. Two Norwegian studies based on patients' own medication lists report PIMs in 14-18% of older patients in general practices [92, 93].

Table 2. Explicit prescribing quality indicators (PQI)

Author	Year (revision)	Country	Name PQI	Description
Beers [66, 94, 95]	1991 (1997, 2003)	USA	Beers list	Target population aged ≥65. 68 criteria; 48 single drugs; 20 drug-disease combinations.
McLeod [96]	1997	Canada	McLeods list	Target population: not specified. 38 criteria in four categorises; cardiovascular diseases, psychotropics, NSAIDs/other analgesics, miscellaneous drugs.
Naugler [97]	2000	Canada	IPET	Target population aged ≥70. 14 criteria; 2 drug specific, 12 drug-disease combinations.
Fastbom, Schmidt* [98]	2010	Sweden	Swedish National Board of Welfares' indicators	Target population aged ≥65 (75). 20 criteria; 9 drug specific criteria, 11 diagnosis-specific criteria.
Laroche [99]	2007	France	French consensus list	Target population aged ≥75. 34 criteria; 29 single drugs/classes; 5 criteria regarding specific medical conditions.
Barry [74]	2007	Ireland	START	Target population aged ≥65. 22 criteria of drugs indicated for use.
Gallagher [100]	2008	Ireland	STOPP	Target population aged ≥65. 65 different criteria divided in 10 major criteria; 7 organ-specific. 2 of drugs regarding side effects; 1 for drug duplication.
Basger [75]	2008	Australia	Australian Prescribing Indicators Tool	Target population aged >65. 48 drug-disease specific criteria.
Rognstad [77]	2009	Norway	NORGEP	Target population aged ≥70. 36 criteria; 21 single drugs. 15 drug combinations. Recommended by authors for use in general practice

* Project leaders. IPET= Improving Prescribing in the Elderly Tool, START=Screening Tool to Alert doctors to the Right Treatment, STOPP=Screening Tool of Older Persons' potentially inappropriate Prescriptions, NORGEP=The Norwegian General Practice criteria, NSAIDs=Non-Steroidal Anti-Inflammatory Drugs.

Although comparison should be done cautiously due to differences in used indicators and drug-markets between countries, the proportion of PIMs appears to be higher in older Americans than in older Europeans, Table 3. Furthermore, drugs most commonly denoted as PIMs vary according to the criteria set used and the population under

investigation. Predictors for receiving PIMs comprise female gender, 'younger' older age (66-70 years) and multiple drug use [101]. A study advocates that patients with highest disease burden who are eligible for NH placement but who receive HNS, are at highest risk of being prescribed PIMs, compared to other community-dwelling older patients or to patients in NHs [102]. The high prevalence of PIMs in different settings emphasizes the importance of focusing on prescribing quality in both HNS and NHs.

Table 3. Potentially inappropriate medication (PIMs) use in older patients

Author	Year	Country	Study participants	Setting	Criteria	Proportion (%) of patients using PIMs
Strand [92]	1999	Norway	Not reported	GP	Own list*	14
Dhall [85]	2002	USA	44 562	NH	Beers modified*	33
Nygaard [24]	2003	Norway	1 024	NH	Beers modified*	25
Lau [83]	2004	USA	3 372	NH	Beers	50
Roth [90]	2005	USA	100	HNS*	Beers	34
Fialova [15]	2005	Europe	2 707	HNS	Beers* McLeod	20
Perri [91]	2005	USA	1 117	NH	Beers	47
Niwata [87]	2006	Japan	1 669	NH	Beers	18
Cannon [16]	2006	USA	786	HNS	Beers	31
Lapane [86]	2007	USA	164 889	NH	Beers*	40
Brekke [93]	2008	Norway	85 836	GP	13 explicit indicators	18
Hosia-Randell [21]	2008	Finland	1 987	NH	Beers	35
Ryan [103]	2009	Ireland	1 329	GP	Beers STOPP	18 21
Olsson [22]	2010	Sweden	3 705	NH and SCUD	Swedish National Board of Welfares' indicators	*
Kölzsch [84]	2011	Germany	8 685	NH	French consensus list	22

*See original article for further details. NH=nursing home, HNS=home nursing service, GP=General practice. SCUD=Special Care Units for Dementia.

Drug-related problems

A range of 'synonymous' concepts exist for DRPs and include drug therapy problem, medication error, medication related problem, medication therapy problem, treatment related problem, therapy related problem and pharmaceutical care issue [104]. Different classification systems have been developed to identify, categorise and resolve DRPs [105-107]. In 2007 a Norwegian classification system for assessing DRPs was published [107]. This classification tool has a hierarchical structure, with six main categories (see Table 4), and twelve sub-categories. In this thesis a DRP is defined, in accordance to Pharmaceutical Care Network Europe, as *"an event or*

circumstance involving drug therapy that actually or potentially interferes with desired health outcomes" [105].

Table 4. Classification of drug-related problems (DRPs) [107]

Main category	Definitions
Drug choice	One or more drugs are missing according to established national/international guidelines. Deviations from guidelines that are based on the patient's individual treatment goals and risk factors are not considered to be DRPs.
	A drug that is seen as unnecessary if the indication is no longer present, with lack of discontinuation or double prescription of two or more drugs from the same therapeutic group
	Not given reason for deviation from concordance between drug and diagnosis/indication or absolute/relative contraindication because of for example age or co-morbidity. Deviations that are based on the patient's individual treatment goal and risk factors are not considered to be DRPs.
Dose	Suboptimal dosing (including dosing time and formulation) according to established national/international guidelines. Deviations that are based on the patient's individual treatment goal and risk factors are not considered to be DRPs.
Adverse drug reaction	Any noxious, unintended, and undesired effect of a drug, which occurs at doses in humans for prophylaxis, diagnosis, or therapy (WHO)
Interaction	An interaction is occurring when the effect of a drug is changed by the presence of another drug, food, drink or some environmental chemical agent. Drug combinations with intended overall effect are not considered to be DRPs.
Drug use	Patients' real drug use deviate from the doctor's prescription with respect to type of drug, dose or scheme. It is a prerequisite that prescriptions are based on a common understanding (concordance) between prescriber and patient (exception: patient with dementia, emergency situation etc.) Problems with logistics are not considered to be DRPs.
Other	Monitoring with respect to effect and toxicity of drugs is not done or does not adhere to guidelines.
	In general therapy discussions that include several problems and do not belong in any other category.

DRPs can be identified by performing medication reviews at an individual patient level. The performance and comprehensiveness of the review relies on several factors including available clinical information, and health personnel's knowledge and skills. Performed systematically in accordance to the DRP classification, the task is time consuming and resource demanding. Different health disciplines have conducted medication review studies including physicians [108], pharmacists [109] and nurses [110].

The first Norwegian study that examined DRPs in NHs revealed problems in 76% of the patients, with an average of 2.5 DRPs per patient [17]. Other studies have reported 4.6 DRPs in older patients consulted in general practices [111], and 2.5-4.0 DRPs in older NH patients [17, 26, 30, 113], Table 5.

Table 5. Drug-related problems (DRPs) in older patients

Author	Year	Country	Study participants	Setting	DRPs per patient	Proportion (%) of patients With DRPs
Ruths [17]	2003	Norway	1 354	NH	2.5	77
Pit [111]	2007	Australia	452	GP	-	88
Finkers [30]	2007	The Netherlands	91	NH	3.5	96
Stafford [112]	2009	Australia	234	RC	4.6	-
Kersten [113]	2009	Norway	48	NH	4.0	98
Davidsson [26]	2011	Norway	93	NH	2.5	88
Nishtala [114]	2011	Australia	500	RC	2.9	96

NH=Nursing homes, GP=general practice, RC=Home or residential care.

Drugs for treatment of the alimentary, cardiovascular and nervous system are linked to the majority of DRPs [114, 115]. Recently two small Norwegian studies have addressed DRPs in NHs patients [26, 113]. The majority of problems concerned unnecessary drug treatment [113], which in about half of the cases led to drug discontinuation [26].

Clinical pharmacists and multidisciplinary collaboration

Clinical pharmacy is according to the European Society of Clinical Pharmacy defined as; "*a health specialty, which describes the activities and services of the clinical pharmacist to develop and promote the rational and appropriate use of medicinal products and devices. Clinical pharmacy includes all the services performed by pharmacists practising in hospitals, community pharmacies, nursing homes, home-based care services, clinics and any other setting where medicines are prescribed and used*" [116]. According to this definition, clinical pharmacy has a wide scope in various health care settings. Nevertheless, clinical pharmacy is by many considered to be in its modest beginning in Norway. The first program 'experience-based master's degree in clinical pharmacy' was established in 2009 at the University of Oslo [117]. The late onset of clinical pharmacy in Norway can be explained by the fact that the only education institution for masters in pharmacy until 1994, the University of Oslo, focused mostly on medicinal chemistry and pharmaceutical sciences. Another reason is that pharmacists were defined as health personnel as late as in 1999 [118]. Until then opportunities to act alongside other health personnel in different settings were limited. Pharmacists with responsibility to supervise and monitor drug stocks at institutions

were usually not involved in drug therapy decisions or did not participate in multidisciplinary teams.

Twenty years ago Hepler and Strand outlined the re-professionalization and the importance for pharmacists to "*adopt patient-centred pharmaceutical care as their philosophy of practice*" [119]. Since then the professional role and opportunity to collaborate with other health professions has changed considerably in countries like the U.S., Australia, England, Scotland, The Netherlands, but also in Norway. Although in its infancy, pharmacists work alongside other health professionals, most at hospitals departments, but also in NHs. To the author's knowledge, multidisciplinary collaboration including pharmacists in HNS has not yet been put into the system.

In 2006 the impact of clinical pharmacists in hospital settings has been evaluated in a systematic review. The review concluded that clinical pharmacists improved care, with no evidence of harm [120]. Almost at the same time, another study evaluated the effect of pharmacist-led medication review on hospital admission, mortality and number of drugs prescribed in older patients. This systematic review and meta-analysis concluded that pharmacists had no effect on the outcomes, except from contributing to a slight decrease in number of drugs prescribed [121].

In Norway the Government White Paper No. 18, 2004-2005 '*On course towards more correct use of medicine*' emphasized multidisciplinary collaboration with pharmacists as one way to achieve quality improvement of older patients' drug therapy [122]. Combined with experience from previous research [17, 123], it is important to determine whether pharmacists' knowledge and skills can be utilized in multidisciplinary teams to identify, prevent and resolve DRPs in older patients outside of hospitals.

The Norwegian Knowledge Centre for the Health Services recently evaluated randomized controlled trials aiming to reduce inappropriate drug use in NH [124]. Academic detailing, various educational and teaching initiatives, and drug utilization reviews performed by pharmacists or GPs have been shown to reduce prescribing of psychotropic and other drugs. However, most studies were small and of poor quality [124]. Nonetheless, the report highlighted the importance of further research on these initiatives.

Motivation for the studies and the author's preconceptions

In Norway, only a few studies have investigated the pharmacists' role with regard to prevent inappropriate prescribing and to increase the overall quality of drug use for older patients. At the moment, pharmacist services are growing in NHs, which actualizes research on this topic. Drug utilization studies investigating the quality of drug prescribing in HNS are in general lacking. To my knowledge, studies comparing medication use and prescribing quality in disease-burdened patients in HNS and NHs have not been conducted. With increasing numbers of older persons, and as drug consumption is increasing considerably during the last decade (Table 1), it is important to develop and implement systems that can improve and maintain prescribing quality for these large groups of frail and old patients.

During my undergraduate study period, I often reflected on the possibilities to work clinically with drug-related issues. The pharmacy curricula at the University of Tromsø inspired me, and I especially remember visits to hospital wards and assessments of patients' drug regimens. The undergraduate program including patient stories and case-based learning encourage a growing interest to work multidisciplinary with drug-related issues. By chance during my first job as a consultant pharmacist (pharmacist supervision) in Bergen municipality health care service, I met two enthusiastic researchers (a physician and a pharmacist) who had experience with multidisciplinary collaboration between pharmacists and physicians.

At the same time, I often wondered at what level in the health care system clinical pharmacists could contribute. I developed an interest in the field of drug use in older patients, in particular in primary care. Employed by the municipality as a consultant pharmacist, I experienced that nurses and physicians whom I had to cooperate with in order to improve drug treatment quality perceived me as something entirely different, almost as an inspector or a 'police authority'. This experience aroused a curiosity as to how nurses and physicians viewed multidisciplinary collaboration with pharmacists as well as changes in the distribution of tasks.

AIMS OF THE STUDIES

The aim of this research was to examine and improve prescribing quality in older patients receiving HNS or living in NHs. This has been achieved by conducting two comprehensive quantitative studies, and one supplementary qualitative study. The three sub-studies had the following aims:

Paper I

To examine the quality of drug prescribing for older persons in nursing homes and home nursing services based on explicit prescribing quality indicators.

Paper II

To describe an innovative team intervention to identify and resolve drug-related problems in Norwegian nursing homes.

Paper III

To explore how physicians and nurses working in nursing homes and hospitals experience multidisciplinary collaboration with pharmacists to optimise drug therapy in older patients.

MATERIAL AND METHODS

Design, setting and participants

Table 6. Design, setting and study participants

Paper	Design	Setting	Population/Informants
I	Analytical Cross-sectional study; MDD database	Nursing homes and home nursing services	11 254 patients
II	Descriptive intervention study	Three nursing homes	142 patients
III	Focus group and individual interviews	Nursing homes and Hospitals	12 informants; 4 physicians and 8 nurses

Paper I

Drug databases at suppliers (wholesalers) of MDDs in Norway comprise drug use information on large numbers of HNS and NH patients. One of the main suppliers was contacted and agreed to provide anonymous data for a descriptive cross-sectional study. Data extraction was performed on September 9, 2009. All patients ≥65 years were included. The following variables were obtained: age, gender, care setting (HNS or NH), drug name, strength, formulation, dosage schedule, regular or p.r.n. use, and number of days of dispensed medicines. All drugs were coded according to WHO's Anatomical Therapeutic Chemical (ATC) classification system [23].

Because of lack of clinical information, patients' medication lists were screened by means of Norwegian explicit quality indicators independent of indications; NORGEP [77] was used to identify PIMs, and DRUID [54] for detecting DDIs, respectively. The prevalence of drugs use, PIMs, and DDIs was compared between care setting (HNS or NH).

Paper II

A descriptive intervention study was conducted. Eligible study participants were patients ≥65 years old in three medium-sized (60-75 beds) NHs in Bergen, Norway, using at least one regular drug.

A pilot study comprising 15 patients was conducted at one NH to test and adjust study procedures. Prior to, and during enrolment of study participants, pharmacists and the research group met to discuss and clarify ambiguities regarding study procedures. Data collection was conducted by three pharmacists from February to July 2006. Nurses in charge measured patients' body weight, blood pressure and pulse, while the pharmacists recorded the following data: age, gender, diagnoses, medications (time of initial prescribing, brand or generic name, formulation, strength, dosage time, and regular or p.r.n. medication), and relevant and available laboratory results. Creatinine values recorded in medical charts were entered into the web-based calculator from the National Kidney Foundation[TM] [125] for calculating glomerulus filtration rates.

Pharmacists performed individual comprehensive medication reviews according to a Norwegian classification tool [107], taking into account the gathered information, each patient's clinical characteristics, the Norwegian Drug Formulary [126], the Norwegian drug and therapeutic formulary for health personnel [127], DRUID [54], and the NHs' guidelines for drug handling. The pharmacists identified potential DRPs and classified them according to the classification tool.

Multidisciplinary case conferences

The pharmacists presented the identified potential DRPs to the patients' physician and nurse at the weekly patient-centred case conferences. The clinical team discussed the DRPs until consensus was reached: I) team agreed on DRP identified by the pharmacist, II) team disagreed, III) team agreed of a DRP being identified, but not with the classification of the DRP, and IV) an up till then undiscovered DRP was identified during the multidisciplinary team discussion. After agreement on DRPs classification, the multidisciplinary team discussed relevant actions to resolve acknowledged DRPs. All team members could recommend strategies to achieve treatment improvement. The agreed strategy was recorded by the pharmacist. In cases

of ambiguities, the physician had the final word. Pharmacists examined whether planned interventions were completed by re-visiting the NHs after three weeks. The total number of drugs used was recorded before and after the intervention.

Drugs were coded according to the ATC-classification system [23]. Data was analysed with regard to the following outcome measures: DRPs identified by pharmacists; DRPs acknowledged, altered, refused or added at case conferences; medications involved in DRPs; interventions planned and executed.

Paper III

Focus group interview and individual interviews are useful for examining peoples' knowledge and experience [128-130]. We applied these two methods to gain experience regarding how physicians and nurses had experienced multidisciplinary collaboration with pharmacists. NH informants were selected from study sites described in *Paper II*. All physicians (three men, one woman) and a purposeful sample of six nurses (all women; two from each nursing home) were invited to take part in intra-professional focus-group interviews. One of the physicians did not want to participate in the focus-group. Furthermore, as one of the remaining physicians was prevented from meeting as scheduled, only two physicians (a man and a woman) were interviewed for 2 hours. Later, the third physician was interviewed at his office for an hour. The nurses' focus-group interview lasted for 2 hours; one nurse failed to attend as planned.

To contrast findings from NHs, informants for individual interviews were recruited from two different hospitals by inviting two chief-physicians, from the rheumatology and geriatric departments. Both hospitals were known to include pharmacists in the multidisciplinary healthcare team. The purposeful sampling intended to include informants who had experienced multidisciplinary collaboration with pharmacists over a period of time. Using a semi-structured interview guide an experienced moderator with the presence of a secretary (myself), interviewed first the NH physicians (n=2) and then the NH nurses (n=5). Later, the author of this thesis individually interviewed another NH physician, and the hospital informants, i.e. three nurses and one physician. The semi-structured interview guide developed for the

purpose covered the following topics: i] personal experience with pharmacist collaboration, ii] the impact of the collaboration and iii] the structure of the collaboration. All interviews were audio-taped and transcribed (modified verbatim). The analysis was performed in accordance with the principles of systematic text condensation [131].

Statistical analysis (Paper I and Paper II)

Student's t-test was applied to compare means for continuous data (age, number of drugs used, PIMs, DDIs). Chi-square test was applied to compare categorical data (gender, settings). Correlation between age, number of drugs used, PIMs and DDIs were examined using Pearsons *r* (one-tailed), **Paper I**. Logistic regression was performed to examine the impact of care setting (NH or HNS) on exposure to selected drug groups, PIMs or DDIs, adjusting for patients' age and gender and number of drugs used. Differences were presented as OR with 95% confidence interval (CI), **Paper I**. *p*-values < .05 were considered statistically significant. The statistical package SPSS/PASW version 14/18 was used for data analysis.

Qualitative analysis (Paper III)

To facilitate the analysis of the transcribed interviews we used QSR NVivo version 8. The analysis process transformed interview material to systematized experience and knowledge. As premise for the analysis procedure we used the objective of the study, clarified our self-known presuppositions in the field and made an active choice of theory basis [132, 133]. These premises clarified, the material (transcripts) was read by all the authors, searching for an understanding of the data within our frame of reference. Thus we identified an initial set of themes and consented on the following: resources, quality changes, awareness and change of behaviour, professional knowledge, and multidisciplinary collaboration. The material was searched from the perspective of these themes, selecting text elements (units of meaning) that specifically represented them. These units of meaning were de-contextualized and analogous units were grouped under abstracted headings and expressed in generalized descriptions. Using these categories as a framework, we searched all material for additional

perspectives on the core items. These were: i] introduction of a new team member, ii] consequences for the collaborating health personnel and their patients and iii] perspectives on collaboration development.

Ethics and approvals

All three studies were presented to the Regional Committee for Medical Research of Western Norway; no objections were put forward. In addition, the Norwegian Social Science Data Services gave their approval. The required exemption of professional secrecy was given by the Norwegian Data Inspectorate and the Norwegian Directorate for Health and Social Affairs, *Paper II*.

SYNOPSIS OF THE PAPERS

Paper I

Prescribing quality for older people in Norwegian nursing homes and home nursing services using multi-dose dispensed drugs.

Halvorsen KH, Granas AG, Engeland A, Ruths S. *Pharmacoepidemiol Drug Saf 2011.*

Objective To examine the quality of drug prescribing for older persons in nursing homes and home nursing services based on explicit prescribing quality indicators.

Methods and material Cross-sectional study comprising NHs and HNS patients aged ≥65 years using MDD. PIMs were identified according to NORGEP criteria, and DDIs according to DRUID. The impact of care setting on exposure to selected drug groups, PIMs and DDIs was calculated, adjusting for patients' age, gender, and number of drugs used.

Results Altogether 11 254 patients were included, 2 986 (72% women, 85.3 years) in NHs and 8 268 (69% women, 83.0 years) receiving HNS. In total, 63 936 drug items were analysed. Patients in NHs and HNS used on average 5.7 regular MDD. Drugs for treatment of cardiovascular (79.6%), nervous (68.9%), alimentary (57.1%) and blood (56.5%) system conditions were most frequently prescribed. Figure 4 presents the ten most commonly used MDDs. As compared to NHs, more patients in HNS used cardiovascular drugs and fewer used psychotropic drugs.

Figure 2. Top ten prescribed multi-dose dispensed drugs to nursing home and home nursing service patients in Norway 2009
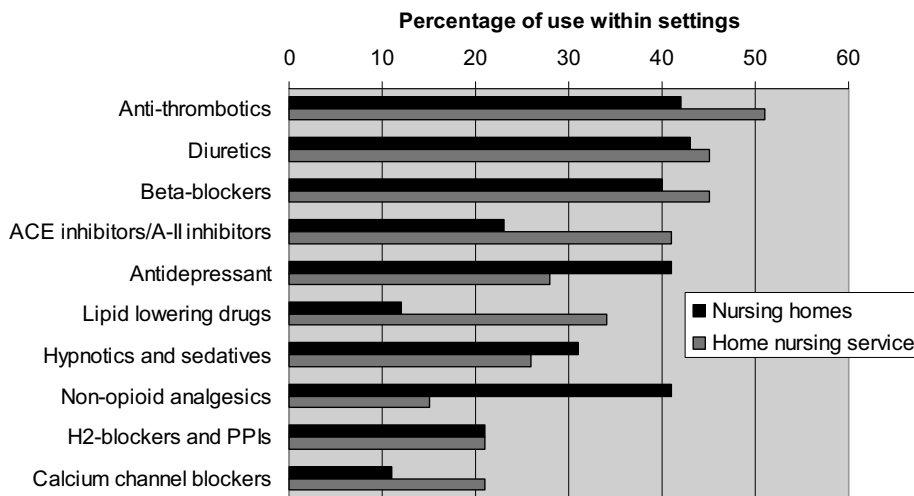
Altogether 26% of the patients used at least one PIM, 31% in NHs and 25% in HNS (*p<.001*). Concomitant use of three or more psychotropic and/or opioid drugs was the criterion most commonly identified in both NHs (18%) and HNS (9%) (*p<.001*). The mean number of PIMs was significantly correlated with numbers of drugs used (*p<.01*).

A total of 8 615 DDIs were identified in 55% of patients, 48% in NH and 57% in HNS (*p<.001*). The mean number was 0.77 DDIs per patients. The number of DDIs was significantly correlated with the number of drugs used (*p<.01*). DDIs were assigned severity level A, B, C and D in 27%, 39%, 9% and 2% of all patients, respectively.

Conclusions PIMs were more often prescribed to patients in NHs, while patients in HNS were more frequently exposed to DDIs. There are significant differences in the quality of drug prescribing in NHs compared to HNS.

Paper II

Multidisciplinary intervention to identify and resolve drug-related problems in Norwegian nursing homes

Halvorsen KH, Ruths S, Granas AG, Viktil KK. *Scand J Prim Health Care 2010; 28: 82-88.*

Objective To describe an innovative team intervention to identify and resolve DRPs in Norwegian NHs.

Methods and materials Descriptive intervention study in three NHs in Bergen, Norway. DRPs were identified by pharmacists, and discussed with patients' physician and nurse at multidisciplinary case conferences. Actions to resolve the DRPs were planned and followed-up.

Results Three pharmacists systematically reviewed 142 long-term care patients (106 women, 86.9 years) which most commonly suffered from dementia (65%), hypertension (35%) and depression (34%). The ten most commonly used regular and p.r.n. medications are presented in Table 7. Pharmacists identified 719 potential DRPs, of which 372 were accepted, 104 accepted but reclassified, 243 rejected, and 28 new DRPs added at case conferences; finally, 504 DRPs were acknowledged. Within three weeks 476 (94%) of the DRPs were resolved. The two most frequently identified DRPs were "Unnecessary drug" (n=194) and "Monitoring required" (n=68). Drugs for treatment of the alimentary and nervous system accounted for the majority of the DRPs. The intervention resulted in a significant mean reduction of 1.5 prescribed drugs per patient ($p<.01$).

Table 7. The ten most commonly prescribed regular and p.r.n. medications to nursing home patients (n=142)

	Regular medications			P.r.n. medications	
ATC code	Generic name	%	ATC code	Generic name	%
A06AD11	Lactulose	81	N02BE01	Paracetamol	89
N02BE01	Paracetamol	58	N05BA04	Oxazepam	46
B01AC06	Aspirin	55	N02AA59	Paracetamol + codeine	29
B03BA03	Hydroxycobalamin	47	N05CF01	Zopiclone	26
C03CA01	Furosemide	39	N02AX02	Tramadol	22
A06AB02	Bisacodyl	28	N05BA01	Diazepam	21
N05CF01	Zopiclone	33	A03FA01	Metoclopramide	19
A11EA-	Vitamin B-complex	32	C01DA02	Glyceroltrinitrate	19
N05BA04	Oxazepam	25	A06AG11	Sodium lauryl sulfate	14
A06AB04	Citalopram	24	A06AB02	Bisacodyl	13

Conclusions The multidisciplinary team intervention was suitable to identify and resolve DRPs in NHs. Systematic medication reviews and involvement of pharmacists in clinical teams should therefore be implemented on a regular basis to achieve and maintain high quality drug therapy.

Paper III

Physicians' and nurses' experiences of multidisciplinary collaboration with pharmacists at case conferences – A qualitative study.

Halvorsen KH, Stensland P, Granas AG. *Int J Pharm Pract 2011; 19: 350-57.*

Objective To explore how physicians and nurses working in NHs and hospitals experience multidisciplinary collaboration with pharmacists to optimize drug therapy in older patients.

Methods and material Qualitative interview study, i.e., focus group and individual interviews, using systematic text condensation. Four physicians and eight nurses from NHs (long-term care) and hospital wards (rheumatology and gerontology) were interviewed.

Results

Introduction of a new team member

Health professionals had different perceptions about collaborating with pharmacists. Lack of a predictable time schedule and knowing what the focus was supposed to be at case conference caused some frustration for collaborating health personnel. The informants reported that pharmacists addressed most of the identified problems towards the physician rather than nurses. The physicians found it challenging to cope with questions demanding clear professional answers regarding established drug therapy, regardless of them being responsible for initiating treatment or not.

Consequences for the collaborating health personnel and their patients

The introduction of pharmacists to the multidisciplinary team changed focus from other care issues towards drug therapy issues to a greater extent than before. Consequently, this led to less attention for discussing nurse-related issues, and caused time strain for the nurses who experienced that their issues were partly unresolved after the case conferences. Nevertheless, according to the informants the process of addressing DRPs resulted in raised awareness on the quality of prescribing, which was considered to outweigh the downsides of other issues given less attention.

Perspectives on collaboration development

The informants had different opinions about how often pharmacists ought to participate at case conferences. While some suggested twice annually, others felt it was important to have pharmacists present continuously. The way pharmacists independently collected data and performed medication reviews prior to case conferences was endorsed by the informants as it required less input from them. The hospital nurses felt that pharmacists' findings, mostly concerning drug treatment decisions, could be raised directly with the physician without their attendance. In contrast, NH nurses felt that their presence was important, and thus wanted to actively take part in the multidisciplinary team when discussing patients' drug treatment.

Conclusions Physicians and nurses valued the pharmacists' services and reported that this collaboration improved patients' drug therapy. However, before implementing this service in NHs, there is a need to make an organisational frame for this collaboration to support the professional role of the pharmacist.

DISCUSSION

Discussion of results

Number of drugs used by older patients in NH and HNS (Paper I and II)

In **Paper I** we report an average of 5.7 regular drugs among MDD users, whereas **Paper II** including all drugs revealed 8.1 regular drugs, respectively. Compared with other studies, our findings suggest that the total number of drugs used per patient in NHs has increased during the last decades. A Norwegian study examining DRPs in 1 552 NH patients in 1997 revealed a mean of 5.0 drugs regular medications [17]. Our study revealed 8.1 regular drugs and concurs well with other Nordic studies reporting an average of 7.5-8.5 regular drugs [21, 22, 26], although caution should be exercised when comparing the total number of drugs used across borders due to differences in therapy traditions, study populations and health care systems.

In **Paper I** the number of prescribed MDD was equal in HNS and NH patients. As mentioned earlier, drug utilization studies from HNS are sparse. The Ad-HOC project (2000-2003) including 2 707 HNS patients in eight European countries revealed that 92% (of N=388) of older Norwegian HNS patients used ≥1 drug, 34% used ≥6 drugs, and 11% used ≥9 drugs, respectively [15]. The data comprised patients' drug use during one week including regular, p.r.n. and over-the-counter medications.

The increasing numbers of drugs used can possibly be explained by i] focus on preventive care such as anti-platelet therapy, lipid-lowering drugs and blood pressure-lowering drugs, ii] adherence to prescribing guidelines recommending complex drug regimens for e.g. cardiovascular diseases, and iii] availability of new treatment alternatives. Although these explanations in most cases may benefit the patients, it also puts high demands on prescribers and health care professionals to evaluate and monitor drugs' effects and ADRs.

Drug utilization patterns in HNS and NH (Paper I)

Drug utilization patterns varied between HNS and NHs, Figure 5; mainly due to differences in use of cardiovascular and psychotropic and/or opioid drugs. Dementia and BSPD are known predictors for institutionalization [12], and subsequent prescribing of psychotropic drugs for symptomatic treatment [134]. On the other hand, use of β-blockers and diuretics varied little between the two settings, suggesting that cardiovascular diseases are highly prevalent also in NHs.

Lipid-lowering drugs were the drugs accounting for the greatest differences between patients in HNS and NHs, *Paper I*. The variation may be explained by adherence to guidelines that advise against prescribing to patients whose life expectancy is less than five years [10, 74]. In general, drug discontinuation is considered appropriate when time to effect is longer than predicted life expectancy [135]. But when it comes to lipid-lowering drugs, controversy exists whether to discontinue the drug or not. While the effect of lipid-lowering drugs in secondary prevention is well-known, their role in primary prevention is questioned [136, 137]. In addition, prescribing physicians need to consider ADRs, DDIs, costs and number needed to treat to prevent one new incident of cardiovascular disease [138]; a demanding task in older patients with a range of co-morbidities using multiple drugs. Moreover, the role of primary prevention in the NH setting is limited, and attention should instead be devoted to palliation.

Quality of drug prescribing in older patients

To determine the quality of drug prescribing, PIMs, DDIs (*Paper I*) and DRPs (*Paper II*) were used as outcome measures. Findings in both papers indicate a need for prescribing quality improvements. Based on explicit criteria, 25% of older patients receiving MDD were exposed to PIMs, *Paper I*. The proportion was higher in NH patients compared to those in NHs (31% vs. 25%, respectively). However, when NORGEP criterion no. 36 (three or more psychotropics and/or opioid drugs) was excluded differences between HNS and NHs disappeared (21% in both settings). Several former studies have identified sub-optimal quality of psychotropic drug use, in

particular in NHs [17, 21]. Our findings suggest that prescribing quality in NHs still needs improvement [24, 139].

A two-fold prevalence of concomitant use of three or more psychotropic drugs and/or opioid drugs was found in NHs compared to HNS, *Paper I* (18% vs. 9%, respectively). Recently, the prognostic value of this criterion has been questioned [140]; In long-term care facilities, mortality risk at 5-years follow-up did not differ between older patients using ≤ 2 vs. ≥ 3 psychotropic drugs, but risk was higher in psychotropic drug users vs. non-users in community-dwelling older persons with dementia [141]. However, it is important to keep in mind that the indicator was intentionally developed to prevent undesirable ADRs such as muscular weakness, falls, fractures, cognitive impairment, or DDIs, and not hard endpoints like mortality [77]. The fact that patients in HNS only have visits from health personnel on demand, while NH patients have continuous surveillance outline the importance of addressing multiple psychotropic drug use in this setting as well. This can be achieved by taking advantage of the possibilities in the computerised MDD system, but so far the possibilities inherent in electronic prescribing support have been neglected. The potential of incorporating alerts, for instance by using explicit criteria [77], and of feed back to GPs have existed for more than ten years [142]. Although the method contributes to reduce PIMs [142], the technology has only been used for feedback regarding DDIs from pharmacies (manually – telephone calls) to physicians in Norway. Finally, the Norwegian Medicines Agency has now taken responsibility and has developed the program "prescribing and dispensing" support (FEST). FEST provides identical up-to-date drug information both to prescribers in different clinical settings and drug dispensers [143].

The far more comprehensive method used to investigate DRPs revealed that most problems concerned unnecessary drug use; this finding gave rise to a significant reduction of 1.5 prescribed drugs per patient, *Paper II*. Former studies have shown that medication reviews can contribute to reduce total drug consumption [121]. In this study, almost all patients (>98%) had DRPs. Alimentary and nervous system drugs caused the majority of acknowledged DRPs; corresponding with findings from a Dutch NH study where DRPs identified in 96% of the patients mostly constituted

'unknown indications'; subsequently leading to drug discontinuation [30]. Compared to the BEDNURS study which identified DRPs in 75% of patients [17], our and other recent studies [26] suggest a decrease in quality of drug treatment during the last years, as the proportion of DRPs in NHs has increased. However, in the BEDNURS study less clinical information was available, like for instance laboratory values and body weight. Neither did they discuss potential DRPs with the patients' physician.

Positively, in *Paper I* less than 3% of patients in both NH and HNS used diazepam or nitrazepam. A former Norwegian study revealed that 22% of NH subjects used benzodiazepines [144]. In addition, NSAIDs were prescribed to less than 4% (result not published), while reported to be issued to 7% of older patients in general practice in harmful combination with other drugs [93].

In contrast to the substantial use of psychotropic drugs in NHs, *Paper I*, ADRs were almost not identified, *Paper II* (< 1%). This questions whether the broad approach undertaken in *Paper II* turned out to focus on selected areas like over-treatment, i.e., unnecessary drug use. The argument is also supported by the fact that under-treatment, reported to be a prevalent problem in NHs [17, 145], was only identified in four patients.

We conducted a comprehensive screening for DDIs by using DRUID [54], and identified 1% severe (class D) DDIs in NH patients and 2% in HNS patients, *Paper I*. For comparison, a Swedish study of older NH patients using in average 8.5 regular drugs reported class D DDIs to comprise 8.1 % of patients [22]. In Finland, 4.8% of older NH patients using 7.9 regular drugs per day were susceptible to class D DDIs [21]. The use of MDD data, excluding drug groups such as warfarin and anti-infectiva, may explain the lower prevalence of clinical significant DDIs identified in our study, and make direct comparison difficult. Surprisingly, HNS patients were more often exposed to DDIs (any class) than NH patients; putting them at a higher risk of experiencing ADRs. Furthermore, the result raises questions if the DDIs screening process of MDD performed in pharmacies is performed properly. The difference may also be explained by poor communication lines and/or collaboration between prescribers and dispensers, or that GPs take DDIs into higher consideration when initiating drug therapy in frail and vulnerable NH patients.

Multidisciplinary collaboration involving pharmacists

Many studies have demonstrated sub-optimal prescribing quality in older patients [21, 93, 103]. Patients' GPs are responsible for overall prescribing quality, but strive of different reasons to achieve desirable quality. Pitfalls are many and explanations are partly related to diagnostic work and whether assimilated information regarding drug therapy is used appropriately [146]. In order to improve the quality of medical care for NH patients, the Norwegian Medical Association has decided to establish a special competence area for NH medicine in 2011 [147].

We investigated whether pharmacists could contribute to improve the quality of drug prescribing for older patients, in cooperation with patients' physicians, ***Paper II and III***. The methodology applied in ***Paper II*** allowed a comprehensive review of the individual patient's medication list to identify DRPs. When pharmacists presented findings at case conferences, the physician in particular was enquired to reconsider prescribing decisions. A series of questions, and drug treatment discussions enabled evaluation of existing drug therapy, thus fulfilling one of the premises for good prescribing [146].

However, ***Paper III*** describes how the physicians experienced challenges when being questioned by pharmacists, a phenomenon also observed by the nurses; demonstrating the novelty of multidisciplinary collaboration involving pharmacists. The importance of clarifying roles prior to implementing a pharmacist-physician collaboration has previously been described [148], and one of the GPs outlined the importance of not presenting prescribing errors in a condescending way; thus humiliating other team members.

In Norway, during the last ten years pharmacists have adapted a patient-centred service in the hospital setting [149, 150], and clinical pharmacists are now even employed at smaller local hospitals. Recently in Sweden, the implementation of a comprehensive pharmacist service for patients 80 years and older in this setting has shown to reduce morbidity and health care costs [151].

To improve prescribing quality in NHs, we recommended implementing medication reviews and multidisciplinary collaboration with pharmacists, ***Paper II***, an intervention endorsed by both physicians and nurses in ***Paper III***. However, there is a

need to consider which patients in NHs (or HNS) should be prioritized for medication reviews and multidisciplinary discussion. It will also be necessary to consider when, and how often reviews should be conducted. In the U.S., medication reviews performed every third month by clinical pharmacists in NH facilities became mandatory through the Omnibus Budged Reconciliation Act in 1987. The frequency was later increased to monthly [148, 152]. A stepwise model, starting at the system level with explicit quality indicators [100] could be a useful approach as demonstrated in *Paper I*. For instance, suppliers of MDD could easily implement such a service and give feedback regularly to prescribers. Then, an individual approach like the model demonstrated in *Paper II* could be implemented. Currently, the Norwegian Directorate of Health is working on a guide for medication reviews in different health care settings.

The pharmacists (*Paper II*) did not interview the patients about their problems related to drug use; an approach which has been used in the hospital setting to identify DRPs [153]. The high prevalence of dementia in the NH setting [9] makes patient interviews difficult. When interviewing hospital nurses (*Paper III*), they at times felt redundant when physicians and pharmacists discussed drug therapy strategies. In contrast, the NH nurses experienced their presence as important, because of their profound patient knowledge; affirming the importance of adjusting collaboration models to the relevant health care setting.

The rather positive evaluation in *Paper III* and the results from *Paper II* propose to reconsider how to utilize the skills and competence of pharmacists. The multidisciplinary team including three different health professions discussed and judged to what extent *potential* DRPs were **real** DRPs. Furthermore, relevant actions were planned and carried out to resolve the acknowledged DRPs; implying that the multidisciplinary team managed to collaborate, and hence improved overall prescribing quality by reducing DRPs.

Comprehensive systematic medication reviews demand clinical information
There has been a growing interest from pharmacy chains during the last years to conduct medication reviews. Studies have questioned the effect of home based

medication reviews on reducing hospitalization, but findings are conflicting [154, 155]. In Norway accessibility to medication records outside the institutional setting is not catered for, meaning that medication reviews as performed in *Paper II* are not possible to conduct outside the NHs or the GP's office. As demonstrated in *Paper II*, accessibility to patient medical records as well as the physicians' clinical input and the nurses' profound patient knowledge are essential to perform comprehensive medication reviews. This underlines the importance of developing collaboration models which bring together these three health professions in the respective settings. These models should also focus on improving collaboration between physicians, nurses and pharmacists [155].

Methodological considerations

The term validity is normally divided into *internal validity*; describing whether the method is applicable to obtain valid knowledge about the studied phenomenon, and *external validity*; dealing with transferability [132]. This section addresses methodological aspects individually for each paper.

Paper I

To my knowledge, this is the first Norwegian study using MDD data to assess prescribing quality for patients in HNS and NHs. Performing 'large-scale' drug utilization studies in HNS and NH patients has previously been difficult due to the lack of prescription databases for the NH setting, and the fact that patients receiving HNS cannot be identified in the Norwegian national prescription database [65]. The study comprised numerous HNS and NHs throughout the country. Patients' age and gender distribution was in concordance with the general HNS and NH population in Norway (SSB), which contributes to external validity.

The MDD database includes some information of other drug formulations than tablets and capsules. However, because of uncertainty regarding the quality of these data we decided to exclude them from the analysis. P.r.n. medications were excluded for the same reason. This systematic selection bias was leading to a certain underestimation of total drug use, PIMs and DDIs.

Assessment of prescribing quality by using the explicit Norwegian quality indicators NORGEP [77] and DRUID [54] was considered advantageous as they correspond to the National Drug formulary [126]. On the other hand, NORGEP addresses only a short list of drugs considered inappropriate in older patients [77], while all other medications are by default considered appropriate. Further, neither over- nor under-prescribing could be identified, e.g. too low dose of paracetamol for pain management. Additionally, we know that off-label prescribing occurs, and that physicians in special cases may choose to prescribe 'inappropriate' drugs; illuminating the problem of lacking clinical information.

Concerns have been raised about explicit quality indicators' appropriateness to determine the quality of drug prescribing [76, 140]. Ideally, quality indicators should be validated in the actual setting before use [156]. However, the NORGEP criteria are recommended, but not validated by their authors for use in the NH setting [77].

Paper II

The relatively small number of included patients (N=142) and NHs (N=3) is a limitation to the external validity of the study. Moreover, we cannot rule out a certain selection bias, as the process of including study participants was left to the collaborating NHs' physicians and nurses.

Internal validity was strengthened by performing a pilot study on 15 patients to adjust study procedures, and a midterm meeting with data collectors and researchers to monitor and discuss the entry of data. Further, the DRP classification system provided the structure for the systematic medication review, and served as a platform for discussing the identified DRPs in patients [107]. Although the clinical skills and knowledge of the GPs will probably affect the accuracy of classification positively, we did neither examine the individual pharmacists' identification or classification of DRPs, nor the multidisciplinary groups' agreements. A way to increase the accuracy of DRP classification, and thus validity, is to present the problems to a group of experts for rating; similar to the method used to develop the DRP classification system [107]. However, such a process is impractical to conduct in a busy clinical setting where the classification of DRPs should be a secondary consideration. Priority should be given to identify and acknowledge that a problem actually exists and then perform relevant actions.

Paper III

Being a novice qualitative researcher this study has limitations and strengths that need to be address more comprehensively.

Sampling, or the selection of informants for the study, is a critical point in qualitative research. Mays describe that the researcher does not seek a random or a representative sample of the population, but a strategic one, which may be able to

describe the phenomenon under investigation in great detail [157]. As multidisciplinary collaboration with pharmacists, particularly in NHs, is at an early phase in Norway, there is not a vast pool of informants to choose from. One could argue that the study design was not optimal as we were only able to conduct the focus group interview with the nurses, and not with the physicians. Furthermore we did not investigate the experiences of pharmacists, nor conducting multi-professional focus group interviews. Both alternatives would have contributed to more data and most likely a broader understanding of the studied phenomenon. However, systematic empirical knowledge has its own value [158] and we only aimed to achieve early experiences and perspectives of this collaboration.

Data collection was performed by using both a semi-structured focus group and individual interviews. The use of open-ended questions in both focus group interviews and individual interviews allow the interviewer and the interviewees to follow ideas regarding the area under exploration [68]. However, in focus group interviews, group dynamics also plays an important role to bring out knowledge. Both methods may gain insight into the informant's own experiences, thoughts and feelings [128, 159].

The phenomenon of transcribing speech to text, and further translating from one written language to another, may introduce ambiguities or errors. Kvale considers audio-taping to cause the first abstraction [130]. The importance of transcripts being close to verbatim have been outlined, and several types of transcribing errors have been described [160], including: i] deliberated alterations; consisting of tiny text adjustments to bring out the meaning better, ii] accidental alterations; providing the text a different meaning than originally intended, and iii] loss of non-verbal communication, i.e., body language. In this paper the entire transcribing process was performed by the same researcher, who was present during all interviews. This ensured equal transcribing from audio-tape to text, and the opportunity to take into account aspects from the interviews and group dynamics in the analytical process [130]. However, danger of nuances and information being lost in translation is always present, thus affecting reliability.

Reliability concerns also whether findings may be reproduced by other researchers based on the same data, or at later moments [130]. In our case pharmacists

acted as interviewers. If a nurse or a physician, both with alternative preconceptions compared to pharmacists (and myself), had conducted the interviews other ideas and perspectives reflecting their own professions may have been followed and explored more extensively. However, in qualitative research repeatability is rarely a relevant criterion for ensuring reliability [132]. Instead, it is of interest to exploit the diversity in qualitative data [161].

When it comes to validity, Kvale describe a seven step process permeating the whole research process from theory basis to whether the main findings are reported consistently. The work of validation should be conducted continuously and not only at the end of knowledge production [130]; most likely why "qualitative analysis should not be left to the novice" [162]. By having two experienced (physician and pharmacist) and one novice researcher (myself) to perform the analysis and interpretation of findings, the reported findings were balanced according to the investigators different preconception and enabled mirror of true experiences. However, both internal and external validity might have benefited from including a nurse in the research and the analytical process; thus better ensuring investigator triangulation [163]. A more thorough work to ensure that all informants met as scheduled, might by providing a richer material also have increased the validity.

Member validation, i.e., selecting one or more of the respondents to read the transcripts or just an abstract of them, is another way to promote validity [164]. This method gives the interviewees the opportunity to confirm or disapprove the interpretations of findings. In our case, the two interviewers summarized thoughts and perspectives to some extent during or at the end of the interviews. But the respondents were not invited to respond to our interpretations, a step that may have strengthened validity. However, such a procedure is demanding [164], and brings both advantages and disadvantages [165].

In my experience, the role of the qualitative researcher has been the most difficult to account for or to describe. Awareness of own preconceptions and to take them into consideration during the entire research process is important [132]. As described in the explanations of my preconceptions, I feared that the role as a pharmacist in the multidisciplinary team (but also as a researcher) would be misjudged

by the other collaborators. The collection of data to *Paper II* and *III* revealed, however, something different. The interest and willingness to share own experiences, and the collaborators' interest to improve the quality of drug treatment differed from what I initially perceived. Still, as described in the preconceptions and in *Paper III*, readers of this thesis and *Paper III* need to take into consideration my motivation of developing clinical pharmacy.

External validity deals with whether findings or experiences can be transferred to other settings than they were obtained in [132]. As multidisciplinary collaboration is in an early phase in Norway, and problems with sampling were experienced, we decided to contrast our findings from nursing homes with findings from hospitals. Collecting experiences from two settings rendered possible comparison between them. Although the experiences varied to some degree for some themes, similarities were also revealed; thus serving as a test for external validity.

IMPLICATIONS AND FURTHER RESEARCH

This thesis demonstrates the need of improving prescribing quality for older patients in HNS (*Paper I*) and NHs (*Paper I and Paper II*). Based on a system audit of drug treatment in NHs, the Norwegian Board of Health has pointed out that improving structures and systems is a prerequisite for providing good quality drug treatment [62]. With the imminent increase in number of older patients, quality system should be implemented to improve and maintain prescribing quality.

Paper II reveals that a multidisciplinary collaboration model involving pharmacists is eligible to identify and resolve DRPs in NHs. This finding is supported by a preliminary evaluation of '*In Safe Hands: the Norwegian patient safety campaign 2011 – 2013*' [166]. However, signals from the national health authorities are contradictory; while the White paper "*On course towards more correct use of medicine*" [122] recommends multidisciplinary collaboration with pharmacists, one of the focus areas in the Norwegian patient safety campaign; "*Proper use of medicines in nursing homes*" was originally planned conducted without pharmacists.

Physicians' and nurses' experience of collaborating multidisciplinary with pharmacists, *Paper III*, are largely positive. Both physicians and nurses expressed that pharmacists were able to give constructive feedback and aided synergistically in the multidisciplinary team to improve quality of prescribing and drug utilization in NH patients.

This thesis advocates for change in strategies to improve prescribing quality. The availability of a national tool kit comprising both explicit and implicit methods can facilitate the work of physicians, nurses and pharmacists. We also need to ensure that prescribing quality is maintained when patients are transferred between health care levels, in particular on implementation of the Coordination reform [42]. Electronic prescriptions (eResept) [167] and FEST [143] provide opportunities to implement guidelines and provide feedback.

Further research should concentrate on the impact of medication reviews on clinical outcomes such as quality of life, ADRs, hospital admissions and mortality. Furthermore, it is important to examine when and how often medications reviews

should be conducted. Findings in *Paper I* imply the need of performing more comprehensive prescribing quality studies among patients receiving HNS. These patients have a high disease burden, and most of them use multiple drugs; I propose to investigate a multidisciplinary collaboration model including GPs, nurses and pharmacists in this setting as well.

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